An automated flow-injection enzyme-linked immunosorbent assay for the detection of Zearalenone

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Lund University
Authors: Jantra, J. (Ekstern), Zor, K. (Intern), Hedström, M. (Ekstern), Mattiasson, B. (Ekstern)
Publication date: 2018
Main Research Area: Technical/natural sciences
Zearalenone, Flow-ELISA, Biosensor
Electronic versions:
Untitled.pdf

Relations
Activities:
An automated flow-injection enzyme-linked immunosorbent assay for the detection of Zearalenone
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2018

A Viscoelastic Catastrophe
We use a differential constitutive equation to model the flow of a viscoelastic flow in a cross-slot geometry, which is known to exhibit bistability above a critical flow rate. The novelty lies in two asymmetric modifications to the geometry, which causes a change in the bifurcation diagram such that one of the stable solutions becomes disconnected from the solution at low flow speeds. First we show that it is possible to mirror one of the modifications such that the system can be forced to the disconnected solution. Then we show that a slow decrease of the flow rate, can cause the system to go through a drastic change on a short time scale, also known as a catastrophe. The short time scale could lead to a precise and simple experimental measurement of the flow conditions at which the viscoelastic catastrophe occurs. Since the phenomena is intrinsically related to the extensional rheology of the fluid, we propose to exploit the phenomena for in-line extensional rheometry.

General information
Cellular effects and delivery propensity of penetratin is influenced by conjugation to parathyroid hormone fragment 1-34 in synergy with pH

The cell-penetrating peptide (CPP) penetratin, has demonstrated potential as a carrier for transepithelial delivery of cargo peptides, such as the therapeutically relevant part of parathyroid hormone, i.e. PTH(1-34). The purpose of the present study was to elucidate the relevance of modifying the pH for PTH(1-34)-penetratin conjugates and for co-administered penetratin with PTH(1-34) in terms of transepithelial permeation of PTH(1-34) and cellular effects. Transepithelial permeation was assessed using monolayers of the Caco-2 cell culture model, and effects on Caco-2 cellular viability kinetics were evaluated by using the Real-Time-GLO assay as well as by microscopy following Tryphan blue staining. Morphological Caco-2 cell changes were studied exploiting the impedance-based xCELLigence system as well as optically using the oCelloscope setup. Finally, the effect of pH on the folding propensity of the PTH(1-34)-penetratin conjugate and its ability to disrupt lipid membranes were assessed by circular dichroism (CD) spectroscopy and the calcein release assay, respectively. The transepithelial PTH(1-34) permeation was not pH-dependent when applying the co-administration approach. However, by applying the conjugation approach, the PTH(1-34) permeation was significantly enhanced by lowering the pH from 7.4 to 5, but also associated with a compromised barrier and a lowering of the cellular viability. The negative effects on the cellular viability following cellular incubation with the PTH(1-34)-penetratin conjugate were moreover confirmed during real-time monitoring of the Caco-2 cell viability as well as by enhanced Tryphan blue uptake. In addition, morphological changes were primarily observed for cells incubated with the PTH(1-34)-penetratin conjugate at pH 5, which was moreover demonstrated to have an enhanced membrane permeating effect following lowering of the pH from 7.4 to 5. The latter observation was, however, not a result of better secondary folding propensity at pH 5 when compared to pH 7.4.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Copenhagen
Authors: Kristensen, M. (Ekstern), Nielsen, L. H. (Intern), Zor, K. (Intern), Boisen, A. (Intern), Christensen, M. V. (Ekstern), Berthelsen, J. (Ekstern), Mørck Nielsen, H. (Ekstern)
Pages: 371-381
Publication date: 2018
Main Research Area: Technical/natural sciences
Development of electrosprayed mucoadhesive chitosan microparticles

The efficacy of chitosan (CS) to be used as drug delivery carrier has previously been reported. However, limited work has been pursued to produce stable and mucoadhesive CS electrosprayed particles for oral drug delivery, which is the aim of this study. Various CS types with different molecular weight (MW), degree of deacetylation (DD), and degree of polymerization (DP) were assessed. In addition, the effect of the solvent composition was also investigated. Results showed that stable CS electrosprayed particles can be produced by dissolving 3% w/v of low MW CS in mixtures of aqueous acetic acid and ethanol (50/50% v/v). The stable CS particles displayed diameters of approximately 1 μm as determined by dynamic light scattering. The zeta potential of these particles was found to be approximately 40 mV confirming the mucoadhesion properties of these CS electrosprayed particles and its potential to be used as drug delivery carrier.

General information
State: Published
Organisations: National Food Institute, Research Group for Nano-Bio Science, Department of Micro- and Nanotechnology, Nanoprobes, University of Munster
Drug loaded biodegradable polymer microneedles fabricated by hot embossing

This study demonstrates a fast low temperature method for fabrication of drug loaded polymer microneedles (MNs). First, arrays of tapered pillar MNs with a length of 275 ± 3 μm (mean ± SD) and a diameter of 84 ± 1 μm were fabricated in Si with a three-step deep reactive ion etching (DRIE) process. The Si MNs were used as a template for fabrication of polydimethylsiloxane (PDMS) stamps. The stamps were applied for replication of the MNs in spin coated poly-ε-caprolactone (PCL) films by hot embossing at 60 °C and a pressure of 1.4 MPa for 3 min. The resulting PCL MNs perfectly resembled the Si MNs and had a length of 270 ± 5 μm and a diameter of 84 ± 3 μm. The MNs had sufficient mechanical strength to penetrate the surface of a 10 w/w% gelatine gel without deformation. Finally, PCL MNs containing 20 w/w% of furosemide were fabricated and drug release by diffusion was demonstrated.
Effects of water-absorption and thermal drift on a polymeric photonic crystal slab sensor

A photonic crystal slab (PCS) sensor is a universal refractive index sensor with possibilities and performance very similar to surface plasmon resonance (SPR), which represents the gold standard of biosensing. Cheap PCS sensors can be made vacuum-free entirely out of polymers, but come with additional challenges, besides those relating to temperature-variations, which must be considered in any refractive index based method: The polymeric waveguide core was found to swell by 0.3% as water absorbed into the waveguide core over 1.5 h. This was investigated by monitoring the wavelength of resonant reflection during absorption, by monitoring the release of water using ellipsometry, and by rigorous coupled-wave analysis (RCWA). The approach presented here enables monitoring of water uptake and thermal fluctuations, for drift-free, high-performance operation of a polymeric PCS sensor.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Optofluidics, Technical University of Denmark
Authors: Sørensen, K. T. (Intern), Ingvorsen, C. B. (Ekstern), Nielsen, L. H. (Intern), Kristensen, A. (Intern)
Number of pages: 7
Pages: 5416-5422
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information

Journal: Optics Express
Volume: 26
Issue number: 5
ISSN (Print): 1094-4087
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 1.567 SJR 1.519
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.48 SJR 1.532 SNIP 1.544
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.91 SNIP 1.674 CiteScore 3.78
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.313 SNIP 2.124 CiteScore 4.18
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.337 SNIP 2.196 CiteScore 4.38
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.562 SNIP 2.108 CiteScore 3.85
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.58 SNIP 2.572 CiteScore 4.04
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.906 SNIP 2.428
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 3.039 SNIP 2.679
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.204 SNIP 2.423
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.284 SNIP 2.11
Web of Science (2007): Indexed yes
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 3.313 SNIP 2.336
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 2.819 SNIP 2.472
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 2.669 SNIP 2.217
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.745 SNIP 1.748
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 1.496 SNIP 1.42
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.98 SNIP 0.761
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 1.442 SNIP 0.843

Original language: English
Electronic versions:
Efficiency enhancement of InGaN amber MQWs using nanopillar structures

We have investigated the use of nanopillar structures on high indium content InGaN amber multiple quantum well (MQW) samples to enhance the emission efficiency. A significant emission enhancement was observed which can be attributed to the enhancement of internal quantum efficiency and light extraction efficiency. The size-dependent strain relaxation effect was characterized by photoluminescence, Raman spectroscopy and time-resolved photoluminescence measurements. In addition, the light extraction efficiency of different MQW samples was studied by finite-different time-domain simulations. Compared to the as-grown sample, the nanopillar amber MQW sample with a diameter of 300 nm has demonstrated an emission enhancement by a factor of 23.8.
enhancements, greater than $10^7$ (>10^8 in hot spots), with unrivalled macroscopic signal uniformity as characterized by a coefficient of variation of only 6% across 4 cm. After SERS analyses, the nanohoodooos can be recycled by complete removal of gold via a one-step, simple, and robust wet etching process without compromising performance. After eight times of recycling, the substrate still exhibits identical SERS performance in comparison to a new substrate. The macroscopic uniformity combined with recyclability at conserved high performance is expected to contribute significantly on the overall competitiveness of the substrates. These findings show that the gold nanoparticles sliding on recyclable nanohoodooo substrate is a very strong candidate for obtaining cost-effective, high-quality, and reliable SERS spectra, facilitating a wide and simple use of SERS for both laboratorial and commercial applications.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Self-Organized Nanoporous Materials, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Wu, K. (Intern), Li, T. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Ndoni, S. (Intern)
Number of pages: 11
Publication date: 2018
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Advanced Functional Materials
Volume: 28
Issue number: 2
Article number: 1704818
ISSN (Print): 1616-301X
Ratings:
- Web of Science (2018): Indexed yes
- Web of Science (2017): Indexed Yes
- Scopus rating (2016): CiteScore 11.56
- Web of Science (2016): Indexed yes
- Scopus rating (2015): CiteScore 11.93
- Web of Science (2015): Indexed yes
- Scopus rating (2014): CiteScore 11.32
- Web of Science (2014): Indexed yes
- Scopus rating (2013): CiteScore 10.6
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- Scopus rating (2012): CiteScore 10.41
- ISI indexed (2012): ISI indexed yes
- Scopus rating (2011): CiteScore 9.47
- ISI indexed (2011): ISI indexed no
- Web of Science (2010): Indexed yes
- Web of Science (2009): Indexed yes
- Web of Science (2008): Indexed yes
- Web of Science (2007): Indexed yes
Original language: English
DOIs: 10.1002/adfm.201704818
Source: FindIt
Source-ID: 2393658476
Publication: Research - peer-review › Journal article – Annual report year: 2018

**Injection molded lab-on-a-disc platform for screening of genetically modified E. coli using liquid-liquid extraction and surface enhanced Raman scattering**

We present the development of an automated centrifugal microfluidic platform with integrated sample pre-treatment (filtration and liquid-liquid extraction) and detection (SERS-based sensing). The platform consists of eight calibration and four assay modules, fabricated with polypropylene using injection molding and bonded with ultrasonic welding. The platform was used for detection of a secondary bacterial metabolite (p-coumaric acid) from bacterial supernatant. The obtained extraction efficiency was comparable to values obtained in batch experiments and the SERS-based sensing showed a good correlation with HPLC analysis.
Laser ablation and injection moulding as techniques for producing micro channels compatible with Small Angle X-Ray Scattering

Microfluidic mixing is an important means for in-situ sample preparation and handling while Small Angle X-Ray Scattering (SAXS) is a proven tool for characterising (macro-)molecular structures. In combination those two techniques enable investigations of fast reactions with high time resolution (< 1 ms). The goal of combining a micro mixer with SAXS, however, puts constraints on the materials and production methods used in the device fabrication. The measurement channel of the mixer needs good X-ray transparency and a low scattering background. While both depend on the material used, the requirement for low scattering especially limits the techniques suitable for producing the mixer, as the fabrication process can induce molecular orientations and stresses that can adversely influence the scattering signal. Not only is it important to find a production method that results in a device with low background scattering, but it also has to be versatile enough to produce appropriate mixer designs. Here we discuss two methods – laser ablation of polycarbonate and injection moulding of Topas – which were found suitable for our needs, provided care is taken in aligning the mixing/reaction channel, where the actual measurements will be carried out. We find injection moulding to be the better of the two methods.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Polymer Micro & Nano Engineering, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Crete, Graz University of Technology
Authors: Haider, R. (Ekstern), Marmiroli, B. (Ekstern), Gavalas, I. (Ekstern), Wolf, M. (Ekstern), Matteucci, M. (Intern), Taboryski, R. (Intern), Boisen, A. (Intern), Stratakis, E. (Ekstern), Amenitsch, H. (Ekstern)
Pages: 7-12
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Microelectronic Engineering
Volume: 195
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
Micropatterned Carbon-on-Quartz Electrode Chips for Photocurrent Generation from Thylakoid Membranes

Harvesting the energy generated by photosynthetic organisms through light-dependent reactions is a significant step towards a sustainable future energy supply. Thylakoid membranes are the site of photosynthesis, and thus particularly suited for developing photo-bioelectrochemical cells. Novel electrode materials and geometries could potentially improve the efficiency of energy harvesting using thylakoid membranes. For commercial applications, electrodes with large surface areas are needed. Photolithographic patterning of a photoresist, followed by pyrolysis, is a flexible and fast approach for the fabrication of carbon electrodes with tailored properties. In this work, electrode chips consisting of patterned carbon supported on quartz were designed and fabricated. The patterned electrode area is 1 cm$^2$, and the measurement chamber footprint is 0.5 cm$^2$, one order of magnitude larger than previously-tested electrodes for thylakoid membrane immobilization. The use of a transparent substrate allows back-side illumination, protecting the bioelectrochemical system from the environment and vice versa. Two different mediators, monomeric ([Ru(NH$_3$)$_6$]$^{3+}$) and polymeric ([Os(2,2-bipyridine)$_2$-poly(N-vinylimidazole)10Cl]$^{7/2+}$) are used for evaluating photocurrent generation from thylakoid membranes with different electrode geometries. Current densities up to 71 µA cm$^{-2}$ are measured upon illumination through the transparent electrode chip with solar simulated irradiance (1000 W m$^{-2}$).
Tailoring stress in pyrolytic carbon for fabrication of nanomechanical string resonators

In order to achieve high resonance frequencies and quality factors of pyrolytic carbon MEMS string resonators the resonator material needs to have a large tensile stress. In this study, the influence of pyrolysis temperature, dwell time and ramping rate on the residual stress in thin pyrolytic carbon films is investigated with the bending plate method. The results show that the pyrolysis temperature is the most important parameter for tailoring the residual stress, with a transition from tensile stress at temperature below 800ºC to compressive stress at temperatures above 800ºC. Two kinds of photoresist: positive (AZ5214E) and negative (SU-8) and different pyrolysis conditions are used to fabricate pyrolytic carbon string resonators at variable pyrolysis conditions. The best performance is obtained for devices with a length of 400 µm fabricated at a pyrolysis temperature of 700ºC, ramping rate of 30ºC/min and 10 minutes dwell time corresponding to the conditions for maximum tensile stress in pyrolytic carbon thin films. The optimized pyrolytic carbon string resonators had resonant frequencies above 300 kHz and quality factors (Q) in the order of 10⁴, which is suitable for their application as nanomechanical sensors.

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Temperature Modulated Nanomechanical Thermal Analysis

The response of microcantilever deflection to complex heating profiles was used to study thermal events like glass transition and enthalpy relaxation on nanograms of the biopolymer Poly(lactic-co-glycolic acid) (PLGA). The use of two heating rates enables the separation of effects on the deflection response that depends on previous thermal history (non-reversing signal) and effects that depends only on the heating rate variation (reversing signal). As these effects may appear superposed in the total response, temperature modulation can increase the measurement sensitivity to some thermal events when signals are isolated. Initially, it was shown how the signal can be processed to extract reversing, total and non-reversing signals and how the temperature modulation affects the cantilever sensitivity to temperature. Then, this technique was used to study how the different aging times affects the non-reversing curve but has no effect on the reversing curve, enabling more precise extraction of glass transition (Tg) in aged samples. With non-reversing data at different aging times, we measured the aging rate by means of average relaxation time (τ) using the Cowie-Ferguson model, obtaining τ = 348 minutes for PLGA aged at 20 °C and at 50 % RH. Tg for PLGA at 50 % RH was measured 37.8 °C using the reversing signal with 0.32 °C of variation between aging times.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of São Paulo
Using microcantilever sensors to measure poly(lactic-co-glycolic acid) plasticization by moisture uptake
Polymeric materials absorb water when exposed to humidity or in contact with aqueous solutions. The polymer and water molecules interact, changing the physicochemical parameters of the material; the most noticeable effect is a decreased glass transition temperature ($T_g$), known as plasticization. We used microcantilever sensors to measure the $T_g$ versus moisture content in poly(lactic-co-glycolic acid) (PLGA), a biodegradable polymer used in implants and as a drug carrier. We demonstrate a concomitant measurement of the mass absorption and $T_g$ using nanograms of material and an inexpensive setup. The standard deviation of $T_g$ for this system was 0.025 °C, and the variation in $T_g$ with respect to a 1% RH change was clearly resolved. The decrease in the $T_g$ of PLGA was linear ($R^2 = 0.99$) at a rate of $6.03 \pm 0.57$ °C per mass% of water absorbed. The initial dry $T_g$ of PLGA was extrapolated to $41.24 \pm 0.07$ °C.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of São Paulo
Authors: Alves, G. M. A. (Ekstern), Bose-Goswami, S. (Intern), Mansano, R. D. (Ekstern), Boisen, A. (Intern)
Number of pages: 7
Pages: 407-413
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Polymer Testing
Volume: 65
ISSN (Print): 0142-9418
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.251 SJR 0.669
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.82 SJR 0.827 SNIP 1.582
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.898 SNIP 1.606 CiteScore 2.58
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.01 SNIP 1.984 CiteScore 2.46
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.859 SNIP 1.924 CiteScore 2.17
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.845 SNIP 1.826 CiteScore 1.91
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.979 SNIP 1.791 CiteScore 2.12
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.083 SNIP 1.803
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.876 SNIP 1.37
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.005 SNIP 1.575
Scopus rating (2007): SJR 0.986 SNIP 1.626
Scopus rating (2006): SJR 0.79 SNIP 1.378
A METHOD FOR PREPARING A SUBSTRATE BY APPLYING A SAMPLE TO BE ANALYSED

The invention relates to a method for preparing a substrate (105a) comprising a sample reception area (110) and a sensing area (111). The method comprises the steps of: 1) applying a sample on the sample reception area; 2) rotating the substrate around a predetermined axis; 3) during rotation, at least part of the liquid travels from the sample reception area to the sensing area due to capillary forces acting between the liquid and the substrate; and 4) removing the wave of particles and liquid formed at one end of the substrate. The sensing area is closer to the predetermined axis than the sample reception area. The sample comprises a liquid part and particles suspended therein.

A METHOD FOR THE PREPARATION OF A SUBSTRATE

Although mechanical cues are known to affect stem cell fate and mechanobiology, the significance of such stimuli on the osteogenic differentiation of human adipose stem cells (hASCs) remains unclear. In this study, we investigated the effect of long-term mechanical stimulation on the attachment, osteogenic differentiation and mechanical properties of hASCs. Tailor-made, pneumatic cell stretching devices were used to expose hASCs to cyclic equiaxial stretching in osteogenic medium. Cell attachment and focal adhesions were visualised using immunocytochemical vinculin staining on days 3 and 6, and the proliferation and alkaline phosphatase activity, as a sign of early osteogenic differentiation, were analysed on days 0, 6 and 10. Furthermore, the mechanical properties of hASCs, in terms of apparent Young's modulus and normalised contractility, were obtained using a combination of atomic force microscopy based indentation and computational approaches. Our results indicated that cyclic equiaxial stretching delayed proliferation and promoted osteogenic differentiation of hASCs. Stretching also reduced cell size and intensified focal adhesions and actin cytoskeleton. Moreover, cell stiffening was observed during osteogenic differentiation and especially under mechanical stimulation. These results suggest that cyclic equiaxial stretching modifies cell morphology, focal adhesion formation and mechanical properties of hASCs. This could be exploited to enhance osteogenic differentiation.

The effect of equiaxial stretching on the osteogenic differentiation and mechanical properties of human adipose stem cells

Although mechanical cues are known to affect stem cell fate and mechanobiology, the significance of such stimuli on the osteogenic differentiation of human adipose stem cells (hASCs) remains unclear. In this study, we investigated the effect of long-term mechanical stimulation on the attachment, osteogenic differentiation and mechanical properties of hASCs. Tailor-made, pneumatic cell stretching devices were used to expose hASCs to cyclic equiaxial stretching in osteogenic medium. Cell attachment and focal adhesions were visualised using immunocytochemical vinculin staining on days 3 and 6, and the proliferation and alkaline phosphatase activity, as a sign of early osteogenic differentiation, were analysed on days 0, 6 and 10. Furthermore, the mechanical properties of hASCs, in terms of apparent Young's modulus and normalised contractility, were obtained using a combination of atomic force microscopy based indentation and computational approaches. Our results indicated that cyclic equiaxial stretching delayed proliferation and promoted osteogenic differentiation of hASCs. Stretching also reduced cell size and intensified focal adhesions and actin cytoskeleton. Moreover, cell stiffening was observed during osteogenic differentiation and especially under mechanical stimulation. These results suggest that cyclic equiaxial stretching modifies cell morphology, focal adhesion formation and mechanical properties of hASCs. This could be exploited to enhance osteogenic differentiation.

The effect of equiaxial stretching on the osteogenic differentiation and mechanical properties of human adipose stem cells

Although mechanical cues are known to affect stem cell fate and mechanobiology, the significance of such stimuli on the osteogenic differentiation of human adipose stem cells (hASCs) remains unclear. In this study, we investigated the effect of long-term mechanical stimulation on the attachment, osteogenic differentiation and mechanical properties of hASCs. Tailor-made, pneumatic cell stretching devices were used to expose hASCs to cyclic equiaxial stretching in osteogenic medium. Cell attachment and focal adhesions were visualised using immunocytochemical vinculin staining on days 3 and 6, and the proliferation and alkaline phosphatase activity, as a sign of early osteogenic differentiation, were analysed on days 0, 6 and 10. Furthermore, the mechanical properties of hASCs, in terms of apparent Young's modulus and normalised contractility, were obtained using a combination of atomic force microscopy based indentation and computational approaches. Our results indicated that cyclic equiaxial stretching delayed proliferation and promoted osteogenic differentiation of hASCs. Stretching also reduced cell size and intensified focal adhesions and actin cytoskeleton. Moreover, cell stiffening was observed during osteogenic differentiation and especially under mechanical stimulation. These results suggest that cyclic equiaxial stretching modifies cell morphology, focal adhesion formation and mechanical properties of hASCs. This could be exploited to enhance osteogenic differentiation.
Animal models for evaluation of oral delivery of biopharmaceuticals

Biopharmaceuticals are increasingly important for patients and the pharmaceutical industry due to their ability to treat and, in some cases, even cure chronic and potentially life-threatening diseases. Most biopharmaceuticals are administered by injection, but intensive focus on development of systems for oral delivery of biopharmaceuticals may result in new treatment modalities to increase the patient compliance and reduce product cost. In the preclinical development phase, use of experimental animal models is essential for evaluation of new formulation designs. In general, the limited oral bioavailability of biopharmaceuticals, of just a few percent, is expected, and therefore, the animal models and the experimental settings must be chosen with utmost care. More knowledge and focus on this topic is highly needed, despite experience from the numerous studies evaluating animal models for oral drug delivery of small molecule drugs. This review highlights and discusses pros and cons of the most currently used animal models and settings. Additionally, it also looks into the influence of anesthetics and sampling methods for evaluation of drug delivery systems for oral delivery of biopharmaceuticals primarily with examples on insulin.
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.763 SNIP 2.089 CiteScore 6.33
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.225 SNIP 2.307
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.922 SNIP 2.033
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 2.272 SNIP 1.895
Scopus rating (2007): SJR 2.168 SNIP 1.81
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.788 SNIP 1.779
Scopus rating (2005): SJR 1.57 SNIP 1.826
Scopus rating (2004): SJR 1.485 SNIP 1.775
Scopus rating (2003): SJR 1.61 SNIP 1.687
Scopus rating (2002): SJR 1.442 SNIP 1.539
Scopus rating (2001): SJR 1.26 SNIP 1.363
Scopus rating (2000): SJR 0.956 SNIP 1.391
Scopus rating (1999): SJR 1.036 SNIP 1.294
Original language: English
In situ perfusion, In vivo, Insulin, Macromolecules, Peptides, Proteins

An integrated lab-on-a-disc approach to detect inflammatory biomarkers from whole blood

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems, Academia Sinica Taiwan, BluSense Diagnostics
Authors: Uddin, R. (Intern), Donolato, M. (Ekstern), Fock, J. (Intern), Hansen, M. F. (Intern), Hwu, E. (Ekstern), Boisen, A. (Intern)
Publication date: 2017
Main Research Area: Technical/natural sciences

A pseudo-Voigt component model for high-resolution recovery of constituent spectra in Raman spectroscopy
Raman spectroscopy is a well-known analytical technique for identifying and analyzing chemical species. Since Raman scattering is a weak effect, surface-enhanced Raman spectroscopy (SERS) is often employed to amplify the signal. SERS signal surface mapping is a common method for detecting trace amounts of target molecules. Since the method produces large amounts of data and, in the case of very low concentrations, low signal-to-noise (SNR) ratio, ability to extract relevant spectral features is crucial. We propose a pseudo-Voigt model as a constrained source separation model, that is able to directly and reliably identify the Raman modes, with overall performance similar to the state of the art non-negative matrix factorization approach. However, the model provides better interpretation and is a step towards enabling the use of SERS in detection of trace amounts of molecules in real-life settings.

General information
State: Published
Blu-Ray-based micromechanical characterization platform for biopolymer degradation assessment

Degradable biopolymers are used as carrier materials in drug delivery devices. A complete understanding of their degradation behaviour is thus crucial in the design of new delivery systems. Here we combine a reliable method, based on spray coated micromechanical resonators and a disposable microfluidic chip, to characterize biopolymer degradation under the action of enzymes in controlled flow condition. The sensing platform is based on the mechanics and optics from a Blu-Ray player, which automatically localize individual sensors within the array, and sequentially measure and record the resonance frequency of up to twelve resonators within 4 min. Such fast and automated measuring technology, combined with the use of thin polymers layers in the degradation experiments, allows to reduce the experimental time needed for degradation studies from 6 weeks to 8 h. We first present a full characterization of sensor properties and then perform degradation studies of poly(lactic-co-glycolic acid) (PLGA) in steady flow for three different enzyme concentrations. The degradation has been performed in liquid environment. Before each resonator measurement, the measuring chamber has been automatically dried, since the resonator characteristics are much approved when measuring in air compared to liquid. The obtained degradation profiles are comparable to profiles obtained by conventional approaches, which have shown to require up to 6 weeks of experimental time frame.
Butyrate-Loaded Chitosan/Hyaluronan Nanoparticles: A Suitable Tool for Sustained Inhibition of ROS Release by Activated Neutrophils

Tissue damage caused by excessive amounts of neutrophil-derived reactive oxygen species (ROS) occurs in many inflammatory diseases. Butyrate is a short-chain fatty acid (SCFA) with known anti-inflammatory properties, able to modulate several neutrophil functions. Evidence is provided here that butyrate inhibits neutrophil ROS release in a dose and time-dependent fashion. Given the short half-life of butyrate, chitosan/hyaluronan nanoparticles are next designed and developed as controlled release carriers able to provide cells with a long-lasting supply of this SCFA. Notably, while the
inhibition of neutrophil ROS production by free butyrate declines over time, that of butyrate-loaded chitosan/hyaluronan nanoparticles (B-NPs) is sustained. Additional valuable features of these nanoparticles are inherent ROS scavenger activity, resistance to cell internalization, and mucoadhesiveness. B-NPs appear as promising tools to limit ROS-dependent tissue injury during inflammation. Particularly, by virtue of their mucoadhesiveness, B-NPs administered by enema can be effective in the treatment of inflammatory bowel diseases.
**Challenges in the integration of silicon SERS substrates into a polypropylene injection moulded microfluidic chip**

**General information**

State: Published

Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Authors: Serioli, L. (Intern), Morelli, L. (Intern), Matteucci, M. (Intern), Zor, K. (Intern), Boisen, A. (Intern)

Publication date: 2017


Main Research Area: Technical/natural sciences

Integration, SERS, Microfluidics

Electronic versions:

Untitled.pdf

Source: PublicationPreSubmission

Source-ID: 140300954

Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

**Chemical Engineering in the "BIO" world**

Modern Chemical Engineering was born around the end of the 19th century in Great Britain, Germany, and the USA, the most industrialized countries at that time. Milton C. Whitaker, in 1914, affirmed that the difference between Chemistry and Chemical Engineering lies in the capability of chemical engineers to transfer laboratory findings to the industrial level. Since then, Chemical Engineering underwent huge transformations determining the detachment from the original Chemistry nest. The beginning of the sixties of the 20th century saw the development of a new branch of Chemical Engineering baptized Biomedical Engineering by Peppas and Langer and that now we can name Biological Engineering. Interestingly, although Biological Engineering focused on completely different topics from Chemical Engineering ones, it resorted to the same theoretical tools such as, for instance, mass, energy and momentum balances. Thus, the birth of Biological Engineering may be considered as a Darwinian evolution of Chemical Engineering similar to that experienced by mammals which, returning to water, used legs and arms to swim. From 1960 on, Biological Engineering underwent a considerable evolution as witnessed by the great variety of topics covered such as hemodialysis, release of synthetic drugs, artificial organs and, more recently, delivery of small interfering RNAs (siRNA). This review, based on the activities developed in the frame of our PRIN 2010-11 (20109PLMH2) project, tries to recount origins and evolution of Chemical Engineering illustrating several examples of recent and successful applications in the biological field. This, in turn, may stimulate the discussion about the Chemical Engineering students curriculum studiorum update.

**General information**

State: Published

Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics


Pages: 158-178

Publication date: 2017

Main Research Area: Technical/natural sciences
Ciprofloxacin-loaded sodium alginate/poly (lactic-co-glycolic acid) electrospun fibrous mats for wound healing

Wound dressings should ideally be able to maintain high humidity, remove excess wound exudate, permit thermal insulation, provide certain mechanical strength, and in some cases deliver antibiotics to prevent infections. Until now, none of the existing wound dressing products can meet all these requirements. To design a wound dressing with as many of the aforementioned features as possible, in this study, we attempted to prepare ciprofloxacin (CIP), an antibiotic, loaded electrospun hydrophobic poly (lactic-co-glycolic acid) (PLGA) fibrous mats modified with hydrophilic sodium alginate (ALG) microparticles. The results showed that ALG could improve the wettability, water absorption capacity, and enhance the release rate of ciprofloxacin from the PLGA fibrous mats. In addition, the addition of ALG reduced the stiffness of PLGA fibrous mats for better protection of the injured area as indicated by the Young's Modulus. Moreover, the burst release of CIP resulted from the addition of ALG seemed to provide an improved antibacterial effect to the PLGA mats. This study demonstrated the potential of combining hydrophilic and hydrophobic polymers to design the desired wound dressings via the electrospinning process.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, University of Southern Denmark
Authors: Liu, X. (Ekstern), Nielsen, L. H. (Intern), Klodzinska, S. N. (Ekstern), Nielsen, H. M. (Ekstern), Qu, H. (Ekstern), Christensen, L. P. (Ekstern), Rantanen, J. (Ekstern), Yang, M. (Ekstern)
Pages: 42-49
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: European Journal of Pharmaceutics and Biopharmaceutics
Volume: 123
ISSN (Print): 0939-6411
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 1.378 SJR 1.342
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.49 SJR 1.411 SNIP 1.416
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.437 SNIP 1.471 CiteScore 4.37
Web of Science (2015): Indexed yes
Design and development of electrochemical polymer-based lab-on-a-disc devices for biological applications

The need for reliable, fast, easy to use, portable and cost effective analytical tools has led to several novel approaches in the development of miniaturized microfluidic platforms integrated with electrochemical sensors. This thesis presents the design and development of an electrochemical detection based centrifugal microfluidic platforms towards applications in bioprocess monitoring, medical diagnostics, food and environmental analysis, etc. Stencil based electrode fabrication approach was developed and optimized to pattern reliable and reproducible electrodes on a polymeric substrate. Also, a fast, easy to use and simplified approach was established for interfacing the electrodes integrated with the polymeric Lab-on-a-disc (LoD) devices. On-disc filtration and supported liquid membrane (SLM) extraction was adapted on LoD devices for sample pre-treatment (e.g., filtration, extraction, enrichment). The applicability of the developed microfluidic systems was demonstrated by monitoring a biological process, namely quantifying the amount of the bacterial metabolite p-Coumaric acid (pHCA) produced by genetically modified E. coli cells. The first generation LoD device (with integrated filtration) was used to quantify pHCA at the end of bacterial culture (24 hours) when the cell density is the highest. We demonstrated the efficiency of the centrifugal filtration, which enabled cell-free electrochemical detection eliminating the effect of high cell density on electrochemical quantification of pHCA. The second generation LoD device (with integrated SLM extraction) was more advanced and facilitated extraction, enrichment, as well as electrochemical detection of pHCA from the complex sample matrix, i.e., E. coli supernatant at different time points during the cell culture. Realizing the need for more advanced sensors that can be integrated with microfluidic devices, we developed dual functionality sensors facilitating surface-enhanced Raman spectroscopy (SERS) based sensing as well as electrochemical detection. Moreover, to eliminate the need for bulky peripheral instrumentation connected through slip rings for on-disc electrochemical measurements, we present a miniaturized smartphone controlled wireless potentiostat, which can be integrated on a...
rotating microfluidic platform.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Sanger, K. (Intern), Boisen, A. (Intern), Zor, K. (Intern), Heiskanen, A. (Intern)
Number of pages: 118
Publication date: 2017

Publication information
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
PhD_Thesis_Kuldeep_Final_tilhjemmeside.pdf

Relations
Projects:
Design and development of electrochemical polymer-based lab-on-a-disc devices for biological applications
Source: PublicationPreSubmission
Source-ID: 140389290
Publication: Research › Ph.D. thesis – Annual report year: 2017

Detection of melamine in milk using nanopillar filters and Raman spectroscopy

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Durucan, O. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Matteucci, M. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2017

Host publication information
Title of host publication: Book of Abstracts, Sustain 2017
Publisher: Technical University of Denmark (DTU)
Article number: F-8
Main Research Area: Technical/natural sciences
Conference: Sustain 2017, Kgs. Lyngby, Denmark, 06/12/2017 - 06/12/2017
Electronic versions:
SustainAbstracts2017c.compressed_66.pdf
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2017

Detection of p-coumaric acid from cell supernatant using surface enhanced Raman scattering

A standard protocol for analysis of microbial factories requires the screening of several populations in order to find the bestperforming ones. Standard analytical methods usually include high performance liquid chromatography (HPLC), thin layerchromatography (TLC) or spectrophotometry, which are expensive and time-consuming processes. Surface Enhanced Raman Spectroscopy (SERS), instead, is a highly sensitive spectroscopic technique for specific, fast and real-time sensing of biological samples. Here we demonstrate the use of SERS to discriminate between two different bacterial populations based on detection of p-coumaric acid (pHCA) in cell supernatant. SERS active substrates, based on leaning gold-capped silicon nanopillars, were used for detection. They were successfully used to detect culture medium spiked with pHCA, and the effect of medium dilution was studied. For analysis of biological production of pHCA, triplicate cultures of E. coli strains expressing a pHCA-forming enzyme (P) as well as of a non-producing strain (C) were grown. Then, supernatant samples were collected and their pHCA content was measured using SERS and HPLC for comparison. The intensity of the pHCA Raman mode at 1169 cm⁻¹ (CH-rocking motion) showed different trends for P and C strains, similar to the results obtained using the HPLC method. Results illustrate that SERS can be used for quick and semiquantitative discrimination of pHCA concentrations in cell supernatant medium.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Research Groups, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Morelli, L. (Intern), Jendresen, C. B. (Intern), Zor, K. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)
Detection of Surface-Linked Polychlorinated Biphenyls using Surface-Enhanced Raman Scattering Spectroscopy

We present an improved procedure for analytical detection of toxic polychlorinated biphenyls (PCB) using surface-enhanced Raman scattering (SERS) spectroscopy. A gold-capped silicon nanopillar substrate was utilized to concentrate PCB molecules within an area of high electromagnetic fields through formation of microsized nanopillar clusters, and consequently, so-called “hot spots” can be formed. In order to improve PCB detection limit, 3,3′,4,4′-tetrachlorobiphenyl (PCB77) compounds were chemically modified with a –SCH$_3$ (PCB77-SCH$_3$) group. Experimental and numerical analysis of vibrational modes showed only minor differences between standard PCB77 and PCB77-SCH$_3$. Consequently, we observe significantly increased SERS signals for –SCH$_3$ modified PCB77 while retaining most vibrational modes that characterize standard PCB77. Results point towards more efficient path for detecting different PCB congeners from real-life samples. We interpret the result as PCB77-SCH$_3$ link to gold surface via sulfur atoms that facilitates accumulation of the modified PCB molecules on the metal surface. For similar SERS experimental conditions most spectral characteristics of PCB77 are identifiable down to concentrations of ~10$^{-5}$ M while PCB77-SCH$_3$ spectral fingerprint is retained in ~10$^{-8}$ M range.
Development of a Video-Microscopic Tool To Evaluate the Precipitation Kinetics of Poorly Water Soluble Drugs: A Case Study with Tadalafil and HPMC

Many drug candidates today have a low aqueous solubility and, hence, may show a low oral bioavailability, presenting a major formulation and drug delivery challenge. One way to increase the bioavailability of these drugs is to use a supersaturating drug delivery strategy. The aim of this study was to develop a video-microscopic method, to evaluate the effect of a precipitation inhibitor on supersaturated solutions of the poorly soluble drug tadalafil, using a novel video-microscopic small scale setup. Based on preliminary studies, a degree of supersaturation of 29 was chosen for the supersaturation studies with tadalafil in FaSSIF. Different amounts of hydroxypropyl methyl cellulose (HPMC) were predissolved in FaSSIF to give four different concentrations, and the supersaturated system was then created using a solvent shift method. Precipitation of tadalafil from the supersaturated solutions was monitored by video-microscopy as a function of time. Single-particle analysis was possible using commercially available software; however, to investigate the entire population of precipitating particles (i.e., their number and area covered in the field of view), an image analysis algorithm was developed (multiparticle analysis). The induction time for precipitation of tadalafil in FaSSIF was significantly prolonged by adding 0.01% (w/v) HPMC to FaSSIF, and the maximum inhibition was reached at 0.1% (w/v) HPMC, after which additional HPMC did not further increase the induction time. The single-particle and multiparticle analyses yielded the same ranking of the HPMC concentrations, regarding the inhibitory effect on precipitation. The developed small scale method to assess the effect of precipitation inhibitors can speed up the process of choosing the right precipitation inhibitor and the concentration to be used.
Extraction And SERS Based Detection Of Bacterial Metabolites In Mixture On A Centrifugal Microfluidic Device
Fabrication and characterization of Au dimer antennas on glass pillars with enhanced plasmonic response

We report on the fabrication and dark-field spectroscopy characterization of Au dimer nanoantennas placed on top of SiO2 nanopillars. The reported process enables the fabrication of nanopillar dimers with gaps down to 15 nm and heights up to 1 μm. A clear dependence of the plasmonic resonance position on the dimer gap is observed for smaller pillar heights, showing the high uniformity and reproducibility of the process. It is shown how increasing the height of nanopillars significantly affects the recorded elastic scattering spectra from Au nanoantennas. The results are compared to finite-difference time-domain (FDTD) and finite-element method (FEM) simulations. Additionally, measured spectra are accompanied by dark-field microscopy images of the dimers, showing the pronounced change in color. Placing nanoantennas on nanopillars with a height comparable to the in-plane dimer dimensions results in an enhancement of the scattering response, which can be understood through reduced interaction of the near-fields with the substrate. When increasing the pillar height further, scattering by the pillars themselves manifests itself as a strong tail at lower wavelengths. Additionally, strong directional scattering is expected as a result of the interface between the nanoantennas and nanopillars, which is taken into account in simulations. For pillars of height close to the plasmonic resonance wavelength, the scattering spectra become more complex due to additional scattering peaks as a result of larger geometrical nonuniformities.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technische Universität Wien
Authors: Sadeghi, P. (Ekstern), Wu, K. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Schmid, S. (Ekstern)
Pages: 497-505
Publication date: 2017
Main Research Area: Technical/natural sciences
Fabrication of completely free-standing pyrolytic carbon string resonator

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Nguyen, Q. L. (Intern), Larsen, P. E. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Number of pages: 1
Publication date: 2017
Main Research Area: Technical/natural sciences

Fabrication of completely free-standing pyrolytic carbon string resonators

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Nguyen, Q. L. (Intern), Larsen, P. E. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Publication date: 2017
Main Research Area: Technical/natural sciences

From concept to in vivo testing: Microcontainers for oral drug delivery
This work explores the potential of polymeric micrometer sized devices (microcontainers) as oral drug delivery systems (DDS). Arrays of detachable microcontainers (D-MCs) were fabricated on a sacrificial layer to improve the handling and facilitate the collection of individual D-MCs. A model drug, ketoprofen, was loaded into the microcontainers using supercritical CO2 impregnation, followed by deposition of an enteric coating to protect the drug from the harsh gastric environment and to provide a fast release in the intestine. In vitro, in vivo and ex vivo studies were performed to assess the viability of the D-MCs as oral DDS. D-MCs improved the relative oral bioavailability by 180% within 4h, and increased the absorption rate by 2.4 times compared to the control. This work represents a significant step forward in the translation of these devices from laboratory to clinic.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Applied Mathematics and Computer Science, Cognitive Systems, Department of Physics, Neutrons and X-rays for Materials Physics, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Copenhagen
Pages: 343-351
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Controlled Release
Volume: 268
Enteric coating, Microtechnology, Oral drug delivery, Supercritical impregnation

DOIs:
10.1016/j.jconrel.2017.10.013

Original language: English

Relations
Projects:
From concept to in vivo testing: Microcontainers for oral drug delivery
Source: FindIt
Source-ID: 2392221100
Geometrically Optimized 3D Printed Mini-Devices for Oral Drug Delivery

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Mechanical Engineering, Manufacturing Engineering, Technical University of Denmark
Authors: Vaut, L. (Intern), Juszczyk, J. J. (Ekstern), Jensen, K. E. (Intern), Andersen, A. J. (Intern), Tosello, G. (Intern), Boisen, A. (Intern)
Publication date: 2017
Event: Poster session presented at 44th Annual Meeting & Exposition of the Controlled Release Society, Boston, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
Untitled.pdf
Source: PublicationPreSubmission
Source-ID: 134459839
Publication: Research - peer-review › Poster – Annual report year: 2017

Gold nanomaterials for the selective capturing and SERS diagnosis of toxins in aqueous and biological fluids

A highly sensitive nanosensing method for the combined selective capture and SERS detection of Microcystin-LR (MC-LR) in blood plasma has been developed. The new method utilizes gold coated magnetic nanoparticles that are functionalized with anti MC-LR antibody Fab' fragments for the selective capture of MC-LR from aqueous media and blood plasma. Using an oriented immobilization approach, the Fab' fragments are covalently attached to gold surface to form a monolayer with high capture efficiency towards the toxin. After the selective capture, the purified MC-LR molecules were released from the extractor nanoparticles within 5min by manipulating the pH environment of the nanoparticles. The regenerated extractor nanoparticles maintained their capture efficiency and, therefore, were re-used to capture of MC-LR from successive samples. The released purified toxin was screened within 10min on gold coated silicon nanopillars and a new paper-based SERS substrate by handheld Raman spectrometer. The SERS enhancement factors of the nanopillars and the new paper-based substrate were 2.5×10⁶ and 3×10⁵ respectively. The lower limit of quantification (LOQ) of MC-LR by SERS on the nanopillar substrate was 10fM (R²=0.9975) which is well below the clinically required detection limit of the toxin. The SERS determination of MC-LR was cross validated against ELISA. By using antibody fragments that are specific to the target biomolecule, the new methodology can be extended to the rapid extraction and detection of other toxins and proteins.

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Queensland University of Technology
Authors: Hassanain, W. A. (Ekstern), Izake, E. L. (Ekstern), Schmidt, M. S. (Intern), Ayoko, G. A. (Ekstern)
Number of pages: 9
Pages: 664-672
Publication date: 2017
Main Research Area: Technical/natural sciences

**Publication information**
Journal: Biosensors and Bioelectronics
Volume: 91
ISSN (Print): 0956-5663
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.65 SJR 2.373
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.22 SJR 2.095 SNIP 1.619
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.044 SNIP 1.671 CiteScore 7.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.057 SNIP 1.716 CiteScore 6.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.029 SNIP 1.726 CiteScore 6.34
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.397 SNIP 1.592 CiteScore 5.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.126 SNIP 1.704 CiteScore 5.85
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.143 SNIP 1.609
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.991 SNIP 1.771
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.495 SNIP 1.782
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.111 SNIP 1.962
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.911 SNIP 1.658
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.455 SNIP 1.596
Scopus rating (2004): SJR 1.436 SNIP 1.603
Scopus rating (2003): SJR 1.245 SNIP 1.568
Scopus rating (2002): SJR 1.016 SNIP 1.252
Scopus rating (2001): SJR 1.188 SNIP 1.558
Scopus rating (2000): SJR 1.11 SNIP 1.33
Scopus rating (1999): SJR 0.985 SNIP 0.919

Original language: English
Antibody fragments, Biological fluids, Functionalized nanoparticles, Microcystin-LR, Molecular diagnosis, Paper SERS substrate

DOIs:
10.1016/j.bios.2017.01.032
Source: FindIt
Source-ID: 2351198724
Publication: Research - peer-review › Journal article – Annual report year: 2017
Hand-Held Femtogram Detection of Hazardous Picric Acid with 2 Hydrophobic Ag Nanopillar SERS Substrates and Mechanism of 3 Elasto-Capillarity

Picric acid (PA) is a severe environmental and security risk due to its unstable, toxic, and explosive properties. It is also challenging to detect in trace amounts and in situ because of its highly acidic and anionic character. Here, we assess sensing of PA under nonlaboratory conditions using surface-enhanced Raman scattering (SERS) silver nanopillar substrates and hand-held Raman spectroscopy equipment. The advancing elasto-capillarity effects are explained by molecular dynamics simulations. We obtain a SERS PA detection limit on the order of 20 ppt, corresponding attomole amounts, which together with the simple analysis methodology demonstrates that the presented approach is highly competitive for ultrasensitive analysis in the field.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Science and Technology of China, Uppsala University, Swedish Defense Research Agency FOI, University of Hyderabad, Dezhou University, Chalmers University of Technology
Authors: Hakonen, A. (Ekstern), Wang, F. (Ekstern), Andersson, P. O. (Ekstern), Wingfors, H. (Ekstern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Soma, V. R. (Ekstern), Xu, S. (Ekstern), Li, Y. (Ekstern), Boisen, A. (Intern), Wu, H. (Ekstern)
Number of pages: 5
Pages: 198-202
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: ACS Sensors
Volume: 2
Issue number: 2
ISSN (Print): 2379-3694
Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): SNIP 1.241 SJR 1.895
Web of Science (2017): Indexed yes
Original language: English
SERS, Picric acid, Elasto-capillarity, Hydrophobic ag nanopillars, Flexible hot-spots, Molecular dynamics simulations
DOIs:
10.1021/acssensors.6b00749
Source: PublicationPreSubmission
Source-ID: 128987400
Publication: Research - peer-review › Journal article – Annual report year: 2017

High-Throughput Fabrication of Nanocone Substrates through Polymer Injection Moulding For SERS Analysis in Microfluidic Systems

Metal-coated nanostructured surfaces have shown promise as substrates for surface-enhanced Raman spectroscopy (SERS) as they allow chemical trace detection with high sensitivity and rapid response. This sensitivity and specificity makes SERS especially interesting for environmental and biological analysis. Metal-capped silicon nanopillars, fabricated through a maskless ion etch, are state-of-the-art for on-chip SERS substrates. A dense cluster of high aspect ratio polymer nanocones was achieved by using high-throughput polymer injection moulding over a large area replicating a silicon nanopillar structure. Gold-capped polymer nanocones display similar SERS sensitivity as silicon nanopillars, while being easily integrable into a microfluidic chips.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Spectro Inlets ApS
Authors: Viehrig, M. (Intern), Matteucci, M. (Intern), Thilsted, A. H. (Ekstern), Schmidt, M. S. (Intern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2017
Event: Abstract from 21st International Conference on Miniaturized Systems for Chemistry and Life Sciences, Savannah, United States
Main Research Area: Technical/natural sciences
Lithography-free, Reactive Ion Etching, Polymer Injection, Nanopillars, SERS, Sensors
Electronic versions:
Untitled.pdf
Immobilisation of barley aleurone layers enables parallelisation of assays and analysis of transient gene expression in single cells

The barley aleurone layer is an established model system for studying phytohormone signalling, enzyme secretion and programmed cell death during seed germination. Most analyses performed on the aleurone layer are end-point assays based on cell extracts, meaning each sample is only analysed at a single time point. By immobilising barley aleurone layer tissue on polydimethylsiloxane pillars in the lid of a multiwell plate, continuous monitoring of living tissue is enabled using multiple non-destructive assays in parallel. Cell viability and menadione reducing capacity were monitored in the same aleurone layer samples over time, in the presence or absence of plant hormones and other effectors. The system is also amenable to transient gene expression by particle bombardment, with simultaneous monitoring of cell death. In conclusion, the easy to handle and efficient experimental setup developed here enables continuous monitoring of tissue samples, parallelisation of assays and single cell analysis, with potential for time course studies using any plant tissue that can be immobilised, for example leaves or epidermal peels.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Systems Biology, Bioanalytics, Fluidic Array Systems and Technology, Aarhus University
Number of pages: 6
Pages: 71-76
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Plant Physiology and Biochemistry
Volume: 118
ISSN (Print): 0981-9428
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.092 SJR 1.125
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.4 SJR 1.187 SNIP 1.16
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.185 SNIP 1.276 CiteScore 3.19
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.061 SNIP 1.17 CiteScore 2.86
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.078 SNIP 1.369 CiteScore 3.24
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.144 SNIP 1.327 CiteScore 3.07
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.197 SNIP 1.258 CiteScore 3.1
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
IR spectroscopy with pyrolytic carbon string resonator as a tool for particle detection

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Nguyen, Q. L. (Intern), Larsen, P. E. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Publication date: 2017
Event: Poster session presented at 14th International Workshop on Nanomechanical Sensors, Keauhou Bay, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
Untitled.pdf
Source: PublicationPreSubmission
Source-ID: 140842833
Publication: Research - peer-review › Poster – Annual report year: 2017

Lab-on-a-disc platform for screening of genetically modified E. coli cells via cell-free electrochemical detection of p-Coumaric acid

We present a robust easy to use lab-on-a-disc (LoD) device with integrated sample pre-treatment and electrochemical detection system for cell-free detection of a secondary metabolite, p-Coumaric acid (pHCA), produced by genetically modified E. coli. In the LoD device, which incorporates eight filtration and electrochemical detection units, the sample filtration was performed by rotating the disc using a programmable closed-loop stepper motor. The electrodes, patterned on plastic substrate, were connected through a printed circuit board to the slip ring using a robust magnetic clamping.

system that enables easy assembly and robust electrical connections. pHCA was quantified in a linear range from 0.125 up to 2 mM using square wave voltammetry. The platform was successfully used for the quantification of pHCA produced by two genetically modified E. coli strains after 24 h of cell culture. The data obtained from the electrochemical measurements showed good correlation with high performance liquid chromatographic analysis. The developed LoD system offers fast and easy detection of pHCA, enabling screening of genetically modified organisms based on the quantity of produced secondary metabolites.

