Wednesday Afternoon, October 21, 2015

Biomaterial Interfaces
Room: 211D - Session BI-WeA

Biophysics, Membranes and Nanoscale Biological Interfaces
Moderator: Stephanie Allen, The University of Nottingham, UK

2:20pm **BI-WeA1 Direct Measurement of Single Molecule Interaction Free Energies at Solid/Liquid Interfaces for the Prediction of Macroscopic Properties**, ***Markus Valtiner***, *S. Raman, T. Utzig, P. Stock*, Max Planck Institut fur Eisenforschung GmbH, Germany

Unraveling the complexity of the macroscopic world based on molecular level details relies on understanding the scaling of single molecule interactions towards integral interactions at the meso- and macroscopic scale. Here, we discuss how one can decipher the scaling of individual single binding interactions at solid/liquid interactions towards the macroscopic level [1], where a large number of these bonds interacts simultaneously. We developed a synergistic experimental approach combining Surface Forces Apparatus (SFA) experiments and single molecule force spectroscopy (SMFS). We show that equilibrium SFA measurements scale linearly with the number density of a model acid-base bond at an interface, providing acid-amine interaction energies of 10.9 ± 0.2 kT. Using Bell-Evans theory together with Jarzynski's equality, we can demonstrate how a set of single molecule interaction forces measured by SMFS similarly converges to an interaction energy of 11 ± 1 kT, with unbinding energy barriers of 25 kT ± 5 kT. This indicates excellent predictive power of our newly developed scaling approach.

In addition, we tested a number of other bonds including hydrophobic, ligand-receptor and metal-polymer bonds with our model and find that our model is widely applicable. Hence, we will discuss in detail how single molecule unbinding energy landscapes can be utilized to predict scenarios where a large number of molecules simultaneously interact, giving rise to both macroscopic equilibrated and non-equilibrated interaction energies during adhesive failure. As such, our experimental strategy provides a unique framework for molecular design of novel functional materials through predicting of large-scale properties such as adhesion, self-assembly or cell-substrate interactions based on single molecule energy landscapes.

[1] S. Raman et al. *inNature Communications*, 5**(2014)**, 5539.

[2] T. Utzig et al. *in Langmuir*, 31(9) **(2015)**, 2722.

2:40pm **BI-WeA2 Multipurpose Biomembranes of Sandwiches Layers: Deposition and Characterization with Surface and Biological Methods**, *H. Heidari Zare,* Munich University of Applied Sciences, Germany, *D. Jocham,* University Hospital of Schleswig-Holstein, Germany, ***Gerhard Franz***, Munich University of Applied Sciences, Germany

For coating of medical implants, two different strategies have been evolved, either films which can be decomposed after a certain time of impact, or "eternal" layers. Both types can be composed as a homogeneous film or a heterogeneous sandwich layer, which have the charm that the same coating layer can be used not only to protect different pharmaceutical depot layers on top of different substrates but also to allow a retarded emission of drugs, which can be adjusted by its porosity. Our coatings are made of FDA-passed poly-(p-xylylene), or parylene, PPX. It is employed it two systems: for coronary stents, or in antibacterial urinary catheters. In the first case, it protects a restenotic drug which is applied on top of a plasma-roughened metallic surface, in the second application, the porous cap layer protects a silver film, which is deposited on the interior walls of a catheter in a random zebra-stripe design without application of a mask technology. Its morphology can be adjusted by the conditions of preparation.

For capillaries, one challenge is the homogeneous thickness on the interior sidewall from the mouth to the dead end of the capillary, which has been solved by application of a temperature seesaw: Since condensation is an exothermic process, application of the principle of Le Chatelier moves the equilibrium of diffusion with deposition loss to the side with higher internal energy, i. e. to the vaporous phase, thereby equalizing the deposition rate, downward at the mouth and upward at the dead end.

The porosity of the cap layer can be adjusted by its thickness between zero and approx. 1000 nm [1]. Especially for the Gorham method, which is widely applied for the deposition of PPX, thicknesses below 1 µm are difficult to obtain. Applying a method which resembles Papin's principle, this challenge could also be met [2].

