MEMS and NEMS
Room 102B - Session MN+BI-ThM
'Fantastic Voyage' – the New Micro/Nano/Bio Systems Frontiers

Moderators: Reza Ghodssi, University of Maryland, College Park, Christian Zorman, Case Western Reserve University

8:00am **MN+BI-ThM1 Living Micromachines*, M. Taher Saif,*** *B. Williams,* University of Illinois at Urbana Champaign **INVITED**

Industrial revolution of the 19th century marked the onset of the era of machines that transformed societies. Late 20tthe century marked the beginning of miniaturization resulting in micro-nano electronics and MEMS/NEMS. This revolution connected every individual with all the others in the planet. However, all of these machines are non-living, and they do not have inherent intelligence. On the other hand, since the discovery of genes, there is a considerable body of knowledge on engineering living cells. It is thus appropriate to envision biohybrid micro machines that are made from microfabricated scaffolds and living cells. These machines have the potential of unprecedented capabilities, as they would carry the footprints of millions of years of evolution. These machines may emerge from an interaction between the living cells and the micro-nano scaffolds. Thus, they might be the unique products of both the bottom-up and top-down methods. In this talk we will present such an elementary micro machine consisting of a soft slender string and rat cardiomyocytes. The string is made from PDMS by filling a microfabricated channel using capillary draw. Cells are cultured on one region of the string. These cells interact with the string as well as with each other, and beat in synchrony as a single actuator. This living actuator bends the string, and a bending wave propagates from the actuator site towards the end, as a bending of a sperm. This artificial machine thus swims in fluids as the engineered living swimmer. These swimmers might be used in vivo for autonomous intelligent drug delivery.

8:40am **MN+BI-ThM3 Inertial Imaging with Nanoelectromechanical Systems*, Selim Hanay,*** Bilkent University, Turkey

Nanoelectromechanical Systems (NEMS) resonators can be used as exquisite sensors of physical quantities, such as mass, force and spin. As the size of a mechanical sensor shrinks, its responsivity increases: combining this advantage with low-noise readout schemes has enabled extreme sensitivity levels to be achieved such as the detection of electronic spins, single-cells in liquid and volatile chemicals at low concentration. It has become possible to use NEMS sensors for single-molecule analysis: for instance, the mass of single molecules can be measured by NEMS, paving the road for sensitive biochemical analysis. Another sensing modality, for single-biomolecule analysis, has been recently discovered. It was shown that spatial properties of analyte particles, such as its size and degree of asymmetry, can be extracted by tracking multiple mechanical modes of a sensor. Such multimodal mesaurement provides both size and shape information, as well as, the mass of the analyte. Furthermore, by combining spatial information, an image of the analyte can be constructed. The new technique, Inertial Imaging, transforms the capabilities of nanomechanical sensors to a new level: the combined data of molecular mass, size and shape of the analyte can enable previously unattainable information in biomolecular analytics. In this talk details for the implementation of this technique as well as experimental progress for single molecule detection will be presented.

9:00am **MN+BI-ThM4 Dynamic Patterning of Breast Cancer Cells Using Silicon Nitride Multimode Membrane Resonators*, Hao Jia**[*]**,*** *H. Tang, P.X.-L. Feng,* Case Western Reserve University

Manipulating and patterning biological cells on surfaces has gained great interest due to its fundamental importance for cell-level biophysical studies, and implications for potential biomedical applications.[1] In this work, we report the first experimental demonstration of non-invasive, fast, dynamic patterning of clusters of cancer cells with micrometer-scale spatial precision, by using multimode silicon nitride (Si_3N_4) membrane resonators that feature very large aspect ratios (~600nm-thick, and hundreds of microns in lateral dimensions), in rectangular and square shapes. The fabricated Si_3N_4 membranes exhibit robust multiple flexural resonances (within 50–500 kHz) in liquid solutions. We observe that the breast cancer cells (MDA-MB-231) can be dynamically manipulated into diverse Chladni patterns[2] within a few seconds, via the multimode resonances of the membrane. Multiple spatially signatory cell patterns are observed for rectangles (~300×120μm^2) and squares (~350×350μm^2), respectively. We further demonstrate that cell patterns can be dynamically switched. We model and explain the cell patterns by oscillating boundary induced acoustic steaming flows of the fluid.

