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)
Publication date: 9 Nov 2017

Publication information
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.

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

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

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

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

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

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)
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Publication date: 2017

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Main Research Area: Technical/natural sciences
Conference: 42nd IEEE International Conference on Acoustics, Speech and Signal Processing, New Orleans, United States, 05/03/2017 - 05/03/2017
Electronic versions: Untitled.pdf
DOIs: 10.1109/ICASSP.2017.7952570
Source: PublicationPreSubmission
Source-ID: 128987321
Publication: Research - peer-review › Article in proceedings – Annual report year: 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.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Academia Sinica Taiwan, Technische Universität Wien
Authors: Casci Ceccacci, A. (Intern), Chen, C. (Ekstern), Hwu, E. (Ekstern), Morelli, L. (Intern), Bose-Goswami, S. (Intern), Bosco, F. (Intern), Schmid, S. (Ekstern), Boisen, A. (Intern)
Number of pages: 7
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Main Research Area: Technical/natural sciences

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BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.07 SJR 1.333 SNIP 1.463
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.25 SNIP 1.509 CiteScore 4.84
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.229 SNIP 1.679 CiteScore 4.37
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.242 SNIP 1.622 CiteScore 4.25
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.405 SNIP 1.679 CiteScore 3.92
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.474 SNIP 1.744 CiteScore 4.08
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.409 SNIP 1.437
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.297 SNIP 1.509
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.436 SNIP 1.576
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.434 SNIP 1.592
Scopus rating (2006): SJR 1.336 SNIP 1.526
Scopus rating (2005): SJR 1.267 SNIP 1.849
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1.336 SNIP 1.504
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 1.159 SNIP 1.381
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 1.086 SNIP 1.07
Scopus rating (2001): SJR 0.835 SNIP 1.128
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 0.928 SNIP 1.2
Web of Science (2000): Indexed yes
Challenges in the integration of silicon SERS substrates into a polypropylene injection moulded microfluidic chip

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Serioli, L. (Intern), Morelli, L. (Intern), Matteucci, M. (Intern), Zor, K. (Intern), Boisen, A. (Intern)
Publication date: 2017
Main Research Area: Technical/natural sciences
Integration, SERS, Microfluidics

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 –SCH3 (PCB77-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)
Number of pages: 6
Pages: 1-6
Publication date: 2017
Main Research Area: Technical/natural sciences
Fabrication of completely free-standing pyrolytic carbon string resonator

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes
Authors: Nguyen, Q. L. (Intern), Larsen, P. E. (Intern), Boisen, A. (Intern), Keller, S. S. (Intern)
Number of pages: 1
Publication date: 2017
Main Research Area: Technical/natural sciences
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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
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Pyrolytic carbon, MEMS resonator, Mass sensor
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Hand-Held Femtogram Detection of Hazardous Picric Acid with 2 Hydrophobic Ag Nanopillar SERS Substrates and Mechanism of 3 Elasto-Capillarity

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

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

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

**General information**

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

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

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

We present a robust easy to use lab-on-a-disc (LoD) device with integrated sample pre-treatment and electrochemical detection system for cell-free detection of a secondary metabolite, p-Coumaric acid (pHCA), produced by genetically modified E. coli. In the LoD device, which incorporates eight filtration and electrochemical detection units, the sample filtration was performed by rotating the disc using a programmable closed-loop stepper motor. The electrodes, patterned on plastic substrate, were connected through a printed circuit board to the slip ring using a robust magnetic clamping system that enables easy assembly and robust electrical connections. pHCA was quantified in a linear range from 0.125 up to 2 mM using square wave voltammetry. The platform was successfully used for the quantification of pHCA produced by two genetically modified E. coli strains after 24 h of cell culture. The data obtained from the electrochemical measurements showed good correlation with high performance liquid chromatographic analysis. The developed LoD system offers fast and easy detection of pHCA, enabling screening of genetically modified organisms based on the quantity of produced secondary metabolites.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, Novo Nordisk Foundation Center for Biosustainability, Bacterial Cell Factory Optimization, Bioanalytics, Research Groups
Authors: Sanger, K. (Intern), Zor, K. (Intern), Jendresen, C. B. (Intern), Heiskanen, A. (Intern), Amato, L. (Intern), Nielsen, A. T. (Intern), Boisen, A. (Intern)
Pages: 999-1005
Publication date: 2017
Main Research Area: Technical/natural sciences

