A modular reconfigurable digital microfluidics platform
Miniaturizing the traditional wet lab processes and realizing the full potential of lab-on-a-chip technology (LOC) has been a great challenge for scientists and engineers in the quest of providing health care where such does not exist, or to increase lab efficiency and lower the operational cost. A range of practical LOC fabrication technologies has already been demonstrated, and as a result, the research of real life applications has been steadily increasing. However, due to the variety of used technologies and LOC form factors, it often requires a modification or even a complete redesign of the available instrumentation systems. Standardization and flexible instrumentation has seen limited development in the LOC field even though developing on all application levels has been proven as an effective way to stimulate a growth in a research field. To address this, we present a modular digital microfluidics (DMF) instrumentation platform and a concept of integrated chip-instrument co-design that has the potential to solve a wide range of LOC instrumentation challenges.
Direct detection of candida albicans with a membrane based electrochemical impedance spectroscopy sensor

Candidemia and invasive candidiasis is a cause of high mortality and morbidity rates among hospitalized patients worldwide. The occurrence of the infections increases due to the complexity of the patients and overuse of the antifungal therapy. The current Candida detection method includes blood culturing which is a lengthy procedure and thus delays the administration of the antifungal therapy. Even though the results are available after 48 h it is still the gold standard in pathogen detection in a hospital setting. In this work we present an electrochemical impedance sensor that is capable of detecting Candida albicans yeast. The yeast cells are captured on electrodes specifically functionalized with anti-Candida antibodies and detection is achieved by electrochemical impedance spectroscopy. The sensor allows for detection of the yeast cells at clinically relevant concentrations in less than 1 h.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Copenhagen University Hospital , Technical University of Denmark
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Sensors
Volume: 18
Issue number: 7
Article number: 2214
ISSN (Print): 1424-8220
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): CiteScore 3.23 SJR 0.584 SNIP 1.55
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.78 SJR 0.623 SNIP 1.614
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.647 SNIP 1.643 CiteScore 2.21
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.707 SNIP 1.796 CiteScore 2.4
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.636 SNIP 1.758 CiteScore 2.72
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.671 SNIP 1.709 CiteScore 2.53
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.641 SNIP 1.439 CiteScore 2.44
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.579 SNIP 1.244
Web of Science (2010): Indexed yes
Model-Based Systems Engineering for Life-Sciences Instrumentation Development

General information
State: Accepted/In press
Organisations: Department of Management Engineering, Engineering Systems, Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Copenhagen Center for Health Technology, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering
Authors: Patou, F. (Intern), Dimaki, M. (Intern), Maier, A. (Intern), Svendsen, W. E. (Intern), Madsen, J. (Intern)
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: Systems Engineering
ISSN (Print): 1098-1241
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.612 SJR 0.285 CiteScore 1.18
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.67 SJR 0.494 SNIP 1.026
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.456 SNIP 1.655 CiteScore 1.58
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.519 SNIP 1.732 CiteScore 1.36
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.46 SNIP 1.725 CiteScore 1.67
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.373 SNIP 1.228 CiteScore 1.2
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.524 SNIP 2.207 CiteScore 1.07
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 0.403 SNIP 1.444
Pyocyanin is a toxin produced by Pseudomonas aeruginosa. Here we describe a novel paper-based electrochemical sensor for pyocyanin detection, manufactured with a simple and inexpensive approach based on electrode printing on paper. The resulting sensors constitute an effective electrochemical method to quantify pyocyanin in bacterial cultures without the conventional time consuming pretreatment of the samples. The electrochemical properties of the paper-based sensors were evaluated by ferric/ferrocyanide as a redox mediator, and showed reliable sensing performance. The paper-based sensors readily allow for the determination of pyocyanin in bacterial cultures with high reproducibility, achieving a limit of detection of 95 nM and a sensitivity of 4.30 μA/μM in standard culture media. Compared to the similar commercial ceramic based sensors, it is a 2.3-fold enhanced performance. The simple in-house fabrication of sensors for pyocyanin quantification allows researchers to understand in vitro adaptation of P. aeruginosa infections via rapid screenings of bacterial cultures that otherwise are expensive and time-consuming.

General information
State: Published
Organisations: Department of Biotechnology and Biomedicine, Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Infection Microbiology, Novo Nordisk Foundation Center for Biosustainability, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering, Copenhagen Center for Health Technology, Roskilde University, University of Copenhagen
Number of pages: 9
Publication date: 2018
Main Research Area: Technical/natural sciences

Publication information
Journal: P L o S One
Volume: 13
Issue number: 3
Article number: e0194157
ISSN (Print): 1932-6203
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.01 SJR 1.164 SNIP 1.111
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.11 SJR 1.236 SNIP 1.101
Web of Science (2016): Indexed yes
ELECTROCHEMICAL DEVICE FOR DETECTION OF SELECTED QUORUM SENSING SIGNALS

For diagnostic purposes, and particularly point-of-care diagnostic purposes, there is a need for devices capable of detecting quorum sensing molecules such as AHL within a biological sample with high precision, and which furthermore are fast and simple to use. The present invention relates to an electrochemical device, comprising: 5 - at least one reference electrode (RE), - at least one counter electrode (CE), - two or more working electrodes (WEs), wherein each working electrode differ from the other working electrode(s) with respect to at least one of the following characteristics: surface area, 10 size, material, and coating, - a sample receiving area for receiving a biological sample, wherein the electrodes and the sample receiving area is fluidly connected - means for transferring the sample to the electrodes for measurement, and - means for displaying a result of the measurement. 15

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Alzahra, F. A. A. (Ekstern), Svendsen, W. E. (Intern)
Publication date: 19 Oct 2017

Publication information
IPC: G01N 33/ 487 A I
Patent number: WO2017178455
Concentration of nanoparticles and/or microparticles in flow conditions by dielectrophoresis

A device for concentration of nanoparticles and/or microparticles in liquid flow conditions by dielectrophoresis is disclosed in this invention.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Rozlosnik, N. (Intern), Dimaki, M. (Intern), Olsen, M. H. (Ekstern), Svendsen, W. E. (Intern)
Publication date: 8 Sep 2017

Publication information
IPC: B01L 3/00 A1
Patent number: WO2017148785
Date: 08/09/2017
Priority date: 01/03/2016
Priority number: EP20160157983
Original language: English
Electronic versions:
WO2017148785A1.pdf
Main Research Area: Technical/natural sciences
Source: espacenet
Source-ID: WO2017148785
Publication: Research › Patent – Annual report year: 2017

Helbredstjek af dansk sundhedsteknologi: Sektorudviklingsrapport
Sådan kan samarbejde mellem industrien, universiteterne og sundhedsvæsenet skabe gode løsninger til forebyggelse, diagnostik, patientbehandling og rehabilitering

General information
State: Published
Organisations: Office for Innovation & Sector Services, Copenhagen Center for Health Technology, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering, Center for Energy Resources Engineering, Scientific Computing, Department of Management Engineering, Technology and Innovation Management, Department of Electrical Engineering, Biomedical Engineering, Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Department of Photonics Engineering, Diode Lasers and LED Systems, Department of Energy Conversion and Storage, Electrofunctional materials, IT Service, National Space Institute, Innovation and Research-based consultancy, Department of Chemical and Biochemical Engineering, The Danish Polymer Centre, Office for Research and Relations, It-branchen, manjour.dk
Number of pages: 72
Publication date: 2017

Publication information
Publisher: Technical University of Denmark (DTU)
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
2017.02.16.DTU_Sektorudviklingsrapport_Helbredstjek_af_dansk_sundhedsteknologi.pdf
Publication: Commissioned › Report – Annual report year: 2017
In-situ doped junctionless polysilicon nanowires field effect transistors for low-cost biosensors

Silicon nanowire (SiNW) field effect transistor based biosensors have already been proven to be a promising tool to detect biomolecules. However, the most commonly used fabrication techniques involve expensive Silicon-On-Insulator (SOI) wafers, E-beam lithography and ion-implantation steps. In the work presented here, a top down approach to fabricate SiNW junctionless field effect biosensors using novel in-situ doped polysilicon is demonstrated. The p-type polysilicon is grown with an optimum boron concentration that gives a good metal-silicon electrical contact while maintaining the doping level at a low enough level to provide a good sensitivity for the biosensor. The silicon nanowires are patterned using standard photolithography and a wet etch method. The metal contacts are made from magnetron sputtered TiW and e-beam evaporation of gold. The passivation of electrodes has been done by sputtered Si3N4 which is patterned by a lift-off process. The characterization of the critical fabrication steps is done by Secondary Ion Mass Spectroscopy (SIMS) and by statistical analysis of the measurements made on the width of the SiNWs. The electrical characterization of the SiNW in air is done by sweeping the back gate voltage while keeping the source drain potential to a constant value and surface characterization is done by applying liquid gate in phosphate buffered saline (PBS) solution. The fabricated SiNW sensors functionalized with (3-aminopropyl)triethoxysilane (APTES) have demonstrated good sensitivity in detecting different pH buffer solutions.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Technical University of Denmark
Pages: 88-95
Publication date: 2017
Main Research Area: Technical/natural sciences

System-Level Sensitivity Analysis of SiNW-bioFET-Based Biosensing Using Lockin Amplification

Although Silicon Nanowire biological Field-Effect Transistors (SiNW-bioFETs) have steadily demonstrated their ability to detect biological markers at ultra-low concentration, they have not yet translated into routine diagnostics applications. One of the challenges inherent to the technology is that it requires an instrumentation capable of recovering ultra-low signal variations from sensors usually designed and operated in a highly-resistive configuration. Often overlooked, the SiNWbioFET/instrument interactions are yet critical factors in determining overall system biodetection performances. Here, we carry out for the first time the system-level sensitivity analysis of a generic SiNW-bioFET model coupled to a custom-design instrument based on the lock-in amplifier. By investigating a large parametric space spanning over both sensor and instrumentation specifications, we demonstrate that systemwide investigations can be instrumental in identifying the design trade-offs that will ensure the lowest Limits-of-Detection. The generic character of our analytical model allows us to elaborate on the most general SiNW-bioFET/instrument interactions and their overall implications on detection performances. Our model can be adapted to better match specific sensor or instrument designs to either ensure that ultra-high sensitivity SiNW-bioFETs are coupled with an appropriately sensitive and noise-rejecting instrumentation, or to best tailor SiNW-bioFET design to the specifications of an existing instrument.

General information
State: Published
Organisations: Department of Management Engineering, Engineering Systems, Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Center for Bachelor of Engineering Studies, Afdelingen for El-teknologi,
A new application of plant virus nanoparticles as drug delivery in breast cancer

Nanoparticles based on non-pathogenic viruses have opened up a novel sector in nanotechnology. Viral nanoparticles based on plant viruses have clear advantages over any synthetic nanoparticles as they are biocompatible and biodegradable self-assembled and can be produced inexpensively on a large scale. From several such under-development platforms, only a few have been characterized in the target-specific drugs into the cells. Potato virus X is presented as a carrier of the chemotherapeutic drug Herceptin that is currently used as a targeted therapy in (HER2+) breast cancer patients. Here, we used nanoparticles formed from the potato virus X to conjugate the Herceptin (Trastuzumab) monoclonal antibody as a new option in specific targeting of breast cancer. Bioconjugation was performed by EDC/sulfo-N-hydroxysuccinimide (sulfo-NHS) in a two-step protocol. Then, the efficiency of conjugation was investigated by different methods, including sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), Western blot, ELISA, Zetasizer, and transmission electron microscopy. SDS-PAGE and Western blot analysis confirmed an 82-kDa protein band that resulted from conjugation of potato virus X (PVX) coat protein (27 kDa) to heavy chain of Herceptin (55 kDa). Zeta potential values for conjugated particles, PVX, and HER were −7.05, −21.4, and −1.48, respectively. We investigated the efficiency of PVX-Herceptin to induce SK-OV-3 and SK-BR-3 cells (HER2 positive cell lines) apoptosis. We therefore counted cells and measured apoptosis by flow cytometry assay, then compared with Herceptin alone. Based on our data, we confirmed the conjugation of PVX and Herceptin. This study suggests that the PVX-Herceptin conjugates enable Herceptin to become more potential therapeutic tools.
Aptasensor development for detection of virus in water

Contamination of water by waterborne viruses causes serious health issues worldwide. The current virus detection methods are expensive and time-consuming and require access to well-equipped laboratories. This thesis describes the development of an impedimetric all-polymer aptasensor for detection of three types of waterborne viruses: norovirus, rotavirus and hepatitis A virus. The development of the aptasensor involved sample preparation for aptamer selection of rotavirus and hepatitis A virus, an iterative design process of the aptasensor, investigation of the surface immobilisation of aptamers and finally an impedimetric electrical characterisation of the sensor.

The sample preparation of the rotavirus was based on purification and biotinylation of the virus to meet the requirements of the aptamer selection process. The selection process, performed by an external collaborator, was based on streptavidin coated magnetic bead separation, hence the needed biotinylation. It was found that the BPH linker gave the highest yield when the biotinylated rotavirus were immobilised onto the beads.

The design of the viral aptasensor was determined by an iterative design process. The final chip design was based on a SD card design with an injection moulded PC substrate and lid. The electrodes were screen-printed PEDOT:PSS. The surface immobilisation of aptamers through UV cross-linking onto different polymer substrates was tested. As the success of this step is crucial for the aptasensor specificity and performances, the surface immobilisation was thoroughly
investigated. The aptamer UV cross-linking onto PEDOT:PSS was promising. Furthermore, some passive absorption of the aptamers onto the PEDOT:PSS was found. The impedimetric electrical characterisation of the aptasensor chip was done with different media salinity and different pH values. The impedimetric measurements of the different media salinity showed the expected behaviour with the greatest change present in the region representing the solution resistance. The pH measurements did not show any significant change of the impedance, hence the chip was stable in the measured pH range, which corresponds to the expected pH range of water samples. The stability of the aptasensor chip was tested over a 2 week period in continuous flow. It was found that the electrodes were not damaged or degraded during the time period, as a constant impedance signal was measured.

A solid foundation for the further development of the aptasensor for viral detection has been established and from this a new cheap and simple viral detection method can emerge.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics, National Veterinary Institute, Virology, Nano Bio Integrated Systems
Authors: Kirkegaard, J. (Intern), Rozlosnik, N. (Intern), Larsen, L. E. (Intern), Svendsen, W. E. (Intern)
Number of pages: 214
Publication date: 2016

**Publication information**

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

**Relations**

Projects:
Aptasensor development for detection of virus in water
Source: PublicationPreSubmission
Source-ID: 128311006
Publication: Research › Ph.D. thesis – Annual report year: 2017

**Electrochemical sensing of biomarker for diagnostics of bacteria-specific infections**

**Aim:** *Pseudomonas aeruginosa* is a pathogen that is prevalent in serious infections in compromised patients worldwide. A unique virulence factor of this bacterium is the redox-active molecule pyocyanin, which is a potential biomarker for the identification of *P. aeruginosa* infections. Here we report a direct, selective and rapid detection technique of pyocyanin.

