Spatio-temporal pattern formation in predator-prey systems with fitness taxis

We pose a spatial predator–prey model in which the movement of animals is not purely diffusive, but also contains a drift term in the direction of higher specific growth rates. We refer to this as fitness taxis. We conduct a linear stability analysis of the resulting coupled reaction–advection–diffusion equations and derive conditions under which spatial patterns form. We find that for some parameters the problem is ill posed and short waves grow with unbounded speeds. To eliminate this, we introduce spatial kernels in the model, yielding coupled integro-differential equations, and conduct a similar stability analysis for this system. Through numerical simulation, we find that a variety of patterns can emerge, including stationary spatial patterns, standing and travelling waves, and seemingly chaotic spatio-temporal patterns. We argue that fitness taxis represents a simple and generic extension of diffusive motion, is ecologically plausible, and provides an alternative mechanism for formation of patterns in spatially explicit ecosystem models, with emphasis on non-stationary spatio-temporal dynamics.
A General Microscopic Traffic Model Yielding Dissipative Shocks

We consider a general microscopic traffic model with a delay. An algebraic traffic function reduces the equation to the Aw-Rascle microscopic model while a sigmoid function gives the standard “follow the leader”. For zero delay we prove that the homogeneous solution is globally stable. For a positive delay, it becomes unstable and develops dispersive and dissipative shocks. These are followed by a finite time singularity for the algebraic traffic function and by kinks for the sigmoid function.

General information

State: Published
Organisations: Department of Applied Mathematics and Computer Science, Department of Physics, Plasma Physics and Fusion Energy, Dynamical Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Bogolyubov Institute for Theoretical Physics, INSA Rouen
Authors: Gaididei, Y. B. (Ekstern), Caputo, J. G. (Ekstern), Christiansen, P. L. (Intern), Rasmussen, J. J. (Intern), Sørensen, M. (Intern)
Pages: 375-382
Publication date: 2018

Host publication information

Title of host publication: Progress in Industrial Mathematics at ECMI 2016
Volume: 26
Publisher: Springer
ISBN (Print): 9783319630823
Series: Mathematics in Industry
Volume: 26
Main Research Area: Technical/natural sciences
DOIs:
10.1016/j.ecocom.2018.04.003
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), Merck Nielsen, H. (Ekstern)
Pages: 371-381
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Bioconjugate Chemistry
Volume: 29
Issue number: 2
ISSN (Print): 1043-1802
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.984 SJR 1.801 CiteScore 4.4
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.63 SJR 1.802 SNIP 1.065
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.664 SNIP 1.065 CiteScore 4.64
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.711 SNIP 1.175 CiteScore 4.85
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.02 SNIP 1.201 CiteScore 5.12
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.064 SNIP 1.263 CiteScore 4.8
Detecting forensic substances using commercially available SERS substrates and handheld Raman spectrometers

Ultra-sensitive in-field measurements of most forensic substances still today remain a challenge for first responders and forensic investigators. Handheld Raman spectroscopy equipment is getting more and more routinely used in the field for evidence collection, however, restricted to measurements of pure or high concentration samples. Here, surface-enhanced Raman scattering (SERS) sensing of common forensic substances with commercially available SERS substrates and handheld spectrometers, have been investigated. 3D Finite Element Method (FEM) and Density Functional Theory (DFT) simulations were used to interpret the high SERS enhancement of the Ag nanopillar substrate and the detection of the substances, respectively. The forensic generality and high performance of the analytical method were demonstrated by explicit detection of close to unprecedented amounts, down to femtograms, of Cyclosarin, RDX, Amphetamine and Picric acid. Implications are ultra-sensitive in-field SERS detection of these substances with commercial equipment.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Sensor Visions AB, Swedish Defense Research Agency FOI
Authors: Hakonen, A. (Ekstern), Wu, K. (Intern), Schmidt, M. S. (Intern), Andersson, P. O. (Ekstern), Boisen, A. (Intern), Rindzviecius, T. (Intern)
Number of pages: 4
Pages: 649-652
Publication date: 2018
Main Research Area: Technical/natural sciences

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Journal: Talanta
Volume: 189
ISSN (Print): 0039-9140
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.26 SJR 1.186 SNIP 1.163
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.19 SJR 1.168 SNIP 1.276
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.173 SNIP 1.316 CiteScore 3.99
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.192 SNIP 1.284 CiteScore 3.71
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.2 SNIP 1.385 CiteScore 3.74
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.417 SNIP 1.451 CiteScore 3.74
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.432 SNIP 1.507 CiteScore 3.91
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.466 SNIP 1.368
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.328 SNIP 1.332
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.35 SNIP 1.304
Scopus rating (2007): SJR 1.439 SNIP 1.483
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 1.308 SNIP 1.353
Scopus rating (2005): SJR 1.115 SNIP 1.438
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.169 SNIP 1.514
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.989 SNIP 1.337
Scopus rating (2002): SJR 0.859 SNIP 1.252
Web of Science (2002): Indexed yes
Scopus rating (2001): SJR 0.925 SNIP 1.148
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.817 SNIP 1.181
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.907 SNIP 1.089
Original language: English
SERS, Raman, Forensic detection, Chemical warfare agents, Explosives, Narcotics
DOIs:
10.1016/j.talanta.2018.07.009
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.

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: Andersen, T. E. (Ekstern), Andersen, A. J. (Intern), Petersen, R. S. (Intern), Nielsen, L. H. (Intern), Keller, S. S. (Intern)
Pages: 57-61
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): CiteScore 1.87 SJR 0.604 SNIP 0.937
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
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.