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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.07 SJR 1.333 SNIP 1.463
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.25 SNIP 1.509 CiteScore 4.84
Large-scale, Lithography-free Production of Transparent Nanostructured Surface for Dual-functional Electrochemical and SERS Sensing

In this work, we present a dual-functional sensor that can perform surface-enhanced Raman spectroscopy (SERS) based identification and electrochemical (EC) quantification of analytes in liquid samples. A lithography-free reactive ion etching process was utilized to obtain nanostructures of high aspect ratios distributed homogeneously on a 4-inch fused silica wafer. The sensor was made up of three-electrode array, obtained by subsequent e-beam evaporation of Au on nanostructures in selected areas through a shadow mask. The SERS performance was evaluated through surface-averaged enhancement factor (EF), which was \( \sim 6.2 \times 10^5 \), and spatial uniformity of EF, which was \( \sim 13\% \) 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 ($\Delta E_p \sim 90\text{mV}$) and higher peak currents ($I_{pa}/I_{pc} \sim 1$), comparing to planar electrodes ($\Delta E_p \sim 560\text{mV}$). The oxidation potential of PAR was also lowered by $\sim 80 \text{mV}$ on nanostructured electrodes. To illustrate dual-functional sensing, quantitative evaluation of PAR ranging from 30 $\mu\text{M}$ to 3 mM was realized through EC detection, and presence of PAR was verified by its SERS fingerprint.

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

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DOIs:
10.1021/acssensors.7b00783
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Loading of Drug-Polymer Matrices in Microreservoirs for Oral Drug Delivery

For major advances in microfabricated drug delivery systems (DDS), fabrication methods with high throughput using biocompatible polymers are required. Once these DDS are fabricated, loading of drug poses a significant challenge. Here, hot punching is presented as an innovative method for drug loading in microfabricated DDS. The microfabricated DDS are microcontainers fabricated in photoresist SU-8 and biopolymer poly-$\varepsilon$-lactic-acid (PLLA). Furosemide (F) drug is embedded in poly-$\varepsilon$-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.

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

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Volume: 302
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Web of Science (2018): Indexed yes
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Scopus rating (2016): CiteScore 3.01 SJR 0.894 SNIP 0.971
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.
Lipid self-assembly, Micro devices, Oral drug delivery, Oral vaccine delivery, Particulates, Spray drying
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.

General information
State: Published
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
Authors: Kurek, M. (Intern), Carnoy, M. (Ekstern), Larsen, P. E. (Intern), Nielsen, L. H. (Intern), Hansen, O. (Intern), Rades, T. (Ekstern), Schmid, S. (Ekstern), Boisen, A. (Intern)
Numerical Optimization in Microfluidics

Numerical modelling can illuminate the working mechanism and limitations of microfluidic devices. Such insights are useful in their own right, but one can take advantage of numerical modelling in a systematic way using numerical optimization. In this chapter we will discuss when and how numerical optimization is best used.

General information

State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes
Authors: Jensen, K. E. (Intern)
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Chapter: 5
Main Research Area: Technical/natural sciences
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Activities:
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Source: Findit
Source-ID: 2372109739
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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.