**Materials & methods:** Pyocyanin was detected by amperometry at a relatively high potential where the pyocyanin signal was unaffected by background contributions. Results & conclusion: Pyocyanin was detected at concentrations down to 125 nM in a 50 μM mixture of interfering compounds with a reproducibility of $r^2 = 0.999$ ($n = 5$) within 200 s. The results document a step toward apoint-of-care technique for diagnosis of *P. aeruginosa* infections.

**General information**

State: Published
Organisations: Department of Systems Biology, Infection Microbiology, Department of Micro- and Nanotechnology, Novo Nordisk Foundation Center for Biosustainability, Department of Microbiology, Risø National Laboratory for Sustainable Energy, Department of Photonics Engineering, Nano Bio Integrated Systems
Number of pages: 11
Pages: 2185-2195
Publication date: 2016
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Nanomedicine
Volume: 11
Issue number: 16
ISSN (Print): 1743-5889
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.19 SJR 1.302 SNIP 0.89
Evolvable Smartphone-Based Platforms for Point-Of-Care In-Vitro Diagnostics Applications

The association of smart mobile devices and lab-on-chip technologies offers unprecedented opportunities for the emergence of direct-to-consumer in vitro medical diagnostics applications. Despite their clear transformative potential, obstacles remain to the large-scale disruption and long-lasting success of these systems in the consumer market. For instance, the increasing level of complexity of instrumented lab-on-chip devices, coupled to the sporadic nature of point-of-care testing, threatens the viability of a business model mainly relying on disposable/consumable lab-on-chips. We argued recently that system evolvability, defined as the design characteristic that facilitates more manageable transitions between system generations via the modification of an inherited design, can help remedy these limitations. In this paper, we discuss how platform-based design can constitute a formal entry point to the design and implementation of evolvable smart device/lab-on-chip systems. We present both a hardware/software design framework and the implementation details of a platform prototype enabling at this stage the interfacing of several lab-on-chip variants relying on current- or impedance-based biosensors. Our findings suggest that several change-enabling mechanisms implemented in the higher abstraction software layers of the system can promote evolvability, together with the design of change-absorbing hardware/software interfaces. Our platform architecture is based on a mobile software application programming interface coupled to a modular hardware accessory. It allows the specification of lab-on-chip operation and post-analytic functions at the mobile software layer. We demonstrate its potential by operating a simple lab-on-chip to carry out the detection of dopamine using various electroanalytical methods.

General information
Evolvable Smartphone-Based Point-of-Care Systems For In-Vitro Diagnostics

Recent developments in the life-science -omics disciplines, together with advances in micro- and nanoscale technologies offer unprecedented opportunities to tackle some of the major healthcare challenges of our time. Lab-on-Chip technologies coupled with smart-devices in particular, constitute key enablers for the decentralization of many in-vitro medical diagnostics applications to the point-of-care, supporting the advent of a preventive and personalized medicine. Although the technical feasibility and the potential of Lab-on-Chip/smart-device systems is repeatedly demonstrated, direct-to-consumer applications remain scarce. This thesis addresses this limitation. After identifying system evolvability as a key enabler to the adoption and long-lasting success of next-generation point-of-care systems by favoring the integration of new technologies, streamlining the reengineering efforts for system upgrades and limiting the risk of premature system obsolescence. Among possible strategies, platform-based design represents a particularly suitable entry point to the development of evolvable systems. One necessary condition, is for change-absorbing and change-enabling mechanisms to be incorporated in the platform architecture at initial design-time. Important considerations arise as to where in Lab-on-Chip/smart-device platforms can these mechanisms be integrated, and how to implement them.

Our investigation revolves around the silicon-nanowire biological field effect transistor, a promising biosensing technology for the detection of biological analytes at ultra low concentrations. We discuss extensively the sensitivity and instrumentation requirements set by the technology before we present the design and implementation of an evolvable smartphone-based platform capable of interfacing lab-on-chips embedding such sensors. We elaborate on the implementation of various architectural patterns throughout the platform and present how these facilitated the evolution of the system towards one accommodating for electrochemical sensing. Model-based development was undertaken throughout the engineering process. A formal SysML system model fed our evolvability assessment process. We introduce, in particular, a model-based methodology enabling the evaluation of modular scalability: the ability of a system to scale the current value of one of its specification by successively reengineering targeted system modules.

The research work presented in this thesis provides a roadmap for the development of evolvable point-of-care systems, including those targeting direct-to-consumer applications. It extends from the early identification of anticipated change, to the assessment of the ability of a system to accommodate for these changes. Our research should thus interest industrials
eager not only to disrupt, but also to last in a shifting socio-technical paradigm.

**Fast Selective Detection of Pyocyanin Using Cyclic Voltammetry**

Pyocyanin is a virulence factor uniquely produced by the pathogen *Pseudomonas aeruginosa*. The fast and selective detection of pyocyanin in clinical samples can reveal important information about the presence of this microorganism in patients. Electrochemical sensing of the redox-active pyocyanin is a route to directly quantify pyocyanin in real time and in situ in hospitals and clinics. The selective quantification of pyocyanin is, however, limited by other redox-active compounds existing in human fluids and by other metabolites produced by pathogenic bacteria. Here we present a direct selective method to detect pyocyanin in a complex electroactive environment using commercially available electrodes. It is shown that cyclic voltammetry measurements between –1.0 V to 1.0 V reveal a potential detection window of pyocyanin of 0.58–0.82 V that is unaffected by other redox-active interferents. The linear quantification of pyocyanin has an R² value of 0.991 across the clinically relevant concentration range of 2–100 nM. The proposed method was tested on human saliva showing a standard deviation of 2.5% ±1% (n = 5) from the known added pyocyanin concentration to the samples. This inexpensive procedure is suggested for clinical use in monitoring the presence and state of *P. aeruginosa* infection in patients.
This thesis deals with the development of a novel biosensor for the detection of biomolecules based on a silicon nanowire biologically gated field-effect transistor and its integration into a point-of-care device. The sensor and electrical on-chip integration was developed in a different project. The presented research is based on this sensor structure and investigates its potential as a versatile biomarker detection platform by evaluating different functionalization approaches. The functionalization of the silicon sensor surface with organic molecules was investigated in detail to determine the suitability of different methods for the preparation of organic interfaces for protein attachment. Oxide-free silicon surfaces offer unique possibilities to create highly sensitive sensor surfaces for charge detection due to the lack of an insulating oxide layer, but the highly reactive surface presents a challenge for modification under ambient conditions. Self-assembled monolayer formation by hydrosilylation with alkenes and alkynes was thus investigated under different conditions, both ambient and controlled, and quantified using x-ray photoelectron spectroscopy.
With the aim to create a platform for subsequent immobilization of receptor molecules, amine- and carboxylic acid- as well as alkyne-terminated surfaces were prepared that allow for the conjugation of biomolecules using established cross-linking schemes. Using a receptor-ligand model system protein detection experiments were performed with nanowire sensors functionalized using different modification schemes. To facilitate functionalization and measurement and as a first step towards integration into a point-of-care device, several microfluidic tools were developed for sample delivery to the sensor surface and as a modular platform for the further development of automated functionalization and sample preparation schemes.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, University of Copenhagen
Authors: Pfreundt, A. (Intern), Svendsen, W. E. (Intern), Dimaki, M. (Intern), Andresen, L. (Ekstern)
Number of pages: 210
Publication date: 2016

**Publication information**

Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
PhD_Thesis_anpf.pdf
Publication: Research › Ph.D. thesis – Annual report year: 2016

---

**Micro fluidic System for Culturing and Monitoring of Neuronal Cells and Tissue**

The aim of this Ph.D. project was to combine experience within cell and tissue culturing, electrochemistry and microfabrication in order to develop an in vivo-like fluidic culturing platform, challenging the traditional culturing methods. The first goal was to develop a fluidic system for culturing of brain tissue. The second goal was to develop a sensor system with the potential for incorporation into both conventional culture systems and fluidic culturing systems. The third and final goal of this project was to develop a system for culturing of neuronal cells with the possibility of incorporating the developed sensor system. The project was conducted in collaboration with researchers at KU to ensure that the end product is actually desired by the community.

This thesis demonstrates some of the work carried out during the course of this Ph.D. project. First it describes culturing of primary neuronal cells on a Peptide Nano Wires (PNW) modified substrate aiming to bring conventional neuronal cultures closer to mimic the in vivo situation. The work describes both the fabrication of the culture substrates and results comparing the performance of PNW cultured neurons and conventional cultures. Tests show that the function of neurons cultured on PNWs lies closer to neurons in vivo than neurons cultured on conventional plastic substrates.

The second part of the thesis describes a fluidic system for culturing of brain slices. It describes the fabrication and use of the system as well as results on culturing of hippocampal tissue slices. We found that the tissues cultured in the microfluidic system were of similar or better quality compared to tissues cultured conventionally.

The third part of the thesis is about the development, characterisation and test of a membrane based sensor system. As the membranes are used for culturing, the introduction of electrodes on these will allow for the real time measurement of relevant cell/tissue products during culturing.

The last part of the thesis is about, i.e. the integration of the membrane based sensors with the fluidic system, in a way compatible with mass production. The last part of this thesis also includes perspectives on how to expand the latest designed device to facilitate culturing of tissue and co-culturing of cells.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Bakmand, T. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern), Waagepetersen, H. S. (Ekstern)
Number of pages: 110
Publication date: 2016

**Publication information**

Publisher: DTU Nanotech
Original language: English
Main Research Area: Technical/natural sciences

**Relations**

Projects:
Micro fluidic System for Culturing and Monitoring of Neuronal Cells and Tissue
Source: PublicationPreSubmission
Source-ID: 127667528
Publication: Research › Ph.D. thesis – Annual report year: 2016
Model-Based Evaluation Of System Scalability: Bandwidth Analysis For Smartphone-Based Biosensing Applications

Scalability is a design principle often valued for the engineering of complex systems. Scalability is the ability of a system to change the current value of one of its specification parameters. Although targeted frameworks are available for the evaluation of scalability for specific digital systems, methodologies enabling scalability analysis of multidomain, complex systems, are still missing. In acknowledgment of the importance for complex systems to present the ability to change or evolve, we present in this work a system level model-based methodology allowing the multidisciplinary parametric evaluation of scalability. Our approach can be used to determine how a set of limited changes to targeted system modules could affect design specifications of interest. It can also help predict and trace system bottlenecks over several product generations, offering system designers the chance to better plan re-engineering efforts for scaling a system specification efficaciously.

We demonstrate the value of our methodology by investigating a smartphone-based biosensing instrumentation platform. Specifically, we carry out scalability analysis for the system’s bandwidth specification: the maximum analog voltage waveform excitation frequency the system could output while allowing continuous acquisition and wireless streaming of bioimpedance measurements. We rely on several SysML modelling tools, including dependency matrices, as well as a fault-detection Simulink Stateflow executable model to conclude on how the successive re-engineering of 5 independent system modules, from the replacement of a wireless Bluetooth interface, to the revision of the ADC sample-and-hold operation could help increase system bandwidth.

Smartphone-based biosensing platform evolution: implementation of electrochemical analysis capabilities

Lab-on-Chip technologies offer great opportunities for the democratization of in-vitro medical diagnostics to the consumer-market. Despite the limitations set by the strict instrumentation and control requirements of certain families of these devices, new solutions are emerging. Smartphones now routinely demonstrate their potential as an interface of choice for operating complex, instrumented Lab-on-Chips. The sporadic nature of home-based in-vitro medical diagnostics testing calls for the development of systems capable of evolving with new applications or new technologies for Lab-on-Chip devices. We present in this work how we evolved the first generation of a smartphone/Lab-on-Chip platform designed for evolvability. We demonstrate how reengineering efforts can be confined to the mobile-software layer and illustrate some of the benefits of building evolvable systems. We implement electrochemical capabilities on our platform prototype and carry out cyclic voltammetry to measure dopamine concentrations over several orders of magnitude.
A Lab-on-a-disc platform for trapping of cells, monitoring of cell behaviour and evaluation of redox metabolism

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Bioanalytics, Center for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics
Authors: Amato, L. (Intern), Kuldeep, K. (Intern), Esmail Tehrani, S. (Intern), Burger, R. (Intern), Caviglia, C. (Intern), Andreasen, S. Z. (Intern), Heiskanen, A. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
Pages: 1299-1301
Publication date: 2015

Host publication information
Title of host publication: Proceedings MicroTAS 2015
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 128950322
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2015

All Polymer Lab-on-a-chip System for Virus Detection in Water

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics, Nano Bio Integrated Systems
Authors: Kirkegaard, J. (Intern), Olsen, M. H. (Intern), Dimaki, M. (Intern), Rozlosnik, N. (Intern)
Number of pages: 1
Publication date: 2015
Event: Poster session presented at Microfluidics Congress 2015, London, United Kingdom.
Main Research Area: Technical/natural sciences

An easy-to-use microfluidic interconnection system to create quick and reversibly interfaced simple microfluidic devices

The presented microfluidic interconnection system provides an alternative for the individual interfacing of simple microfluidic devices fabricated in polymers such as polymethylmethacrylate, polycarbonate and cyclic olefin polymer. A modification of the device inlet enables the direct attachment of tubing (such as polytetrafluoroethylene tubing) secured and sealed by using a small plug, without the need for additional assembly, glue or o-rings. This provides a very clean connection that does not require additional, potentially incompatible, materials. The tightly sealed connection can withstand pressures above 250 psi and therefore supports applications with high flow rates or highly viscous fluids. The ease of incorporation, configuration, fabrication and use make this interconnection system ideal for the rapid prototyping of simple microfluidic devices or other integrated systems that require microfluidic interfaces. It provides a valuable addition to the toolbox of individual and small arrays of connectors suitable for micromachined or template-based injection molded devices since it does not require protruding, threaded or glued modifications on the inlet and avoids bulky and expensive fittings.
A Smart Mobile Lab-on-Chip-Based Medical Diagnostics System Architecture Designed For Evolvability

Unprecedented knowledge levels in life sciences along with technological advances in micro- and nanotechnologies and microfluidics have recently conditioned the advent of Lab-on-Chip (LoC) devices for In-Vitro Medical Testing (IVMT). Combined with smart-mobile technologies, LoCs are pervasively giving rise to opportunities to better diagnose disease, predict and monitor personalised treatment efficacy, or provide healthcare decision-making support at the Point-of-Care (PoC). Although made increasingly available to the consumer market, the adoption of LoC-based PoC In-Vitro Medical Testing (IVMT) systems is still in its infancy. This attrition partly pertains to the intricacy of designing and developing complex systems, destined to be used sporadically, in a fast-pace evolving technological paradigm. System evolvability is therefore key in the design process and constitutes the main motivation for this work.

