Biomaterial Interfaces
Room 2014 - Session BI+MN-TuA

Microfluidics, MEMS, Lab-on-Chip
Moderator: M. Lochhead, Accelr8 Technology Corporation

2:00pm **BI+MN-TuA1 Disposable Molecular Diagnostics: Microfluidic Laboratories for the Field**, ***C.M. Klapperich,*** Boston University **INVITED**
The impact of infectious disease on resource poor areas of the world is devastating. It is unlikely that the financial climate surrounding drug development for diseases prevalent in third world countries will soon change. Our best approach at dealing with some of these diseases will be prevention efforts assisted by the widespread availability of inexpensive and accurate diagnostics. Probes to amplify and identify microbial or viral nucleic acids are available for almost every well known disease vector. Assays for serum antibodies to many organisms are also well documented. Dedicated engineering of test protocols (patient sample preparation, dilutions, washing, blocking, and detection) and devices is required to move these technologies out of the research laboratory and into the field where they can have a more immediate impact on world health. We are focused on designing and prototyping disposable microfluidic platforms to enable molecular diagnostic testing using patient samples in locations far from a full service laboratory. Device design goals are low production costs, long shelf lives and relative ease of use. This talk will cover the formulation, fabrication and testing of microfluidic solid phase extraction columns based on polymer monoliths impregnated with nanoparticulate inclusions for protein and nucleic acid isolation from patient samples. Mammalian and bacterial cell lysis in microfluidic chips will be covered in addition to a discussion of strategies for micro and nanoscale enzyme linked immunosorbent assays. Practical concerns about the direct use of patient samples (blood, urine, saliva, and stool) will also be addressed.

2:40pm **BI+MN-TuA3 Surface Modification of Microfluidic Devices for Biological Applications**, *M. Salim, G.J.S. Fowler, B O'Sullivan, P.C. Wright,* ***S.L. McArthur,*** University of Sheffield, UK
Microfluidic systems are becoming increasingly important for bioanalytical and biochemical research such as proteomics, genomics, clinical diagnostics and drug discovery. Miniaturisation has been applied to bioassays and biological applications such as electrophoresis, DNA sequencing, DNA separation, immunoassays, polymerase chain reaction (PCR), cell counting, enzymatic assays, cell sorting and cell culture onto a chip. In all of these applications the ability of control biomolecule interactions with the device surface is critical. In this study we use ELISA, fluorescence microscopy, XPS and ToF-SIMS to investigate a range of surface modification methods for controlling the non-specific adsorption and immobilisation of biomolecules on glass microfluidic devices and micro-capillaries. The results highlight that protein adsorption occurs rapidly on the devices and that while varying concentration, residences time, flow, pH all influenced the adsorption profiles, none of these were able to completely eliminate protein adsorption. Plasma polymerisation has proved to be a flexible system for controlling the interactions along microfluidic channels. The wide range of monomers available for polymerisation has enabled us to develop low-fouling channels, functionalised substrates for the immobilisation of enzymes and antibodies and spatially control the surface chemistry along a channel length.

3:00pm **BI+MN-TuA4 Study of FET Flow Control and Electrostatic Response of Charged Molecules in Nanofluidic Channels**, *Y. Oh, D.N. Petsev,* University of New Mexico*; C.F. Ivory,* Washington State University*; C.H. Chung,* Sungkyunkwan University, Korea*; S.R.J. Brueck, G.P. Lopez,* ***S.M. Han,*** University of New Mexico
Using scanning laser confocal fluorescence microscopy (SL-CFM) and multiple internal reflection Fourier transform infrared spectroscopy (MIR-FTIRS), we have studied the field-effect-transistor (FET) flow control of charged dye molecules (Alexa 488 and Rhodamine B) in a parallel array (~10@sup 5@) of nanochannels during electroosmosis. For fluidic FET, a DC potential is applied to the gate surrounding an isolated mid-section of the channels. The gate potential controls the surface charge on SiO@sub 2@ channel walls and therefore the @xi@-potential. Depending the polarity and magnitude, the gate potential can accelerate, decelerate, or reverse the flow. We observe that the isolated gate, which is heavily doped with B (~10@sup 19@ cm@sup -3@), shows more pronounced control than applying the bias to the entire substrate. We also demonstrate a pH shift in nanochannels, when bulk electrolyte solutions enter the channels. This outcome illustrates that the solution pH can be further controlled by the gate bias. To improve the controllability of flow and to introduce a pH gradient along the channels for isoelectric focusing, our latest nanochannel device contains multiple gates. A different potential is applied to each gate to differentially control the surface charge on the SiO@sub 2@ channel walls and to create a pH gradient along the channels. Since the nanochannels are integrated into a MIR infrared waveguide, we can also probe the molecular orientation, segregation, and reaction of charged molecules in nanochannels in response to the gate bias. For instance, the xenthene-skeletal C-C vibrational modes at 1617 and 1552 cm@sup -1@ of Rhodamine B shift upon gate biasing, indicating a conformational change. The control of pH gradient as a function of gate bias as well as molecular orientation will be further discussed in this presentation.