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, University of Melbourne
Authors: Larsen, T. (Intern), Schmid, S. (Intern), Dohn, S. (Intern), Sader, J. E. (Ekstern), Boisen, A. (Intern), Villanueva, L. (Ekstern)
Number of pages: 5
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
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Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.606 SNIP 0.999
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.533 SNIP 0.856 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.592 SNIP 0.897 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.602 SNIP 1.001 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.745 SNIP 0.983 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.818 SNIP 1.169 CiteScore 1.8
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.946 SNIP 1.119
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.847 SNIP 1.127
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.05 SNIP 1.077
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.065 SNIP 1.155
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.979 SNIP 1.101
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.96 SNIP 1.001
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 0.99 SNIP 1.117
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.814 SNIP 0.986
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.726 SNIP 0.722
Scopus rating (2001): SJR 0.552 SNIP 0.646
Scopus rating (2000): SJR 0.748 SNIP 0.573
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.654 SNIP 0.574
Original language: English
Microcontainers, Shadow mask, Micro-milling, Drug delivery systems, Microtomography, Oral drug delivery
DOIs:
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Relations
Projects:
Powder embossing method for selective loading of polymeric microcontainers with drug formulation
Source: Findit
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Publication: Research - peer-review › Journal article – Annual report year: 2017

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Department of Physics, Experimental Surface and Nanomaterials Physics, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Thilsted, A. H. (Intern), Schmidt, M. S. (Intern), Rindzevicius, T. (Intern), Boisen, A. (Intern)
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Publication information
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Date: 05/10/2016
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Original language: English
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Source: espacenet
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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
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Department of Applied Mathematics and Computer Science, Cognitive Systems, Magnetic Systems, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Columbia University, University of the Basque Country, Yonsei University, CIC nanoGUNE Consolider
Authors: Yang, J. (Ekstern), Donolato, M. (Intern), Pinto, A. (Ekstern), Bosco, F. (Intern), Hwu, E. (Ekstern), Chen, C. (Ekstern), Alstrem, T. S. (Intern), Lee, G. (Ekstern), Schäfer, T. (Ekstern), Vavassori, P. (Ekstern), Boisen, A. (Intern), Lin, Q. (Ekstern), Hansen, M. F. (Intern)
Pages: 396-403
Publication date: 2016
Main Research Area: Technical/natural sciences
Publication information
Journal: Biosensors and Bioelectronics
Volume: 75
Detection methods for centrifugal microfluidic platforms

Centrifugal microfluidics has attracted much interest from academia as well as industry, since it potentially offers solutions for affordable, user-friendly and portable biosensing. A wide range of so-called fluidic unit operations, e.g. mixing, metering, liquid routing, and particle separation, have been developed and allow automation and integration of complex assay protocols in lab-on-a-disc systems. Besides liquid handling, the detection strategy for reading out the assay is crucial for developing a fully integrated system. In this review, we focus on biosensors and readout methods for the centrifugal microfluidics platform and cover optical as well as mechanical and electrical detection principles.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Burger, R. (Intern), Amato, L. (Intern), Boisen, A. (Intern)
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
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Scopus rating (2016): CiteScore 7.22 SJR 2.092 SNIP 1.633
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.077 SNIP 1.694 CiteScore 7.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.059 SNIP 1.74 CiteScore 6.57
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 2.033 SNIP 1.744 CiteScore 6.34
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.4 SNIP 1.605 CiteScore 5.7
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.121 SNIP 1.717 CiteScore 5.85
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.129 SNIP 1.62
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.981 SNIP 1.79
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.498 SNIP 1.806
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 Authors: Hakonen, A. (Ekstern), Rindzevicius, T. (Intern), Schmidt, M. S. (Intern), Andersson, P. O. (Ekstern), Juhlin, L. (Ekstern), Svedendahl, M. (Ekstern), Boisen, A. (Intern), Käll, M. (Ekstern)
Number of pages: 4
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Web of Science (2017): Indexed Yes
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Scopus rating (2016): CiteScore 7.46 SJR 2.769 SNIP 1.459
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 2.842 SNIP 1.588 CiteScore 7.97
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 2.651 SNIP 1.676 CiteScore 7.64
Web of Science (2014): Indexed yes
In this study, we perform experimental studies as well as simulations for cyclic voltammetry (CV) of the redox couple FeIII(CN)63-/FeII(CN)64- on a gold plated ECC biosensor encapsulated by a microfluidic system. We examine the effect of flow rate, scan rate, varying supporting electrolyte, exchange current density and the position of electrode on the CV measurements. The results show that at a relatively high flow (250 μL) and low scan rates (50 - 200 mV/s), the current response is limited by the convection due to quick supply of fresh ions at the electrode surface which leads to fading hysteresis of the recorded CV. However, at high scan rates (250 mV/s) and slow flow rates (50 - 200 μL), peak currents are recorded which means that mass transport is dominated by the diffusion mechanism and a quasi-steady state of CV is recorded. In the case of insufficient supporting electrolyte, the excess charges generated during scan will lead to ohmic distortion of the electrolyte solution and consequently result into a ramping effect of the recorded CV. However, for sufficient amount of supporting electrolyte (200 mM), the simulation results show good agreement with the experimental data. In addition, the results also show that a decrease in exchange current density leads to a shift in the peak current of the recorded CV. Finally, the results also demonstrate that the working electrode at the center of the fluidic cell records accurate measurement than placing the electrode at the bottom of the cell. The numerical results and the experimental data show both qualitative good agreement and quantitative good agreement.
Lab-on-a-disc agglutination assay for protein detection by optomagnetic readout and optical imaging using nano- and micro-sized magnetic beads