General information
State: Published
Organisations: Department of Photonics Engineering, Diode Lasers and LED Systems, Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, King Abdullah University of Science and Technology, Sun Yat-Sen University
Authors: Ou, Y. (Intern), Iida, D. (Ekstern), Liu, J. (Ekstern), Wu, K. (Intern), Ohkawa, K. (Ekstern), Boisen, A. (Intern), Petersen, P. M. (Intern), Ou, H. (Intern)
Pages: 317-322
Publication date: 2018
Main Research Area: Technical/natural sciences
Gold Nanoparticles Sliding on Recyclable Nanohoodoos as SERS Substrates – Bridging the Gap between Low Cost and Excellent Performance

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Self-Organized Nanoporous Materials
Authors: Wu, K. (Intern), Li, T. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Ndoni, S. (Intern), Boisen, A. (Intern)
Publication date: 2018
Event: Abstract from Fifth International Conference on Frontiers of Plasmonics, Nanjing, China.
Main Research Area: Technical/natural sciences
Electronic versions:
DOI: 10.1515/nanoph-2017-0057
Source: FindIt
Source-ID: 2392914335
Publication: Research - peer-review › Journal article – Annual report year: 2018

Gold Nanoparticles Sliding on Recyclable Nanohoodoos-Engineered for Surface-Enhanced Raman Spectroscopy
Robust, macroscopically uniform, and highly sensitive substrates for surface-enhanced Raman spectroscopy (SERS) are fabricated using wafer-scale block copolymer lithography. The substrate consists of gold nanoparticles that can slide and aggregate on dense and recyclable alumina/silicon nanohoodoos. Hot-spot engineering is conducted to maximize the SERS performance of the substrate. The substrate demonstrates remarkably large surface-averaged SERS 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 nanohoodoos 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 nanohoodoo 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, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Center for Nanostructured Graphene, Self-Organized Nanoporous Materials, University College London
Authors: Wu, K. (Intern), Li, T. (Ekstern), 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
Hacking CD/DVD/Blu-ray for Biosensing

The optical pickup unit (OPU) within a CD/DVD/Blu-ray drive integrates 780, 650, and 405 nm wavelength lasers, diffraction-limited optics, a high-bandwidth optoelectronic transducer up to 400 MHz, and a nano-resolution x-, z-axis and tilt actuator in a compact size. In addition, the OPU is a remarkable piece of engineering and could enable different scientific applications such as sub-angstrom displacement sensing, micro and nanoimaging, and nanolithography. Although off-the-shelf OPUs can be easily obtained, manufacturers protect their datasheets under non-disclosure agreements to impede their availability to the public. Thus, OPUs are black boxes that few people can use for research, and only experienced researchers can access all their functions. This review details the OPU mechanism and components. In addition, we explain how to utilize three commercially available triple-wavelength OPUs from scratch and optimize sensing quality. Then, we discuss scientific research using OPUs, from standard optical drive-based turnkey-biomarker array reading and OPU direct bio-applications (cytometry, optical tweezing, bioimaging) to modified OPU-based biosensing (DNA chip fluorescence scanning, biomolecular diagnostics). We conclude by presenting future trends on optical storage devices and potential applications. Repurposing low-cost and high-performance OPUs may spread micro and nanoscale biosensing research from research labs to citizen scientists around the globe. 

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Hwu, E. E. (Intern), Boisen, A. (Intern)
Number of pages: 11
Pages: 1222-1232
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: ACS Sensors
Volume: 3
InGaN/GaN ultraviolet LED with a graphene/AZO transparent current spreading layer

We report an approach of using an interlayer of single layer graphene (SLG) for electroluminescence (EL) enhancement of an InGaN/GaN-based near-ultraviolet (NUV) light-emitting diode (LED) with an aluminum-doped zinc oxide (AZO)-based current spreading layer (CSL). AZO-based CSLs with and without a SLG interlayer were fabricated on the NUV LED epitaxial wafers. The current-voltage (I-V) characteristic and the EL intensity were measured and compared. We find that the LED without the SLG interlayer can possess a 40% larger series resistance. Furthermore, a 95% EL enhancement was achieved by the employment of the SLG interlayer.
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.

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, Politecnico di Torino
Number of pages: 9
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Lab on a Chip
ISSN (Print): 1473-0197
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 6.05 SJR 2.158 SNIP 1.586
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
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
Optoelectric scaffold for photo-responsive biological components.
According to one aspect, an optoelectric scaffold for accommodating photo-responsive biological components is provided. The scaffold comprises an optical waveguide configured for confining light propagating in a longitudinal direction thereof. The optical waveguide comprises at least one leaky section with enhanced emission of light in a direction transverse or lateral to the longitudinal direction. The scaffold further comprises an electrically conductive layer arranged on an outer surface of the optical waveguide, wherein the electrically conductive layer has an immobilisation or growth support surface for the immobilisation or cultivation of photo-responsive biological components thereon. The electrically conductive layer comprises transparent regions at least partially overlapping the leaky section. The transparent region is configured so as to transmit light from the leaky section of the waveguide to the immobilisation and/or growth support surface. According to a further aspect, an optoelectric device comprises an optoelectric scaffold and a photo-responsive biological component arranged on the immobilisation/growth support surface. The growth support surface is arranged so as to transmit light received from the leaky section of the optical waveguide to the biological component placed thereon.