The porosity is judged by atomic force microscopy (AFM) and electrochemical impedance spectroscopy (EIS), the loss rate by ICP-OES and polarography, the medical impact by measuring the optical density and applying a growth inhibition test [3]. One of the medical challenges is the confirmation of the minimum inhibition concentration of these compound layers.

[1] F. Schamberger, A. Ziegler, and G. Franz, J. Vac. Sci. Technol. B 30, 051801 (2012)

[2] G. Franz and F. Schamberger,. J. Vac. Sci. Technol. A 31, 061602 (2013)

[3] H. Heidari Zare, St. Sudhop, F. Schamberger, and G. Franz, Biointerphases 9, 031002 (2014)

3:00pm **BI-WeA3 Vascularized Micro-Tissue Engineered Constructs for Drug Screening**, ***Noo Li Jeon***, Seoul National University, Korea **INVITED**

Vasculature is a fundamental building block of tissues. In order to design and fabricate in-vitro organ-on-chip systems, vasculature needs to be integrated with the micro-tissue constructs.

This presentation will describe the development of a novel microfluidic device with perfusable network of blood vessels that: 1) reproduce angiogenesis and vasculogenesis, 2) allow formation of network of perfusable endothelial vessels in 3D tissue, 3) allow observation of cancer and immune cell intravasation and extravasation, and 3) allow measurement of microvessel permeability. Cancer cells can be introduced and their intravasation and extravasation can be observed with live-cell imaging for extended periods and thus control the tumor microenvironment for investing different steps of metastatic cascade. Characterization of the vessels with immuno-histochemical techniques show that tight-junctions form between the endothelial cells and laminin and collagen IV are deposited along the length of the vessel.

The development of vascularized micro-tissue represents a step forward in building organ-on-chip systems. Drug screening and other assays can be performed using live-cell imaging and immunohistochemistry techniques enabling high throughput testing of multiple conditions simultaneously.

4:20pm **BI-WeA7 Controlling Cell Adhesion on Device Surfaces by Nanotopography**, ***Elena Liang***, *E. Mah, S. Wu, A. Yee*, University of California, Irvine

The ability to control cell adhesion on material surfaces is critical to the performance and biointegration of implanted medical devices. Of particular interest to our research is developing an understanding of what role surface topography plays in cell adhesion, which could lead to simple and durable ways to engineer surfaces without having to chemically modify the surface of biomaterials. Our group found that human embryonic stem cells grown on nanopillar structures have a significantly reduced number of focal adhesions per cell and concordantly exhibit increased cell motility on the nanopillars (Kong *et al*. 2013). We hypothesized that pillar nanostructures would prevent cells from adhering. To test this hypothesis, we counted the number of fibroblasts adhering to a variety of surface topographies, which consisted of a flat surface, nanolines, and nanopillars, and examined cell morphology on these surfaces. We created a library of nanopillared polymethylmethacrylate (PMMA) surfaces, including a biomimetic cicada wing replicate (the surface of the wing has a high density of nanopillars with dimensions that are ideal for our studies) made by compressing a negative hPDMS stamp of the cicada wing into PMMA, and pillar arrays of approximately 200 nm diameter nanopillars with center-to-center spacing ranging from 320 nm to 692 nm fabricated with nanoimprint lithography. We also observed the focal adhesions using fibroblasts transfected with paxillin-GFP and tracked migration. After 24 hours, we found that the fibroblasts showed a spread-like morphology on the flat film while those on pillars were smaller and more equiaxed. Preliminary results show that there are noticeably fewer cells on PMMA pillars than on flat PMMA. The focal adhesions on cells on nanopillars appear smaller than focal adhesions of cells on a flat surface. Lastly, cells on nanopillars on average traveled a greater distance than cells on a flat surface. Our study shows that protruding structures in the 100-500 nm size range affect cell adhesion dynamics and structure dimensions modulate the adhesion of cells. This may provide researchers a useful means of controlling cell adhesion on surfaces of implants.