**General information**

State: Published

Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Bioanalytics, Research Groups

Authors: Sanger, K. (Intern), Zor, K. (Intern), Jendresen, C. B. (Intern), Heiskanen, A. (Intern), Amato, L. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)

Pages: 999-1005

Publication date: 2017

Main Research Area: Technical/natural sciences

**Publication information**

Journal: Sensors and Actuators B: Chemical

Volume: 253

ISSN (Print): 0925-4005

Ratings:

BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes

BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.453 SJR 1.406
Web of Science (2017): Indexed yes

BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.07 SJR 1.343 SNIP 1.464
Web of Science (2016): Indexed yes

BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.225 SNIP 1.484 CiteScore 4.84
Web of Science (2015): Indexed yes

BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.229 SNIP 1.658 CiteScore 4.37
Web of Science (2014): Indexed yes

BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.261 SNIP 1.638 CiteScore 4.25

ISI indexed (2013): ISI indexed yes

Web of Science (2013): Indexed yes

BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.412 SNIP 1.674 CiteScore 3.92

ISI indexed (2012): ISI indexed yes

Web of Science (2012): Indexed yes

BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.485 SNIP 1.752 CiteScore 4.08

ISI indexed (2011): ISI indexed yes

Web of Science (2011): Indexed yes

BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.434 SNIP 1.437
Web of Science (2010): Indexed yes

BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.317 SNIP 1.518
Web of Science (2009): Indexed yes

BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.448 SNIP 1.566
Web of Science (2008): Indexed yes
Large-scale, Lithography-free Production of Transparent Nanostructured Surface for Dual-functional Electrochemical and SERS Sensing

In this work, we present a dual-functional sensor that can perform surface-enhanced Raman spectroscopy (SERS) based identification and electrochemical (EC) quantification of analytes in liquid samples. A lithography-free reactive ion etching process was utilized to obtain nanostructures of high aspect ratios distributed homogeneously on a 4-inch fused silica wafer. The sensor was made up of three-electrode array, obtained by subsequent e-beam evaporation of Au on nanostructures in selected areas through a shadow mask. The SERS performance was evaluated through surface-averaged enhancement factor (EF), which was ~6.2 x 10^5, and spatial uniformity of EF, which was ~13% in terms of relative standard deviation. Excellent electrochemical performance and reproducibility were revealed by recording cyclic voltammograms. On nanostructured electrodes, paracetamol (PAR) showed an improved quasi-reversible behavior with decrease in peak potential separation (∆Ep ~90mV) and higher peak currents (Ipa/Ipc ~1), comparing to planar electrodes (∆Ep ~560mV). The oxidation potential of PAR was also lowered by ~80 mV on nanostructured electrodes. To illustrate dual-functional sensing, quantitative evaluation of PAR ranging from 30 µM to 3 mM was realized through EC detection, and presence of PAR was verified by its SERS fingerprint.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Bioanalytics
Authors: Sanger, K. (Intern), Durucan, O. (Intern), Wu, K. (Intern), Thilsted, A. H. (Intern), Heiskanen, A. R. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Zor, K. (Intern), Boisen, A. (Intern)
Pages: 1869–1875
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: ACS Sensors
Volume: 2
Issue number: 12
ISSN (Print): 2379-3694
Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): SNIP 1.241 SJR 1.895
Web of Science (2017): Indexed yes
Original language: English
Lithography-free, Dual-functional, Electrochemical, SERS, Paracetamol
DOIs:
10.1021/acssensors.7b00783
Loading of Drug-Polymer Matrices in Microreservoirs for Oral Drug Delivery

For major advances in microfabricated drug delivery systems (DDS), fabrication methods with high throughput using biocompatible polymers are required. Once these DDS are fabricated, loading of drug poses a significant challenge. Here, hot punching is presented as an innovative method for drug loading in microfabricated DDS. The microfabricated DDS are microcontainers fabricated in photoresist SU-8 and biopolymer poly-ε-caprolactone (PLLA). Furosemide (F) drug is embedded in poly-ε-caprolactone polymer matrix. This F-PCL drug polymer matrix is loaded in SU-8 and PLLA microcontainers using hot punching with >99% yield. Thus, it is illustrated that hot punching allows high-throughput, parallel loading of 3D polymer microcontainers with drug-polymer matrices in a single process step.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Petersen, R. S. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern)
Number of pages: 6
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Macromolecular Materials & Engineering
Volume: 302
Issue number: 3
Article number: 1600366
ISSN (Print): 1438-7492
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.945 SJR 0.755
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.01 SJR 0.905 SNIP 0.972
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.847 SNIP 1.072 CiteScore 2.88
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.009 SNIP 1.294 CiteScore 2.81
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.956 SNIP 1.24 CiteScore 2.66
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.963 SNIP 1.181 CiteScore 2.34
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.972 SNIP 1.058 CiteScore 2.18
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.922 SNIP 0.916
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.072 SNIP 0.992
BFI (2008): BFI-level 1
Low surface damage dry etched black silicon

Black silicon (bSi) is promising for integration into silicon solar cell fabrication flow due to its excellent light trapping and low reflectance, and a continuously improving passivation. However, intensive ion bombardment during the reactive ion etching used to fabricate bSi induces surface damage that causes significant recombination. Here, we present a process optimization strategy for bSi, where surface damage is reduced and surface passivation is improved while excellent light trapping and low reflectance are maintained. We demonstrate that reduction of the capacitively coupled plasma power, during reactive ion etching at non-cryogenic temperature (-20°C), preserves the reflectivity below 1% and improves the effective minority carrier lifetime due to reduced ion energy. We investigate the effect of the etching process on the surface morphology, light trapping, reflectance, transmittance, and effective lifetime of bSi. Additional surface passivation using atomic layer deposition of Al₂O₃ significantly improves the effective lifetime. For n-type wafers, the lifetime reaches 12 ms for polished and 7.5 ms for bSi surfaces. For p-type wafers, the lifetime reaches 800 ls for both polished and bSi surfaces.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, DTU Danchip, Nanoprobes, Department of Energy Conversion and Storage, Anhalt University of Applied Sciences, Fraunhofer Center for Silicon Photovoltaics CSP
Authors: Plakhotnyuk, M. M. (Intern), Gaudig, M. (Ekstern), Davidsen, R. S. (Intern), Michael-Lindhard, J. (Intern), Hirsch, J. (Ekstern), Lausch, D. (Ekstern), Schmidt, M. S. (Intern), Stamate, E. (Intern), Hansen, O. (Intern)
Number of pages: 9
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Applied Physics
Volume: 122
Issue number: 14
Article number: 143101
ISSN (Print): 0021-8979
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.953 SJR 0.739
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.72 SJR 0.906 SNIP 0.977
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.821 SNIP 0.996 CiteScore 1.57
Macroscale SERS Uniformity and Reproducibility Using Densely Clustered Nanopillars
Magnetic Bead-Based Biosensing on an Automated & Integrated Lab-on-a-Disc Platform

The PhD thesis presents the development and utilization of magnetic bead-based agglutination assays for the detection of biomarkers in biofluids as well as discovery of a biomarker relevant to the mechanism of action of a type-2 diabetes (T2D) drug while integrating the assays on an automated centrifugal microfluidic platform with incorporated readout units. The assays were developed through surface functionalization of micro or nano-sized magnetic beads with specific antibodies or aptamers to specifically bind with the biomarker of interest resulting in the formation of the biomarker-bridged magnetic bead clusters and hence called ‘agglutination’ assay. The concentration of the analyte or biomarker was quantified based on the size of the clusters. The model biomarkers studied in this project were thrombin – a blood coagulation protein; C-reactive protein – an acute phase protein-biomarker for inflammatory diseases; and mononuclear white blood cell count – a biomarker for the prognosis of different medical conditions. Furthermore, the concept of the agglutination assay was utilized for a biomarker discovery application by investigating the mechanism of action of a T2D drug - metformin through the analysis and quantification of the aggregation and disaggregation phenomena of the magnetic beads in response to the presence of the drug.

The assays were either partially or fully integrated on disc-shaped polymeric microfluidic substrates i.e. microfluidic discs for incorporating the advantages of centrifugal microfluidics e.g. eliminating the need for external fluidic connectors or pumps, and facilitating simple, compact and low-cost instrumentation along with effective multiplexing of microfluidic units. All the discs were fabricated in-house using multiple layers of polymeric substrates. Two specific valving mechanisms namely centrifugo-pneumatic and event-triggered valving were incorporated into the microfluidic platform in order to facilitate the integration of the assay from sample-to-answer. The readouts were performed by two different optical methods: Blu-ray based optomagnetic readout and optical imaging method. The readout instruments were customized and incorporated with the automated centrifugation microfluidic platform to produce an integrated and automated biosensing platform with a potential for operating in an out-of-lab setting which can pave the way for further development of a point-of-care diagnostic tool.
condition of the phenomena under test, are better controlled. As proof of concept to test the capabilities of the system, we studied the biopolymer degradation of Poly Lactic-co-Glycolic Acid (PLGA), which is of high relevance in the biomedical research field. A second version of the system is currently under development, and it aims to increase the throughput of the system allowing to read out multiple microbridge arrays.

For material characterization, spectroscopy analysis is often considered a benchmark technology. Conventional infrared spectroscopy approaches commonly require milligram amount of sample. Considering the frame of reference given by the overall aim of the project, mechanical sensors can be exploited to provide a unique tool for performing spectroscopy on a limited amount of sample. In this project, a nanomechanical photothermal sensor has been designed, developed and exploited to perform thin film Infrared Spectroscopy. Contrary to what has been previously shown, this work has focused on a membrane sensor providing a robust experimental approach which better suit sample quantification and preparation. The purpose of the studies presented here is to show the real potential of photothermal spectroscopy based on a nanomechanism sensor and to provide a method to maximise the signal to noise ratio (SNR) from a single acquisition. The methodology presented showed that it is possible obtaining a high SNR of 300 on a 20nm thick polymer layer showing a substantial improvement compared to the benchmark technique, attenuated total reflectance spectroscopy (ATR-FTIR). This high sensitivity allowed us to observe the chemical modification occurring during the gelification of a submicron thick layer of poly-vinyl-pyrrrolidone (PVP) corresponding to picogram quantity of material.

Microcontainers as an oral delivery system for spray dried cubosomes containing ovalbumin

The purpose of this study was to prepare cubosomes encapsulating the model antigen ovalbumin (OVA) via spray drying, and to characterise such cubosomes with a view for their potential application in oral vaccine delivery. Furthermore the cubosome formulation was loaded into polymeric microcontainers intended as an oral drug delivery system. The cubosomes consisted of commercial glyceryl monooleate, Dimodan®, containing OVA and were surrounded with a dextran shell prepared by spray drying. Cryo-TEM was used to confirm that cubosomes were formed after hydration of the spray dried precursor powder. The precursor powder had a mean particle size of 1.3±0.1μm, whereas the mean diameter of the dispersed cubosomes was 282±7nm (PDI: 0.18) measured by dynamic light scattering. 8.5±0.3% (w/w) of OVA was present in the cubosome powder and OVA was found released slowly over the first 70h, followed by a more rapid release. Total release of 47.9±2.8% of loaded OVA occurred over 96h in a buffer at pH 6.8. When the powder was filled into microcontainers, and the opening covered with the pH sensitive polymer Eudragit S100, the pH sensitive ‘lid’ was intact at gastric pH, but release of OVA from the cubosomes and microcontainers occurred at pH 6.8, releasing 44.1±5.6% of the OVA in 96h. Small-angle X-ray scattering (SAXS) revealed that the ‘dry’ particles possessed an internal ordered lipid structure (lamellar and inverse micellar phase) by virtue of a small amount of residual water, and after hydration in buffer at pH 6.8, the particles formed the hexagonal inverse cubic phases, thereby indicating that cubosomes were formed when released from microcontainers.
MICROCONTAINERS FOR INTESTINAL DRUG DELIVERY: in vivo and ex vivo study

General information
State: Published
Nanomechanical Infrared Spectroscopy with Vibrating Filters for Pharmaceutical Analysis

Standard infrared spectroscopy techniques are well-developed and widely used. However, they typically require milligrams of sample and can involve time-consuming sample preparation. A promising alternative is represented by nanomechanical infrared spectroscopy (NAM-IR) based on the photothermal response of a nanomechanical resonator, which enables the chemical analysis of picograms of analyte directly from a liquid solution in only a few minutes. Herein, we present NAM-IR using perforated membranes (filters). The method was tested with the pharmaceutical compound indomethacin to successfully perform a chemical and morphological analysis on roughly 100 pg of sample. With an absolute estimated sensitivity of 109±15 fg, the presented method is suitable for ultrasensitive vibrational spectroscopy.
**Nanopillar Filters for Surface-Enhanced Raman Spectroscopy**

We present a simple, robust, and automated molecule extraction technique based on a centrifugal microfluidic platform. Fast and facile extraction of a food adulterant (melamine) from a complex sample medium (milk) on a SERS substrate is demonstrated. The unique characteristic of the detection method is the obtained “filter paper/chromatographic” effect which combines centrifugal force and wetting properties of the SERS substrate. The work addresses issues related to SERS-based detection of analytes in complex media, which is important for realizing next generation SERS platforms applicable for a broad variety of real-life applications.

**General information**
- **State:** Published
- **Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
- **Authors:** Durucan, O. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Matteucci, M. (Intern), Boisen, A. (Intern)
- **Pages:** 1400-1404
- **Publication date:** 2017
- **Main Research Area:** Technical/natural sciences

**Publication information**
- **Journal:** ACS Sensors
- **Volume:** 2
- **Issue number:** 10
- **ISSN (Print):** 2379-3694
- **Ratings:**
  - Web of Science (2018): Indexed yes
  - Scopus rating (2017): SNIP 1.241 SJR 1.895
  - Web of Science (2017): Indexed yes
- **Original language:** English
- **SERS, Wicking, Microfluidics, Nanopillars, Filtration, Melamine**
- **DOIs:**
  - 10.1021/acssensors.7b00499
- **Source:** FindIt
- **Source-ID:** 2390574014
- **Publication:** Research - peer-review › Letter – Annual report year: 2017

**New Evidence for the Mechanism of Action of a Type-2 Diabetes Drug Using a Magnetic Bead-Based Automated Biosensing Platform**

The mechanism of action (MOA) of the first line type-2 diabetes drug metformin remains unclear despite its widespread usage. However, recent evidence suggests that the mitochondrial copper (Cu)-binding action of metformin may contribute toward the drug's MOA. Here, we present a novel biosensing platform for investigating the MOA of metformin using a magnetic microbead-based agglutination assay which has allowed us to demonstrate for the first time the interaction between Cu and metformin at clinically relevant low micromolar concentrations of the drug, thus suggesting a potential pathway of metformin's blood-glucose lowering action. In this assay, cysteine-functionalized magnetic beads were agglutinated in the presence of Cu due to cysteine's Cu-chelation property. Addition of clinically relevant doses of metformin resulted in disaggregation of Cu-bridged bead-clusters, whereas the effect of adding a closely related but blood-glucose neutral drug propanediimidamide (PDI) showed completely different responses to the clusters. The entire assay was integrated in an automated microfluidics platform with an advanced optical imaging unit by which we investigated these aggregation-disaggregation phenomena in a reliable, automated, and user-friendly fashion with total assay time of 17 min requiring a sample (metformin/PDI) volume of 30 μL. The marked difference of Cu-binding action between the blood-glucose lowering drug metformin and its inactive analogue PDI thus suggests that metformin's distinctive Cu-binding properties may be required for its effect on glucose homeostasis. The novel automated platform demonstrating this novel investigation thus holds the potential to be utilized for investigating significant and sensitive molecular interactions via magnetic bead-based agglutination assay.

**General information**
- **State:** Published
- **Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Tampere University of Technology, University of Dundee, Academia Sinica Taiwan
- **Authors:** Uddin, R. (Intern), Nur-E-Habiba (Ekstern), Rena, G. (Ekstern), Hwu, E. T. (Ekstern), Boisen, A. (Intern)
- **Number of pages:** 8
- **Pages:** 1329–1336
- **Publication date:** 2017
- **Main Research Area:** Technical/natural sciences
Numerical Optimization in Microfluidics
Numerical modelling can illuminate the working mechanism and limitations of microfluidic devices. Such insights are useful in their own right, but one can take advantage of numerical modelling in a systematic way using numerical optimization. In this chapter we will discuss when and how numerical optimization is best used.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes
Authors: Jensen, K. E. (Intern)
Number of pages: 14
Pages: 95-108
Publication date: 2017

Host publication information
Title of host publication: Complex Fluid-Flows in Microfluidics
Publisher: Springer
ISBN (Print): 978-3-319-59593-1_5
ISBN (Electronic): 978-3-319-59593-1
Chapter: 5
Main Research Area: Technical/natural sciences
DOIs: 10.1007/978-3-319-59593-1_5

Relations
Activities:
1st Summer School on Complex Fluid-Flows in Microfluidics
Source: FindIt
Source-ID: 2372109739
Publication: Research - peer-review › Book chapter – Annual report year: 2017

Optimizing silver-capped silicon nanopillars to simultaneously realize macroscopic, practical-level SERS signal reproducibility and high enhancement at low costs
The ideal surface-enhanced Raman spectroscopy (SERS) substrate should fulfil the following: (a) predictable SERS enhancement, (b) macroscale SERS signal uniformity, and (c) suitability for mass production at low costs. Macroscale SERS uniformity and reproducibility at practical levels are big obstacles, which have been preventing most SERS substrates from reliable sensing applications. We have previously shown that SERS-active nanopillar structures, fabricated by lithography-free processes, exhibit high average SERS enhancements and are mass producible. Here, we report an optimized process and show that the improved structures exhibit unrivalled macroscale SERS uniformities (RSD: ~2.5% in millimeter scale, ~7% in wafer scale) and reproducibility (RSD: ~1.5% across 3 wafers), while at the same time exhibiting a very large average SERS enhancement factor of >10^8. The obtained SERS uniformity (~2.5% RSD in millimeter scale) is the best to date measured on large-area solid SERS substrates. Fast and reproducible SERS analysis of trans-1,2-bis (4-pyridyl) ethylene down to 4x10^-13 mol is demonstrated using the optimized structures. We emphasize that achieving simultaneously macroscopic, practical-level SERS signal reproducibility and high enhancement via a lithography-free process is a notable advance towards industrialization of substrate-based SERS sensors.
Photothermal Transport of DNA in Entropy-Landscape Plasmonic Waveguides

The ability to handle single, free molecules in lab-on-a-chip systems is key to the development of advanced biotechnologies. Entropic confinement offers passive control of polymers in nanofluidic systems by locally asserting a molecule's number of available conformation states through structured landscapes. Separately, a range of plasmonic configurations have demonstrated active manipulation of nano-objects by harnessing concentrated electric fields. The integration of these two independent techniques promises a range of sophisticated and complementary functions to handle, for example, DNA, but numerous difficulties, in particular, conflicting requirements of channel size, have prevented progress. Here, we show that metallic V-groove waveguides, embedded in fluidic nanoslits, form entropic potentials that trap and guide DNA molecules over well-defined routes while simultaneously promoting photothermal transport of DNA through the losses of plasmonic modes. The propulsive forces, assisted by in-coupling to propagating channel plasmon polaritons, extend along the V-grooves with a directed motion up to ≈0.5 μm·mW⁻¹ away from the input beam and λ-DNA velocities reaching ≈0.2 μm·s⁻¹·mW⁻¹. The entropic trapping enables the V-grooves to be flexibly loaded and unloaded with DNA by variation of transverse fluid flow, a process that is selective to biopolymers versus fixed-shape objects and also allows the technique to address the challenges of nanoscale interaction volumes. Our self-aligning, light-driven actuator provides a convenient platform to filter, route, and manipulate individual molecules and may be realized wholly by wafer-scale fabrication suitable for parallelized investigation.
Position and mode dependent optical detection back-action in cantilever beam resonators

Optical detection back-action in cantilever resonant or static detection presents a challenge when striving for state-of-the-art performance. The origin and possible routes for minimizing optical back-action have received little attention in literature. Here, we investigate the position and mode dependent optical back-action on cantilever beam resonators. A high power heating laser (100 μW) is scanned across a silicon nitride cantilever while its effect on the first three resonance modes is detected via a low-power readout laser (1 μW) positioned at the cantilever tip. We find that the measured effect of back-action is not only dependent on position but also the shape of the resonance mode. Relevant silicon nitride material parameters are extracted by fitting finite element (FE) simulations to the temperature-dependent frequency response of the first three modes. In a second round of simulations, using the extracted parameters, we successfully fit the FEM results with the measured mode and position dependent back-action. From the simulations, we can conclude that the observed frequency tuning is due to temperature induced changes in stress. Effects of changes in material properties and dimensions are negligible. Finally, different routes for minimizing the effect of this optical detection back-action are described, allowing further improvements of cantilever-based sensing in general.
Powder embossing method for selective loading of polymeric microcontainers with drug formulation

The present study introduces powder embossing as a novel method to enhance loading of polymeric microcontainers with drug. With current loading approaches, it is not possible to handle pure powder drug in a scalable, homogenous and reproducible manner. In this work, we demonstrate simultaneous loading of 625 microcontainers with powder formulation. This is achieved in a single step by aligning a shadow mask prepared by micro-milling to an array of microcontainers in order to limit drug deposition to the container cavities with diameters of 220 μm. A pressure of 8.9 MPa is applied by a bonding press and thereby the desired powder is embossed into the container cavities. Powder in the form of pure drug, lipid-based microparticles, and pure polymer was successfully loaded with minimal residues in between the microcontainers and with 100% loaded cavities demonstrating the versatility of the method. The current work is thus contributing to the loading of powder formulations into microscale drug delivery systems such as microcontainers in a facile and reproducible manner.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Department of Physics, Neutrons and X-rays for Materials Physics, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Number of pages: 5
Pages: 20-24
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Microelectronic Engineering
Volume: 171
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.737 SNIP 0.949 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.813 SNIP 1.148 CiteScore 1.8
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.934 SNIP 1.093
Web of Science (2010): Indexed yes
Quantification of a bacterial secondary metabolite by SERS combined with SLM extraction for bioprocess monitoring

During the last few decades, great advances have been reached in high-throughput design and building of genetically engineered microbial strains, leading to a need for fast and reliable screening methods. We developed and optimized a microfluidic supported liquid membrane (SLM) extraction device and combined it with surface enhanced Raman scattering (SERS) sensing for the screening of a biological process, namely for the quantification of a bacterial secondary metabolite, p-coumaric acid (pHCA), produced by Escherichia coli. The microfluidic device proved to be robust and reusable, enabling efficient removal of interfering compounds from the real samples, reaching more than 13-fold up-concentration of the donor at 10 μL min⁻¹ flow rate. With this method, we quantified pHCA directly from the bacterial supernatant, distinguishing between various culture conditions based on the pHCA production yield. The obtained data showed good correlation with HPLC analysis.
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.92
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.11
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.88
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.16
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Web of Science (2006): Indexed yes
Web of Science (2005): Indexed yes
Web of Science (2002): Indexed yes
Web of Science (2001): Indexed yes
Original language: English
DOIs:
10.1039/c7an01393k
Source: FindIt
Source-ID: 2392200631

Quantitative Detection of Trace Level Cloxacillin in Food Samples Using Magnetic Molecularly Imprinted Polymer Extraction and Surface-Enhanced Raman Spectroscopy Nanopillars

There is an increasing demand for rapid, sensitive, and low cost analytical methods to routinely screen antibiotic residues in food products. Conventional detection of antibiotics involves sample preparation by liquid-liquid or solid-phase extraction, followed by analysis using liquid chromatography-mass spectrometry (LC-MS), capillary electrophoresis (CE), or gas chromatography (GC). The process is labor-intensive, time-consuming, and expensive. In this study, we developed a new analytical method that combines magnetic molecularly imprinted polymer (MMIP)-based sample preparation with surface-enhanced Raman spectroscopy (SERS)-based detection for quantitative analysis of cloxacillin in pig serum. MMIP microspheres were synthesized using a core-shell technique. The large loading capacity and high selectivity of the MMIP microspheres enabled efficient extraction of cloxacillin, while the magnetically susceptible characteristics greatly simplified sample handling procedures. Low cost and robust SERS substrates consisting of vertical gold capped silicon nanopillars were fabricated and employed for the detection of cloxacillin. Quantitative SERS was achieved by normalizing signal intensities using an internal standard. By coherently combining MMIP extraction and silicon nanopillar-based SERS biosensor, good sensitivity toward cloxacillin was achieved. The detection limit was 7.8 pmol. Cloxacillin recoveries from spiked pig plasma samples were found to be more than 80%.
Recent advances in smart biotechnology: Hydrogels and nanocarriers for tailored bioactive molecules depot

Over the past ten years, the global biopharmaceutical market has remarkably grown, with ten over the top twenty worldwide high performance medical treatment sales being biologics. Thus, biotech R&D (research and development) sector is becoming a key leading branch, with expanding revenues. Biotechnology offers considerable advantages compared to traditional therapeutic approaches, such as reducing side effects, specific treatments, higher patient compliance and therefore more effective treatments leading to lower healthcare costs. Within this sector, smart nanotechnology and colloidal self-assembling systems represent pivotal tools able to modulate the delivery of therapeutics. A comprehensive understanding of the processes involved in the self-assembly of the colloidal structures discussed therein is essential for the development of relevant biomedical applications. In this review we report the most promising and best performing platforms for specific classes of bioactive molecules and related target, spanning from siRNAs, gene/plasmids, proteins/growth factors, small synthetic therapeutics and bioimaging probes.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Istituto Italiano di Tecnologia, University of Coimbra, University of Algarve, University of Trieste
Authors: Milcovich, G. (Ekstern), Lettieri, S. (Ekstern), Antunes, F. E. (Ekstern), Medronho, B. (Ekstern), Fonseca, A. C. (Ekstern), Coelho, J. F. (Ekstern), Marizza, P. (Intern), Perrone, F. (Ekstern), Farra, R. (Ekstern), Dapas, B. (Ekstern), Grassi, G. (Ekstern), Grassi, M. (Ekstern), Giordani, S. (Ekstern)
Pages: 163-180
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Advances in Colloid and Interface Science
Volume: 249
ISSN (Print): 0001-8686
Ratings:
  BFI (2018): BFI-level 1
  Web of Science (2018): Indexed yes
  BFI (2017): BFI-level 1
  Scopus rating (2017): SNIP 2.907 SJR 1.977
  Web of Science (2017): Indexed Yes
  BFI (2016): BFI-level 1
  Scopus rating (2016): CiteScore 8 SJR 2.155 SNIP 2.757
  BFI (2015): BFI-level 1
  Scopus rating (2015): SJR 2.221 SNIP 2.913 CiteScore 7.9
  BFI (2014): BFI-level 1
  Scopus rating (2014): SJR 2.823 SNIP 4.325 CiteScore 9.47
  BFI (2013): BFI-level 1
  Scopus rating (2013): SJR 2.405 SNIP 3.574 CiteScore 7.64
  ISI indexed (2013): ISI indexed yes
  BFI (2012): BFI-level 1
  Scopus rating (2012): SJR 2.773 SNIP 4.029 CiteScore 7.78
  ISI indexed (2012): ISI indexed yes
  BFI (2011): BFI-level 1
  Scopus rating (2011): SJR 2.759 SNIP 4.247 CiteScore 7.91
  ISI indexed (2011): ISI indexed yes
  BFI (2010): BFI-level 1
  Scopus rating (2010): SJR 2.912 SNIP 3.764
  Web of Science (2010): Indexed yes
  BFI (2009): BFI-level 1
  Scopus rating (2009): SJR 2.464 SNIP 3.189
  BFI (2008): BFI-level 1
  Scopus rating (2008): SJR 2.249 SNIP 2.499
SERS detection of the biomarker hydrogen cyanide from Pseudomonas aeruginosa cultures isolated from cystic fibrosis patients

Pseudomonas aeruginosa is the primary cause of chronic airway infections in cystic fibrosis (CF) patients. Persistent infections are seen from the first P. aeruginosa culture in about 75% of young CF patients, and it is important to discover new ways to detect P. aeruginosa at an earlier stage. The P. aeruginosa biomarker hydrogen cyanide (HCN) contains a triple bond, which is utilized in this study because of the resulting characteristic C≡N peak at 2135 cm⁻¹ in a Raman spectrum. The Raman signal was enhanced by surface-enhanced Raman spectroscopy (SERS) on a Au-coated SERS substrate. After long-term infection, a mutation in the patho-adaptive lasR gene can alter the expression of HCN, which is why it is sometimes not possible to detect HCN in the breath of chronically infected patients. Four P. aeruginosa reference strains and 12 clinical P. aeruginosa strains isolated from CF children were evaluated, and HCN was clearly detected from overnight cultures of all wild type-like isolates and half of the later isolates from the same patients. The clinical impact could be that P. aeruginosa infections could be detected at an earlier stage, because daily breath sampling with an immediate output could be possible with a point-of-care SERS device.
SERS spectroscopy for detection of hydrogen cyanide in breath from children colonised with P. aeruginosa

There is a need for a fast and non-invasive tool to detect Pseudomonas aeruginosa airway colonisation in cystic fibrosis (CF) patients unable to expectorate. Fifty CF children and 19 controls aged 5–17 years were included in the feasibility study. A surface-enhanced Raman spectroscopy (SERS) nanochip optimised for detection of trace amounts of the P. aeruginosa biomarker hydrogen cyanide (HCN) was mounted inside a Tedlar bag, which the patient breathed into. The SERS chip was then analysed in a Raman spectrometer, investigating the C≡N peak at 2131 cm⁻¹ and correlated with sputum cultures. One new P. aeruginosa colonisation occurred during the trial period. The C≡N peak intensity was enhanced in this sample in contrast to the subject's 3 other samples. Three additional patients had intense C≡N SERS signals from their breath, but no P. aeruginosa was cultured from their sputum. It is concluded that SERS spectroscopy can be developed into an easy to use hypersensitive clinical prescreening method for detection of HCN in human breath.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Infection Microbiology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Rigshospitalet, University of Copenhagen, Copenhagen University Hospital
Number of pages: 6
Pages: 5757-5762
Publication date: 2017
Main Research Area: Technical/natural sciences
Single step fabrication and loading of biopolymer microcontainers for oral drug delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Abid, Z. (Intern), Petersen, R. S. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Publication date: 2017
Main Research Area: Technical/natural sciences
Microcontainers, Hot punching, Oral drug delivery, Embossing
Electronic versions:
Untitled.pdf
Source: PublicationPreSubmission
Source-ID: 140300863
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Surface Enhanced Raman Scattering for Quantification of p-Coumaric Acid Produced by Escherichia coli
The number of newly developed genetic variants of microbial cell factories for production of biochemicals has been rapidly growing in recent years, leading to an increased need for new screening techniques. We developed a method based on surface-enhanced Raman scattering (SERS) coupled with liquid-liquid extraction (LLE) for quantification of p-coumaric acid (pHCA) in the supernatant of genetically engineered Escherichia coli (E. coli) cultures. pHCA was measured in a dynamic range from 1 μM up to 50 μM on highly uniform SERS substrates based on leaning gold-capped nanopillars, which showed an in-wafer signal variation of only 11.7%. LLE using dichloromethane as organic phase was combined with the detection in order to increase selectivity and sensitivity by decreasing the effect of interfering compounds from the analytes of interest. The difference in pHCA production yield between three genetically engineered E. coli strains was successfully evaluated using SERS and confirmed with high-performance liquid chromatography. As this novel approach has potential to be automated and parallelized, it can be considered for high-throughput screening in metabolic engineering.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Research Groups, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Morelli, L. (Intern), Zor, K. (Intern), Jendresen, C. B. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)
Number of pages: 7
Pages: 3981-3987
Publication date: 2017
Main Research Area: Technical/natural sciences

Publication information
Journal: Analytical Chemistry
Volume: 89
ISSN (Print): 0003-2700
Ratings:
  BFI (2018): BFI-level 2
  Web of Science (2018): Indexed yes
  BFI (2017): BFI-level 2
  Web of Science (2017): Indexed yes
  BFI (2016): BFI-level 2
  Scopus rating (2016): CiteScore 6.08
  Web of Science (2016): Indexed yes
  BFI (2015): BFI-level 2
  Scopus rating (2015): CiteScore 6
  Web of Science (2015): Indexed yes
  BFI (2014): BFI-level 2
  Scopus rating (2014): CiteScore 5.79
  BFI (2013): BFI-level 2
  Scopus rating (2013): CiteScore 6.01
  ISI indexed (2013): ISI indexed yes
  Web of Science (2013): Indexed yes
  BFI (2012): BFI-level 2
  Scopus rating (2012): CiteScore 5.8
  ISI indexed (2012): ISI indexed yes
  Web of Science (2012): Indexed yes
  BFI (2011): BFI-level 2
  Scopus rating (2011): CiteScore 5.86
  ISI indexed (2011): ISI indexed yes
  Web of Science (2011): Indexed yes
  BFI (2010): BFI-level 2
  Web of Science (2010): Indexed yes
  BFI (2009): BFI-level 2
  Web of Science (2009): Indexed yes
  BFI (2008): BFI-level 2
  Web of Science (2008): Indexed yes
  Web of Science (2007): Indexed yes
  Web of Science (2006): Indexed yes
  Web of Science (2005): Indexed yes
  Web of Science (2004): Indexed yes
  Web of Science (2003): Indexed yes
  Web of Science (2002): Indexed yes
  Web of Science (2000): Indexed yes
Original language: English
DOIs: 10.1021/acs.analchem.6b04428
Source: FindIt
Source-ID: 2352823102
Publication: Research - peer-review › Journal article – Annual report year: 2017

Wireless Powered Lab-on-Disc Platform for Measurements on the Spin

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Taiwan University
Wireless, smartphone controlled potentiostat integrated with lab-on-disc platform

A smartphone controlled wireless data transmitting and inductive powering Power Lab-on-disc (PLoD) platform is developed based on 2.4 GHz Bluetooth and 205 kHz Qi techniques, respectively. A potentiostat is integrated on the PLoD platform, and amperometric measurements are performed. The wireless potentiostat can provide -3~3 V with 14-bit resolution for amperometry in a range of -300~300 μA with a readout noise floor of 1.2 μA (p-p) in a static condition. A 0~3000 rpm spinning test shows that a phosphate buffer saline (400 mV potential) baseline noise is proportional to spinning acceleration and deceleration.

A substrate and a method of using it

A substrate for a plurality of different measurement set-ups such as SERS, SPR and LSPR which substrate has a base and a plurality of elongate elements with metallic tips. A metallic layer is present on the base surface between the elongate elements and gaps or cavities exist between the layer and the tips or elongate elements. When the elongate elements and the base are transparent, transmission measurement set-ups are also possible.
A Centrifugal Microfluidic Platform Using SLM Extraction: for combined sample clean-up and enrichment of trace analytes

Here we present a pump-less microfluidic platform which performs sample clean-up and enrichment in a single step, by integrating Supported Liquid Membrane (SLM) extraction. Our platform offers a simple, yet very efficient, method for achieving sample pre-treatment and enrichment of rare analytes, in an easy to use and highly efficient device.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics
Authors: Andreasen, S. Z. (Intern), Burger, R. (Intern), Ernéus, J. (Intern), Boisen, A. (Intern)
Publication date: 2016
Main Research Area: Technical/natural sciences
Electronic versions:
   Andreasen_Biosensors2016_poster_final1.pdf Source: PublicationPreSubmission Source-ID: 127192804 Publication: Research - peer-review › Poster – Annual report year: 2016

A comprehensive investigation of copper binding properties of metformin using on-disc magnetic microbead agglomeration with real-time analysis

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems
Authors: Uddin, R. (Intern), Quan, X. (Intern), Donolato, M. (Intern), Burger, R. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2016
Main Research Area: Technical/natural sciences
Electronic versions:
   abstract_biosensors_Uddin_Rokon.pdf Source: PublicationPreSubmission Source-ID: 131347570 Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Analyzing Engineered Nanoparticles using Photothermal Infrared Spectroscopy

Nanoparticles, particles having one or more dimensions smaller than 100 nm, show novel properties and functions that differ significantly from those of their corresponding bulk counterparts. Due to their small size and large surface to volume ratio they can e.g. diffuse easily and be highly reactive. To facilitate occupational safety and health there is a need to develop instruments to monitor and analyze nanoparticles in the industry, research and urban environments. The aim of this Ph.D. project was to develop new sensors that can analyze engineered nanoparticles. Two sensors were studied: (i) a miniature toxicity sensor based on electrochemistry and (ii) a photothermal spectrometer based on tensile-stressed mechanical resonators (string resonators).

Miniaturization of toxicity sensor targeting engineered nanoparticles was explored. This concept was based on the results of the biodurability test using redox activity measurements. With a new setup adapted to miniaturization, stable pH was achieved, platinum was found to be more suitable than gold for open circuit potential-time measurements, miniaturized platinum working electrodes and quasi silver/silver chloride reference electrodes were fabricated, and Gambles solution with dispersed iron oxide nanoparticles showed lowered potential as expected. Despite the potential of this concept instability and lack of reproducibility continued to be an unneglectable issue. The concept of utilizing string resonators for photothermal spectroscopy was, for the first time, studied in details both theoretically and experimentally. The string-based photothermal spectrometer consists of a string resonator on which an analyte is collected. Wavelength-dependent absorption by the analyte leads to heating of the string which is reflected in its resonance frequency. This setup allows for spectroscopic measurement of the analyte. An analytical model describing the resonance frequency of a string resonator locally heated was developed. The developed model was in agreement with FEM simulations and experimental results. Theoretical and experimental work lead to a set of design rules for the responsivity of the string-based photothermal spectrometer. Responsivity is maximized for a thin, narrow and long string irradiated by high power radiation.

Various types of nanoparticles and binary mixtures of them were successfully detected and analyzed. Detection of copper-chelation of the antidiabetic drug metformin was demonstrated as well. The estimated detection limit for the developed system is an analyte with a mass of $\sim 150$ ag ($1$ ag = $10^{-18}$ g). In short, it has been demonstrated that the string-based photothermal spectrometer is a promising technique for nanoparticle detection and analysis.
Black silicon laser-doped selective emitter solar cell with 18.1% efficiency

We report fabrication of nanostructured, laser-doped selective emitter (LDSE) silicon solar cells with power conversion efficiency of 18.1% and a fill factor (FF) of 80.1%. The nanostructured solar cells were realized through a single step, mask-less, scalable reactive ion etch (RIE) texturing of the surface. The selective emitter was formed by means of laser doping using a continuous wave (CW) laser and subsequent contact formation using light-induced plating of Ni and Cu. The combination of RIE-texturing and a LDSE cell design has to our knowledge not been demonstrated previously. The resulting efficiency indicates a promising potential, especially considering that the cell reported in this work is the first proof-of-concept and that the fabricated cell is not fully optimized in terms of plating, emitter sheet resistance and surface passivation. Due to the scalable nature and simplicity of RIE-texturing as well as the LDSE process, we consider this specific combination a promising candidate for a cost-efficient process for future Si solar cells.
This paper describes an aptamer-based optomagnetic biosensor for detection of a small molecule based on target binding-induced inhibition of magnetic nanoparticle (MNP) clustering. For the detection of a target small molecule, two mutually exclusive binding reactions (aptamer-target binding and aptamer-DNA linker hybridization) are designed. An aptamer specific to the target and a DNA linker complementary to a part of the aptamer sequence are immobilized onto separate MNPs. Hybridization of the DNA linker and the aptamer induces formation of MNP clusters. The target-to-aptamer binding on MNPs prior to the addition of linker-functionalized MNPs significantly hinders the hybridization reaction, thus reducing the degree of MNP clustering. The clustering state, which is thus related to the target concentration, is then quantitatively determined by an optomagnetic readout technique that provides the hydrodynamic size distribution of MNPs and their clusters. A commercial Blu-ray optical pickup unit is used for optical signal acquisition, which enables the establishment of a low-cost and miniaturized biosensing platform. Experimental results show that the degree of MNP clustering correlates well with the concentration of a target small molecule, adenosine triphosphate (ATP).
in this work, in the range between 10µM and 10mM. This successful proof-of-concept indicates that our optomagnetic
aptasensor can be further developed as a low-cost biosensing platform for detection of small molecule biomarkers in an
out-of-lab setting.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Applied Mathematics and
Computer Science, Cognitive Systems, Magnetic Systems, Center for Intelligent Drug Delivery and Sensing Using
Microcontainers and Nanomechanics, Columbia University, University of the Basque Country, Yonsei University, CIC
nanoGUNE Consolider
Authors: Yang, J. (Ekstern), Donolato, M. (Intern), Pinto, A. (Ekstern), Bosco, F. (Intern), Hwu, E. (Ekstern), Chen, C.
(Ekstern), Alstrøm, T. S. (Intern), Lee, G. (Ekstern), Schäfer, T. (Ekstern), Vavassori, P. (Ekstern), Boisen, A. (Intern), Lin,
Q. (Ekstern), Hansen, M. F. (Intern)
Pages: 396-403
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Biosensors and Bioelectronics
Volume: 75
ISSN (Print): 0956-5663
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.65 SJR 2.373
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.22 SJR 2.095 SNIP 1.619
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.044 SNIP 1.671 CiteScore 7.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.057 SNIP 1.716 CiteScore 6.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.029 SNIP 1.726 CiteScore 6.34
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.397 SNIP 1.592 CiteScore 5.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.126 SNIP 1.704 CiteScore 5.85
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.143 SNIP 1.609
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.991 SNIP 1.771
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.495 SNIP 1.782
Web of Science (2008): Indexed yes
Click chemistry based biomolecular conjugation monitoring using surface-enhanced Raman spectroscopy mapping

We describe here a novel surface-enhanced Raman spectroscopy (SERS) based technique for monitoring the conjugation of small molecules by the well-known click reaction between an alkyne and azido moiety on the partner molecules. The monitoring principle is based on the loss of the characteristic alkyne/azide Raman signal with triazole formation in the reaction as a function of time. Since these universal Raman reporter groups are specific for click reactions, this method may facilitate a broad range of applications for monitoring the conjugation efficiency of molecules in diverse areas such as bioconjugation, material science or drug discovery. Additionally, as an attractive advantage of this technique, no significant background signal is expected during the measurements, since these signals reside in a Raman silent region of 2000–2300 cm⁻¹, where virtually all biological molecules are transparent.

Comparison of optomagnetic and AC susceptibility readouts in a magnetic nanoparticle agglutination assay for detection of C-reactive protein

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Uppsala University
Authors: Fock, J. (Intern), Parmvi, M. (Intern), Strömberg, M. (Ekstern), Svedlindh, P. (Ekstern), Donolato, M. (Intern), Hansen, M. F. (Intern)
Comparison of Ultrasonic Welding and Thermal Bonding for the Integration of Thin Film Metal Electrodes in Injection Molded Polymeric Lab-on-Chip Systems for Electrochemistry

We compare ultrasonic welding (UW) and thermal bonding (TB) for the integration of embedded thin-film gold electrodes for electrochemical applications in injection molded (IM) microfluidic chips. The UW bonded chips showed a significantly superior electrochemical performance compared to the ones obtained using TB. Parameters such as metal thickness of electrodes, depth of electrode embedding, delivered power, and height of energy directors (for UW), as well as pressure and temperature (for TB), were systematically studied to evaluate the two bonding methods and requirements for optimal electrochemical performance. The presented technology is intended for easy and effective integration of polymeric Lab-on-Chip systems to encourage their use in research, commercialization and education.
Detection methods for centrifugal microfluidic platforms
Centrifugal microfluidics has attracted much interest from academia as well as industry, since it potentially offers solutions for affordable, user-friendly and portable biosensing. A wide range of so-called fluidic unit operations, e.g. mixing, metering, liquid routing, and particle separation, have been developed and allow automation and integration of complex assay protocols in lab-on-a-disc systems. Besides liquid handling, the detection strategy for reading out the assay is crucial for developing a fully integrated system. In this review, we focus on biosensors and readout methods for the centrifugal microfluidics platform and cover optical as well as mechanical and electrical detection principles.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Burger, R. (Intern), Amato, L. (Intern), Boisen, A. (Intern)
Pages: 54-67
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Biosensors and Bioelectronics
Volume: 76
ISSN (Print): 0956-5663
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.65 SJR 2.373
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.22 SJR 2.095 SNIP 1.619
Web of Science (2016): Indexed yes
Detection of nerve gases using surface-enhanced Raman scattering substrates with high droplet adhesion

Threats from chemical warfare agents, commonly known as nerve gases, constitute a serious security issue of increasing global concern because of surging terrorist activity worldwide. However, nerve gases are difficult to detect using current analytical tools and outside dedicated laboratories. Here we demonstrate that surface-enhanced Raman scattering (SERS) can be used for sensitive detection of femtomol quantities of two nerve gases, VX and Tabun, using a handheld Raman device and SERS substrates consisting of flexible gold-covered Si nanopillars. The substrate surface exhibits high droplet adhesion and nanopillar clustering due to elasto-capillary forces, resulting in enrichment of target molecules in plasmonic hot-spots with high Raman enhancement. The results may pave the way for strategic life-saving SERS detection of chemical warfare agents in the field.

General information
Development of a video-microscopic method to compare the effect of a precipitation inhibitor
DNA self-assembly on graphene surface studied by SERS mapping

The self-assembly of double-stranded DNA (dsDNA) segments on two variations of graphene surfaces having nano-platelets with different lateral sizes and thicknesses was investigated using surface enhanced Raman spectroscopy (SERS) and electrical impedance spectroscopy (EIS) techniques. Due to the strong local field-enhancement, the SERS signals from functional molecules bound to the graphene edges and from DNA moieties were recorded. Relative intensities of specific Raman modes were used as contrast parameters to build Raman signal intensity maps. The observed variation in the SERS signal intensity was related to the different configuration (tilted or flattened) in which dsDNA segments are assembled on the carbon surface, depending on the graphene platelet size. EIS was used to characterize the conductive properties of nano-structured films containing pristine or DNA-functionalized graphene nano-platelets. Results from the EIS analysis supported the SERS findings and confirmed that SERS mapping is a reliable method for a rapid monitoring of the procedures used to interface DNA with graphene surfaces. The present study, linking DNA anchoring morphology to the conductive properties of nano-structured hybrid films, contribute to define a new approach in the optimization of biosensor design.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Italian National Agency for New Technologies, University of Rome La Sapienza, Horiba Italia
Authors: Botti, S. (Ekstern), Rufoloni, A. (Ekstern), Laurenzi, S. (Ekstern), Gay, S. (Ekstern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Santonicola, M. G. (Ekstern)
Number of pages: 10
Pages: 363-372
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Carbon
Volume: 109
ISSN (Print): 0008-6223
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SJR 2.226 SNIP 1.666
Web of Science (2017): Indexed yes
Electrospraying Chitosan Particles for Oral Vaccine Delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Food Institute, Research Group for Nano-Bio Science
Authors: Nielsen, L. H. (Intern), Sevilla Moreno, J. A. (Intern), Boutrup Stephansen, K. (Intern), Chronakis, I. S. (Intern), Boisen, A. (Intern)

DOI: 10.1016/j.carbon.2016.07.069
Source: FindIt
Source-ID: 2307069586
Publication: Research - peer-review > Journal article – Annual report year: 2016
Electrospraying particles for loading into microcontainers for drug delivery

General information
State: Published
Organisations: National Food Institute, Research Group for Nano-Bio Science, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Sevilla Moreno, J. A. (Intern), Boutrup Stephansen, K. (Intern), Nielsen, L. H. (Intern), Chronakis, I. S. (Intern), Boisen, A. (Intern)
Publication date: 2016
Event: Abstract from 42nd International conference on Micro and Nano Engineering, Vienna, Austria.
Main Research Area: Technical/natural sciences
Electronic versions:
Electrospraying_particles_for_loading_into_microcontainers_for_drug_delivery.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 127315846
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016

Engineering Plasmonic Nanopillar Arrays for Surface-enhanced Raman Spectroscopy

This Ph.D. thesis presents (i) an in-depth understanding of the localized surface plasmon resonances (LSPRs) in the nanopillar arrays (NPs) for surface-enhanced Raman spectroscopy (SERS), and (ii) systematic ways of optimizing the fabrication process of NPs to improve their SERS efficiencies. This Ph.D. project is part of the NAPLAS - NAnoPLAsmonic Sensors project, funded by The Danish Council for Independent Research. LSPRs in silver capped silicon NPs are studied using numerical simulations and dark-field scattering microscopy. Simulations show that a standalone NP supports two LSPR modes, i.e., the particle mode and the cavity mode. The particle mode can be hybridized via leaning of pillars. The LSPR wavelength of the cavity mode is dominant only by the diameter of the Si pillar. The presence of a substrate dramatically changes the intensities of these two LSPR modes, by introducing constructive and destructive interference patterns with the excitation fields. Experimental scattering spectra can be interpreted using theoretical simulations. The processes, which affect the SERS efficiencies of the silver NPs, are systematically evaluated. Short exposures to the O2-plasma and the use of 1-3 nm Cr adhesion layers are advantageous for reducing the SERS background signals. Influence of the NP height and silver deposition thickness on SERS intensities is also investigated. Using an optimized recipe, the measured SERS enhancement factor (EF) reaches 108, and the SERS signal intensity exhibits a standard deviation of ~14% (660 data points) across a 5 x 5 mm2 surface area. Lastly, a further improved process shows that high-density NPs exhibit unrivalled macroscale SERS uniformities (RSD: ~2.5% in mm scale, ~7% in inch scale) and SERS reproducibilities (RSD: ~1.5% across three wafers), while at the same time displaying a very large average SERS EF of >108. From a practical point of view, the developed SERS substrates are particularly interesting, since they are easy to handle and store and the fabrication is scalable, facilitating a wide and simple use of SERS in sensing applications.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Wu, K. (Intern), Boisen, A. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern)
Number of pages: 152
Publication date: 2016

Publication information
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
Experimentation and numerical modeling of cyclic voltammetry for electrochemical micro-sized sensors under the influence of electrolyte flow

In this study, we perform experimental studies as well as simulations for cyclic voltammetry (CV) of the redox couple FeIII(CN)63-/FeII(CN)64- on a gold plated ECC biosensor encapsulated by a microfluidic system. We examine the effect of flow rate, scan rate, varying supporting electrolyte, exchange current density and the position of electrode on the CV measurements. The results show that at a relatively high flow (250 μL) and low scan rates (50 - 200 mV/s), the current response is limited by the convection due to quick supply of fresh ions at the electrode surface which leads to fading hysteresis of the recorded CV. However, at high scan rates (250 mV/s) and slow flow rates (50 - 200 μL), peak currents are recorded which means that mass transport is dominated by the diffusion mechanism and a quasi-steady state of CV is recorded. In the case of insufficient supporting electrolyte, the excess charges generated during scan will lead to ohmic distortion of the electrolyte solution and consequently result into a ramping effect of the recorded CV. However, for sufficient amount of supporting electrolyte (200 mM), the simulation results show good agreement with the experimental data. In addition, the results also show that a decrease in exchange current density leads to a shift in the peak current of the recorded CV. Finally, the results also demonstrate that the working electrode at the center of the fluidic cell records accurate measurement than placing the electrode at the bottom of the cell. The numerical results and the experimental data show both qualitative good agreement and quantitative good agreement.
Fabrication and characterization of Au dimer antennas on glass pillars with enhanced plasmonic response

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technische Universität Wien
Authors: Sadeghi, P. (Ekstern), Wu, K. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Schmid, S. (Ekstern)
Pages: 23-24
Publication date: 2016

Host publication Information

Title of host publication: Nanophotonics and Micro/Nano Optics International Conference 2016 : Book of Abstracts
Article number: 415
Main Research Area: Technical/natural sciences
Electronic versions:
Untitled.pdf
Source: PublicationPreSubmission
Source-ID: 131447664
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2017

Fabrication and characterization of pyrolytic carbon string resonators
Fabrication of scalable tissue engineering scaffolds with dual-pore microarchitecture by combining 3D printing and particle leaching

Limitations in controlling scaffold architecture using traditional fabrication techniques are a problem when constructing engineered tissues/organisms. Recently, integration of two pore architectures to generate dual-pore scaffolds with tailored physical properties has attracted wide attention in tissue engineering community. Such scaffolds features primary structured pores which can efficiently enhance nutrient/oxygen supply to the surrounding, in combination with secondary random pores, which give high surface area for cell adhesion and proliferation. Here, we present a new technique to fabricate dual-pore scaffolds for various tissue engineering applications where 3D printing of poly(vinyl alcohol) (PVA) mould is combined with salt leaching process. In this technique the sacrificial PVA mould, determining the structured pore architecture, was filled with salt crystals to define the random pore regions of the scaffold. After crosslinking the casted polymer the combined PVA-salt mould was dissolved in water. The technique has advantages over previously reported ones, such as automated assembly of the sacrificial mould, and precise control over pore architecture/dimensions by 3D printing parameters. In this study, polydimethylsiloxane and biodegradable poly(-caprolactone) were used for fabrication. However, we show that this technique is also suitable for other biocompatible/biodegradable polymers. Various physical and mechanical properties of the dual-pore scaffolds were compared with control scaffolds with either only structured or only random pores, fabricated using previously reported methods. The fabricated dual-pore scaffolds supported high cell density, due to the random pores, in combination with uniform cell distribution throughout the scaffold, and higher cell proliferation and viability due to efficient nutrient/oxygen transport through the structured pores. In conclusion, the described fabrication technique is rapid, inexpensive, scalable, and compatible with different polymers, making it suitable for engineering various large scale organs/tissues.
Geometric Optimization of Microcontainers for Oral Drug Delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Jensen, K. E. (Intern), Vaut, L. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2016
Event: Abstract from Modelling and experiments in drug delivery systems, Coimbra, Portugal.
Main Research Area: Technical/natural sciences
Electronic versions:
KristianE.pdf

Relations
Activities:
Modelling and experiments in drug delivery systems
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017

Gold Nanoparticle Aggregations on Recyclable Hierarchical Nanotrays for Surface-enhanced Raman Spectroscopy with Macroscale Uniformity

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Self-Organized Nanoporous Materials
Authors: Wu, K. (Intern), Li, T. (Intern), Schmidt, M. S. (Intern), Wang, Z. (Intern), Rindzevicius, T. (Intern), Ndoni, S. (Intern), Boisen, A. (Intern)
Publication date: 2016
Event: Abstract from XXV International Conference on Raman Spectroscopy, Eusébio, Brazil.
Main Research Area: Technical/natural sciences
Electronic versions:
Untitled.pdf

Hollow MEMS: An Integrated Sensor for Combined Density, Viscosity, Buoyant Mass and IR Absorption Spectrometry

Miniaturization of electro mechanical sensor systems to the micro range and beyond has shown impressive sensitivities measuring sample properties like mass, viscosity, acceleration, pressure and force just to name a few applications. In order to enable these kinds of measurements on liquid samples a hollow MEMS sensor has been designed, fabricated and tested. Combined density, viscosity, buoyant mass spectrometry and IR absorption spectroscopy are possible on liquid samples and micron sized suspended particles (e.g. single cells). Measurements are based on changes in the resonant behavior of these sensors.
Optimization of the microfabrication process has led to a process yield of almost 100%. This is achieved despite the fact, that the process still offers a high degree of flexibility. By simple modifications the Sensor shape can be optimized for different size ranges and sensitivities.