We introduce a smart-mobile and LoC-based system architecture designed for evolvability. By propagating LoC programmability, instrumentation, and control tools to the highlevel abstraction smart-mobile software layer, our architecture facilitates the realisation of new use-cases and the accommodation for incremental LoC-technology developments. We demonstrate these features with an implementation allowing the interfacing of LoCs embedding current- or impedance-based biosensors such as Silicon Nanowire Field Effect Transistors (SiNW-FETs) or electrochemical transducers. Structural modifications of these LoCs or changes in their specific operation may be addressed by the sole reengineering of the mobilesoftware layer, minimising system upgrade development and validation costs and efforts.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Center for Bachelor of Engineering Studies, Afdelingen for El-teknologi, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering
Authors: Patou, F. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern), Kjærgaard, C. (Intern), Madsen, J. (Intern)
Pages: 390-398
Publication date: 2015

Host publication information
Title of host publication: Proceedings of the Euromicro Conference on Digital System Design 2015
Publisher: IEEE
ISBN (Print): 9781467380355
BFI conference series: Euromicro Conference on Digital System Design (5000380)
Main Research Area: Technical/natural sciences
Lab-on-Chip, Smartphone, Point-of-care, In-vitro medical diagnostics, System evolvability, System architecting
Electronic versions:
Certified_DSD2015_paper.pdf
DOIs:
10.1109/DSD.2015.11
Source: PublicationPreSubmission
Source-ID: 115264502
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015
Basic Microfluidics Theory

Flow in microsystems behaves very different than flow on the macroscale, i.e., the flow we are used to in our everyday life. The most obvious difference is that the chaotic turbulent flow we most often observe, e.g., rivers flowing or tap water running does not appear on the microscale. Here, the flow is more smooth and most often what we call laminar flow. Other parameters considered important on the macroscale such as inertia are insignificant on the microscale, whereas viscosity becomes extremely important. Diffusion, which on large scale is a hopeless parameter to use for transport, becomes significant on microscale. The surface of your system has to be considered more carefully as the surface to volume ratio (S/V) increases dramatically as you downscale your system. Take for example a cubic macrosystem with sides of 1 m, here S/V=6 m⁻¹, whereas for a system with sides of 1 μm the V/S=600,000 m⁻¹, which is a huge difference and has a large impact on flow behavior. In this chapter the basic microfluidic theory will be presented, enabling the reader to gain a comprehensive understanding of how liquids behave at the microscale, enough to be able to engage in design of micro systems and to support the theory used in other chapters in the book, but without going into the deep underlying theoretical approach.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Svendsen, W. E. (Intern)
Pages: 17-26
Publication date: 2015

Host publication information
Title of host publication: Lab-on-a-Chip Devices and Micro-Total Analysis Systems
Publisher: Springer
ISBN (Print): 978-3-319-08686-6
ISBN (Electronic): 978-3-319-08687-3
Chapter: 2
Main Research Area: Technical/natural sciences
DOI: 10.1007/978-3-319-08687-3_2
Publication: Research - peer-review › Book chapter – Annual report year: 2015

Coplanar Electrode Layout Optimized for Increased Sensitivity for Electrical Impedance Spectroscopy

This work describes an improvement in the layout of coplanar electrodes for electrical impedance spectroscopy. We have developed, fabricated, and tested an improved electrode layout, which improves the sensitivity of an impedance flow cytometry chip. The improved chip was experimentally tested and compared to a chip with a conventional electrode layout. The improved chip was able to discriminate 0.5 μm beads from 1 μm as opposed to the conventional chip. Furthermore, finite element modeling was used to simulate the improvements in electrical field density and uniformity between the electrodes of the new electrode layout. Good agreement was observed between the model and the obtained experimental results.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, SBT Aqua ApS
Authors: Clausen, C. H. (Intern), Skands, G. E. (Intern), Bertelsen, C. V. (Intern), Svendsen, W. E. (Intern)
Number of pages: 11
Pages: 110-120
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Micromachines
Volume: 6
Issue number: 1
ISSN (Print): 2072-666X

Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): CiteScore 2.31 SJR 0.493 SNIP 0.987
Web of Science (2017): Indexed yes
Scopus rating (2016): CiteScore 1.83 SJR 0.395 SNIP 0.791
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 0.463 SNIP 0.925 CiteScore 1.78
Web of Science (2015): Indexed yes
Design and Simulation of Lab-on-a-Chip Devices

Microfluidic channels are an essential part of any lab-on-a-chip system. They usually perform various functions, such as transporting liquids from A to B or mixing or separating liquids. As production costs for such systems are not insignificant, it is essential that the systems are designed properly before the fabrication, in order to avoid unnecessary fabrication repetitions. The use of simulations can give a good idea of how microfluidic systems work, to the point where a significant part of the design optimisation can be done theoretically. This chapter will provide some basic information on how to embark on these types of simulations, explaining the basics of microfluidic modelling and providing examples.

Early Detection Of Bacterial Infections By Electrochemistry

Early Detection Of Bacterial Infections By Electrochemistry.pdf
Early Detection Of Chronic Bacterial Infections By Microsensors

General information
State: Published
Organisations: Department of Systems Biology, Infection Microbiology, Department of Micro- and Nanotechnology, Novo Nordisk Foundation Center for Biosustainability, Nano Bio Integrated Systems
Number of pages: 1
Publication date: 2015
Event: Poster session presented at The 3rd International Conference on Nanotechnology in Medicine (NANOMED), Manchester, United Kingdom.
Main Research Area: Technical/natural sciences
Electronic versions:
Early_Detection_Of_Chronic_Bacterial_Infections_By_Microsensors.pdf
Source: PublicationPreSubmission
Source-ID: 118548801
Publication: Research - peer-review › Poster – Annual report year: 2015

Electrochemical detection of pyocyanin as a biomarker for bacterial infections

General information
State: Published
Organisations: Department of Systems Biology, Infection Microbiology, Department of Micro- and Nanotechnology, Novo Nordisk Foundation Center for Biosustainability, Nano Bio Integrated Systems, Bacterial Cell Factories
Number of pages: 1
Publication date: 2015
Event: Poster session presented at 25th European Congress of Clinical Microbiology and Infectious Diseases, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Electronic versions:
Alatraktchi_ECCMID_2015.pdf
Source: PublicationPreSubmission
Source-ID: 110696576
Publication: Research - peer-review › Poster – Annual report year: 2015

Fabrication and Characterisation of Membrane-Based Gold Electrodes
This work presents a versatile, membrane based electrochemical sensor with thin film electrodes fabricated through Ebeam evaporation directly on porous materials (membranes). Here, the fabrication of the electrodes is described along with possible methods for integration in fluidic systems and characterisation of the electrodes through cyclic voltammetry (CV). The continued porous nature of the membranes after metal deposition is documented and its robustness and stability is investigated. Furthermore, amperometric sensing of dopamine is demonstrated as a proof of concept to validate the usability of the membrane sensor.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Pages: 217-224
Publication date: 2015
Main Research Area: Technical/natural sciences
Publication information
Journal: Electroanalysis
Volume: 27
Issue number: 1
ISSN (Print): 1040-0397
Fabrication of polyimide based microfluidic channels for biosensor devices

The ever-increasing complexity of the fabrication process of Point-of-care (POC) devices, due to high demand of functional versatility, compact size and ease-of-use, emphasizes the need of multifunctional materials that can be used to simplify this process. Polymers, currently in use for the fabrication of the often needed microfluidic channels, have limitations in terms of their physicochemical properties. Therefore, the use of a multipurpose biocompatible material with better resistance to the chemical, thermal and electrical environment, along with capability of forming closed channel...
microfluidics is inevitable. This paper demonstrates a novel technique of fabricating microfluidic devices using polyimide (PI) which fulfills the aforementioned properties criteria. A fabrication process to pattern microfluidic channels, using partially cured PI, has been developed by using a dry etching method. The etching parameters are optimized and compared to those used for fully cured PI. Moreover, the formation of closed microfluidic channel on wafer level by bonding two partially cured PI layers or a partially cured PI to glass with high bond strength has been demonstrated. The reproducibility in uniformity of PI is also compared to the most commonly used SU8 polymer, which is a near UV sensitive epoxy resin. The potential applications of PI processing are POC and biosensor devices integrated with microelectronics.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Zulfiqar, A. (Intern), Pfreundt, A. (Intern), Svendsen, W. E. (Intern), Dimaki, M. (Intern)
Number of pages: 8
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Micromechanics and Microengineering
Volume: 25
Issue number: 3
ISSN (Print): 0960-1317
Ratings:
BFI (2018): BFI-level 1
BFI (2017): BFI-level 1
Web of Science (2017): Indexed yes
Scopus rating (2017): CiteScore 2.02 SJR 0.554 SNIP 0.968
Web of Science (2016): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.74 SJR 0.63 SNIP 1.067
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.687 SNIP 1.265 CiteScore 1.96
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.802 SNIP 1.316 CiteScore 1.84
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.737 SNIP 1.233 CiteScore 1.74
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 0.936 SNIP 1.491 CiteScore 1.92
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.036 SNIP 1.443 CiteScore 2.43
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.013 SNIP 1.637
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.144 SNIP 1.5
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.243 SNIP 1.616
Web of Science (2008): Indexed yes
Fluidic system for long-term in vitro culturing and monitoring of organotypic brain slices

Brain slice preparations cultured in vitro have long been used as a simplified model for studying brain development, electrophysiology, neurodegeneration and neuroprotection. In this paper an open fluidic system developed for improved long term culturing of organotypic brain slices is presented. The positive effect of continuous flow of growth medium, and thus stability of the glucose concentration and waste removal, is simulated and compared to the effect of stagnant medium that is most often used in tissue culturing. Furthermore, placement of the tissue slices in the developed device was studied by numerical simulations in order to optimize the nutrient distribution. The device was tested by culturing transverse hippocampal slices from 7 days old NMRI mice for a duration of 14 days. The slices were inspected visually and the slices cultured in the fluidic system appeared to have preserved their structure better than the control slices cultured using the standard interface method.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Technical University of Denmark, University of Copenhagen, University of Southern Denmark
Authors: Bakmand, T. (Intern), Troels-Smith, A. R. (Ekstern), Dimaki, M. (Intern), Nissen, J. D. (Ekstern), Andersen, K. B. (Intern), Sasso, L. (Intern), Waagepetersen, H. S. (Ekstern), Gramsbergen, J. B. (Ekstern), Svendsen, W. E. (Intern)
Number of pages: 7
Publication date: 2015
Main Research Area: Technical/natural sciences

Publication information
Journal: Biomedical Microdevices
Volume: 17
Issue number: 4
Article number: 71
ISSN (Print): 1387-2176
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.639 SJR 0.538 CiteScore 2.07
Web of Science (2017): Indexed Yes
Integrating Electrochemical Detection with Centrifugal Microfluidics for Real-Time and Fully Automated Sample Testing

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

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

**Publication information**
Journal: R S C Advances
Volume: 5
ISSN (Print): 2046-2069
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.01 SJR 0.863 SNIP 0.736
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.06 SJR 0.889 SNIP 0.757
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.947 SNIP 0.834 CiteScore 3.42
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.113 SNIP 0.962 CiteScore 3.87
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.119 SNIP 0.904 CiteScore 3.74
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 0.872 SNIP 0.619 CiteScore 2.4
ISI indexed (2012): ISI indexed no
Web of Science (2012): Indexed yes
Original language: English
Electronic versions:
Integrating_Electrochemical_Detection_with_Centrifugal_Microfluidics_for_Real_Time_and_Fully_Automated_Sample_Testing.pdf
DOIs: 10.1039/c4ra16858e
Source: PublicationPreSubmission
Source-ID: 105957472
Publication: Research - peer-review › Journal article – Annual report year: 2015

**Lab-on-a-chip devices and micro-total analysis systems: a practical guide**

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Castillo, J. (ed.) (Intern), Svendsen, W. E. (ed.) (Intern)
Publication date: 2015

**Publication information**
Publisher: Springer
ISBN (Print): 978-3-319-08686-6
ISBN (Electronic): 978-3-319-08687-3
Micro and Nanofabrication Using Self-Assembled Biological Nanostructures

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Castillo, J. (ed.) (Intern), Svendsen, W. E. (ed.) (Intern)
Number of pages: 126
Publication date: 2015

Novel culturing platform for brain slices and neuronal cells
In this paper we demonstrate a novel culturing system for brain slices and neuronal cells, which can control the concentration of nutrients and the waste removal from the culture by adjusting the fluid flow within the device. The entire system can be placed in an incubator. The system has been tested successfully with brain slices and PC12 cells. The culture substrate can be modified using metal electrodes and/or nanostructures for conducting electrical measurements while culturing and for better mimicking the in vivo conditions.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, University of Copenhagen
Number of pages: 4
Pages: 346-349
Publication date: 2015

Host publication information
Title of host publication: 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society
Publisher: IEEE
Main Research Area: Technical/natural sciences
DOIs: 10.1109/EMBC.2015.7318370
Source: FindIt
Source-ID: 276551057
Publication: Research - peer-review › Article in proceedings – Annual report year: 2015

Novel Diagnostic Method for Personalized Treatment of Cancer
Point-Of-Care (POC) devices, due to their better portability and easy-to-use functions, have already found their way into the domestic house hold appliances. The technologies developed for these devices have enabled the mankind to monitor the health related problems at home such as the blood pressure, glucose, hemoglobin, cholesterol level in the blood and many more. The efforts are now being made to develop a Point-Of-Care Technology (POCT) that can detect cancer at an early and potentially treatable stage. To fulfill this requirement, a highly sensitive sensing technology is needed that can detect very small amount of cancer markers in the blood drop to be used in a POC device.

Silicon Nanowires (SiNW) in a field effect setup have been demonstrated as a highly sensitive tool that can be used to detect very small amount of biomolecules. However, the manufacturing method to produce them relies on highly expensive tools e.g. e-beam lithography, and expensive substrates e.g. Silicon-On-Insulator (SOI) which poses hurdle in cheap and fast production of the devices that can be used for both research purposes and for domestic use.

