Biomaterial Interfaces
Room: Taos - Session BI+MN-FrM

Sensors & Fluidics for Biomedical Applications
Moderator: S.L. McArthur, Swinburne University of Technology, Australia

8:20am **BI+MN-FrM1 Release of Biomolecues from a Photovoltaic Device for Targeted Drug Delivery**, ***S.L. Ambure***, University of Texas at el Paso, *D. Terreros*, Texas Tech Univerity Health Sciences Center, *T. Xu*, University of Texas at el Paso

Introduction

An important goal of targeted drug delivery is to minimize the exposure of normal tissues to the drugs while maintaining their therapeutic concentration in diseased parts of the body. However, current methodologies are not yet ideal for such goal; therefore, new strategies for targeted drug delivery are needed. A photovoltaic device (PD) is a system that converts lights into electricity as well as induces charge transfer by photovoltaic effect. Motivated by such unique property, we have hypothesized that a PD can serve as a new drug delivery system to carry chemotherapeutic drugs and release them upon external photo stimulation, such as near Near-Infrared (NIR) light or Laser source. Taking advantage of repulsion between a photovoltaic device and a substance is proposed to serve as a new drug delivery method. In this study, we have investigated if the if the charged molecules can be effectively released from the PV device upon photon stimulation.

Methodology

As proof of principle, we have first experimented coating of commercially available photovoltaic devices with positively charged poly-l-lysine and negatively charged bovine serum albumin (BSA) tested the release of the molecules upon photo stimulation. These molecules were physically absorbed onto the surface of the PDs before exposed to an IR LED illuminator, which was used as an external light source. Moreover, the pure glass slide was used as a control of the device with non-photovoltaic effect for drug delivery.

Results and Discussion

During the series of experiments, we have found that, the PD has a capability to release the charged drugs by photovoltaic effect. Compared to no light stimulation, the positively charged poly-l-lysine and the negatively charged BSA when exposed to IR illuminator for 3 hours were released about 2.0 folds and 2.1 folds respectively. Moreover, in the control group (pure glass slide with no photovoltaic effect), there was no significant release of both poly-l-lysine and BSA when exposed to the IR illustrator.

Conclusion

These data showed that the new PD can effectively carry either positively or negative charged molecules on its surface and release them upon external photo stimulation, which suggests the PD has potential to be used as a new drug delivery system to carry cancer chemotherapeutic drugs. Further experiments are planned on the micro-fabricated photovoltaic devices (Size 300µm to 500 µm). With this project a new approach for targeted drug delivery with micro- photovoltaic devices will be developed.

(*Proprietary: an IP application based on this study is pending)

8:40am **BI+MN-FrM2 Enzymatic Activity Enhancement on Nano-structured TiO_2 Platforms by Ru doping for Biosensor Applications**, ***R.R. Pandey***, Centre for Cellular and Molecular Biology, India, *K.K. Saini*, National Physical Laboratory, India, *M. Dhayal*, Centre for Cellular and Molecular Biology, India

Devices based on nanomaterials platforms are emerging as a powerful tool for ultrasensitive sensors for the direct detection of biological and chemical species. In this work, we will report the preparation and the full characterization of Ru doped TiO2 nanostructured platforms those have been used for electrochemical detection of enzymatic activity for biosensor applications. Ru doped TiO2 platforms were prepared by sol-gel deposition onto conducting substrates and as test model cholesterol oxidase, urease and gucose oxidase were loaded onto the nanostructured platforms. Cholesterol /Urease/Glucose oxidase immobilized onto Ru doped TiO2-based nanostructured surfaces exhibited a pair of well-defined and quasireversible voltammetric peaks in CV measurements. The electron exchange between the enzyme and the electrodes was greatly enhanced in the Ru doped TiO2 nanostructured environment. The electrocatalytic activity of cholesterol, uresae and glucose oxidase embedded on Ru doped TiO2 electrodes had enhanced significantly toward detection of low concentrations of cholesterol, urea and glucose.