Microfluidic interfacing has been realized using high throughput and low cost technologies such as injection molding and ultra-sonic welding. Standard fluidic LUER connections were used that are widely applied in other micro fluidic projects at DTU Nanotech to enable future interfacing of the system with other technologies and pre-concentration approaches.

A thorough theoretical analysis of the expected sensor responsivity and sensitivity is performed. Predictions made are confirmed by finite element simulations. Using these tools the sensor geometry is optimized for ideal performance in both mass density and IR spectroscopy measurements of samples, the size of single yeast cells (~ 5 μm). A relative frequency shift of 69 ppm/single cell buoyant mass in case of the mass spectroscopy measurements and 40 ppm/μW in case of the IR absorption spectroscopy measurements are calculated and confirmed by FE simulations for the sensor geometry fabricated.

In order to verify sufficient frequency stability, Allan Deviation measurements are performed on the fabricated sensors. In combination with the calculated responsivities these measurements confirm that the sensor sensitivity will enable single cell measurements.

Initial experiments confirming the calculated responsivities are performed. Experiments filling the sensor with liquids of different densities confirmed the predicted mass responsivity. The resonance frequency shifts 29% when filled with water compared to air.

By irradiating the sensor with a tunable IR laser source and tracking the resonance frequency the capability of the sensor to perform spectroscopic measurements is tested. Experiments with both an empty and a paraffin wax filled channel confirm the predicted heating responsivity. A resonance shift of >8000 ppm at the absorption peak of paraffin is observed. Individual absorption peaks can be resolved with a wavenumber resolution below 1 cm⁻¹.

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General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Larsen, P. E. (Intern), Boisen, A. (Intern), Schmid, S. (Intern)
Number of pages: 139
Publication date: 2016

Publication information
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 125027797
Publication: Research › Ph.D. thesis – Annual report year: 2016

Lab-on-a-disc agglutination assay for protein detection by optomagnetic readout and optical imaging using nano- and micro-sized magnetic beads

We present a biosensing platform for the detection of proteins based on agglutination of aptamer coated magnetic nano- or microbeads. The assay, from sample to answer, is integrated on an automated, low-cost microfluidic disc platform. This ensures fast and reliable results due to a minimum of manual steps involved. The detection of the target protein was achieved in two ways: (1) optomagnetic readout using magnetic nanobeads (MNBs); (2) optical imaging using magnetic microbeads (MMBs). The optomagnetic readout of agglutination is based on optical measurement of the dynamics of MNB aggregates whereas the imaging method is based on direct visualization and quantification of the average size of MMB aggregates. By enhancing magnetic particle agglutination via application of strong magnetic field pulses, we obtained identical limits of detection of 25 pM with the same sample-to-answer time (15 min 30 s) using the two differently sized beads for the two detection methods. In both cases a sample volume of only 10 μl is required. The demonstrated automation, low sample-to-answer time and portability of both detection instruments as well as integration of the assay on a low-cost disc are important steps for the implementation of these as portable tools in an out-of-lab setting.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, BluSense Diagnostics
Authors: Uddin, R. (Intern), Burger, R. (Ekstern), Donolato, M. (Ekstern), Fock, J. (Intern), Creagh, M. (Ekstern), Hansen, M. F. (Intern), Boisen, A. (Intern)
Number of pages: 7
Pages: 351-357
Publication date: 2016
Main Research Area: Technical/natural sciences
Publication information
Journal: Biosensors and Bioelectronics
Magnetic bead, Agglutination assay, Thrombin, Microfluidic disc, Optomagnetic readout method, Optical imaging method

Electronic versions:
Lab_on_a_disc_agglutination_assay_for_protein_detection_by_optomagnetic...pdf. Embargo ended: 14/05/2018

DOIs:
Lab-on-a-disc device for screening of genetically engineered E.coli cells

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Research Groups
Authors: Sanger, K. (Intern), Zor, K. (Intern), Jendresen, C. B. (Intern), Amato, L. (Intern), Burger, R. (Intern), Boisen, A. (Intern), Nielsen, A. T. (Intern)
Number of pages: 1
Publication date: 2016
Main Research Area: Technical/natural sciences
Electronic versions:
Biosensors_poster.pdf

Relations
Activities:
Biosensors 2016
Publication: Research - peer-review › Poster – Annual report year: 2017

Lifetime of ALD Al2O3 Passivated Black Silicon Nanostructured for Photovoltaic Applications
Black silicon nano-structures provide significant reduction of silicon surface reflection due to highly corrugated nano-structures with excellent light trapping properties. However, most recent RIE techniques for black silicon nano-structuring have one very important limitation for PV applications – high surface recombination velocity due to intensive plasma ion bombardment of the silicon surface. In an attempt to optimize black silicon for PV applications we develop a mask-less one step reactive ion nano-structuring of silicon with low ion surface damage with reflectance below 0.5%. For passivation purposes we used 37 nm ALD Al2O3 films and conducted lifetime measurements and found 1220 µs and to 4170 µs, respectively, for p- and n-type CZ silicon wafers. Such results are promising results to introduce for black silicon RIE nano-structuring in solar cell process flow.

General information
State: Published
Organisations: Department of Energy Conversion and Storage, Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes, Department of Photonics Engineering, Plasmonics and Metamaterials, Experimental Surface and Nanomaterials Physics
Authors: Plakhotnyuk, M. (Intern), Davidsen, R. S. (Intern), Schmidt, M. S. (Intern), Malureanu, R. (Intern), Stamate, E. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2016
Event: Poster session presented at 32nd European Photovoltaic Solar Energy Conference and Exhibition, Munich, Germany.
Main Research Area: Technical/natural sciences
Electronic versions:
2AV.2.34_PVSEC_M._Plakhotnyuk_poster.pdf

Relations
Activities:
32nd European Photovoltaic Solar Energy Conference and Exhibition
Publication: Research - peer-review › Poster – Annual report year: 2017

Lifetime of Nano-Structured Black Silicon for Photovoltaic Applications
In this work, we present recent results of lifetime optimization for nano-structured black silicon and its photovoltaic applications. Black silicon nano-structures provide significant reduction of silicon surface reflection due to highly corrugated nano-structures with excellent light trapping properties. We applied reactive ion etching technology at -20ºC to create nano-structures on silicon samples and obtained an average reflectance below 0.5%. For passivation purposes, we used 37 nm ALD Al2O3 films. Lifetime measurements resulted in 1220 µs and to 4170 µs for p- and n-type CZ silicon wafers, respectively. This is promising for use of black silicon RIE nano-structuring in a solar cell process flow.
Lithography-Free Fabrication of Silica Nanocylinders with Suspended Gold Nanorings for LSPR-Based Sensing

Tunable plasmonic platforms are important for a variety of applications such as photovoltaics, LED's, optoelectronics, medical research, and biosensors. In particular, development of label-free plasmonic biosensors is one of the key research areas that utilizes plasmonic nanostructures for detection of biologically relevant molecules at low concentrations. The authors have developed a cost-effective, fast, and lithography-free method to fabricate transparent fused silica nanocylinders. The technique allows tuning of nanocylinder height, diameter, and density and can be scaled to large surface areas, such as 8 in. wafers. The authors demonstrate that gold coated nanocylinders support localized surface plasmon resonances (LSPR) from visible to near infrared wavelengths. The plasmonic platform can be characterized as suspended gold nanorings and exhibits a sensitivity of 658 nm RIU\(^{-1}\) with a figure-of-merit of 10, comparable to other state-of-the-art LSPR sensing platforms that utilize more complex nanofabrication pathways. It was observed that the LSPR peak positions can be controlled by varying the geometry of the nanocylinders. The authors illustrate surface functionalization, biosensing, and surface regeneration properties of the platform using thiols and detection of bovine serum albumin (BSA). The observed LSPR shifts for 11-mercaptoundecanoic acid and BSA was 12 and 26 nm, respectively.
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 8.11 SJR 3.45 SNIP 1.505
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 3.212 SNIP 1.596 CiteScore 8.11
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 3.165 SNIP 1.652 CiteScore 7.74
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 3.628 SNIP 1.685 CiteScore 8.13
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 4.52 SNIP 1.902 CiteScore 8.17
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 4.17 SNIP 1.832 CiteScore 8.15
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 3.789 SNIP 1.732
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 3.485 SNIP 1.685
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 3.884 SNIP 1.542
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 3.345 SNIP 1.506
Web of Science (2006): Indexed yes
Original language: English
Electronic versions:
Lithography_Free_Fabrication_of_Silica_Nanocylinders_with_Suspended_Gold_Nanorings_for_LSPR_Based_Sensing.pdf
DOIs:
10.1002/smll.201602299
Source: FindIt
Source-ID: 2347368370
Publication: Research - peer-review › Journal article – Annual report year: 2016

**Macroscale SERS Uniformity and Reproducibility Using Densely Clustered Nanopillars**

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Wu, K. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Thilsted, A. H. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2016
Event: Abstract from 43rd Annual North American Meeting of the Federation of Analytical Chemistry and Spectroscopy Societies, Minneapolis, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
Untitled.pdf
Source: PublicationPreSubmission
Source-ID: 136956791
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2017
Microcontainers - an oral drug delivery system for poorly soluble drugs

In oral delivery, it can sometimes be necessary to employ drug delivery systems to achieve targeted delivery to the intestine. Microcontainers are polymeric, cylindrical devices in the micrometer size range (Figure 1), and are suggested as a promising oral drug delivery system [1],[2]. The purpose of these studies was to fabricate microcontainers in either SU-8 or biodegradable poly-L-lactic acid (PLLA), and fill the microcontainers with poorly soluble drugs. Furthermore, the application of the microcontainers as an oral drug delivery system was investigated in terms of release, in situ intestinal perfusion and oral bioavailability. SU-8 microcontainers were fabricated using lithography resulting in microcontainers with an inner diameter of 220 μm. The PLLA microcontainers were prepared by hot embossing with inner diameter of 240 μm (Figure 1). In terms of drug filling, the SU-8 microcontainers were filled with polyvinylpyrrolidone (PVP) by inkjet printing followed by supercritical CO2 impregnation of ketoprofen into the PVP matrix. As an alternative filling method, the powder of amorphous sodium salt of furosemide, (ASSF) was filled into the SU-8 microcontainers. The PLLA microcontainers were filled with drug formulation by embossing the microcontainers into a polycaprolactone (PCL) and furosemide (4:1 w/w) layer. For the ASSF-filled microcontainers, an enteric-resistant lid of Eudragit L100 was spray coated onto the cavity of the microcontainers. From coated ASSF-filled microcontainers, a fast release in simulated intestinal medium at pH 6.5 was observed. In situ intestinal perfusions were performed in rats of the Eudragit-coated ASSF-filled microcontainers and compared to a furosemide solution. At the end of the study, the small intestine was harvested from the rat and imaged under a light microscope. The absorption rate constant of ASSF was 1.5 fold higher, when ASSF was confined in the microcontainers compared to a furosemide solution. Micrographs of the small intestine after the perfusion showed that the microcontainers were engulfed by the intestinal mucus. For the in vivo studies, the rats were dosed orally with capsules containing ASSF-filled microcontainers coated with Eudragit L100. As control, capsules were filled with the powder of ASSF and the capsules were coated with Eudragit L100. The oral bioavailability study showed that the relative oral bioavailability of ASSF in microcontainers is 220±43% when compared to drug-filled capsules coated with Eudragit.
Microcontainers as an oral drug delivery system

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Petersen, R. S. (Intern), Marizza, P. (Intern), Keller, S. S. (Intern), Melero, A. (Ekstern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Publication date: 2016
Event: Abstract from 10th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Glasgow, United Kingdom.
Main Research Area: Technical/natural sciences

Bibliographical note
Oral presentation at conference, 10TH WORLD MEETING on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Glasgow, Scotland, April 2016
Source: PublicationPreSubmission
Source-ID: 125164766
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016

Microcontainers as an Oral Drug Delivery System

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Publication date: 2016
Event: Abstract from 2016 AAPS Annual Meeting and Exposition, Denver, CO, United States.
Main Research Area: Technical/natural sciences
Electronic versions: Abstract_AAPS_2016_microcontainers_1.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 127315863
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016

Microcontainers as effective drug delivery vehicles: advances in the drug loading

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark
Authors: Marizza, P. (Intern), Leonardi, L. (Ekstern), Mazzoni, C. (Intern), Tentor, F. (Intern), Petersen, R. S. (Intern), Abid, Z. (Intern), Boisen, A. (Intern)
Publication date: 2016
Event: Abstract from 11th Central European Symposium on Pharmaceutical Technology, Belgrade, Serbia.
Main Research Area: Technical/natural sciences
Electronic versions: Chiara_Mazzoni_2.pdf

Relations
Activities:
Central European Symposium on Pharmaceutical Technology
Source: PublicationPreSubmission
Source-ID: 127259103
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016
Microcontainers for Intestinal Drug Delivery

Among all the drug administration routes, the oral one is the most preferred by the patients being less invasive, faster and easier.

Oral drug delivery systems designed to target the intestine are produced by powder technology and capsule formulations. Those systems including micro- and nano-particulate systems (i.e. vesicles, polymer nanoparticles, dendrimers etc.) suffer the non-unidirectional release of the drug to the epithelium of the intestine, which entails an inevitable loss in the lumen and, therefore, the reduction of the drug delivered to the intestinal epithelium. A new promising approach focuses on reservoir based microdevices serving as carriers for poorly soluble drugs, hereby called microcontainers (1).

Microcontainers have a cylindrical geometry and provide a unidirectional release due to their design meanwhile protecting the drug formulation from the low gastric pH and the enzymatic degradation. Here, we present the preparation of microcontainers with enteric coating (2) efficiently loaded with drug and able to target the intestine as a multi-particulate system.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Tentor, F. (Intern), Mazzoni, C. (Intern), Keller, S. S. (Intern), Marizza, P. (Intern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2016
Event: Abstract from 11th Central European Symposium on Pharmaceutical Technology, Belgrade, Serbia.
Main Research Area: Technical/natural sciences
Electronic versions:
Fabio_Tentor.pdf

Micromechanical Pyrolytic Carbon String Resonators

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark
Authors: Kurek, M. (Intern), Larsen, F. K. (Ekstern), Larsen, P. E. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Number of pages: 2
Publication date: 2016
Main Research Area: Technical/natural sciences
Electronic versions:
Micromechanical_Pyrolytic_Carbon_String_Resonators.pdf
Source: PublicationPreSubmission
Source-ID: 126456729
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2016

Monitoring intra- and extracellular redox capacity of intact barley aleurone layers responding to phytohormones

Redox regulation is important for numerous processes in plant cells including abiotic stress, pathogen defence, tissue development, seed germination and programmed cell death. However, there are few methods allowing redox homeostasis to be addressed in whole plant cells, providing insight into the intact in vivo environment. An electrochemical redox assay that applies the menadione-ferricyanide double mediator is used to assess changes in the intracellular and extracellular redox environment in living aleurone layers of barley (Hordeum vulgare cv. Himalaya) grains, which respond to the phytohormones gibberellic acid and absciscic acid. Gibberellic acid is shown to elicit a mobilisation of electrons as detected by an increase in the reducing capacity of the aleurone layers. By taking advantage of the membrane-permeable menadione/menadiol redox pair to probe the membrane-impermeable ferricyanide/ferrocyanide redox pair, the mobilisation of electrons was dissected into an intracellular and an extracellular, plasma membrane-associated component. The intracellular and extracellular increases in reducing capacity were both suppressed when the aleurone layers were incubated with abscistic acid. By probing redox levels in intact plant tissue, the method provides a complementary approach to assays of reactive oxygen species and redox-related enzyme activities in tissue extracts.

General information
State: Published
Organisations: Agricultural and Environmental Proteomics, Department of Systems Biology, Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Fluidic Array Systems and Technology
Nanomechanical IR spectroscopy for fast analysis of liquid-dispersed engineered nanomaterials

The proliferated use of engineered nanomaterials (ENMs), e.g. in nanomedicine, calls for novel techniques allowing for fast and sensitive analysis of minute samples. Here we present nanomechanical IR spectroscopy (NAM-IR) for chemical analysis of picograms of ENMs. ENMs are nebulized directly from dispersion and efficiently collected on nanomechanical string resonators through a non-diffusion limited sampling method. Even very small amounts of sample can convert absorbed IR light into a measurable frequency detuning of the string through photothermal heating. An IR absorption spectrum is thus readily obtained by recording this detuning of the resonator over a range of IR wavelengths. Results recorded using NAM-IR agree well with corresponding results obtained through ATR-FTIR, and remarkably, measurement including sample preparation takes only a few minutes, compared to ~2 days sample preparation for ATR-FTIR. Resonator dimensions play an important role in NAM-IR, a relationship which will be elaborated here.
Nanomechanical Pyrolytic Carbon Resonators: Novel Fabrication Method and Characterization of Mechanical Properties

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark
Authors: Kurek, M. (Intern), Larsen, F. K. (Ekstern), Larsen, P. E. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Number of pages: 11
Pages: 1097
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Sensors
Volume: 16
Issue number: 7
ISSN (Print): 1424-8220
Ratings:
BFI (2018): BFI-level 2
Nanostructuring of Solar Cell Surfaces

Solar energy is by far the most abundant renewable energy source available, but the levelized cost of solar energy is still not competitive with that of fossil fuels. Therefore there is a need to improve the power conversion efficiency of solar cells without adding to the production cost.

The main objective of this PhD thesis is to develop nanostructured silicon (Si) solar cells with higher power conversion efficiency using only scalable and cost-efficient production methods. The nanostructures, known as "black silicon", are
fabricated by single-step, maskless reactive ion etching and used as front texturing of different Si solar cells. Theoretically the nanostructure topology may be described as a graded refractive index in a mean-field approximation between air and Si. The optical properties of the developed black Si were simulated and experimentally measured. Total AM1.5G-weighted average reflectance well below 1% was measured for different crystalline grades of Si. Furthermore, the reflectance of RIE-textured Si remains below that of KOH-textured Si at all incident angles below 70°. RIE- and conventionally textured, screen-printed Si solar cells were fabricated on 156x156 mm² CZ Si wafers and characterized for comparison. Power conversion efficiency of 16.5% was obtained for this batch of RIE-textured Si solar cells. The efficiency of the KOH-textured reference cell was 17.8%. Quantum Efficiency measurements and carrier loss analysis show that the lower efficiency of the RIE-textured cells is primarily due to increased emitter and surface recombination. The large-area screen-printed solar cells were furthermore characterized at varying incident angles. The angle-dependent analysis shows that RIE-textured cells have a higher normalized power output averaged over the range of incident angles between 0 and 90. This result indicates the potential of improved cell performance and higher output power at diffuse light conditions and during daily and yearly operation. A second batch of RIE-textured solar cells with laser-doped selective emitters (LDSE) was fabricated. A power conversion efficiency of 18.1% and a fill factor of 80.1% were obtained by laser doping and subsequent Ni/Cu plating in combination with RIE-texturing. This result shows the potential of improved efficiency of RIE-textured compared to conventionally textured cells, especially when laser doping on black Si is combined with improved surface passivation schemes such as atomic layer deposition (ALD) of Al₂O₃, ALD Al₂O₃ passivation on black Si yields surface recombination velocity (SRV) below 80 cm/s and implied open-circuit voltage (iVOC) of 680 mV. Surface recombination velocity of 20 cm/s and implied open-circuit voltage of 695 mV is obtained for black Si passivated by doped poly-Si and a tunnel oxide.
On-chip RF-to-optical transducer

Recent advances in the fabrication of nano- and micromechanical elements enable the realization of high-quality mechanical resonators with masses so small that the forces from optical photons can have a significant impact on their motion. This facilitates a strong interaction between mechanical motion and light, or phonons and photons. This interaction is the corner stone of the field of optomechanics and allows, for example, for ultrasensitive detection and manipulation of mechanical motion using laser light. Remarkably, today these techniques can be extended into the quantum regime, in which fundamental fluctuations of light and mechanics govern the system’s behavior. Micromechanical elements can also interact strongly with other physical systems, which is the central aspect of many micro-electro-mechanical based sensors. Micromechanical elements can therefore act as a bridge between these diverse systems, plus technologies that utilize them, and the mature toolbox of optical techniques that routinely operates at the quantum limit.

In a previous work [1], we demonstrated such a bridge by realizing simultaneous coupling between an electronic LC circuit and a quantum-noise limited optical interferometer. The coupling was mediated by a mechanical oscillator forming a mechanically compliant capacitor biased with a DC voltage. The latter enhances the electromechanical interaction all the way to the strong coupling regime. That scheme allowed optical detection of electronic signals with effective noise temperatures far below the actual temperature of the mechanical element. On-chip integration of the electrical, mechanical and optical elements is necessary for an implementation of the transduction scheme that is viable for commercial applications. Reliable assembly of a strongly coupled electromechanical device, and inclusion of an optical cavity for enhanced optical readout, are key features of the new platform. Both can be achieved with standard cleanroom fabrication techniques. We will furthermore present ongoing work to couple our transducer to an RF or microwave antenna, for low-noise detection of electromagnetic signals, including sensitive measurements of magnetic fields in an MRI detector.

Suppression of thermomechanical noise is a key feature of electro-optomechanical transducers, and, more generally,
hybrid systems involving mechanical degrees of freedom. We have shown that engineering of the phononic density of states allows improved isolation of the relevant mechanical modes from their thermal bath [2], enabling coherence times sufficient to realize quantum-coherent optomechanical coupling. This proves the potential of the employed platform for complex transducers all the way into the quantum regime.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Simonsen, A. (Ekstern), Tsaturyan, Y. (Ekstern), Seis, Y. (Ekstern), Schmid, S. (Intern), Schliesser, A. (Ekstern), Polzik, E. S. (Ekstern)
Number of pages: 1
Publication date: 2016
Conference: Quantum Optics, Brussels, Belgium, 05/04/2016 - 05/04/2016
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Proceedings of SPIE, the International Society for Optical Engineering
Volume: 9900
ISSN (Print): 0277-786X
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.289 SJR 0.243
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.42 SNIP 0.258 SJR 0.226
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.212 SNIP 0.239 CiteScore 0.3
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.217 SNIP 0.249 CiteScore 0.3
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.234 SNIP 0.273 CiteScore 0.26
ISI indexed (2013): ISI indexed no
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.219 SNIP 0.275 CiteScore 0.27
ISI indexed (2012): ISI indexed no
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.217 SNIP 0.286 CiteScore 0.31
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.233 SNIP 0.277
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.236 SNIP 0.312
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.245 SNIP 0.3
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.247 SNIP 0.376
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.323 SNIP 0.676
Scopus rating (2005): SJR 0.162 SNIP 0.372
Web of Science (2004): Indexed yes
Web of Science (2002): Indexed yes
Original language: English
Electronic versions: 99000X.pdf
Optical two-beam trap in a polymer microfluidic chip

An optical two-beam trap, composed from two counter propagating laser beams, is an interesting setup due to the ability of the system to trap, hold, and stretch soft biological objects like vesicles or single cells. Because of this functionality, the system was also named "the optical stretcher" by Jochen Guck, Josep Käs and co-workers some 15 years ago. In a favorable setup, the two opposing laser beams meet with equal intensities in the middle of a fluidic channel in which cells may flow past, be trapped, stretched, and allowed to move on, giving the promise of a high throughput device. Yet, single beam optical traps, aka optical tweezers, by far outnumber the existing optical stretchers in research labs throughout the world. The ability to easily construct an optical stretcher setup in a low-cost material would possibly imply more frequent use of the optical stretching technique. Here, we will outline the design, the production procedures, and results obtained in a fiber-based experimental setup built within an injection molded microfluidic polymer chip. The microfluidic chip is constructed with a three layer technology in which we ensure both horizontal and vertical focusing of the cells we wish to trap, thereby preventing too many cells to flow below the line of focus of the two counter propagating laser beams that are positioned perpendicular to the direction of flow of the cells. Results will be compared to that from other designs from previous work in the group.

General information

State: Published
Organisations: Department of Physics, Biophysics and Fluids, Department of Micro- and Nanotechnology, Optofluidics, Nanoprobes, NIL Technology ApS
Authors: Palanco, M. E. (Intern), Catak, D. (Intern), Marie, R. (Intern), Matteucci, M. (Intern), Bilenberg, B. (Ekstern), Kristensen, A. (Intern), Berg-Sørensen, K. (Intern)
Number of pages: 10
Publication date: 2016

Host publication information

Title of host publication: Proceedings of SPIE 9922, Optical Trapping and Optical Micromanipulation XIII
Volume: 9922
Publisher: SPIE - International Society for Optical Engineering
Series: S P I E - International Society for Optical Engineering. Proceedings
Volume: 9922
ISSN: 0277-786X
Main Research Area: Technical/natural sciences
Optical trapping, Fiber-based optical trap, Polymer injection molding, Hydrodynamic focusing
Electronic versions:
Palanco_2016_optical_two_beam_trap_in_a_polymer_microfluidic_chip_SPIE_992213_2.pdf
DOIs:
10.1117/12.2236465
Source: FindIt
Source-ID: 2349370130
Publication: Research - peer-review › Article in proceedings – Annual report year: 2016

Orientation of Pterin-6-Carboxylic Acid on Gold Capped Silicon Nanopillars Platforms: Surface Enhanced Raman Spectroscopy and Density Functional Theory Studies

The orientation of pterin-6-carboxylic acid on gold nanopillars was investigated by surface enhanced Raman spectroscopy and density functional theory methods. The experimentally vibrations from pterin-6-COOH free and attached to the Au surface display vibration features indicating chemical interaction of the pterin with the metal surface. The spectral feature evidenced that the pterin would adsorb on gold surface with a "lying down" configuration through the high intensity vibration of NH scissoring and rocking OH modes. The orientation study of pterins on gold nanopillars presented herein is believed to lead to new applications in biosensing field for detecting pterins of physiological importance.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Universidad Industrial de Santander, Universidad Santo Tomas, Bogota
Authors: Castillo, J. J. (Ekstern), Rozo, C. E. (Ekstern), Bertel, L. (Ekstern), Rindzevicius, T. (Intern), Mendez-Sanchez, S. C. (Ekstern), Martinez Ortega, F. (Ekstern), Boisen, A. (Intern)
Perforated SiN membrane resonators for nanomechanical IR spectroscopy poster

Constant progress in micro- and nanofabrication provides a great opportunity in development of micro- and nanomechanical resonators that can be used for sensing purposes. These sensors usually consist of singly-clamped cantilever beams, doubly-clamped bridges or membranes that exhibit resonant behavior. The principle of operation is based on the monitoring of the resonance frequency shift due to various external factors such as change of temperature. It
has been shown that photothermal infrared (IR) spectroscopy based on nanomechanical silicon nitride (SiN) string resonators (NAM-IR) enables the exceptionally fast chemical analysis of pictograms of analytes directly from liquid solution in only a few minutes [1]. However in this technique the coupling of the IR laser beam to the nanometer wide string resonators is difficult and inefficient. Therefore perforated SiN membranes with thickness of 100 nm, lateral dimension of $1 \times 1 \text{ mm}^2$ and 2 $\mu$m perforation grid pitch were used instead of strings which makes the IR beam alignment significantly simpler while maintaining similar sampling efficiency and photothermal IR absorption sensitivity.

### General information

**State:** Published  
**Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark  
**Authors:** Kurek, M. (Intern), Carnoy, M. (Ekstern), Boisen, A. (Intern), Schmid, S. (Intern)  
**Number of pages:** 1  
**Publication date:** 2016  
**Event:** Poster session presented at 42nd International conference on Micro and Nano Engineering, Vienna, Austria.  
**Main Research Area:** Technical/natural sciences  
**Electronic versions:**  
- **Perforated SiN membrane resonators for nanomechanical IR spectroscopy poster.pdf**  
- **Source:** PublicationPreSubmission  
- **Source-ID:** 126456655  
- **Publication:** Research - peer-review › Poster – Annual report year: 2016

### Plasmonic nanopillar structures for surface-enhanced raman scattering applications

Noble metal nanostructures support localized surface plasmon (LSPR) resonances that depend on their dimensions, shapes and compositions. Particle LSPR's can be used to spatially confine the incident light and produce enormous electromagnetic (EM) field enhancement spots, i.e. hot spots. Hot spots have been utilized in surface enhanced Raman spectroscopy (SERS) for biological and chemical sensing. We present Au nanopillar (NP) SERS structures that are excellent for molecular detection. The NP structures can be fabricated using a simple two-step process. We analyze NP optical properties experimentally and theoretically. Simulations show that that a single Agcoated NP supports two LSPR modes, i.e. the particle mode and the Ag cap resonant cavity mode. The Ag cap resonant cavity mode contributes most to the enhancement of the Raman scattering signal. The electric field distribution calculations show that the EM hot spots are located at the bottom of the Ag cap which is important observation for practical SERS sensing. Reproducible and repeatable SERS signal intensities can be obtained across large surface areas (>mm$^2$). Application examples include detection of TAMRA-labeled vasopressin and cyanide (KCN).

### General information

**State:** Published  
**Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Harvard University, Columbia University  
**Authors:** Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Wu, K. (Intern), Thilsted, A. H. (Intern), Lauridsen, R. K. (Intern), Alstrøm, T. S. (Intern), Palla, M. (Ekstern), Yang, J. (Ekstern), Boisen, A. (Intern)  
**Number of pages:** 4  
**Pages:** 243-246  
**Publication date:** 2016  
**Host publication information**  
- **Title of host publication:** Techconnect Briefs 2016  
- **Volume:** 4  
- **ISBN (Electronic):** 978097511734  
- **Main Research Area:** Technical/natural sciences  
- **Conference:** 10th Annual TechConnect World Innovation Conference and Expo, Washington, D.C., United States, 22/05/2016 - 22/05/2016  
- **Source:** FindIt  
- **Source-ID:** 2347144588  
- **Publication:** Research - peer-review › Article in proceedings – Annual report year: 2016

### Polymeric microcontainers improve oral bioavailability of furosemide

Microcontainers with an inner diameter of 223$\mu$m are fabricated using the polymer SU-8, and evaluated in vitro, in situ and in vivo for their application as an advanced oral drug delivery system for the poorly water soluble drug furosemide. An amorphous sodium salt of furosemide (ASSF) is filled into the microcontainers followed by applying a lid using Eudragit L100. It is possible to control the drug release in vitro, and in vitro absorption studies show that the microcontainers are not a hindrance for absorption of ASSF. In situ perfusion studies in rats are performed with ASSF-filled microcontainers coated with Eudragit and compared to a furosemide solution. The absorption rate constant of ASSF confined in microcontainers is found to be significantly different from the solution, and by light microscopy, it is observed that the microcontainers are engulfed by the intestinal mucus. An oral bioavailability study in rats is performed with ASSF confined in microcontainers coated with Eudragit and a control group with ASSF in Eudragit-coated capsules. A relative bioavailability of 220% for the ASSF in microcontainers compared to ASSF in capsules is found. These studies indicate that the microcontainers could serve as a promising oral drug delivery system.
Rapid Voltammetric Measurements at Conducting Polymer Microelectrodes Using Ultralow-Capacitance Poly(3,4-ethylenedioxythiophene)-Tosylate

We use a vapor-phase synthesis to generate conducting polymer films with low apparent capacitance and high conductance enabling rapid electrochemical measurements. Specifically, oxidative chemical vapor deposition was used to create thin films of poly(3,4-ethylenedioxythiophene):tosylate (PEDOT:tosylate). These films had a conductance of 17.1 ± 1.7 S/cm. Furthermore, they had an apparent capacitance of 197 ± 14 μF/cm², which is an order of magnitude lower than current commercially available and previously reported PEDOT. Using a multistage photolithography process, these films were patterned into PEDOT:tosylate microelectrodes and were used to perform fast-scan cyclic voltammetry (FSCV) measurements. Using a scan rate of 100 V/s, we measured ferrocene carboxylic acid and dopamine by FSCV. In contrast to carbon-fiber microelectrodes, the reduction peak showed higher sensitivity when compared to the oxidation peak. The adsorption characteristics of dopamine at the polymer electrode were fit to a Langmuir isotherm. The low apparent capacitance and the microlithographic processes for electrode design make PEDOT:tosylate an attractive material for future applications as an implantable biosensor for FSCV measurements. Additionally, the integration of PEDOT:tosylate electrodes on plastic substrates enables new electrochemical measurements at this polymer using FSCV.
SERS detection of pneumonia in breath of children with cystic fibrosis

Cystic fibrosis (CF) is the most frequently inherited disease in the Western world, and also the one with the highest morbidity and mortality. The main reason is chronic lung infections caused by the pathogenic bacterium Pseudomonas aeruginosa, which is well-adapted to the thick and dehydrated mucous in the CF airways. Established methods to detect P. aeruginosa in young CF children are invasive and lack sensitivity, which is why novel approaches are being investigated. P. aeruginosa emits hydrogen cyanide (HCN) gas, which can possibly be used as a biomarker for early P. aeruginosa colonisation, if it can be detected in the breath. It was investigated if a nanopillar substrate for surface-enhanced Raman spectroscopy (SERS), developed in the Nanoprobes group, could be optimised for gas phase detection of HCN. The project consisted of 3 steps, of which the first was to establish a chemical method to detect cyanide on the...
substrate in relevant concentrations, preferably in gas. Step I was split up into two parts; one for HCN detection in the gas phase, and one for detection of potassium cyanide (KCN) in serial dilutions to reach sufficiently low CN concentrations and verify the limit of detection. Once this was done, Step II was to measure HCN(g) from emissions of *P. aeruginosa*; first from the established reference strain, the wild type PAO1. Secondly, it was relevant to study clinical *P. aeruginosa* strains, isolated for the first time from CF children (the wild type-like strains), and then compare to SERS measurements on later strains, isolated from the same patients after their infection became chronic and the *P. aeruginosa* had mutated in the lasR gene, which is essential to HCN production. Step III was a clinical trial, where children with CF would blow into a bag containing the SERS substrate, which was then measured, to see if HCN was detected when a new *P. aeruginosa* colonisation occurred; and data was correlated to culturing of sputum from the patient’s lungs.

The SERS substrate was optimised, and setups were developed for HCN(g) detection, for SERS detection of HCN from bacterial volatiles, and for collection and SERS substrate exposure to human breath. Five ppm HCN was successfully detected in gas phase, and KCN was detected down to 10-6 M. HCN detection was demonstrated from cultures of *P. aeruginosa* wild types, starting from the end of exponential / beginning of stationary growth phase. HCN was also detected from lasR mutated clinical *P. aeruginosa* strains isolated from the airways of children with CF, when the mutation was located at the 5’ terminal (downstream) of the gene. *P. aeruginosa* isolates with a mutation at the 3’ terminal of the lasR gene (upstream) did not emit detectable HCN. Application for ethics’ committee was submitted and permission granted to conduct a 4 months’ clinical pilot study at Rigshospitalet, including 50 CF patients aged 5-17 years and 19 age-matched control subjects. One CF patient had a new *P. aeruginosa* lung colonisation during the trial, and it was probably detected on the SERS substrate, which had an increased HCN signal compared to the patient’s other visits. Additional cases of increased SERS cyanide signal were seen in the breath of some of the children, and it was speculated if they could come from prolonged exposure time or from children being exposed to passive smoking at home. The SERS substrate has a background peak in the Raman spectrum, which needs to be addressed, because it is located very close to the cyanide peak.
The present study is aimed to enhance the oral bioavailability of ketoprofen by inserting it into the matrix of poly(vinylpyrrolidone) (PVP) K10 spatially confined into microcontainers, by means of supercritical CO2-aided impregnation. Microcontainers are cylindrical reservoirs, with typical sizes in the micrometer range, with a cavity open on one side, where the drug formulation is loaded. Differently to traditional tablets, microcontainers have a higher surface area per unit volume, and release the drug only in one direction. This design is meant to enhance the absorption of problematic drugs, like those with poor solubility in water. In a previous study we introduced a novel technique for drug loading of microcontainers, based on inkjet printing and supercritical impregnation (SCI). We showed that SCI produces accurate and reproducible drug loading for large arrays of microcontainers. In the attempt of enhancing the throughput of the loading methods, we propose the replacement of polymer inkjet printing with an easier manual compression of the PVP powder into the microcontainers. As the second step, the polymer powder-filled microcontainers were submitted to SCI. The separate role of different impregnation parameters (temperature, pressure, time, drug concentration in the supercritical phase) was elucidated with respect to the loading capacity. The microcontainer filling was observed by means of optical macroimaging, X-ray microtomography and scanning electron microscopy. The physical state of the drug was investigated by means of Raman spectroscopy and compared with selected representative PVP-ketoprofen physical mixtures. Finally, the drug loading was estimated by means of in vitro dissolution tests. The characterization study shows that the present loading method is a valuable alternative to the one previously described. The drug loading can be controlled with high accuracy and reproducibility and the impregnated drug is in amorphous state. These results demonstrate that SCI can be used as a high-throughput loading technique for microfabricated devices for oral drug delivery.
Surface-enhanced Raman spectroscopic study of DNA and 6-mercapto-1-hexanol interactions using large area mapping

The emergence of 2D SERS substrates with large areas of hot spots has enabled data to be gathered at large scale. This work presents a statistical tool for analysing large amounts of SERS data by utilizing a peak-fitting model in a specific spectral range. By analysing the distributions of Raman intensities and peak positions it is possible to directly inspect the interplay between DNA and 6-mercapto-1-hexanol on gold covered nanopillars. It is demonstrated that optimised functionalization parameters can be extracted from the Raman spectra directly. Using the peak-fitting approach it is possible to avoid miss-interpretation of intensity histograms, where contamination might contribute with an enhanced background and not a peak.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Department of Applied Mathematics and Computer Science, Cognitive Systems, Nanoprobes, Copenhagen Center for Health Technology, Surface Engineering, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Frøhling, K. B. (Intern), Alstrøm, T. S. (Intern), Bache, M. (Intern), Schmidt, M. S. (Intern), Schmidt, M. N. (Intern), Larsen, J. (Intern), Jakobsen, M. H. (Intern), Boisen, A. (Intern)
Pages: 331-336
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: Vibrational Spectroscopy
Volume: 86
ISSN (Print): 0924-2031
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Surface Enhanced Raman Spectroscopy detection of p-coumaric acid from cell supernatant using gold-capped silicon nanopillar substrates

A standard protocol for analysis of microbial factories requires the screening of several populations in order to find the best performing ones. This is done with standard analytical methods (e.g. HPLC) with an expensive and time-consuming process. Surface Enhanced Raman Spectroscopy (SERS) is a highly sensitive spectroscopic technique which only requires drying a small volume of solution on an active substrate, with an analysis time of few minutes. Here we demonstrate the use of SERS to discriminate between two different bacterial populations based on detection of p-coumaric acid (pHCA) in cell supernatant. pHCA is a valuable secondary metabolite of genetically modified E. coli[1]. It is produced through deamination of tyrosine, and it has strong Raman and SERS activity[2],[3]. Gold capped silicon nanopillars were used as sensing substrates[4]. At first, they were successfully used to detect pHCA spiked in culture medium, in the same concentration range ($10^{-4}$ – $10^{-5}$ M) commonly found in cell supernatant. For supernatant analysis, triplicate cultures of FjTAL modified (P strains) and control (C strains) E.coli strains were carried out according to the methods described by[5] and shown in Fig.1. Samples of cell supernatant were extracted from each culture at 0, 3, 24 and 48 h post seeding and their pHCA content was measured with HPLC[5]. For SERS analysis, aliquots of supernatant were diluted 10-fold with MilliQ water, and 1 μL droplets were dried on the SERS substrates. A MatLab analysis was performed to extract the height of the significant peak at 1169cm$^{-1}$, with the results shown in Fig.2. The amplitude of the peak shows a different trend for P and C strains. A similar trend is obtained from HPLC. These promising results open up new
possibilities for the use of SERS for high-throughput and automated evaluation of bacterial factories, allowing parallel analysis and discrimination of different strains.

**General information**

**State:** Published  
**Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Research Groups  
**Authors:** Morelli, L. (Intern), Jendresen, C. B. (Intern), Burger, R. (Intern), Rindzevicius, T. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)  
**Publication date:** 2016

**Surface Enhanced Raman Spectroscopy detection of p-coumaric acid from cell supernatant using gold-capped silicon nanopillar substrates**

The purpose of the project is to use Surface Enhanced Raman Spectroscopy (SERS) to discriminate between two different bacterial populations, based on their p-coumaric acid (pHCA) production. The pHCA concentration is measured in a droplet of diluted supernatant dried on SERS substrates, using a Raman microscope. By analyzing the SERS signal of pHCA from the supernatant, considering the peak height at the characteristic frequency (1169 cm⁻¹) it is possible to distinguish between a producing and control strain, as also confirmed by HPLC analysis.

**General information**

**State:** Published  
**Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Research Groups  
**Authors:** Morelli, L. (Intern), Jendresen, C. B. (Intern), Burger, R. (Intern), Rindzevicius, T. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)  
**Number of pages:** 1  
**Publication date:** 2016

**Synthesis and characterization of UV photocrosslinkable hydrogels with poly(N-vinyl-2-pyrrolidone): Determination of the network mesh size distribution**

Hydrogels of poly(N-vinyl-2-pyrrolidone) were produced by UV irradiation of aqueous solutions of the polymer in presence of hydrogen peroxide, used as initiator. The mechanical and the nanostructural properties of the gels were characterized by a combination of experimental techniques including rheology, low field nuclear magnetic resonance spectroscopy (LF-NMR), and small angle X-ray scattering. Different irradiation doses as well as polymer and initiator concentrations were tested in the characterization. The study elucidates the relationship between different methods to estimate the mesh size of the gel polymeric network. Moreover, a novel correlation model was developed based on Chui and Scherer theories for the interpretation of LF-NMR dataset of polymer solutions and networks.

**General information**

**State:** Published  
**Organisations:** Department of Micro- and Nanotechnology, Nanoprobes, Department of Chemical and Biochemical Engineering, The Danish Polymer Centre, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Trieste, National Research Council of Italy  
**Authors:** Marizza, P. (Intern), Abrami, M. (Ekstern), Keller, S. S. (Intern), Posocco, P. (Ekstern), Laurini, E. (Ekstern), Goswami, K. (Intern), Skov, A. L. (Intern), Boisen, A. (Intern), Larobina, D. (Ekstern), Grassi, G. (Ekstern), Grassi, M. (Ekstern)  
**Pages:** 516-525  
**Publication date:** 2016

**Publication Information**

**Journal:** International Journal of Polymeric Materials and Polymeric Biomaterials  
**Volume:** 65  
**Issue number:** 10  
**ISSN (Print):** 0091-4037
Translucent Substrates for Plasmonic Sensing by Lithography-Free Fabrication

This Ph.D. thesis presents fabrication and optimization of translucent plasmonic substrates that can be used for biological and chemical sensing by surface enhanced Raman spectroscopy (SERS) sensing and localized surface plasmon resonance refractive index (LSPR RI) sensing. These substrates are: glass nanopillars with gold caps for SERS sensing; polymer nanopillars with gold caps for SERS sensing; transferred gold nanocaps to polymer foil for SERS sensing; and glass hollow-core nanocylinders with gold nanorings for LSPR RI sensing. These substrates were achieved using lithography-free fabrication methods, and resulted in large-area, high throughput and low cost production techniques. The fabrication techniques consisted of using aluminum patterned areas and reactive
ion etching (RIE) to achieve nanopillars or nanocylinders in glass; using RIE to achieve nanopillars in silicon as a mould for polymer injection; and using RIE and imprinting to transfer gold nanocaps to a polymer foil. The SERS substrates showed a 91%, a 94% and 8% Raman signal intensity compared to gold-capped silicon nanopillars for the glass nanopillars, the polymer injected nanopillars and the transferred gold nanocaps, respectively. As the substrates were transparent, measurements from the backside were possible, showing a 44%, 1.7% and 71% Raman signal intensity in comparison to the measurements from the front, for the glass nanopillars, the polymer injected nanopillars and the transferred metal nanocaps, respectively.

For LSPR, the glass hollow-core nanocylinders with suspended gold nanorings showed a sensitivity of 658 nm RIU with a figure-of-merit of 10. The LSPR wavelengths could be shifted by tuning the plasma etching parameters. Due to the low electrical conductivity of glass substrates, electrodes could be incorporated onto the glass nanopillars, resulting in a device that could be used for both electrochemistry and SERS measurements. The polymer injected nanopillars used an industrial high throughput and robust fabrication technique. The substrate was integrated into high throughput fluidic devices for in-situ SERS measurements. The fabrication methods presented in this Ph.D. thesis are scalable, high throughput and low cost, and result in high performance plasmonic surfaces for sensing.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Thilsted, A. H. (Intern), Boisen, A. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern)
Number of pages: 158
Publication date: 2016

Publications information
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions: Untitled.pdf

Relations
Projects:
Transparent Substrates for Plasmonic Sensing by Lithography-Free Fabrication
Source: PublicationPreSubmission
Source-ID: 128589069
Publication: Research › Ph.D. thesis – Annual report year: 2017

Triple co-culture cell model as an in vitro model for oral particulate vaccine systems
A triple co-culture cell model of Caco-2 cells, dendritic cells and macrophages (Figure 1) has previously been developed for studying intestinal permeability in a state of inflammation [1],[2]. The aim of this study was to investigate the applicability of this cell model for testing the immunostimulatory ability of particulate vaccine formulations designed for oral delivery. Levels of cytokine production in response to vaccine administration were measured following particulate vaccine administration, as an indication of dendritic cell and macrophage activation. Precursors of cubosomes containing the model antigen ovalbumin was spray dried to obtain a particulate vaccine model system for testing in the cell model. The precursors were shown to form cubosomes when dispersed in aqueous medium, and was therefore used as the vaccine formulation for testing the co-cultures. After 11 days, the TEER values of the co-cultures were found to be 860-1340 Ω·cm²; the formulations were incubated with the co-cultures at this time point. From confocal microscopy images, it was observed that the THP-1 cells (macrophages) migrated into the overlying Caco-2 cell monolayer when the co-cultures were incubated with particle formulations. This was not the case when incubating with ovalbumin solution or blank. The ELISA screening assay showed production of a wide range of cytokines following culture incubation with cubosomes (with and without ovalbumin) and LPS solutions, indicative of a stimulatory effect; this was not observed with ovalbumin and blank solution. An example of the results is shown in Figure 2 for IL-17A. An established co-culture of Caco-2, THP-1 and MUTZ-3 cells showed promise as an in vitro model for testing of oral vaccine formulations. Mobility of co-culture immune cells as well as cytokine production observed following treatment with spray dried cubosomes as a particulate vaccine formulation will be further investigated.

