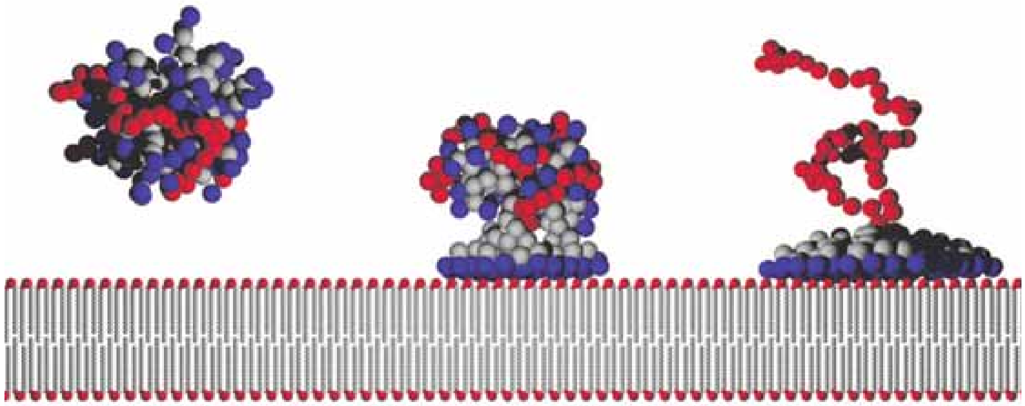
NewsBytes



Snapshots of a simulation of a dendrimer-DNA complex arriving and docking at a model cell membrane. Reprinted with permission from The Journal of Chemical Physics *130, 155101, 2009. Copyright 2009, American Institute of Physics.*

“There's a growing appreciation of how important mechanical forces are for many biological processes ranging from directing stem cell differentiation, to tissue formation, to how cells respond to drugs,” says **Ali Khademhosseini, PhD**, an assistant professor of medicine at Harvard and MIT. “This work generates a powerful model that can be used for many different applications. There's a lot of scientific follow-up as well as many potential technological and engineering advances that can come out of it.”

—By Rachel Tompa, PhD

Modeling A Gene Therapy Delivery Vehicle

Gene therapy to correct inherited illnesses hinges on successful delivery of DNA into a person's cells. Most gene therapists work with viruses to ferry their DNA cargo. Yet the body tends to fight even disarmed viruses that should be harmless. As an alternative, researchers have devised dendrimers, branched molecules whose endings can be tailored to package DNA. Now, in the first molecular-level simulation of a gene therapy vector in action, researchers have simulated a dendrimer docking at a model cell surface and shown how long it can hold on to its DNA cargo.

“With our simple tinker toy model we're going to throw out a lot of information that is certainly important, but it gives us the basic physics,” says Paul Welch.

The simulation rendered a quick but clear sketch of what happens at the cell membrane. “With our simple tinker toy model we're going to throw out a lot of information that is certainly important, but it gives us the basic physics,” says **Paul Welch, PhD**, a materials physicist at Los Alamos National Laboratory and lead author on the study published in the April 2009 issue of *The Journal of Chemical Physics*.

In previous work, other researchers have modeled dendrimers interacting with membranes, but no one had simulated them transporting DNA.

Welch and his team created a molecular dynamics model of a dendrimer with an attached DNA strand. In their simulations, they let the dendrimer-DNA complex loose near a simple, planar membrane model to see whether it would bind or wander off. They found that both the propensity to bind and the duration of binding decreased in the presence of a more negatively charged membrane. There is a range of surface charges which allow binding for the optimal length of time—long enough for the complex to transit the membrane but not so long that the dendrimer retains a grip on the DNA after entry. In addition, the researchers found that big burly dendrimers are not necessarily the best delivery vehicles for DNA. In future simulations, Welch's team hopes to use a more realistic model of the membrane's lipid bilayer. Ideally, Welch says, the membrane would undulate, deform and perhaps form a little liposome (bubble) around the complex to pull it in, much as one would expect a membrane to behave in nature.

Ron Larson, PhD, a polymer physicist at the University of Michigan in Ann Arbor who models the use of dendrimers to poke holes in membranes to kill bacteria or deliver drugs, wonders whether the model should address possible interactions between the four bases of the DNA and the membrane. And he looks forward to experiments that would test the model. “People make these different particles by the seat of their pants and see how many go in,” Larson says. “When things go wrong, they often don't know why. It's really helpful to have a theoretical model.”

—By Roberta Friedman, PhD

Different But Equal

Kids often claim they are just as smart—if not smarter—than their parents. Childish nonsense? Perhaps not, according to a recent study. It turns out that young children's brains are as efficient in solving information-processing tasks as their adult versions, despite being very differently organized. This finding could improve our understanding of normal brain development as well as of disorders such as autism and Tourette syndrome.

“Whether you are a kid or an adult your brain is organized in a pretty damn efficient way,” says **Steven Peterson, PhD**, a neurophysiologist at the Washington University School of Medicine in St. Louis, and senior author of the study which appeared in the May 2009 issue of *PLoS Computational Biology*.