In this project, a novel fabrication method, using in-situ doped polysilicon, has been developed for SiNW based devices that does not require the above mentioned expensive tools and resources thereby enabling faster and cost effective production of devices as compared to the already developed methods. In addition to this, the device has been made even
more compact and portable by using a novel polyimide based technology to integrate microfluidics on top of SiNW sensor. Various generations of prototype devices have been used for bio-sensing experiments to detect antibodies and DNA hybridization that has shown very promising results and potential application of the device in clinical and patient level diagnostics.

In the first part of this thesis, the fabrication process of producing the SiNW based devices is explained in detail where three generations of the process are developed in order to obtain highly sensitive device. Different characterization techniques have been used to ensure better reproducibility and high throughput while keeping the sensitivity of the SiNW to a high level.

In the second part, the fabrication process to produce microfluidic channel on top of bio sensors by using polyimide is developed. The fabrication process to integrate closed-microfluidic system on top of SiNW is demonstrated. The durability of the microfluidic system has also been tested.

In the third part, different functionalization methods are explained and used to demonstrate the bio sensing on the SiNW sensor. The detection of cancer biomarker is also tested on these devices.

Lastly, the alternative fabrication processes developed during this PhD project are discussed along with the problems faced during the development. These devices could not be tested due to time constraints.
A compact microelectrode array chip with multiple measuring sites for electrochemical applications

In this paper we demonstrate the fabrication and electrochemical characterization of a microchip with 12 identical but individually addressable electrochemical measuring sites, each consisting of a set of interdigitated electrodes acting as a working electrode as well as two circular electrodes functioning as a counter and reference electrode in close proximity. The electrodes are made of gold on a silicon oxide substrate and are passivated by a silicon nitride membrane. A method for avoiding the creation of high edges at the electrodes (known as lift-off ears) is presented. The microchip design is highly symmetric to accommodate easy electronic integration and provides space for microfluidic inlets and outlets for integrated custom-made microfluidic systems on top. © 2014 by the authors; licensee MDPI, Basel, Switzerland.
A compact multifunctional microfluidic platform for exploring cellular dynamics in real-time using electrochemical detection

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Nano Bio Integrated Systems, Fluidic Array Systems and Technology, University of Genoa, University Autónoma de Madrid, Lund University, Tel Aviv University, Hungarian Academy of Sciences, University College Cork, University of Potsdam, Politecnico di Milano
A flexible mobile-device biosensing instrumentation platform for point-of-care medical diagnostics applications

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Department of Electrical Engineering, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 24th Anniversary World Congress on Biosensors, Melbourne, Australia.
Main Research Area: Technical/natural sciences
Source: PublicationPreSubmission
Source-ID: 101856297
Publication: Research - peer-review › Poster – Annual report year: 2014
A flexible mobile-device biosensing instrumentation platform for point-of-care medical diagnostics applications

The early diagnosis and monitoring of chronic diseases still constitutes today one of the major healthcare challenges in our society. Advances in nanotechnology and microfluidics have been increasingly empowering researchers and engineers with tools to develop integrated biosensing solutions helping to address this challenge. Specifically, Lab-on-Chip (LoC) devices have a key role to play in the advent of Point-of-Care (PoC) medical applications, driving a shift of the medical diagnostics paradigm and the transition from a centralized, technical, high-throughput biological sample analysis process to a diagnostician and patient-oriented field decision-making support system.

The success of such systems requires the development of highly sensitive and specific biosensors to reliably detect small amounts of relevant biological markers. Nevertheless, the socio-technical complexity of the PoC medical diagnostics context necessitates considering broader requirements, notably in terms of usability, flexibility, and integration capabilities. These characteristics call for multi-disciplinary design methodologies inspired from the field of systems engineering and constitute the motivations for this work.

We present a mobile-device based, PoC biosensing instrumentation platform, designed for multiplexed high-impedance sensing and the electrochemical detection of biological species on a LoC. The proposed system is thus designed as a flexible, user-friendly hardware and software platform allowing programmable electrical readout from LoCs potentially comprehending varied transducers addressing different targeted biological markers. A smart-phone/tablet docking-station embeds the hardware interface necessary for the implementation of a smart-phone digital lock-in amplifier. The platform is tested with high-impedimetric measurements from Silicon-nanowire Field Effect Transistors embedded in a LoC. Programmable firmware and flexible hardware will in turn allow for standard voltammetry and electrical impedance spectroscopy to be performed. The design of a mobile app and standard mobile software libraries will ensure system evolvability, enabling application-specific biosensors readouts and adapted user interfacing.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Department of Electrical Engineering, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering
Number of pages: 1
Publication date: 2014
and an implementation of a simple and rapid calibration scheme for instrument-based PoC blood biomarker analysis systems. Motivated by the complexity of associating high-accuracy biosensing using silicon nanowire field effect transistors with ease of use for the PoC system user, we propose a novel one-step, multipoint calibration method for LoC-based systems. Our approach specifically addresses the important interfaces between a novel microfluidic unit to integrate the sensor array and a mobile-device hardware accessory. A multi-point calibration curve is obtained by generating a defined set of reference concentrations from a single input. By consecutively splitting the flow perpendicular to the diffusion interface only one mixing step is required for each of the generated calibration solutions. This results in a compact design with a very small footprint of the microfluidic layout.

**General information**

**State:** Published

**Organisations:** Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Department of Applied Mathematics and Computer Science, Embedded Systems Engineering

**Authors:** Pfreundt, A. (Intern), Patou, F. (Intern), Zulfiqar, A. (Intern), Dimaki, M. (Intern), Madsen, J. (Intern), Svendsen, W. E. (Intern)

**Publication date:** 2014

---

**Applicanion of versatile electrochemical sensor in cell culturing**

**General information**

**State:** Published

**Organisations:** Department of Micro- and Nanotechnology, Nano Bio Integrated Systems

**Authors:** Bakmand, T. (Intern), Al Atrakchi, F. A. (Intern), Svendsen, W. E. (Intern)

**Number of pages:** 1

**Publication date:** 2014

---

**AquaVir- Portable Analyzer for Water Borne Infectious Viruses**

Viral contamination in waters intended for human consumption or human contact poses a high health risk. In worst-case, lead to viral outbreaks. The waterborne virus, norovirus is a major cause of viral gastroenteritis. Conventional detection methods of norovirus rely on microbiological methods like polymerase chain reaction and a variety of sample preparations. These methods are time consuming, expensive and require highly trained personnel. Thus, viral surveillance cannot be done continuously and only provide an instant overview of the water quality. We are developing an all polymer detection system for online viral surveillance of waters. The detection is based on differential impedance measurements between a reference and an electrode functionalized with a bio-recognition element. The bio-recognition element is an aptamer specific to the target virus. We have previously shown very low detection limits with influenza virus as proof of concept of the technology. The electrode material is the intrinsic conducting polymer PEDOT:PSS screen-printed on TOPAS for easy scaling of production. Finite element simulations of the electrode potential confirm the electrode viability in waters with conductivities similar to tap water, see figure 1. Substantial pre-concentration is required to reach the limit of detection needed in surface water. We employ both filter and on-chip based concentration techniques to accomplish this. In figure 2, virus presence and successful bio-recognition to the electrodes is established as an initial test. On-chip concentration is done by electric focusing of the virus particles. From extensive finite element modelling, we have designed dielectrophoresis channels with embedded microelectrodes to focus the virus particles in the center and thus facilitate concentration of the particles.

**General information**
A Semi-Closed Device for Chromosome Spreading for Cytogenetic Analysis

Metaphase chromosome spreading is the most crucial step required for successful karyotyping and FISH analysis. These two techniques are routinely used in cytogenetics to assess the chromosome abnormalities. The spreading process has been studied for years but it is still considered an art more than a science. The chromosome spreading greatly depends on the environmental conditions such as humidity and temperature, which govern the evaporation of fixative, in which the cells are suspended. The spreading is normally performed manually in ambient conditions on glass slides, which are hydrophilic, and thus allow for better quality spreads. Further cytogenetic analysis depends on the quality of the spreads, which is dependent on the skills of the personnel and is thus limited to laboratory settings. Here, we present a semi-closed microfluidic chip for preparation of the metaphase spreads on a glass and a Topasr substrate rendered more hydrophilic by oxygen plasma treatment coupled with photografting. The device consists of a microfluidic chamber with perfusion holes that facilitate the evaporation of fixative and reliable formation of the spreads. The usability of the chromosome spreads formed on the glass and the Topasr slide is tested by performing FISH analysis.
Electrochemical detection of chromosome translocation

Cytophenetics is a study of the cell structure with a main focus on chromosomes content and their structure. Chromosome abnormalities, such as translocations may cause various genetic disorders and hematological malignancies. Chromosome translocations are structural rearrangements of two chromosomes that results in formation of derivative chromosomes with a mixed DNA sequence. The method currently used for their detection is Fluorescent In Situ Hybridization, which requires a use of expensive, fluorescently labeled probes that target the derivative chromosomes. We present here a double hybridization approach developed for label-free detection of the chromosome translocations. For specific translocation detection it is necessary to determine that the two DNA sequences forming a derivative chromosome are connected, which is achieved by two subsequent hybridization steps. The electrochemical impedance spectroscopy was selected as the sensing method on a microfabricated chip with array of 12 electrode sets. Two independent chips (Chip1 and Chip2) were used for targeting the chromosomal fragments involved in the translocation. Each chip was differentially functionalized with DNA probes matching the derivative chromosomes. The observed increase in the charge transfer resistance for both chips serves as a way of detection the presence of the selected translocation in the analyzed sample. The developed sensor was reliable and could in the future be implemented in cytophenetic laboratories as a supplementary method for the existing techniques.

Electrochemistry in a centrifugal microfluidic system: Towards a novel point-of-care technology platform

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Technical University of Denmark
Authors: Andreasen, S. Z. (Intern), Kwasny, D. (Intern), Bregger, A. L. (Intern), Bosco, F. (Intern), Andersen, K. B. (Intern), Svendsen, W. E. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern)
Number of pages: 1
Pages: 37-37
Publication date: 2014
Host publication information
Title of host publication: Oral presentations – ESEAC2014
Main Research Area: Technical/natural sciences
Electronic versions:
Full_Oral_Presentations_ESEAC_2014.pdf
Finger prick blood plasma separation using a standard lab equipment

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Amphiphilic Polymers in Biological Sensing
Authors: Kwasny, D. (Intern), Andersen, K. B. (Intern), Pfreundt, A. (Intern), Levinsen, S. (Intern), Svendsen, W. E. (Intern)
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 4th National Conference on Nano- and Micromechanics
Main Research Area: Technical/natural sciences
Electronic versions:
Kwasny_KKNM_Wroclaw_2014.pdf

Bibliographical note
Oral presentation at a National Conference in nano and Micromechanics in Wroclaw, Poland in July 2014
Source: PublicationPreSubmission
Source-ID: 93752615
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

Finger prick blood plasma separation using a standard lab equipment
Blood is a complex biological matrix that has a huge potential for diagnostics as it contains various analytes and biomarkers. Traditionally the analysis is performed on plasma and white blood cells separated from venous blood. However, the collection of venous blood samples is painful and requires a few milliliters of blood. It has been demonstrated that the blood taken from finger prick contains the same analytes as venous blood in sufficient abundance and could therefore be used for diagnosis as an alternative in many cases. Various approaches towards analysis of finger prick blood with plasma separation and analyte detection on-chip are reported in the literature [1]. Although versatile, these plasma separation techniques often require sample dilution prior to separation and use low flow rates resulting in longer processing times which greatly hinders their use in commercial systems.

Here we present a device for analysis of minute blood volumes using a standard laboratory tabletop spinner. The microfabricated polymer device fits in a 1.5 mL eppendorf tube and takes between 10-20 μl of whole blood. The blood is layered over a pre-loaded Ficoll paque® that is used to separate the plasma and white blood cells for further analysis. The procedure requires 2 min spinning and can efficiently separate the plasma and white blood cells from red blood cells. The device allows for handling blood with varying hematocrit levels readout of which is included in the device design. After separation the plasma and white blood cells are simply pipetted or pushed out of the device by pressing a flexible chamber. Plasma quality is assessed by spectrophotometry to determine the amount of proteins in the extracted plasma and the degree of undesired hemolysis.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Amphiphilic Polymers in Biological Sensing
Authors: Kwasny, D. (Intern), Andersen, K. B. (Intern), Pfreundt, A. (Intern), Levinsen, S. (Intern), Svendsen, W. E. (Intern)
Number of pages: 1
Publication date: 2014
Event: Poster session presented at 4th International Workshop on Analytical Miniaturization and NANOtechnologies, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences

Bibliographical note
Poster
Source: PublicationPreSubmission
Source-ID: 93752606
Publication: Research - peer-review › Poster – Annual report year: 2014

Finger prick blood plasma separation using standard lab equipment
Label-free protein detection using a microfluidic Coulter-counter device

A new method for measuring specific protein concentrations in solutions has been developed. The technique makes use of the Coulter effect for detecting and sizing of micro-scaled objects suspended in a buffer fluid. The method is completely label-free as it is only based on the electrical readout when a suspension of microscopic beads flows over a set of electrodes in a microfluidic device. Since no electrode functionalization is needed the same device can be used in a number of different assays. Using goat-anti-rat IgG functionalized polystyrene beads we have shown proof of principle detecting rat IgG in solution. When the analyte (rat IgG) is present oligomers of beads are formed. The electrical readout of the oligomers is different compared to a zero control sample with no rat IgG. Detection of the protein has been performed in a concentration as small as 14 ng/mL. The dynamic range of the system has been demonstrated to be relatively large, ranging from 1 g/mL to 14 ng/mL. The microfluidic system is made from polymer and glass and very little volume of sample (<10 L) is needed for analysis.
Multifunctional sensing membrane-based platform for tissue or cell culturing and monitoring

The present application discloses a water-permeable sensor membrane comprising i) a first layer of a conductive material defining at least one electrode and having a thickness of 0.1-0.000 [μm]; ii) a second layer of a nanostructure material build on the first layer; and iii) a third, topmost, layer of a conducting polymer material defining at least one electrode and having a thickness of 0.001-1.0 [μm]. The application also discloses a tissue or cell culture sample monitoring assembly comprising a sensor assembly and a tissue sample or a cell culture sample arranged on top of the third layer of the sensor membrane, and a method of monitoring the concentration or presence of a tissue analyte in the proximity of a tissue sample or cell culture sample.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Sasso, L. (Intern), Andersen, K. B. (Intern), Castillo, J. (Intern), Gramsbergen, J. B. (Ekstern), Svendsen, W. E. (Intern)
Publication date: 2014

Publication information
IPC: C12Q1/00
Nanoscaled biological gated field effect transistors for cytogenetic analysis

Cytogenetic analysis is the study of chromosome structure and function, and is often used in cancer diagnosis, as many chromosome abnormalities are linked to the onset of cancer. A novel label free detection method for chromosomal translocation analysis using nanoscaled field effect transistors (FET) is presented here. The FET is gated by the hybridization of the target DNA on the semiconducting nanowire. The results show an extreme sensitivity to the hybridization process, so that the hybridization and dehybridisation can be followed in real time. The nanoscaled FET is made of polysilicon using standard UV lithography enabling batch processing of the sensors.