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Centre for Infection Research (HZI), Saarland University, University of Copenhagen, Monash University
Authors: Nielsen, L. H. (Intern), De Rossi, C. (Ekstern), Lehr, C. (Ekstern), Rades, T. (Ekstern), Boyd, B. (Ekstern), Boisen, A. (Intern), Gordon, S. (Ekstern)
Number of pages: 1
Publication date: 2016
Event: Poster session presented at BioBarriers 2016, Saarbrücken, Germany.
Triple co-culture cell model as an in vitro model for oral particulate vaccine systems

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Centre for Infection Research (HZI), University of Copenhagen, Monash University
Authors: Nielsen, L. H. (Intern), De Rossi, C. (Ekstern), Lehr, C. (Ekstern), Rades, T. (Ekstern), Boyd, B. (Ekstern), Boisen, A. (Intern), Gordon, S. (Ekstern)
Number of pages: 1
Publication date: 2016
Event: Poster session presented at 10th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Glasgow, United Kingdom.
Main Research Area: Technical/natural sciences
Electronic versions:
BB2016_cell_model.pdf

Bibliographical note
Poster at conference, 10TH WORLD MEETING on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
Source: PublicationPreSubmission
Source-ID: 125164776
Publication: Research - peer-review › Poster – Annual report year: 2016

Triple co-culture cell model as an in vitro model for oral particulate vaccine systems

Wafer-Scale Nanopillars Derived from Block Copolymer Lithography for Surface-Enhanced Raman Spectroscopy
We report a novel nanofabrication process via block copolymer lithography using solvent vapor annealing. The nanolithography process is facile and scalable, enabling fabrication of highly ordered periodic patterns over entire wafers as substrates for surface-enhanced Raman spectroscopy (SERS). Direct silicon etching with high aspect ratio templated by the block copolymer mask is realized without any intermediate layer or external precursors. Uniquely, an atomic layer deposition (ALD)-assisted method is introduced to allow reversing of the morphology relative to the initial pattern. As a result, highly ordered silicon nanopillar arrays are fabricated with controlled aspect ratios. After metallization, the resulting nanopillar arrays are suitable for SERS applications. These structures readily exhibit an average SERS enhancement factor of above $10^9$, SERS uniformities of $8.5\%$ relative standard deviation across $4 \text{ cm}$, and $6.5\%$ relative standard deviation over $5 \times 5 \text{ mm}^2$ surface area, as well as a very low SERS background. The as-prepared SERS substrate, with a good enhancement and large-area uniformity, is promising for practical SERS sensing applications.
**A method for the chemical modification of polychlorinated biphenyls for improved affinity towards noble metal surfaces.**

The present application discloses a method for the modification and analysis of a field sample suspected of containing contaminant(s) like polychlorinated biphenyls (PCBs). The invention also relates to a corresponding kit for the modification of samples suspected of containing such contaminant(s).
Electrochemical method for transferring graphene

The present application discloses a method for separating a graphene-support layer laminate from a conducting substrate-graphene-support layer laminate, using a gentle, controllable electrochemical method. In this way, substrates which are fragile, expensive or difficult to manufacture can be used - and even re-used - without damage or destruction of the substrate or the graphene.

Adsorption and Vibrational Study of Folic Acid on Gold Nanopillar Structures Using Surface-enhanced Raman Scattering Spectroscopy

This paper presents a study of adsorption and vibrational features of folic acid, using surface-enhanced Raman scattering (SERS). A gold-capped silicon nanopillar (Au NP) with a height of 600 nm and a width of 120 nm was utilized to study the vibrational features of FA molecules adsorbed on the nanopillars within the high electromagnetic field areas. The adsorption behaviour of folic acid and the band assignment of the main vibrations together with the optimized geometry of folic acid and folic acid in the presence of a cluster of 10 gold atoms were assessed using the density functional theory (B3LYP(6-31G(d))) and the scalar relativistic effective core potential with a double-zeta basis set (LANL2DZ). The vibrations obtained from the solid-state folic acid and the folic acid on a gold cluster were in accordance with those observed experimentally. The analysis of the main vibrations indicated that the interaction of folic acid with the Au NP occurred primarily through the nitrogen atoms, from their pteridine ring. Finally, the obtained adsorption isotherm for folic acid was deduced from the analysis of the SERS spectra and it followed a negative cooperative binding model.
A Lab-on-a-Disc Platform for Trapping of Cell Population, Monitoring of Cell growth and Evaluation of Redox Metabolism

In this work, we demonstrate an integrated electrochemical system on a centrifugal microfluidic platform for cell studies by combining electrochemical impedance spectroscopy and amperometry, and comparison of different cleaning protocols for gold electrodes on plastic substrate.

A Lab-on-a-disc platform for trapping of cells, monitoring of cell behaviour and evaluation of redox metabolism

In this work, we demonstrate an integrated electrochemical system on a centrifugal microfluidic platform for cell studies by combining electrochemical impedance spectroscopy and amperometry, and comparison of different cleaning protocols for gold electrodes on plastic substrate.
Angle resolved characterization of nanostructured and conventionally textured silicon solar cells

We report angle resolved characterization of nanostructured and conventionally textured silicon solar cells. The nanostructured solar cells are realized through a single step, mask-less, scalable reactive ion etching (RIE) texturing of the surface. Photovoltaic properties including short circuit current, open circuit voltage, fill factor (FF) and power conversion efficiency are each measured as function of the relative incident angle between the solar cell and the light source. The relative incident angle is varied from 0° to 90° in steps of 10° in orthogonal axes, such that each solar cell is characterized at 100 different angle combinations. The angle resolved photovoltaic properties are summarized in terms of the average, angle-dependent electrical power output normalized to the power output at normal incidence and differently textured cells on different silicon substrates are compared in terms of angle resolved performance. The results show a 3% point improvement in average electrical power output normalized with respect to normal incidence power output of RIE textured, multicrystalline Si cells compared to conventional multicrystalline Si cells and above 1% point improvement of RIE textured monocrystalline Si cells compared to conventional monocrystalline Si cells.
An impedance method for spatial sensing of 3D cell constructs – towards applications in tissue engineering

We present the characterisation and validation of multiplexed 4-terminal (4T) impedance measurements as a method for sensing the spatial location of cell aggregates within large three-dimensional (3D) gelatin scaffolds. The measurements were performed using an array of four rectangular chambers, each having eight platinum needle electrodes for parallel analysis. The electrode positions for current injection and voltage measurements were optimised by means of finite element simulations to maximise the sensitivity field distribution and spatial resolution. Eight different 4T combinations were experimentally tested in terms of the spatial sensitivity. The simulated sensitivity fields were validated using objects (phantoms) with different conductivity and size placed in different positions inside the chamber. This provided the detection limit (volume sensitivity) of 16.5%, i.e. the smallest detectable volume with respect to the size of the measurement chamber. Furthermore, the possibility for quick single frequency analysis was demonstrated by finding a common frequency of 250 kHz for all the presented electrode combinations. As final proof of concept, a high density of human hepatoblastoma (HepG2) cells were encapsulated in gelatin to form artificial 3D cell constructs and detected when placed in different positions inside large gelatin scaffolds. Taken together, these results open new perspectives for impedance-based sensing technologies for non-invasive monitoring in tissue engineering applications providing spatial information of constructs within biologically relevant 3D environments.
Baking-powder driven centripetal pumping controlled by event-triggering of functional liquids

This paper reports radially inbound pumping by the event-triggered addition of water to on-board stored baking powder in combination with valving by an immiscible, high-specific weight liquid on a centrifugal microfluidic platform. This technology allows making efficient use of precious real estate near the center of rotation by enabling the placement of early sample preparation steps as well as reagent reservoirs at the spacious, high-field region on the perimeter of the disc-shaped rotor. This way the number of process steps and assays that can be integrated on these of this “Lab-on-a-Disc” (LoaD) cartridge can be significantly enhanced while maintaining minimum requirements on the intrinsically simple, spindle-motor based instrumentation.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Dublin City University
Authors: Kinahan, D. J. (Ekstern), Burger, R. (Intern), Vembadi, A. (Ekstern), Kilcawley, N. A. (Ekstern), Lawlor, D. (Ekstern), Glynn, M. T. (Ekstern), Ducree, J. (Ekstern)
Number of pages: 4
Pages: 504-507
Publication date: 2015

Host publication information
Title of host publication: Proceedings of 28th International Conference on Micro Electro Mechanical Systems (MEMS)
Publisher: IEEE
ISBN (Electronic): 978-1-4799-7955-4
Main Research Area: Technical/natural sciences
Conference: 28th International Conference on Micro Electro Mechanical Systems (MEMS), Estoril, Portugal, 18/01/2015 - 18/01/2015
DOIs: 10.1109/MEMSYS.2015.7051002
Source: Findit
Source-ID: 274206830
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015

Carbon nanopillars for stem cell differentiation and dopamine detection

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Biomaterial Microsystems, Polymer Microsystems for Cell Processing
Authors: Bunea, A. (Intern), Amato, L. (Intern), Heiskanen, A. (Intern), Keller, S. S. (Intern), Larsen, N. B. (Intern), Emnéus, J. (Intern)
Number of pages: 1
Publication date: 2015

Host publication information
Title of host publication: Book of Abstracts. DTU's Sustain Conference 2015
Place of publication: Lyngby
Publisher: Technical University of Denmark (DTU)
Article number: Q-3
Main Research Area: Technical/natural sciences
Conference: DTU Sustain Conference 2015, Lyngby, Denmark, 17/12/2015 - 17/12/2015
Electronic versions: Q3_DTU_Sustain_2015.pdf
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

Centrifugal Microfluidic Platform Using Supported Liquid Membrane Extraction for Combined Sample Clean-Up and Enrichment of Trace Analytes

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Andreasen, S. Z. (Intern), Burger, R. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
Number of pages: 1
Centrifugal Microfluidic Platform Using Supported Liquid Membrane Extraction for Combined Sample Clean-Up and Enrichment of Trace Analytes

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics
Authors: Andreasen, S. Z. (Intern), Burger, R. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015
Event: Poster session presented at Microfluidics Congress 2015, London, United Kingdom.
Main Research Area: Technical/natural sciences
Electronic versions:
GlobalEngagePoster_AndreasenSune.pdf
Source: PublicationPreSubmission
Source-ID: 118025081
Publication: Research - peer-review › Poster – Annual report year: 2015

Degradation studies of spray coated polymer films using cantilever sensors

General information
State: Published
Organisations: Center for Nanostructured Graphene, Department of Micro- and Nanotechnology, Amphiphilic Polymers in Biological Sensing, Nanoprobes, Biomaterial Microsystems, Department of Applied Mathematics and Computer Science, Cognitive Systems
Authors: Almdal, K. (Intern), Bose, S. (Intern), Keller, S. S. (Intern), Alstrøm, T. S. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015
Event: Poster session presented at Fourth International Symposium Frontiers in Polymer Science, Riva del Garda, Italy.
Main Research Area: Technical/natural sciences
Electronic versions:
Frontiers_2015_poster_A3.pdf
Source: PublicationPreSubmission
Source-ID: 110839877
Publication: Research - peer-review › Poster – Annual report year: 2015

Dense high-aspect ratio 3D carbon pillars on interdigitated microelectrode arrays
In this work we present high-aspect ratio carbon pillars (1.4 μm in diameter and ~11 μm in height) on top of interdigitated electrode arrays to be used for electrochemical applications. For this purpose, different types of 2D and 3D pyrolysed carbon structures were fabricated and characterised including surface- and microstructure, electrical and electrochemical properties. A pre-treatment of oxidised Si wafers is introduced to eliminate electrode delamination and ensure structure stability in water during long time-experiments. Additionally, a heat treatment method is reported for regeneration of pyrolysed carbon films with increased film resistance due to oxidation during storage.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Lund University, Capres A/S, Technical University of Denmark
Authors: Amato, L. (Intern), Heiskanen, A. (Intern), Hansen, R. (Ekstern), Gammelgaard, L. (Ekstern), Rindzevicius, T. (Intern), Tenje, M. (Ekstern), Emnéus, J. (Intern), Keller, S. S. (Intern)
Number of pages: 12
Pages: 792-803
Detection of bacterial metabolites through dynamic acquisition from surface enhanced raman spectroscopy substrates integrated in a centrifugal microfluidic platform

In this work we present a novel technology that combines the advantages of centrifugal microfluidics with dynamic in-situ Surface Enhanced Raman Spectroscopy (SERS) sensing. Our technology is based on an automated readout system that allows on-line SERS acquisition on a rotating centrifugal microfluidic platform with embedded gold nanopillar substrates. While spinning, the disc platform enables dynamic SERS acquisition of multiple chips, significantly reducing time-to-result and improving the reproducibility of the acquired spectra, reducing the fluctuation by a factor of 2.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Durucan, O. (Intern), Morelli, L. (Intern), Schmidt, M. S. (Intern), Burger, R. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Number of pages: 3
Pages: 1831-1833
Publication date: 2015

Host publication information
Title of host publication: 19th International Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2015
Publisher: Chemical and Biological Microsystems Society
ISBN (Electronic): 9780979806483
Main Research Area: Technical/natural sciences
Surface Enhanced Raman Spectroscopy (SERS), Dynamic SERS, Centrifugal microfluidics
Source: FindIt
Source-ID: 2342840484
Publication: Research - peer-review › Article in proceedings – Annual report year: 2016

Development of a SERS aptasensor for detection of medical residues
Low levels of medical residues in environmental, industrial and domestic water systems is a growing concern. The biosensor industry is trying to accomodate the need of sensitive and specific sensor systems capable of ultra-low level detection of medical residues. In this PhD project a surface enhanced Raman spectroscopy (SERS) sensor for the female sexhormone 17β-estradiol was attempted. It is commonly used in contraceptive pills from where it find its way through waste water treatment plants and into the environment. The SERS substrate was fabricated in a cleanroom facility using techniques well known from the electronics industry. The substrate consisted of silver or gold covered silicon nanopillars. The nanopillars were chemically functionalised with a DNA aptamer specific towards 17β-estradiol using thiol chemistry. At first, an entire functionalisation protocol was carried out to detect Estradiol Glow, which is fluorescently labelled 17β-estradiol. It was shown that Estradiol Glow exhibit very strong Raman activity and was such ideal for initial test. Since a large amount of data was gathered for this experiment it was necessary to develop an algorithm capable of analysing large data sets. Non-negative Matrix Factorization (NMF) was utilised to effectively improve the detection limit of the system by one order of magnitude.

Due to issues relating to the functionalisation protocol it was secondly investigated whether the aptamer was properly immobilised on the nanopillar surface. By hybridisation to a labelled complementary strand it was proven that aptamer was indeed immobilised. It was also found that stronger binding to the gold covered nanopillars could be obtained by a short treatment in reactive O₂ plasma. Likewise it was found that the addition of a detergent to the washing buffer had a great influence on the unspecific binding to the nanopillars.

A thorough study of the parameters influencing the degree of functionalisation was then conducted. By utilizing a developed peak-fitting model it was possibile to directly inspect the interplay between DNA aptamer and 6-mercapto-1-hexanol (MCH) used for blocking unspecific binding to gold. By inspecting the spectra of the molecules and their combination it was possible to observe attachment of DNA aptamer and MCH. Displacement/removal of DNA aptamer was also observed for high concentrations of MCH.

The final study was an attempt to detect pure 17β-estradiol using the developed functionalisation parameters. Unfortunately the inherent weak Raman signal of 17β-estradiol proved to faint for direct detection. Therefore Estradiol Glow was employed, however without success. Despite several attempts with varying degree of stringency successful detection was never accomplished.

In conclusion, this PhD project successfully characterised the chemical functionalisation parameters needed for generic SERS aptasensor development using only the Raman signals of the molecules. The SERS substrate was successfully fabricated repeatedly and showed great enhancement of Raman signals. Two analysis methods (NMF and peak-fitting) was developed in collaboration with DTU Compute in order to accomodate for the large amount of data gathered.
throughout the project. This work displays the complexity in SERS aptasensor development, which is needed for sensitive and selective capture of medical residues.

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Surface Engineering, Nanoprobes
Authors: Frøhling, K. B. (Intern), Jakobsen, M. H. (Intern), Boisen, A. (Intern), Bache, M. (Intern)
Number of pages: 162
Publication date: 2015

**Publication information**
Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
PhD_Thesis_web.pdf
Source: PublicationPreSubmission
Source-ID: 117515076
Publication: Research › Ph.D. thesis – Annual report year: 2015

**Exploring Plasmonic Resonances of Silver Capped Silicon Nanopillars**

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Fluidic Array Systems and Technology
Authors: Wu, K. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Mogensen, K. B. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015

**Host publication information**
Title of host publication: Proceedings of the 7th International Conference on Surface Plasmon Photonics
Main Research Area: Technical/natural sciences
Conference: 7th International Conference on Surface Plasmon Photonics, Jerusalem, Israel, 31/05/2015 - 31/05/2015
Electronic versions:
Kaiyu_SPP7_ABSTRACT_v1_mssc_comments.pdf
Source: PublicationPreSubmission
Source-ID: 110867882
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

**Explosive and chemical threat detection by surface-enhanced Raman scattering: A review**

Acts of terror and warfare threats are challenging tasks for defense agencies around the world and of growing importance to security conscious policy makers and the general public. Explosives and chemical warfare agents are two of the major concerns in this context, as illustrated by the recent Boston Marathon bombing and nerve gas attacks on civilians in the Middle East. To prevent such tragic disasters, security personnel must be able to find, identify and deactivate the threats at multiple locations and levels. This involves major technical and practical challenges, such as detection of ultra-low quantities of hazardous compounds at remote locations for anti-terror purposes and monitoring of environmental sanitation of dumped or left behind toxic substances and explosives. Surface-enhanced Raman scattering (SERS) is one of today’s most interesting and rapidly developing methods for label-free ultrasensitive vibrational "fingerprinting" of a variety of molecular compounds. Performance highlights include attomolar detection of TNT and DNT explosives, a sensitivity that few, if any, other technique can compete with. Moreover, instrumentation needed for SERS analysis are becoming progressively better, smaller and cheaper, and can today be acquired for a retail price close to 10,000 US$. This contribution aims to give a comprehensive overview of SERS as a technique for detection of explosives and chemical threats. We discuss the prospects of SERS becoming a major tool for convenient in-situ threat identification and we summarize existing SERS detection methods and substrates with particular focus on ultra-sensitive real-time detection. General concepts, detection capabilities and perspectives are discussed in order to guide potential users of the technique for homeland security and anti-warfare purposes.

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Chalmers University of Technology, Swedish Defence Research Agency
Authors: Hakonen, A. (Ekstern), Andersson, P. O. (Ekstern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Käll, M. (Ekstern)
Fabrication and improvement of nanopillar InGaN/GaN light-emitting diodes using nanosphere lithography

Surface-patterning technologies have enabled the improvement of currently existing light-emitting diodes (LEDs) and can be used to overcome the issue of low quantum efficiency of green GaN-based LEDs. We have applied nanosphere lithography to fabricate nanopillars on InGaN/GaN quantum-well LEDs. By etching through the active region, it is possible to improve both the light extraction efficiency and, in addition, the internal quantum efficiency through the effects of lattice strain relaxation. Nanopillars of different sizes are fabricated and analyzed using Raman spectroscopy. We have shown that nanopillar LEDs can be significantly improved by applying a combination of ion-damage curing techniques, including thermal and acidic treatment, and have analyzed their effects using x-ray photoelectron spectroscopy.

General information
State: Published
Organisations: Department of Photonics Engineering, Diode Lasers and LED Systems, Department of Micro- and Nanotechnology, Nanoprobes, Chinese Academy of Sciences, Lund University
Number of pages: 9
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Nanophotonics
Volume: 9
Article number: 093062
ISSN (Print): 1934-2608
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.551 SJR 0.438
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.518 SNIP 0.618 CiteScore 1.17
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.61 SNIP 0.661 CiteScore 1.34
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.584 SNIP 0.644 CiteScore 1.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.723 SNIP 0.751 CiteScore 1.2
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.893 SNIP 0.828 CiteScore 1.16
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.998 SNIP 1.209 CiteScore 1.59
ISI indexed (2011): ISI indexed no
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.015 SNIP 0.862
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.938 SNIP 1.072
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.614 SNIP 0.981
Original language: English
Light-emitting diodes, Gallium nitride, Nanopillar, Damage treatment
DOIs:
Fabrication and loading of microcontainers for oral drug delivery

Oral drug delivery is considered as the most patient compliant delivery route. However, it faces many obstacles, especially due to the ever-increasing number of drugs that are poorly soluble and barely absorbed in the gastro-intestinal tract. Moreover, drugs can degrade in the harsh acidic environment of stomach before they reach the intestine. These issues lead to reduced bioavailability of active ingredients. To combat that novel oral drug delivery systems have been developed. Some of these systems that have gained significant interest in this field are reservoir based drug delivery microdevices. These microreservoir based-systems have dimension ranging from 10 μm to 500 μm. Additional functionalities are added to control the site and profile of drug release through mucoadhesive layers, asymmetric geometry and unidirectional drug release. Most of these devices have been fabricated using microfabrication methods with materials such as Si and photoresists. However, there is a need to shift from these materials towards biocompatible and biodegradable polymers such as poly-l-lactic acid (PLLA) or poly-e-caprolactone (PCL). Hot embossing is one of the most viable and matured methods to fabricate microstructures in such biopolymers. However, hot embossing is unable to produce discrete 3D microdevices due to the inherent problem of a residual layer that connects all the microdevices to each other. Therefore, hot punching which is combination of hot embossing and mechanical punching has been developed in this project. This process utilizes a stamp in connection with the ability to apply heat and pressure to transfer the stamp pattern to a film. Processes have been optimized for fabrication of nickel stamps with two layered, high aspect ratio microstructures. Bosch deep reactive ion etching of Silicon producing sloped sidewalls required for stamp production has been developed. The sloped sidewalls ensure a successful separation of stamp and film after patterning. High aspect ratio, 3D, discrete microcontainers in PLLA and PCL are fabricated using hot punching. High throughput and replication fidelity is achieved. Characterization of spin coating of drug-polymer films is thoroughly performed using microscopy, profilometry, differential scanning calorimetry, Raman spectroscopy, X-ray diffraction and microdissolution release tests. These films are applied for loading of microcontainers. Furosemide which is an important loop diuretic drug with low solubility and permeability is used as a model drug and embedded in a PCL matrix. The crystallinity of the drug is tailored by the process parameters of spin coating. Release profiles ranging from rapid burst release to sustained zero-order release are obtained by tuning spin coating. The hot punching technique is then applied for loading of microcontainers with the spin coated drug-polymer matrix. It has been demonstrated that hot punching is a fast, parallel, single step process that can load containers with high yield. Furthermore, the drug-polymer matrix loaded in the containers is characterized using the above mentioned techniques. Finally, zero-order sustained release of furosemide drug from microcontainers is successfully demonstrated.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Petersen, R. S. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Number of pages: 176
Publication date: 2015
Fabrication of Ni stamp with high aspect ratio, two-leveled, cylindrical microstructures using dry etching and electroplating:

Paper

We describe a process for the fabrication of a Ni stamp that is applied to the microstructuring of polymers by hot embossing. The target devices are microcontainers that have a potential application in oral drug delivery. Each container is a 3D, cylindrical, high aspect ratio microstructure obtained by defining a reservoir and a separating trench with different depths of 85 and 125 μm, respectively, in a single embossing step. The fabrication of the required two leveled stamp is done using a modified DEEMO (dry etching, electroplating and molding) process. Dry etching using the Bosch process and electroplating are optimized to obtain a stamp with smooth stamp surfaces and a positive sidewall profile. Using this stamp, hot embossing is performed successfully with excellent yield and high replication fidelity.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Individual Nanoparticle Functionality, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Petersen, R. S. (Intern), Keller, S. S. (Intern), Hansen, O. (Intern), Boisen, A. (Intern)
Number of pages: 12
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information

Journal: Journal of Micromechanics and Microengineering
Volume: 25
Issue number: 5
Article number: 055021
ISSN (Print): 0960-1317
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.968 SJR 0.554
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.74 SJR 0.63 SNIP 1.067
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.687 SNIP 1.265 CiteScore 1.96
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.802 SNIP 1.316 CiteScore 1.84
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.737 SNIP 1.233 CiteScore 1.74
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.936 SNIP 1.491 CiteScore 1.92
Fiber-Based, Injection-Molded Optofluidic Systems: Improvements in Assembly and Applications

We present a method to fabricate polymer optofluidic systems by means of injection molding that allow the insertion of standard optical fibers. The chip fabrication and assembly methods produce large numbers of robust optofluidic systems that can be easily assembled and disposed of, yet allow precise optical alignment and improve delivery of optical power. Using a multi-level chip fabrication process, complex channel designs with extremely vertical sidewalls, and dimensions that range from few tens of nanometers to hundreds of microns can be obtained. The technology has been used to align optical fibers in a quick and precise manner, with a lateral alignment accuracy of 2.7 ± 1.8 μm. We report the production, assembly methods, and the characterization of the resulting injection-molded chips for Lab-on-Chip (LoC) applications. We demonstrate the versatility of this technology by carrying out two types of experiments that benefit from the improved optical system: optical stretching of red blood cells (RBCs) and Raman spectroscopy of a solution loaded into a hollow core fiber. The advantages offered by the presented technology are intended to encourage the use of LoC technology for commercialization and educational purposes.
Hot embossing and mechanical punching of biodegradable microcontainers for oral drug delivery

A process has been developed to fabricate discrete three-dimensional microcontainers for oral drug delivery application in Poly-L-Lactic Acid (PLLA) polymer. The method combines hot embossing for the definition of holes in a PLLA film and mechanical punching to penetrate the polymer layer around the holes, after filling them with drug. Here, we demonstrate the fabrication of microcontainers with a diameter of 340 lm and a height of 50 lm. The process is temperature benign so that the compositional integrity of the drug is preserved. It also provides a good flexibility for creating different sizes and shapes of microcontainers. Finally, the process is compatible with roll-to-roll processing that could lead to low cost high volume production. © 2014 Elsevier B.V. All rights reserved.
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.737 SNIP 0.949 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.813 SNIP 1.148 CiteScore 1.8
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.934 SNIP 1.093
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.834 SNIP 1.098
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.027 SNIP 1.06
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.045 SNIP 1.138
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.966 SNIP 1.093
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.952 SNIP 0.989
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1 SNIP 1.1
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.812 SNIP 0.956
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.712 SNIP 0.711
Scopus rating (2001): SJR 0.558 SNIP 0.645
Scopus rating (2000): SJR 0.502 SNIP 0.568
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.595 SNIP 0.555
Original language: English
Hot embossing, Mechanical punching, Biodegradable polymer, Drug delivery, Microcontainers
Hot punching of high-aspect-ratio 3D polymeric microstructures for drug delivery


General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Petersen, R. S. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern)
Number of pages: 4
Pages: 2576-2579
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Lab on a Chip
Volume: 15
Issue number: 12
ISSN (Print): 1473-0197
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.586 SJR 2.158
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.98 SJR 2.162 SNIP 1.569
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.239 SNIP 1.721 CiteScore 5.74
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.555 SNIP 1.797 CiteScore 5.6
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.397 SNIP 1.693 CiteScore 5.9
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.405 SNIP 1.731 CiteScore 5.35
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 2.54 SNIP 1.788 CiteScore 5.76
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.718 SNIP 1.876
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.673 SNIP 2.164
Hydrodynamics studies of cyclic voltammetry for electrochemical micro biosensors

We investigate the effect of flow rate on the electrical current response to the applied voltage in a micro electrochemical system. To accomplish this, we considered an ion-transport model that is governed by the Nernst-Planck equation coupled to the Navier-Stokes equations for hydrodynamics. The Butler-Volmer relation provides the boundary conditions, which represent reaction kinetics at the electrode-electrolyte interface. The result shows that convection drastically affects the rate of surface kinetics. At a physically sufficient high flow rates and lower scan rates, the current response is limited by the convection due to fresh ions being brought to the electrode surface and immediately taken away before any surface reaction. However, at high flow and scan rates, the Faradaic current overrides current due to convection. The model also allows predicting the effect of varying electrolyte concentration and scan rates respectively.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Adesokan, B. J. (Intern), Quan, X. (Intern), Evgrafov, A. (Intern), Heiskanen, A. (Intern), Boisen, A. (Intern)
Number of pages: 5
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Physics: Conference Series (Online)
Volume: 574
Issue number: 012008
ISSN (Print): 1742-6596
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.447 SJR 0.241
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.45 SJR 0.24 SNIP 0.401
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Impedimetric Toxicity Assay Evaluating Free and Liposome-loaded Anticancer drugs

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Colloids and Biological Interfaces, Bioanalytics, University of Genoa, Politecnico di Milano
Authors: Caviglia, C. (Intern), Garbarino, F. (Intern), Zor, K. (Intern), Brogaard, R. Y. (Intern), Melander, F. (Intern), Eliassen, R. (Intern), Carminati, M. (Ekstern), Ferrari, G. (Ekstern), Raiteri, R. (Ekstern), Andresen, T. L. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from XXIII International Symposium on Bioelectrochemistry and Bioenergetics, Malmö, Sweden.
Main Research Area: Technical/natural sciences
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015
Impedimetric toxicity assay in microfluidics using free and liposome-encapsulated anticancer drugs

In this work, we have developed a microfluidic cytotoxicity assay for a cell culture and detection platform, which enables both fluid handling and electrochemical/optical detection. The cytotoxic effect of anticancer drugs doxorubicin (DOX), oxaliplatin (OX) as well as OX-loaded liposomes, developed for targeted drug delivery, was evaluated using real-time impedance monitoring. The time-dependent effect of DOX on HeLa cells was monitored and found to have a delayed onset of cytotoxicity in microfluidics compared with static culture conditions based on data obtained in our previous study. The result of a fluorescent microscopic annexin V/propidium iodide assay, performed in microfluidics, confirmed the outcome of the real-time impedance assay. In addition, the response of HeLa cells to OX-induced cytotoxicity proved to be slower than toxicity induced by DOX. A difference in the time-dependent cytotoxic response of fibrosarcoma cells (HT1080) to free OX and OX-loaded liposomes was observed and attributed to incomplete degradation of the liposomes, which results in lower drug availability. The matrix metalloproteinase (MMP)-dependent release of OX from OX-loaded liposomes was also confirmed using laryngopharynx carcinoma cells (FaDu). The comparison and the observed differences between the cytotoxic effects under microfluidic and static conditions highlight the importance of comparative studies as basis for implementation of microfluidic cytotoxic assays.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Molecular Windows, Colloids and Biological Interfaces, Bioanalytics, University of Siena, University of Genoa, Politecnico di Milano
Authors: Caviglia, C. (Intern), Zor, K. (Intern), Montini, L. (Ekstern), Tilli, V. (Ekstern), Canepa, S. (Intern), Melander, F. (Intern), Larsen, L. B. (Intern), Carminati, M. (Ekstern), Ferrari, G. (Ekstern), Raiteri, R. (Ekstern), Heiskanen, A. (Intern), Andresen, T. L. (Intern), Emnéus, J. (Intern)
Number of pages: 9
Pages: 2204-2212
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Analytical Chemistry
Volume: 87
Issue number: 4
ISSN (Print): 0003-2700
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.08
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 6
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 5.79
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 6.01
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 5.8
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 5.86
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Integrating Electrochemical Detection with Centrifugal Microfluidics for Real-Time and Fully Automated Sample Testing

Here we present a robust, stable and low-noise experimental set-up for performing electrochemical detection on a centrifugal microfluidic platform. By using a low-noise electronic component (electrical slip-ring) it is possible to achieve continuous, on-line monitoring of electrochemical experiments, even when the microfluidic disc is spinning at high velocities. Automated sample handling is achieved by designing a microfluidic system to release analyte sequentially, utilizing on-disc passive valving. In addition, the microfluidic system is designed to trap and keep the liquid sample stationary during analysis. In this way it is possible to perform cyclic voltammetry (CV) measurements at varying spin speeds, without altering the electrochemical response. This greatly simplifies the interpretation and quantification of data. Finally, real-time and continuous monitoring of an entire electrochemical experiment, including all intermediate sample handling steps, is demonstrated by amperometric detection of on-disc mixing of analytes (PBS and ferricyanide).

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Andreasen, S. Z. (Intern), Kwasny, D. (Intern), Amato, L. (Intern), Brøgger, A. L. (Intern), Bosco, F. (Intern), Andersen, K. B. (Intern), Svendsen, W. E. (Intern), Boisen, A. (Intern)
Pages: 17187–17193
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: R S C Advances
Volume: 5
ISSN (Print): 2046-2069
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.736 SJR 0.863
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.06 SJR 0.889 SNIP 0.757
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.947 SNIP 0.834 CiteScore 3.42
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.113 SNIP 0.962 CiteScore 3.87
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.119 SNIP 0.904 CiteScore 3.74
We present a novel strategy for thrombin detection by combining a magnetic bead-based agglutination assay and a low-cost microfluidic disc. The detection method is based on an optomagnetic readout system implemented using a Blu-ray optical pickup unit (OPU) as a main optoelectronic component. The assay, from sample to answer, is fully integrated on a microfluidic disc which embeds on-disc mixing ensuring full automation of the assay along with less sample-to-answer time compared to similar methods. Moreover, we compare the optomagnetic readout to the cluster size distribution determined using a commercial optical scanning imaging instrument.
Interdependence of initial cell density, drug concentration and exposure time revealed by real-time impedance spectroscopic cytotoxicity assay

We investigated the combined effect of the initial cell density (12,500, 35,000, 75,000, and 100,000 cells cm\(^{-2}\)) and concentration of the anti-cancer drug doxorubicin on HeLa cells by performing time-dependent cytotoxicity assays using real-time electrochemical impedance spectroscopy. A correlation between the rate of cell death and the initial cell seeding density was found at 2.5 μM doxorubicin concentration, whereas this was not observed at 5 or 100 μM. By sensing the changes in the cell–substrate interaction using impedance spectroscopy under static conditions, the onset of cytotoxicity was observed 5 h earlier than when using a standard colorimetric end-point assay (MTS) which measures changes in the mitochondrial metabolism. Furthermore, with the MTS assay no cytotoxicity was observed after 15 h of incubation with 2.5 μM doxorubicin, whereas the impedance showed at this time point cell viability that was below 25%. These results indicate that impedance detection reveals cytotoxic events undetectable when using the MTS assay, highlighting the importance of combining impedance detection with traditional drug toxicity assays towards a more in depth understanding of the effect of anti-cancer drugs on in vitro assays. Moreover, the detection of doxorubicin induced toxicity determined with impedance under static conditions proved to be 6 times faster than in perfusion culture.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Molecular Windows, Colloids and Biological Interfaces, University of Genoa, Politecnico di Milano
Authors: Caviglia, C. (Intern), Zor, K. (Intern), Canepa, S. (Intern), Carminati, M. (Ekstern), Larsen, L. B. (Intern), Raiteri, R. (Ekstern), Andresen, T. L. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern)
Number of pages: 7
Pages: 3623-3629
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Analyst
Volume: 140
Issue number: 10
ISSN (Print): 0003-2654
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.92
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.11
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.88
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.16
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
Interdigitated Carbon Electrodes for Stem Cell Differentiation and Dopamine Detection

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Polymer Microsystems for Cell Processing, Biomaterial Microsystems
Authors: Bunea, A. (Intern), Amato, L. (Intern), Heiskanen, A. (Intern), Larsen, N. B. (Intern), Keller, S. S. (Intern), Emnéus, J. (Intern)
Publication date: 2015
Event: Poster session presented at XXIII International Symposium on Bioelectrochemistry and Bioenergetics, Malmö, Sweden.
Main Research Area: Technical/natural sciences
Links:
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Luminescence enhancement of green InGaN/GaN nanopillar LEDs

General information
State: Published
Organisations: Department of Photonics Engineering, Diode Lasers and LED Systems, Department of Micro- and Nanotechnology, Nanoprobes, Tokyo University of Technology
Number of pages: 2
Publication date: 2015
Main Research Area: Technical/natural sciences
Electronic versions:
Maskless Nanostructure Definition of Submicron Rear Contact Areas for Advanced Solar Cell Designs

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes
Authors: Davidsen, R. S. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2015
Main Research Area: Technical/natural sciences

Mathematical model for biomolecular quantification using large-area surface-enhanced Raman spectroscopy mapping
Surface-enhanced Raman spectroscopy (SERS) based on nanostructured platforms is a promising technique for quantitative and highly sensitive detection of biomolecules in the field of analytical biochemistry. Here, we report a mathematical model to predict experimental SERS signal (or hotspot) intensity distributions of target molecules on receptor-functionalized nanopillar substrates for biomolecular quantification. We demonstrate that by utilizing only a small set of empirically determined parameters, our general theoretical framework agrees with the experimental data particularly well in the picomolar concentration regimes. This developed model may be generally used for biomolecular quantification using Raman mapping on SERS substrates with planar geometries, in which the hotspots are approximated as electromagnetic enhancement fields generated by closely spaced dimers. Lastly, we also show that the detection limit of a specific target molecule, TAMRA-labeled vasopressin, approaches the single molecule level, thus opening up an exciting new chapter in the field of SERS quantification.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Applied Mathematics and Computer Science, Cognitive Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Harvard University, Columbia University
Authors: Palla, M. (Ekstern), Bosco, F. (Intern), Yang, J. (Ekstern), Rindzevicius, T. (Intern), Alstrøm, T. S. (Intern), Schmidt, M. S. (Intern), Lin, Q. (Ekstern), Ju, J. (Ekstern), Boisen, A. (Intern)
Pages: 85845-85853
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: RSC Advances
Volume: 5
Issue number: 104
ISSN (Print): 2046-2069
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.736 SJR 0.863
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.06 SJR 0.889 SNIP 0.757
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.947 SNIP 0.834 CiteScore 3.42
This paper presents the development of a novel statistical method for quantifying trace amounts of biomolecules by surface-enhanced Raman spectroscopy (SERS) using a rigorous, single molecule (SM) theory based mathematical derivation. Our quantification framework could be generalized for planar SERS substrates, in which the nanostructured features can be approximated as a closely spaced electromagnetic dimer problem. The potential for SM detection was also shown, which opens up an exciting opportunity in the field of SERS quantification.

Method for manufacturing carrier containing e.g. proteins for human during oral drug delivery operation for food and drug administration application in pharmaceutical industry, involves providing active ingredient to core layer

NOVELTY - The method involves preparing a multi-layered film comprising a core layer and a barrier layer, where the core layer comprises active ingredient. The multi-layered film is subjected to a hot embossing step using an embossing stamp including protrusions that allows for generation of the micro-containers containing an active ingredient or containing a core layer that is configured to accept the active ingredient such that the barrier layer partially encloses the core layer. The active ingredient is provided to the core layer when the core layer is configured to accept the active ingredient.

USE - Method for manufacturing a multi-layered micro-container i.e. carrier, containing an active ingredient e.g. small organic molecules, proteins, peptides, vitamins, antibodies, antibody fragments, vaccines, RNA, DNA and antibiotics, for a patient e.g. human and animal, during an oral drug delivery operation for a food and drug administration (FDA) application in a pharmaceutical industry.
ADVANTAGE - The method enables allowing an individual micro-structure stuck in an embossing stamp to be demolded under the conditions such that demolding operation is done by treating elastically or plastically deformable layer to increase stiction of the release layer. The method enables manufacturing the micro-container including an outer diameter of 200-500 μm and a height of 2-70 μm such that wall thickness is larger than 5 μm to increase geometrical stability and reduce buckling. The method enables manufacturing a multi-layered micro-container to enable unidirectional release at a site of absorption, thus increasing bioavailability of drugs.

DETAILED DESCRIPTION - The barrier layer is made out of polycaprolactone (PCL), polylactic acid (PLA), polyglycolic acid (PGA), hydroxypropylmethyl cellulose (HPMC), polymethacrylate (PMMA), Eudragits Poly-methacylic acid-co-methyl methacrylate, ethyl cellulose (EC), polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), polyethylene glycol methacrylate (PEGMA), polyethylene glycol dimethacrylate (PEGDMA), poly-lactic-co-glycolic acid (PLGA), polyacrylic acid (PAA) and copolymer. An INDEPENDENT CLAIM is also included for a micro-container.

Method of Manufacturing A Porous Polymer Component Involving Use of A Dissolvable, Sacrificial Material

The present invention relates to a method of manufacturing a porous polymer component 1 with structured and/or random pores 4 and/or channels 5. The method comprises arranging a dissolvable, sacrificial material 2 in a geometrical arrangement corresponding to an inner structure to be obtained in the polymer component 1. A component material 3, which is to form the final component 1, is arranged so that it surrounds at least a majority of the sacrificial material 2, and subsequently the sacrificial material 2 is dissolved and removed from the component material 3. The sacrificial material 2 and thereby the resulting inner structure of the component 1 is arranged in a controlled and reproducible manner. The sacrificial material 2 and possibly also the component material 3 may e.g. be arranged by use of a 3D-printer or manually. The method may e.g. be used to manufacture a three-dimensional scaffold for tissue engineering.

Microcantilever sensors for fast analysis of enzymatic degradation of poly (D, L-lactide)

In this work we have performed a detailed analysis of enzymatic degradation of amorphous poly (d, l-lactide) (PDLLA) by measuring the resonance frequencies of polymer coated microcantilevers before and after degradation. The miniaturized cantilever system provides a fast analysis of the biodegradation rate of PDLLA with a minute amount of sample and without the need of thermal and chemical acceleration. The degradation rate of the polymer has been estimated by multilayer cantilever theory and model simulation. A bulk degradation rate of 0.24 μg mm⁻² hour⁻¹ is estimated which
agrees well with values reported in literature. The role of enzyme concentrations, pre-hydration in buffer, surface morphologies of PDLLA films and adsorption time of enzymes on the rate of degradation has been investigated. An increase in degradation rate is observed with an increase in enzyme concentration and after pre-hydration in buffer. A polymer film with a non-uniform surface degrades faster than the uniform one due to the preference of enzyme attack at film defects. A threshold time of around 3 h is estimated for irreversible enzyme adsorption on the polymer surface after which degradation can proceed even in buffer solution in the absence of enzyme.
Microcontainers - an oral drug delivery system for poorly soluble drugs

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Petersen, R. S. (Intern), Marizza, P. (Intern), Keller, S. S. (Intern), Melero, A. (Ekstern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2015
Event: Abstract from 2015 AAPS Annual Meeting and Exposition, Orlando, FL, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
Abstract_AAPS_2015_microcontainers.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 118685843
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Microcontainers as an oral drug delivery system

General information
State: Published
Organisations: Biomaterial Microsystems, Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, University of Copenhagen
Authors: Petersen, R. S. (Intern), Nielsen, L. H. (Intern), Marizza, P. (Intern), Keller, S. S. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015

Host publication information
Title of host publication: Book of Abstracts. DTU's Sustain Conference 2015
Place of publication: Lyngby
Publisher: Technical University of Denmark (DTU)
Article number: Q-5
Main Research Area: Technical/natural sciences
Conference: DTU Sustain Conference 2015, Lyngby, Denmark, 17/12/2015 - 17/12/2015
Electronic versions:
Q5_DTU_Sustain_2015.pdf
Microcontainers improve oral bioavailability of furosemide

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Biomaterial Microsystems, University of Valencia, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Melero, A. (Ekstern), Keller, S. S. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015
Event: Poster session presented at 1st European Conference on Pharmaceutics, Reims, France.
Main Research Area: Technical/natural sciences
Electronic versions:
Poster_Reims_2015_LHN.pdf
Source: PublicationPreSubmission
Source-ID: 110810681
Publication: Research - peer-review › Poster – Annual report year: 2015

Micromechanical Fast Quasi-Static Detection of α and β Relaxations with Nanograms of Polymer
Micromechanical string resonators are used as a highly sensitive tool for the detection of glass transition (Tg or α relaxation) and sub-Tg (β relaxation) temperatures of polystyrene (PS) and poly (methyl methacrylate) (PMMA). The characterization technique allows for a fast detection of mechanical relaxations of polymers with only few nanograms of sample in a quasi-static condition. The polymers are spray coated on one side of silicon nitride (SiN) microstrings. These are pre-stressed suspended structures clamped on both ends to a silicon frame. The resonance frequency of the microstrings is then monitored as a function of increasing temperature. α and β relaxations in the polymer affect the net static tensile stress of the microstring and result in measurable local frequency slope maxima. Tg of PS and PMMA is detected at 91 ±2°C and 114 ±2°C, respectively. The results match well with the glass transition values of 93.6°C and 114.5°C obtained from differential scanning calorimetry of PS and PMMA, respectively. The β relaxation temperatures are detected at 30 ±2°C and 33 ±2°C for PS and PMMA which is in accordance with values reported in literature.