9:00am **BI+MN-FrM3 A Microfluidic Single Cell Isolation Device for Ensemble Measurements of Viral Hemorrhagic Fever Pathogenesis in Macrophages**, *M.W. Moorman, J.B. Ricken, R.F. Renzi, R.P. Manginell, C.S. Branda, O.A. Negrete,* ***C.D. James****, B.D. Carson*, Sandia National Laboratories **INVITED**

Arenaviruses are a particular class of viruses that cause lethal hemorrhagic fever in humans, and a fundamental problem in understanding their pathogenicity is that many effects of viral infection are not mediated directly by the virus itself (primary immune response) but by the response of the immune system (secondary immune response). Thus, population level experiments on cells make it difficult to elucidate the timing of signaling events during pathogenesis in order to lay the groundwork for improved antiviral therapeutics, vaccines, and biological countermeasures. Our objective here is to deconvolute the pathogenic response by isolating and infecting individual macrophage host cells followed by real-time measurements of response-critical cytokines. We have developed a microfluidic cell isolation platform that can trap up to 150 individual host cells in fluidically isolated microchambers. The chip design eliminates chamber-to-chamber fluidic communication, thus signaling molecules that are secreted from infected cells are prevented from interacting with uninfected cells. This configuration allows us to differentiate between primary and secondary immune response when compared to bulk cell population level studies. The chip is made with a three level reactive-ion etch process in silicon that produces trapping features that place cells adjacent to an anodically-bonded coverslip to permit high-resolution confocal imaging. The microfluidic device is operated with a custom pressure controller system that permits computer-controlled delivery and routing of up to 10 different reagents. Currently, we are using experimental and computational techniques to identify the mechanisms by which arenaviruses provoke lethal cytokine production in host cells. This is accomplished with a fluorescent reporter fusion construct that we developed to measure the cytoplasm-to-nucleus translocation dynamics of a transcription factor. This construct allows us to assess the early (< 1 hour) response of host cells to viral infection and when combined with a second reporter construct for real-time monitoring of cytokine induction, we are also able to monitor a late (>1 hour) immune response event. Initial studies using a viral mimic challenge showed oscillation of the transcription factor in and out of the nucleus over the first several hours of pathogen exposure, and a rapid 2X increase in cytokine induction over the first five hours post-infection. Future work will use a live Pichinde virus to examine transcription factor (NFkappaB) translocation and cytokine (TNFalpha, IFNbeta) induction dynamics.

9:40am **BI+MN-FrM5 Elastomeric Microparticles that Exhibit Negative Acoustic Contrast in Bioassays**, ***K.W. Cushing***, *M.E. Piyasena, B.A. Lopez, N. Carroll, T. Woods, D.N. Petsev, S. Graves*, University of New Mexico, *G.P. Lopez*, Duke University

The development of more sensitive and rapid medical assays is imperative to decreasing time-to-diagnosis in diseased state individuals, and thus to improving patient outcomes. Enhanced detection limits afford the ability to detect the presence of low concentrations of biomarkers that may be present during the early-onset stages of a disease. Reduction in sample preparation requirements can further decrease assay time and the expertise level of the user. Our research aims to develop a sensitive and rapid bioassay platform using elastomeric capture microparticles (ECµPs) coupled to an acoustic sample preparation chamber and a flow cytometer. ECµPs possess unique physical and mechanical properties enabling the separation of ligand-bound ECµPs from biological particles (e.g., red blood cells) within a collected fluid sample (e.g., whole blood) by placing them under acoustic pressure. ECµPs have acoustic properties (negative contrast) that allow their positioning separately from many biological particles, which typically exhibit positive contrast, (e.g., cells) within an acoustic pressure field. Hence, an in-line acoustic sample preparation instrument can be used to separate unwanted biological particles (along with interfering soluble molecules) from ligand-bound ECµPs within biological fluids, The acoustic field will also concentrate the ECµPs, and so combined with removal of unwanted biological particles, much higher analysis rates of ECµPs may be possible. Since the acoustic sample preparation system operates continuously and can be mounted to feed separated ECµPs directly into a flow cytometer, this approach may decrease sample preparation time. Our studies show that simple emulsion polymerization methods using commercially available silicone precursors can be used to easily form elastomeric microparticles that exhibit negative contrast.

