Seed: Probing interactions between particles and membranes: adhesion, deformation, and assembly

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Cellular membranes are astonishingly complex. In addition to their roles in protection and compartmentalization, membranes are responsible for a variety of other functions, such as signaling, transport, and adhesion, many of which are executed by membrane proteins. In fact, the cell membrane is loaded with proteins: Roughly half of its mass is comprised of proteins bound to or embedded within the membrane. The physical forces acting between these inclusions are essential to their assembly and function, yet understanding how such forces assemble bacteriorhodopsin into two-dimensional crystals or fold the membrane itself into complex gyroid structures, like those found in butterfly wings, is challenging.

In vitro model systems consisting of few, well-controlled components could help to tease out the underlying physical principles at work. Indeed, great progress in understanding the physics of the bilayer membrane itself has been made using binary mixtures of amphiphiles and water; the conformational behavior of lipid membranes, such as their preferred shapes and shape fluctuations, has been studied extensively. These efforts have resulted in a quantitative understanding of the structure and dynamics of membranes. However, similar model systems for studying the physical forces between membrane inclusions, as well as how these forces give rise to organization of membrane-bound objects, are lacking.

The seed project in the Rogers lab seeks to develop such an experimental system, in which the key determinants of membrane-inclusion interactions—the adhesion and membrane curvature energies—can be controlled independently, and to measure the resulting interactions with high precision. They will use DNA hybridization to control the adhesive interactions. By grafting complementary DNA onto colloidal particles (0.1-1 micrometer diameter) and unilamellar vesicles (1-100 micrometer diameter), either by direct conjugation or by doping the vesicles with DNA-labeled cholesterol, they will use the effective interactions that emerge from Watson-Crick base pairing to control adhesion with remarkable precision: The interactions can be tuned from roughly 0-100 $k_B T$ simply by lowering the temperature 15°C. The vesicles will be composed of lipids or block copolymers, providing a handle over their membrane properties, and made using microfluidics. Finally, the lab will utilize a combination of optical tweezers, microscopy, and particle tracking to tackle a hierarchy of questions: (1) How does the degree of deformation from one colloidal particle depend on the balance of adhesion and membrane-curvature energies? (2) How do the warp fields due to binding of two neighboring particles interact with one another? and (3) How can these deformation-mediated interactions combine with other lateral interactions to organize many bound particles in interesting ways?

The Rogers lab is uniquely positioned to pursue this solution. They have refined synthetic schemes for fabricating DNA-grafted colloidal particles, built optical-tweezers instruments and particle tracking routines for measuring DNA-induced interactions with nm- and $k_B T$-scale precision, and developed tractable models for predicting the interactions quantitatively. A postdoc partially supported by the seed, Gaël Prado, who will start February 16, 2016, will bring these skills to bear on an exciting new problem—the study of interactions between membrane inclusions—that could help shed light on the mechanisms of organization in cellular membranes, as well as provide insight into new ways of building colloidal materials. Going forward, the techniques developed here could complement the directions of IRG 1: Membrane-based Materials, presenting opportunities for synergistic activity with Dogic (colloidal membranes), Rodal (real membranes and proteins), Dinsmore (nanoparticles and large vesicles), and Hagan (theory and multiscale simulation).