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes, Amphiphilic Polymers in Biological Sensing, Stanford University
Authors: Bose, S. (Intern), Schmid, S. (Intern), Larsen, T. (Ekstern), Keller, S. S. (Intern), Boisen, A. (Intern), Almdal, K. (Intern)
Pages: 1035-1039
Publication date: 2015
Main Research Area: Technical/natural sciences
Novel Nanostructured Electrodes Obtained by Pyrolysis of Composite Polymeric Materials

In this work, we compare pyrolyzed carbon derived from the photoresist SU‐8 alone or in combination with polystyrene and poly(styrene)-block-poly(dimethylsiloxane) copolymer (PS-b-PDMS), to be used as novel materials for micro- and nanoelectrodes. The pyrolyzed carbon films are evaluated with scanning electron microscopy, thermal gravimetric analysis, X‐ray photoelectron spectroscopy, contact angle analysis, and Raman spectroscopy. Furthermore, the standard rate constant for electron transfer is determined from cyclic voltammograms and found to be lower for PS‐b‐PDMS compared to PS and SU‐8 films. This may be related to the lower carbon content of PS-b-PDMS, as well as to its higher microstructural disorder.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Self-Organized Nanoporous Materials, Bioanalytics, Biomaterial Microsystems, Center for Nanostructured Graphene
Authors: Amato, L. (Intern), Schulte, L. (Intern), Heiskanen, A. (Intern), Keller, S. S. (Intern), Ndoni, S. (Intern), Emnéus, J. (Intern)
Number of pages: 6
Pages: 1544-1549
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Electroanalysis
Volume: 27
Issue number: 7
ISSN (Print): 1040-0397
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.643 SJR 0.692
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.673 SNIP 0.712 CiteScore 2.57
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.671 SNIP 0.727 CiteScore 2.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.672 SNIP 0.761 CiteScore 2.26
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.861 SNIP 0.894 CiteScore 2.74
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.11 SNIP 0.857 CiteScore 2.86
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.017 SNIP 0.877 CiteScore 2.86
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.087 SNIP 0.851
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.027 SNIP 0.896
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.313 SNIP 0.892
Web of Science (2008): Indexed yes
Novel Readout Method for Molecular Diagnostic Assays Based on Optical Measurements of Magnetic Nanobead Dynamics

We demonstrate detection of DNA coils formed from a Vibrio cholerae DNA target at picomolar concentrations using a novel optomagnetic approach exploiting the dynamic behavior and optical anisotropy of magnetic nanobead (MNB) assemblies. We establish that the complex second harmonic optical transmission spectra of MNB suspensions measured upon application of a weak uniaxial AC magnetic field correlate well with the rotation dynamics of the individual MNBs. Adding a target analyte to the solution leads to the formation of permanent MNB clusters, namely, to the suppression of the dynamic MNB behavior. We prove that the optical transmission spectra are highly sensitive to the formation of permanent MNB clusters and, thereby to the target analyte concentration. As a specific clinically relevant diagnostic case, we detect DNA coils formed via padlock probe recognition and isothermal rolling circle amplification and benchmark against a commercial equipment. The results demonstrate the fast optomagnetic readout of rolling circle products from bacterial DNA utilizing the dynamic properties of MNBs in a miniaturized and low-cost platform requiring only a transparent window in the chip.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Silicon Microtechnology, Uppsala University, Stockholm University, CIC nanoGUNE Consolider
Pages: 1622-1629
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Analytical Chemistry
Volume: 87
ISSN (Print): 0003-2700
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.08
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 6
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 5.79
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 6.01
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 5.8
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 5.86
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 2
Web of Science (2008): Indexed yes
Web of Science (2007): Indexed yes
Web of Science (2006): Indexed yes
Web of Science (2005): Indexed yes
Web of Science (2004): Indexed yes
Web of Science (2003): Indexed yes
Web of Science (2002): Indexed yes
Web of Science (2000): Indexed yes
Original language: English
DOIs: 10.1021/ac503191v
Source: PublicationPreSubmission
Source-ID: 105335096
Publication: Research - peer-review › Journal article – Annual report year: 2015

**On-line monitoring of 2D and 3D cell cultures: electrode configurations for impedance based sensors**

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Biomaterial Microsystems, Nanoprobes, Colloids and Biological Interfaces, BioLabChip, Fluidic Array Systems and Technology, University of Oslo
Number of pages: 2
Publication date: 2015
Event: Abstract from World Congress on Medical Physics and Biomedical Engineering 2015, Toronto, Canada.
Main Research Area: Technical/natural sciences
Electronic versions: Canali_2_IUPESM15.pdf

**Relations**
Activities:
World Congress on Medical Physics and Biomedical Engineering 2015
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

**Parallelized system for biopolymer degradation studies through automated microresonator measurement in liquid flow**
In this work we present a novel automated system which allows the study of enzymatic degradation of biopolymer films coated on micromechanical resonators. The system combines an optical readout based on Blu-Ray technology with a software-controlled scanning mechanism. Integrated with a microfluidic setup unit, the system allows high-throughput measurements of resonance frequency over microresonator arrays under controlled flow conditions. We here demonstrate the acquisition of statistical data on biopolymer films degradation under enzymatic reaction over a large sample of
Micromechanical resonators. The system has been proved to be able to perform measurements both in air and in liquid environment.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Academia Sinica Taiwan
Authors: Casci Ceccacci, A. (Intern), Morelli, L. (Intern), Bosco, F. (Intern), Burger, R. (Intern), Chen, C. H. (Ekstern), Hwu, E. T. (Ekstern), Boisen, A. (Intern)
Number of pages: 3
Pages: 1870-1872
Publication date: 2015

Host publication information
Title of host publication: 19th International Conference on Miniaturized Systems for Chemistry and Life Sciences, MicroTAS 2015
Publisher: Chemical and Biological Microsystems Society
ISBN (Electronic): 9780979806483
Main Research Area: Technical/natural sciences
Control and Systems Engineering, Automation, Biomolecules, Resonators, Blu-ray technology, Enzymatic Degradation, Enzymatic reaction, High-throughput measurements, Liquid environment, Micro-resonator arrays, Resonance frequencies, Scanning mechanisms, Micromechanical resonators
Source: FindIt
Source-ID: 2342835041
Publication: Research - peer-review › Article in proceedings – Annual report year: 2016

pH-triggered drug release from biodegradable microwells for oral drug delivery
Microwells fabricated from poly-L-lactic acid (PLLA) were evaluated for their application as an oral drug delivery system using the amorphous sodium salt of furosemide (ASSF) as a model drug. Hot embossing of PLLA resulted in fabrication of microwells with an inner diameter of 240 μm and a height of 100 μm. The microwells were filled with ASSF using a modified screen printing technique, followed by coating of the microwell cavities with a gastroresistant lid of Eudragit® L100. The release behavior of ASSF from the coated microwells was investigated using a μ-Diss profiler and a UV imaging system, and under conditions simulating the changing environment of the gastrointestinal tract. Biorelevant gastric medium (pH 1.6) was employed, after which a change to biorelevant intestinal release medium (pH 6.5) was carried out. Both μ-Diss profiler and UV imaging release experiments showed that sealing of microwell cavities with an Eudragit® layer prevented drug release in biorelevant gastric medium. An immediate release of the ASSF from coated microwells was observed in the intestinal medium. This pH-triggered release behavior demonstrates the future potential of PLLA microwells as a site-specific oral drug delivery system.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Saarland University, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Nagstrup, J. (Intern), Gordon, S. (Ekstern), Keller, S. S. (Intern), Østergaard, J. (Ekstern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 7
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Biomedical Microdevices
Volume: 17
Issue number: 3
ISSN (Print): 1387-2176
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.639 SJR 0.538
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.29 SJR 0.606 SNIP 0.743
Web of Science (2016): Indexed yes
Biodegradable polymer, Oral drug delivery, Micro delivery systems, Furosemide, μ-Diss profiler, UV imaging

Plasmon resonances of Ag capped Si nanopillars fabricated using mask-less lithography.
Localized surface plasmon resonances (LSPR) and plasmon couplings in Ag capped Si Nanopillar (Ag NP) structures are studied using 3D FEM simulations and dark-field scattering microscopy. Simulations show that a standalone Ag NP supports two LSPR modes, i.e. the particle mode and the cavity mode. The LSPR peak position of the particle mode can be tuned by changing the size of the Ag cap, and can be hybridized by leaning of pillars. The resonance position of the cavity resonance mode can be tuned primarily via the diameter of the Si pillar, and cannot be tuned via leaning of Ag NPs. The presence of a substrate dramatically changes the intensity of these two LSPR modes by introducing constructive and destructive interference patterns with incident and reflected fields. Experimental scattering spectra can be interpreted using theoretical simulations. The Ag NP substrate displays a broad plasmonic resonance band due to the contribution from both the hybridized particle LSPR and the cavity LSPR modes.
Polymeric microcontainers improve oral bioavailability of a poorly soluble drug

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Valencia, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Melero, A. (Ekstern), Keller, S. S. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2015
Main Research Area: Technical/natural sciences
Electronic versions:
Polymeric_microcontainers_improve_oral_bioavailability_of_a_poorly_soluble_drug.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 118685806
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Pyrolysed carbon microelectrode in a self-aligning electrochemical batch system

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics
Authors: Hemanth, S. (Intern), Amato, L. (Intern), Caviglia, C. (Intern), Emnéus, J. (Intern), Keller, S. S. (Intern)
Number of pages: 1
Publication date: 2015
Event: Abstract from XXIII International Symposium on Bioelectrochemistry and Bioenergetics, Malmö, Sweden.
Main Research Area: Technical/natural sciences
Links:
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Quantification of NS1 dengue biomarker in serum via optomagnetic nanocluster detection
Dengue is a tropical vector-borne disease without cure or vaccine that progressively spreads into regions with temperate climates. Diagnostic tools amenable to resource-limited settings would be highly valuable for epidemiologic control and containment during outbreaks. Here, we present a novel low-cost automated biosensing platform for detection of dengue fever biomarker NS1 and demonstrate it on NS1 spiked in human serum. Magnetic nanoparticles (MNPs) are coated with high-affinity monoclonal antibodies against NS1 via bio-orthogonal Cu-free ‘click’ chemistry on an anti-fouling surface molecular architecture. The presence of the target antigen NS1 triggers MNP agglutination and the formation of
Quantification of rolling circle amplified DNA using magnetic nanobeads and a Blu-ray optical pick-up unit

We present the first implementation of a Blu-ray optical pickup unit (OPU) for the high-performance low-cost readout of a homogeneous assay in a multichamber microfluidic disc with a chamber thickness of 600 μm. The assay relies on optical measurements of the dynamics of magnetic nanobeads in an oscillating magnetic field applied along the light propagation direction.
direction. The laser light provided by the OPU is transmitted through the sample chamber and reflected back onto the photo detector array of the OPU via a mirror. Spectra of the 2nd harmonic photo detector signal vs. the frequency of the applied magnetic field show a characteristic peak due to freely rotating magnetic nanobeads. Beads bound to ~1 μm coils of DNA formed off-chip by padlock probe recognition and rolling circle amplification show a different dynamics and the intensity of the characteristic peak decreases. We have determined the optimum magnetic bead concentration to 0.1 mg/mL and have measured the response vs. concentration of DNA coils formed from Escherichia Coli. We have found a limit of detection of 10 pM and a dynamic range of about two orders of magnitude, which is comparable to the performance obtained using costly and bulky laboratory equipment. The presented device leverages on the advanced but low-cost technology of Blu-ray OPUs to provide a low-cost and high-performance magnetic bead-based readout of homogeneous bioassays. The device is highly flexible and we have demonstrated its use on microfluidic chambers in a disc with a thickness compatible with current optical media mass-production facilities.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Uppsala University, Academia Sinica Taiwan
Authors: Donolato, M. (Intern), Antunes, P. S. M. (Intern), Gómez del a Torre, T. Z. (Ekstern), Hwu, E. (Ekstern), Chen, C. (Ekstern), Burger, R. (Intern), Rizzi, G. (Intern), Bosco, F. (Intern), Strømme, M. (Ekstern), Boisen, A. (Intern), Hansen, M. F. (Intern)
Number of pages: 7
Pages: 649-655
Publication date: 2015
Main Research Area: Technical/natural sciences

**Publication Information**

Journal: Biosensors and Bioelectronics
Volume: 67
ISSN (Print): 0956-5663

Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.65 SJR 2.373
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.22 SJR 2.095 SNIP 1.619
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.044 SNIP 1.671 CiteScore 7.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.057 SNIP 1.716 CiteScore 6.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.029 SNIP 1.726 CiteScore 6.34
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.397 SNIP 1.592 CiteScore 5.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.126 SNIP 1.704 CiteScore 5.85
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.143 SNIP 1.609
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scalable DNA-Based Magnetic Nanoparticle Agglutination Assay for Bacterial Detection in Patient Samples

We demonstrate a nanoparticle-based assay for the detection of bacteria causing urinary tract infections in patient samples with a total assay time of 4 h. This time is significantly shorter than the current gold standard, plate culture, which can take several days depending on the pathogen. The assay is based on padlock probe recognition followed by two cycles of rolling circle amplification (RCA) to form DNA coils corresponding to the target bacterial DNA. The readout of the RCA products is based on optomagnetic measurements of the specific agglutination of DNA-bound magnetic nanoparticles (MNPs) using low-cost optoelectronic components from Blu-ray drives. We implement a detection approach, which relies on the monomerization of the RCA products, the use of the monomers to link and agglutinate two populations of MNPs functionalized with universal nontarget specific detection probes and on the introduction of a magnetic incubation scheme. This enables multiplex detection of Escherichia coli, Proteus mirabilis and Pseudomonas aeruginosa at clinically relevant concentrations, demonstrating a factor of 30 improvement in sensitivity compared to previous MNP-based detection schemes. Thanks to the universal probes, the same set of functionalized MNPs can be used to read out products from a multitude of RCA targets, making the approach truly scalable for parallel detection of multiple bacteria in a future integrated point of care molecular diagnostics system.
SERS sensors for DVD platform

This Ph.D. thesis explores the engineering of a portable sensor system for detection of rare and small molecules. The Ph.D. project is part of the research
The project ‘Multi-Sensor DVD platform’ (MUSE), aiming to integrate different sensors on a rotating disc. The sensors are chosen to complement each other, creating more reliable and stable results for the end user. The rotating disc comprises microfluidic channels, which can be utilized for handling and manipulating liquid samples such as blood or water.

The focus of this Ph.D. thesis, is on the integration of one specific sensor on a rotating disc. The sensor is based upon surface enhanced Raman spectroscopy (SERS), which detects molecular vibrations. The aim of this thesis is to cover the different aspects of the sensor system.

SERS substrates, consisting of nanorods with gold or silver caps on top, have been fabricated by standard micro and nano fabrication techniques. These substrates possess plasmonic properties and can therefore enhance Raman signals from even small molecules in close proximity to the surface of the caps. By introducing high temperature annealing to the fabrication process, the SERS background signal, originating from etch residues, has been reduced, further improving the SERS signal.

Microfluidic sample handling are, in combination with the SERS sensor, to be used with the DVD system. Nanoparticles has been investigated as a mean to capture and handle the target molecules. This enables the use of sandwich assays between the substrate and nanoparticles for biodetection. It is demonstrated that the SERS substrate maintains its enhancing properties when the nanoparticles are immobilized on the surface.

By introducing a dynamic measuring method called DynaSERS it is demonstrated how the stability of the Raman signal can be improved. Additionally, the assignment of vibrational modes is made easier, as the peak width is reduced and the peak position is shifted.

Finally, the instrumentation for a portable sensor system has been investigated and SERS measurements on a rotating microfluidic disc has been demonstrated.
Silver Capped Silicon Nanopillars as Surface Enhanced Raman Spectroscopy Substrates

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Wu, K. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015

Host publication information
Title of host publication: Proceedings of the 36th Progress In Electromagnetics Research Symposium
Main Research Area: Technical/natural sciences
Conference: 36th Progress In Electromagnetics Research Symposium, Prague, Czech Republic, 06/07/2015 - 06/07/2015
Electronic versions:
150416025429_abstract.pdf
Source: PublicationPreSubmission
Source-ID: 112799073
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

Simple electrodynamic transduction scheme for micromechanical resonators

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Kurek, M. (Intern), Larsen, P. E. (Intern), Schmid, S. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2015
Main Research Area: Technical/natural sciences
Electronic versions:
Simple_electrodynamic_transduction_scheme_for_micromechanical_resonators_poster_2.pdf
Source: PublicationPreSubmission
Source-ID: 119092722
Publication: Research - peer-review › Poster – Annual report year: 2015

Simulation and Measurement of Angle Resolved Reflectance from Black Si Surfaces
In this work angle-resolved reflectance from nanostructured Si surfaces realized by maskless RIE texturing has been simulated and measured. The simulation and experimental measurement data show the same trend. Experimentally a total reflectance below 1% for incident angles below 30o and specular reflectance below 0.1% at incident angles below 70o is seen. In both simulation and experiment the specular reflectance is below 10% at incident angles below 65o and below 1% at incident angles below 45o in the case of non-linear graded refractive index. From the simulation results the non-linear graded refractive index yields lower reflectance than the linearly graded refractive index.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes
Authors: Davidsen, R. S. (Intern), Wu, K. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern)
Number of pages: 3
Publication date: 2015

Host publication information
Title of host publication: Proceedings of the 31st European Photovoltaic Solar Energy Conference and Exhibition
Series: EU PVSEC Proceedings
ISSN: 2196-100X
Main Research Area: Technical/natural sciences
Black silicon, Reactive ion etching, Angle dependence, Reflectance, Nanostructures
Electronic versions:
2BV.8.25_paper.pdf
Source: PublicationPreSubmission
Source-ID: 117670602
Simulation and Measurement of Angle Resolved Reflectance from Black Si Surfaces

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes
Authors: Davidsen, R. S. (Intern), Wu, K. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2015
Main Research Area: Technical/natural sciences
Electronic versions:
2BV.8.25_poster.pdf
Source: PublicationPreSubmission
Source-ID: 117670617
Publication: Research - peer-review › Poster – Annual report year: 2015

Spray drying of cubosomes for oral vaccine delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Institute for Pharmaceutical Research Saarland, University of Copenhagen, Monash University
Authors: Nielsen, L. H. (Intern), Gordon, S. (Ekstern), Rades, T. (Ekstern), Boyd, B. (Ekstern)
Number of pages: 2
Publication date: 2015
Event: Abstract from 2015 AAPS Annual Meeting and Exposition, Orlando, FL, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
Abstract_AAPS_2015_cubosomes.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 118685856
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

Stabilisation of amorphous furosemide increases the oral drug bioavailability in rats
A glass solution of the amorphous sodium salt of furosemide (ASSF) and polyvinylpyrrolidone (PVP) (80: 20 w/w%) was prepared by spray drying. It was investigated if PVP was able to stabilise ASSF during storage and dissolution and whether this influenced the in vivo performance of the glass solution after oral dosing to rats. The glass solution had a glass transition temperature of 121.3 +/- 0.5 degrees C, which was significantly higher than that of the pure drug (101.2 degrees C). ASSF in the glass solution was stable for at least 168 days when stored at 20 degrees C and 0% relative humidity. The glass solution exhibited fast dissolution in simulated intestinal medium, pH 6.5; the intrinsic dissolution rate was found to be 10.1 +/- 0.6 mg/cm(2)/min, which was significantly faster than the pure ASSF. When investigating the stability during dissolution in simulated intestinal medium at pH 6.5, the ASSF in the glass solution showed signs of crystallinity after 1 min of dissolution, but crystallised to a lesser extent than pure ASSF. The stabilising effect of PVP on ASSF, led to improved relative oral bioavailability in rats of 263%, when compared to the pure ASSF. (C) 2015 Elsevier B.V. All rights reserved.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern)
Number of pages: 7
Pages: 334-340
Publication date: 2015
Main Research Area: Technical/natural sciences
Publication information
Journal: International Journal of Pharmaceutics
Stabilisation of amorphous furosemide increases the oral drug bioavailability in rats post_print.pdf

DOIs:
10.1016/j.ijpharm.2015.05.063
Statistical analysis of large areas of Raman mapped DNA functionalized gold coated silicon nanopillar SERS substrates

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Surface Engineering, Department of Applied Mathematics and Computer Science, Cognitive Systems, Nanoprobes
Authors: Frøhling, K. B. (Intern), Alstrøm, T. S. (Intern), Bache, M. (Intern), Schmidt, M. S. (Intern), Schmidt, M. N. (Intern), Larsen, J. (Intern), Jakobsen, M. H. (Intern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2015
Event: Abstract from 8th International Conference on Advanced Vibrational Spectroscopy, Vienna, Austria.
Main Research Area: Technical/natural sciences
SERS, Area map, Peak fitting, Statistics, Sensor
Electronic versions: ICAVS8_abstract.pdf

Relations
Activities:
Statistical analysis of large areas of Raman mapped DNA functionalized gold coated silicon nanopillar SERS substrates
Source: PublicationPreSubmission
Source-ID: 112913529
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2015

The copper binding properties of metformin - QCM-D, XPS and nanobead agglomeration
Study of the copper binding properties of metformin is important for revealing its mechanism of action as a first-line type-2 diabetes drug. A quantitative investigation of interactions between metformin and l-cysteine-copper complexes was performed. The results suggest that metformin could interact with biological copper, which plays a key role in mitochondrial function.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, DTU Danchip, Magnetic Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Dundee
Authors: Quan, X. (Intern), Uddin, R. (Intern), Heiskanen, A. (Intern), Parmvi, M. (Intern), Nilson, K. (Intern), Donolato, M. (Intern), Hansen, M. F. (Intern), Rena, G. (Ekstern), Boisen, A. (Intern)
Pages: 17313-17316
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication Information
Journal: Chemical Communications
Volume: 51
Issue number: 97
ISSN (Print): 1359-7345
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SJR 2.555 SNIP 1.127
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 6.06 SJR 2.538 SNIP 1.16
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.601 SNIP 1.295 CiteScore 6.7
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Lung infections with *Pseudomonas aeruginosa* (PA) is the most common cause of morbidity and mortality in cystic fibrosis (CF) patients. Due to its ready adaptation to the dehydrated mucosa of CF airways, PA infections tend to become chronic, eventually killing the patient. Hydrogen cyanide (HCN) at ppb level has been reported to be a PA biomarker. For early PA detection in CF children not yet chronically lung infected a non-invasive Surface-Enhanced Raman Spectroscopy (SERS)-based breath nanosensor is being developed. The triple bond between C and N in cyanide, with its characteristic band at \(\sim 2133 \text{ cm}^{-1}\), is an excellent case for the SERS-based detection due to the infrequent occurrence of triple bonds in nature. For demonstration of direct HCN detection in the gas phase, a gold-coated silicon nanopillar substrate was exposed to 5...
ppm HCN in N₂. Results showed that HCN adsorbed on the SERS substrate can be consistently detected under different experimental conditions and up to 9 days after exposure. For detection of lower cyanide concentrations serial dilution experiments using potassium cyanide (KCN) demonstrated cyanide quantification down to 1 μM in solution (corresponding to 18 ppb). Lower KCN concentrations of 10 and 100 nM (corresponding to 0.18 and 1.8 ppb) produced SERS intensities that were relatively similar to the reference signal. Since HCN concentration in the breath of PA colonized CF children is reported to be ~13.5 ppb, the detection of cyanide is within the required range.

Wafer-Scale Leaning Silver Nanopillars for Molecular Detection at Ultra-Low Concentrations

Wafer-scale surface-enhanced Raman scattering (SERS) substrates fabricated using maskless lithography are important for scalable production targets. Large-area, leaning silver-capped silicon nanopillar (Ag NP) structures suitable for SERS molecular detection at extremely low analyte concentrations are investigated. Theoretical results show that isolated Ag NPs essentially support two localized surface plasmon (LSP) modes. The most prominent LSP resonance is observed in the near-infrared region (~800 nm) and can be tuned by changing the diameter of the silicon nanopillars (Si NPs). The corresponding electric field distribution maps indicate that the maximum E-field enhancement is found at the Ag cavity, i.e., the bottom part of the Ag cap. We argue that the plasmon coupling between the resonant Ag cap cavities contributes most to the enhancement of the Raman signal. We experimentally evaluate these findings and show that by exposing Si NPs to an O₂-plasma the average Ag NP cluster size, and thus the overall interpillar coupling, can be systematically reduced. We show that deposition of Cr adhesion layers on Si NPs (>3 nm) introduces plasmon coupling loss to the Ag NP LSP cavity mode that significantly reduces the SERS intensity. Results also show that short exposures to the O₂-plasma and the use of 1–3 nm Cr adhesion layers are advantageous for reducing the signal background noise from Ag NPs. In addition, the influence of the Ag NP height and Ag metal thickness on SERS intensities is investigated and optimal fabrication process parameters are evaluated. Finally, the SERS spectrum from 100 pM trans-1,2-bis(4-pyridyl) ethylene (BPE) is recorded, showing distinct characteristic Raman vibrational modes. The calculated enhancement factor is of the order of 10⁸, and the SERS signal intensity exhibits a standard deviation of around 14% (660 data points) across a 5 × 5 mm² surface area.
Biosensor based on the measurements of clustering dynamics of magnetic particles using a double pass setup

Disclosed herein is a biosensor for optical detection of Brownian relaxation dynamics of magnetic particles measured by light transmission. The magnetic particles can be functionalized with biological ligands for the detection of target analytes in a sample. The setup may be implemented in a disc and optical pick-up head configuration.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Academia Sinica Taiwan
Authors: Donolato, M. (Intern), Bosco, F. (Intern), Hansen, M. F. (Intern), Boisen, A. (Intern), Hwu, E. T. (Ekstern)
Publication date: 31 Dec 2014

Publication information
IPC: G01N21/17; G01N33/543
Patent number: WO2014206583
Date: 31/12/2014
Priority date: 28/06/2013
Priority number: EP20130174311
Original language: English
Electronic versions:
WO2014206583A1.pdf
Main Research Area: Technical/natural sciences
Publication: Research › Patent – Annual report year: 2015

A Centrifugal Microfluidic Platform for Biomarker Detection in Blood using BluRay Technology

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems, Department of Applied Mathematics and Computer Science , Cognitive Systems, Copenhagen University Hospital
Publication date: 2014
Event: Poster session presented at 24th Anniversary World Congress on Biosensors, Melbourne, Australia.
Main Research Area: Technical/natural sciences
Electronics versions:
import_1401278051292
Source: PublicationPreSubmission
Source-ID: 92650093
Publication: Research - peer-review › Poster – Annual report year: 2014

A compact multifunctional microfluidic platform for exploring cellular dynamics in real-time using electrochemical detection

Downscaling of microfluidic cell culture and detection devices for electrochemical monitoring has mostly focused on miniaturization of the microfluidic chips which are often designed for specific applications and therefore lack functional flexibility. We present a compact microfluidic cell culture and electrochemical analysis platform with in-built fluid handling and detection, enabling complete cell based assays comprising on-line electrode cleaning, sterilization, surface functionalization, cell seeding, cultivation and electrochemical real-time monitoring of cellular dynamics. To demonstrate the versatility and multifunctionality of the platform, we explored amperometric monitoring of intracellular redox activity in yeast (Saccharomyces cerevisiae) and detection of exocytotically released dopamine from rat pheochromocytoma cells (PC12). Electrochemical impedance spectroscopy was used in both applications for monitoring cell sedimentation and adhesion as well as proliferation in the case of PC12 cells. The influence of flow rate on the signal amplitude in the detection of redox metabolism as well as the effect of mechanical stimulation on dopamine release were demonstrated using the programmable fluid handling capability. The here presented platform is aimed at applications utilizing cell based assays, ranging from e.g. monitoring of drug effects in pharmacological studies, characterization of neural stem cell differentiation, and screening of genetically modified microorganisms to environmental monitoring.
Advanced dry etching studies for micro- and nano-systems

Dry etching is a collective term used for controlled material removal by means of plasma generated ions. Dry etching includes several techniques, with reactive ion etching as one of the most used of its many derivatives. In this work inductively coupled plasma reactive ion etching has been applied for structuring of sapphire and many polymers. Metals and metal alloys have been structured by physical sputtering with argon ions in an ion beam etching system. The materials for which etch characteristics have been investigated are commonly used in device fabrication at DTU-Danchip. Ion beam etching was first used for structuring of a magnetic device containing four different materials in nine layers. The materials, tantalum, tantalum oxide, iridium manganese, and permalloy, can all be etched by reactive ion etching, however...
A magnetic nanoparticle-clustering biosensor for Blu-ray based optical detection of small-molecules

In magnetic nanoparticle (MNP)-clustering assays, a target molecule is bound to multiple receptors tethered onto MNPs, triggering MNP-clustering and leading to changes in the size of clusters. However, sandwich-type clustering requires multiple binding-sites on a target molecule, which is often unavailable for small-molecules. Furthermore, measuring magnetic properties as signals is not intrinsically selective regarding MNP-cluster size. Thus, the detection of few MNP-clusters is readily interfered by background signals from predominantly-existing single MNPs. Additionally, bulky and high-cost instruments limit the advancement of MNP-based assays. We report here a novel MNP-clustering small-molecule assay on an optical readout platform to overcome the limitations aforementioned with the following improvements. First, a facile MNP-clustering assay applicable to diverse small-molecules was realized by adopting an inhibition mechanism. Next, frequency-dependent optical measurements enabled us to resolve signals depending on the cluster size. Lastly, a low-cost and miniaturized optical readout setup was established by implementing a Blu-ray pickup head. Consequently, our low-cost optical biosensor using MNP-clustering facilitates high-resolution small-molecule assays.

For experiments, aptamer-functionalized MNPs (Apt-MNPs) were first incubated with adenosine-5'-triphosphate (ATP) followed by adding MNPs with linker strands (linker-MNPs). The linker hybridizes with a region of aptamer sequences in the absence of ATP, forming MNP-clusters. Conversely, when aptamers are preoccupied by ATP inhibiting the hybridization, the cluster formation is hindered. Consequently, higher ATP-concentrations result in smaller and fewer cluster formations. Blu-ray optical transmission measurements through an MNP-solution reveal that the 2nd harmonic component of the signal is related to the frequency of Brownian relaxation dynamics of MNPs induced by alternating magnetic field. Following measurement characterization and analyze-control experiments, we demonstrated the ATP concentration dependent behavior of signals in micromolar ranges. These results support that our MNP-clustering optical biosensor is capable of specific and quantitative detection of small-molecules.
Can engineering solutions really provide a sustainable future?
Sustainability is a word which is very often (mis)used in various public debates. In engineering, however, it is perhaps easier to define the term, then in other academic fields. We advocate the principle that only those activities, which can be sustained for at least a few centuries using known technology and resources, should be called sustainable. Using this definition of sustainability one particularly big challenge field is energy supply, but the importance of the issue - “The energy problem” - is clear.
To illustrate one central aspect of the energy problem we introduce the "1 TW benchmark". On this backdrop we proceed to discuss the practical availability of chemical elements for energy technologies and the implications this has for industrial scalability. The issue will be exemplified by how some, otherwise promising, emerging technologies are limited in ultimate scale by scarcity of key elements. Finally, we discuss a few specific recent research highlights from DTU-Physics within the field of energy harvesting and conversion.

Characterization of Electromechanical Behavior of an Electrochemical Cantilever System

Characterization of the time-evolving bending profile of micro-cantilevers
Conducting 3D-carbon scaffolds induce spontaneous differentiation of human neural stem cells and measure neurotransmitter release in real-time

Demonstration of suppressed phonon tunneling losses in phononic bandgap shielded membrane resonators for high-Q optomechanics

Dielectric membranes with exceptional mechanical and optical properties present one of the most promising platforms in quantum optomechanics. The performance of stressed silicon nitride nanomembranes as mechanical resonators notoriously depends on how their frame is clamped to the sample mount, which in practice usually necessitates delicate, and difficult-to-reproduce mounting solutions. Here, we demonstrate that a phononic bandgap shield integrated in the membrane’s silicon frame eliminates this dependence, by suppressing dissipation through phonon tunneling. We dry-etch the membrane’s frame so that it assumes the form of a cm-sized bridge featuring a 1-dimensional periodic pattern, whose phononic density of states is tailored to exhibit one, or several, full band gaps around the membrane’s high-Q modes in the MHz-range. We quantify the effectiveness of this phononic bandgap shield by optical interferometry measuring both the suppressed transmission of vibrations, as well as the influence of frame clamping conditions on the membrane modes. We find suppressions up to 40 dB and, for three different realized phononic structures, consistently observe significant suppression of the dependence of the membrane’s modes on sample clamping—if the mode’s frequency lies in the bandgap. As a result, we achieve membrane mode quality factors of $5 \times 10^6$ with samples that are tightly bolted to the 8 K-cold finger of a cryostat. Qxf-products of $6 \times 10^{12}$ Hz at 300 K and $14 \times 10^{12}$ Hz at 8 K are observed, satisfying one of the main requirements for optical cooling of mechanical vibrations to their quantum ground-state.
Development of an electrochemical cantilever platform

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, McGill University, Lund University
Authors: Quan, X. (Intern), Heiskanen, A. (Intern), Grütter, P. (Ekstern), Tenje, M. (Ekstern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 11th Nanomechanical Sensing Workshop
Main Research Area: Technical/natural sciences
Conference: 11th International Workshop on Nanomechanical Sensing, Madrid, Spain, 30/04/2014 - 30/04/2014

Efficient Excitation of Channel Plasmons in Tailored, UV-Lithography-Defined V-Grooves
We demonstrate the highly efficient (>50%) conversion of freely propagating light to channel plasmon-polaritons (CPPs) in gold V-groove waveguides using compact 1.6 μm long waveguide-termination coupling mirrors. Our straightforward fabrication process, involving UV-lithography and crystallographic silicon etching, forms the coupling mirrors innately and ensures exceptional-quality, wafer-scale device production. We tailor the V-shaped profiles by thermal silicon oxidation in order to shift initially wedge-located modes downward into the V-grooves, resulting in well-confined CPPs suitable for nanophotonic applications.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Optofluidics, Nanoprobes, Department of Photonics Engineering, University of Southern Denmark
Authors: Smith, C. L. C. (Intern), Thilsted, A. H. (Intern), Garcia-Ortiz, C. E. (Ekstern), Radko, I. P. (Forskerdatabase), Marie, R. (Intern), Jeppesen, C. (Intern), Vannahme, C. (Intern), Bozhevolnyi, S. I. (Ekstern), Kristensen, A. (Intern)
Pages: 1659-1664
Publication date: 2014
Main Research Area: Technical/natural sciences
Electrochemistry in a centrifugal microfluidic system: Towards a novel point-of-care technology platform

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Bioanalytics
Authors: Andreasen, S. Z. (Intern), Kwasny, D. (Intern), Bregger, A. L. (Intern), Bosco, F. (Intern), Andersen, K. B. (Intern), Svendsen, W. E. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
Number of pages: 1
Pages: 37-37
Publication date: 2014

Host publication information
Title of host publication: Oral presentations – ESEAC2014
Main Research Area: Technical/natural sciences
Electronic versions:
Full_Oral_Presentations_ESEAC_2014.pdf
Source: PublicationPreSubmission
Source-ID: 118025115
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

Evidence of surface loss as ubiquitous limiting damping mechanism in SiN micro- and nanomechanical resonators
Silicon nitride (SiN) micro- and nanomechanical resonators have attracted a lot of attention in various research fields due to their exceptionally high quality factors (Qs). Despite their popularity, the origin of the limiting loss mechanisms in these structures has remained controversial. In this Letter we propose an analytical model combining acoustic radiation loss with intrinsic loss. The model accurately predicts the resulting mode-dependent Qs of low-stress silicon-rich and high-stress stoichiometric SiN membranes. The large acoustic mismatch of the low-stress membrane to the substrate seems to minimize radiation loss and Qs of higher modes (n≥m≥3) are limited by intrinsic losses. The study of these intrinsic losses in low-stress membranes reveals a linear dependence with the membrane thickness. This finding was confirmed by comparing the intrinsic dissipation of arbitrary (membranes, strings, and cantilevers) SiN resonators extracted from literature, suggesting surface loss as ubiquitous damping mechanism in thin SiN resonators with $Q_{surf} = \beta h$ and $\beta = 6 \times 10^{10} \pm 4 \times 10^{10} \text{m}^{-1}$. Based on the intrinsic loss the maximal achievable Qs and Qf products for SiN membranes and strings are outlined.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Ecole Polytechnique Federale de Lausanne (EPFL)
Authors: Villanueva, L. G. (Ekstern), Schmid, S. (Intern)
Number of pages: 6
Pages: 227201
Publication date: 2014
Main Research Area: Technical/natural sciences
Fabrication and Process Optimization of Wafer-scale Silicon Nanopillar SERS Substates

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Wu, K. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 40th International Conference on Micro and Nano Engineering, Lausanne, Switzerland.
Main Research Area: Technical/natural sciences
Electronic versions:
2014.09.MNE.v2.pdf
Source: PublicationPreSubmission
Source-ID: 100597072
Publication: Research - peer-review › Poster – Annual report year: 2014

Fabrication of drug-laden poly(vinylpyrrolidone)(PVP) microgels by UV-photolithography and supercritical impregnation

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Polymer Microsystems for Cell Processing, Center for Electron Nanoscopy, University of Copenhagen
Authors: Marizza, P. (Intern), Keller, S. S. (Intern), Faralli, A. (Intern), Mateiu, R. V. (Intern), Müllertz, A. (Ekstern), Larsen, N. B. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of The 40th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Electronic versions:
import_1403702671013
Source: PublicationPreSubmission
Source-ID: 93522892
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Gold Nanoparticle Doped Polymer Materials for Micro- and Nanofabrication

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Surface Engineering, Nanoprobes
Authors: Fischer, S. V. (Intern), Masuda, N. (Ekstern), Keller, S. S. (Intern), Uthuppu, B. (Intern), Jakobsen, M. H. (Intern)
Number of pages: 2
Publication date: 2014
High Excitation Efficiency of Channel Plasmon Polaritons in Tailored, UV-Lithography-Defined V-Grooves

We demonstrate >50% conversion of light to V-groove channel plasmon-polaritons (CPPs) via compact waveguide-termination mirrors. Devices are fabricated using UV-lithography and crystallographic silicon etching. The V-shape is tailored by thermal oxidation to support confined CPPs.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Optofluidics, Nanoprobes, Department of Photonics Engineering, University of Southern Denmark
Number of pages: 2
Pages: 1-2
Publication date: 2014

Host publication information
Title of host publication: Proceedings of 2014 Conference on Lasers and Electro-Optics (CLEO)
Publisher: IEEE
ISBN (Print): 9781557529992
Main Research Area: Technical/natural sciences
Conference: Conference on Lasers and Electro-Optics 2014, San Jose, CA, United States, 08/06/2014 - 08/06/2014
Electronic versions:
CLEO14_CLCS_UV_Vgrvs.pdf
Source: PublicationPreSubmission
Source-ID: 93684927
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Hollow micro string based calorimeter device
The present invention relates to a micron-scale calorimeter and a calorimetry method utilizing the micron-scale calorimeter. In accordance with the invention, there is provided a micron-scale calorimeter comprising a micro-channel string, being restrained at least two longitudinally distanced positions so as to form a free released double clamped string in-between said two longitudinally distanced positions said micro-channel string comprising a microfluidic channel having a closed cross section and extending in the longitudinal direction of the hollow string, acoustical means adapted to oscillate the string at different frequencies by emitting sound waves towards the string, optical means adapted to detect oscillating frequencies of the string, and controlling means controlling the strength and frequency of the sound wave emitted by the acoustical means and receiving a signal from the optical means representing the detected oscillating frequencies.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Khan, F. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Larsen, T. (Intern)
Publication date: 2014

Publication information
IPC: G01K17/00
Patent number: WO2014161553
Date: 09/10/2014
Priority date: 05/04/2013
Priority number: EP20130162524
Imaging based agglutination measurement of magnetic micro-particles on a Lab-on-a-Disc platform

In this work we present a magnetic micro beads based agglutination assay on a centrifugal microfluidic platform. An imaging based method is used to quantify bead agglutination and measure the concentration of antibodies or C-reactive protein in solution.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems, Malmö University
Number of pages: 2
Publication date: 2014
Event: Poster session presented at 18th International Conference on Miniaturized Systems for Chemistry and Life Sciences, San Antonio, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
4050563_MicroTAS_Burger_2.pdf
Source-ID: 102456688
Publication: Research - peer-review › Poster – Annual report year: 2014

Impedance spectroscopic monitoring of the effect of phytochemical compounds on wound healing in microfluidics

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark, University of Siena
Authors: Tilli, V. (Ekstern), Montini, L. (Ekstern), Caviglia, C. (Intern), Bin, C. (Ekstern), Biaggi, M. (Ekstern), Giachetti, D. (Ekstern), Heiskanen, A. (Intern), Zor, K. (Intern), Emnéus, J. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 18th International Conference on Miniaturized Systems for Chemistry and Life Sciences
Publisher: Chemical and Biological Microsystems Society
Main Research Area: Technical/natural sciences
Conference: 18th International Conference on Miniaturized Systems for Chemistry and Life Sciences, San Antonio, United States, 26/10/2014 - 26/10/2014
Lab-on-a-disc, Centrifugal microfluidics, Bead based immunoassay
Source-ID: 102496130
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014
Improvement of Infrared Detectors for Tissue Oximetry using Black Silicon Nanostructures

We present a nanostructured surface, made of dry etched black silicon, which lowers the reflectance for light incident at all angles. This surface is fabricated on infrared detectors used for tissue oximetry, where the detection of weak diffuse light signals is important. Monte Carlo simulations performed on a model of a neonatal head shows that approximately 60% of the injected light will be diffuse reflected. However, the change in diffuse reflected light due to the change in cerebral oxygenation is very low and the light will be completely isotropic scattered. The reflectance of the black silicon surface was measured for different angels of incident and was fund to be below 10% for angles of incident up to 70°. The quantum efficiency of detectors with the black silicon nanostructures was measured and compared to detectors with a simple anti-reflection coating. The result was an improvement in quantum efficiency for both normal incident light and light incident at 38°.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Silicon Microtechnology, Nanoprobes
Authors: Petersen, S. D. (Intern), Davidsen, R. S. (Intern), Alcala, L. R. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern), Thomsen, E. V. (Intern)
Number of pages: 4
Pages: 652-655
Publication date: 2014
Main Research Area: Technical/natural sciences
Journal: Procedia Engineering
Volume: 87
ISSN (Print): 1877-7058
Ratings:
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 0.74
Scopus rating (2015): CiteScore 0.56
Scopus rating (2014): CiteScore 0.53
Scopus rating (2013): CiteScore 0.4
ISI indexed (2013): ISI indexed no
Scopus rating (2012): CiteScore 0.28
ISI indexed (2012): ISI indexed no
Scopus rating (2011): CiteScore 0.45
ISI indexed (2011): ISI indexed no
Web of Science (2010): Indexed yes
Original language: English
Tissue oximetry, Infrared detectors, Black detectors, Black silicon, Quantum efficiency, Diffuse reflected light
Electronic versions:
procedia_engineering_eurosensors2014_petersen.pdf
DOIs:
10.1016/j.proeng.2014.11.572
Publication: Research - peer-review › Conference article – Annual report year: 2014
Improving spectral resolution of SERS using moving AG nanopillar substrate

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Applied Mathematics and Computer Science, Cognitive Systems
Authors: Brøgger, A. L. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 24th International Conference on Raman Spectroscopy, Jena, Germany.
Main Research Area: Technical/natural sciences
Electronic versions:
Poster_ICORS.pdf
Source: PublicationPreSubmission
Source-ID: 101141519
Publication: Research - peer-review › Poster – Annual report year: 2014

Improving the robustness of Surface Enhanced Raman Spectroscopy based sensors by Bayesian Non-negative Matrix Factorization

Due to applications in areas such as diagnostics and environmental safety, detection of molecules at very low concentrations has attracted recent attention. A powerful tool for this is Surface Enhanced Raman Spectroscopy (SERS) where substrates form localized areas of electromagnetic “hot spots” where the signal-to-noise (SNR) ratio is greatly amplified. However, at low concentrations hot spots with target molecules bound are rare. Furthermore, traditional detection relies on having uncontaminated sensor readings which is unrealistic in a real world detection setting. In this paper, we propose a Bayesian Non-negative Matrix Factorization (NMF) approach to identify locations of target molecules. The proposed method is able to successfully analyze the spectra and extract the target spectrum. A visualization of the loadings of the basis vector is created and the results show a clear SNR enhancement. Compared to traditional data processing, the NMF approach enables a more reproducible and sensitive sensor.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Cognitive Systems, Department of Micro- and Nanotechnology, Surface Engineering, Nanoprobes
Authors: Alstrøm, T. S. (Intern), Frøhling, K. B. (Intern), Larsen, J. (Intern), Schmidt, M. N. (Intern), Bache, M. (Intern), Schmidt, M. S. (Intern), Jakobsen, M. H. (Intern), Boisen, A. (Intern)
Number of pages: 6
Publication date: 2014
Host publication information
Title of host publication: Proceedings of the 2014 IEEE International Workshop on Machine Learning for Signal Processing (MLSP)
Publisher: IEEE
Editors: Mboup, M., Adali, T., Moreau, É., Larsen, J.
ISBN (Print): 978-1-4799-3694-6
Main Research Area: Technical/natural sciences
Bioengineering, Communication, Networking and Broadcast Technologies, Computing and Processing, Engineering Profession, Signal Processing and Analysis, 17β-Estradiol, Abstracts, Biosensing, Non-negative Matrix Factorization
In-situ monitoring of potential enhanced DNA related processes using electrochemical quartz crystal microbalance with dissipation (EQCM-D)

The effect of applied potential pulses on DNA functionalization (thiolated single stranded DNA) and hybridization processes has been monitored in-situ on gold surfaces using electrochemical quartz crystal microbalance with dissipation (EQCM-D). The applied potentials were chosen with respect to the potential of zero charge ($E_{pzc}$) of the gold surfaces: a positive potential to attract the negatively charged DNA molecules and a negative potential to enhance the vertical alignment due to electrostatic repulsion. The obtained results clearly show that both DNA modification and hybridization are strongly enhanced by applying potential pulses. Based on the EQCM-D results, we present a model to explain the influence of the potential pulsing. Aside from the effect of applied potentials on DNA related processes, this work also demonstrates the versatility of the combination of electrochemistry and quartz crystal microbalance with dissipation in facilitating real-time in situ monitoring of such processes.
Integrated cantilever-based flow sensors with tunable sensitivity for in-line monitoring of flow fluctuations in microfluidic systems

For devices such as bio-/chemical sensors in microfluidic systems, flow fluctuations result in noise in the sensor output. Here, we demonstrate in-line monitoring of flow fluctuations with a cantilever-like sensor integrated in a microfluidic channel. The cantilevers are fabricated in different materials (SU-8 and SiN) and with different thicknesses. The integration of arrays of holes with different hole size and number of holes allows the modification of device sensitivity, theoretical detection limit and measurement range. For an average flow in the microliter range, the cantilever deflection is directly proportional to the flow rate fluctuations in the microfluidic channel. The SiN cantilevers show a detection limit below 1 nL/min and the thinnest SU-8 cantilevers a detection limit below 5 nL/min. Finally, the sensor is applied for in-line monitoring of flow fluctuations generated by external pumps connected to the microfluidic system. © 2013 by the authors; licensee MDPI, Basel, Switzerland.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Noeth, N. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern)
Pages: 229-244
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Sensors
Volume: 14
Issue number: 1
ISSN (Print): 1424-8220
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SJR 0.584 SNIP 1.55
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.78 SJR 0.623 SNIP 1.614
Interface losses in multimaterial resonators

We present an extensive study shedding light on the role of surface and bulk losses in micromechanical resonators. We fabricate thin silicon nitride membranes of different sizes and we coat them with different thicknesses of metal. We later characterize the 81 lowest out-of-plane flexural vibrational modes to achieve a total of more than 3000 experimental points that allow us to quantify the contribution of surface and volume intrinsic (material related) losses in MEMS resonators. We conclude that the losses in the interface between silicon nitride and aluminum is a very important contributor to the overall energy loss.

General information
State: Published
In vitro characterization of microcontainers as an oral drug delivery system.
We here present in vitro studies showing the promise of microcontainers (fabricated in either SU-8 or Poly(lactic acid) (PLLA)) as an oral drug delivery system for the poorly watersoluble drug, furosemide.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Petersen, R. S. (Intern), Jacobsen, J. (Ekstern), Boisen, A. (Intern), Müllertz, A. (Ekstern)
Publication date: 2014
Event: Abstract from 10th International Conference and Workshop on Biological Barriers, Saarbrücken, Germany.
Main Research Area: Technical/natural sciences
Electronic versions:
Biblio_ical_characterization_of_microcontainers_as_an_oral_drug_delivery_system.pdf

Bibliographical note
Conference poster contribution: 10th International Conference and Workshop on Biological Barriers, Saarbrücken, Germany.
Source: PublicationPreSubmission
Source-ID: 97048489
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014
Lab-on-Blu-ray: Low-cost analyte detection on a disk

In this work, we present for the first time a centrifugal microfluidic system for the detection of analytes in blood using a low cost (< 10$) blu-ray pickup head for detection. The microfluidic operations are carried out on a disk, while the detection method is based on optical measurements of the rotation dynamics of functionalized magnetic nanobeads (MNBs) in an oscillating uniaxial magnetic field.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Technical University of Denmark, Columbia University, Academia Sinica Taiwan
Authors: Donolato, M. (Intern), Antunes, P. S. M. (Intern), Burger, R. (Intern), Bosco, F. (Intern), Olsson, M. (Ekstern), Yang, J. (Ekstern), Chen, C. (Ekstern), Lin, Q. (Ekstern), Hwu, E. T. (Ekstern), Boisen, A. (Intern), Hansen, M. F. (Intern)
Pages: 2044-2046
Publication date: 2014
Loading of microcontainers for oral drug delivery

The pharmaceutical research is facing several obstacles in the development of drug products for the oral delivery. The main problem deals with the intrinsic chemical nature of the new drug candidates, which are often poorly soluble and barely absorbed in the gastro-intestinal tract. Furthermore, they are usually degraded before they are absorbed. These combined factors considerably reduce the bioavailability of many active ingredients. Several strategies have been developed to overcome these challenges. One of them are microfabricated drug delivery devices. Microreservoir based-systems are characterized by small dimensions (100-500 μm), mucoadhesive properties, asymmetric geometry and unidirectional drug release. In the fabrication of these microcontainers, an important task is the drug loading. The state of the art in this field is based on traditional methods used in microtechnology, which for this application in most cases are cost ineffective and unsuitable for large scale production.

The goal of this project was to develop novel techniques for loading of poorly soluble drugs and macromolecules in microcontainers. The research focused on simple and cost effective methods, suitable for a large group of drugs and with the perspective of mass production.

In a first instance, the suitability of inkjet printing as filling method was elucidated. Solutions containing furosemide and lipid based formulations of insulin were dispensed into microcontainers. Secondly, this technique was successfully utilized for the deposition of polymer matrices in microcontainers, which afterwards were loaded with the drug. For this purpose, inkjet printing of solutions of poly(vinylpyrrolidone) was developed. The polymer deposition was homogeneous and reproducible, which demonstrated that inkjet printing is a valuable technology to dispense controlled amounts of polymer into microcontainers. Subsequently, polymer filled-containers were loaded with drug. To achieve this, supercritical impregnation technology was successfully employed. Furthermore, in vitro drug dissolution studies showed that the loading yields and the release properties of the microdevices can be tuned. The effect of different impregnation process parameters on the loading yields was studied, and the drug-polymer interactions were characterized with various spectroscopic techniques. This technique allowed loading of large arrays of the microcontainers in one single operation with high accuracy and repeatability. Furthermore, the combination of inkjet printing and supercritical impregnation allows to minimize the waste of possibly expensive active ingredients.

A successful process for the definition of micropatterns of poly(vinylpyrrolidone) hydrogel by means of UV photolithography was developed. The fabrication of polymer patterns was optimized and loading with both small hydrophobic drugs and proteins was demonstrated. Finally, structural properties of hydrogels were elucidated by rheology and NMR with the perspective of controlling the drug release.

The loading techniques developed in this thesis represent a novelty in the field of microfabricated drug delivery devices. The methods utilized in this research work are potentially integrated in the fabrication process of biopolymer microcontainers.

Low-Power Photothermal Probing of Single Plasmonic Nanostructures with Nanomechanical String Resonators

We demonstrate the direct photothermal probing and mapping of single plasmonic nanostructures via the temperature-induced detuning of nanomechanical string resonators. Single Au nanoslits and nanorods are illuminated with a partially polarized focused laser beam (λ = 633 nm) with irradiances in the range of 0.26–38 μW/μm2. Photothermal heating maps with a resolution of ∼375 nm are obtained by scanning the laser over the nanostructures. Based on the string sensitivities, absorption efficiencies of 2.3 ± 0.3 and 1.1 ± 0.7 are extracted for a single nanoslit (53 nm × 1 μm) and nanorod (75 nm × 185 nm). Our results show that nanomechanical resonators are a unique and robust analysis tool for the low-power investigation of thermoplasmonic effects in plasmonic hot spots.
Mediated amperometric monitoring of DT-diaphorase induction in cancer cells: tool for screening phytotherapeutical drugs

General Information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark, University of Siena
Authors: Montini, L. (Ekstern), Tilli, V. (Ekstern), Caviglia, C. (Intern), Biagi, M. (Ekstern), Giachetti, D. (Ekstern), Zor, K. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 15th International Conference on Electroanalysis
Main Research Area: Technical/natural sciences

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 102790061

Micro and nano structures for biosensing and oral drug delivery

The optics and mechanics from a DVD player can be used to realize compact and sensitive sensor systems. By rotating a disc with integrated microfluidic channels it is possible to manipulate liquid samples such as blood – performing crucial operations like separation, valving and mixing. We integrate sensors such as cantilevers, nanoparticles and resonating strings with centrifugal microfluidics. The sensors are read out by a DVD pick-up head which can perform transmission/absorption measurements and which can detect nm deflections. Also, electrodes are integrated on a disc platform, facilitating electrochemical measurements. In cantilever—based sensing, micrometer sized cantilevers are functionalized on one side with probe molecules. As target analytes bind to the probe molecules the cantilever deflects due to changes in surface stress. This deflection is typically in the nm range and normally only a few cantilevers can be read—out simultaneously. Using a rotating disc system hundreds of cantilevers can be read—out in one second. We will demonstrate how this approach can be used for detection of biomarkers. Hollow cantilevers will be briefly discussed as a new way of performing IR spectroscopy on picoliter amount of sample. Vibrating micrometer sized strings can be used for efficient and sensitive mass detection and for chemical analysis of single nanoparticles. We will show examples from drug characterization and illustrate how the strings can be read—out using blu—ray optics. Finally, we will show how agglutination based assays can be handled and read—out using the disc platform – here targeting biomarkers for rapid diagnostics and prognostics. Micrometer sized containers can be used for oral drug delivery. The hypothesis is that oral drug delivery can be improved significantly by utilizing micrometer sized containers loaded with drug(s) and sealed by intelligent lids that open at specific locations in the body. The containers will, among other features, protect active pharmaceutical ingredients (APIs) during the passage through the stomach and facilitate adhesion to the wall of the intestine for controlled and unidirectional release, followed by absorption through the intestinal wall. We will show our recent findings and results.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Abstract Book - DTU Sustain Conference 2014
Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Main Research Area: Technical/natural sciences
Conference: DTU Sustain Conference 2014, Lyngby, Denmark, 17/12/2014 - 17/12/2014
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Microcontainers, an innovative oral drug delivery system for poorly soluble drugs

General information
Microcontainers as an oral drug delivery system.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Jacobsen, J. (Ekstern), Rades, T. (Ekstern), Boisen, A. (Intern), Müllertz, A. (Ekstern)
Publication date: 2014
Event: Abstract from Globalization of Pharmaceutics Education Network biennial meeting, Helsinki, Finland.
Main Research Area: Technical/natural sciences
Electronic versions:
Nielsen_Abstract.pdf
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2014

Microcontainers as oral drug delivery systems for small molecules and proteins

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Rønholt, S. (Ekstern), Nielsen, L. H. (Intern), Davidsen, A. B. (Ekstern), Keller, S. S. (Intern), Müllertz, A. (Ekstern), Boisen, A. (Intern), Nielsen, H. M. (Ekstern)
Publication date: 2014
Event: Poster session presented at 2014 AAPS Annual Meeting and Exposition, San Diego, CA, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
AAPS_abstract_microcontainers_20140528_1.pdf
Source: PublicationPreSubmission
Source-ID: 101975268
Publication: Research - peer-review › Poster – Annual report year: 2014
Microcontainers for Unidirectional Release in the Upper Intestine

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Marizza, P. (Intern), Keller, S. S. (Intern), Nielsen, L. H. (Intern), Petersen, R. S. (Intern), Nagstrup, J. (Intern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 13th European Symposium on Controlled Drug Delivery
Main Research Area: Technical/natural sciences
Conference: 13th European Symposium on Controlled Drug Delivery, Egmond aan Zee, Netherlands, 16/04/2014 - 16/04/2014
Electronic versions:
ESCCDD_2014_Egmond_aan_Zee_PAOLO_MARIZZA_2.pdf
Source: PublicationPreSubmission
Source-ID: 93522990
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Microfabricated containers for oral drug delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Keller, S. S. (Intern), Nielsen, L. H. (Intern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 40th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Drug delivery, Microcontainers, Spray coating
Electronic versions:
Keller_MNE2014.pdf

Bibliographical note
For oral presentation
Source: PublicationPreSubmission
Source-ID: 103224898
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Microfabricated containers for pH-triggered drug release in the upper intestine

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Keller, S. S. (Intern), Nielsen, L. H. (Ekstern), Marizza, P. (Intern), Petersen, R. S. (Intern), Nagstrup, J. (Intern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 10th International Conference and Workshop on Biological Barriers
Main Research Area: Technical/natural sciences
Conference: 10th International Conference and Workshop on Biological Barriers, Saarbrücken, Germany, 16/02/2014 - 16/02/2014
Electronic versions:
Keller_Biobarrriers2014.pdf

Bibliographical note
Micromechanical photothermal analyser of microfluidic samples.
The present invention relates to a micromechanical photothermal analyser of microfluidic samples comprising an oblong micro-channel extending longitudinally from a support element, the micro-channel is made from at least two materials with different thermal expansion coefficients, wherein the materials are arranged relatively to each other so that heating of the micro-channel results in a bending of the micro-channel, the first material has a first thermal expansion coefficient and is made from a light-specific transparent penetrable material so that when exposed to ultraviolet, visible, or infrared light, the specific light radiates into the channel through said light transparent material, the second material has a second thermal expansion coefficient being different from the first thermal expansion coefficient. The micromechanical photothermal analyser also comprises an irradiation source being adapted to controlled radiate ultraviolet, visible, or infrared light towards and through the transparent micro-channel, and a deflection detector being adapted to detect the amount of deflection of the micro-channel. The wavelength-deflection plot provides a spectrum of an analyte inside the oblong microchannel. To characterize the analyte the plot is compared with the standard database of spectroscopy.