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

**General information**

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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 (2016): Indexed yes
- BFI (2015): BFI-level 1
- Scopus rating (2015): SJR 2.077 SNIP 1.694 CiteScore 7.07
- Web of Science (2015): Indexed yes
- BFI (2014): BFI-level 1
- Scopus rating (2014): SJR 2.059 SNIP 1.74 CiteScore 6.57
- Web of Science (2014): Indexed yes
- BFI (2013): BFI-level 1
- Scopus rating (2013): SJR 2.033 SNIP 1.744 CiteScore 6.34
- ISI indexed (2013): ISI indexed yes
- Web of Science (2013): Indexed yes
- BFI (2012): BFI-level 1
- Scopus rating (2012): SJR 2.4 SNIP 1.605 CiteScore 5.7
- ISI indexed (2012): ISI indexed yes
- Web of Science (2012): Indexed yes
- BFI (2011): BFI-level 1
- Scopus rating (2011): SJR 2.121 SNIP 1.717 CiteScore 5.85
- ISI indexed (2011): ISI indexed yes
- Web of Science (2011): Indexed yes
- BFI (2010): BFI-level 2
- Scopus rating (2010): SJR 2.129 SNIP 1.62
- Web of Science (2010): Indexed yes
- BFI (2009): BFI-level 1
- Scopus rating (2009): SJR 1.981 SNIP 1.79
- Web of Science (2009): Indexed yes
- BFI (2008): BFI-level 1
- Scopus rating (2008): SJR 2.498 SNIP 1.806
- Web of Science (2008): 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.
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 measureable 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)
Number of pages: 11
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Main Research Area: Technical/natural sciences

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Journal: Sensors
Volume: 16
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ISSN (Print): 1424-8220
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BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
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Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.78 SJR 0.576 SNIP 1.393
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.591 SNIP 1.478 CiteScore 2.21
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.636 SNIP 1.705 CiteScore 2.4
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.627 SNIP 1.826 CiteScore 2.72
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.668 SNIP 1.736 CiteScore 2.53
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.636 SNIP 1.488 CiteScore 2.44
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.574 SNIP 1.196
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.525 SNIP 1.132
Web of Science (2009): Indexed yes
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.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, University of Valencia, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Melero, A. (Ekstern), Keller, S. S. (Intern), Jacobsen, J. (Ekstern), Garrigues, T. (Ekstern), Rades, T. (Ekstern), Müllertz, A. (Ekstern), Boisen, A. (Intern)
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Web of Science (2017): Indexed yes
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Scopus rating (2016): CiteScore 4.24 SJR 1.284 SNIP 1.395
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 1.297 SNIP 1.465 CiteScore 4.2
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
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**

State: Published
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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Ratings:
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Web of Science (2018): Indexed yes
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Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.01 SJR 0.976 SNIP 1.266
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.921 SNIP 1.216 CiteScore 2.71
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.139 SNIP 1.461 CiteScore 2.89
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.097 SNIP 1.503 CiteScore 3.18
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.329 SNIP 1.669 CiteScore 3.38
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.055 SNIP 1.483 CiteScore 3.03
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.337 SNIP 1.571
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.288 SNIP 1.431
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.231 SNIP 1.496
Scopus rating (2007): SJR 1.197 SNIP 1.576
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.902 SNIP 1.383
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 misinterpretation of intensity histograms, where contamination might contribute with an enhanced background and not a peak.