4:40pm **BI-WeA8 Condensation-Mediated "Living" Chain Growth Polymerization: Towards New DNA Nanostructures**, *L. Tang, R. Gu,* Duke University, *J. Lamas,* Texas State University, *N. Li,* North Carolina State University, *S. Rastogi,* Texas State University, *A. Chilkoti,* Duke University, *W. Brittain,* Texas State University, *Y.G. Yingling,* North Carolina State University, ***Stefan Zauscher***, Duke University

Polynucleotide co-polymers promise a rich micellization behavior in solution and hold promise for novel functional materials in nano- and biotechnological applications. We report on the synthesis of biologically-inspired polynucleotides with well-defined sequence, dispersity, and assembly function that have large potential for applications ranging from delivery vehicles of medical therapeutics, sensing applications, to scaffolds for nanowires. Specifically, we exploit the ability of the DNA polymerase, terminal deoxynucleotidyl transferase (TdT), to polymerize long chains of single strand DNA (ssDNA) and to incorporate unnatural nucleotides with useful functional groups into the growing polynucleotide chain. Furthermore, we demonstrate the reversible micellar aggregation of a DNA-azobenzene conjugate, in which the photoisomerization of the initially apolar *trans*-azobenzene moiety to the polar *cis* isomer causes disassembly of the aggregates. Finally, we show how coarse-grained simulations can be used to describe the conformational characteristics of the engineered ssDNA blocks and their self-assembly into a rich spectrum of biomolecular nanostructures in solution and on surfaces.

5:00pm **BI-WeA9 Simple Routes to All-Polymeric Corrals, Flow-Channels and Traps for Studies of Lipid and Protein Diffusion in Supported Lipid Bilayers**, *A. Johnson, P.M. Chapman, A.M. Alswieleh,* University of Sheffield, UK, *P. Bao,* University of Leeds, UK, *A. Tsargorodska, S.P. Armes,* University of Sheffield, UK, *S.D. Evans,* University of Leeds, UK, ***Graham Leggett***, University of Sheffield, UK

We describe simple routes to the fabrication of corrals, channels, traps and other structures for the fabrication of spatially organized lipid bilayers and membrane proteins. These utilize photochemistry and polymer brushes. In the first approach, UV exposure of films of (chloromethylphenyl)trichlorosilane (CMPTS) causes dehalogenation of the surface creating carboxylic acid groups to create hydrophilic, anionic regions, in which lipid mobilities are observed that are similar to those observed on glass surfaces. In masked regions, the halogen remains intact, and is used to grow poly(oligoethyleneglycol methacrylate) (POEGMA) brushes by atom-transfer radical polymerization (ATRP), defining lipid-free walls within which SLBs may be formed by vesicle fusion. Two-component structures are fabricated by using an aminosilane film in which the amine group is protected by a photoremovable nitrophenyl group. Selective exposure, through a mask or using a Lloyd's mirror interferometer, causes patterned deprotection of the film leading to patterned brush growth by ATRP. Poly(Cysteine methacrylate) (PCysMA) is a new, highly biocompatible, stimulus-responsive zwitterionic polymer that forms thick brushes when grown from surfaces by atom transfer radical polymerization (ATRP). Lipid mobility similar to that observed on glass is observed on PCysMA brushes. Measurements of membrane protein diffusion have been made using ac trap structures. After lithographic definition of corrals, channels and other structures, PCysMA is end-capped and the remainder of the surface deprotected; POEGMA brushes are grown by ATRP, enclosing the PCysMA structures. Using interferometric lithography, arrays of close-packed gold nanostructures may be defined on the substrate. These are strongly coupled to photosynthetic membrane proteins, yielding intense extinction spectra. These gold nanostructures are incorporated into brush corrals and other structures, with polymer brushes grown to the same height as the gold nanostructures, enabling the formation of a continuous SLB with integral plasmonic reporters for membrane protein activity.