Micromechanical resonators as a tool for polymer characterization
The aim of this Ph.D. project was the evaluation of micromechanical resonators like cantilevers and strings as analytical tools for characterization of polymers. Spray coating was used as the technique to coat one side of the micromechanical resonators with polymer. Process optimization of different spray coating parameters was carried out with two polymer-solvent systems to obtain homogeneous films with uniform thickness and low roughness. Full factorial experimental design was employed to identify the most important parameter among the crucial parameters of spray coating such as nozzle-substrate distance, the temperature of the substrate and the speed of the spraying nozzle. Micromechanical string resonators were successfully developed as an analytical tool for sensitive and fast thermal characterization of polymers with only a few nanograms of sample. Both the glass transition (T_g) and sub-T_g transition of different polymers were detected and confirmed by conventional thermal polymer characterization techniques. An analytical model was derived to validate the resonance frequency response of the polymer coated microstrings during heating cycles. The resonance frequency change provided the quasi-static T_g of polymers while the quality factor change provided the frequency dependent shift of T_g to higher temperature. Microcantilevers were successfully employed as a platform for fast estimation of polymer degradation rate with minute amount of sample compared to conventional techniques. A detailed investigation of enzymatic degradation of poly (D, L-lactide) was done in buffered proteinase K solution. The influence of concentration of the enzyme solution, pre-hydration in buffer, surface morphology and adsorption time of enzymes on the rate of degradation was studied. The bulk degradation rate estimated from the experimental results and model simulation of multilayered cantilever structures matched well with values reported in literature. The basic understanding of the spray coating process and the newly developed approaches of microstrings and microcantilevers as analytical tools show promising potential for investigation of different polymers and pharmaceutical systems.
Micromechanical String Resonators: Analytical Tool for Thermal Characterization of Polymers

Resonant microstrings show promise as a new analytical tool for thermal characterization of polymers with only few nanograms of sample. The detection of the glass transition temperature (Tg) of an amorphous poly(d,l-lactide) (PDLLA) and a semicrystalline poly(l-lactide) (PLLA) is investigated. The polymers are spray coated on one side of the resonating microstrings. The resonance frequency and quality factor (Q) are measured simultaneously as a function of temperature. Change in the resonance frequency reflects a change in static tensile stress, which yields information about the Young’s modulus of the polymer, and a change in Q reflects the change in damping of the polymer-coated string. The frequency response of the microstring is validated with an analytical model. From the frequency independent tensile stress change, static Tg values of 40.6 and 57.6 °C were measured for PDLLA and PLLA, respectively. The frequency-dependent damping from Q indicates higher Tg values of 62.6 and 88.8 °C for PDLLA and PLLA, respectively, at ~105 Hz. Resonant microstrings facilitate thermal analysis of nanogram polymer samples measuring the static and a dynamic glass transition temperature simultaneously.
Molecular diagnostics based on magnetic nanobead clustering dynamics monitored using a Blu-ray optomagnetic readout system

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Uppsala University, Stockholm University, Academia Sinica Taiwan, CIC nanoGUNE Consolider
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 24th Anniversary World Congress on Biosensors, Melbourne, Australia.
Main Research Area: Technical/natural sciences

Electronic versions:
import_1401279983766
Source: PublicationPreSubmission
Source-ID: 92650195
Publication: Research - peer-review › Poster – Annual report year: 2014

Nanoimprinted DWDM laser arrays on indium phosphide substrates
Dense wavelength division multiplexing lasers play a major role in today's long-haul broadband communication. Typical distributed feedback laser cavities consist of long half-pitch gratings in InGaAsP on InP substrates with grating periods of around 240 nm. The lasers include a quarter wavelength shift in the grating, and are single mode with high side-mode suppression. Typically, such lasers are patterned using e-beam lithography (EBL). We present a fabrication method based on patterning by thermal nanoimprint lithography, which is potentially less costly and faster than EBL. Thermal nanoimprint lithography of laser gratings raises two types of challenges: (1) The imprint process itself is delicate due to the mechanical fragility of indium phosphide substrates and the thermal mismatch between the substrate and the silicon stamp. (2) The subsequent processing puts requirements on the imprint resist thickness after patterning, and the alignment between the crystallographic direction of the substrate and the grating pattern. Working laser arrays were produced, with >40 mW optical power and side mode suppression ratios of more than 50 dB in all 12 channels.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Optofluidics, Nanoprobes, Silicon Microtechnology, NIL Technology ApS, NeoPhotonics Corporation
Authors: Smistrup, K. (Ekstern), Nørregaard, J. (Ekstern), Mironov, A. (Ekstern), Bro, T. H. (Ekstern), Bilenberg, B. (Ekstern), Nielsen, T. (Ekstern), Eriksen, J. (Intern), Thilsted, A. H. (Intern), Hansen, O. (Intern), Kristensen, A. (Intern), Rishton, S. (Ekstern), Khan, F. (Ekstern), Emanuel, M. (Ekstern), Ma, Y. (Ekstern), Zhang, Y. (Ekstern)
Pages: 149-153
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Microelectronic Engineering
Volume: 126
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
Nanomechanical identification of liquid reagents in a microfluidic channel

Integration of promising technologies that can enhance sensitivity, selectivity, and throughput into micro total analysis systems (μTAS) are important in making them useful in precise screening of reaction byproducts in analytical chemistry, cellular biology and pharmaceutical industries. But unfortunately so far a method to precisely determine molecular signatures of reagents is missing in μTAS. We have developed a technique whereby molecular signatures of 50 pL of liquid reagents confined within a bimetallic microchannel cantilever can be obtained. This is achieved using wavelength dependent mechanical bending of the cantilever under infrared (IR) radiation. This technique also allows simultaneous physical characterization of the liquid reagent using variations in resonance frequency. It is useful in lab-on-a-chip devices and has a myriad of applications in drug screening, bioreactor monitoring, and petrochemical analysis.
Nanomechanical IR Spectroscopy for the fast analysis of picogram samples of engineered nanomaterials

The proliferation of engineered nanomaterials (ENMs), e.g. in nanomedicine, demands for novel sensitive techniques allowing for the analysis of minute samples. We present nanoelectromechanical system-based IR spectroscopy (NEMS-IR) of picograms of polymeric micelles. The micelles are nebulized with electrospray directly from dispersion and then efficiently collected on the sensor, which detects the IR-wavelength-dependent photothermal sample heating. Only 10 nL of sample (~0.1 mg/mL) is required for the acquisition of an IR spectrum. Measurement, including sample preparation, takes only a few minutes, compared to 2 days for analysis by ATR-FT-IR. NEMS-IR constitutes a promising technique for the fast analysis of ENMs.

Non-labeling multiplex surface enhanced Raman scattering (SERS) detection of volatile organic compounds (VOCs)

In this paper, we report multiplex SERS based VOCs detection with a leaning nano-pillar substrate. The VOCs analyte molecules adsorbed at the tips of the nano-pillars produced SERS signal due to the field enhancement occurring at the localized surface plasmon hot spots between adjacent leaning nano-pillars. In this experiment, detections of acetone and ethanol vapor at different concentrations were demonstrated. The detection limits were found to be 0.0017 ng and 0.0037 ng for ethanol and acetone vapor molecules respectively. Our approach is a non-labeling method such that it does not require the incorporation of any chemical sensing layer for the enrichment of gas molecules on sensor surface. The leaning nano-pillar substrate also showed highly reproducible SERS signal in cyclic VOCs detection, which can reduce the detection cost in practical applications. Further, multiplex SERS detection on different combination of acetone and ethanol vapor was also successfully demonstrated. The vibrational fingerprints of molecular structures provide specific Raman peaks for different VOCs contents. To the best of our knowledge, this is the first multiplex VOCs detection using SERS. We believe that this work may lead to a portable device for multiplex, specific and highly sensitive detection of complex VOCs samples that can find potential applications in exhaled breath analysis, hazardous gas analysis, homeland security and environmental monitoring.
Surface enhanced Raman scattering, SERS, Volatile organic compounds (VOCs) detection, Multiplex detection, Non-labeling

DOIs: 10.1016/j.aca.2014.06.043

Publication: Research - peer-review › Journal article – Annual report year: 2014
Optical detection of radio waves through a nanomechanical transducer.

Low-loss transmission and sensitive recovery of weak radio-frequency and microwave signals is a ubiquitous challenge, crucial in radio astronomy, medical imaging, navigation, and classical and quantum communication. Efficient up-conversion of radio-frequency signals to an optical carrier would enable their transmission through optical fibres instead of through copper wires, drastically reducing losses, and would give access to the set of established quantum optical techniques that are routinely used in quantum-limited signal detection. Research in cavity optomechanics has shown that nanomechanical oscillators can couple strongly to either microwave or optical fields. Here we demonstrate a room-temperature optoelectromechanical transducer with both these functionalities, following a recent proposal using a high-quality nanomembrane. A voltage bias of less than 10 V is sufficient to induce strong coupling between the voltage fluctuations in a radio-frequency resonance circuit and the membrane's displacement, which is simultaneously coupled to light reflected off its surface. The radio-frequency signals are detected as an optical phase shift with quantum-limited sensitivity. The corresponding half-wave voltage is in the microvolt range, orders of magnitude less than that of standard optical modulators. The noise of the transducer—beyond the measured 800 pV Hz-1/2 Johnson noise of the resonant circuit—consists of the quantum noise of light and thermal fluctuations of the membrane, dominating the noise floor in potential applications in radio astronomy and nuclear magnetic imaging. Each of these contributions is inferred to be 60 pV Hz-1/2 when balanced by choosing an electromechanical cooperativity of ~150 with an optical power of 1 mW. The noise temperature of the membrane is divided by the cooperativity. For the highest observed cooperativity of 6,800, this leads to a projected noise temperature of 40 mK and a sensitivity limit of 5 pV Hz-1/2. Our approach to all-optical, ultralow-noise detection of classical electronic signals sets the stage for coherent up-conversion of low-frequency quantum signals to the optical domain.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Institute of Standards and Technology, University of Copenhagen
Authors: Bagci, T. (Forskerdatabase), Simonsen, A. (Ekstern), Schmid, S. (Intern), Villanueva Torrijo, L. G. (Intern), Zeuthen, E. (Forskerdatabase), Appel, J. (Forskerdatabase), Taylor, J. M. (Ekstern), Sørensen, A. (Ekstern), Usami, K. (Forskerdatabase), Schliesser, A. (Forskerdatabase), Polzik, E. (Forskerdatabase)
Pages: 81-85
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Nature
Volume: 507
Issue number: 7490
ISSN (Print): 0028-0836
Ratings:
BFI (2018): BFI-level 3
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 13.33
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 14.38
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 14.22
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 14.96
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 14.01
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 13.96
Optical, Nanomechanical and Electrochemical Sensing on a DVD Disc

Our vision is to create a platform where optical, nanomechanical and electrochemical sensors can be integrated and read-out using the mechanics and the optics from DVDs and Blu-Rays. Integrating sensors on a disc allows us to use centrifugal microfluidics which has been developed for more than 50 years and which has proven to be a simple and powerful way to manipulate liquid samples without the need of external pumps [1]. As an example, serum can be separated from a whole blood sample in a few minutes by simply spinning the disc and allowing the cellular components to sediment. Cantilever-like sensors have been integrated on a disc [2] and we now have a method of obtaining large amount of data – allowing us to do statistics on the measurements. Currently, we are studying the specific detection of biomarkers, such as suPAR [3]. Additionally, we try to implement optical microscopy on the spinning platform in order to study and count larger objects such as cells. In this way it will be possible to analyze a given sample for several parameters simultaneously. Electrodes can also be integrated on the spinning platform [4] and hereby it is possible to perform electrochemical measurements at the same time as having the benefit of the centrifugal liquid handling. As an example it is simple to measure in flow conditions and to perform continuous cyclic voltammograms in different concentrations of electrolytes using built-in valves. In conclusion, the merger of sensors and centrifugal microfluidics combined with sensitive and compact read-out possibilities from optical pick-up heads makes it possible to realize full sample pretreatment and read-out in a both fast and compact manner. References: 1. M. Madou et al., Lab on a CD, Annual Review of Biomedical Engineering, Vol. 8: 601-628, 2016 2. F.G Bosco et al., High throughput label-free platform for statistical bio-molecular sensing, Lab on a Chip, 11(14) 2411-2416, 2011 3. M. Bache et al., Nanomechanical recognition of prognostic biomarker suPAR with DVD-ROM optical technology, Nanotechnology 24 (44), 444011, 2013 4. A.L. Brøeger et al., Centrifugal microfluidic platform with real-time electrochemical detection, 224th Electrochemical Society Meeting, 2013
Optimizing Signal-to-Noise Ratio of SERS Ag Capped Si Nanopillars

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Wu, K. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014
Event: Poster session presented at Third International Conference on Frontiers of Plasmonics, Xiamen, China.
Main Research Area: Technical/natural sciences
Electronic versions:
2014.03.FOP3.v6.pdf
Source: dtu
Publication: Research - peer-review › Poster – Annual report year: 2014

Photothermal probing of plasmonic hotspots with nanomechanical resonator
Plasmonic nanostructures (hotspots) are key components e.g. in plasmon-enhanced spectroscopy, plasmonic solar cells, or as nano heat sources. The characterization of single hotspots is still challenging due to a lack of experimental tools. We present the direct photothermal probing and mapping of single plasmonic nanoslits via the thermally induced detuning of nanomechanical string resonators. A maximum relative frequency detuning of 0.5 % was measured for a single plasmonic nanoslit for a perpendicularly polarized laser with a power of 1350 nW. Finally, we show the photothermal scan over a nanoslit array.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Schmid, S. (Intern), Wu, K. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
Pages: 1205-1208
Publication date: 2014

Host publication information
Title of host publication: 2014 IEEE 27th International Conference on Micro Electro Mechanical Systems (MEMS)
Publisher: IEEE
ISBN (Print): 9781479935093
Main Research Area: Technical/natural sciences
Laser beams, Nanoelectromechanical devices, Nanophotonics, Plasmonics, Resonators, Fields, Waves and Electromagnetics
DOIs:
10.1109/MEMSYS.2014.6765864
Source: dtu
Source-ID: n::oai:DTIC-ART:iel/441685379::38408
Publication: Research - peer-review › Article in proceedings – Annual report year: 2014

Photothermal resonance
The present invention relates to a method for detecting photo-thermal absorbance of a material utilising a mechanically temperature sensitive resonator (20) and a sample being arrange in thermal communication with the temperature sensitive resonator. The present invention further relates to an apparatus for detecting photo-thermal absorbance of a sample.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Yamada, S. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Larsen, T. (Intern)
Publication date: 2014

Publication information
IPC: G01N21/17
Patent number: WO2014063712
Physical characterization of photocrosslinked poly(vinyl pyrrolidone) (PVP) hydrogels for drug delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Chemical and Biochemical Engineering, The Danish Polymer Centre, University of Trieste, University of Copenhagen
Number of pages: 2
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 8th Symposium of The Pharmaceutical Solid State Research Cluster
Main Research Area: Technical/natural sciences
Electronic versions:
Marizza_PSSRC2014_1.pdf

Bibliographical note
8th Symposium of The Pharmaceutical Solid State Research Cluster (PSSRC), Ljubljana, Slovenia, September 16-18 2014,
Source: PublicationPreSubmission
Source-ID: 103224915
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Polymer drug matrix loading in micro-containers using hot punching

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Petersen, R. S. (Intern), Nagstrup, J. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 40th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Hot embossing, Microcontainers, Oral drug delivery, SU-8, Photolithography
Electronic versions:
Petersen_MNE2014.pdf

Bibliographical note
For poster presentation
Source: PublicationPreSubmission
Source-ID: 103224970
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Polymer-filled microcontainers for oral delivery loaded using supercritical impregnation
In the last years a large variety of drug delivery systems have been developed to improve bioavailability of therapeutics in oral administration. An increasing interest has arisen in reservoir-based microdevices designed for active ingredients like water insoluble compounds and fragile biomolecules. Such microdevices are designed to protect the active ingredient against degradation and deactivation, and to allow cytoadhesion and unidirectional drug release. There are few works which optimize the drug loading step and often therapeutics are dosed in the microdevices through laborious and time consuming procedures. This work proposes an effective loading technique for a poorly soluble model drug in microcontainers, by combining inkjet printing and supercritical fluid impregnation. Well defined quantities of poly(vinyl
Pyrrolidone) (PVP) solutions are dispensed into microcontainers by inkjet printing with a quasi-no-waste performance. Then ketoprofen is impregnated in the polymer matrix by using supercritical carbon dioxide (scCO₂) as loading medium. The amount of polymer is controlled by the volume and the number of droplets of dispensed polymer and drug loading is tuned by varying the impregnation parameters. Compared to solid dispersions of the same drug and polymer, scCO₂-impregnated microcontainers exhibit a more reproducible drug loading and a faster dissolution rate of the active compound which allows drug release to be modulated. The combination of these loading techniques potentially allows the high throughput fabrication of microdevices for oral drug delivery with a safe and solvent-free solution. © 2013 Published by Elsevier B.V.
Pyrolysed 3D-Carbon Scaffolds Induce Spontaneous Differentiation of Human Neural Stem Cells and Facilitate Real-Time Dopamine Detection

Structurally patterned pyrolysed three-dimensional carbon scaffolds (p3Dcarbon) are fabricated and applied for differentiation of human neural stem cells (hNSCs) developed for cell replacement therapy and sensing of released dopamine. In the absence of differentiation factors (DF) the pyrolysed carbon material induces spontaneous hNSC differentiation into mature dopamine-producing neurons and the 3D-topography promotes neurite elongation. In the presence and absence of DF, ≈73–82% of the hNSCs obtain dopaminergic properties on pyrolysed carbon, a to-date unseen efficiency in both two-dimensional (2D) and 3D environment. Due to conductive properties and 3D environment, the p3D-carbon serves as a neurotransmitter trap, enabling electrochemical detection of a significantly larger dopamine fraction released by the hNSC derived neurons than on conventional 2D electrodes. This is the first study of its kind, presenting new conductive 3D scaffolds that provide highly efficient hNSC differentiation to dopaminergic phenotype combined with real-time in situ confirmation of the fate of the hNSC-derived neurons.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark, University of California, Irvine, Capres A/S, Universidad Autónoma de Madrid
Number of pages: 11
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Advanced Functional Materials
ISSN (Print): 1616-301X
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 11.56
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 11.93
Web of Science (2015): Indexed yes
**Quadratic measurement and conditional state preparation in an optomechanical system**

We experimentally demonstrate, for the first time, quadratic measurement of mechanical motion in an optomechanical system. We use this nonlinear measurement to conditionally prepare classical non-Gaussian states of motion of a micromechanical oscillator.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Queensland
Authors: A. Brawley, G. (Ekstern), Vanner, M. A. (Ekstern), Bowen, W. P. (Ekstern), Schmid, S. (Intern), Boisen, A. (Intern)
Number of pages: 3
Publication date: 2014

**Host publication information**

Title of host publication: Proceedings of CLEO 2014
Publisher: Optical Society of America (OSA)
ISBN (Electronic): 9781557529992
Series: Optics Infobase Conference Papers
ISSN: 2162-2701
Main Research Area: Technical/natural sciences
Conference: Conference on Lasers and Electro-Optics 2014, San Jose, CA, United States, 08/06/2014 - 08/06/2014
Instrumentation, Atomic and Molecular Physics, and Optics, Conditional state, Mechanical motions, Micromechanical oscillators, Non-Gaussian state, Nonlinear measurement, Opto-mechanical systems, Oscillistors
Source: FindIt
Source-ID: 22011111210
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015

**Real-time monitoring of drug-induced cytotoxicity kinetics using a tailor-made impedance platform**

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Colloids and Biological Interfaces, Molecular Windows
Real-time multi-parameter cell-based analysis platform: towards new tools for biomedical research

Monitoring cellular dynamics such as cell surface interactions, metabolic processes and exocytosis, can help unravelling the causes behind the evolution of diseases associated with cellular dysfunction. A better understanding of cellular behaviour opens up possibilities for the development of new biomedical diagnostic techniques, drug discovery and screening.

My project focused on the further development, improvement and exploration of the EXCELL microfluidic platform with particular interest in drug kinetic monitoring and neurotransmitter detection. The aim was to perform multi-parameter real-time cell based assays for their future application as complementary tools in biomedical research. Specifically, the research has focused on: (1) Characterization of the cell culture and detection platforms (batch system for static conditions and microfluidics for perfusion conditions) and optimization of protocols and procedures for performing different cellular assays. (2) Electrochemical impedance spectroscopy (EIS) applied for drug screening and drug delivery in cancer research and wound healing studies. (3) Amperometry for monitoring of neurotransmitter exocytosis, relevant in research on Parkinson’s disease. (4) The combination of amperometry, EIS monitoring and microscopic visualization in microfluidics assays for real-time multi-parameter analysis on the same cell population.

The research carried out in this thesis branches out from the context of the EU-funded FP7 project EXCELL (Exploring Cellular Dynamics at Nanoscale) aimed at developing innovative systems for the investigation of real time cellular dynamics. The main focus of the EXCELL project was related to the development of a multi-parameter microfluidic cell culture and detection platform, combining electrochemical and optical techniques.
Removal of residues from reactive ion etched silicon surfaces characterized with XPS and Raman spectroscopy

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Brøgger, A. L. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 40th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Electronic versions:
MNEabstract_alibr.pdf
Source: PublicationPreSubmission
Source-ID: 101141566
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Sensitive Blu-ray detection of clustered rolling circle products for molecular diagnostics

In this paper we present a method for low cost and rapid sensing of nucleic acids (NA) for infectious diagnostics, where isothermal rolling circle amplification (RCA) products, specifically generated by the presence of the human pathogen Pseudomonas aeruginosa (PA), are bound to magnetic nanoparticles (MNP). Samples are injected into a microfluidic disc chip and analyzed on a novel magneto-optical platform. The sensing approach is based on the clustering pattern of MNP in a magnetic field and measures the effect of cluster formation on transmitted light using a standard Blu-Ray pickup head. The concentration of DNA target is correlated with an increase of clustered particles.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Silicon Microtechnology, Stockholm University
Sensitive Blu-ray detection of clustered rolling circle products for molecular Diagnostics

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Magnetic Systems, Nanoprobes, Silicon Microtechnology, Stockholm University
Number of pages: 2
Publication date: 2014

Single-layer graphene on silicon nitride micromembrane resonators
Due to their low mass, high quality factor, and good optical properties, silicon nitride (SiN) micromembrane resonators are widely used in force and mass sensing applications, particularly in optomechanics. The metallization of such membranes would enable an electronic integration with the prospect for exciting new devices, such as optoelectromechanical transducers. Here, we add a single-layer graphene on SiN micromembranes and compare electromechanical coupling and mechanical properties to bare dielectric membranes and to membranes metallized with an aluminium layer. The electrostatic coupling of graphene covered membranes is found to be equal to a perfectly conductive membrane, without significantly adding mass, decreasing the superior mechanical quality factor or affecting the optical properties of pure SiN micromembranes. The concept of graphene-SiN resonators allows a broad range of new experiments both in applied physics and fundamental basic research, e.g., for the mechanical, electrical, or optical characterization of graphene.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Institute of Standards and Technology, Harvard University, Technical University of Denmark, Massachusetts Institute of Technology, University of Copenhagen
Authors: Schmid, S. (Intern), Bagci, T. (Forskerdatabase), Zeuthen, E. (Forskerdatabase), Taylor, J. M. (Ekstern), Herring, P. K. (Ekstern), Cassidy, M. C. (Ekstern), Marcus, C. M. (Ekstern), Villanueva Torrijio, L. G. (Intern), Armato, B. (Ekstern), Boisen, A. (Intern), Shin, Y. C. (Ekstern), Kong, J. (Ekstern), Sørensen, A. S. (Ekstern), Usami, K. (Ekstern), Polzik, E. S. (Ekstern)
Pages: 054513
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Applied Physics
Surface-enhanced Raman scattering (SERS)-based volatile organic compounds (VOCs) detection using plasmonic bimetallic nanogap substrate

In this paper, we present surface-enhanced Raman scattering (SERS)-based volatile organic compounds (VOCs) detection with bimetallic nanogap structure substrate. Deep UV photolithography at the wavelength of 250 nm is used to pattern circular shape nanostructures. The nanogap between adjacent circular patterns is 30 +/- 5 nm. Silver (30 nm) and gold (15 nm) plasmonic active layers are deposited on the nanostructures subsequently. SERS measurements on different concentrations of acetone vapor ranged from 0.7, 1.5, 3.5, 10.3, 24.5 % and control have been performed with the substrate. The measurement results are found reproducible, and the detection limit is found to be 9.5 pg (acetone molecule). The detection sensitivity is 28.7 % higher than that of the recent reported leaning silicon nanopillar substrate. With further system miniaturization, the sensing technique can work as a portable SERS-based VOCs detection platform for point-of-care breath analysis, homeland security, chemical sensing and environmental monitoring.
Synthesis and characterization of covalent diphenylalanine nanotube-folic acid conjugates

Herein, we describe the synthesis and characterization of a covalent nanoscale assembly formed between diphenylalanine micro/nanotubes (PNT) and folic acid (FA). The conjugate was obtained via chemical functionalization through coupling of amine groups of PNTs and carboxylic groups of FA. The surface analysis of PNT-FA indicated the presence of FA aggregates on the surface of PNTs. The covalent interaction between FA and self-assembled PNTs was further investigated using fluorescence microscopy, Raman and surface-enhanced Raman scattering (SERS) spectroscopies. The SERS experiments were performed on a large area silver-capped (diameter of 62 nm) silicon nanopillars with an approximate height of 400 nm and a width of 200 nm. The results showed that the PNT-FA synthesis procedure preserves the molecular structure of FA. The PNT-FA conjugate presented in this study is a promising candidate for applications in the detection and diagnosis of cancer or tropical diseases such as leishmaniasis and as a carrier nanosystem delivering drugs to malignant tumors that overexpress folate receptors.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Electron Nanoscopy, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics
Synthesis and characterizations of high permittivity ultraviolet cured soft elastomeric networks and composites applicable as dielectric electroactive polymer

The objective of this thesis was preparation and characterizations of high permittivity ultraviolet (UV) cured elastomeric networks and composites applicable as dielectric electroactive polymers (DEAPs). At present, none of the commercially available elastomers such as acrylics, poly (dimethyl siloxane) (PDMS) and polyurethanes are designed with the requirements specific for DEAPs. Thus there is a need to develop elastomers with low elastic modulus, low viscous and dielectric losses and high relative permittivity. Interpenetrating networks and fumed silica reinforced composites of poly (propylene oxide) (PPO) were prepared which showed marked improvements in properties compared to the acrylic elastomers. But difficulties in curing by industrial processes and handling of these elastomers posed as limitations. So the focus was on optimizing UV induced thiol-ene reactions for curing commercially available PDMS. UV curing of PDMS was successfully established which eliminated the major drawbacks of widely used platinum catalyzed addition curing of PDMS. An advanced sequential curing used to form the PDMS networks showed low elastic modulus and low viscous losses than the former-developed processes due to better control over the heterogeneity of the networks. The sequential curing approach was successfully used to incorporate conductive multiwalled carbon nanotubes (MWCNTs) in higher concentrations than usual without making the elastomers conductive. The PDMS-MWCNT composites also showed high relative permittivity, low elastic modulus and low viscous and dielectric losses. Thus the elastomers developed in this project show promising properties to be considered as potential DEAPs.

Tailoring the structure and the properties of pyrolysed carbon electrodes

This paper presents a microchip incorporating an aptamer-functionalized nanopillar substrate, enabling the specific detection of low-abundance biomolecules using surface enhanced Raman spectroscopy (SERS). In a temperature controlled microchannel, aptamers immobilized on the nanostructure surface specifically recognize target molecules.
Raman-tagged biomolecules trapped within a cluster of leaning nanopillars report greatly enhanced Raman signals due to the coupling effect of localized surface plasmons. It was demonstrated that integrated intensities of spatially collected Raman responses are linearly proportional to analyte concentrations in the low picomolar regime (10/ 50/ 100/ 200 pM), showing the capability of our device for sensitive and quantitative detection of analyte molecules.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Columbia University
Authors: Yang, J. (Ekstern), Palla, M. (Ekstern), Bosco, F. G. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Ju, J. (Ekstern), Lin, Q. (Ekstern)
Pages: 1799-1802
Publication date: 2013

**Host publication information**

Title of host publication: Proceedings of the The 17th International Conference on Solid-State Sensors, Actuators and Microsystems
Publisher: IEEE
ISBN (Print): 9781467359832
Main Research Area: Technical/natural sciences
Conference: 17th International Conference on Solid-State Sensors, Actuators and Microsystems, Barcelona, Spain, 16/06/2013 - 16/06/2013
bioMEMS, biosensors, microfluidics, microsensors, molecular biophysics, nanobiotechnology, nanosensors, optical sensors, Raman spectroscopy, surface enhanced Raman scattering, surface plasmons, Computing and Processing, Engineering Profession, General Topics for Engineers, Geoscience, Nuclear Engineering
DOIs: 10.1109/Transducers.2013.6627138
Source: dtu
Source-ID: n::oai:DTIC-ART:iel/409255442::36273
Publication: Research - peer-review › Article in proceedings – Annual report year: 2013

A slow cooling rate of indomethacin melt spatially confined in microcontainers increases the physical stability of the amorphous drug without influencing its biorelevant dissolution behaviour

Amorphous indomethacin was prepared by melting the γ-form of indomethacin, spatially confined within microcontainers (inner diameter of 223 μm), followed by cooling of the melt at a rate of 14, 23 or 36 K/min. The physical stability of the amorphous indomethacin within microcontainers was investigated using Raman microscopy. Furthermore, the dissolution behaviour of confined amorphous indomethacin was evaluated in biorelevant intestinal media at pH 6.5. After 30 days of storage, 10.3±1.2 % of the amorphous indomethacin cooled at 14 K/min and confined within microcontainers was found to be crystalline. When the melt of indomethacin was cooled at 23 or 36 K/min, 20.7±1.5 and 31.0±2.6% of the indomethacin were found to be crystalline after storage for 30 days. Scanning electron microscopy showed a smooth surface of amorphous indomethacin within the microcontainers when cooling the melt at 14 K/min, whereas cracks and an uneven surface were observed when cooling at rates of 23 and 36 K/min. The uneven surface is hypothesised to be the main reason for the lower physical stability, as the cracks could act as nucleation sites for crystal growth. The rate of cooling was not seen to have any effect on the dissolution of amorphous indomethacin from the microcontainers.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Müllertz, A. (Ekstern), Rades, T. (Ekstern)
Pages: 268-274
Publication date: 2013

**Publication information**

Journal: Drug Delivery and Translational Research
Volume: 4
Issue number: 3
ISSN (Print): 2190-393X
Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): SNIP 0.832 SJR 0.944
Web of Science (2017): Indexed Yes
Scopus rating (2016): SJR 0.976 SNIP 0.71 CiteScore 2.76
Biodegradable microcontainers as an oral drug delivery system for poorly soluble drugs.

PURPOSE: To fabricate microcontainers in biodegradable polyactic acid (PLLA) polymer films using hot embossing, and investigate the application of fabricated microcontainers as an oral drug delivery system for a poorly soluble drug.

METHODS: For fabrication of the PLLA microcontainers, a film of PLLA was produced by spin coating. The film was heated above the polymer glass transition temperature (Tg), and a stamp was forced into the film. Following cooling of the film the stamp was removed, exposing the formed microcontainers. Microcontainers were filled with amorphous furosemide sodium salt (produced by spray drying) using a simplified version of a screen printing technique. An enteric-resistant lid of Eudragit L-100 was subsequently spray coated onto the cavity of the microcontainers. Release of amorphous furosemide salt from the coated microcontainers was investigated using a μ-Diss profiler. Release experiments were carried out in biorelevant gastric medium (pH 1.6) for 2 h, followed by 3 h in a biorelevant intestinal medium (pH 6.5). Moreover, biorelevant flow through dissolution was also carried out in conjunction with UV imaging to visualize the release of amorphous furosemide salt from the coated microcontainers.

RESULTS: Fabricated PLLA microcontainers had an inner diameter of 220 μm and a height of 100 μm. The screen printing technique was shown to be an optimized set-up to fill the microcontainers with drug. From the release experiments it was observed that the Eudragit layer prevented drug release in biorelevant gastric medium, while an immediate release of the amorphous furosemide salt was seen in the biorelevant intestinal medium. The same trend was observed in the UV imaging experiments – negligible drug release was observed in gastric medium, whereas following re-equilibration of the dissolution cell with the intestinal medium, a release of furosemide was observed after 1 min with an increased release after 5 min of dissolution.

CONCLUSIONS: Biodegradable microcontainers were successfully fabricated and loaded with drug. Coating with Eudragit L-100 proved to be useful for protecting drug release from microcontainers in gastric medium, and facilitated an immediate release in the intestinal medium. The fabricated microcontainers therefore show considerable future potential as oral drug delivery systems.
Black silicon maskless templates for carbon nanotube forests

We present here a proof of concept for a novel fabrication method of vertically aligned carbon nanotube forests, utilizing black silicon nanograss (a forest of silicon nanometer-sized spikes created with reactive ion etching) coated with titanium tungsten diffusion barrier as a template. The method allows maskless definition of carbon nanotube forests with control of their density, nanotube diameter and height. Four nanograss reactive ion etching recipes are investigated and their wafer-to-wafer repeatability, wafer uniformity, and density control is discussed. Evaluation of carbon nanotube forests grown on the nanograss substrates is presented with discussion of their morphology, diameter distribution, and catalyst thickness influence.
A cost-effective method for fabricating antireflective subwavelength structures on silicon carbide is demonstrated. The nanopatterning is performed in a 2-step process: aluminum deposition and reactive ion etching. The effect of the deposited aluminum film thickness and the reactive ion etching conditions, on the average surface reflectance and nanostructure landscape have been investigated systematically. The average reflectance of silicon carbide surface is significantly suppressed from 25.4% to 0.05%, under the optimal experimental conditions, in the wavelength range of 390-784 nm. The presence of stochastic nanostructures also changes the wetting properties of silicon carbide surface from hydrophilic (47°) to hydrophobic (108°).
Centrifugal microfluidic platform with real-time electrochemical detection

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems
Authors: Brøgger, A. L. (Intern), Andreasen, S. Z. (Intern), Bosco, F. (Intern), Andersen, K. B. (Intern), Kwasny, D. (Intern), Svendsen, W. E. (Intern), Boisen, A. (Intern)
Pages: 202768
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Electrochemical Society. Meeting Abstracts (Online)
Volume: MA2013-02
ISSN (Print): 2151-2043
Original language: English
Electronic versions:
2013 ECS Abstract ALB.pdf
Source: dtu
Source-ID: u::8332
Publication: Research - peer-review › Journal article – Annual report year: 2013

Compact MEMS/NEMS characterization platform using a DVD optical pick-up unit with optical imaging function

In this work, we present a compact, simple and efficient platform for Micro-electromechanical systems (MEMS)/Nano-electromechanical systems (NEMS) characterization. In this platform, a CCD camera is combined with a DVD optical pick-up unit (OPU). The CCD camera captures optical image of MEMS/NEMS samples and detection laser spot, which makes laser alignment on measurement target easier. The DVD OPU is used for detection of resonant frequency measurements of the samples. Working bandwidth and noise level of the OPU are 100 MHz and 1.3 pmHz^2, respectively. Furthermore, the OPU has a laser spot size of 560 μm (full width at half maximum, FWHM), which is capable of measuring cantilevers and strings with sub-micron width. A homemade nano-scale resolution X-Y-Z positioner with working distances of 12, 12, 5 mm is responsible for laser-sample alignment. Both thermal and excited resonant frequencies of MEMS/NEMS cantilevers and strings are characterized.

General information
Computational and experimental studies of the interaction between single-walled carbon nanotubes and folic acid

This work involved the preparation of a conjugate between single-walled carbon nanotubes and folic acid that was obtained without covalent chemical functionalization using a simple "one pot" synthesis method. Subsequently, the conjugate was investigated by a computational hybrid method: our own Nlayered Integrated Molecular Orbital and Molecular Mechanics (B3LYP(6–31G(d):UFF)). The results confirmed that the interaction occurred via hydrogen bonding between protons of the glutamic moiety from folic acid and π electrons from the carbon nanotubes. The single-walled carbon nanotube-folic acid conjugate presented herein is believed to lead the way to new potential applications as carbon nanotube-based drug delivery systems.
Conducting pyrolysed carbon scaffold for tissue engineering

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, BioLabChip, Nanoprobes, Bioanalytics, Fluidic Array Systems and Technology
Authors: Mohanty, S. (Intern), Amato, L. (Intern), Heiskanen, A. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Dufva, M. (Intern), Emnéus, J. (Intern)
Publication date: 2013

Host publication information
Title of host publication: Proceedings of the 39th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Electronic versions:
prod11389012046900.Conducting_pyrolysed_carbon_scaffold_for_tissue_engineering.pdf
Detection of Airborne Nanoparticles with Mechanical Systems

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark
Authors: Schmid, S. (Intern), Kurek, M. (Intern), Adolphsen, J. (Ekstern), Boisen, A. (Intern)
Number of pages: 3
Publication date: 2013
Main Research Area: Technical/natural sciences

Development of Electrochemical Cantilever Sensors for DNA Applications

In this work, we develop a generic DNA based sensing platform used for characterizing surface functionalization and detecting DNA hybridization. Silicon nitride cantilever sensors are fabricated with an integrated three-electrode system and integrated in a microfluidic chip. Cantilevers with gold electrodes are functionalized with thiol-modified single stranded DNA (ssDNA) probes to detect target DNA. During functionalization and hybridization, information related to nanomechanical changes on the surface are obtained by optical measurements of changes in cantilever deflection. Simultaneously, the process is monitored electrochemically. The results clearly indicate that the electrochemical cantilever sensor is very sensitive for detecting DNA hybridization at the cantilever surface.

General information
State: Published
Organisations: Nanoprobes, Department of Micro- and Nanotechnology, Bioanalytics, BioLabChip, Lund University, McGill University
Authors: Quan, X. (Intern), Heiskanen, A. (Intern), Yi, S. (Intern), Labuda, A. (Ekstern), Wolff, A. (Intern), Dulanto, J. (Ekstern), Grutter, P. (Ekstern), Tenje, M. (Ekstern), Boisen, A. (Intern)
Pages: 2077-81
Publication date: 2013
Main Research Area: Technical/natural sciences
DNA hybridization sensing for cytogenetic analysis

Cytogenetic analysis focuses on studying the cell structure, mainly in respect to chromosome content and their structure. Chromosome abnormalities, such as translocations may cause various genetic disorders, but are also associated with haematological malignancies. Chromosome translocations are rearrangements between two chromosome arms that results in two derivative chromosomes having a mixed DNA sequence. The current detection method is a Fluorescent In situ Hybridization, which requires a use of expensive, fluorescently labeled probes that target the DNA sequences of two chromosomes involved in the translocation (Kwasny et al., 2012).

We have developed a new double hybridization assay that allows for sorting of the DNA chromosomal fragments into separate compartment, moreover allowing for detection of the translocation. To detect the translocation it is necessary to determine that the two DNA sequences forming a derivative chromosome are connected, which is achieved by two subsequent hybridization steps. The first example of the translocation detection was presented on lab-on-a-disc using fluorescently labeled DNA fragments, representing the derivative chromosome (Brøgger et al., 2012). To allow for cheaper detection a label-free approach has been investigated using electrochemical impedance spectroscopy as a sensing method. We present here our recent results in regards to DNA sensing on metallic and conductive polymer electrodes for translocation detection. Our sensors are inexpensive and can be successfully applied in cytogenetic analysis as a replacement of standard techniques.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics, Nanoprobes, Technical University of Denmark
Publication date: 2013

Host publication information
Title of host publication: Proceedings of Analytix 2013
Main Research Area: Technical/natural sciences
Conference: Analytix 2013, Suzhou, China, 21/03/2013 - 21/03/2013
Source: dtu
Source-ID: u::9971
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2013

Drug-polymer filled micro-containers for oral delivery loaded using supercritical CO₂ aided-impregnation

In this work we present an effective loading technique of micro-containers for oral drug delivery of a poorly water soluble drug in a solid dispersion with polymer. By combining inkjet printing and supercritical CO₂ impregnation we load
ketoprofen in a solid dispersion with poly(vinylpyrrolidone) (PVP) into cylindrical micro-containers providing unidirectional release. Both the printing and the impregnation step can be tuned in order to control drug loading with accuracy in the range of micro-grams.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Trieste, University of Copenhagen
Authors: Marizza, P. (Intern), Keller, S. S. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Kikic, I. (Ekstern), Moneghini, M. (Ekstern), De Zordi, N. (Ekstern), Solinas, D. (Ekstern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2013

Host publication information
Title of host publication: Proceedings of the 40th Annual Meeting & Exposition of the Controlled Release Society
Main Research Area: Technical/natural sciences
Electronic versions:
prod11395147470321.CRS_2013_Abstract_FINAL_VERSION.pdf
Source: dtu
Source-ID: u::10866
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Enhanced Light–Matter Interactions in Graphene-Covered Gold Nanovoid Arrays
The combination of graphene with noble-metal nanostructures is currently being explored for strong light–graphene interactions enhanced by plasmons. We introduce a novel hybrid graphene–metal system for studying light–matter interactions with gold-void nanostructures exhibiting resonances in the visible range. Enhanced coupling of graphene to the plasmon modes of the nanovoid arrays results in significant frequency shifts of the underlying plasmon resonances, enabling 30% enhanced absolute light absorption by adding a monolayer graphene and up to 700-fold enhancement of the Raman response of the graphene. These new perspectives enable us to verify the presence of graphene on gold-void arrays, and the enhancement even allows us to accurately quantify the number of layers. Experimental observations are further supported by numerical simulations and perturbation-theory analysis. The graphene gold-void platform is beneficial for sensing of molecules and placing Rhodamine 6G (R6G) dye molecules on top of the graphene; we observe a strong enhancement of the R6G Raman fingerprints. These results pave the way toward advanced substrates for surface-enhanced Raman scattering (SERS) with potential for unambiguous single-molecule detection on the atomically well-defined layer of graphene.

General information
State: Published
Organisations: Department of Photonics Engineering, Structured Electromagnetic Materials, Department of Micro- and Nanotechnology, Nanoprobes, Silicon Microtechnology, Center for Individual Nanoparticle Functionality, Center for Nanostructured Graphene, Fudan University
Authors: Zhu, X. (Intern), Shi, L. (Ekstern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern), Zi, J. (Ekstern), Xiao, S. (Intern), Mortensen, N. A. (Intern)
Pages: 4690–4696
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Nano Letters
Volume: 13
Issue number: 10
ISSN (Print): 1530-6984
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 13.4
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 14.76
Fabrication of antireflective SiC surface using plasma etching with self-assembled nanopattern

General information
State: Published
Organisations: Department of Photonics Engineering, Department of Micro- and Nanotechnology, Nanoprobes, Diode Lasers and LED Systems
Authors: Ou, Y. (Intern), Argyraki, A. (Intern), Ou, H. (Intern)
Publication date: 2013
Main Research Area: Technical/natural sciences
Electronic versions: 2013 MNE A0.ppt

Bibliographical note
39th International Conference on Micro and Nano Engineering
16 – 19 September 2013

Relations
Activities:
39th International Conference on Micro and Nano Engineering
Source: dtu
Ferromagnetic shadow mask for spray coating of polymer patterns

We present the fabrication of a wafer-scale shadow mask with arrays of circular holes with diameters of 150–400 μm. Standard UV photolithography is used to define 700 μm thick SU-8 structures followed by electroplating of nickel and etching of the template. The ferromagnetic properties of the shadow mask allow magnetic clamping to the substrate and spray coating of well defined polymer patterns.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Keller, S. S. (Intern), Bosco, F. (Intern), Boisen, A. (Intern)
Pages: 427-431
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Microelectronic Engineering
Volume: 110
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.737 SNIP 0.949 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.813 SNIP 1.148 CiteScore 1.8
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.934 SNIP 1.093
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.834 SNIP 1.098
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.027 SNIP 1.06
Web of Science (2008): Indexed yes
Fluidic automation of nitrate and nitrite bioassays in whole blood by dissolvable-film based centrifugo-pneumatic actuation

This paper demonstrates the full centrifugal microfluidic integration and automation of all liquid handling steps of a 7-step fluorescence-linked immunosorbent assay (FLISA) for quantifying nitrate and nitrite levels in whole blood within about 15 min. The assay protocol encompasses the extraction of metered plasma, the controlled release of sample and reagents (enzymes, co-factors and fluorescent labels), and incubation and detection steps. Flow control is implemented by a rotationally actuated dissolvable film (DF) valving scheme. In the valves, the burst pressure is primarily determined by the radial position, geometry and volume of the valve chamber and its inlet channel and can thus be individually tuned over an extraordinarily wide range of equivalent spin rates between 1,000 RPM and 5,500 RPM. Furthermore, the vapour barrier properties of the DF valves are investigated in this paper in order to further show the potential for commercially relevant on-board storage of liquid reagents during shelf-life of bioanalytical, ready-to-use discs. © 2013 by the authors; licensee MDPI, Basel, Switzerland.
Graphene-on-dielectric micromembrane for optoelectromechanical hybrid devices

Due to their exceptional mechanical and optical properties, dielectric silicon nitride (SiN) micromembranes have become the centerpiece of many optomechanical experiments. Efficient capacitive coupling of the membrane to an electrical system would facilitate exciting hybrid optoelectromechanical devices. However, capacitive coupling of such SiN membranes is rather weak. Here we add a single layer of graphene on SiN micromembranes (SiN-G) and compare the electromechanical coupling and mechanical properties to bare SiN membranes and to membranes coated with an aluminium layer (SiN-Al). The electrostatic force to external coplanar electrodes of SiN-G membranes is found to be equal to that of the SiN-Al membranes and corresponds to the theoretical value calculated for a perfectly conductive membrane coating. Our results show that a single layer of graphene substantially enhances the electromechanical capacitive coupling of a SiN membrane without significantly adding mass, decreasing the mechanical quality factor or affecting the optical properties.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, National Institute of Standards and Technology, Harvard University, Technical University of Denmark, Massachusetts Institute of Technology, University of Copenhagen
Authors: Schmid, S. (Intern), Bagci, T. (Forskerdatabase), Zeuthen, E. (Forskerdatabase), Taylor, J. M. (Ekstern), Herring, P. K. (Ekstern), Cassidy, M. C. (Ekstern), Marcus, C. M. (Forskerdatabase), Villanueva Torrij, L. G. (Intern), Amato, B. (Ekstern), Boisen, A. (Intern), Shin, Y. C. (Ekstern), Kong, J. (Ekstern), Sørensen, A. S. (Forskerdatabase),
High-performance spinning device for DVD-based micromechanical signal transduction

Here we report a high-throughput spinning device for nanometric scale measurements of microstructures with instrumentation details and experimental results. The readout technology implemented in the designed disc-like device is based on a DVD data storage optical pick-up unit (OPU). With a spinning mechanism, this device can simultaneously measure surface topography, mechanical deflections and resonance frequencies of several microfabricated beams at a high speed. In biochemical sensing applications, the OPU can measure bending changes of functionalized microcantilevers, providing a statistically robust and label-free bio-detection analysis of multiple compounds. The signal-to-noise ratio (S/N) is demonstrated from statistical measurements as 1.2 with arginine detection at 750 nM concentration. Practically, the OPU can measure up to 480 individual cantilever sensors per second with nanometer resolution. The optomechanical optimization of the device design and settings for biochemical detection are described.
Hot punching of individual biopolymer microcontainers for oral drug delivery

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Petersen, R. S. (Intern), Nagstrup, J. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern)
Number of pages: 1
Publication date: 2013

Host publication information
Title of host publication: Proceedings of the 39th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
Electronic versions:
MNE_London_Book_of_Abstracts.pdf
Imaging interferometry to measure surface rotation field

This paper describes a polarized-light imaging interferometer to measure the rotation field of reflecting surfaces. This setup is based on a homemade prism featuring a birefringence gradient. The arrangement is presented before focusing on the homemade prism and its manufacturing process. The dependence of the measured optical phase on the rotation of the surface is derived, thus highlighting the key parameters driving the sensitivity. The system's capabilities are illustrated by imaging the rotation field at the surface of a tip-loaded polymer specimen.
Inkjet printing as a technique for filling of micro-wells with biocompatible polymers

We present an innovative technique to dispense precise amounts of polymer solutions into large arrays of microscopic wells. An inkjet printer (NP 2.1 GeSim, Germany) is used to fill micro-wells with poly (vinyl pyrrolidone) (PVP K10). The micro-wells are fabricated with cavity diameters of 300 μm down to 50 μm with SU-8 with two steps of negative photolithography. Inkjet printing is shown to be a suitable technique to dispense defined volumes of solution (down to 0.3 nL) in a highly reproducible way. The filling with polymer can be controlled varying the concentration of the solution and the number of dispensed droplets. Solutions of up to 20 wt.% PVP in water are successfully spotted.
Loading of micro-containers for oral delivery with supercritical CO$_2$ aided impregnation

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Trieste, University of Copenhagen
Authors: Marizza, P. (Intern), Keller, S. S. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Kikic, I. (Ekstern), Moneghini, M. (Ekstern), Boisen, A. (Intern)
Number of pages: 3
Publication date: 2013

Host publication information
Luminescence enhancement of fluorescent SiC via surface nanostructuring produced by 2-step cost effective method

General information
State: Published
Organisations: Department of Photonics Engineering, Department of Micro- and Nanotechnology, Nanoprobes, Diode Lasers and LED Systems, Linköping University
Authors: Argyraki, A. (Intern), Ou, Y. (Intern), Jokubavicius, V. (Ekstern), Syväjärvi, M. (Ekstern), Ou, H. (Intern)
Publication date: 2013
Main Research Area: Technical/natural sciences
Electronic versions:
Luminescence enhancement of fluorescent SiC via surface nanostructuring produced by

Relations
Activities:
39th International Conference on Micro and Nano Engineering
Source: dtu
Source-ID: u::8779
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2013

Mapping the Complex Morphology of Cell Interactions with Nanowire Substrates Using FIB-SEM
Using high resolution focused ion beam scanning electron microscopy (FIB-SEM) we study the details of cell-nanostructure interactions using serial block face imaging. 3T3 Fibroblast cellular monolayers are cultured on flat glass as a control surface and on two types of nanostructured scaffold substrates made from silicon black (Nanograss) with low- and high nanowire density. After culturing for 72 hours the cells were fixed, heavy metal stained, embedded in resin, and processed with FIB-SEM block face imaging without removing the substrate. The sample preparation procedure, image acquisition and image post-processing were specifically optimised for cellular monolayers cultured on nanostructured substrates. Cells display a wide range of interactions with the nanostructures depending on the surface morphology, but also greatly varying from one cell to another on the same substrate, illustrating a wide phenotypic variability. Depending on the substrate and cell, we observe that cells could for instance: break the nanowires and engulf them, flatten the nanowires or simply reside on top of them. Given the complexity of interactions, we have categorised our observations and created an overview map. The results demonstrate that detailed nanoscale resolution images are required to begin understanding the wide variety of individual cells' interactions with a structured substrate. The map will provide a framework for light microscopy studies of such interactions indicating what modes of interactions must be considered.