New approach of long-term modification of Topas® to acquire surface hydrophilicity for chromosome spreading

A modified and improved photografting procedure of Topas® surface hydrophilization is investigated in order to obtain stable modification of the polymer for long term storage. The achieved hydrophilicity and monitoring of the wettability during one month of storage are presented as well as a description of the optimal cleaning procedure and storage conditions to maintain the modified surface. Three minutes of oxygen plasma activation followed by 4 min of acrylic acid UV-photografting at 50 °C leads to the most stable hydrophilicity that was characterized by an initial water contact angle of 53.5° ± 1.2°. Storage of the modified material in cold water at 4 °C and refraining from ultrasonic cleaning limit water contact angle increase to 5° over 30 days. In comparison with pristine hydrophobic Topas, the proposed treatment improves chromosome spreading ability significantly.
Novel electrochemical sensor for lab-on-a-chip and biomedical technology

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Sol Voltaics AB
Number of pages: 1
Publication date: 2014
Main Research Area: Technical/natural sciences
Electronic versions:
ESEAC2014_Tanya.pdf
Source: PublicationPreSubmission
Source-ID: 101565178
Publication: Research - peer-review › Poster – Annual report year: 2014

This article presents a novel membrane-based sensor for real-time electrochemical investigations of cellular- or tissue cultures. The membrane sensor enables recording of electrical signals from a cell culture without any signal dilution, thus avoiding loss of sensitivity. Moreover, the porosity of the membrane provides optimal culturing conditions similar to existing culturing techniques allowing more efficient nutrient uptake and molecule release. The patterned sensor electrodes were fabricated on a porous membrane by electron-beam evaporation. The electrochemical performance of the membrane electrodes was characterized by cyclic voltammetry and chronoamperometry, and the detection of synthetic dopamine was demonstrated down to a concentration of 3.1 pM. Furthermore, to present the membrane-sensor functionality the dopamine release from cultured PC12 cells was successfully measured. The PC12 cells culturing experiments showed that the membrane-sensor was suitable as a cell culturing substrate for bio-applications. Real-time measurements of dopamine exocytosis in cell cultures were performed, where the transmitter release was recorded at the point of release. The developed membrane-sensor provides a new functionality to the standard culturing methods, enabling sensitive continuous in vitro monitoring and closely mimicking the in vivo conditions.

Novel membrane-based electrochemical sensor for real-time bio-applications.

This article presents a novel membrane-based sensor for real-time electrochemical investigations of cellular- or tissue cultures. The membrane sensor enables recording of electrical signals from a cell culture without any signal dilution, thus avoiding loss of sensitivity. Moreover, the porosity of the membrane provides optimal culturing conditions similar to existing culturing techniques allowing more efficient nutrient uptake and molecule release. The patterned sensor electrodes were fabricated on a porous membrane by electron-beam evaporation. The electrochemical performance of the membrane electrodes was characterized by cyclic voltammetry and chronoamperometry, and the detection of synthetic dopamine was demonstrated down to a concentration of 3.1 pM. Furthermore, to present the membrane-sensor functionality the dopamine release from cultured PC12 cells was successfully measured. The PC12 cells culturing experiments showed that the membrane-sensor was suitable as a cell culturing substrate for bio-applications. Real-time measurements of dopamine exocytosis in cell cultures were performed, where the transmitter release was recorded at the point of release. The developed membrane-sensor provides a new functionality to the standard culturing methods, enabling sensitive continuous in vitro monitoring and closely mimicking the in vivo conditions.
Real-time multiparameter monitoring of cellular dynamics: an automated microfluidic electrochemical analysis platform

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Nano Bio Integrated Systems, Fluidic Array Systems and Technology, Technical University of Denmark
Number of pages: 1
Publication date: 2014

Host publication information
Title of host publication: Proceedings of the 15th International Conference on Electroanalysis
Main Research Area: Technical/natural sciences
Electronic versions: Real_time_multiparameter_monitoring_of_cellular_dynamics_an_automated_microfluidic_electrochemical_analysis_platform.pdf
Silicon as an anisotropic mechanical material: Deflection of thin crystalline plates

While silicon is an anisotropic material it is often in literature treated as an isotropic material when it comes to plate calculations. This leads to considerable errors in the calculated deflection. To overcome this problem, we present an in-depth analysis of the bending behavior of thin crystalline plates. An analysis of the compliance tensor for the 32 different crystal classes shows, that for thin plates, only 5 different types of plates exist. An anisotropic plate equation valid for crystalline thin plates is derived and solved for circular, elliptic, rectangular and square plates using both exact analytical expressions and approximate expressions calculated by the Galerkin method. The results are applied to plates made on silicon (0 0 1), (0 1 1) and (1 1 1) substrates, respectively, and analytical equations for the deflection, strain energy and resonance frequency of such plates are presented. These expressions are in excellent agreement with anisotropic finite element calculations. The calculated deflection differs less than 0.1%, for both circular and rectangular plates, compared to finite element calculations. The results are presented as ready-to-use facilitating accurate analytical models involving crystalline plates, such as those often found in the field of micro electro mechanical systems. The effect of elastic boundary conditions is taken into account by using an effective radius of the plate.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, MEMS-AppliedSensors, Nano Bio Integrated Systems, Experimental Surface and Nanomaterials Physics, Silicon Microtechnology
Authors: Thomsen, E. V. (Intern), Reck, K. (Intern), Skands, G. E. (Intern), Bertelsen, C. V. (Intern), Hansen, O. (Intern)
Number of pages: 18
Pages: 347-364
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Sensors and Actuators A: Physical
Volume: 220
ISSN (Print): 0924-4247
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 1.363 SJR 0.699 CiteScore 2.79
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 2.79 SJR 0.787 SNIP 1.627
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.826 SNIP 1.553 CiteScore 2.73
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.866 SNIP 1.771 CiteScore 2.41
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.819 SNIP 1.762 CiteScore 2.53
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.91 SNIP 2.113 CiteScore 2.34
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 0.909 SNIP 2.103 CiteScore 2.5
ISI indexed (2011): ISI indexed yes
Study of Paclitaxel-Treated HeLa Cells by Differential Electrical Impedance Flow Cytometry

This work describes the electrical investigation of paclitaxel-treated HeLa cells using a custom-made microfluidic biosensor for whole cell analysis in continuous flow. We apply the method of differential electrical impedance spectroscopy to treated HeLa cells in order to elucidate the changes in electrical properties compared with non-treated cells. We found that our microfluidic system was able to distinguish between treated and non-treated cells. Furthermore, we utilize a model for electrical impedance spectroscopy in order to perform a theoretical study to clarify our results. This study focuses on investigating the changes in the electrical properties of the cell membrane caused by the effect of paclitaxel. We observe good agreement between the model and the obtained results. This establishes the proof-of-concept for the application in cell drug therapy.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics, Nano Bio Integrated Systems
Number of pages: 16
Pages: 257-272
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Biosensors
Volume: 4
Synthesis and characterization of covalent diphenylalanine nanotube-folic acid conjugates

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Center for Electron Nanoscopy, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics
Authors: León, J. J. C. (Intern), Rindzevicius, T. (Intern), Wu, K. (Intern), Schmidt, M. S. (Intern), Janik, K. A. (Intern), Boisen, A. (Intern), Svendsen, W. E. (Intern), Rozlosnik, N. (Intern), Castillo, J. (Intern)
Number of pages: 8
Publication date: 2014
Main Research Area: Technical/natural sciences

Publication information
Journal: Journal of Nanoparticle Research
Volume: 16
Issue number: 7
Article number: 2525
ISSN (Print): 1388-0764
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
The aim of this work is to produce polymer modifiers in order to develop hydrophilic polymeric surfaces for use in microfluidics. The use of hydrophilic polymers in microfluidics will have many advantages e.g. preventing protein absorbance. Here we present an amphiphilic diblock copolymer consisting of a bulk material compatible block and a hydrophilic block. To utilize the possibility of incorporating diblock copolymers into ethylenenorbornene copolymers, we have in this work developed a model poly(ethylene-1-butene) polymer compatible with the commercial available ethylenenorbornene copolymer TOPAS. Through matching of the radius of gyration for the model polymer and TOPAS the miscibility was achieved. The poly(ethylene-1-butene) polymer was synthesized from a hydrogenated anionic polymerized polybutadiene polymer. As hydrophilic block poly(ethylene...
oxide) was subsequently added also with anionic polymerization. Recent miscibility results between the model polymer and TOPAS will be presented, as well ongoing efforts to study the hydrophilic surface.

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Amphiphilic Polymers in Biological Sensing, Nano Bio Integrated Systems, Department of Mechanical Engineering, Materials and Surface Engineering
Authors: Levinsen, S. (Intern), Svendsen, W. E. (Intern), Horsewell, A. (Intern), Almdal, K. (Intern)
Number of pages: 1
Publication date: 2014

**Host publication Information**
Title of host publication: Bulletin of the American Physical Society
Volume: 59
Article number: BAPS.2014.MAR.W21.2
Main Research Area: Technical/natural sciences
Conference: APS March Meeting 2014 , Denver, CO, United States, 03/03/2014 - 03/03/2014
Electronic versions:
MWS_MAR14_2013_001179_2.pdf

**Versatile electrochemial sensor for tissue culturing and sample handling**
Culturing of organotypic brain tissues is a routine procedure in neural research. The visual inspection of the medium is the only way of determining the state of the tissue. At the end of culturing, post-processing techniques such as HPLC can be used to measure the concentration of the secreted metabolites in the waste products. Continuous measurements would enable improved monitoring as compared to the end-point assay. Here, we developed a sensor system capable of real time measurements of the analytes directly secreted from the tissue. The presented system can be readily integrated in the standard procedures allowing for better assessment of the progress of the culturing.
The sensor system was initially developed for monitoring of cells and tissue cultures but has lately been considered for, and tested in, a wide range of applications. Some of these include pathogen detection and integration in microfluidic devices for sample preparation.
In this work we present the development of the sensor system along with results on characterization by impedance spectroscopy and cyclic voltammetry. Furthermore we present recent results on integration of the sensor as well as amperometric detection of dopamine as a preliminary proof of concept.

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Number of pages: 1
Publication date: 2014

**Host publication Information**
Title of host publication: Proceedings of the 15th International conference on Electroanalysis
Main Research Area: Technical/natural sciences
Electronic versions:
BakmandTanya.pdf

**Bibliographical note**
For poster presentation
Source: PublicationPreSubmission
Source-ID: 100775812
Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2014

**Versatile electrochemical sensor for cell culturing**
Combined Cell Culture-Biosensing Platform Using Vertically Aligned Patterned Peptide Nanofibers for Cellular Studies

This Article presents the development of a combined cell culture–biosensing platform using vertically aligned self-assembled peptide nanofibers. Peptide nanofibers were patterned on a microchip containing gold microelectrodes to provide the cells with a 3D environment enabling them to grow and proliferate. Gold microelectrodes were functionalized with conductive polymers for the electrochemical detection of dopamine released from PC12 cells. The combined cell culture–biosensing platform assured a close proximity of the release site, the cells and the active surface of the sensor, thereby rendering it possible to avoid a loss of sensitivity because of the diffusion of the sample. The obtained results showed that the peptide nanofibers were suitable as a cell culturing substrate for PC12 cells. The peptide nanofibers could be employed as an alternative biological material to increase the adherence properties of PC12 cells. Dopamine was amperometrically detected at a value of 168 fmole.

General information
State: Published
Organisations: Nano Bio Integrated Systems, Department of Micro- and Nanotechnology, Technical University of Denmark
Authors: Taskin, M. B. (Ekstern), Sasso, L. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern), Castillo, J. (Intern)
Pages: 3323-3328
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: A C S Applied Materials and Interfaces
Volume: 5
Issue number: 8
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 2.561 SNIP 1.536
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 2.262 SNIP 1.555 CiteScore 7.38
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 2.125 SNIP 1.636 CiteScore 6.88
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.992 SNIP 1.548 CiteScore 6.05
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 2.199 SNIP 1.327 CiteScore 4.94
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 2.046 SNIP 1.404 CiteScore 4.41
ISI indexed (2011): ISI indexed no
Web of Science (2011): Indexed yes
Scopus rating (2010): SJR 1.597 SNIP 0.944
Web of Science (2010): Indexed yes
Web of Science (2009): Indexed yes
Original language: English
DOIs:
10.1021/am0400390g
Computational and experimental studies of the interaction between single-walled carbon nanotubes and folic acid

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics, Universidad Santo Tomas, Universidad Industrial de Santander
Authors: Castillo, J. J. (Ekstern), Rozo, C. E. (Ekstern), Castillo-León, J. (Intern), Rindzevicius, T. (Intern), Svendsen, W. E. (Intern), Rozlosnik, N. (Intern), Boisen, A. (Intern), O, F. M. (Ekstern)
Pages: 60-64
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Chemical Physics Letters
Volume: 564
ISSN (Print): 0009-2614
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.61 SJR 0.656 CiteScore 1.64
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 1.71 SJR 0.718 SNIP 0.689
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.709 SNIP 0.707 CiteScore 1.83
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 0.755 SNIP 0.765 CiteScore 1.83
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 0.858 SNIP 0.835 CiteScore 2.07
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.104 SNIP 0.915 CiteScore 2.2
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.159 SNIP 1.004 CiteScore 2.38
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.213 SNIP 0.932
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 1.241 SNIP 0.971
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Culturing of PC12 Cells, Neuronal Cells, Astrocytes Cultures and Brain Slices in an Open Microfluidic System

The brain is the center of the nervous system, where serious neurodegenerative diseases such as Parkinson’s, Alzheimer’s and Huntington’s are products of functional loss in the neural cells (1). Typical techniques used to investigate these diseases lack precise control of the cellular surroundings, in addition to isolating the neural tissue from nutrient delivery and to creating unwanted gradients (2). This means that typical techniques used to investigate neurodegenerative diseases cannot mimic in vivo conditions, as closely as desired. We have developed a novel microfluidic system for culturing PC12 cells, neuronal cells, astrocytes cultures and brain slices. The microfluidic system provides efficient nutrient delivery, waste removal, access to oxygen, fine control over the neurochemical environment and access to modern microscopy. Additionally, the setup consists of an in vitro culturing and electrochemical sensor system that enables real time detection of metabolites, e.g. dopamine from cell cultures and brain slices. In summary we present results on culturing of brain slices and cells in the microfluidic system as well as on the incorporation of an electrochemical sensor system for characterization of exocytotic dopamine release from neural and brain cultures.

