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PHYSICAL FORCES ORGANIZING BIOMOLECULES

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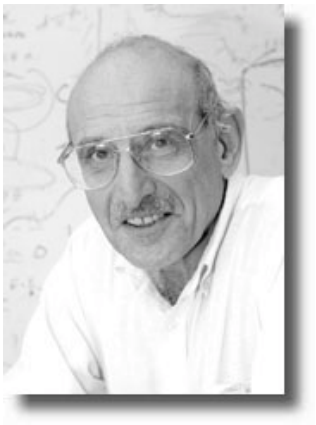

With a long-term goal to build a practical physics of biological material, we measure, characterize, and codify the interactions that govern the organization and self-assembly of different types of biological molecules. In part as a result of the recent NIH-wide interest in nanotechnology, we are building on our experience with van der Waals fluctuation forces to formulate interactions involving carbon nanotubes—not only with regard to their assembly but also, and more important, with respect to their suitability as substrates for biopolymers such as DNA. Our undertaking is strengthened by its strong connection with physical theory. Through a series of measurements and analyses of different types of interactions as revealed in vivo, in vitro, and in computation, we are working with DNA assemblies such as those seen in viral capsids and in vitro; with polypeptides and polysaccharides in suspension; and with lipid/water liquid crystals. In all these systems, we observe the structure of packing and measure intermolecular interaction energies.

Van der Waals forces

Parsegian, Podgornik; in collaboration with Ching, French, Mkrtchian, Rajter

While we recognize that van der Waals forces are the dominant interaction that coheres membranes and proteins, we are now systematically studying—in a collaboration with quantum physicists and biophysicists—the source of the powerful surface tension at membrane interfaces as well as the attraction that creates membrane multilayers or allows membranes to adhere to artificial surfaces. This year, using the quantum-mechanical density functional theory solved for several carbon nanotubes, we computed the forces that cause the nanotubes to cohere and to serve as a substrate for many materials. It is remarkable that quantum chemistry combined with our expertise in macromolecular interactions is allowing us to see properties such as torque and the force between carbon nanotubes. We began our investigations by focusing on the elements of physical theory that relate the polarizability of materials to the fluctuations of charges within them. We have thus been able to design experiments that show how macromolecular organization responds to deliberate changes in solution properties. We demonstrated a tight coupling of the modern quantum theory of structured materials with experiments and measurements that revealed electromagnetic properties.

By teaming with other groups that measure absorption spectra, we formulated and computed van der Waals forces involving lipids, water,

ions, and synthetic structures such as carbon nanotubes. The results have shown how charge fluctuation forces conferred by ions in solution can modify forces between lipid membranes. We measured those forces and computed van der Waals charge fluctuation forces in the same systems.

We also extended the Lifshitz theory of van der Waals interactions in stratified media such as lipid multilamellar systems, thereby enabling us to compute forces between bodies with extended interfaces ranging from the practical—the composite media of electric insulators—to the biological—the action of extended polymer layers on biological membranes.

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Molecular assembly in vitro and in vivo

Bezrukov, Harries, Parsegian, Petrache, Podgornik, Rau; in collaboration with Gelbart, Knobler, Stanley, Todd, Zemb

We have developed new theories and new methods of macromolecular organization by beginning with direct measurements of forces between large molecules, proceeding with observations of molecules under confinement, and building on the statistical physics of molecular organization under the action of organizing forces. In particular, we observed DNA under the osmotic stress of large polymers or confined within the hard walls of a virus capsid.

The osmotic action of small solutes controls a remarkable number of cellular processes, including the gating of ionic channels and specific versus non-specific DNA–protein interactions regulating gene expression. Osmotic sensing at the molecular level can probe the forces acting between and within macromolecules. By varying the salt or neutral “osmolyte” concentration in the bathing solution, we control osmotic pressure.

Most recently, we observed the ejection of DNA from capsids subjected to different salt conditions. Expansive pressures, which are responsible for the initial ejection of DNA, can vary up to many tens of atmospheres. Ionic conditions, in turn, may vary these pressures. An unrecognized feature of many viruses is that ionic conditions can penetrate a virus and even modify the expansive force within it. At one extreme, DNA in simple salts is under great pressure to expand and be ejected from the capsid; under other conditions, where DNA-condensing ions can enter the capsid, DNA may be under no expansive pressure. We have started to measure the motion of DNA within capsids subjected to different ionic conditions to see how ionic surroundings might control ejection. Whether these manipulations ultimately affect viral infectivity is a worthwhile and exciting question for investigation.

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