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Bioanalytics, Department of Photonics Engineering, Programmable Phase Optics, Optofluidics
Authors: Emnéus, J. (Intern), Bunea, A. (Intern), Keller, S. S. (Intern), Kristensen, A. (Intern), Heiskanen, A. (Intern)
Publication date: 2018

Publication information
IPC: C12Q1/00; G01N33/50; G01N33/543
Patent number: WO2018002237
Date: 04/01/2018
Priority date: 29/06/2016
Priority number: EP20160176841
Original language: English
Electronic versions:
WO2018002237A1.pdf
Main Research Area: Technical/natural sciences
Publication: Research › Patent – Annual report year: 2018

Real-time electrochemical detection of paracetamol interaction with intestinal tissue
General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Malmö University
Authors: Thoppe Rajendran, S. (Intern), Ruzgas, T. (Ekstern), Boisen, A. (Intern), Zor, K. (Intern)
Publication date: 2018
Event: Abstract from Biosensors 2018, Miami, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
BIOS2018_0146_Tissue.pdf
Source: PublicationPreSubmission
Source-ID: 150347839
Publication: Research › peer-review › Conference abstract for conference – Annual report year: 2018

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 \(10^4\), which is suitable for their application as nanomechanical sensors.

**General information**

State: Published

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

Authors: Quang, L. N. (Intern), Larsen, P. E. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)

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Publication date: 2018

Main Research Area: Technical/natural sciences

**Publication information**

Journal: Carbon
Volume: 133

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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes

BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 6.76 SJR 2.226 SNIP 1.666
Web of Science (2017): Indexed yes

BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 6.49 SJR 2.091 SNIP 1.648
Web of Science (2016): Indexed yes

BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.988 SNIP 1.71 CiteScore 6.53
Web of Science (2015): Indexed yes

BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.132 SNIP 1.976 CiteScore 6.62
Web of Science (2014): Indexed yes

BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.289 SNIP 2.114 CiteScore 6.54
ISI indexed (2013): ISI indexed yes

BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.518 SNIP 2.102 CiteScore 5.95
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes

BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.193 SNIP 2.048 CiteScore 5.23
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes

BFI (2010): BFI-level 1
Scopus rating (2010): SJR 2.392 SNIP 2.034
Web of Science (2010): Indexed yes

BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.121 SNIP 2.103
Web of Science (2009): Indexed yes

BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.126 SNIP 1.938
Scopus rating (2007): SJR 1.835 SNIP 1.798
Web of Science (2007): Indexed yes

Scopus rating (2006): SJR 1.791 SNIP 1.877
Web of Science (2006): Indexed yes

Scopus rating (2005): SJR 1.444 SNIP 1.7
Scopus rating (2004): SJR 1.523 SNIP 1.879
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.
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 ± 0.57 °C per mass% of water absorbed. The initial dry T_g of PLGA was extrapolated to 41.24 ± 0.07 °C.

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 ± 0.57 °C per mass% of water absorbed. The initial dry T_g of PLGA was extrapolated to 41.24 ± 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)
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Web of Science (2018): Indexed yes
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Microcantilever sensor, Thermal analysis, Temperature modulation, Glass transition, Polymer

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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 ± 0.57 °C per mass% of water absorbed. The initial dry T_g of PLGA was extrapolated to 41.24 ± 0.07 °C.
Wireless, smartphone controlled electrochemical lab-on-a-disc platform for drug dissolution studies from μcontainers

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Eindhoven University of Technology, University of Naples Federico II, National Taiwan University, Politecnico di Milano
Authors: Thoppe Rajendran, S. (Intern), Bergkamp, M. H. (Ekstern), Scarano, E. (Ekstern), Cheng, C. (Ekstern), Wang, J. (Ekstern), Capria, A. M. (Ekstern), Ferrari, G. (Ekstern), Zor, K. (Intern), Hwu, E. T. (Intern), Huang, K. (Ekstern), Boisen, A. (Intern)
Publication date: 2018
Event: Abstract from Biosensors 2018, Miami, United States.
Main Research Area: Technical/natural sciences
Electronic versions:
BIOS2018_PLoD.pdf
Mucin dispersions as a model for the oromucosal mucus layer in in vitro and ex vivo buccal permeability studies of small molecules

The mucus layer is believed to play a part in drug permeation across the oral mucosa. Human freeze-dried saliva (HFDS) and porcine gastric mucin (PGM) was evaluated as model for mucus layer per se or in conjunction with in vitro and ex vivo buccal permeability models. Four small molecules (nicotine, mannitol, propranolol, caffeine) showed decreased permeability across mucin dispersions, compared to controls, and a greater effect was seen with HFDS than with PGM. Permeability of propranolol and caffeine across filter-grown TR146 cells was decreased by the presence of mucin, whereas no effect was found on nicotine and mannitol. Incubation of porcine buccal mucosa with mucin dispersions for 24 h compromised the integrity of the tissue, whereas 30 min incubation did not affect tissue integrity. Tissue incubation with mucin dispersions did not decrease nicotine permeability. For the studied model drugs, it is concluded that mucin dispersions constitute a minor barrier for drug diffusion compared to the epithelium.
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.

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Durucan, O. (Intern), Schmidt, M. S. (Ekstern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
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Publication information
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Original language: English
Electronic versions:
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Main Research Area: Technical/natural sciences
Source: espacenet
Source-ID: WO2017191080
Publication: Research › Patent – Annual report year: 2017

Micro-fabrication of three dimensional pyrolysed carbon microelectrodes

The present invention relates in one aspect to a method of producing a three-dimensional microscale patterned resist template for a pyrolysed carbon microelectrode structure by means of UV-lithography. Coating a planar substrate with an epoxy-based negative photoresist, such as an SU-8 photoresist; soft baking the photoresist layer; performing a full depth exposure with UV light through a first mask; performing a partial depth exposure with UV light through a second mask; wherein the full depth exposure and the partial depth exposure are aligned to ensure that the first and second latent images are connected to each other; post-exposure baking the photoresist layer; and developing the microscale patterned resist template as a free-standing structure of cross-linked resist with lateral hanging structures that are supported by vertical support structures at a free height above the substrate. The method is characterized by a soft baking temperature below 70 °C. Repetitive coating and partial depth exposure allows for the fabrication of multiple level laterally
interconnected structures. Carbonization of the resist template provides truly three-dimensional carbon microelectrode structures.