10:00am **BI+MN-FrM6 Optimization of Biosensors using Selective Chemistry**, ***O. Seitz***, *P.G. Fernandes*, University of Texas at Dallas, *H.C. Wen*, Texas Instruments, Inc., *H.J. Stiegler, R.A. Chapman, E.M. Vogel, Y.J. Chabal*, University of Texas at Dallas

There is currently a strong need to develop sensitive and reliable biosensors, based on electronic detection, such as field-effect transistors (FET). Most of the focus has been on improving sensitivity by decreasing the FET channel size, using nanowires instead of similar devices on planar silicon. Issues of silicon functionalization, important for device reliability have been mostly ignored.

In this work, we present a robust approach to functionalize the channel region of a SOI wafer, thus achieving better reliability and sensitivity to very low analyte concentrations. The process leads to attachment of active SAM on oxide-free (H-terminated) silicon through formation of a Si-C bond on the channel. Combining IR absorption (IRAS) and X-ray photoelectron (XPS) spectroscopies, photoluminescence, atomic force microscopy (AFM) and electrical measurements, we find that this configuration results in a stable device where the active SAM is more strongly attached to the Si than silane molecules do on oxides. This functionalization is achieved by immersion in carboxylic acid (COOH)-terminated alkene molecules to functionalize the H-terminated channel. After processing, XPS and IRAS confirm that the channel remains oxide-free, that the packing of the SAM on the channel is dense. Photoluminescence measurements confirm the high quality of the interface on the channel where non-radiative recombination (interface states) is not detected. The AFM pictures confirm that active molecules attach to the channel (imaged by attachment of nanoparticles). Electrical measurements, on these improved devices, indicate excellent response for both pH and protein sensing with sensitivity at least as good as the one of similar structure with a uniform SAM functionalization (i.e. using oxidized Si channels).

10:20am **BI+MN-FrM7 Nanopatterned Pores on a Gel-supported Membrane For On-chip Sample Preparation in Surface Plasmon Resonance Sensing**, ***G.R. Marchesini***, Joint Research Centre, Italy, *S. Rebe Raz*, Wageningen University, the Netherlands, *M.G.E.G. Bremer*, RIKILT – Institute of Food Safety, *P. Colpo, G. Giudetti*, Joint Research Centre, Italy, *W. Norde*, Wageningen University, the Netherlands, *F. Rossi*, Joint Research Centre, Italy

We present a novel approach to tackle the most common drawback of using Surface Plasmon Resonance for analyte screening in complex biological matrices - the nonspecific binding to the sensor chip surface.

By using a perforated membrane supported by a polymeric gel structure that exceeds the evanescent wave penetration depth, we created a filter above the sensing region that prevents the diffusion of large particles or aggregates that bind non specifically to the polymeric gel and interfere with SPR sensing, thus increasing assay's sensitivity, reducing sample preparation steps and shortening the analysis time in total. A 10 nm thick non-fouling membrane with nanopatterned macropores was fabricated by means of colloidal lithography and plasma enhanced chemical vapor deposition of polyethylene oxide-like films. Such a membrane was supported by carboxymethyldextran, a polymeric gel matrix commonly used in surface plasmon resonance analysis. The surface was characterized using surface plasmon resonance imaging, contact angle, atomic force microscopy and scanning electron microscopy.

The performance of this surface in full fat milk and porcine serum was studied using an antibiotic detection immunoassay as a model system. Structurally, the 91.7 ± 14.7 nm diameter pores presented an hexagonal crystal lattice and a clearance of about 5 % of the total surface. Functionally, the nanopatterned macropores showed significant improvements in the quality of the obtained measurements in comparison to bare carboxymethyldextran, displaying 100 fold increase in the limit of detection of the enrofloxacin bioassay when performed in porcine serum.