3:20pm **BI+MN-TuA5 Soft-state Biologic ASICs and nSERS for Quantitative Medicine**, ***L.P. Lee,*** University of California, Berkeley **INVITED**
In order to create high-content Integrated Quantitative Molecular Diagnostics (iQMD) chip, Biologic Application Specific Integrated Circuits (BioASICs) and quantum nanoplasmonic probes such as nanostructured surface enhanced Raman scattering (nSERS) substrates are developed. Soft-state BioASICs are created by connecting existing and novel microfluidic circuits for high-content experimental biology in new ways. We are creating a library of these "building blocks" to develop multifunctional biological microprocessors. To build a solid foundation of future high-speed micro- and nanofluidic bioprocessors for experimental systems biology and biomarker discovery, we have developed design rules and critical modules of BioASICs such as single cell analysis chip, integrated multiple patch-clamp array, dynamic cell culture array, on-chip cell lysing device, sample preparation chip, cell separation device, high-density single cell analysis chip, molecular harvesting device, cell-cell communication array, animals on a chip, and nanofluidic SERS substrate. For nanoscale spectroscopic molecular imaging and photothermal therapeutic applications, nanocrescent SERS probes are developed. The formation of asymmetric nanophotonic crescent structure is accomplished by the interfacing both bottom-up and top-down methods, which allows to create effective local field enhancement structures, batch nanofabrication, and precise controls of hot spot coupling distance for in-vivo molecular imaging. Gold-based nanocrescents have structures with a sub-10 nm sharp edge, which can enhance local electromagnetic field at the edge area. The advanced nanocrescent SERS probes can be applied for sensitive molecular detection and electron transfers of biomolecules. The functional BioASICs and quantum nanoplasmonics have a potential to impact on systems biology and quantitative medicine.

4:00pm **BI+MN-TuA7 Challenges in Microfluidic Technology Development and Commercialization**, ***A. Chow,*** Caliper Life Sciences
Research activities in microfluidics have exploded in the past decade and a half from just in a handful of laboratories to becoming an important research area in most major universities and research institutes in the world. Commercialization of microfluidics technologies, on the other hand, has been much less ubiquitous. In this presentation, the successes and key challenges in product development and commercialization will be examined, focusing on analyzing the role of scientific and engineering innovations that may be required to bring new microfluidics products and applications to the market.

4:20pm **BI+MN-TuA8 Biomolecule Assembly and Functionality in Completely Packaged Microfluidic Devices**, ***X. Luo,*** *J.J. Park, H. Yi, R. Ghodssi,* University of Maryland*; G.W. Rubloff,* University of Maryland, US
We demonstrate in situ biomolecule assembly at readily addressable sites in a completely packaged bioMEMS device. Chitosan's pH responsive properties for site-selective electrodeposition and its amine functionality for biomolecular conjugation allow this aminopolysaccharide to be employed as the platform for electric signal-guided assembly of biomolecules onto conductive inorganic surfaces from aqueous environment, preserving the activity of biomolecules being assembled. Our completely packaged microfluidic device features consistently leak-free sealing, fluidic inputs/outputs for solution transport, electrical ports to guide the assembly onto selective sites, and simple in situ and ex situ examination of the assembly procedures within the channel for 4 different cases. (1)We electrodeposited fluorescently labeled chitosan at specific electrodes to directly demonstrate the potential of biomolecule assembly inside a microfluidic channel. (2)We assembled fluorescent marker molecules (fluorescein and green fluorescent protein (GFP)) onto an electrodeposited chitosan scaffold to illustrate the in situ biomolecule assembly at readily addressible sites, with GFP's biofunctionality retained through the assembly process. (3)We covalently assembled probe single-stranded DNA onto an electrodeposited chitosan scaffold, then exposed

the scaffold to mismatching and matching fluorescently labeled target DNA to show the ability to assemble probe species and to detect sequence-specific hybridization through sequences of reactions. (4)We compared fluorescence images to post-process profilometer measurements, confirming the relation between the active chitosan sites and the observed fluorescence. These results demonstrate the first signal-directed chitosan-mediated in situ biomolecule assembly in the microfluidic environment after complete packaging of the bioMEMS device, preserving the biological activities of assembled biomolecules.

4:40pm **BI+MN-TuA9 A Bio-MEMS Device for Modeling the Reflex-arc**, ***K.A. Wilson***, *M. Das, J.W. Rumsey, P. Molnar, J.J. Hickman,* University of Central Florida

The reflex-arc is the most basic functional unit of the animal nervous system and consists of three elements: a muscle fiber, a motoneuron (MN), and a dorsal root ganglion cell (DRG). These elements form a circuit that serves to control functions such as breathing, digestion, and involuntary muscle contraction. Due to the importance of this biological circuit it is of great interest in the study of neurodegenerative disease (ND), traumatic spinal cord injury (SCI), and bioprosthetics/biorobotics. However, due to the complex interactions of the cell types involved, novel strategies are required to study this circuit in vitro. Our objective is to develop a MEMS device for recreating the spinal reflex-arc as a model system for studying ND, SCI, and bioprosthetics/biorobotics. As a first step we have demonstrated the ability to culture the various elements of the reflex-arc in a defined serum-free culture system. We have also developed a MEMS platform for integrating these elements into a format that allows stringent control of physiological parameters as well as selective stimulation of the individual elements of the reflex-arc. Furthermore we are now able to measure contractile forces generated by the muscle component of the circuit using this system. Ultimately this device will allow the controlled interrogation of the reflex-arc for basic science and therapeutic research applications.

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