**General information**
- **State:** Published
- **Organisations:** Department of Micro- and Nanotechnology, Biomaterial Microsystems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
- **Authors:** Hemanth, S. (Intern), Keller, S. S. (Intern), Caviglia, C. (Intern), Amato, L. (Intern)
- **Publication date:** 30 Mar 2017

**Publication information**
- **Country:** International Bureau of the World Intellectual Property Organization (WIPO)
- **IPC:** G03F 7/38 A1
- **Patent number:** WO2017050808
- **Date:** 30/03/2017
- **Priority date:** 21/09/2015
- **Priority number:** EP20150186066
- **Original language:** English
- **Electronic versions:** WO2017050808A1.pdf
- **Main Research Area:** Technical/natural sciences
- **Source:** espacenet
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- **Publication:** Research › Patent – Annual report year: 2017

A nanofiltration technique for analyte extraction from complex matrix and surface enhanced Raman spectroscopy based sensing

**General information**
- **State:** Published
- **Organisations:** Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
- **Authors:** Durucan, O. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Ilichenko, O. (Intern), Boisen, A. (Intern)
- **Number of pages:** 1
- **Publication date:** 2017
- **Event:** Abstract from 43rd International conference on Micro and Nano Engineering, Braga, Portugal.
- **Main Research Area:** Technical/natural sciences
- **Electronic versions:** Onur_Durucan_MNE_Abstract.pdf

**Relations**
- **Activities:**
  - A nanofiltration technique for analyte extraction from complex matrix and surface enhanced Raman spectroscopy based sensing
  - A pseudo-Voigt component model for high-resolution recovery of constituent spectra in Raman spectroscopy

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
- **Organisations:** Department of Applied Mathematics and Computer Science, Cognitive Systems, Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
- **Authors:** Alstrøm, T. S. (Intern), Schmidt, M. N. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Larsen, J. (Intern)
- **Pages:** 2317-21
- **Publication date:** 2017
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.
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
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Integration, SERS, Microfluidics
Electronic versions:
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.

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State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
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Main Research Area: Technical/natural sciences

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Scopus rating (2017): CiteScore 1.67 SJR 0.443 SNIP 0.608
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 2.02 SJR 0.504 SNIP 0.768
Scopus rating (2015): SJR 0.513 SNIP 0.712 CiteScore 1.76
Scopus rating (2014): SJR 0.599 SNIP 0.737 CiteScore 1.85
Scopus rating (2013): SJR 0.677 SNIP 0.861 CiteScore 2.17
Scopus rating (2012): SJR 0.804 SNIP 0.937 CiteScore 2.43
Scopus rating (2011): SJR 0.599 SNIP 0.743 CiteScore 1.94
Scopus rating (2010): SJR 0.673 SNIP 1.163
Scopus rating (2009): SJR 0.808 SNIP 0.88
Scopus rating (2008): SJR 1.055 SNIP 1.015
Scopus rating (2007): SJR 0.959 SNIP 1.154
Scopus rating (2006): SJR 0.498 SNIP 0.52
Scopus rating (2005): SJR 0.377
Original language: English
Biological engineering, Chemical engineering, Evolution, siRNA delivery
DOIs:
10.2174/1567201813666160602230550
Source: FindIt
Source-ID: 2350805722
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 best-performing ones. Standard analytical methods usually include high performance liquid chromatography (HPLC), thin layer chromatography (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)
Number of pages: 3
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Publication date: 2017
Conference: Biosensors 2016, Gothenburg, Sweden, 25/05/2016 - 25/05/2016
Main Research Area: Technical/natural sciences

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 –SCH₃ group. Experimental and numerical analysis of vibrational modes showed only minor differences between standard PCB77 and PCB77-SCH₃. Consequently, we observe significantly increased SERS signals for –SCH₃ 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-SCH₃ 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-SCH₃ spectral fingerprint is retained in ~10⁻⁸ M range.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Hansa Fine Chemicals GmbH, Universidad Industrial de Santander
Authors: Rindzevicius, T. (Intern), Barten, J. (Ekstern), Vorobiev, M. (Ekstern), Schmidt, M. S. (Intern), Castillo, J. J. (Ekstern), Boisen, A. (Intern)
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, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technische Universität Wien
Authors: Sadeghi, P. (Ekstern), Wu, K. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern), Schmid, S. (Ekstern)
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Web of Science (2016): Indexed yes
Scopus rating (2015): SNIP 1.963 SJR 3.411
Web of Science (2015): Indexed yes
Scopus rating (2014): SNIP 2.714 SJR 3.475
Scopus rating (2013): SNIP 2.247 SJR 3.023
ISI indexed (2013): ISI indexed no
Web of Science (2013): Indexed yes
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Electronic versions:
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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
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
Pyrolytic carbon, MEMS resonator, Mass sensor

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
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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
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BFI (2017): BFI-level 2
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 7.56 SJR 2.463 SNIP 1.85
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.738 SNIP 2.074 CiteScore 8.11
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
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.
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.

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)  
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**Publication date:** 2017  
**Main Research Area:** Technical/natural sciences

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BFI (2017): BFI-level 1  
Scopus rating (2017): CiteScore 5.67 SJR 1.406 SNIP 1.453  
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
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 (ΔE_p ~90mV) and higher peak currents (I_p/A ~1), comparing to planar electrodes (ΔE_p ~580mV). 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.
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 photosist SU-8 and biopolymer poly-ε-caprolactone (PCL). Furosemide (F) drug is embedded in poly-ε-caprolactone (PCL) 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.

