Biomolecular-Scale Engineering

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The proliferation of inexpensive electronic devices in virtually every area of our lives, along with the enormous processing power of computers, would probably not have occurred if not for our ability to scale the dimensions of individual device and circuit components to smaller and smaller sizes. Using advanced lithographic patterning, the semiconductor industry is already producing integrated circuits with transistor elements that are only a few tens of nanometers, i.e., around the size of large biomolecules. This has opened up new opportunities where the tools of micro- and nanofabrication can be used to address questions in biology and medicine.

We have been exploring new approaches which combine traditional lithographic patterning with new surface chemistries and biomolecular assembly to fabricate devices and structures with dimensions of only a few nanometers, where we can begin to manipulate individual molecules. Exploiting the chemical and structural specificity of biomolecular recognition enables the assembly of biologically functional patterns with single-molecule precision. Based on this strategy, we have begun developing biomolecular patterned surfaces[1] with which we can study how the geometric arrangement of components of the extracellular matrix (ECM) affects cell behavior.

Using a self-aligned nanoimprint lithography pattern transfer process, we have created arrays of sub-10 nm metal dots (in some cases as small as 3 – 4 nm).[2] We have developed new surface chemistries to enable the selective binding of an assortment of biomolecules to these nanodots. One class of molecules we have been studying is the integrins, which are transmembrane protein which serve as the primary link between components of the extracellular matrix and the actin cytoskeleton. Lithographic patterning allows us to explore cell behavior on a variety of geometric arrangements of integrin-binding ligands, in which ligand spacing, number and density can be varied independently. This has led to the discovery of a minimal cell adhesion unit which controls cell motility, where a minimum number of integrin binding sites clustered within ~ 60 nm or less are required for cell adhesion. Similar lithographically-directed patterning schemes enable us to explore how other physical cues, such as rigidity, force and curvature, affect cell behavior.

Another biomolecular patterning scheme we are exploring involves DNA. Nanoscale barriers, which control the flow of supported lipid bilayers, are used to create "DNA curtains" which facilitate the study of DNA-protein interactions on a massively parallel, single-molecule basis.[3] In addition, highly selective binding of single-stranded DNA to lithographically patterned anchors allows us to study cooperative effects in DNA hybridization. We have been able to observe localized hybridization, followed by restriction enzyme cleaving, confirming that single-stranded DNA bound to nanodots maintains its native conformation. This has, in turn, enabled lithographically-directed assembly of DNA origami, which we are presently exploring for the hierarchical assembly of electronically functional nanostructures, such as semiconductor nanowires, carbon nanotubes and nanotube/molecule hybrids.

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