General information
State: Published
Organisations: Center for Electron Nanoscopy, Molecular Windows, Department of Micro- and Nanotechnology, DTU Admission Course, Nanoprobes, Fluidic Array Systems and Technology, University of Copenhagen
Number of pages: 12
Pages: e53307
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: PLoS One
Volume: 8
Issue number: 1
ISSN (Print): 1932-6203
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
Micro fabrication of biodegradable polymer drug delivery devices

The pharmaceutical industry is presently facing several obstacles in developing oral drug delivery systems. This is primarily due to the nature of the discovered drug candidates. The discovered drugs often have poor solubility and low permeability across the gastrointestinal epithelium. Furthermore, they are often degraded before they can be absorbed.
The result is low bioavailability of the drugs. To overcome these challenges, better drug delivery systems need to be developed. Recently, micro systems have emerged as promising candidates to solve the challenges of poor solubility, low permeability and degradation. These systems are for the majority based on traditional materials used in micro technology, such as SU-8, silicon, poly(methyl methacrylate). The next step in developing these new drug delivery systems is to replace classical micro fabrication materials with biodegradable polymers. In order to successfully do this, methods for fabricating micro structures in biodegradable polymers need to be developed.

The goal of this project has been to develop methods for micro fabrication in biodegradable polymers and to use these methods to produce micro systems for oral drug delivery. This has successfully been achieved by fabrication of micro container systems made of poly(L-lactic acid) and polycaprolactone. To achieve this, polymer solutions have been developed using the theory of Hansen’s solubility parameters. The solutions are used to fabricate polymer films by spin coating, which are used in the fabrication of micro devices for oral drug delivery. Films consisting of both polymer and pharmaceuticals have also been developed by spin coating. A deep reactive ion etch producing sloped sidewalls for stamp production has been developed. The sloped sidewalls ensure a successful separation of stamp and film after patterning. Large scale methods for filling of micro reservoirs based on embossing, screen printing and solvent casting have been developed.

In vitro drug release experiments on both type of micro devices have been performed. The experiments show that most of the drug is released from the developed devices. Additionally, it has been shown that it is possible to control the release of drug by adding polymeric coatings.
Micro string resonators as temperature sensors

The resonance frequency of strings is highly sensitive to temperature. In this work we have investigated the applicability of micro string resonators as temperature sensors. The resonance frequency of strings is a function of the tensile stress which is coupled to temperature by the thermal expansion of the string and the frame clamping it. The sensitivity improves when the length and pre-stress are reduced and the difference in thermal expansion, Young's modulus and resonant mode are increased. At low tensile stress, the sensitivity becomes highly dependent on temperature. The investigation was done with silicon rich silicon nitride (SiNx), nickel (Ni) and aluminum (Al) micro strings. Aluminum strings show a relative sensitivity of up to 15±1 ‰/°C, which is more than 100 times higher than values reported by other groups for similar devices. Sub-millisecond time constants can be achieved due to the low thermal mass of the strings. A temperature resolution of 2.5×10^{-4} °C has been achieved with silicon nitride strings. The theoretical limit for the temperature resolution of 8×10^{-8} °C has not been reached yet and requires further improvement of the sensor.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark
Authors: Larsen, T. (Ekstern), Schmid, S. (Intern), Boisen, A. (Intern)
Pages: 931-936
Publication date: 2013
Conference: Ninth International Temperature Symposium, Los Angeles, United States, 19/03/2012 - 19/03/2012
Main Research Area: Technical/natural sciences

Publication information

Journal: A I P Conference Proceedings Series
Volume: 1552
ISSN (Print): 0094-243X
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Scopus rating (2017): SJR 0.165 SNIP 0.3
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 0.21 SJR 0.165 SNIP 0.246
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.18 SNIP 0.218 CiteScore 0.18
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.171 SNIP 0.202 CiteScore 0.17
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.164 SNIP 0.187 CiteScore 0.16
ISI indexed (2013): ISI indexed no
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.176 SNIP 0.193 CiteScore 0.14
ISI indexed (2012): ISI indexed no
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.161 SNIP 0.16 CiteScore 0.12
ISI indexed (2011): ISI indexed no
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.166 SNIP 0.158
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.163 SNIP 0.156
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 0.17 SNIP 0.132
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 0.171 SNIP 0.176
Scopus rating (2006): SJR 0.184 SNIP 0.187
Scopus rating (2005): SJR 0.217 SNIP 0.416
Scopus rating (2004): SJR 0.198 SNIP 0.249
Web of Science (2004): Indexed yes
Mikrosensorer skal hjælpe skadestuer med prioritering af patienter

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Surface Engineering
Authors: Brøgger, A. L. (Intern), Frøhling, K. B. (Intern)
Pages: 12-14
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Dansk kemi
Volume: 94
Issue number: 9
ISSN (Print): 0011-6335
Ratings:
ISI indexed (2013): ISI indexed no
ISI indexed (2012): ISI indexed no
ISI indexed (2011): ISI indexed no
Web of Science (2007): Indexed yes
Web of Science (2004): Indexed yes
Original language: Danish
Source: dtu
Source-ID: n::oai:DTIC-ART:dkart/408719335::38042
Publication: Research › Journal article – Annual report year: 2014

Nanomechanical recognition of prognostic biomarker suPAR with DVD-ROM optical technology
In this work the use of a high-throughput nanomechanical detection system based on a DVD-ROM optical drive and cantilever sensors is presented for the detection of urokinase plasminogen activator receptor inflammatory biomarker (uPAR). Several large scale studies have linked elevated levels of soluble uPAR (suPAR) to infectious diseases, such as HIV, and certain types of cancer. Using hundreds of cantilevers and a DVD-based platform, cantilever deflection response from antibody–antigen recognition is investigated as a function of suPAR concentration. The goal is to provide a cheap and portable detection platform which can carry valuable prognostic information. In order to optimize the cantilever response the antibody immobilization and unspecific binding are initially characterized using quartz crystal microbalance technology. Also, the choice of antibody is explored in order to generate the largest surface stress on the cantilevers, thus increasing the signal. Using optimized experimental conditions the lowest detectable suPAR concentration is currently around 5 nM. The results reveal promising research strategies for the implementation of specific biochemical assays in a portable and high-throughput microsensor-based detection platform.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Surface Engineering, Department of Applied Mathematics and Computer Science, Cognitive Systems, Academia Sinica Taiwan, Copenhagen University Hospital
Number of pages: 7
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Nanotechnology
Volume: 24
Issue number: 44
Article number: 444011
ISSN (Print): 0957-4484
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.788 SJR 1.079
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.87 SJR 1.339 SNIP 0.945
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.257 SNIP 1.035 CiteScore 3.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.497 SNIP 1.269 CiteScore 3.09
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.602 SNIP 1.231 CiteScore 2.74
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.861 SNIP 1.307 CiteScore 3.34
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.899 SNIP 1.451 CiteScore 3.86
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.844 SNIP 1.252
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.809 SNIP 1.27
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.857 SNIP 1.32
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.899 SNIP 1.348
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.938 SNIP 1.364
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.958 SNIP 1.435
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.892 SNIP 1.47
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.475 SNIP 1.364
Web of Science (2003): Indexed yes
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.93 SNIP 0.929
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.89 SNIP 0.818
Scopus rating (1999): SJR 0.956 SNIP 0.9
Non-covalent conjugates of single-walled carbon nanotubes and folic acid for interaction with cells overexpressing folate receptors

We here present a method to form a noncovalent conjugate of single-walled carbon nanotubes and folic acid aimed to interact with cells over-expressing folate receptors. The bonding was obtained without covalent chemical functionalization using a simple, rapid “one pot” synthesis method. The zeta potential for the single-walled carbon nanotube–folic acid solution was ~32.4 mV at pH 7.0 and the result indicates that the folic acid coating inhibited aggregation of the carbon nanotubes. Properties of the single-walled carbon nanotube–folic acid conjugate were analyzed using ultraviolet-visible, fluorescence and Raman spectroscopies. While the folic acid fluorescence signature was significantly quenched by the presence of single-walled carbon nanotubes, the Raman spectra of the conjugate displayed a decreased distribution of sp3 sites. Both results were attributed to the noncovalent functionalization of the single-walled carbon nanotubes with folic acid. A more detailed investigation of the single-walled carbon nanotube–folic acid conjugates utilizing scanning electron microscopy, atomic force microscopy and energy-dispersive X-ray spectroscopy confirmed the presence of the well-defined folic acid coating on the individual single-walled carbon nanotubes. The single-walled carbon nanotube–folic acid conjugates were incubated with THP-1 cells and the internalization was evaluated by Giemsa staining with light microscopy, and cytotoxicity was evaluated using the MTT reduction assay. The cytotoxicity studies presented a low toxicity of the conjugates in the THP-1 cells. The low toxicity and the cellular uptake of single-walled carbon nanotube–folic acid by cancer cells suggest their potential use in carbon nanotube-based drug delivery systems and in the diagnosis of cancer or tropical diseases such as leishmaniasis.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics, Nanoprobes, Universidad Industrial de Santander
Authors: Castillo, J. J. (Ekstern), Rindzevicius, T. (Intern), Novoa, L. V. (Ekstern), Svendsen, W. E. (Intern), Rozlosnik, N. (Intern), Boisen, A. (Intern), Escobar, P. (Ekstern), Martínez, F. (Ekstern), Castillo-Léon, J. (Intern)
Pages: 1475–1481
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Materials Chemistry B
Volume: 1
Issue number: 10
ISSN (Print): 2050-750X
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.024 SJR 1.561
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 1.468 SNIP 1.005 CiteScore 4.8
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.537 SNIP 1.144 CiteScore 5.14
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.332 SNIP 1.002 CiteScore 4.69
BFI (2013): BFI-level 1
ISI indexed (2013): ISI indexed no
Original language: English
RAMAN-SPECTROSCOPY, CANCER-CELLS, FUNCTIONALIZATION, CHITOSAN, NANOPARTICLES, RECOGNITION, MICROSCOPY, DISPERSION
Electronic versions:
Castillo_2013.pdf
Nonlinearity in nanomechanical cantilevers

Euler-Bernoulli beam theory is widely used to successfully predict the linear dynamics of micro- and nanocantilever beams. However, its capacity to characterize the nonlinear dynamics of these devices has not yet been rigorously assessed, despite its use in nanoelectromechanical systems development. In this article, we report the first highly controlled measurements of the nonlinear response of nanomechanical cantilevers using an ultralinear detection system. This is performed for an extensive range of devices to probe the validity of Euler-Bernoulli theory in the nonlinear regime. We find that its predictions deviate strongly from our measurements for the nonlinearity of the fundamental flexural mode, which show a systematic dependence on aspect ratio (length/width) together with random scatter. This contrasts with the second mode, which is always found to be in good agreement with theory. These findings underscore the delicate balance between inertial and geometric nonlinear effects in the fundamental mode, and strongly motivate further work to develop theories beyond the Euler-Bernoulli approximation. DOI: 10.1103/PhysRevB.87.024304
Online measurement of mass density and viscosity of pL fluid samples with suspended microchannel resonator

Physical characterization of viscous samples is crucial in chemical, pharma and petroleum industry. For example, in the refining industry of petroleum, water percentage is verified by measuring the density of a sample. In this article we present a suspended microchannel resonator (SMR) which uses 5 pL of a fluid sample and measures its density with a resolution of 0.01 kg/m^3 and a sensitivity of 16 Hz/kg/m^3. The resonator can also simultaneously measure viscosity of the solutions with an accuracy of 0.025 mPa s. The SMR is part of a system which contains packaging and tubing to deliver samples to the resonator. The system can easily handle multiple viscous fluids to measure their densities and viscosities. The SMR is transparent, facilitating visual inspection of the microchannel content. © 2013 Elsevier B.V.
Optical detection of radio waves through a nanomechanical transducer

Low-loss transmission and sensitive recovery of weak radio-frequency (rf) and microwave signals is an ubiquitous technological challenge, crucial in fields as diverse as radio astronomy, medical imaging, navigation and communication,
including those of quantum states. Efficient upconversion of rf-signalsto an optical carrier would allow transmitting them via optical fibers instead of copper wires dramatically reducing losses, and give access to the mature toolbox of quantum optical techniques, routinely enabling quantum-limited signal detection. Research in the field of cavity optomechanics [1, 2] has shown that nanomechanical oscillators can couple very strongly to either microwave [3–5] or optical fields [6, 7]. An oscillator accommodating both these functionalities would bear great promise as the intermediate platform in a radio-to-optical transduction cascade. Here, we demonstrate such an opto-electro-mechanical transducer following a recent proposal [8] utilizing a high-Q nanomembrane. A moderate voltage bias (Vdc < 10V) is sufficient to induce strong coupling [4, 6, 7] between the voltage fluctuations in a radio-frequency resonance circuit and the membrane’s displacement, which is simultaneously coupled to light reflected off its metallized surface. The circuit acts as an antenna; the voltage signals it induces are detected as an optical phase shift with quantum-limited sensitivity. The corresponding half-wave voltage is in the micovolt range, orders of magnitude below that of standard optical modulators. The noise added by the mechanical interface is suppressed by the electro-mechanical cooperativity Cem 6800 and has a temperature of TN = Tm/Cem 40mK, where Tm is the room temperature at which the entire device is operated. This corresponds to a sensitivity limit as low as 5 pV/pHz, or −210dBm/Hz in a narrow frequency band around 1MHz. Our work introduces an entirely new approach to all-optical, ultralow-noise detection of classical electronic signals, and sets the stage for coherent upconversion of low-frequency quantum signals to the optical domain [8–12].
Optical readout of coupling between a nanomembrane and an LC circuit at room temperature

Summary form only given. Opto- and electromechanical systems have separately shown great progress in reaching ultrasensitive displacement readout and manipulation of nano- and micromechanical resonators at the quantum level [1,2,3]. Besides that, combining optical and electrical degrees of freedom via a mechanical interface is of potential interest, as it would allow for low noise optical detection and laser cooling of weak electrical excitations. In a recent paper [4], a scheme was proposed for room temperature applications where a membrane converts rf electrical excitations in an LC circuit to optical excitations in a high finesse cavity. In this work, we have experimentally realized both optical and electrical detection of coupling in a roomtemperature electromechanical system composed of an LC circuit and a 100-nm thick SiN nanomembrane coated by 50 nm Aluminum. We follow an approach similar to the one described in [4] (cf. Fig 1a): The displacement of the high Q membrane is capacitively coupled to a plate capacitor that is connected in parallel to a ferrite inductor. A change in capacitance alters the LC resonance frequency, thereby creating coupling between the membrane and the LC circuit. A DC bias voltage applied to the capacitor amplifies the coupling. We confirm two-way coupling by observing broadening in the membrane vibrations via optical readout (Doppler vibrometry, Fig. 1b) and an MIT (Mechanically Induced Transparency) dip in the electrical probe (Fig. 1c). The two different methods show fairly good agreement. We note that a similar phenomenon (EMIT) was reported recently in an electromechanical system [5], however at cryogenic temperatures with a superconducting circuit. At 60V DC bias voltage, we extract a promising cooperativity parameter (C) of around 50, corresponding to a coupling strength of roughly g/2π=1 kHz, whereas the LC decay rate is around 7 kHz. Our setup serves as a sensitive optical loudspeaker [4] for rf excitations circulating in the LC circuit which may eventually compete with cryogenic amplifiers. With an optimized design, strong electromechanical coupling is within reach. Furthermore the electromechanical part can be placed in an optical cavity for simultaneous readout and laser cooling of electrical excitations in an LC circuit.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, National Institute of Standards and Technology
Authors: Bagci, T. (Ekstern), Simonsen, A. (Ekstern), Zeuthen, E. (Ekstern), Taylor, J. M. (Ekstern), Villanueva Torrijo, L. G. (Intern), Schmid, S. (Intern), Sørensen, A. (Ekstern), Schliesser, A. (Ekstern), Usami, K. (Ekstern), Polzik, E. S. (Ekstern)
Number of pages: 1
Publication date: 2013
Photochemical Synthesis of the Bioconjugate Folic Acid-Gold Nanoparticles

In this paper we present a rapid and simple one-pot method to obtain gold nanoparticles functionalized with folic acid using a photochemistry method. The bioconjugate folic acid-gold nanoparticle was generated in one step using a photo-reduction method, mixing hydrogen tetrachloroaurate with folic acid in different ratios and varying the illumination time of a mercury lamp (λ= 255 nm). Scanning electron microscopy showed a particle size of around 40-50 nm and dynamic light scattering exhibited that the zeta potential varies from -41 to -50 mV with different illumination times. Storage in the dark at 4°C prolongs the stability of folic acid-gold nanoparticle suspensions to up to 26 days. Ultraviolet visible and Fourier transform infrared spectroscopy showed a surface plasmon band of around 534 nm and fluorescence spectroscopy exhibited a quenching effect on gold nanoparticles in the fluorescence emission of folic acid and thus confirmed the conjugation of folic acid to the surface of gold nanoparticles. In this study we demonstrate the use of a photochemistry method to obtain folic acid-gold nanoparticles in a simple and rapid way without the use of surfactants and long reaction times. The photochemical synthesis of FA-AuNPs opens new perspectives for creating novel functional nanomaterials for biomedical applications.
Photothermal analysis of individual nanoparticulate samples using micromechanical resonators

The ability to detect and analyze single sample entities such as single nanoparticles, viruses, spores, or molecules is of fundamental interest. This can provide insight into the individual specific properties which may differ from the statistical sample average. Here we introduce resonant photothermal spectroscopy, a novel method that enables the analysis of individual nanoparticulate samples. Absorption of light by an individual sample placed on a microstring resonator results in local heating of the string, which is reflected in its resonance frequency. The working principle of the spectrometer is demonstrated by analyzing the optical absorption of different micro- and nanoparticles on a microstring. We present the measurement of a simple absorption spectrum of multiple polystyrene microparticles illuminated with an unfocused LED light source. Using a diode laser, single 170 nm polystyrene nanoparticles are detected. With the current setup, nanoparticulate samples with a mass of ~40 ag are detectable. By using nanostrings, visible and infrared photothermal spectroscopy in the subattogram mass regime is possible and single molecule detection is within reach. © 2013 American Chemical Society.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Larsen, T. (Intern), Schmid, S. (Intern), Villanueva Torrijo, L. G. (Intern), Boisen, A. (Intern)
Pages: 6188-6193
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: ACS Nano
Volume: 7
Issue number: 7
ISSN (Print): 1936-0851
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 2.58 SJR 7.203
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 13.65 SJR 6.948 SNIP 2.604
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 5.981 SNIP 2.721 CiteScore 12.49
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 6.672 SNIP 2.735 CiteScore 13.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 7.162 SNIP 2.685 CiteScore 11.92
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Scopus rating (2011): SJR 6.282 SNIP 2.453 CiteScore 11.05
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 5.344 SNIP 2.069
Web of Science (2010): Indexed yes
Scopus rating (2009): SJR 4.114 SNIP 1.735
Micromechanical photothermal infrared spectroscopy is a promising technique, where absorption-related heating is detected by frequency detuning of microstring resonators. We present photothermal infrared spectroscopy with mechanical string resonators providing rapid identification of femtogram-scale airborne samples. Airborne sample material is directly collected on the microstring with an efficient nondiffusion limited sampling method based on inertial impaction. Resonance frequency shifts, proportional to the absorbed heat in the microstring, are recorded as monochromatic IR light is scanned over the mid-infrared range. As a proof-of-concept, we sample and analyze polyvinylpyrrolidone (PVP) and the IR spectrum measured by photothermal spectroscopy matches the reference IR spectrum measured by an FTIR spectrometer. We further identify the organic surface coating of airborne TiO2 nanoparticles with a total mass of 4 pg. With an estimated detection limit of 44 fg, the presented sensor demonstrates a new paradigm in ultrasensitive vibrational spectroscopy for identification of airborne species.
Plasma etching on large-area mono-, multi- and quasi-mono crystalline silicon

We use plasma etched Black Si (BS) nanostructures to achieve low reflectance due to the resulting graded refractive index at the Si-air interface. The goal of this investigation is to develop a suitable texturing method for Si solar cells. Branz et al. [3] report below 3% average reflectance for their 16.8% efficient black Si cell using a metal-assisted, chemical etching method on FZ mono-crystalline Si substrates. Yoo et al. [4] use RIE similar to this work on large-area, multi-crystalline Si cells and achieve a 16.1% efficiency despite a relatively high reflectance of 13.3%. Despite several advantages such as; (i) excellent light trapping, (ii) dry, single-sided and scalable process method and (iii) etch independence on crystallinity of Si, RIE-texturing has so far not been proven superior to standard wet texturing, primarily as a result of lower power conversion efficiency due to increased surface recombination. This work shows promising potential of future improvements in power conversion efficiency, since excellent light absorption has been shown for large-area, industry grade CZ Si wafers with several identified areas of improvement. We show that the RIE nanostructures lead to superior light absorption independent of crystalline grade and incident angle. A texturing method which is applicable to all industrially relevant grades of Si and which yields improved performance at non-ideal incident angles has a major scientific and commercial relevance. The nanostructures were fabricated using maskless RIE in a O2 and SF6 plasma, and the surface topology was optimized for solar cell applications by varying gas flows, pressure, power and process time. The starting substrates were 156x156 mm p-type, CZ mono-, multi- and quasi-mono crystalline Si wafers, respectively, with a thickness of 200 μm. Reflectance measurements of the RIE-textured mono-, multi and quasi-mono Si surfaces were performed using a broadband light source (Mikropack DH-2000), an integrating sphere (Mikropack ISP-30-6-R), and a spectrometer (Ocean Optics QE65000, 280-1000 nm). The reference solar spectral irradiance for AM 1.5 was used to calculate the weighted average reflectance in the wavelength range from 280-1000 nm. Our maskless, scalable RIE nanostructuring of the Si surface is shown to reduce the AM1.5-weighted average reflectance to a level below 1% in a fully optimized RIE texturing, and thus holds a significant potential for improvement of solar cell performance compared to current industrial standards. The reflectance is shown to remain below that of conventional textured cells also at high angle of incidence. The process is shown to be equally applicable to mono-, multi- and quasi-mono-crystalline Si.
Plasma etching on large-area mono-, multi- and quasi-mono crystalline silicon

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes
Authors: Davidsen, R. S. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2013
Main Research Area: Technical/natural sciences

Plasma texturing on large-area industrial grade CZ silicon solar cells

We report on an experimental study of nanostructuring of silicon solar cells using reactive ion etching (RIE). A simple mask-less, scalable RIE nanostructuring of the solar cell surface is shown to reduce the AM1.5-weighted average reflectance to a level below 1% in a fully optimized RIE texturing, and thus holds a significant potential for improvement of the cell performance compared to current industrial standards. The reflectance is shown to remain below that of conventional textured cells also at high angle of incidence. The process is shown to be equally applicable to mono-, multi- and quasi-mono-crystalline Si. The process was successfully integrated in fabrication of solar cells using only industry standard processes on a Czochralski (CZ) silicon starting material. The resulting cell performance was compared to cells with conventional texturing. For cells, where the nanostructuring was not fully optimized (reflectance larger than 2%), an efficiency of 16.5% at 1 sun was demonstrated.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes, Department of Physics, Experimental Surface and Nanomaterials Physics, Institute for Energy Technology
Authors: Davidsen, R. S. (Intern), Nordseth, Ø. (Ekstern), Boisen, A. (Intern), Schmidt, M. S. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2013
Main Research Area: Technical/natural sciences

Plasma texturing on large-area industrial grade CZ silicon solar cells

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Silicon Microtechnology, Nanoprobes, Institute for Energy Technology
Authors: Davidsen, R. S. (Intern), Nordseth, Ø. (Ekstern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Hansen, O. (Intern)
Number of pages: 1
Publication date: 2013
Process optimization of ultrasonic spray coating of polymer films

In this work we have performed a detailed study of the influence of various parameters on spray coating of polymer films. Our aim is to produce polymer films of uniform thickness (500 nm to 1 μm) and low roughness compared to the film thickness. The coatings are characterized with respect to thickness, roughness (profilometer), and morphology (optical microscopy). Polyvinylpyrrolidone (PVP) is used to do a full factorial design of experiments with selected process parameters such as temperature, distance between spray nozzle and substrate, and speed of the spray nozzle. A mathematical model is developed for statistical analysis which identifies the distance between nozzle and substrate as the most significant parameter. Depending on the drying of the sprayed droplets on the substrate, we define two broad regimes, "dry" and "wet". The optimum condition of spraying lies in a narrow window between these two regimes, where we obtain a film of desired quality. Both with increasing nozzle-substrate distance and temperature, the deposition moves from a wet state to a dry regime. Similar results are also achieved for solvents with low boiling points. Finally, we study film formation during spray coating with poly (d,l-lactide) (PDLLA). The results confirm the processing knowledge obtained with PVP and indicate that the observed trends are identical for spraying of other polymer films. © 2013 American Chemical Society.
Pyrolysed carbon resonators: Fabrication and characterization

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark
Authors: Amato, L. (Intern), Armato, B. (Ekstern), Villanueva Torrijo, L. G. (Intern), Emnéus, J. (Intern), Heiskanen, A. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Schmid, S. (Intern)
Publication date: 2013
Main Research Area: Technical/natural sciences
Electronic versions:
prod11389011885927.Pyrolysed_carbon_resonators_Fabrication_and_characterization.pdf
Source: dtu
Source-ID: u::10307
Publication: Research - peer-review › Poster – Annual report year: 2013

Pyrolyzed Photoresist Electrodes for Integration in Microfluidic Chips for Transmitter Detection from Biological Cells
In this study, we show how pyrolyzed photoresist carbon electrodes can be used for amperometric detection of potassium-induced transmitter release from large groups of neuronal PC 12 cells. This opens the way for the use of carbon film electrodes in microfabricated devices for neurochemical drug screening applications. We also investigated the effect of using two different photoresists for fabrication of pyrolyzed photoresist electrodes. We observed a significant difference in the cross-sectional profile of band electrodes made of AZ 4562 and AZ 5214 photoresist. This difference can be explained by the difference in photoresist viscosity. By adding a soft bake step to the fabrication procedure, the flatness of pyrolyzed...
AZ 5214 electrodes could be improved which would facilitate their integration in microfluidic chip devices.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Polymer Micro & Nano Engineering, Bioanalytics, Nanoprobes, Polymer Microsystems for Medical Diagnostics
Authors: Larsen, S. T. (Intern), Argyraki, A. (Intern), Amato, L. (Intern), Tanzi, S. (Intern), Keller, S. S. (Intern), Rozlosnik, N. (Intern), Taboryski, R. J. (Intern)
Pages: B5-B7
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: E C S Electrochemistry Letters
Volume: 2
Issue number: 5
ISSN (Print): 2162-8726
Ratings:
Scopus rating (2017): SNIP 0.819 SJR 0.688
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.631 SNIP 0.78 CiteScore 1.76
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.767 SNIP 0.685 CiteScore 1.97
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.643 SNIP 0.771 CiteScore 1.77
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.639 SNIP 0.696 CiteScore 1.48
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.068 SNIP 1.006
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.056 SNIP 0.984
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.183 SNIP 1.01
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.231 SNIP 1.003
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.323 SNIP 1.107
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.432 SNIP 1.132
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.474 SNIP 1.227
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.48 SNIP 1.227
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.962 SNIP 1.565
Scopus rating (2003): SJR 2.36 SNIP 1.499
Real-time single airborne nanoparticle detection with nanomechanical resonant filter-fiber

Nanomechanical resonators have an unprecedented mass sensitivity sufficient to detect single molecules, viruses or nanoparticles. The challenge with nanomechanical mass sensors is the direction of nano-sized samples onto the resonator. In this work we present an efficient inertial sampling technique and gravimetric detection of airborne nanoparticles with a nanomechanical resonant filter-fiber. By increasing the nanoparticle momentum the dominant collection mechanism changes from diffusion to more efficient inertial impaction. In doing so we reach a single filter-fiber collection efficiency of $65 \pm 31\%$ for 28 nm silica nanoparticles. Finally, we show the detection of single 100 nm silver nanoparticles. The presented method is suitable for environmental or security applications where low-cost and portable monitors are demanded. It also constitutes a unique technique for the fundamental study of single filter-fiber behavior. We present the direct measurement of diffusive nanoparticle collection on a single filter-fiber qualitatively confirming Langmuir's model from 1942.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Schmid, S. (Intern), Kurek, M. (Intern), Adolphsen, J. Q. (Ekstern), Boisen, A. (Intern)
Number of pages: 5
Pages: 1288
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Scientific Reports
Volume: 3
ISSN (Print): 2045-2322
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.245 SJR 1.533
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.692 SNIP 1.354
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.034 SNIP 1.597 CiteScore 5.3
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.163 SNIP 1.554 CiteScore 4.75
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.998 SNIP 1.57 CiteScore 4.06
ISI indexed (2013): ISI indexed yes
Resonant fiber based aerosol particle sensor and method
The present invention relates to methods and devices for determining the weight of small particles, typically being nano-sized particles by use of resonating fibers in the form of elongate members being driven into resonance by an actuator or e.g. thermal noise/fluctuation. The frequency shift in resonance frequency due to depositing of nano-sized particles is correlated with the mass deposited on the elongate member and the vibration frequency of the elongate member is determined by a detector. The read-out from the detector is transformed into a mass deposited on the elongate member. Particles are deposited by letting a fluid with the particles flow past the elongate member.

Resonant photothermal IR spectroscopy of picogram samples with microstring resonator
Here, we report a demonstration of resonant photothermal IR spectroscopy using microstrings in mid-infrared region providing rapid identification of picogram samples. In our microelectromechanical resonant photothermal IR spectroscopy system, samples are deposited directly on microstrings using an in-situ sampling method and the resonance frequency of the string is measured optically. Resonance frequency shifts, proportional to the absorbed heat, are recorded in real time as monochromatic infrared light is being scanned over the mid-infrared range. These resonant photothermal IR spectroscopy spectra, obtained from picogram samples, suggest promising future applications of this approach.
Sensitive determination of the Young’s modulus of thin films by polymeric microcantilevers

A method for the highly sensitive determination of the Young’s modulus of TiO₂ thin films exploiting the resonant frequency shift of a SU-8 polymer microcantilever (MC) is presented. Amorphous TiO₂ films with different thickness ranging from 10 to 125 nm were grown at low temperature (90 °C) with subnanometer thickness resolution on SU-8 MC arrays by means of atomic layer deposition. The resonant frequencies of the MCs were measured before and after coating and the elastic moduli of the films were determined by a theoretical model developed for this purpose. The Young’s modulus of thicker TiO₂ films (>75 nm) was estimated to be about 110 GPa, this value being consistent with the value of amorphous TiO₂. On the other hand we observed a marked decrease of the Young’s modulus for TiO₂ films with a thickness below 50 nm. This behavior was found not to be related to a decrease of the film mass density, but to surface effects according to theoretical predictions on size-dependent mechanical properties of nano- and microstructures.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, CSMT Gestione S.c.a.r.l., Università di Brescia
Authors: Colombi, P. (Ekstern), Bergese, P. (Ekstern), Bontempi, E. (Ekstern), Borgese, L. (Ekstern), Federici, S. (Ekstern), Keller, S. S. (Intern), Boisen, A. (Intern), Depero, L. E. (Ekstern)
Pages: 125603
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Measurement Science and Technology
Volume: 24
Issue number: 12
ISSN (Print): 0957-0233
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 1.061 SJR 0.53
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.75 SJR 0.672 SNIP 1.234
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.704 SNIP 1.368 CiteScore 1.71
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.704 SNIP 1.416 CiteScore 1.58
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.639 SNIP 1.417 CiteScore 1.53
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.748 SNIP 1.604 CiteScore 1.65
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.851 SNIP 1.704 CiteScore 1.77
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Spray coating of microcontainers with Eudragit using ferromagnetic shadow masks for controlled oral release of poorly water soluble drugs.

PURPOSE: To form a lid of Eudragit S-100 or L-100 on the cavity of drug-filled microcontainers (micro scale oral drug delivery devices) by utilizing ferromagnetic masks. Furthermore, investigations of drug release in biorelevant gastric and intestinal media were evaluated for testing the ability of controlling the drug release of poorly soluble drugs from the microcontainers.

METHODS: Cylindrical microcontainers (inner diameter of 240 μm) were fabricated in SU-8, using photolithography on silicon substrate. The microcontainers were filled with either cinnarizine (weak base) or amorphous furosemide salt (weak acid). The cavity of the drug-filled microcontainers were spray coated with a 2 wt% solution of either Eudragit S-100 (soluble below pH 5) or Eudragit L-100 (soluble above pH 6) in isopropanol. The spray coating process was performed using ferromagnetic shadow masks (380 μm) allowing for magnetic clamping to the substrate and therefore precise deposition of the polymer on the microcontainers to form a lid. The release of cinnarizine and amorphous furosemide salt from the coated microcontainers was performed in fasted biorelevant gastric (pH 1.6) and intestinal media (pH 6.5), respectively.

RESULTS: By use of the ferromagnetic shadow masks it was possible to deposit the Eudragit precisely and therefore possible to form a lid of the cavity of the microcontainers. The thickness of the Eudragit layer on the cavity of the microcontainers was approximately 8-10 μm for both types of Eudragit. It was possible to control the drug release of cinnarizine by using Eudragit L-100 in the gastric medium and also possible to control the release of amorphous furosemide salt by the Eudragit E-100 coating in the intestinal medium.

CONCLUSIONS: The ferromagnetic shadow masks made it possible to deposit a lid of Eudragit on the cavity of the microcontainers and this is important in terms of utilizing the microcontainers as an oral drug delivery system as the drug release can be controlled.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Müllertz, A. (Ekstern)
Number of pages: 1
Publication date: 2013
SU-8 etching in inductively coupled oxygen plasma

Structuring or removal of the epoxy based, photo sensitive polymer SU-8 by inductively coupled plasma reactive ion etching (ICP-RIE) was investigated as a function of plasma chemistry, bias power, temperature, and pressure. In a pure oxygen plasma, surface accumulation of antimony from the photo-initiator introduced severe roughness and reduced etch rate significantly. Addition of SF6 to the plasma chemistry reduced the antimony surface concentration with lower roughness and higher etch rate as an outcome. Furthermore the etch anisotropy could be tuned by controlling the bias power. Etch rates up to 800 nm min-1 could be achieved with low roughness and high anisotropy. © 2013 The Authors. Published by Elsevier B.V. All rights reserved.
Surface-Enhanced Raman Spectroscopy Based Quantitative Bioassay on Aptamer-Functionalized Nanopillars Using Large-Area Raman Mapping

Surface-enhanced Raman spectroscopy (SERS) has been used in a variety of biological applications due to its high sensitivity and specificity. Here, we report a SERS-based biosensing approach for quantitative detection of biomolecules. A SERS substrate bearing gold-decorated silicon nanopillars is functionalized with aptamers for sensitive and specific detection of target molecules. In this study, TAMRA-labeled vasopressin molecules in the picomolar regime (1 pM to 1 nM) are specifically captured by aptamers on the nanostructured SERS substrate and monitored by using an automated SERS signal mapping technique. From the experimental results, we show concentration-dependent SERS responses in the picomolar range by integrating SERS signal intensities over a scanning area. It is also noted that our signal mapping approach significantly improves statistical reproducibility and accounts for spot-to-spot variation in conventional SERS quantification. Furthermore, we have developed an analytical model capable of predicting experimental intensity distributions on the substrates for reliable quantification of biomolecules. Lastly, we have calculated the minimum needed area of Raman mapping for efficient and reliable analysis of each measurement. Combining our SERS mapping analysis with an aptamer-functionalized nanopillar substrate is found to be extremely efficient for detection of low-abundance biomolecules.
**Tailoring channeled plasmon polaritons in metallic V-grooves**

Channeled plasmon polaritons (CPPs) are electromagnetic excitations that are bound to and propagate along metallic V-groove waveguides [1]. CPPs offer subwavelength lateral confinement, an ability to turn sharp bends with near-zero loss and are considered to be one of the most suitable forms of propagating plasmons to optimize the trade-off between lateral confinement and loss [2]. Accordingly, the traits of CPPs in metallic V-grooves suggest their widespread implementation,
with applications ranging from ultracompact photonic circuitry [3] to lab-on-a-chip sensing. Current CPP research focuses on the optimisation of their properties (e.g. propagation length, confinement) and improving both the quality and cost of fabrication techniques [4]. © 2013 IEEE.

**Temperature Stable Mass Sensors**

**General information**
State: Published  
Organisations: Department of Micro- and Nanotechnology, Nanoprobes  
Authors: Khan, F. (Intern), Boisen, A. (Intern), Schmid, S. (Intern)  
Publication date: 2013

**Publication information**
Place of publication: Kgs. Lyngby  
Publisher: Technical University of Denmark (DTU)  
Original language: English  
Main Research Area: Technical/natural sciences  
Publication: Research › Ph.D. thesis – Annual report year: 2013

**Towards airborne nanoparticle mass spectrometry with nanomechanical string resonators**

Airborne nanoparticles can cause severe harm when inhaled. Therefore, small and cheap portable airborne nanoparticle monitors are highly demanded by authorities and the nanoparticle producing industry. We propose to use nanomechanical resonators to build the next generation cheap and portable airborne nanoparticle sensors. Recently, nanomechanical mass spectrometry was established. One of the biggest challenges of nanomechanical sensors is the low efficiency of diffusion-based sampling. We developed an inertial-based sampling method that enables the efficient sampling of airborne nanoparticles on a nanomechanical sensor operating directly in air. We measured a sampling rate of over 1000 particles per second, for 28 nm silica nanoparticles with a concentration of 380000 #/cm³, collected on a 500 nm wide nanomechanical string resonator. We show that it is possible to reach a saturated sampling regime in which 100% of all nanoparticles are captured that are owing in the projection of the nanostring. We further show that it is possible to detect single airborne nanoparticles by detecting 50 nm Au particles with a 250 nm wide string resonator. Our resonators are currently operating in the first bending mode. Mass spectrometry of airborne nanoparticles requires the simultaneous operation in the first and second mode, which can be implemented in the transduction scheme of the resonator. The presented results lay the cornerstone for the realization of a portable airborne nanoparticle mass spectrometer.

**General information**
State: Published  
Organisations: Department of Micro- and Nanotechnology, Nanoprobes  
Authors: Schmid, S. (Intern), Kurek, M. (Intern), Boisen, A. (Intern)  
Pages: 872525  
Publication date: 2013
Towards Picomolar Detection with DVD-ROM Optical Technology

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Surface Engineering, Academia Sinica Taiwan, Copenhagen University Hospital
Number of pages: 2
Publication date: 2013

Host publication information
Title of host publication: Proceedings of 2013 Nanomechanical Sensing Workshop
Main Research Area: Technical/natural sciences
Workshop: 10th International Workshop on Nanomechanical Sensing, San Francisco, CA, United States, 01/05/2013 - 01/05/2013
Electronic versions:
NMC2013_Abstract V9.pdf
Source: dtu
Source-ID: u::9886
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2013

Using Experience From Explosives Detection in Development of Biosensors Based On Nanomechanical Responses

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Boisen, A. (Intern)
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Electrochemical Society. Meeting Abstracts (Online)
Volume: MA2013-02
ISSN (Print): 2151-2043
Original language: English
Electronic versions:
Meet._Abstr._2013_Boisen_2791.pdf

Bibliographical note
© 2013 The Electrochemical Society
Source: dtu
Source-ID: n::oai:DTIC-ART:highwire/390424873::35350
Publication: Research - peer-review › Conference abstract in journal – Annual report year: 2013

Centrifugally driven microfluidic disc for detection of chromosomal translocations
Chromosome translocations are a common cause of congenital disorders and cancer. Current detection methods require use of expensive and highly specialized techniques to identify the chromosome regions involved in a translocation. There is a need for rapid yet specific detection for diagnosis and prognosis of patients. In this work we demonstrate a novel, centrifugally-driven microfluidic system for controlled manipulation of oligonucleotides and subsequent detection of chromosomal translocations. The device is fabricated in the form of a disc with capillary burst microvalves employed to control the fluid flow. The microvalves in series are designed to enable fluid movement from the center towards the
periphery of the disc to handle DNA sequences representing translocation between chromosome 3 and 9. The translocation detection is performed in two hybridization steps in separate sorting and detection chambers. The burst frequencies of the two capillary burst microvalves are separated by 180 rpm enabling precise control of hybridization in each of the chambers. The DNA probes targeting a translocation are immobilized directly on PMMA by a UV-activated procedure, which is compatible with the disc fabrication method. The device performance was validated by successful specific hybridization of the translocation derivatives in the sorting and detection chambers.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Kennedy Center, University of Copenhagen
Authors: Brøgger, A. L. (Intern), Kwasny, D. (Intern), Bosco, F. G. (Intern), Silahtaroglu, A. (Forskerdatabase), Tümer, Z. (Forskerdatabase), Boisen, A. (Intern), Svendsen, W. E. (Intern)
Pages: 4628-4634
Publication date: 2012
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Lab on a Chip
Volume: 12
Issue number: 22
ISSN (Print): 1473-0197
Ratings:
- BFI (2018): BFI-level 1
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 1
- Scopus rating (2017): SNIP 1.586 SJR 2.158
- Web of Science (2017): Indexed Yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 5.98 SJR 2.162 SNIP 1.569
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 2.239 SNIP 1.721 CiteScore 5.74
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 2.555 SNIP 1.797 CiteScore 5.6
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 2
- Scopus rating (2013): SJR 2.397 SNIP 1.693 CiteScore 5.9
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 2
- Scopus rating (2012): SJR 2.405 SNIP 1.731 CiteScore 5.35
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 2
- Scopus rating (2011): SJR 2.54 SNIP 1.788 CiteScore 5.76
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 2.718 SNIP 1.876
- Web of Science (2010): Indexed yes
- BFI (2009): BFI-level 2
- Scopus rating (2009): SJR 2.673 SNIP 2.164
- Web of Science (2009): Indexed yes
- BFI (2008): BFI-level 1
- Scopus rating (2008): SJR 2.833 SNIP 1.849
- Web of Science (2008): Indexed yes
Dense high aspect ratio pillar arrays for carbon MEMS electrodes

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark, Capres A/S, Ecole Polytechnique, University of California, Irvine, University of Canterbury, Lund University
Authors: Amato, L. (Intern), Hansen, R. J. (Ekstern), Heiskanen, A. (Intern), Gammelgard, L. (Ekstern), Rindzevicius, T. (Intern), Martinez-Duarte, R. (Ekstern), Singh Bisht, G. (Ekstern), Downard, A. (Ekstern), Baronian, K. (Ekstern), Tenje, M. (Ekstern), Madou, M. (Ekstern), Boisen, A. (Intern), Emnéus, J. (Intern), Keller, S. S. (Intern)
Number of pages: 1
Publication date: 2012

Host publication information
Title of host publication: Proceedings of the 38th International Conference on Micro and Nano Engineering
Main Research Area: Technical/natural sciences
3D microelectrodes, Pyrolysed micropillars, Carbon MEMS electrodes
Electronic versions:
Dense high aspect ratio pillar arrays for carbon MEMS electrodes.pdf
Source: dtu
Source-ID: u::10312
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2013

Electrochemical evaluation of dopamine detection on pyrolysed carbon and gold electrodes

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Nano Bio Integrated Systems, Lund University
Publication date: 2012
Event: Poster session presented at 63rd Annual Meeting of the International Society of Electrochemistry, Prague, Czech Republic.
Main Research Area: Technical/natural sciences
Electronic versions:
prod11389012746102.Electrochemical_evaluation_of_dopamine_detection_on_pyrolysed_carbon_and_gold_electrodes.pdf
Source: dtu
Source-ID: u::10310
Publication: Research - peer-review › Poster – Annual report year: 2013
Electrochemical evaluation of pyrolysed high-aspect ratio 3D electrodes for biofuel cell applications

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Bioanalytics, Technical University of Denmark, Lund University
Authors: Amato, L. (Intern), Hansen, R. J. (Ekstern), Tenje, M. (Ekstern), Ortiz, R. (Ekstern), Gorton, L. (Ekstern), Keller, S. S. (Intern), Heiskanen, A. (Intern), Boisen, A. (Intern), Emnéus, J. (Intern)
Publication date: 2012
Event: Poster session presented at 63rd Annual Meeting of the International Society of Electrochemistry, Prague, Czech Republic.
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::10311
Publication: Research - peer-review › Poster – Annual report year: 2013

Fabrication of high-aspect ratio SU-8 micropillar arrays
SU-8 is the preferred photoresist for development and fabrication of high aspect ratio (HAR) three dimensional patterns. However, processing of SU-8 is a challenging task, especially when the film thickness as well as the aspect ratio is increasing and the size of the features is close to the resolution limit of photolithography. This paper describes process optimization for the fabrication of dense SU-8 micropillar arrays (2.5μm spacing) with nominal height 20μm and nominal diameter 2.5μm (AR 8). Two approaches, differing in temperature, ramping rate and duration of the baking steps were compared as part of the photolithographic processing, in order to evaluate the effect of baking on the pattern resolution. Additionally, during the post-processing, supercritical point drying and hard baking were introduced yielding pillars with diameter 1.8μm, AR=11 and an improved temporal stability.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Nano Bio Integrated Systems
Authors: Amato, L. (Intern), Keller, S. S. (Intern), Heiskanen, A. (Intern), Dimaki, M. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern), Tenje, M. (Intern)
Pages: 483-487
Publication date: 2012
Main Research Area: Technical/natural sciences
Publication information
Journal: Microelectronic Engineering
Volume: 98
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Graphene on silicon nitride micromembranes for optoelectromechanical devices

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Harvard University, University of Maryland, University of Copenhagen
Authors: Schmid, S. (Intern), Bagci, T. (Forskerdatabase), Rasmussen, A. N. (Forskerdatabase), Herring, P. (Ekstern), Cassidy, M. (Ekstern), Marcus, C. M. (Forskerdatabase), Taylor, J. (Ekstern), Sørensen, A. (Ekstern), Usami, K. (Forskerdatabase), Polzik, E. S. (Forskerdatabase)
Pages: 12
Publication date: 2012

Host publication information
Title of host publication: Carbonhagen 2012 : 3rd Symposium on graphene and carbon nanotubes
Inkjet printing as a novel drug loading technique of micro-containers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark
Authors: Marizza, P. (Intern), Keller, S. S. (Intern), Rades, T. (Ekstern), Boisen, A. (Intern)
Publication date: 2012

Investigation of cleaning and regeneration methods for reliable construction of DNA cantilever biosensors

Biosensing systems based on detecting changes in cantilever surface stress have attracted great interest. To achieve high reliability of measurements, high quality and high reproducibility in functionalization of the sensor surface are key points. In this paper, we investigate different methods to clean and regenerate the sensing surface of cantilever biosensors.