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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)
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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
Scopus rating (2008): SJR 0.952 SNIP 0.942
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.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Copenhagen, Monash University
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Microcontainers as an oral delivery system for spray-dried cubosomes containing ovalbumin.pdf. Embargo ended: 18/12/2017

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MICROCONTAINERS FOR INTESTINAL DRUG DELIVERY: in vivo and ex vivo study

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Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, Københavns Universitet, University of Copenhagen
Authors: Mazzoni, C. (Intern), Tentor, F. (Intern), Andersen, S. S. S. (Forskerdatabase), Nielsen, L. H. (Intern), Keller, S. S. (Intern), Müllertz, A. (Ekstern), Marizza, P. (Intern), Boisen, A. (Intern)
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Modelling the thermal properties of large diameter fibre ropes

General information
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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Southern Denmark
Authors: Oland, E. (Ekstern), Bossolini, E. (Intern), Nielsen, O. W. (Ekstern), Sørensen, M. P. (Intern), Veje, C. (Ekstern)
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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.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Silicon Microtechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark, University of Copenhagen, Technische Universität Wien
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Scopus rating (2016): CiteScore 10.8 SJR 5.954 SNIP 2.146
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 5.888 SNIP 2.225 CiteScore 11.13
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
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
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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
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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
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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.

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 fulfill 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 $4\times 10^{-13}$ 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.
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
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.
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%.

General information
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Organisations: Department of Micro- and Nanotechnology, BioLabChip, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Magnetic Systems
Authors: Ashley, J. (Intern), Wu, K. (Intern), Hansen, M. F. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Sun, Y. (Intern)
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Scopus rating (2017): CiteScore 6.24
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
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
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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.
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.

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Authors: Thilsted, A. H. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
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Blu-ray based optomagnetic aptasensor for detection of small molecules
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
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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
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.22 SJR 2.095 SNIP 1.619
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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
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Carbon nanopillars for enhanced stem cell differentiation and dopamine detection

Parkinson’s disease is characterized by a deficit of dopamine in the brain, a neurotransmitter involved in the motor function. One of the future ideas for treatment is cell replacement therapy. Our group has previously shown that pyrolysed 3D carbon micropillars induce spontaneous differentiation of human neural stem cells (hNSCs) into dopaminergic neurons and that they can also be employed for detecting dopamine release from mature neurons attached to them [1]. Here, we report 3D carbon nanopillars, fabricated through colloidal lithography, with even more pronounced effect on the electrochemical detection of dopamine

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Organisations: Department of Photonics Engineering, Programmable Phase Optics, Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Polymer Microsystems for Cell Processing, Bioanalytics, European Commission - Joint Research Center
Authors: Bunea, A. (Intern), Amato, L. (Intern), Valsesia, A. (Ekstern), Pellacani, P. (Ekstern), Casci Ceccacci, A. (Intern), Keller, S. S. (Intern), Larsen, N. B. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern)
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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.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Columbia University
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Number of pages: 3
Publication date: 2016

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**

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Authors: Burger, R. (Intern), Amato, L. (Intern), Boisen, A. (Intern)
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ISI indexed (2013): ISI indexed yes
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BFI (2009): BFI-level 1
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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
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
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Chalmers University of Technology, Swedish Defence Research Agency
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 7.46 SJR 2.789 SNIP 1.441
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
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Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
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Web of Science (2014): Indexed yes
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Scopus rating (2013): SJR 2.558 SNIP 1.467 CiteScore 6.89
ISI indexed (2013): ISI indexed yes
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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 μ/L) 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 μ/L), 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.
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.

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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)
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Web of Science (2017): Indexed yes
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BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.057 SNIP 1.716 CiteScore 6.57
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Scopus rating (2013): SJR 2.029 SNIP 1.726 CiteScore 6.34
ISI indexed (2013): ISI indexed yes
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BFI (2012): BFI-level 1
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Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
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ISI indexed (2011): ISI indexed yes
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BFI (2010): BFI-level 2
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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
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.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Thilsted, A. H. (Intern), Pan, J. Y. (Intern), Wu, K. (Intern), Zor, K. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern)
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Web of Science (2017): Indexed Yes
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
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.
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
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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)
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Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.647 SNIP 1.643 CiteScore 2.21
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.707 SNIP 1.796 CiteScore 2.4
Web of Science (2014): Indexed yes
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Scopus rating (2013): SJR 0.636 SNIP 1.758 CiteScore 2.72
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.671 SNIP 1.709 CiteScore 2.53
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Web of Science (2012): Indexed yes
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Scopus rating (2011): SJR 0.641 SNIP 1.439 CiteScore 2.44
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.579 SNIP 1.244
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Nonlinear optomechanical measurement of mechanical motion

Precision measurement of nonlinear observables is an important goal in all facets of quantum optics. This allows measurement-based non-classical state preparation, which has been applied to great success in various physical systems, and provides a route for quantum information processing with otherwise linear interactions. In cavity optomechanics much progress has been made using linear interactions and measurement, but observation of nonlinear mechanical degrees-of-freedom remains outstanding. Here we report the observation of displacement-squared thermal motion of a micro-mechanical resonator by exploiting the intrinsic nonlinearity of the radiation-pressure interaction. Using this measurement we generate bimodal mechanical states of motion with separations and feature sizes well below 100 pm. Future improvements to this approach will allow the preparation of quantum superposition states, which can be used to experimentally explore collapse models of the wavefunction and the potential for mechanical-resonator-based quantum information and metrology applications.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark, University of Queensland
Authors: Brawley, G. (Ekstern), Vanner, M. R. (Ekstern), Larsen, P. E. (Intern), Schmid, S. (Intern), Boisen, A. (Intern), Bowen, W. (Ekstern)
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 11.8 SJR 6.414 SNIP 2.855
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 6.287 SNIP 2.86 CiteScore 11.23
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.