Detection of cancer cells using a peptide nanotube–folic acid modified graphene electrode

This article describes the preparation of a graphene electrode modified with a new conjugate of peptide nanotubes and folic acid for the selective detection of human cervical cancer cells over-expressing folate receptors. The functionalization of peptide nanotubes with folic acid was confirmed by fluorescence microscopy and atomic force microscopy. The peptide nanotube–folic acid modified graphene electrode was characterized by scanning electron microscopy and cyclic voltammetry. The modification of the graphene electrode with peptide nanotube–folic acid led to an increase in the current signal. The human cervical cancer cells were bound to the modified electrode through the folic acid–folate receptor
interaction. Cyclic voltammograms in the presence of [Fe(CN)6]3/4 as a redox species demonstrated that the binding of the folate receptor from human cervical cancer cells to the peptide nanotube–folic acid modified electrode lowered the electron transfer resulting in a decrease in the measured current. A detection limit of 250 human cervical cancer cells per mL was obtained. Control experiments confirmed that the peptide nanotube–folic acid electrode specifically recognized folate receptors. The modified electrode described here opens up new possibilities for future applications in early stage diagnoses of diseases where cells over-express folate receptors, such as in cancer or leishmaniasis disease.

**General information**

State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics, Universidad Industrial de Santander
Authors: Castillo, J. J. (Intern), Svendsen, W. E. (Intern), Rozlosnik, N. (Intern), Escobar, P. (Ekstern), Martinez, F. (Ekstern), Castillo-León, J. (Intern)
Pages: 1026-1031
Publication date: 2013
Main Research Area: Technical/natural sciences

**Publication information**

Journal: Analyst
Volume: 138
ISSN (Print): 0003-2654
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.8
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.92
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.11
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.88
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): CiteScore 4.16
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Web of Science (2008): Indexed yes
Web of Science (2007): Indexed yes
Web of Science (2006): Indexed yes
Web of Science (2005): Indexed yes
Web of Science (2004): Indexed yes
Web of Science (2003): Indexed yes
Web of Science (2002): Indexed yes
Web of Science (2001): Indexed yes
Dielectrophoretic manipulation and solubility of protein nanofibrils formed from crude crystallins

Protein nanofibrils and nanotubes are now widely accepted as having potential for use in the field of bionanotechnology. For this to be a feasible alternative to existing technologies, there is a need for a commercially viable source. Previous work has identified amyloid fibrils formed from crude crystallin proteins as such a source, since these fibrils can be produced in large quantities at a low cost. Applications include use of fibrils as templates for the formation of nanowires or as biosensing scaffolds. There remains a number of practical considerations, such as stability and the ability to control their arrangement. In this study, crude crystallin amyloid fibrils are shown to be stable in a range of biological and clean room solvents, with the fibril presence confirmed by transmission electron microscopy and the thioflavin T fluorescent assay. The fibrils were also immobilised between microelectrodes using dielectrophoresis, which enabled the recording of I–V curves for small numbers of fibrils. This investigation showed the fibrils to have low conductivity, with current values in the range of 10–10 A recorded. This low conductivity could be increased through modification, or alternately, the fibrils could be used unmodified for applications where they can act as templates or high surface area nanoscaffolds.

General information
State: Published
Organisations: Nano Bio Integrated Systems, Department of Micro- and Nanotechnology, University of Canterbury
Authors: Domigan, L. (Ekstern), Andersen, K. B. (Intern), Sasso, L. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern), Gerrard, J. A. (Ekstern), Castillo, J. (Intern)
Pages: 1105-1112
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Electrophoresis
Volume: 34
Issue number: 7
ISSN (Print): 0173-0835
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 0.703 SJR 0.745 CiteScore 2.4
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.64 SJR 0.848 SNIP 0.773
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): SJR 0.847 SNIP 0.812 CiteScore 2.53
BFI (2014): BFI-level 1
Scopus rating (2014): SJR 1.054 SNIP 0.884 CiteScore 2.88
BFI (2013): BFI-level 1
Scopus rating (2013): SJR 1.152 SNIP 0.987 CiteScore 3.13
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): SJR 1.361 SNIP 0.98 CiteScore 3.24
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Scopus rating (2011): SJR 1.527 SNIP 0.923 CiteScore 3.17
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 1
Scopus rating (2010): SJR 1.598 SNIP 0.928
DNA hybridization sensing for cytogenetic analysis

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

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

A surface modification of interdigitated gold microelectrodes (IDEs) with a doped polypyrrole (PPy) film for detection of dopamine released from populations of differentiated PC12 cells is presented. A thin PPy layer was potentiostatically electropolymerized from an 10 aqueous pyrrole solution onto electrode surfaces. The conducting polymer film was doped during electropolymerization by introducing counter ions in the monomer solution. Several counter ions were tested and the resulting electrode modifications were characterized electrochemically to find the optimal dopant that increases sensitivity in dopamine detection. Overoxidation of the PPy films was shown to contribute to a significant enhancement in sensitivity to dopamine. The changes caused by overoxidation in the electrochemical behavior and electrode morphology were investigated using cyclic voltammetry and SEM as well as AFM, respectively. The optimal dopant for dopamine detection was found to be polystyrenesulfonate anion (PSS-15 ). Rat pheochromocytoma (PC12) cells, a suitable model to study exocytotic dopamine release, were differentiated on IDEs functionalized with an overoxidized PSS--doped PPy film. The modified electrodes were used to amperometrically detect dopamine released by populations of cells upon triggering cellular exocytosis with an elevated K+ concentration. A comparison between the generated current on bare gold electrodes and gold electrodes modified with overoxidized doped PPy illustrates the clear advantage of the modification, yielding 2.6-fold signal amplification. The results also illustrate how to use cell population based dopamine exocytosis measurements to obtain biologically significant information that can be relevant in, for instance, the study of neural stem cell differentiation into dopaminergic neurons.

General Information

State: Published
Organisations: Nano Bio Integrated Systems, Department of Micro- and Nanotechnology, Bioanalytics, Technical University of Denmark, University of Genoa, Politecnico di Milano
Pages: 3651-3659
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication Information

Journal: Analyst
Volume: 138
ISSN (Print): 0003-2654
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 3.8
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 3.92
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.07
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 4.1
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 4.11
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 3.88
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 1
Exploring the properties and possibilities of self-assembling

The study (and potential application) of diphenylalanine peptide nanotubes is a popular topic that in recent years has experienced a boost in activity. This activity has been propelled forward by new articles continuously being published presenting even more spectacular properties of the nanotube structures ranging from piezo electricity over semi conductance to fluorescence. If such peptide nanotubes could be controlled and incorporated in sensors such as a biological field effect transistor it would greatly reduce the fabrication costs while at the same time providing researchers with new and exciting possibilities. The major driving forces supporting the interest in the peptide nanotubes is the fast and simple assembly process combined with their remarkable stability towards alcohols, organic solvents, and biological analytes that was presented shortly after the self-assembling properties of the diphenylalanine peptide was reported. The self-assembly process of the peptide nanotubes is entropy driven relying solely on hydrophobic packing of the aminoacid side groups and - interactions of the phenyl rings as stabilizing entities. As such it seems surprising that the peptide nanotubes should be as stable as reported. In this work, a more detailed study has demonstrated that the peptide nanotubes dissolve in most liquids including water. Despite the solubility of the peptide nanotubes in most liquids they remain remarkable stable under bombardment with heavy ions in dry conditions. This makes the peptide nanotubes excellent candidates as a water soluble alternative to traditional photolithography masks. In the present work we have demonstrated a rapid and low cost fabrication of silicon nanowires, in which process the silicon nanowire was dened in a dry etching procedure masked by the peptide nanotubes. To utilize this fabrication approach a manipulation method capable of orienting the peptide nanotubes at wafer scale has been developed. Furthermore, we have demonstrated that the peptide nanotubes can be used as a lift off material for the fabrication of nanoslits in metal surfaces. The water solubility of the peptide nanotubes allow the patterning of polymer materials not compatible with the organic solvents (used to remove the photoresists in traditional microfabrication techniques). In the final part of the project we have demonstrated a rapid and mild fabrication of conducting polymer nanowire devices and illustrated their potential use as sensitive temperature sensor.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Andersen, K. B. (Intern), Svendsen, W. E. (Intern), Castillo, J. (Intern)
Number of pages: 101
Publication date: 2013

Publication information
Original language: English
Main Research Area: Technical/natural sciences
Electronic versions:
Exploring the properties and possibilities of self-assembling.pdf
Source: dtu
Source-ID: u::7547
Publication: Research › Ph.D. thesis – Annual report year: 2013
Fabrication and characterization of PEDOT nanowires based on self-assembled peptide nanotube lithography

In this article we demonstrate the use of self-assembled peptide nanotube structures as masking material in a rapid, mild and low cost fabrication of polymerized p-toluenesulfonate doped poly(3,4-ethylenedioxythiophene) (PEDOT:TsO) nanowire device. In this new fabrication approach the PEDOT:TsO nanowire avoids all contact with any organic solvents otherwise traditionally used in clean room fabrication. This can be achieved due to the intriguing properties of the self-assembled peptide nanotubes utilized as a dry etching mask for the patterning of the PEDOT:TsO nanowire. The peptide nanotubes, despite remaining stable during the reactive ion etching procedure, can be dissolved rapidly in water afterwards. The fabricated PEDOT:TsO nanowire devices exhibit excellent electrical characteristics. Finally, the potential of PEDOT:TsO nanowires as temperature sensors has been demonstrated and the high resolution of the sensor was illustrated.

General information
State: Published
Organisations: Nano Bio Integrated Systems, Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics
Authors: Andersen, K. B. (Intern), Christiansen, N. O. (Intern), Castillo, J. (Intern), Rozlosnik, N. (Intern), Svendsen, W. E. (Intern)
Pages: 1370–1375
Publication date: 2013
Main Research Area: Technical/natural sciences

Publication information
Journal: Organic Electronics
Volume: 14
Issue number: 5
ISSN (Print): 1566-1199
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.884 SJR 1.085 CiteScore 3.44
Web of Science (2017): Indexed Yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 3.4 SJR 1.081 SNIP 0.944
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 1.135 SNIP 1.082 CiteScore 3.6
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 1.346 SNIP 1.188 CiteScore 3.85
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 1.456 SNIP 1.268 CiteScore 3.94
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 1.955 SNIP 1.458 CiteScore 4.25
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 1.941 SNIP 1.466 CiteScore 4.09
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 2.028 SNIP 1.395
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 2.046 SNIP 1.268
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 2.217 SNIP 1.452
Web of Science (2008): Indexed yes
NanoKaryotyping: Application of Micro- and Nanotechnologies in Cytogenetics

Chromosome abnormalities, such as translocations may cause various genetic disorders and are also associated with hematological malignancies. Translocation is a rearrangement between two chromosome arms that results in two derivative chromosomes. The current detection methods such as karyotyping and FISH require a use of expensive
reagents and can only be performed in specialized laboratories. This PhD project aims at developing new strategies for point-of-care detection of chromosome translocations by applying micro- and nanotechnologies to increase the sensitivity. The project started with development of a microfluidic device for controlled chromosome spreading. The device, made in Topas®, was used to facilitate the evaporation of the fixative solution to achieve proper spreading. In the device we obtained a comparable spreading efficiency to the traditional methods but with reduced reagents volume.

To propose a new strategy for chromosome translocation detection we developed a double hybridisation assay. To detect the translocation it is necessary to determine that the two DNA sequences forming a derivative chromosome are connected, which is achieved by two subsequent hybridization steps. The first example of the translocation detection was presented on lab-on-a-disc using fluorescently labeled DNA fragments, representing the derivative chromosome. It allows for sorting of the DNA chromosomal fragments into separate compartments followed by translocation detection.

To allow for cheaper detection an electrical label-free approach has been investigated using silicon nanowires BioFETs, metallic and conductive polymer electrodes. We present here our findings regarding the DNA hybridisation sensing using these sensors. They showed an improved sensitivity and are all label-free, which makes them inexpensive candidates for a novel cytogenetic analysis as a replacement of standard techniques. The metallic electrodes as the most reliable were selected for further development of a complete device for translocation detection. We developed a setup enabling electrochemical measurements on a spinning lab-on-a-disc platform. An electrical swivel was used to provide reliable connections between the electrodes on a disc and a potentiostat. We have demonstrated the applicability of the setup to standard electrochemical techniques. Lab-on-a-chip devices are being constantly developed to improve the analysis at a reduced cost and time. The presented devices that were developed using microand nanotechnologies are label-free and due to their sensitivity show a potential to be applied to chromosome translocation analysis with an improved detection efficiency.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Kennedy Center
Authors: Kwasny, D. (Intern), Svendsen, W. E. (Intern), Tümer, Z. (Ekstern), Dimaki, M. (Intern)
Number of pages: 184
Publication date: 2013

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

Bibliographical note
PhD Thesis
Source: dtu
Source-ID: u::9650
Publication: Research › Ph.D. thesis – Annual report year: 2013

Non-covalent conjugates of single-walled carbon nanotubes and folic acid for interaction with cells overexpressing folate receptors
We here present a method to form a noncovalent conjugate of single-walled carbon nanotubes and folic acid aimed to interact with cells over-expressing folate receptors. The bonding was obtained without covalent chemical functionalization using a simple, rapid "one pot" synthesis method. The zeta potential for the single-walled carbon nanotube–folic acid solution was _32.4 mV at pH 7.0 and the result indicates that the folic acid coating inhibited aggregation of the carbon nanotubes. Properties of the single-walled carbon nanotube–folic acid conjugate were analyzed using ultraviolet-visible, fluorescence and Raman spectroscopies. While the folic acid fluorescence signature was significantly quenched by the presence of single-walled carbon nanotubes, the Raman spectra of the conjugate displayed a decreased distribution of sp3 sites. Both results were attributed to the noncovalent functionalization of the single-walled carbon nanotubes with folic acid. A more detailed investigation of the single-walled carbon nanotube–folic acid conjugates utilizing scanning electron microscopy, atomic force microscopy and energy-dispersive X-ray spectroscopy confirmed the presence of the well-defined folic acid coating on the individual single-walled carbon nanotubes. The single-walled carbon nanotube–folic acid conjugates were incubated with THP-1 cells and the internalization was evaluated by Giemsa staining with light microscopy, and cytotoxicity was evaluated using the MTT reduction assay. The cytotoxicity studies presented a low toxicity of the conjugates in the THP-1 cells. The low toxicity and the cellular uptake of single-walled carbon nanotube–folic acid by cancer cells suggest their potential use in carbon nanotube-based drug delivery systems and in the diagnosis of cancer or tropical diseases such as leishmaniasis.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Polymer Microsystems for Medical Diagnostics, Nanoprobes, Universidad Industrial de Santander
Novel fabrication method of conductive polymer nanowires for sensor applications

