## Bioengineering Subgroup

**1-Subg**
**Mapping Cell Surface Adhesion by Rotation Tracking and Adhesion Footprinting**
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Rolling adhesion is the behaviour that leukocytes and circulating tumour cells exhibit as they passively roll along blood vessel walls under flow. It plays a critical role in capturing cells in the blood, guiding them toward inflammation sites, and activating cell signalling pathways to enable their subsequent transmigration. Rolling adhesion is mediated by catch-bond-like interactions between selectins expressed on endothelial cells lining blood vessels and P-selectin glycoprotein ligand-1 found at microvilli tips of leukocytes. Despite our understanding of individual components of this process, how the molecular details of adhesion bonds scale to cell-surface adhesion and rolling behaviour remains poorly understood. Here, we developed 2 label-free methods that map the functional adhesion sites and their strength on a leukocyte surface. The first method relies on tracking the rotational angle of a single rolling cell, which confers advantages over standard methods that track the centre-of-mass alone. Constructing the adhesion map from the instantaneous angular velocity reveals that the adhesion profile along the rolling circumference is inhomogeneous. We corroborated these findings with a second method that allowed us to obtain a footprint of molecular adhesion events using DNA-based molecular force probes. Our results reveal that adhesion at the functional level is not uniformly distributed over the leukocyte surface as previously assumed, but is instead patchy.

**2-Subg**
**Interactions of Engineered Nanomaterials with Lipid Interfaces**
**Amir Farnoud**.
Chemical and Biomolecular Engineering, Ohio University, Athens, OH, USA.
The emergent applications of nanomaterials in food, cosmetics, bio-sensing, electronics, and medical products necessitates evaluation of their toxicity upon human exposure. Once inside the body, nanomaterials can interact with human cells. The cell membrane, a lipid bilayer that separates the cell from the outer environment, is the first cellular entity that ''meets'' the nanoparticles. Thus, understanding the interactions of nanoparticles with the cell membrane is expected to provide an understanding of the potential toxicity of such materials. However, despite a number of studies, a clear understanding of the mechanisms of nanoparticle-cell membrane interactions is still lacking and the role of nanoparticle physicochemical properties in such interactions remains ill-defined. In this talk, I will give an overview of my studies on the interactions of engineered nanoparticles with lipid interfaces, including lipid monolayers and bilayers representing simple models of biological membranes. Mechanisms of interactions between engineered polystyrene and silica nanoparticles and lipid interfaces will be discussed and an overview on how nanoparticle physicochemical properties might affect their interactions with lipid interfaces will be provided.

**3-Subg**
**Biomembrane Inspired Engineering**
**Marjorie Longo**.
UC Davis, Davis, CA, USA.
Since the invention of the optical microscope in the 17$^{th}$ century it has been observed that biological membranes compartmentalize the cellular machinery of life. Then, nearly 100 years ago, it was concluded, through surface science, that the cell membrane is a lipid bilayer. Since that time, many observations and theories have been put forward to try to explain how complex behavior emerges in living systems from the ubiquitous lipid bilayer structure and its integrated proteins and carbohydrates. We are now in a period of time when some of the most important paradigms posited in the last several decades for emergence of complex behavior in living cell membranes are being tested and questioned. These include the membrane (or lipid) raft hypothesis and mechanisms for generation of curvature and lipid asymmetry. An important outcome of this work may be the engineering of new micro- and nano-scale self-assembled systems and composites. This talk will focus upon our work in lipid phase behavior, crowding-induced mixing, biomembrane mechanical properties, nanoscale curvature generation, and bionanocomposites that may contribute toward the design of new biological membrane-inspired technology.

