their initial contact or by going through a "hemifused" halfway point, where the outside layers have merged but the insides remain separate. "We show that both could happen," says Kasson. The work was published in the August 8, 2006, issue of the *Proceedings of the National Academy of Sciences*.

"Ultimately we'd like to be able to control fusion in biological systems and induce or inhibit it for therapeutic purposes," says Peter Kasson.

Observing two membranes combining in a lab is difficult because it happens so quickly—on the order of microseconds. Earlier models haven't represented membranes in as much detail, over such long timescales, or with as many simulations as this one does, says Kasson.

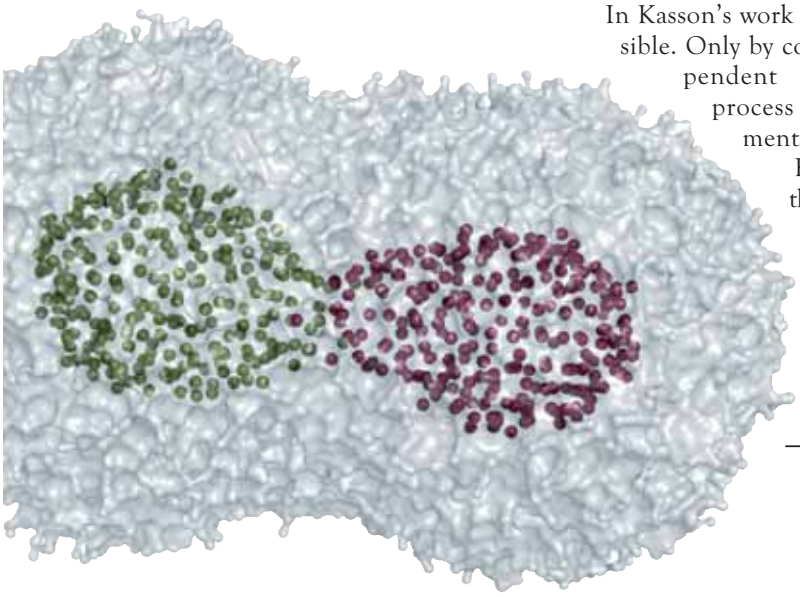
The team ran 10,000 separate simulations of membrane fusion using a distributed computing network called Folding@Home, in which people around the world donate screensaver time to biological research. In each simulation, the fusing membranes began with different starting conditions and evolved based on laws of physics and chemistry. The result: The simulated membranes merged through either of the two routes rather than exclusively through one or the other.

Erik Lindahl, **PhD**, professor of bioinformatics at Stockholm University, Sweden, thinks the project sets the pace for future work in the field. "The key thing is that they're not doing one simulation, they're doing many," he says. "In ten years nobody will publish a single simulation anymore."

Siewert-Jan Marrink, **PhD**, head of the molecular dynamics group at the University of Groningen, the Netherlands, and creator of a previous model of membrane fusion, agrees. "I do consider this work to be a significant step forward," he says. "In my original publication of the fusion process of the same system I was only able to look at a few events, but I could not tell how relevant these were. In Kasson's work this has become possible. Only by comparing many independent instances of the process can global assessments be made."

Kasson is delighted that his model explains experimental observations and can help in planning new experiments. "That's the most exciting part," he says, "when we can come full circle."

—Clara Moskowitz



As a pore forms between two vesicles, the phosphate groups from the membrane's outer leaflet (red from one vesicle, green from the other) mingle with one another in the pore region. Courtesy of Peter Kasson.