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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)
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BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.597 SJR 0.357 CiteScore 1.46
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.21 SJR 0.363 SNIP 0.57
BFI (2015): BFI-level 1
Polymeric microcontainers improve oral bioavailability of furosemide

Microcontainers with an inner diameter of 223μm 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.
Supercritical impregnation of polymer matrices spatially confined in microcontainers for oral drug delivery: Effect of temperature, pressure and time

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.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Biomaterial Microsystems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Trieste, University of Cambridge
Authors: Marizza, P. (Intern); Pontoni, L. (Ekstern); Rindzevicius, T. (Intern); Alopaeus, J. (Ekstern); Su, K. (Ekstern); Zeitler, J. (Ekstern); Keller, S. S. (Intern); Kikic, I. (Ekstern); Moneghini, M. (Ekstern); De Zordi, N. (Ekstern); Solinas, D. (Ekstern); Cortesi, A. (Ekstern); Boisen, A. (Intern)
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.01 SJR 0.982 SNIP 1.278
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.904 SNIP 1.195 CiteScore 2.71
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.128 SNIP 1.461 CiteScore 2.89
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.099 SNIP 1.5 CiteScore 3.18
ISI indexed (2013): ISI indexed yes
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 mis-interpretation of intensity histograms, where contamination might contribute with an enhanced background and not a peak.

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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)
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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  
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Main Research Area: Technical/natural sciences

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BFI (2016): BFI-level 1  
Scopus rating (2016): CiteScore 1.47 SJR 0.401 SNIP 0.545  
Web of Science (2016): Indexed yes  
BFI (2015): BFI-level 1  
Scopus rating (2015): SJR 0.427 SNIP 0.718 CiteScore 1.63  
BFI (2014): BFI-level 1  
Scopus rating (2014): SJR 0.79 SNIP 1.113 CiteScore 2.78  
BFI (2013): BFI-level 1  
Scopus rating (2013): SJR 0.827 SNIP 1.167 CiteScore 2.41  
ISI indexed (2013): ISI indexed yes  
BFI (2012): BFI-level 1  
Scopus rating (2012): SJR 0.695 SNIP 1.038 CiteScore 1.62  
ISI indexed (2012): ISI indexed yes  
Web of Science (2012): Indexed yes  
BFI (2011): BFI-level 1  
Scopus rating (2011): SJR 0.374 SNIP 0.854 CiteScore 1.03  
ISI indexed (2011): ISI indexed no  
BFI (2010): BFI-level 1  
Scopus rating (2010): SJR 0.261 SNIP 0.469  
BFI (2009): BFI-level 1  
Scopus rating (2009): SJR 0.289 SNIP 0.419  
BFI (2008): BFI-level 1  
Scopus rating (2008): SJR 0.22 SNIP 0.497  
Scopus rating (2007): SJR 0.197 SNIP 0.403  
Scopus rating (2006): SJR 0.216 SNIP 0.347  
Scopus rating (2005): SJR 0.265 SNIP 0.465  
Scopus rating (2004): SJR 0.228 SNIP 0.42  
Scopus rating (2003): SJR 0.24 SNIP 0.33  
Scopus rating (2002): SJR 0.184 SNIP 0.28
Thermal properties of Fiber ropes

There is a trend within the oil and gas market to shift from steel wire ropes to fiber ropes for lifting, hoisting and mooring applications. The cost of fiber ropes is about 2-3 times that of steel wire ropes, but the natural buoyancy of fiber ropes reduces the overall weight resulting in smaller cranes and thereby reduces the overall costs. For heave compensation, a rope is typically of 3-4000 meters long, such that one rope costs in the order of 7.5 million dollars. The current practice on when to discard a fiber rope is through visual inspections done manually with large safety factors. This means that the rope is discarded before it is necessary, increasing the overall life-cycle costs. The offshore industry wants a better monitoring system to understand when the fiber rope must be replaced.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Technical University of Denmark, University of Southern Denmark
Authors: Bossolini, E. (Intern), Nielsen, O. W. (Ekstern), Oland, E. (Ekstern), Sørensen, M. P. (Intern), Veje, C. (Ekstern)
Number of pages: 4
Publication date: 2016
Main Research Area: Technical/natural sciences
Electronic versions:
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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 on 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
Triple co-culture cell model as an in vitro model for oral particulate vaccine systems

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 $10^8$, SERS uniformities of 8.5% relative standard deviation across 4 cm, and 6.5% relative standard deviation over $5 \times 5$ 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.

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 $10^8$, SERS uniformities of 8.5% relative standard deviation across 4 cm, and 6.5% relative standard deviation over $5 \times 5$ 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.
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.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Universidad Santo Tomas, Universidad Industrial de Santander
Authors: Castillo, J. J. (Ekstern), Rindzevicius, T. (Intern), Rozo, C. E. (Ekstern), Boisen, A. (Intern)
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.

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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Bioanalytics, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Amato, L. (Intern), Kuldeep, K. (Intern), Esmail Tehrani, S. (Intern), Burger, R. (Intern), Caviglia, C. (Intern), Andreasen, S. Z. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
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Centrifugal Microfluidic Platform Using Supported Liquid Membrane Extraction for Combined Sample Clean-Up and Enrichment of Trace Analytes

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

Fabrication and loading of oral drug delivery microcontainers using hot punching

In this paper, poly-l-lactic acid (PLLA) solution is spin coated to achieve a PLLA layer of 55 μm thickness. Hot punching with a Ni stamp is optimized to fabricate microcontainers in PLLA. Process optimization of thermal bonding of the microcontainers to a poly acrylic acid (PAA) layer is performed by modifying sample preparation and varying temperature. The fabricated microcontainers are loaded by hot punching in a spin coated drug polymer film of furosemide and poly-e-caprolactone (PCL).
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.
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.
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BFI (2018): BFI-level 2
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BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 1.87 SJR 0.604 SNIP 0.937
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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
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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
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Hot punching of high-aspect-ratio 3D polymeric microstructures for drug delivery

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

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Authors: Adesokan, B. J. (Intern), Quan, X. (Intern), Evgrafov, A. (Intern), Heiskanen, A. (Intern), Boisen, A. (Intern)
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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
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).