In this work we demonstrate a new, quick and low cost fabrication of PEDOT:TsO nanowires using self-assembled peptide nanotubes as a masking material. The peptide nanotubes show a remarkably stability during reactive ion etching and can be dissolved in water afterwards. We have shown that the impedance of the nanowire is changing with backgating the wire, this gives promising possibility for application as a sensor.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Polymer Microsystems for Medical Diagnostics, Nano Bio Integrated Systems
Authors: Christiansen, N. O. (Intern), Andersen, K. B. (Intern), Castillo, J. (Intern), Svendsen, W. E. (Intern), Rozlosnik, N. (Intern)
Pages: 458-461
Publication date: 2013
Translating silicon nanowire BioFET sensor-technology to embedded point-of-care medical diagnostics

**General information**
- **State**: Published
- **Organisations**: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
- **Authors**: Pfreundt, A. (Intern), Zulfiqar, A. (Intern), Andresen, L. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern)
- **Publication date**: 2013
- **Event**: Poster session presented at The Gordon Research Conference on the Physics and Chemistry of Microfluidics, Lucca, Italy.
- **Main Research Area**: Technical/natural sciences
- **Electronic versions**: Poster_GRC_Microfluidics2013.pdf
- **Source**: PublicationPreSubmission
- **Source-ID**: 101678063
- **Publication**: Research - peer-review › Poster – Annual report year: 2014

**Translating silicon nanowire BioFET sensor-technology to embedded point-of-care medical diagnostics**

Silicon nanowire and nanoribbon biosensors have shown great promise in the detection of biomarkers at very low concentrations. Their high sensitivity makes them ideal candidates for use in early-stage medical diagnostics and further disease monitoring where low amounts of biomarkers need to be detected. However, in order to translate this technology from the bench to the bedside, a number of key issues need to be taken into consideration: Integrating nanobiosensors-based technology requires to overcome the difficult tradeoff between imperatives for high device reproducibility and associated rising fabrication costs. Also the translation of nano-scale sensor technology into daily-use point-of-care devices requires acknowledgement of the end-user requirements, making device portability and human-interfacing a focus point in device development. Sample handling or purification for instance, should be addressed in an automated way. Here, we are presenting the concept of a polysilicon nanoribbon sensor array integrated with multiplexed microfluidic functionalization, automated calibration and sample handling for flexible diagnostics from finger prick blood samples.

Functionalization of the sensor surface is performed in a controlled microfluidic environment and can be monitored in real-time to ensure reproducible results. In a simple temporary PDMS device, multiple parallel pathways enable straightforward selective functionalization for different biomarkers. Common diagnostic essays, which require a specific set of biomarkers to be identified and quantified simultaneously, can thus be readily translated onto this platform. After hydrogen termination of the silicon surface an alkyne monolayer is formed based on a hydrosilylation process. Antibodies and other receptor proteins can then be immobilized in a parallel manner without the use of a spotting system using various chemistries depending on the chosen headgroup in the monolayer. The system is designed to work with a single tube at the outlet and is able to mix and deliver immobilization reactants and antibody solution as well as washing buffer to the sensor surface.

**General information**
- **State**: Published
- **Organisations**: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
- **Authors**: Pfreundt, A. (Intern), Zulfiqar, A. (Intern), Patou, F. (Intern), Andresen, L. (Intern), Dimaki, M. (Intern), Svendsen, W. E. (Intern)
- **Publication date**: 2013
- **Host publication information**
  - **Title of host publication**: Proceedings of The Gordon Research Conference on the Physics and Chemistry of Microfluidics
  - **Main Research Area**: Technical/natural sciences
  - **Conference**: The Gordon Research Conference on the Physics and Chemistry of Microfluidics, Lucca, Italy, 09/06/2013 - 09/06/2013
  - **Source**: PublicationPreSubmission
  - **Source-ID**: 101678057
  - **Publication**: Research › Conference abstract in proceedings – Annual report year: 2014

**Alignment and Use of Self-Assembled Peptide Nanotubes as Dry-Etching Mask**

Self-assembled diphenylalanine peptide nanotubes provide a means of achieving nanostructured materials in a very simple and fast way. Recent discoveries have shown that this unique material, in addition to remaining stable under dry conditions, rapidly dissolves in water making it a promising candidate for controlled nanofabrication without organic solvents. The present work demonstrates how this unique structure can be aligned, manipulated and used as both an etching mask in a dry etching procedure and as a lift-off material. As a further demonstration of the
potential of this technique, the peptide nanotubes were utilized to fabricate silicon nanowire devices and gold nanoslits in a rapid manner.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Andersen, K. B. (Intern), Castillo, J. (Intern), Bakmand, T. (Intern), Svendsen, W. E. (Intern)
Number of pages: 5
Publication date: 20 Jun 2012
Main Research Area: Technical/natural sciences

Publication information
Volume: 51
ISSN (Print): 0021-4922
Ratings:
Web of Science (2018): Indexed yes
Scopus rating (2017): CiteScore 1.13 SJR 0.497 SNIP 0.668
Web of Science (2017): Indexed Yes
Scopus rating (2016): CiteScore 0.67 SJR 0.497 SNIP 0.768
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 0.426 SNIP 0.682 CiteScore 0.58
Scopus rating (2014): SJR 0.209 SNIP 0.189 CiteScore 0.73
Scopus rating (2013): SJR 0.111 SNIP 0 CiteScore 0.65
ISI indexed (2013): ISI indexed no
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 0.151 SNIP 0.171 CiteScore 0.7
ISI indexed (2012): ISI indexed no
Scopus rating (2011): SJR 0.61 SNIP 1.476 CiteScore 0.94
ISI indexed (2011): ISI indexed no
Scopus rating (2010): SJR 0.574 SNIP 1.066
Scopus rating (2009): SJR 0.585 SNIP 1.039
Scopus rating (2008): SJR 0.764 SNIP 0.689
Scopus rating (2007): SJR 0.858 SNIP 0.877
Scopus rating (2006): SJR 0.829 SNIP 0.969
Scopus rating (2005): SJR 0.764 SNIP 0.889
Scopus rating (2004): SJR 0.842 SNIP 0.998
Scopus rating (2003): SJR 0.92 SNIP 0.994
Scopus rating (2002): SJR 0.961 SNIP 1.134
Scopus rating (2001): SJR 1.061 SNIP 1.013
Web of Science (2001): Indexed yes
Scopus rating (2000): SJR 1.105 SNIP 0.916
Scopus rating (1999): SJR 1.166 SNIP 1.044
Original language: English
DOIs:
10.1143/JJAP.51.06FF13
Source: dtu
Source-ID: u::4016
Publication: Research - peer-review › Journal article – Annual report year: 2012

Advanced microtechnologies for cytogenetic analysis
Cytogenetic and molecular cytogenetic analyses, which aim to detect chromosome abnormalities, are routinely performed in cytogenetic laboratories all over the world. Traditional cytogenetic studies are performed by analyzing the banding pattern of chromosomes, and are complemented by molecular cytogenetic techniques such as fluorescent in situ hybridization (FISH). To improve FISH application in cytogenetic analysis the issues with long experimental time, high volumes of expensive reagents and requirement for trained technicians need to be addressed. The protocol has recently evolved towards on chip detection of chromosome abnormalities with the development of microsystems for FISH analysis. The challenges addressed by the developed microsystems are mainly the automation of the assay performance, reduction in probe volume, as well as reduction of assay time. We present here our efforts to introduce automation in the cytogenetic laboratories at a microscale. We have developed membrane based micro perfusion systems capable of expansion of
lymphocytes in a shorter time and at a smaller scale. The simulated and experimental results show very efficient exchange of the growth medium to the hypotonic solution and fixative. These are commonly used solutions required for proper preparation of a metaphase chromosomes analysis. Further we developed a microfluidic chip for preparation of metaphase chromosome spreads and their analysis by metaphase FISH on chip. All developed devices are capable of performing the entire metaphase FISH protocol in a shorter time and at the same quality as standard methods.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Kennedy Center, University of Copenhagen
Number of pages: 1
Publication date: 2012
Event:
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::6275
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

All-polymer microfluidic device for metaphase FISH on chip

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Kennedy Center
Number of pages: 1
Publication date: 2012
Event: Abstract from Lab on a Chip European Congress 2012, Edinburgh, United Kingdom.
Main Research Area: Technical/natural sciences

Bibliographical note
Poster presentation at Lab on a Chip Conference Edinburgh, 2012
Source: dtu
Source-ID: u::6274
Publication: Research - peer-review › Conference abstract for conference – Annual report year: 2012

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

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

Publication information
Journal: Lab on a Chip
Volume: 12
Compact potentiostat for cellular electrochemical imaging with 54 parallel channels

A novel potentiostat containing 54 current amplifiers matched to an array of custom-fabricated 5μm microelectrodes for electrochemical imaging of released neurotransmitters is presented. The board is integrated with a programmable microfluidic cell culture system and the whole assembly is thin and compact enough to be placed under the objective of a standard microscope for simultaneous optical and electrochemical monitoring. Each channel, scanned every 54μs, features 3pA current resolution over a 5kHz bandwidth, suitable for detecting single exocytotic events. The design and electrical characterization of the system are reported together with its functionality, certified by a 54-pixel electrochemical imaging of the diffusion of a 10μl droplet of a target analyte inside the cell culture chamber.

Electrochemical evaluation of dopamine detection on pyrolysed carbon and gold electrodes

Fabrication of 3D nano/microelectrodes via two-photon-polymerization

The integration of two-photon polymerization technology with standard microfabrication techniques is imperative for the use of this tool in micro- and nanotechnology and especially for the future commercialization of the technology. In this work, we report a novel method for the fabrication of 3D polymeric structures via a two-photon polymerization based system. The method consists of combining a two-photon polymerization system with conventional photolithography techniques in order to create 3D polymer electrodes. The functionality of the final structures was confirmed by electrochemical characterization techniques.
Fabrication of high-aspect ratio SU-8 micropillar arrays

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

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Nanoprobes, Nano Bio Integrated Systems
Authors: Amato, L. (Intern), Keller, S. S. (Intern), Heiskanen, A. (Intern), Dimaki, M. (Intern), Emnéus, J. (Intern), Boisen, A. (Intern), Tenje, M. (Intern)
Pages: 483-487
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: Microelectronic Engineering
Volume: 98
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604 CiteScore 1.87
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.737 SNIP 0.949 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Fabrication of single vertically aligned carbon nanotubes for cellular electrochemistry

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Molecular Windows, Nano Bio Integrated Systems, Bioanalytics, Technical University of Denmark
Publication date: 2012
Main Research Area: Technical/natural sciences
Electronic versions:
Fabrication of single vertically aligned carbon nanotubes for cellular electrochemistry.pdf
Source: dtu
Source-ID: u::10313
Publication: Research - peer-review › Poster – Annual report year: 2013

Label Free Chromosome Translocation Detection with Silicon nanowires
HROMOSOME translocation, which is a rearrangement of arms between two chromosomes, is a major group of chromosome abnormalities leading to cancer. As a result, two derivative chromosomes with sequences coming from both chromosomes are formed. The current translocation detection method is a Fluorescent In Situ Hybridization, which is laborious and involves use of expensive reagents [1]. Here we present a label free technique for detection of chromosome
translocations. As a proof of concept detection of chromosome translocation between chromosome 3 (Chr3) and chromosome 9 (Chr9) was chosen.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Surface Engineering, Kennedy Center, University of Copenhagen
Authors: Kwasny, D. (Intern), Andersen, K. B. (Intern), Frøhling, K. B. (Intern), Silahtaroglu, A. (Forskerdatabase), Tumer, Z. (Eksterm), Castillo, J. (Intern), Svendsen, W. E. (Intern)
Number of pages: 1
Publication date: 2012
Event: Poster session presented at EMBS Micro- and Nanoengineering Conference, Ka'anapali, United States.
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::6273
Publication: Research - peer-review › Poster – Annual report year: 2012

Lab-on-Chip Silicon nanowire biosensors, for biomedical applications

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Pedersen, L. G. (Intern), Zulfiqar, A. (Intern), Pfreundt, A. (Intern), Andresen, L. (Intern), Svendsen, W. E. (Intern)
Number of pages: 2
Publication date: 2012
Event: Poster session presented at III International Workshop on Analytical Miniaturization and NANOtechnologies, Barcelona, Spain.
Main Research Area: Technical/natural sciences
Electronic versions:
NANO_WAM_poster_final.pdf
Source: PublicationPreSubmission
Source-ID: 101678142
Publication: Research - peer-review › Poster – Annual report year: 2012

Host publication information
Title of host publication: Proceedings of WAM-Nano 2012
Main Research Area: Technical/natural sciences
Workshop: III International Workshop on Analytical Miniaturization and NANOtechnologies, Barcelona, Spain, 11/06/2012 - 11/06/2012

Electronic versions:
WAM_NANO2012_poster_abstradt_SiNW_LS1.pdf
Source: PublicationPreSubmission
Source-ID: 101678137

Publication: Research - peer-review › Conference abstract in proceedings – Annual report year: 2012

Micro device for multiple disease diagnostic and monitoring

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Office for Study Programmes and Student Affairs
Number of pages: 1
Publication date: 2012
Microfluidic System for Long Term Culturing of Organotypic Brain Tissue

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Authors: Bakmand, T. (Intern), Sørensen, A. R. (Ekstern), Andersen, K. B. (Intern), Sasso, L. (Intern), Svendsen, W. E. (Intern)
Number of pages: 1
Publication date: 2012

**Host publication information**
Title of host publication: Proceedings of the IEEE-EMBS Micro and Nanotechnology in Medicine Conference
Main Research Area: Technical/natural sciences
Conference: IEEE-EMBS Micro and Nanotechnology in Medicine Conference, Maui, United States, 03/12/2012 - 03/12/2012
Electronic versions:
MNMC2012_Bakmand.pdf
Source: PublicationPreSubmission
Source-ID: 101565408

Microfluidic System With Capillary Burst Valves For Detection Of Chromosomal Translocations

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nanoprobes, Nano Bio Integrated Systems
Authors: Brøgger, A. L. (Intern), Kwasny, D. (Intern), Bosco, F. (Intern), Boisen, A. (Intern), Svendsen, W. E. (Intern)
Publication date: 2012

**Host publication information**
Title of host publication: Proceedings of the IEEE-EMBS Micro and Nanotechnology in Medicine Conference
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::6276