As an important cell line for breast cancer metastasis studies, MDA-MB-231 cells are selected in this work and genetically-engineered to express green florescent protein (GFP), a biomarker for gene expression and cell identification. Dilution in EDTA solution allows suspended individual cells with reduced surface viscosity. Cancer cells are locally delivered to the device area using micropipettes, and the cell distributions are imaged in real time by a high-speed fluorescent microscope. We observe that cancer cells are allocated into '1D' array of clusters on the rectangular membrane under excitation frequencies corresponding to its 1st, 2nd and 3rd modes (in Fig. 1), while they cluster into multiple '2D' patterns when the multiple modes of square membrane are excited individually (in Fig. 2). Furthermore, the cell patterns can be readily changed when switching between resonance frequencies.

The demonstrated Si_3N_4 membrane platform provides new capabilities for manipulating breast cancer cells, which could further lead to studies involving cancer cell signaling and interaction with neighboring cells, probing and controlling cancer cell metastatic behaviors using multimode mechanical resonators.

[1] B. Guillotin, *et al.*, *Trends in Biotechnology***4**, 2011.

[2] E.F.F. Chladni, *Entdeckungen über die Theory des Klanges*, 1787.

9:20am **MN+BI-ThM5 Smart Drug Delivery through Gut*, W. Yu, R. Rahimi, M. Ochoa, Babak Ziaie,*** Purdue University **INVITED**

This paper reports on a magnetic-proximity-fuse method for site-specific drug release in the gut. As an embodiment, a capsule is comprised of two compartments; one houses a charged capacitor and a reed switch (magnetic switch) while the other accommodates the drug reservoir, whose lid is latched by a taut nylon thread intertwined with a NiCr wire. Meanwhile, the wire is connected to the capacitor via the switch. Once within the proximity of a magnet, the switch closes and the capacitor discharges on the wire, melting the fusible thread and opening the reservoir.

Pharmaceutical companies have been interested in releasing medications at specific sites in the gut. Many drug absorption studies (DASs) use Enterion [1] capsule which incorporates a loaded spring that is RF-actuated, pushes a piston and forces the drug out through a hole. The capsule location is monitored via γ-ray scintillating-imaging. Other similar devices include InteliSite [2] (tracked by x-ray) and IntelliCap (tracked by pH). Though suitable for DASs in clinical settings, these approaches are not practical for use in larger populations. This is mainly due to the problems related to the need for real-time localizing the capsule. Thus, we present an alternative approach using a Smart Capsule incorporating a magnetic-proximity fuse.

Fig. 1 depicts a capsule traveling through the gut in proximity to a magnet. The capsule consists of two chambers. The right one contains a capacitor (1F, 2.7V) and a reed switch. The capacitor is charged before use. A NiCr wire is connected to the capacitor and the switch, with two ends in the right chamber and the rest intertwined with a nylon fuse in the drug reservoir. Along the axis is a rubber band linking the fuse to a cap, covering the reservoir with an elastic layer for reliable sealing. Additionally, an elastic rod is used as a loaded spring pushing the cap out once the fuse breaks. As in Fig. 2, the band holds the cap initially. When the capsule meets a magnetic field to close the switch, the NiCr wire is heated, melting the fuse (60~85ºC) and opening the cap. Fig. 3 shows a photo of a Smart Capsule (9mm×26mm).

Fig. 4 shows snapshots of the capsule traveling in a tubing at various points with respect to the magnetic marker. The capsule starts to open in frame "a" (1sec) at a separation distance of 1mm from the magnet, with the opening completed (cap totally separated from the capsule) in frame "e" (17sec). Considerable diffusion and mixing of the powdered dye in water is observed within a minute, frame "f". Fig. 5 shows the relationship between the capacitance and the charging voltage necessary for melting the fuse through a NiCr wire (~0.23ohms).