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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
Integration of agglutination assay for protein detection in microfluidic disc using Blu-ray optical pickup unit and optical fluid scanning

We present a novel strategy for thrombin detection by combining a magnetic bead based agglutination assay and low-cost microfluidic disc. The detection method is based on an optomagnetic readout system implemented using a Blu-ray optical pickup unit (OPU) as 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.

General information
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Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Magnetic Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Uddin, R. (Intern), Burger, R. (Intern), Donolato, M. (Intern), Fock, J. (Intern), Creagh, M. (Intern), Hansen, M. F. (Intern), Boisen, A. (Intern)
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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.
Mathematical model for biomolecular quantification using surface-enhanced Raman spectroscopy based signal intensity distributions

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.

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.
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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.44 SJR 1.041 CiteScore 3.59
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.57 SJR 1.056 SNIP 1.577
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.209 SNIP 1.62 CiteScore 3.48
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.282 SNIP 1.89 CiteScore 3.37
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.336 SNIP 2.102 CiteScore 3.35
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.411 SNIP 2.086 CiteScore 3.25
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.346 SNIP 2.075 CiteScore 3.17
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.245 SNIP 1.637
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 1.345 SNIP 1.612
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.284 SNIP 1.723
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.452 SNIP 1.555
Scopus rating (2006): SJR 1.38 SNIP 1.811
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 1.226 SNIP 1.467
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.064 SNIP 1.421
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.934 SNIP 1.262
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.789 SNIP 1.05
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Scopus rating (2000): SJR 0.654 SNIP 1.069
Scopus rating (1999): SJR 0.737 SNIP 1.176
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Microcontainers as an oral drug delivery system

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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)
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Publication: Research - peer-review › Conference abstract in proceedings – 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

Publication information
Journal: Journal of Polymer Science. Part B, Polymer Physics
Volume: 53
Issue number: 15
ISSN (Print): 0887-6266
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 2.52 SJR 0.837 SNIP 0.88
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.12 SJR 1.067 SNIP 0.97
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
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.
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.
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.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Photonics Engineering, Structured Electromagnetic Materials, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Wu, K. (Intern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Mogensen, K. B. (Intern), Xiao, S. (Intern), Boisen, A. (Intern)
Pages: 12965-12978
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Optics Express
Volume: 23
Issue number: 10
ISSN (Print): 1094-4087

Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 3.74 SJR 1.519 SNIP 1.567
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
Silver-capped silicon nanopillar platforms for adsorption studies of folic acid using surface enhanced Raman spectroscopy and density functional theory

The study of the interactions of folic acid (FA) with surface enhanced Raman scattering substrates is relevant for understanding its adsorption mechanism for fabricating analytical devices for detection of malignant cells over-expressing folate receptors. This paper presents a study of the adsorption of FA on silver-capped silicon nanopillar substrates employing surface enhanced Raman scattering spectroscopy and density functional theory calculations. The experimentally observed vibrations from free FA and FA bound to the Ag surface display different vibrational spectra indicating chemical interaction of the molecule with the metal surface. Density functional theory calculations show that the Ag–FA interaction is primarily through the nitrogen from the pteridine ring anchoring to the Ag metal surface. To investigate the Ag–FA binding behavior further, the adsorption isotherm of FA on the silver-capped silicon nanopillar surface is estimated. The results show a positive cooperative Ag–FA binding mechanism. That is, adsorbed FA increases the affinity of new incoming FA molecules.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Universidad Santo Tomas
Authors: Castillo, J. (Intern), Rindzevicius, T. (Intern), Wu, K. (Intern), Rozo, C. E. (Ekstern), Schmidt, M. S. (Intern), Boisen, A. (Intern)
Pages: 1087-1094
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information

Journal: Journal of Raman Spectroscopy
Volume: 46
Issue number: 11
ISSN (Print): 0377-0486
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.05 SJR 0.888 CiteScore 2.58
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.71 SJR 0.926 SNIP 1.115
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.02 SNIP 0.891 CiteScore 2.25
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.15 SNIP 1.071 CiteScore 2.53
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.029 SNIP 1.073 CiteScore 2.49
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Simulating cyclic voltammetry under advection for electrochemical cantilevers

We present a mathematical model describing an electrochemical system involving electrode–electrolyte interaction. The model is governed by a system of advection–diffusion equations with a nonlinear reaction term at the boundary. Our calculations based on such model demonstrate the dynamics of ionic currents in the electrolyte. The model allows us to predict the effect of varying flow rates, scan rates, and electrolyte concentration of the electrochemical system.

General information
State: Published
Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Adesokan, B. J. (Intern), Evgrafov, A. (Intern), Sørensen, M. P. (Intern)
Pages: 3384-3391
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Mathematical Methods in the Applied Sciences
Volume: 38
Issue number: 16
ISSN (Print): 0170-4214
Ratings: 
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.778 SJR 0.666 CiteScore 1.08

Original language: English
SERS, Nanopillar, Silver, Folic acid, Adsorption isotherm

DOIs: 10.1002/jrs.4734
Source: PublicationPreSubmission
Source-ID: 112799151
Publication: Research - peer-review › Journal article – 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 stimulated intestinal medium at pH 6.5, the ASSF in the glass solution showed signs of crystallinity after 1 min of dissolution, but crystalised 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
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.
Towards quantitative SERS detection of hydrogen cyanide at ppb level for human breath analysis

Lung infections with *Pseudomonas aeruginosaa* (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 N$_2$. 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 $\mu$M 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 $\sim 13.5$ ppb, the detection of cyanide is within the required range.