Cancer Proteins Show Off Their Networking Skills

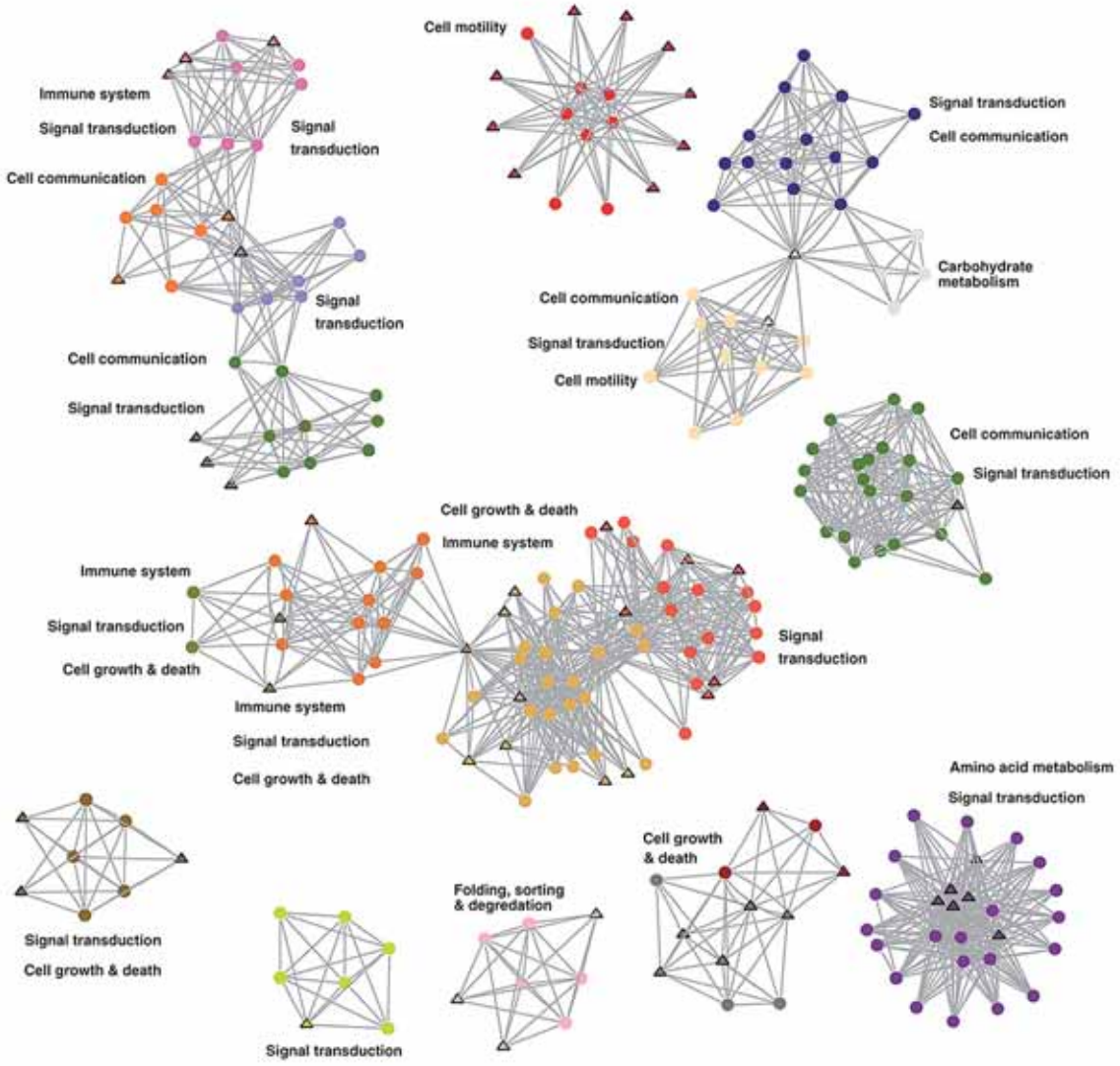
New research suggests that cancer proteins, like influential people, have the most connections. These results, from an extensive study of how human proteins interact with one another, could help explain why cancer wreaks such havoc in cells.

"We haven't gotten to the bottom of what the increased connectivity really means, but perhaps highly connected proteins, once mutated, are more likely to cause disease," says coauthor **Paul Bates**, **PhD**, who heads the Biomolecular Modelling Laboratory at the Cancer Research UK London Research Institute. The research was published in the September 15, 2006, issue of *Bioinformatics*.

Bates and his graduate student **Pall Jonsson** built a model of the human proteome that contained more than 108,000 interactions using experimental information on proteins in other species, including yeast and worms. The typical protein can connect with a limited number of other proteins. The researchers scored the data and linked proteins known to interact, leading to a protein-protein interaction network, also known as the "interactome." Then, using information from a 2004 census of 346 human genes known to mutate in cancer, Bates and Jonsson mapped 509 human cancer proteins onto their network.

The average cancer protein was linked to 23 other proteins in the network, more than twice as many as the typical protein. By analyzing protein clusters, the researchers also found the proteins from cancer genes tend to occupy intersections between protein communities that govern crucial functions such as regulating cell growth and death. This makes sense, says Bates, as proteins that are changed by cancerous mutations tend to disrupt many cellular functions. Bates adds that understanding the network properties around these proteins could help researchers identify drug targets.

Shinichiro Wachi, a doctoral candi-



A sampling of protein communities identified in the interactome. Each community is labeled by the general classes of functions in which it belongs. Cancer proteins are shown as triangles. Note that this figure shows only one community assignment per protein, although they can belong to more than one. Courtesy of Pall Jonsson and Paul Bates.

The average cancer protein is linked to 23 other proteins in the network, more than twice as many as the typical protein.

date at the University of California, Davis, says the results are hard to interpret. The mapped cancer proteins were based on genetic information rather than experimental data on how they interact, he says. "A gene may perform a function in the cell, but the mutation could either reduce the function or result in higher activity. ... It could go either way," says Wachi, who has studied the network properties of proteins in lung cancer tissues. Wachi also cautions that because the list of cancer genes is changing dramatically, the researchers may soon need to re-examine their model.

Bates would like to do further analysis. "We've only got 108,000 interactions. There's likely to be more than that—400,000, maybe 700,000," he says. "We want to increase the map and validate it further."

—Rachel Courtland

Watching Blood Vessels Grow and Shrink

Microscopic capillaries grow on demand, snaking toward hungry cells needing their blood supply. Understanding how to control this process could help scientists promote wound healing or halt cancer in its path. A new computer model simulates how a key molecule (VEGF, or vascular endothelial growth factor) summons vessels to sprout: It spills out of a hungry cell and travels toward a vessel, with increased concentrations in areas with few vessels. The two-dimensional model also predicts the actual number of VEGF molecules at that edge, another novel advance.

"There have been over 10,000 papers published on VEGF and not one shows a molecular-level computation," says **Aleksander Popel, PhD**, professor of biomedical engineering at the Johns Hopkins