**4-Subg**
**Physical Engineering of Behaviour and Function at the Cell and Tissue Levels**
**Andrew Pelling**.
Department of Physics, University of Ottawa, Ottawa, ON, Canada.
Living cells possess an exquisite ability to sense and respond to physical information in their microenvironment. Although this ability plays a key role in many fundamentally important physiological and pathological processes, it can also be exploited to control and manipulate biological behaviour and function. In recent years, the lab has become increasingly interested in created augmented biological systems by exploiting topographical, mechanical and physical cues to direct cellular organization, sorting and complex morphogenesis in three dimensions. This work has also yielded new insights into how cells respond to nano- and micro- scale physical information in highly artificial environments. I will review several projects in which cells are exposed artificial topographies to induce spontaneous cell-sorting in 3D, artificial mechanical stimuli that reveals unexpected physical properties of sub-cellular architecture, and plant-derived 3D scaffolds that can be used to create artificial hybrid mammalian tissues. These results provide insights in how key components of biological and physical feedback loops can be employed to control and govern the life of a cell.

**5-Subg**
**Optical Imaging of Protein Aggregation Reactions In Vitro and in Cells**
**Clemens Kaminski**.
Dept. Chem Engineering and Biotech, Cambridge University, Cambridge, United Kingdom.
The self-assembly of proteins into ordered macromolecular units is fundamental to a variety of diseases. For example, in Alzheimer's Disease (AD) and Parkinson's Disease (PD), proteins that are usually harmless are found to adopt aberrant shapes; one says they 'misfold'. In the misfolded state the proteins are prone to aggregate into highly ordered, toxic structures, called protein amyloids and these make up the insoluble deposits found in the brains of patients suffering from these devastating disorders. A key requirement to gain insights into molecular mechanisms of disease and to progress in the search for therapeutic intervention is a capability to image the protein assembly process in situ i.e. in cellular models of disease. In this talk I will give an overview of research to gain insight on the aggregation state neurotoxic proteins in vitro (1), in cells (2, 3) and in live model organisms (4). In particular, we wish to understand how these and similar proteins nucleate to form toxic structures and to correlate such information with phenotypes of disease (3). I will show how direct stochastic optical reconstruction microscopy, dSTORM, and multiparametric imaging techniques, such as spectral and lifetime imaging, are capable of tracking amyloidogenesis in vitro, and in vivo, and how we can correlate the appearance of certain aggregate species with toxic phenotypes of relevance to PD and AD (5-7).
(1) Pinotsi et al, *Nano Letters* (2013) (2) Kaminski Schierle, et al, *JACS* (2011) (3) Esbjörner, et al, *ChemBiol* (2014) (4) Kaminski Schierle, et al, *ChemPhys Chem* (2011) (5) Michel, et al, *JBC* (2014) (6) Pinotsi, et al, PNAS (2016) (7) Murakami, et al, *Neuron* (2015)

## Mechanobiology Subgroup

**6-Subg**
**Mechanical Aspects of Mitochondrial Alterations in Apoptosis**
**Ana J. Garcia-Saez**.
Membrane Biophysics, University of Tübingen, Tübingen, Germany.
Bax permeabilization of the MOM during apoptosis proceeds via the opening of toroidal membrane pores that are large enough to allow the passage of proteins like cytochrome c. These pores are special in that lipids form part of the pore walls, where they bend to avoid exposure of the hydrophobic tails so that both monolayers form a continuous surface. As a result, toroidal pores are unstable structures whose lifetime depends on the balance between membrane tension, opening the pore, and line tension at the pore rim due to the very high lipid curvature, closing the pore. However, how Bax alters the mechanical properties of the membrane to induce the apoptotic pores remains unknown. We have shown that Bax forms large and stable pores, which are tunable in size. Moreover, it remodels membranes and stabilizes highly curved geometries. Atomic force microscopy data suggest that Bax does so by reorganizing the lipids and reducing the line tension at the pore edge. In addition, Bax accumulates at discrete foci, which are also enriched in Drp1, a dynamin-like protein responsible for mitochondrial fragmentation. Despite their relevant interplay during apoptosis, the mechanisms and mechanical consequences remain obscure. By combining FCS, superresolution microscopy and fluorescence exchange assays, we have discovered that Bax and Drp1 directly interact