5:20pm **BI-WeA10 Measuring Cardiomyocyte Contractions on Silicon Carbide Micromechanical Resonators**, ***Hao Tang***, *H. Jia, P.X.-L. Feng*, Case Western Reserve University

Heart functions are mainly determined by its contractility. Monitoring the contraction curve at single cell level may help attain a deeper understanding of cardiomyocyte contraction process[1], heart failure mechanism[2] and potential methods for drug screening. The contraction frequency, contraction amplitude as well as contraction and relaxation rates of cardiomyocytes all together compose the contraction curve and reflect the health condition of heart tissues.

At the single-cell level, most contractility measurement methods are based on measuring the length change[2] or force change[3] of single cardiomyocyte. Methods based on length change often require massive and fast image processing, therefore, its time resolution is restricted by the capturing and processing speed, and spatial resolution is limited by the diffraction of optical system (typically 0.2um). Methods based on force change require complex readout elements that are compatible with biological environments, which on the other hand results in complex fabrication process.

In this work, we take an initial step to measure the cardiomyocyte contraction in a dynamic mode using SiC micromechanical resonators. As a superior material for bioMEMS platforms, SiC has excellent mechanical, optical, chemical, thermal properties as well as unique biocompatibility[4],[5]. Frequency-shift-based sensing using micromechanical resonators[6],[7] offers possibilities of monitoring mass distribution changes during cardiomyocyte contraction process with high sensitivity. Our dynamic sensing method provides an alternative for cardiomyocyte contraction measurement, with promising applications in heart failure research and drug screening.

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[1] D.M. Bers, *Nature*, vol. 415, no. 6868, pp. 198-205, 2002.

[2] R.V. Yelamarty, et al., *Am. J. Physiol.*, vol. 262, no. 4, pp. C980-C990, 1992.

[3] G. Lin, et al., *IEEE Trans. Biomed. Eng.*, vol. 48, no. 9, pp. 996-1006, 2001.

[4] H. Jia, et al., *MEMS 2015*, pp. 698-701, Estoril, Portugal, Jan. 18-22, 2015.

[5] C. Coletti, et al., *Silicon Carbide Biotechnology*, 1st Edition, pp. 119-152, 2012.

[6] K. Park, et al., *Proc. Natl. Acad. Sci. U.S.A.*, vol. 107, no. 48, pp. 20691-20696, 2010.

[7] M.S. Hanay, et al., *Nature Nanotech.*, vol. 10, no. 4, pp. 339-344, 2015.

5:40pm **BI-WeA11 Programming the Robust Self-organization of Human Tissues using Interfacial Interactions**, ***Zev Gartner***, University of California, San Francisco **INVITED**

Developing tissues contain motile populations of cells that can self-organize into spatially ordered tissues based on differences in their interfacial surface energies. However, it is unclear how self-organization by this mechanism remains robust when interfacial energies become heterogeneous in either time or space. The ducts and acini of the human mammary gland are prototypical heterogeneous and dynamic tissues comprising two concentrically arranged cell types. To investigate the consequences of cellular heterogeneity and plasticity on cell positioning in the mammary gland, we reconstituted its self- organization from aggregates of primary cells in vitro. We find that self-organization is dominated by the interfacial energy of the tissue–ECM boundary, rather than by differential homo- and heterotypic energies of cell–cell interaction. Surprisingly, interactions with the tissue–ECM boundary are binary, in that only one cell-type interacts appreciably with the boundary. Using mathematical modeling and cell-type-specific knockdown of key regulators of cell–cell cohesion, we show that this strategy of self-organization is robust to severe perturbations affecting cell–cell contact formation. We also find that this mechanism of self-organization is conserved in the human prostate. Therefore, a binary interfacial interaction with the tissue boundary provides a flexible and generalizable strategy for forming and maintaining the structure of tissues that exhibit abundant heterogeneity and plasticity. Our model also predicts that mutations affecting binary cell–ECM interactions are catastrophic and could contribute to loss of tissue architecture in diseases such as breast cancer.

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