General information

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

Publication information
Journal: Vibrational Spectroscopy
Volume: 86
ISSN (Print): 0924-2031
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.76
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 1.88
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 2.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 1.68
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.
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.
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 oral vaccine formulations. Mobility of co-culture immune cells as well as cytokine production observed following treatment with spray dried cubosomes as a particulate vaccine formulation will be further investigated.

General information
State: Published
Organisations: Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Department of Micro- and Nanotechnology, Nanoprobes, Helmholtz Centre for Infection Research (HZI), Saarland University, University of Copenhagen, Monash University
Authors: Nielsen, L. H. (Intern), De Rossi, C. (Ekstern), Lehr, C. (Ekstern), Rades, T. (Ekstern), Boyd, B. (Ekstern), Boisen, A. (Intern), Gordon, S. (Ekstern)
Number of pages: 1
Publication date: 2016
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Main Research Area: Technical/natural sciences
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Source: PublicationPreSubmission
Source-ID: 125164729
Publication: Research - peer-review › Poster – Annual report year: 2016
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.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Self-Organized Nanoporous Materials, Nanoprobes, Center for Nanostructured Graphene, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Li, T. (Intern), Wu, K. (Intern), Rindzevicius, T. (Intern), Wang, Z. (Intern), Schulte, L. (Intern), Schmidt, M. S. (Intern), Boisen, A. (Intern), Ndoni, S. (Intern)
Number of pages: 8
Pages: 15668-75
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information
Journal: A C S Applied Materials and Interfaces
Volume: 8
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ISSN (Print): 1944-8244
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 7.6 SJR 2.524 SNIP 1.528
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.299 SNIP 1.568 CiteScore 7.38
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.126 SNIP 1.64 CiteScore 6.88
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.979 SNIP 1.543 CiteScore 6.05
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.18 SNIP 1.309 CiteScore 4.94
Fabrication of Ni stamp with high aspect ratio, two-leveled, cylindrical microstructures using dry etching and electroplating: Paper

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

General information

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

Publication information

Journal: Journal of Micromechanics and Microengineering
Volume: 25
Issue number: 5
Article number: 055021
ISSN (Print): 0960-1317
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BFI (2018): BFI-level 1
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.74 SJR 0.595 SNIP 1.017
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.64 SNIP 1.211 CiteScore 1.96
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.725 SNIP 1.224 CiteScore 1.84
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.611 SNIP 1.055 CiteScore 1.74
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 µm and a height of 50 µm. 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.
Hot punching of high-aspect-ratio 3D polymeric microstructures for drug delivery


**General information**

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

**Publication information**

Journal: Lab on a Chip
Volume: 15
Issue number: 12
ISSN (Print): 1473-0197
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.98 SJR 2.147 SNIP 1.611
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.26 SNIP 1.764 CiteScore 5.74
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.534 SNIP 1.801 CiteScore 5.6
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 2.374 SNIP 1.703 CiteScore 5.9
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 2.382 SNIP 1.738 CiteScore 5.35
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Hydrodynamics studies of cyclic voltammetry for electrochemical micro biosensors

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

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

Publication information
Journal: Journal of Physics: Conference Series (Online)
Volume: 574
Issue number: 012008
ISSN (Print): 1742-6596
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.
Micromechanical Fast Quasi-Static Detection of $\alpha$ and $\beta$ Relaxations with Nanograms of Polymer