Perchloric acid potential sweep, potassium hydroxide-hydrogen peroxide, and piranha cleaning are investigated here. Peak-current potential differences from cyclic voltammetry, X-ray photo-electron spectroscopy and fluorescence detection are applied to characterize surface cleanliness. The experimental results show that piranha cleaning is the most reliable and efficient cleaning procedure.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, BioLabChip, Bioanalytics, McGill University
Authors: Quan, X. (Intern), Yi, S. (Intern), Heiskanen, A. (Intern), Wolff, A. (Intern), Grutter, P. (Ekstern), Boisen, A. (Intern)
Number of pages: 2
Publication date: 2012
Main Research Area: Technical/natural sciences
Electronic versions:
NMC_2012_Final

Relations
Activities:
9th International Nanomechanical Sensing Workshop
Publication: Research - peer-review › Paper – Annual report year: 2012

Investigations by Raman Microscopy if Spatial Confinement of Amorphous Indomethacin Can Lead to Increased Stability

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, University of Otago
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Gordon, K. C. (Ekstern), Boisen, A. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern)
Number of pages: 2
Publication date: 2012
Main Research Area: Technical/natural sciences

Bibliographical note
Poster presentation.
Source: PublicationPreSubmission
Microfluidic System With Capillary Burst Valves For Detection Of Chromosomal Translocations

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems
Authors: Brøgger, A. L. (Intern), Kwasny, D. (Intern), Bosco, F. (Intern), Boisen, A. (Intern), Svendsen, W. E. (Intern)
PUBLICATION DATE: 2012
Event: Poster session presented at III International Workshop on Analytical Miniaturization and NANOtechnologies, Barcelona, Spain.
Main Research Area: Technical/natural sciences
Source: dtu
Publication: Research - peer-review › Poster – Annual report year: 2012

Micromechanical aptasensor-based protein detection using a compact-disc format microfluidics system

A plug-and-play CD-like platform is used to perform a statistical detection of Platelet Derived Growth Factor (PDGF) proteins through aptamer-based surface functionalization of microcantilevers. When PDGF proteins bind to the aptamers, the cantilevers deflect. This deflection is monitored by optical readout heads from a DVD-ROM. The improved sensing platform facilitates measurements in continuous liquid flow with temperature control. Also, the wobbling of the CD platform has been reduced to a minimum and the scanning system has been optimized in order to detect cantilever deflections in liquid in the nanometer range. The capability of the sensing platform is demonstrated by detection of clinically relevant concentrations of PDGF proteins. We have performed statistical measurements on 100 microcantilevers at different concentrations of PDGF, ranging from 10 nM to 400 nM. Hereby it is possible to reliably characterize the averaged mechanical response of cantilevers as a function of protein concentration.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Columbia University, Academia Sinica Taiwan
Authors: Bosco, F. (Intern), Yang, J. (Ekstern), Chen, C. H. (Ekstern), Hwu, E. (Ekstern), Keller, S. S. (Intern), Bache, M. (Intern), Lin, Q. (Ekstern), Boisen, A. (Intern)
Pages: 858 - 861
Publication date: 2012

Host publication information
Title of host publication: Proceedings of IEEE micro electro mechanical systems
ISBN (Print): 9781467303248
Main Research Area: Technical/natural sciences
biosensors, cantilevers, digital versatile discs, micromechanical devices, proteins, statistical analysis
DOIs: 10.1109/MEMSYS.2012.6170321
Source: dtu
Source-ID: n:oai:DTIC-ART:iel/363098251::26984
Publication: Research - peer-review › Article in proceedings – Annual report year: 2013

Micro-Mechanical Temperature Sensors
Temperature is the most frequently measured physical quantity in the world. The field of thermometry is therefore constantly evolving towards better temperature sensors and better temperature measurements. The aim of this Ph.D. project was to improve an existing type of micro-mechanical temperature sensor or to develop a new one. Two types of micro-mechanical temperature sensors have been studied: Bilayer cantilevers and string-like beam resonators. Both sensor types utilize thermally generated stress.

Bilayer cantilevers are frequently used as temperature sensors at the micro-scale, and the goal was therefore to improve their sensitivity. Bilayer cantilevers are usually made by coating a ceramic cantilever with a metal. They were in this case coated with the polymer SU-8 to increase the sensitivity. The measured sensitivity of the fabricated cantilevers turned out to be one half of the expected value. The reduced sensitivity was due to initial bending of the cantilevers and poor adhesion between the two cantilever materials. No further attempts were made to improve the sensitivity of bilayer cantilevers.

The concept of using string-like resonators as temperature sensors has, for the first time, been studied in details both theoretically and experimentally. The measured sensitivity of silicon nitride, nickel and aluminum strings scales in accordance with the theory. A relative change of -15+/-1%/°C was demonstrated using low stressed aluminum strings. This value is more than 100 times higher than values reported by other groups for similar devices. A temperature
resolution of $2.5 \times 10^{-4}$ °C was achieved using high Q silicon nitride strings. This temperature resolution is better than for other types of micro-scale resonating temperature sensors.

The anelastic behavior observed for the strings was least pronounced for the silicon nitride strings. This combined with their better temperature resolution makes them the best temperature sensor candidate.

The concept of using a string-based photothermal spectrometer for microand nano-particle detection has been investigated. Detection and identification of single micro-particles have been demonstrated successfully using a single color irradiation source. The current setup has the potential of detecting single sub-micrometer particles. The detection of wavelength dependent light absorption by micro-particles has also been demonstrated with success.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Larsen, T. (Intern), Boisen, A. (Intern), Schmid, S. (Intern)
Number of pages: 124
Publication date: 2012

**Publication information**

Place of publication: Kgs. Lyngby
Publisher: Technical University of Denmark (DTU)
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:

- ThesisTom.pdf

**Multi-colorimetric sensor array for detection of illegal materials**

The detection of low pressure illegal compounds is an important analytical problem which requires reliable, selective and sensitive detection methods which provide the highest level of confidence in the result. Therefore, to contribute in the successful development of the recognition technology and signal processing enhancements to sensing methods, recognition ability, data acquisition time and data processing algorithms are necessary. In this research we work towards the development of a rapid, easy in use, highly sensitive, specific (minimal false positives) sensor based on a colorimetric sensing technology.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanointegration, Nanoprobes, Surface Engineering, Department of Applied Mathematics and Computer Science, Cognitive Systems
Authors: Kostesha, N. (Intern), Boisen, A. (Intern), Jakobsen, M. H. (Intern), Alstrøm, T. S. (Intern), Larsen, J. (Intern)
Number of pages: 4
Publication date: 2012

**Host publication information**

Title of host publication: 2012 IEEE Sensors
Publisher: IEEE
ISBN (Print): 978-1-4577-1766-6
Series: I E E E Sensors. Proceedings
ISSN: 1930-0395
Main Research Area: Technical/natural sciences
Conference: 2012 IEEE Sensors, Taipei, Taiwan, Province of China, 28/10/2012 - 28/10/2012
DOIs:

10.1109/ICSENS.2012.6411474
Source: dtu
Source-ID: n:oat:DTIC-ART:iel/377909958::25510
Publication: Research - peer-review » Article in proceedings – Annual report year: 2013


M. S. Schmidt et al. describe on page OP11 a simple, two-step fabrication process to assemble flexible, freestanding nanopillars into large-area substrates. These substrates can be made using readily available silicon-processing equipment and are suitable for SERS, having a large, uniform Raman enhancement.

**General information**

State: Published
Physical stability and dissolution of spatially confined amorphous indomethacin: The effect of different heating and cooling rates

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern)
Number of pages: 1
Publication date: 2012
Event: Abstract from Annual Meeting and Exposition of the American Association of Pharmaceutical Scientists (AAPS), Chicago, United States.
Main Research Area: Technical/natural sciences

Bibliographical note
Poster presentation.
Source: PublicationPreSubmission
Source-ID: 97539280
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

Process Optimization for Spray Coating of Poly (vinyl pyrrolidone)
Poly(vinyl pyrrolidone) (PVP) is an important synthetic polymer which has a wide variety of applications in the biomedical field because of its film forming properties including adhesion, excellent physiological compatibility, low toxicity, and reasonable solubility in water and most organic solvents [1]. Recently some studies have been published [2, 3] using micromechanical sensors to characterize thin polymer coatings under various conditions. With the final aim to deposit thin PVP film on cantilevers we studied the process optimization of PVP by spray coating on microscope glass slides. Here, we present a study of the parameters determining the quality of the deposited film. Spray Coating was done in an Exacta Coat Ultrasonic Spraying System (Sonotek, USA). The main components are illustrated in fig. 1. The tip of the ultrasonic atomizer nozzle was actuated at a frequency of 120 kHz. Nitrogen gas was connected to the inlet of the air focusing shroud. The nitrogen pressure was monitored by a pressure sensor and regulated by a valve. The gas flow and the position of the air focusing shroud allowed the control of the diameter and shape of the spray-coating beam. The movement of the nozzle was controlled by an x-y-z stage. A shadow mask was put on a glass slide before deposition to cover some area from spraying. The masked areas acted as a baseline for characterizing the final coating by a surface profilometer (Veeco Dektak8) from where the thickness and roughness value were calculated as shown schematically in fig. 2. The surface texture was observed with an Optical Microscope (Zeiss). A 0.5 wt. % solution of PVP in water was prepared and introduced in the central column of the nozzle using a syringe pump. Each slide was coated 10 times with a flow rate of 0.1 ml/min and nitrogen pressure of 0.03 Bar which was kept constant for all the experiments. The parameters varied are speed of the moving nozzle while spraying (nozzle path shown schematically in fig. 2), temperature of the substrate and distance between nozzle and substrate. Surface morphology of the films is governed mainly by the rate of drying of the spray on the substrate. The depositions can be broadly classified into a dry state, a wet state and an optimized condition in between. The profilometer scan in fig. 3 and the microscope images in fig. 4 show the surface for a distance between the nozzle and the substrate of (a) 100mm, (b) 70mm and (c) 90mm respectively. The further the nozzle is away from the substrate the faster the deposited polymer film dries. Spraying with a distance of 100mm gives rise to the dry state (fig. 3a) with avg. roughness (Ra) 158 nm. When the distance between nozzle and substrate decreases to 70 mm, i.e., at the wet state, Ra reduces to 22 nm. The disadvantage of the wet condition is that as the polymer remains wet for a longer time it accumulates at the edge of the deposition to form peaks of few microns in height (fig. 3b). The optimized condition (fig. 3c) lies in between at a distance of 90 mm where we get a compromise between the dry and the wet state where Ra is 76 nm but there are no edge peaks as shown before. With an increase in temperature (fig. 5a, b and c) the deposition moves from the wet to dry state were roughness increases due to rapid drying of the sprayed drops. Same dry state is observed for coating with an aqueous solution at 60°C (fig. 5c) and when a low boiling solvent like dichloromethane (fig. 5d) is used for deposition at room temperature. The speed of the spraying nozzle influences both the final thickness and roughness of the film. The roughness becomes significant when the nozzle is very fast and the amount of polymer sprayed is not enough to coalesce and form a continuous film. This study shows the inter-correlation of different parameters for uniform film formation by spray coating. The findings will be used for coating of cantilevers and for studies of material characteristics of thin polymer films used for example drug delivery.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Amphiphilic Polymers in Biological Sensing, Nanoprobes
Authors: Bose, S. (Intern), Keller, S. S. (Intern), Boisen, A. (Intern), Almdal, K. (Intern)
Publication date: 2012
Main Research Area: Technical/natural sciences
Electronic versions: MNESanjukta

Relations
Spatial confinement can lead to increased stability of amorphous indomethacin

The aim of this study was to investigate whether the physical stability of amorphous indomethacin can be improved by separating the drug material into small units by the use of microcontainers. Crystallisation from the spatially confined amorphous indomethacin in the microcontainers was determined and compared with the crystallisation kinetics of amorphous bulk indomethacin. Amorphous indomethacin in both a bulk form and contained within microcontainers was prepared by melting of bulk or container-incorporated γ-indomethacin, respectively, followed by quench-cooling. Microcontainers of three different sizes (diameters of 73μm, 174μm and 223μm) were used for the confinement of amorphous indomethacin, in order to elucidate whether the size of the microcontainer had an influence on the stability of the amorphous form. Following preparation, all samples were stored at 30°C and 23% RH. A sample of 100 microcontainers of each size was selected and measured on a Raman microscope over a period of 30 days to ascertain whether the indomethacin in each container was amorphous or crystalline. Over time, a crystallisation number was obtained for the amorphous indomethacin in the microcontainers. The crystallisation numbers from the microcontainers were compared with the crystallisation kinetics of the amorphous bulk indomethacin, as determined by FT-Raman spectroscopy. Comparison of the numeric crystallisation in the microcontainers with the crystallisation kinetics of the amorphous bulk indomethacin showed that spatial confinement of indomethacin led to a significantly lower extent of crystallisation of the amorphous form. In the 174μm microcontainers, 29.0±2.6% of the amorphous indomethacin crystallised to the stable γ-form over a period of 30 days, whilst 38.3±1.5% of the amorphous indomethacin crystallised in the 223μm microcontainers. Both these values were significantly different from that observed in the amorphous bulk indomethacin, where 51.0% crystallised to the γ-form after 30 days. Comparing the 174 and 223μm microcontainers also revealed a significantly greater stabilising effect of the 174μm microcontainers (p-value of 0.0061). Surprisingly, for microcontainers with an inner diameter of 73μm, no stability improvement was found when compared to amorphous bulk indomethacin. It was observed that the amorphous indomethacin within these containers converted to the α-form of indomethacin (a metastable polymorph) which was unexpected at the storage conditions at 30°C and 23% RH.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Otago, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Gordon, K. C. (Ekstern), Boisen, A. (Intern), Rades, T. (Forskerdatabase), Müllertz, A. (Forskerdatabase)
Pages: 418-425
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: European Journal of Pharmaceutics and Biopharmaceutics
Volume: 81
Issue number: 2
ISSN (Print): 0939-6411
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 1.378 SJR 1.342
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 4.49 SJR 1.411 SNIP 1.416
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.437 SNIP 1.471 CiteScore 4.37
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.481 SNIP 1.583 CiteScore 4.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.566 SNIP 1.696 CiteScore 4.64
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Stability of amorphous drug formulations in microcontainers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, University of Copenhagen, University of Otago
Authors: Nielsen, L. H. (Intern), Keller, S. S. (Intern), Gordon, K. C. (Ekstern), Boisen, A. (Intern), Rades, T. (Ekstern)
Number of pages: 1
Publication date: 2012
Event: Abstract from Day of Research, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences

Bibliographical note
Oral presentation.
Source: PublicationPreSubmission
Source-ID: 97539232
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

Statistical analysis of DNT detection using chemically functionalized microcantilever arrays

The need for miniaturized and sensitive sensors for explosives detection is increasing in areas such as security and demining. Micrometer sized cantilevers are often used for label-free detection, and have previously been reported to be able to detect explosives. However, only a few measurements from 1 to 2 cantilevers have been reported, without any information on repeatability and reliability of the presented data. In explosive detection high reliability is needed and thus a statistical measurement approach needs to be developed and implemented. We have developed a DVD-based read-out system capable of generating large sets of cantilever data for vapor and liquid phase detection of 2,4-dinitrotoluene (DNT). Gold coated cantilevers are initially functionalized with tetraTTF-calix[4]pyrrole molecules, specifically designed to bind nitro-aromatic compounds. The selective binding of DNT molecules on the chemically treated surfaces results in significant bending of the cantilevers and in a decrease of their resonant frequencies. We present averaged measurements obtained from up to 72 cantilevers being simultaneously exposed to the same sample. Compared to integrated reference cantilevers with non-selective coatings the tetraTTF-calix[4]pyrrole functionalized cantilevers reveal a
uniform and reproducible behavior.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Academia Sinica Taiwan, University of Southern Denmark
Authors: Bosco, F. (Intern), Bache, M. (Intern), Hwu, E. (Ekstern), Chen, C. (Ekstern), Andersen, S. (Ekstern), Nielsen, K. (Ekstern), Keller, S. S. (Intern), Jeppesen, J. (Forskerdatabase), Kwang, I. (Ekstern), Boisen, A. (Intern)
Pages: 1054-1059
Publication date: 2012
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Sensors and Actuators B: Chemical
Volume: 171-172
ISSN (Print): 0925-4005
Ratings:
- BFI (2018): BFI-level 2
- Web of Science (2018): Indexed yes
- BFI (2017): BFI-level 1
- Scopus rating (2017): SNIP 1.453 SJR 1.406
- Web of Science (2017): Indexed yes
- BFI (2016): BFI-level 1
- Scopus rating (2016): CiteScore 5.07 SJR 1.343 SNIP 1.464
- Web of Science (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 1.225 SNIP 1.484 CiteScore 4.84
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 1.229 SNIP 1.658 CiteScore 4.37
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 1.261 SNIP 1.638 CiteScore 4.25
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 1.412 SNIP 1.674 CiteScore 3.92
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 1.485 SNIP 1.752 CiteScore 4.08
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 1
- Scopus rating (2010): SJR 1.434 SNIP 1.437
- Web of Science (2010): Indexed yes
- BFI (2009): BFI-level 1
- Scopus rating (2009): SJR 1.317 SNIP 1.518
- Web of Science (2009): Indexed yes
- BFI (2008): BFI-level 1
- Scopus rating (2008): SJR 1.448 SNIP 1.566
- Web of Science (2008): Indexed yes
- Scopus rating (2007): SJR 1.446 SNIP 1.598
- Scopus rating (2006): SJR 1.359 SNIP 1.535
- Scopus rating (2005): SJR 1.28 SNIP 1.843
- Web of Science (2005): Indexed yes
Test system and method

The present invention relates to an apparatus for detecting compounds, the apparatus having a device defining a disk-shaped geometry, the device having a centre, a plurality of fluid channels each comprising a fluid inlet positioned at a first distance from the centre and a fluid channel end at a second distance from the centre, the second distance being larger than the first distance, one or more sensors arranged at each fluid channel, wherein the sensors each comprise at least one optical detectable member, the test apparatus further comprising one or more optical sensing devices arranged for sensing the at least one optical detectable member of the one or more sensors, and a rotation device adapted for rotating the device so that the sensors pass over the one or more optical sensing devices. Further the present invention relates to a method for determining compounds comprising providing an apparatus for detecting compounds having a device defining a disk-shaped geometry, the device having a centre, a plurality of fluid channels each comprising a fluid inlet positioned at a first distance from the centre and a fluid channel end at a second distance from the centre, the second distance being larger than the first distance, one or more sensors arranged at each fluid channel, wherein the sensors each comprise at least one optical detectable member, the test apparatus further comprising one or more optical sensing devices arranged for sensing the at least one optical detectable member of the one or more sensors, and a rotation device adapted for rotating the device so that the sensors pass over the one or more optical sensing devices, the method comprising: providing a fluid at an inlet near the centre of the device, rotating the device, and obtaining properties of the sensors using the optical sensing devices.

Ultra-low power hydrogen sensing based on a palladium-coated nanomechanical beam resonator

Hydrogen sensing is essential to ensure safety in near-future zero-emission fuel cell powered vehicles. Here, we present a novel hydrogen sensor based on the resonant frequency change of a nanoelectromechanical clamped-clamped beam. The beam is coated with a Pd layer, which expands in the presence of H2, therefore generating a stress build-up that causes the frequency of the device to drop. The devices are able to detect H2 concentrations below 0.5% within 1 s of the onset of the exposure using only a few hundreds of pW of power, matching the industry requirements for H2 safety sensors. In addition, we investigate the strongly detrimental effect that relative humidity (RH) has on the Pd responsivity to H2, showing that the response is almost nullified at about 70% RH. As a remedy for this intrinsic limitation, we applied a mild heating current through the beam, generating a few μW of power, whereby the responsivity of the sensors is fully
restored and the chemo-mechanical process is accelerated, significantly decreasing response times. The sensors are fabricated using standard processes, facilitating their eventual mass-production. © 2012 The Royal Society of Chemistry.

Various heating and cooling conditions influence the release of amorphous indomethacin from microcontainers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Henriksson, J. (Ekstern), Villanueva Torrijo, L. G. (Intern), Brugger, J. (Ekstern)
Pages: 5059-5064
Publication date: 2012
Main Research Area: Technical/natural sciences
Dynamic in situ chromosome immobilisation and DNA extraction using localized poly(N-isopropylacrylamide) phase transition

A method of in situ chromosome immobilisation and DNA extraction in a microfluidic polymer chip was presented. Light-induced local heating was used to induce poly(N-isopropylacrylamide) phase transition in order to create a hydrogel and embed a single chromosome such that it was immobilised. This was achieved with the use of a near-infrared laser focused on an absorption layer integrated in the polymer chip in close proximity to the microchannel. It was possible to proceed to DNA extraction while holding on the chromosome at an arbitrary location by introducing protease K into the microchannel.

© 2011 American Institute of Physics.

General information
State: Published
Organisations: NSE-Optofluidics Group, NanoSystemsEngineering Section, Department of Micro- and Nanotechnology, Nanoprobes, The Danish Polymer Centre, Department of Chemical and Biochemical Engineering
Authors: Eriksen, J. (Ekstern), Thilsted, A. H. (Intern), Marie, R. (Intern), Lüscher, C. J. (Intern), Nielsen, L. B. (Ekstern), Svendsen, W. E. (Intern), Szabo, P. (Intern), Kristensen, A. (Intern)
Pages: 031101
Publication date: 2011
Main Research Area: Technical/natural sciences

Publication information
Journal: Biomicrofluidics
Volume: 5
Issue number: 3
ISSN (Print): 1932-1058
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.655 SJR 0.592
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.831 SNIP 0.841 CiteScore 2.55
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.855 SNIP 0.888 CiteScore 2.49
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.143 SNIP 1.011 CiteScore 2.5
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.165 SNIP 1.132 CiteScore 2.98
ISI indexed (2013): ISI indexed yes
Scopus rating (2012): SJR 0.922 SNIP 0.976 CiteScore 2.75
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Scopus rating (2011): SJR 0.905 SNIP 1.159 CiteScore 3.23
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 1.227 SNIP 1.256
Scopus rating (2009): SJR 0.728 SNIP 0.856
SERS substrate and a method of providing a SERS substrate

Source: US2011116089A

A substrate primarily for SERS determination, the substrate has a number of elongate elements with a density of at least 1x108 elongate elements per cm² and having metal coated tips. When the elements may be made to lean toward each other, such as by providing a drop of a liquid thereon and allowing the liquid to dry, groups of tips of elongate elements are formed and the Raman enhancement is extremely high.

Spatial confinement of amorphous indomethacin increases stability

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Nielsen, L. H. (Intern), Rades, T. (Ekstern), Gordon, K. C. (Ekstern), Müllertz, A. (Ekstern)
Publication date: 2011
Event: Poster session presented at Annual meeting of the American Association of Pharmaceutical Scientists (AAPS), Washington, United States.
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 97539226
Publication: Research - peer-review › Poster – Annual report year: 2011
Nanostructured surface enhanced Raman scattering substrates for explosives detection

Here we present a method for trace detection of explosives in the gas phase using novel surface enhanced Raman scattering (SERS) spectroscopy substrates. Novel substrates that produce an exceptionally large enhancement of the Raman effect were used to amplify the Raman signal of explosives molecules adsorbed onto the substrate. The substrates were fabricated in a cleanroom process which only requires two steps to produce well controlled nano-sized high aspect ratio metal pillars. These substrates had superior chemical sensing performance in addition to a more cost effective fabrication process compared to existing commercial substrates. Therefore it is believed that these novel substrates will be able to make SERS more applicable in mobile explosives detection systems to be deployed in for example landmine clearance actions.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes
Authors: Schmidt, M. S. (Intern), Olsen, J. K. (Intern), Boisen, A. (Intern), Hübner, J. (Intern)
Pages: 2634 - 2637
Publication date: 2010

Windowless microfluidic platform based on capillary burst valves for high intensity x-ray measurements

We propose and describe a microfluidic system for high intensity x-ray measurements. The required open access to a microfluidic channel is provided by an out-of-plane capillary burst valve (CBV). The functionality of the out-of-plane CBV is characterized with respect to the diameter of the windowless access hole, ranging from 10 to 130 Åm. Maximum driving pressures from 22 to 280 mbar corresponding to refresh rates of the exposed sample from 300 Hz to 54 kHz is demonstrated. The microfluidic system is tested at beamline ID09b at the ESRF synchrotron radiation facility in Grenoble, and x-ray scattering measurements are shown to be feasible and to require only very limited amounts of sample, <1 ml/h of measurements without recapturing of sample. With small adjustments of the present chip design, scattering angles up to 30 can be achieved without shadowing effects and integration on-chip mixing and spectroscopy appears straightforward. (C) 2009 American Institute of Physics.

General information
State: Published
Organisations: NSE-Optofluidics Group, NanoSystemsEngineering Section, Department of Micro- and Nanotechnology, Nanoprobes, Technical University of Denmark, University of Copenhagen
Pages: 115114
Publication date: 2009
Main Research Area: Technical/natural sciences
I propose the utilisation of biopolymer microcontainers as an oral vaccine delivery system. These microcontainers (MCs) will be filled with a particulate vaccine formulation and sealed with a mucoadhesive layer followed by a pH-sensitive lid. The MCs will provide: 1) protection of the vaccine against enzymatic degradation, 2) adherence to the desired site of action and 3) provision of a unidirectional drug release. In the design of such a system, it is intended that the vaccine will be released only upon reaching the intestine, in close proximity to the epithelial cell barrier, allowing for effective uptake of the antigen and the initiation of an immune response. The project will be based at DTU Nanotech with collaborations to KU Pharma, Denmark, Helmholtz Institute for Pharmaceutical Research Saarland, Saarbrücken, Germany and University of Otago, Dunedin, New Zealand.
Heterojunction Silicon Solar Cells

One of the most severe challenges man is facing today is to fulfill the need for energy without harmful environmental consequences. This complicated, grand challenge must be met by a wide range of solutions; among these are more efficient use of resources and replacement of fossil fuels by renewable energy sources. Any sustainable, renewable energy system must directly or indirectly rely on solar energy. Photovoltaic or solar cells are already efficient and reliable sources of electricity from solar light, but even though the cost has decreased significantly in recent years, solar cells are still far too costly for a competitive production of bulk grid power. The challenge within the solar cell field is thus to reduce the costs involved in solar cell production without sacrificing efficiency and reliability; actually, the efficiency should better improve towards 25% or more, since the cell efficiency strongly affects the overall economy of a solar cell power plant. Currently, most of the solar cell market is based on 180-300 micrometer thick crystalline silicon wafers, and approximately 50% of the cost is due to the cost of the material. To reduce material costs thin film cells are promising alternatives, but a limitation in thin film solar cell technologies is that the absorbance of light is quite weak in particular for indirect band gap materials like silicon. This limitation may be lifted by application of photon trapping strategies that can increase the absorptivity of thin photo-absorbers by orders of magnitude at longer wavelengths. Another proved approach in solar cell optimization is carrier selective contacts, such as conventional amorphous silicon, or wide bandgap metal oxide semiconductor.

In this project, we will explore several new ideas for novel silicon-based solar cells to develop efficient solar cells that can be fabricated in a low thermal budget, low-cost fabrication procedure using only abundant elements. The main photo-absorber will be lightly doped p-type silicon (1.12 eV band gap) with a thin n-type TiO₂ (3.2 eV band gap) film on top. This structure forms a p-n heterojunction that effectively separates the photo-generated electron hole-pairs, since the titania and silicon conduction bands are aligned facilitating electron transport, while a ~2 eV energy barrier will prevent hole transport. The electrons transported through the titania to the surface will be conducted laterally by a metal grid or continuous transparent conductive oxides such as Aluminum Zinc Oxide (AZO) with high conductivity, highly transparent (loss 10 %) electrode layer. On the backside, silicon will be coated with complementary to TiO₂ thin film of NiO. NiO is p-type wide bandgap (3.6 eV) semiconductor. In connection to Si it will form p-p isotype heterojunction with excellent valence band matching, and creating hole conducting and electron blocking layer. A back contact will be formed using a high work-function metal to form additional a potential barrier against electron transport, while the holes are easily conducted to the metal. This basic structure will be combined with micro and nanostructuring of the silicon surface prior to fabrication to form a light trapping structure. All fabrication procedures may be done at temperatures close to room temperature with a maximum of ~200°C necessary in a single step, and thus the thermal budget becomes unusually low. At the same time, a high open circuit voltage for the structure is expected due to the efficient carrier separation in the structure.

The overall project will have four main research phases. In the first phase of the project, the basic TiO₂-Si heterostructure will be optimized on planar silicon wafers. Here the focus will be on the development of optimized fabrication procedures that results in high-performance junctions and efficient lateral transport. In this phase of the project, we also want to fabricate silicon alumina-titania heterostructures. Alumina has properties similar to titania: a wide bandgap and transparency to visible wavelengths, hole transport blocking and passivation of a silicon surface. In the process, alumina will be deposited on top of silicon and then the lithographic windows will be opened for titania deposition and formation of localized titania-silicon heterojunctions. On top of titania areas aluminum contacts will be introduced. It is planned to fabricate and test such structures since they have a potential to show both high open circuit voltage and short circuit current. Other metal with close by work function will be tested to minimize current blocking effects in diode structure. In the second stage, NiO-Si isotype heterostructure will be tested and optimized to meet the best ohmic (hole conductive) properties. We will fabricate and characterize NiO-Si structure similar to TiO₂-Si structure. Next micro- and nanostructured silicon surfaces, including “Black silicon”, for light trapping will be developed and characterized. In this stage, nanostructured surfaces should be optimized to obtain the lowest surface recombination velocity in comparison to plain silicon. Then the optimized heterostructure cell fabrication procedure will be ported to these structures.

Finally, after the previous three stages will be developed, different solar cell architectures will be tested for solar cell fabrication and characterization. We consider Pasha, HIT and IBC architecture as the most promising for solar cell test since they showed the world records of efficiencies for conventional silicon solar cells.
Department of Physics
Experimental Surface and Nanomaterials Physics

Nanoprobes

**Nanointegration**
*Period: 15/02/2014 → 15/02/2017*
*Number of participants: 4*
*Silicon Solar Cell, ALD, Carrier Selective Contacts, Transition Metal Oxides*
*Project ID: 3315*
*Project participant:*
Plakhotnyuk, Maksym (Intern)
*Supervisor:*
Schmidt, Michael Stenbæk (Intern)
Booth, Tim (Intern)
*Main Supervisor:*
Hansen, Ole (Intern)

**Relations**
*Activities:*
26th International Photovoltaic Science and Engineering Conference
European Advanced Material Congress
Fraunhofer Center for Silicon Photovoltaics (CSP)
Discovering Challenges in Fabrication of Nanostructured c-Si Solar Cells with Metal Oxides Carrier Selective Contacts
6th Symposium on Carbon and Related Nanomaterials

*Publications:*
Low surface damage dry etched black silicon
Discovering Challenges in Fabrication of Nanostructured c-Si Solar Cells with Metal Oxides Carrier Selective Contacts
Enhanced Passivation And Characterization Of Titania Silicon Heterojunction With Tunneling Oxide Interlayers
Hole Selective NiO Contact for Silicon Solar Cells
Phosphorous Doping of Nanostructured Crystalline Silicon
Behind the Nature of Titanium Oxide Excellent Surface Passivation and Carrier Selectivity of c-Si
TiO2-Si solar cells with carrier selective contacts and low temperature processing
Graphene transfer on highly corrugated black silicon surface
Lifetime of Nano-Structured Black Silicon for Photovoltaic Applications
Phosphorous Doping of Nanostructured Crystalline Silicon

**Micro punching of micro containers for oral drug delivery**
Department of Mechanical Engineering
Manufacturing Engineering

Department of Micro- and Nanotechnology

Nanoprobes
*Period: 21/01/2013 → 13/11/2014*
*Number of participants: 3*
*Project participant:*
Petersen, Ritika Singh (Intern)
Mahshid, Rasoul (Intern)
Hansen, Hans Nørgaard (Intern)

*Activities:*
3D printed system for testing intestinal drug transport
*Period: 21 Mar 2018*
Morten Leth Jepsen (Other)
Line Hagner Nielsen (Other)
Kristoffer Almdal (Other)
Anja Boisen (Other)
Martin Dufva (Other)

Department of Micro- and Nanotechnology
Fluidic Array Systems and Technology
Nanoprobes

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Applied Mathematics and Computer Science

Related event

11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
21/03/2018 → …
Granada, Spain
Activity: Talks and presentations › Conference presentations

Loading of poorly soluble drugs by supercritical CO2 impregnation into microcontainers for oral drug delivery
Period: 19 Mar 2018 → 22 Mar 2018
Chiara Mazzoni (Other)
Anastasia Antalaki (Other)
Rasmus Due Jacobsen (Other)
Jacob Mortensen (Other)
Fabio Tentor (Other)
Roman Slipets (Other)
Oleksii Ilchenko (Other)
Stephan Sylvest Keller (Other)
Line Hagner Nielsen (Other)
Anja Boisen (Other)

Department of Micro- and Nanotechnology
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Nanoprobes

Department of Applied Mathematics and Computer Science

Related event

11th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
21/03/2018 → …
Granada, Spain
Activity: Talks and presentations › Conference presentations

An automated flow-injection enzyme-linked immunosorbent assay for the detection of Zearalenone
Period: 7 Feb 2018 → 9 Feb 2018
Jongjit Jantra (Other)
Kinga Zor (Other)
Martin Hedström (Other)
Bo Mattiasson (Other)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Micro- and Nanotechnology
Nanoprobes
Description
Pure and Applied Chemistry International Conference 2018 (PACCON 2018), Hat Yai, Songkhla, Thailand, 7th-9th February 2018
Degree of recognition: International

Related event
Pure and Applied Chemistry International Conference 2018
07/02/2018 → 09/02/2018
Hat Yai, Thailand
Activity: Talks and presentations › Conference presentations

3D printed system for based on hydrogels for drug transport
Period: 29 Jan 2018
Morten Leth Jepsen (Other)
Line Hagner Nielsen (Other)
Kristoffer Almdal (Other)
Anja Boisen (Other)
Martin Dufva (Other)
Department of Micro- and Nanotechnology
Fluidic Array Systems and Technology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Applied Mathematics and Computer Science

Description
3D printed system for based on hydrogels for drug transport

Related external organisation
University of Southern Denmark
Odense, Denmark
Activity: Talks and presentations › Conference presentations

Loading of poorly soluble drugs by supercritical CO2 impregnation into microcontainers for oral drug delivery
Period: 29 Jan 2018 → 31 Jan 2018
Chiara Mazzoni (Speaker)
Anastasia Antalaki (Other)
Rasmus Due Jacobsen (Other)
Jacob Mortensen (Other)
Fabio Tentor (Other)
Roman Slipets (Other)
Oleksii Ilichenko (Other)
Stephan Sylvest Keller (Other)
Line Hagner Nielsen (Other)
Anja Boisen (Other)
Department of Micro- and Nanotechnology
Office for Study Programmes and Student Affairs
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Related event
Northern Pharma Network Meeting
29/01/2018 → 31/01/2018
Odense, Denmark
Activity: Talks and presentations › Conference presentations

**Microcontainers for oral vaccine delivery**
Period: 29 Jan 2018 → 31 Jan 2018
Line Hagner Nielsen (Guest lecturer)

Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobess

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

**Description**
Oral presentation

Documents:
Odense meeting_Microcontainers for oral vaccine delivery

**Related event**

**Northern Pharma Network Meeting**
29/01/2018 → 31/01/2018
Odense, Denmark
Activity: Talks and presentations › Conference presentations

**26th International Meshing Roundtable**
Period: 21 Sep 2017
Kristian Ejlebjærg Jensen (Organizer)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobess

Documents:
IMR26_fixed

**Related event**

**26th International Meshing Roundtable**
18/09/2017 → 21/09/2017
Barcelona, Spain
Activity: Attending an event › Participating in or organising a conference

**A nanofiltration technique for analyte extraction from complex matrix and surface enhanced Raman spectroscopy based sensing**
Period: 20 Sep 2017
Onur Durucan (Guest lecturer)
Tomas Rindzevicius (Other)
Michael Stenbæk Schmidt (Other)
Oleksii Ilchenko (Other)
Anja Boisen (Other)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobess

**Description**
Our novel proof-of-concept centrifugal microfluidics sensing platform (Fig.1), allows to perform fast and facile purification (nanofiltration) of the complex sample by incorporating inertial (centrifugal) and capillary forces. Furthermore, integrated in the platform, highly uniform Au capped Si nanopillar (NP) substrates for surface enhanced Raman spectroscopy (SERS) are capable to detect analyte molecules in trace amounts [1]. However, in most of the cases SERS based sensing
applications are accompanied with complicated sample manipulation and external purification steps. This can be addressed to various experimental difficulties of SERS based measurements when handling real-life complex samples. Therefore, we believe that combination with the nanofiltration technique would sufficiently increase sensitivity and applicability of SERS based sensors. In addition to that, the nanofiltration of the sample and SERS based sensing of analyte is carried out on the same chip (Au NP surface) which provides robustness to the platform.

Degree of recognition: International

Related event

43rd International conference on Micro and Nano Engineering
18/09/2017 → 22/09/2017
Braga, Portugal
Activity: Talks and presentations › Conference presentations

Photothermal probing of metallic nanoparticles on nanomechanical string resonators to study plasmonic heating effects
Period: 20 Sep 2017
Varadarajan Padmanabhan Rangacharya (Speaker)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes

Description
In this work, we present the use of nanomechanical string resonators as accurate and reliable tools to study plasmonic heating in gold nanoparticles (AuNPs)
Degree of recognition: International
Documents:
Varadarajan MNE abstract_final1

Related event

43rd International conference on Micro and Nano Engineering
18/09/2017 → 22/09/2017
Braga, Portugal
Activity: Talks and presentations › Conference presentations

Microcontainers for oral vaccine delivery
Period: 18 Sep 2017 → 22 Sep 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Oral presentation
Documents:
MNE2017 Microcontainers for oral vaccine delivery

Related event

43rd International conference on Micro and Nano Engineering
18/09/2017 → 22/09/2017
Braga, Portugal
Activity: Talks and presentations › Conference presentations

Electrospraying Chitosan Particles for Oral Vaccine Delivery
Period: 16 Jul 2017 → 19 Jul 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Poster presentation
Documents:
Abstract CRS 2017_electrospray

Related event
44th Annual Meeting & Exposition of the Controlled Release Society
16/07/2017 → 19/07/2017
Boston, United States
Activity: Talks and presentations › Conference presentations

Microcontainers as an Oral Drug Delivery System
Period: 16 Jul 2017 → 19 Jul 2017
Line Hagner Nielsen (Guest lecturer)
Department of Applied Mathematics and Computer Science
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
Poster presentation
Documents:
Abstract CRS 2017_microcontainers

Related event
44th Annual Meeting & Exposition of the Controlled Release Society
16/07/2017 → 19/07/2017
Boston, United States
Activity: Talks and presentations › Conference presentations

1st Summer School on Complex Fluid-Flows in Microfluidics
Period: 14 Jul 2017
Kristian Ejlebjærg Jensen (Speaker)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes
Links:
http://galindorosales.com/SummerSchool2017/Programme.html

Related external organisation
Campus da Faculdade de Engenharia da Universidade do Porto
Portugal
Activity: Talks and presentations › Guest lectures, external teaching and course activities at other universities

Structural aspects of hydrates – insight into phase transformations using nanomechanical sensors
Period: 28 Jun 2017 → 30 Jun 2017
Peter Ouma Okeyo (Guest lecturer)
Peter Emil Larsen (Guest lecturer)
Oleksii Ilychenko (Guest lecturer)
Tomas Rindzevicius (Guest lecturer)
Roman Slipets (Guest lecturer)
Anja Boisen (Guest lecturer)
Thomas Rades (Guest lecturer)
Jukka Rantanen (Guest lecturer)

Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Degree of recognition: International

Related event

11th annual meeting of the Pharmaceutical Solid State Research Cluster
28/06/2017 → 30/06/2017
Graz, Austria
Activity: Talks and presentations › Conference presentations

Integration of Nanopillar SERS Substrates in a Microfluidic Platform for Analyte Separation and Quantitative Sensing
Period: 11 Jun 2017 → 17 Jun 2017
Onur Durucan (Guest lecturer)
Lidia Morelli (Guest lecturer)
Kaiyu Wu (Guest lecturer)
Marlitt Viehrig (Guest lecturer)
Oleksii Ilychenko (Guest lecturer)
Kinga Zor (Guest lecturer)
Marco Matteucci (Guest lecturer)
Tommy Sonne Alstrøm (Guest lecturer)
Tomas Rindzevicius (Guest lecturer)
Michael Stenbæk Schmidt (Guest lecturer)
Anja Boisen (Guest lecturer)

Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Cognitive Systems

Related event

9th International Conference on Advanced Vibrational Spectroscopy
11/06/2017 → 17/06/2017
Victoria, Canada
Activity: Talks and presentations › Conference presentations

SERS combiner for high-speed and high-sensitive quantitative analysis
Period: 11 Jun 2017 → 17 Jun 2017
Oleksii Ilychenko (Guest lecturer)
Tomas Rindzevicius (Guest lecturer)
Onur Durucan (Guest lecturer)
Michael Stenbæk Schmidt (Guest lecturer)
Roman Slipets (Other)
Lidia Morelli (Guest lecturer)
Anja Boisen (Guest lecturer)
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Related event

9th International Conference on Advanced Vibrational Spectroscopy
11/06/2017 → 17/06/2017
Victoria, Canada
Activity: Talks and presentations › Conference presentations

SERS combiner for high-speed and high-sensitive quantitative analysis
Period: 11 Jun 2017 → 17 Jun 2017
Oleksii Ilchenko (Guest lecturer)
Tomas Rindzevicius (Guest lecturer)
Michael Stenbæk Schmidt (Guest lecturer)
Roman Slipets (Guest lecturer)
Onur Durucan (Guest lecturer)
Lidia Morelli (Guest lecturer)
Anja Boisen (Guest lecturer)
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Related event

9th International Conference on Advanced Vibrational Spectroscopy
11/06/2017 → 17/06/2017
Victoria, Canada
Activity: Talks and presentations › Conference presentations

Solving 2D/3D Heat Conduction Problems by Combining Topology Optimization and Anisotropic Mesh Adaptation
Period: 8 Jun 2017
Kristian Ejlebjærg Jensen (Guest lecturer)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes
Documents:
paperID62_KristianE

Related event

12th World Congress of Structural and Multidisciplinary Optimization
05/06/2017 → 09/06/2017
Braunschweig, Germany
Activity: Talks and presentations › Conference presentations

Non-Invasive Delivery of Macromolecules Conference
Period: 23 Feb 2017
Chiara Mazzoni (Guest lecturer)
Department of Micro- and Nanotechnology
Nanoprobes
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Description
MICROCONTAINERS FOR INTESTINAL DRUG DELIVERY: in vivo and ex vivo study
Degree of recognition: International
Documents:
Abstract_Mazzoni

Related event
Non-Invasive Delivery of Macromolecules Conference
21/02/2017 → 24/02/2017
San Diego, United States
Activity: Talks and presentations › Conference presentations

11th Central European Symposium on Pharmaceutical Technology
Period: 23 Sep 2016 → 24 Sep 2016
Fabio Tentor (Speaker)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes

Description
Poster session at the 11th Central European Symposium on Pharmaceutical Technology (Belgrade, Serbia)
Documents:
MICROCONTAINERS FOR INTESTINAL DRUG DELIVERY

Related event
11th Central European Symposium on Pharmaceutical Technology
22/09/2016 → 24/09/2016
Belgrade, Serbia
Activity: Talks and presentations › Conference presentations

Central European Symposium on Pharmaceutical Technology
Period: 23 Sep 2016
Chiara Mazzoni (Speaker)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes

Description
MICROCONTAINERS AS EFFECTIVE DRUG DELIVERY VEHICLES: ADVANCES IN THE DRUG LOADING
Oral presentation
Documents:
MICROCONTAINERS AS EFFECTIVE DRUG DELIVERY VEHICLES: ADVANCES IN THE DRUG LOADING

Related event
Central European Symposium on Pharmaceutical Technology
22/09/2016 → 24/09/2016
Belgrade, Serbia
Activity: Talks and presentations › Conference presentations

Perforated SiN membrane resonators for nanomechanical IR spectroscopy
Period: 19 Sep 2016 → 23 Sep 2016
Maksymilian Kurek (Speaker)
Department of Micro- and Nanotechnology

Nanoprobess

**Description**
Poster together with Matthias Carnoy, Anja Boisen and Silvan Schmid

**Poster**

**Documents:**

**Perforated SiN membrane resonators for nanomechanical IR spectroscopy poster**

**Related event**

**42nd International conference on Micro and Nano Engineering**
19/09/2016 → 23/09/2016
Vienna, Austria
Activity: Talks and presentations › Conference presentations

**Micromechanical pyrolytic carbon string resonators**
Maksymilian Kurek (Speaker)

Department of Micro- and Nanotechnology

Nanoprobess

**Description**
Presented work done together with Frederik Kjær Larsen, Peter Emil Larsen, Silvan Schmid, Anja Boisen and Stephan Sylvest Keller

**Documents:**

**Micromechanical Pyrolytic Carbon String Resonators**

**Related event**

**13th International Workshop on Nanomechanical Sensing**
22/06/2016 → 24/06/2016
Delft, Netherlands
Activity: Talks and presentations › Conference presentations

**Modelling and experiments in drug delivery systems**
Kristian Ejlebjærg Jensen (Speaker)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Micro- and Nanotechnology

Nanoprobess

**Documents:**

**Geometric Optimization of Microcontainers for Oral Drug Delivery**

**Links:**


**Related event**

**Modelling and experiments in drug delivery systems**
20/06/2016 → 22/06/2016
Coimbra, Portugal
Activity: Talks and presentations › Conference presentations

**Biosensors 2016**
Period: 25 May 2016 → 27 May 2016
Kuldeep Sanger (Participant)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes

Description
Poster presentation
Documents:
Biosensors_poster

Related event
Biosensors 2016: 26th Anniversary World Congress on Biosensors
25/05/2016 → 27/05/2016
Gothenburg, Sweden
Activity: Attending an event › Participating in or organising a conference

11th Workshop on Biosensors and Bioanalytical Microtechniques in Environmental, Food and Clinical Analysis
Period: 26 Sep 2015 → 30 Sep 2015
Kuldeep Sanger (Participant)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes

Description
Poster presentation
Documents:
Kuldeep_BBMEC

Related event
11th Workshop on Biosensors and Bioanalytical Microtechniques in Environmental, Food and Clinical Analysis: International Biosensor Conference
26/09/2015 → 30/09/2015
Regensburg, Germany
Activity: Attending an event › Participating in or organising a conference

41st International conference on Micro and Nano Engineering
Period: 21 Sep 2015 → 24 Sep 2015
Kuldeep Sanger (Participant)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Nanoprobes

Description
Conference abstract
Links:

Related event
41st International conference on Micro and Nano Engineering : MNE 2015
21/09/2015 → 24/09/2015
The Hague, Netherlands
Activity: Attending an event › Participating in or organising a conference

Fabrication and loading of biopolymer microcontainers for oral drug delivery using hot punching
Period: 19 May 2015
Ritika Singh Petersen (Speaker)
Department of Micro- and Nanotechnology
Nanoprobes

Related external organisation

Unknown external organisation
Activity: Talks and presentations › Conference presentations

Microfabrication of containers for oral drug delivery
Period: 10 Apr 2015
Ritika Singh Petersen (Invited speaker)
Department of Micro- and Nanotechnology
Nanoprobes

Description
IDUN Center of Excellence opening ceremony

Related external organisation

Unknown external organisation
Activity: Talks and presentations › Conference presentations

Detection of small organics in water: The MUSE project
Period: 29 Jan 2015
Kasper Bayer Frøhling (Speaker)
Department of Micro- and Nanotechnology
Surface Engineering
Nanoprobes
Documents:
K Frøhling DTU Nanotech
Links:
http://danishwaterforum.dk/Research/Annual%20meeting%202015/Presentations/Session-4/K%20Fr%C3%B8hling%20DTU%20Nanotech.pdf

Related event
Danish Water Forum: 9th Annual Water Research Meeting
29/01/2015 → …
Copenhagen, Denmark
Activity: Talks and presentations › Conference presentations

Microfabrication of containers for oral drug delivery
Period: 1 Oct 2014
Ritika Singh Petersen (Invited speaker)
Department of Micro- and Nanotechnology
Nanoprobes

Description
Department Days, DTU Nanotech, Technical University of Denmark

Related external organisation

Unknown external organisation
Activity: Talks and presentations › Conference presentations
**Pyrolysed 3D-carbon scaffolds induce spontaneous differentiation of human neural stem cells and facilitate real-time dopamine detection**

*Period: 14 Sep 2014*

Letizia Amato (Lecturer)

Department of Micro- and Nanotechnology

**Nanoprobes**

**Description**


**Related event**

1st International Conference on Carbon Micro Electromechanical Systems

*14/09/2014 → 16/09/2014*

Irvine, United States

Activity: Talks and presentations › Conference presentations

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**4th International Workshop on Analytical Miniaturization and NANOtechnologies**

*Period: 23 Jun 2014 → 24 Jun 2014*

Sanjukta Bose-Goswami (Participant)

Department of Micro- and Nanotechnology

**Nanoprobes**

**Description**

Poster Presentation

**Related event**

4th International Workshop on Analytical Miniaturization and NANOtechnologies

*23/06/2014 → 24/06/2014*

Copenhagen, Denmark

Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

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**15th International Conference on Electroanalysis**

*Period: 11 Jun 2014 → 15 Jun 2014*

Xueling Quan (Participant)

Department of Micro- and Nanotechnology

**Nanoprobes**

**Description**

Poster

**Documents:**

Characterization of Electromechanical Behavior of an Electrochemical Cantilever System

**Related event**

15th International Conference on Electroanalysis

*11/06/2014 → 15/06/2014*

Malmö, Sweden

Activity: Attending an event › Participating in or organising a conference

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**11th International Workshop on Nanomechanical Sensing**

*Period: 30 Apr 2014 → 2 May 2014*

Xueling Quan (Participant)

Department of Micro- and Nanotechnology
Nanoprobes

Description
Poster

Related event

11th International Workshop on Nanomechanical Sensing
30/04/2014 → 02/05/2014
Madrid, Spain
Activity: Attending an event › Participating in or organising a conference

Nanoprobes

Description
Poster Presentation

Related event

11th International Workshop on Nanomechanical Sensing
Period: 30 Apr 2014 → 2 May 2014
Sanjukta Bose-Goswami (Participant)
Department of Micro- and Nanotechnology

9th Annual Workshop of Biofilms – Research Center for Biointerfaces
Period: 4 Oct 2013
Paula Soares Martins Antunes (Participant)
Department of Micro- and Nanotechnology

Nanoprobes

Description
Poster

Related event

9th Annual Workshop of Biofilms – Research Center for Biointerfaces
03/10/2013 → 04/10/2013
Malmo, Sweden
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

222th Electrochemical Society meeting
Xueling Quan (Participant)
Department of Micro- and Nanotechnology

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Description
Oral

Related event

222th Electrochemical Society meeting
07/10/2014 → 12/10/2014
Honolulu, HI, United States
Activity: Attending an event › Participating in or organising a conference
9th International Nanomechanical Sensing Workshop
Period: 7 Jun 2012
Xueling Quan (Participant)
Department of Micro- and Nanotechnology
Nanoprobes
Description
Poster presentation: Investigation of cleaning and regeneration methods for reliable construction of DNA cantilever biosensors.
Documents:
NMC 2012-Final

Related event

9th International Nanomechanical Sensing Workshop
06/06/2012 → 08/06/2012
Mumbai, India
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

15th International Conference on Miniaturized Systems for Chemistry and Life Sciences
Xueling Quan (Participant)
Department of Micro- and Nanotechnology
Nanoprobes
Description
Poster

Related event

15th International Conference on Miniaturized Systems for Chemistry and Life Sciences
02/10/2011 → 06/10/2011
Seattle, WA, United States
Activity: Attending an event › Participating in or organising a conference

2nd International Conference on Nanotechnology
Period: 27 Jul 2011 → 29 Jul 2011
Xueling Quan (Participant)
Department of Micro- and Nanotechnology
Nanoprobes
Related event

2nd International Conference on Nanotechnology (ICNFA 2011): Fundamentals and Applications
27/07/2011 → 29/07/2011
Ottawa, Canada
Activity: Attending an event › Participating in or organising a conference

36th International Conference on Micro- and Nano-Engineering
Period: 19 Sep 2010 → 22 Sep 2010
Xueling Quan (Participant)
Department of Micro- and Nanotechnology
Nanoprobes
Description
Poster
Related event

36th International Conference on Micro- and Nano-Engineering
19/09/2010 → 22/09/2010
Genoa, Italy
Activity: Attending an event › Participating in or organising a conference