10:40am **BI+MN-FrM8 Stability and Selectivity of Biorecognition Proteins Immobilized on Diamond Surfaces**, *R.J. Hamers*, ***C.J. Stavis***, University of Wisconsin-Madison, *A. Radadia, R. Brashir*, University of Illinois at Urbana-Champaign, *J.A. Carlisle*, Advanced Diamond Technologies, *W.P. King*, University of Illinois at Urbana-Champaign, *H. Zeng*, Advanced Diamond Technologies

The use proteins, such as antibodies, for the detection of target biological species in water supplies or with *in situ* medical diagnostics will require immobilization of these proteins on surfaces that resist non-specific adsorption and maintain the protein's activity over time. Ultrananocrystalline diamond (UNCD) thin films are a promising material that may address several major challenges for the next generation of biosensors including detection of cellular mass loading, stability throughout multiple uses and regenerations of the sensor surface, and use at elevated temperatures.

We are currently investigating the chemical functionalization of diamond thin films with antibodies for selective recognition and detection of biological cells, using E. coli as a model system. Infrared spectroscopy and X-ray photoelectron spectroscopy measurements have been performed to characterize the covalent attachment of antibodies to the surface and to quantitatively characterize the antibody surface attachment via the N(1s) and S(2p) levels. To determine the factors controlling selectivity and stability, we have performed time-dependent cell capture studies and have correlated the time-dependent changes in cell capture efficiency with corresponding measurements of the surface composition. These measurements are used to establish whether long-term stability and selectivity for biomolecular recognition is limited by loss of the ligands directly linked to the diamond substrate, by removal of the biological layer, or by alteration of the antibody structure. Infrared measurements of the Amide I band is particularly useful in characterizing changes in the antibody secondary structures. These studies provide important fundamental insights into the chemical factors that control biological interactions at surfaces and provide guidance on efforts to make ultra-stable biological sensing platforms.

11:00am **BI+MN-FrM9 Saturated Ionic Conductance at Low Electrolyte Concentration Through Solid-State Nanopores**, ***P. Waggoner***, *H. Peng, S. Harrer, B. Luan, S.M. Rossnagel*, IBM T.J. Watson Research Center

It has been observed that ion currents pass through biased nanopores in electrolyte solutions with bulk conduction properties until the concentration of ions decreases beyond a certain level. At this critical point, the conductance of the pores saturates at a constant value despite further decreasing the concentration of ions, an effect that has been attributed to charge shielding effects of surface charges within the pore. Below the critical concentration, the Debye length associated with screening the surface charges becomes larger and larger compared to the size of the pore and effectively cuts off bulk conduction. However, the conductance of the pore is not affected by the continuing growth of the space-charge region with the Debye length. In the following we present a model describing the nanopore-electrolyte system with an analytical solution that explains the experimentally observed behavior for five different salt solutions at low concentrations, including KCl, KCl in 50% glycerol, Tris-EDTA buffer, phosphate buffered saline, and $CaCl_2$. Conduction through the nanopore at low ion concentrations is analogous to hole extraction in reverse biased diodes and is related only to the diffusion of the minority carrier into the space charge region where it is then accelerated through the nanopore. These results also have important implications for solid-state nanopores being applied for DNA detection and sequencing technologies.

11:20am **BI+MN-FrM10 Fabrication of *in situ* Oligonucleotide Arrays by Inkjet Printing and their use in Gene Assembly**, ***I. Saaem***, *J. Tian*, Duke University

In our studies, we utilized an inkjet based *in situ* oligonucleotide synthesis platform that uses salvaged printheads from commercial printers. The platform utilizes standard four-step phosphoramidite chemistry with some modifications in order to synthesize oligonucleotides on functionalized substrates. A sensitive pressurization system is used to ensure print quality and an on-board vision system enables substrate registration and synthesis monitoring. Using this platform we synthesized oligonucleotide on prepatterned functionalized plastic slides. Such patterned substrates help in proper droplet formation and fluid mixing on the surface while mitigating satellite and irregular drops, which can lead to cumulative synthesis errors. Functional integrity of synthesized oligonucleotides was confirmed by hybridization with complementary strands. Being able to hot emboss microfluidic structures directly onto plastic slides in combination with the ability to generate arbitrary sequences provides diagnostic capabilities as well as the means to harvest pools of cheap oligonucleotides on demand. Importantly, our combination of technologies has allowed formation of genes and large DNA constructs by amplifying oligonucleotides off of the synthesized arrays and assembling them in the on-chip chambers.

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