Micromechanical string resonators are used as a highly sensitive tool for the detection of glass transition ($T_g$ or $\alpha$ relaxation) and sub-$T_g$ ($\beta$ 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. $\alpha$ and $\beta$ relaxations in the polymer affect the net static tensile stress of the microstring and result in measureable local frequency slope maxima. $T_g$ 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 $\beta$ 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.
**pH-triggered drug release from biodegradable microwells for oral drug delivery**

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

**General information**

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

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BFI (2018): BFI-level 1
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BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.29 SJR 0.595 SNIP 0.752
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.783 SNIP 0.922 CiteScore 2.68
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.948 SNIP 1.164 CiteScore 2.98
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.868 SNIP 1.008 CiteScore 3.01
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.993 SNIP 1.114 CiteScore 3.12
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.147 SNIP 1.11 CiteScore 3.45
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.276 SNIP 1.243
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.146 SNIP 1.283
BFI (2008): BFI-level 1
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.

**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
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BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): SJR 0.669 SNIP 0.748 CiteScore 0.92
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.755 SNIP 0.837 CiteScore 0.92
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.73 SNIP 0.896 CiteScore 0.85
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.871 SNIP 0.914 CiteScore 0.95
ISI indexed (2013): ISI indexed yes
BFI (2012): BFI-level 1
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 crystallised to a lesser extent than pure ASSF. The stabilising effect of PVP on ASSF, led to improved relative oral bioavailability in rats of 263%, when compared to the pure ASSF. (C) 2015 Elsevier B.V. All rights reserved.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics, Nanoprobes, University of Copenhagen
Authors: Nielsen, L. H. (Intern), Rades, T. (Ekstern), Müllertz, A. (Ekstern)
Number of pages: 7
Pages: 334-340
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: International Journal of Pharmaceutics
Volume: 490
Issue number: 1-2
ISSN (Print): 0378-5173
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
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**Original language:** English

**Furosemide, Polyvinylpyrrolidone, Glass solution, Solid dispersion, Amorphous, Oral bioavailability**

**Electronic versions:**

Stabilisation_of_amorphous_furosemide_increases_the_oral_drug_bioavailability_in_rats_post_print.pdf

**DOIs:**

10.1016/j.ijpharm.2015.05.063

**Source:** FindIt

**Source-ID:** 275284991

**Publication:** Research - peer-review › Journal article – Annual report year: 2015
**Biological Sample Preparation for Electron Microscopy**

Special Topic Course

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:**

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

Period: 7 Feb 2018 → 9 Feb 2018

Jongjit Jantra (Other)

Kinga Zor (Other)

Martin Hedström (Other)

Bo Mattiasson (Other)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Micro- and Nanotechnology

Nanoprobes

**Description**

Pure and Applied Chemistry International Conference 2018 (PACCON 2018), Hat Yai, Songkhla, Thailand, 7th-9th February 2018

Degree of recognition: International

**Related event**

**Pure and Applied Chemistry International Conference 2018**

07/02/2018 → 09/02/2018

Hat Yai, Thailand

Activity: Talks and presentations › Conference presentations
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 → …
Activity: Talks and presentations › Conference presentations

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

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Micro- and Nanotechnology
Nanoprobes
Documents:
IMR26_fixed

Related event

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

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

Period: 20 Sep 2017
Onur Durucan (Guest lecturer)
Tomas Rindzevicius (Other)
Michael Stenbæk Schmidt (Other)
Oleksii Ilchenko (Other)
Anja Boisen (Other)

Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics

Department of Micro- and Nanotechnology
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

**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

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
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

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

Description
Poster presentation
Documents:
Biosensors_poster

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

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

Description
Poster presentation
Documents:
Kuldeep_BBMEC

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

41st International conference on Micro and Nano Engineering
Period: 21 Sep 2015 → 24 Sep 2015
Kuldeep Sanger (Participant)
Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Nanoprobes

Description
Conference abstract
Links:

Related event
41st International conference on Micro and Nano Engineering: MNE 2015
21/09/2015 → 24/09/2015
The Hague, Netherlands
Activity: Attending an event › Participating in or organising a conference
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.