tant step is modeling heating in a more realistic nanoshell distribution, he says. "This is where their more computational approach would be a big win."
—By Tia Ghose

3D Angiogenesis Modeled

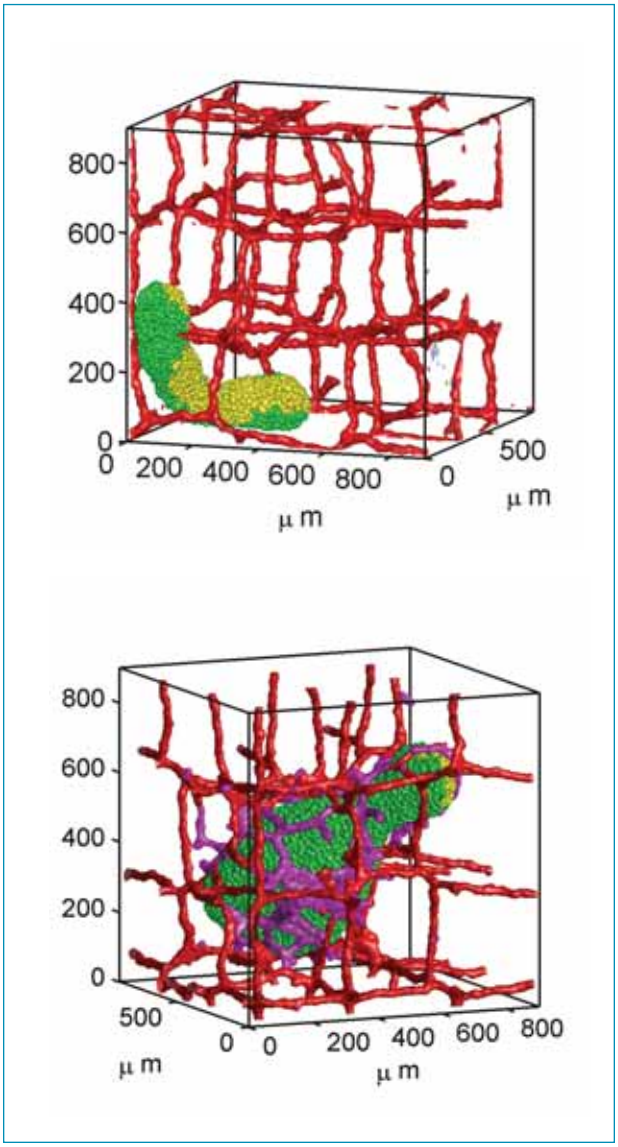
Researchers have successfully simulated how growing blood vessels affect the sizes and shapes of tumors using a 3-D model based solely on how cells behave—without reference to intracellular biochemistry. The simplified modeling system uses open-source cellular behavior "plug-ins" yet compares favorably with models laboriously coded from scratch. It also captures many essential details observed in real tumors.

"Building a computational model based on 10 to 15 behaviors is much easier than building one based on thousands of genes," says **Abbas Shirinifard**, graduate student at Indiana University's Biocomplexity Institute and lead author of the work published in the October 2009 issue of *PLoS One*.

The human body sprouts new blood vessels when they are needed. Cancer cells use this process—called angiogenesis—to their advantage. As a tumor grows, some of its interior cells become starved for oxygen and start emitting distress signals. In response, cells that create new blood vessels grow toward the distressed cells to provide them with oxygen and other nutrients. The result: a larger, actively growing tumor. Until now, researchers have modeled multi-cellular processes—such as angiogenesis—by painstakingly programming interactions among gene and protein cascades. Such models are not easily comparable between research groups, and take much longer to re-program with different conditions.

Shirinifad's team used an open-source platform called CompuCell3D (available at www.compucell3d.org) developed by **James Glazier, PhD**, and **Maciej Swat, PhD**. CompuCell3D models multi-cellular behaviors based on how each cell reacts to environmental conditions. The cells involved in tumor growth respond in defined ways, so Shirinifad and his colleagues modeled them using action-response rules, such as "If oxygen levels fall below X, send out Y signal," or "If protein X reaches concentration Y, divide." When they switched off the rule for cells to create new blood vessels in response to distress signals, the simulated tumors were small and irregular, with contours that followed the existing blood vessels. When they ran the simulation with angiogenesis "turned on," the resulting tumor grew large and rounded. These outcomes matched the appearance of such tumors in models programmed from scratch, as well as observations of real tumors treated with anti-angiogenesis compounds. In CompuCell3D, researchers can change and re-run such models in days—much quicker than if they were adapting a hand-coded algorithm, Shirinifad says.

"The exciting thing is the new technique," says **Mark Chaplain, PhD**, mathematics professor at the University of Dundee, Scotland. He notes that the current model lacks a proper simulation of blood flow; the simulated blood-vessel cells deliver oxygen itself rather than shuttling oxygen-rich blood. "If they develop this technique further by modeling blood flow, they will have a very powerful model," Chaplain says.
—By Jennifer Welsh



After 75 days of simulated growth, a tumor model looks quite different in the presence (A) and absence (B) of new blood vessel formation. Green cells in the tumor are actively dividing, while yellow cells are starved of oxygen. Red cells are blood vessel cells originally present in the model; purple cells are new blood vessel cells, present only in the model that supports angiogenesis. Axes are labeled in microns. Reprinted from Shirinifard, A, et al., 3D Multi-Cell Simulation of Tumor Growth and Angiogenesis, PLoS One, 4(10): e7190. doi:10.1371/journal.pone.0007190 (October 2009). Images provided by Abbas Shirinifard.

Improving the Sense of Touch for Surgical Robots

When a knife cuts into an organ, forces push back in ways that mechanical engineers can, to some extent, predict. But other factors are also at play: Ions shift in solution within cells, causing electromechanical changes that, researchers now say, can be predicted as