Microtechnologies Enable Cytogenetics

**General information**
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems
Pages: 25-40
Publication date: 2012
Monitoring The Functionalization Of Single Walled Carbon Nanotubes With Chitosan And Folic Acid By Two Dimensional Diffusion Ordered NMR Spectroscopy

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Universidad Industrial de Santander
Authors: Castillo, J. J. (Ekstern), Torres, M. H. (Ekstern), Molina, D. R. (Ekstern), León, J. J. C. (Intern), Svendsen, W. E. (Intern), Escobar, P. (Ekstern), Martínez, F. (Ekstern)
Publication date: 2012
Event: Poster session presented at 3rd Symposium on Graphene and Carbon Nanotubes, Copenhagen, Denmark.
Main Research Area: Technical/natural sciences
Single Walled Carbon Nanotube Folic Acid, 2D DOSY Spectroscopy, Diffusion Coefficient
Publication: Research - peer-review › Poster – Annual report year: 2012

Multichannel Bipotentiostat Integrated With a Microfluidic Platform for Electrochemical Real-Time Monitoring of Cell Cultures
An electrochemical detection system specifically designed for multi-parameter real-time monitoring of stem cell culturing/differentiation in a microfluidic system is presented. It is composed of a very compact 24-channel electronic board, compatible with arrays of microelectrodes and coupled to a microfluidic cell culture system. A versatile data acquisition software enables performing amperometry, cyclic voltammetry and impedance spectroscopy in each of the 12 independent chambers over a 100 kHz bandwidth with current resolution down to 5 pA for 100 ms measuring time. The design of the platform, its realization and experimental characterization are reported, with emphasis on the analysis of impact of input capacitance (i.e., microelectrode size) and microfluidic pump operation on current noise. Programmable sequences of successive injections of analytes (ferricyanide and dopamine) and rinsing buffer solution as well as the impedimetric continuous tracking for seven days of the proliferation of a colony of PC12 cells are successfully demonstrated.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Bioanalytics, Fluidic Array Systems and Technology, Nano Bio Integrated Systems, Università Degli Studi Di Genova, University of Potsdam, Politecnico di Milano
Pages: 498-507
Publication date: 2012
Main Research Area: Technical/natural sciences

Publication information
Journal: IEEE Transactions on Biomedical Circuits and Systems
Volume: 6
Issue number: 5
ISSN (Print): 1932-4545
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): SNIP 1.786 SJR 0.865 CiteScore 4.06
Web of Science (2017): Indexed Yes
Novel 3D microelectrodes and pipettes by wet and dry etching

The purpose of this work is to develop novel 3D micro- and nanoelectrodes and pipettes by use of carefully optimised standard microfabrication techniques such as wet (by KOH) and dry silicon etching. Two types of electrodes have been fabricated and characterized: small nanoelectrodes to be used for localised measurements on cell cultures and high aspect ratio scalloped microelectrodes for measurements in brain slices. This paper presents improved fabrication processes for both types of electrodes and the pipettes, as well as the electrical and electrochemical characterization of the small electrodes in order to confirm their functionality. Although functional, an increase in the electrode surface area is needed if they are to be used for electrophysiological measurements. Finally, the pipettes fabricated have openings of the order of 500nm, which makes them ideal candidates for localised stimulation of cell or brain slice cultures.
On-chip cell viability studies using label-free impedance detection

General information
State: Published
Organisations: Office for Study Programmes and Student Affairs, Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Slovak Academy of Sciences
Number of pages: 1
Publication date: 2012
Event: Poster session presented at III International Workshop on Analytical Miniaturization and NANOtechnologies, Barcelona, Spain.
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::6278
Publication: Research - peer-review › Poster – Annual report year: 2012

Rapid Fabrication of Silicon Nanowires Using Self-Assembled Diphenylalanine Peptide Nanostructures

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Surface Engineering
Authors: Kwasny, D. (Intern), Frøhling, K. B. (Intern), Andersen, K. B. (Intern)
Number of pages: 1
Publication date: 2012
Event: Poster session presented at III International Workshop on Analytical Miniaturization and NANOtechnologies, Barcelona, Spain.
Main Research Area: Technical/natural sciences
Source: dtu
Source-ID: u::6277
Publication: Research - peer-review › Poster – Annual report year: 2012

Reactive ion etching of polymer materials for an energy harvesting device
In this paper, we have demonstrated deep reactive ion etching (RIE) of two MEMS compatible polymer materials CYTOP and TOPAS, which may be useful for energy harvesting devices. The CYTOP polymer was patterned and used as the electret for the following corona charging while the TOPAS polymer was used as the wafer bonding material. Three mask materials (Al, photoresist and Si) were investigated for the RIE process. Grass effect was observed for both polymers when Al was used as the etching mask. With an optimized RIE recipe, a 1.5μm-thick photoresist layer served well as an etching mask for 11μm-thick CYTOP and a high selectivity of 9 was achieved. The CYTOP polymer was corona charged with target surface potential after patterning. Wafer-level bonding between CYTOP and TOPAS polymers was successfully performed with a low temperature thermo-compression bonding technique.

General information
State: Published
Organisations: Department of Micro- and Nanotechnology, Nano Bio Integrated Systems, Center for Individual Nanoparticle Functionality, Technical University of Denmark
Authors: Wang, F. (Intern), Bertelsen, C. V. (Intern), Skands, G. (Ekstern), Pedersen, T. (Intern), Hansen, O. (Intern)
Pages: 227-230
Publication date: 2012
Main Research Area: Technical/natural sciences
Publication information
Journal: Microelectronic Engineering
Volume: 97
ISSN (Print): 0167-9317
Ratings:
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Scopus rating (2017): SNIP 0.937 SJR 0.604 CiteScore 1.87
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 1.69 SJR 0.589 SNIP 0.949
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 2
Scopus rating (2015): SJR 0.507 SNIP 0.796 CiteScore 1.35
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 2
Scopus rating (2014): SJR 0.586 SNIP 0.86 CiteScore 1.44
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 2
Scopus rating (2013): SJR 0.595 SNIP 0.964 CiteScore 1.45
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): SJR 0.737 SNIP 0.949 CiteScore 1.44
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): SJR 0.813 SNIP 1.148 CiteScore 1.8
ISI indexed (2011): ISI indexed yes
Web of Science (2011): Indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 0.934 SNIP 1.093
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 1
Scopus rating (2009): SJR 0.834 SNIP 1.098
Web of Science (2009): Indexed yes
BFI (2008): BFI-level 1
Scopus rating (2008): SJR 1.027 SNIP 1.06
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 1.045 SNIP 1.138
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 0.966 SNIP 1.093
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 0.952 SNIP 0.989
Web of Science (2005): Indexed yes
Scopus rating (2004): SJR 1 SNIP 1.1
Web of Science (2004): Indexed yes
Scopus rating (2003): SJR 0.812 SNIP 0.956
Web of Science (2003): Indexed yes
Scopus rating (2002): SJR 0.712 SNIP 0.711
Scopus rating (2001): SJR 0.558 SNIP 0.645
Scopus rating (2000): SJR 0.502 SNIP 0.568
Web of Science (2000): Indexed yes
Scopus rating (1999): SJR 0.595 SNIP 0.555
Original language: English
Energy harvesting, Reactive ion etching, Polymer electret, Wafer bonding
DOIs:
10.1016/j.mee.2012.03.016
Source: dtu
Source-ID: n:oai:DTIC-ART:elsevier/368171921::18936
Publication: Research - peer-review › Journal article – Annual report year: 2012
Vertically aligned patterned peptide nanowires for cellular studies

Over the years, scientific studies have shown that one crucial point when designing biological platforms is the strict environmental conditions required for cell and tissue culturing, such as pH, temperature, medium content and other parameters which affect the system's biocompatibility. Because of these constraints, biological-based substrates such as self-assembled peptide nanostructures make an excellent candidate as a material, due to the inherent properties they hold, such as mechanical and chemical stability, various functionalization options, and mild, fast and cheap synthesis conditions. Recently, our group has demonstrated that vertically aligned diphenylalanine based peptide nanowires (VAPNW) are an useful tool for cellular studies and sensor applications. To expand this study, we patterned VAPNWs into strips of various widths onto an electrode surface to evaluate these structures’ effects on cell growth and adherence using PC12 cells, which are neuronal stem cell models. With this method we are able to obtain important information about the cells’ preference for culture substrate, comparing the adhesion of cells to a forest of VAPNWs with standard protein substrate enhancers such as laminine. Combining this work with other approaches like discrete functionalization of VAPNWs will reveal possible future tools for cellular studies and biosensing.
microorganisms. As glyphosate led to the appearance of resistant species, the pesticide was used more intensively. As a consequence of the heavy use of glyphosate, residues of this compound are increasingly observed in food and water. Recent studies reported a direct link between glyphosate and chronic effects such as teratogenic, tumorigenic and hepatorenal effects although the exposure was below the lowest regulatory limit. Today, pesticides are detected in water by complicated and costly manual procedures conducted by highly skilled personnel. It can take up to several days to get an answer regarding the pesticide content in water. An alternative to this demanding procedure is offered by electrochemical measuring techniques. Electrochemistry is an emerging technology that has the potential of identifying and quantifying several compounds in few minutes. It is currently not possible to detect glyphosate directly in water samples, and intensive research is underway to enable direct selective and quantitative detection of glyphosate in water. This study focuses on developing and modifying a sensor chip that has the ability to selectively measure glyphosate and minimize the signal interference from other compounds. The sensor is a silicon-based chip that is fabricated in a cleanroom facility with dimensions of 10×20 mm. The chip is comprised of a three-electrode configuration. The deposited electrodes consist of a 20 nm layer chromium and 200 nm gold. The working electrode is 4 mm in diameter. The working electrodes are modified by creating molecularly imprinted polymers (MIP) using electrodeposition technique that allows the chip to selectively measure glyphosate at low concentrations. The modification included using gold nanoparticles with a diameter of 10 nm functionalized with 4-aminophenol. This configuration allows the nanoparticles to bind to the working electrode surface and create the template for the glyphosate. The chip was modified using electrodeposition technique. An initial potential for the identification of glyphosate was estimated to be around -0.2 V. The developed sensor was used on 6 different concentrations and it was able to detect glyphosate down to 0.5 mgL⁻¹. This value is below the accepted pesticide limit of 0.7 mgL⁻¹ set by the US regulation. The current focus is to optimize the functionalizing procedure in order to achieve glyphosate detection at the EU regulatory limit of 0.1 µgL⁻¹. To the best of our knowledge, this is the first attempt to modify miniaturized sensor electrodes with functionalized nanoparticles for glyphosate detection.

Degree of recognition: International
Links:
http://dai.waset.org/1307-6892/80426

Related event
20th International Conference on Water Management
16/04/2018 → 17/04/2018
Activity: Talks and presentations › Conference presentations

Microfluidics Congress 2015
Maria Dimaki (Participant)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems
Description
Poster presentation at Microfluidics Congress

Related event
Microfluidics Congress 2015
20/10/2015 → 21/10/2015
London, United Kingdom
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

A Smart Mobile Lab-on-Chip-Based Medical Diagnostics System Architecture Designed For Evolvability
Period: 27 Aug 2015
François Patou (Speaker)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems
Department of Applied Mathematics and Computer Science
Description
Oral presentation

Related event
Digital Systems Design 2015: Special Session on Advanced Systems for Healthcare, Sports and Wellness
26/08/2015 → 28/08/2015
Funchal, Portugal
Activity: Talks and presentations › Conference presentations

**4th International Workshop on Analytical Miniaturization and NANOtechnologies**
Period: 23 Jun 2014 → 24 Jun 2014
Maria Dimaki (Participant)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

**Description**
Lab-on-a-chip system for virus detection in water, Poster

**Related event**

**4th International Workshop on Analytical Miniaturization and NANOtechnologies**
23/06/2014 → 24/06/2014
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising workshops, courses, seminars etc.

**3rd Symposium on Graphene and Carbon Nanotubes**
Jaime Castillo (Participant)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

**Description**
Poster presentation: Monitoring the functionalization of single-walled carbon nanotubes with chitosan and folic acid by two-dimensional diffusion-ordered NMR spectroscopy

**Related event**

**3rd Symposium on Graphene and Carbon Nanotubes**
25/06/2012 → 26/06/2012
Copenhagen, Denmark
Activity: Attending an event › Participating in or organising a conference

**Personalised Medicine**
Period: 18 Jun 2012
Jaime Castillo (Participant)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

**Description**
Poster presentation: Self-assembled Peptide and Protein Nanostructures in Diagnosis

**Related event**

**Personalised Medicine: Better Healthcare for the Future - A Rational Approach Focusing on Bioinformatics, Medicinal Chemistry and Medicine**
17/06/2012 → 22/06/2012
Larnaca, Cyprus
Activity: Attending an event › Participating in or organising a conference

**III International Workshop on Analytical Miniaturization and NANOtechnologies**
Period: 11 Jun 2012 → 12 Jun 2012
Jaime Castillo (Participant)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

Description
Poster presentation: Spin casting of self-assembled peptide nanotubes for cheap and fast cleanroom fabrication

Related event
III International Workshop on Analytical Miniaturization and NanoTechnologies
11/06/2012 → 12/06/2012
Barcelona, Spain
Activity: Attending an event › Participating in or organising a conference

Peptide nanostructures as scaffold for a SERS-based DNA biosensor
Jaime Castillo (Speaker)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems
Links:
http://www.biosensors-congress.elsevier.com/

Related event
22nd World Congress on Biosensors
15/05/2012 → 18/05/2012
Cancun, Mexico
Activity: Talks and presentations › Conference presentations

Self-assembled peptide nanostructures: A new alternative for the development of biosensors
Jaime Castillo (Speaker)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems
Links:
http://www.biosensors-congress.elsevier.com/

Related event
22nd World Congress on Biosensors
15/05/2012 → 18/05/2012
Cancun, Mexico
Activity: Talks and presentations › Conference presentations

Low Cost and Fast Clean Room Fabrication Techniques using Peptide Nanotubes
Period: 11 Dec 2011 → 15 Dec 2011
Jaime Castillo (Speaker)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

Related event
2nd Nano Today conference
11/12/2011 → 15/12/2011
Hawaii, United States
Activity: Talks and presentations › Conference presentations
Self-assembled peptide nanowires as multifunctional sensing platform for cellular studies
Period: 11 Dec 2011 → 15 Dec 2011
Jaime Castillo (Speaker)
Department of Micro- and Nanotechnology
Nano Bio Integrated Systems

Related event
2nd Nano Today conference
11/12/2011 → 15/12/2011
Hawaii, United States
Activity: Talks and presentations › Conference presentations