**General information**

State: Published

Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factories, Department of Chemistry, Department of Applied Mathematics and Computer Science, Cognitive Systems, Amphiphilic Polymers in Biological Sensing, Department of Environmental Engineering, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

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 $10^8$, and the SERS signal intensity exhibits a standard deviation of around 14% (660 data points) across a $5 \times 5$ mm$^2$ surface area.
Center for Electron Nanoscopy
DTU Danchip
Department of Environmental Engineering
Urban Water Engineering
Department of Micro- and Nanotechnology
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Nanoprobes
Amphiphilic Polymers in Biological Sensing
National Food Institute
Research Group for Bioactives – Analysis and Application
Research Group for Nano-Bio Science
Period: 16/11/2015 → 20/11/2015
Number of participants: 6
Project participant:
Schneider, Carina (Intern)
von Halling Laier, Christoffer (Intern)
Ullah, Saif (Intern)
Andersen, Alina Joukainen (Intern)
García Moreno, Pedro Jesús (Intern)
Main Supervisor:
Mateiu, Ramona Valentina (Intern)
Project

Activities:

**Pyrolytic carbon for MEMS string resonantors**
Period: 11 Jun 2018
Quang Long Nguyen (Speaker)
Peter Emil Larsen (Other)
Anja Boisen (Other)
Stephan Sylvest Keller (Invited speaker)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Nanoprobes
Biomaterial Microsystems

**Description**
C-MEMS 2018 oral presentation
Degree of recognition: International
Documents:
Abstract_CMEMS_2018

**Related event**
International Conference on Expanding Frontiers of Carbon MEMS
10/06/2018 → 12/06/2018
San Diego, United States
Activity: Talks and presentations › Conference presentations

**3D printed system for testing intestinal drug transport**
Period: 21 Mar 2018
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
Nanoprobes
Department of Micro- and Nanotechnology
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
**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  
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

**Polarization noise study in all-normal dispersion fiber supercontinuum generation**

Period: 29 Jan 2018  
Ivan Bravo Gonzalo (Speaker)  
Rasmus Dybbro Engelsholm (Other)  
Andreas Falkenstrøm Mieritz (Other)  
Mads Peter Sørensen (Other)  
Ole Bang (Other)  
Department of Photonics Engineering  
Fiber Sensors and Supercontinuum Generation  
Department of Applied Mathematics and Computer Science  
Dynamical Systems  
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

**Related event**

29/01/2018 → ...

**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

Nanoprobes

Documents:  
IMR26_fixed

**Related event**

**26th International Meshing Roundtable**
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
Nanoprobes
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 Ilchenko (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 Ilchenko (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
Department of Applied Mathematics and Computer Science
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 Ilchenko (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

Effects on cells on differentiation.
Period: 11 Nov 2016
Martin Dufva (Lecturer)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Fluidic Array Systems and Technology

Related event
DASCS Stem cell conference
Rungsted, Denmark
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

**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
Nanoprobes

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

**Polymer-derived carbon surfaces for enhancing stem cell differentiation**
Period: 31 May 2016
Ada-Ioana Bunea (Speaker)
Letizia Amato (Other)
Claudia Caviglia (Other)
Andrea Valsesia (Other)
Paola Pellacani (Other)
Andrea Casci Ceccacci (Other)
Stephan Sylvest Keller (Other)
Niels Bent Larsen (Other)
Arto Heiskanen (Other)
Jenny Emnéus (Other)

Department of Photonics Engineering
Programmable Phase Optics
Department of Micro- and Nanotechnology
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Polymer Microsystems for Cell Processing
Bioanalytics

Description
Oral presentation
Degree of recognition: International
Documents:
ECS_San_Diego_2016.pdf

Related event

The 229th ECS Meeting
29/05/2016 → 02/06/2016
San Diego, CA, United States
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

Polymer-derived carbon surfaces for enhancing stem cell differentiation
Period: 27 Nov 2015
Ada-Ioana Bunea (Speaker)
Letizia Amato (Other)
Andrea Valsesia (Other)
Paola Pellacani (Other)
Andrea Casci Ceccacci (Other)
Stephan Sylvest Keller (Other)
Niels Bent Larsen (Other)
Arto Heiskanen (Other)
Jenny Emnéus (Other)
Department of Photonics Engineering
Programmable Phase Optics
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Department of Micro- and Nanotechnology
Polymer Microsystems for Cell Processing
Bioanalytics

Description
Oral presentation for PhD Workshop on Bioanalysis and Enzymology
Degree of recognition: International
Documents:
Luckenwalde_2015.pdf

Related event

PhD Workshop on Bioanalysis and Enzymology
26/11/2015 → 27/11/2015
Luckenwalde, Germany
Activity: Talks and presentations › Conference presentations

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
Department of Micro- and Nanotechnology

Description
Conference abstract
Links:

Related event

41st International conference on Micro and Nano Engineering : MNE 2015
22nd Nordic Rheology Conference
Period: 12 Jun 2013
Kristian Ejlebjærg Jensen (Participant)

Theoretical Microsystems Optimization

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Documents:
Modeling and Optimization with Viscoelastic Differential Constitutive Models

Related event

22nd Nordic Rheology Conference
12/06/2013 → 14/06/2013
Copenhagen, Denmark

Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.