Unraveling Biological Processes at the Nanometer Scale

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Cells respond to their ever changing environment with short-term biochemical catalytic responses that modulate the interaction of existing proteins and longer-term transcriptional responses that elicit the production of entirely new proteins. Both these responses frequently culminate in nanoscopic changes in cell structure that are beyond the resolution of conventional light microscopy, complicating the visualization of dynamic changes in cell structure in real time. A living cell is thus a highly sophisticated, controlled system of nature's nanomachines, proteins and other biomolecules, which self-assemble into a multitude of supramolecular architectures and interact in a highly reproducable manner at the nanometer scale.

Recent advancements in nanotechnology have created a variety of top-down techniques that can consistently produce features of 100 nm or less, approaching a scale that is relevant to cellular systems. At the same time a number of self-assembly techniques have been developed that can be used to create artificial nanostructures mimicking biological systems with similar or even superior performance. The combination of these novel top-down and bottom-up approaches enable us to interact with cellular systems in an unprecedented manner. Proteins, lipid vesicles, macromolecular assemblies, and nanoparticles specifically placed onto predefined artificial patterns can trigger defined cellular responses, reveal the details of cell-surface interactions and allow for the ultimate miniaturization of array-type sensors down to the single molecule level.

Recently, we have focussed our efforts into achieving not only spatial, but also dynamic, control over the properties of biointerfaces. Surfaces that change upon external stimuli provide us with new research tools for studying complex biological problems as well as for tissue engineering purposes. This presentation will highligt the use of biolithography at the nanometer scale, electronically controlled local drug delivery, and the study of muscle cell fusion and division.

The figure below depicts two myoblasts fusing in real time as observed using high-resolution atomic force microscopy in living cells. Alterations of the membrane cytoarchitecture appear soon after initial contact that are not fully resolved using conventional light microscopy. These membrane tubules stain for phosphatidylserine (bottom right), a common requirement for membrane fusogenic systems.