11:00am **MN+BI-ThM10 Biopsy with Untethered Microgrippers*, David Gracias,*** Johns Hopkins University **INVITED**

An important requirement to enable the vision of the Fantastic Voyage is to develop tiny mechanized devices that can be used to perform functional

[*] **MEMS/NEMS Best Paper Award Finalist**

surgical tasks. As an example, I will describe a decade long effort in our laboratory to develop sub-millimeter sized biopsy forceps in the shape of hands or microgrippers. I will discuss challenges in fabrication, materials choice, deployment, guidance, safety, power harvesting and practical surgical operation of these devices. In addition to in vitro and ex vivo studies, I will discuss in vivo operation of such devices in live pigs to enable statistical sampling of tissues, targeted biopsy and drug delivery. I will also discuss the creation of microgrippers out of bioresorbable and biodegradable silicon based and polymer materials as well as devices as small as single red blood cells. Our studies highlight feasibility and proof-of-concept for the implementation of small untethered devices in medicine and surgery.

11:40am **MN+BI-ThM12 Bacterial Biofilms on 3D-printed Implant Materials**, ***Ryan Huiszoon***[*], *S. Subramanian, T.E. Winkler*[†], University of Maryland, College Park; *H.O. Sintim,* Purdue University; *W.E. Bentley, R. Ghodssi,* University of Maryland, College Park

New technologies, like capsule microsystems (Fig.1), have the potential to revolutionize medical care by autonomously locating and treating *in vivo* infections. Such implantable systems require 3D structures that cannot be fabricated using traditional photolithography. Additive manufacturing is the ideal tool that allows for rapid and detailed fabrication of such complex structures. However, 3D-printed implants, like their metal and ceramic counterparts, are vulnerable to biofilm infections [1]. Thus, it is essential to characterize treatments for these films on emerging 3D printable materials. In this work, we evaluate bacterial biofilm treatment on 3D-printed implant materials such as MED610.

Bacterial biofilms are the leading cause of implant infections. They form when planktonic bacteria adhere on a surface, secrete protective extracellular matrix and grow. They are highly resistant to antibiotics, allowing the infection to persist [2,3]. Microfluidics is a common and effective tool to evaluate biofilms in a controlled environment as it offers more clinically relevant data about biofilm growth and treatment [4].

In this work, we 3D printed open microfluidic channels (750µm wide x 400µm deep) on a Stratsys Connex3 polyjet printer. The open channels were sealed using sealing wrap, PDMS and glass, and clamped together using binder clips (Fig.2). *Escherichia coli* W3110 biofilms were grown in the micro-channels under Lysogeny Broth (LB) media flow at 120µl/hr for 24 hours. Subsequently, treatment with LB media (control), 10µg/mL gentamicin, 100µM autoinducer-2 (AI-2) analog (quorum sensing disruptor), or a combination of the latter two treatments was introduced into the various channels at the same flow rate for an additional 24 hours. The biofilms were then imaged through the open channels using an Olympus BX60 microscope (Fig.3). Treatment efficacy was evaluated as a percent change in channel surface coverage quantified using ImageJ. Bacterial biofilm coverage was reduced by 21%, 31% and 50% for gentamicin, analog and combination treatments respectively as compared to the untreated control, consistent with previous results (Fig.4) [2]. The combination treatment proved most effective, reducing biofilm coverage by 37% compared to the standard antibiotic-only therapy [2].

3D printed microfluidic test platforms offer an affordable way to experiment on new materials and can hasten the development of novel treatments. Additionally, the characterization of these materials brings us a step closer to making this technology a viable option for fabricating complex structures for implantable multi-purpose microsystems.

[*] **MEMS/NEMS Best Paper Award Finalist**
[†] **National Student Award Finalist**

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