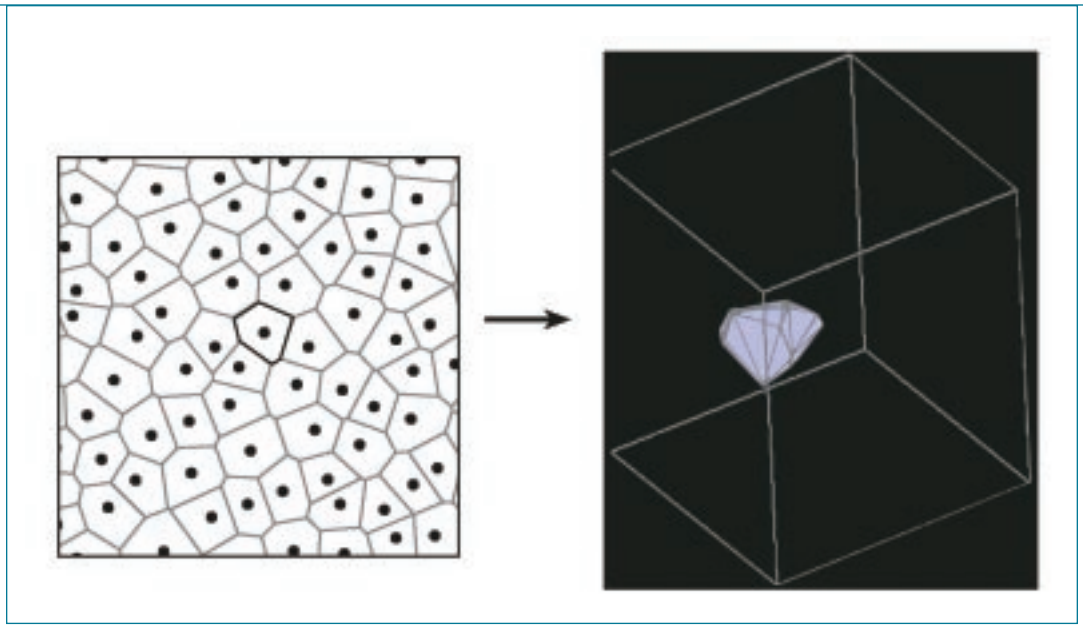


Measuring the geometrical relationships defined by the position of neurons in 3-D, as shown on the right, is far more computationally demanding than doing so for the 2-D version on the left.

in developmental neurobiology, but that may soon change as a result of a National Institute of Mental Health grant to a group of multi-disciplinary researchers at the University of California, Santa Barbara and the University of Cambridge.

"We're creating software tools to analyze how neurons distribute themselves within the brain," says Benjamin Reese, PhD, principal investigator on the grant and a professor of psychology at UCSB. "We understand how neurons are born, the instructions governing their fate and how they then migrate, but virtually nothing about how they distribute themselves in three-dimensional space."

Reese and his colleagues have found that many types of neurons in the retina (essentially a two-dimensional space) respect one rule: they avoid being positioned near one another. This rule results in neurons being spread evenly across the retina, providing a uniform sampling of the visual scene—a characteristic required for good eyesight.

But neurons in other parts of the brain might function under additional or completely different rules. Moreover, 3-D space is harder to model using current software. "The algorithms we've created for studying the distribution of cells in two dimensions are all Matlab-based scripts," Reese says. "Once we add the depth dimension, they become extremely cumbersome." So he and his colleagues, including co-principal investigator Steven Eglen, DPhil, a lecturer at the University of Cambridge, are re-writing portions of the scripts in a lower-level language to improve computational efficiency.

> "By July of 2006, we expect to have a website up and running with both two- and three-dimensional software available for others to download and use."
>
> **—Benjamin Reese.**

The software will both simulate neuronal populations and compare the simulations to real biological data. The first simulation step: throw virtual cells into a defined space with various constraints (e.g., a specified vicinity to similar, or other types of, cells) until the cells achieve the same density as is found within a region in the brain. The researchers will also generate experimental data using transgenic animals that express fluorescently marked populations of nerve cells. They will measure those neurons' x-y-z coordinates and feed them into the software program. The software can then determine the geometry of the simulations repeatedly, looking for the best fit to the real biological data.

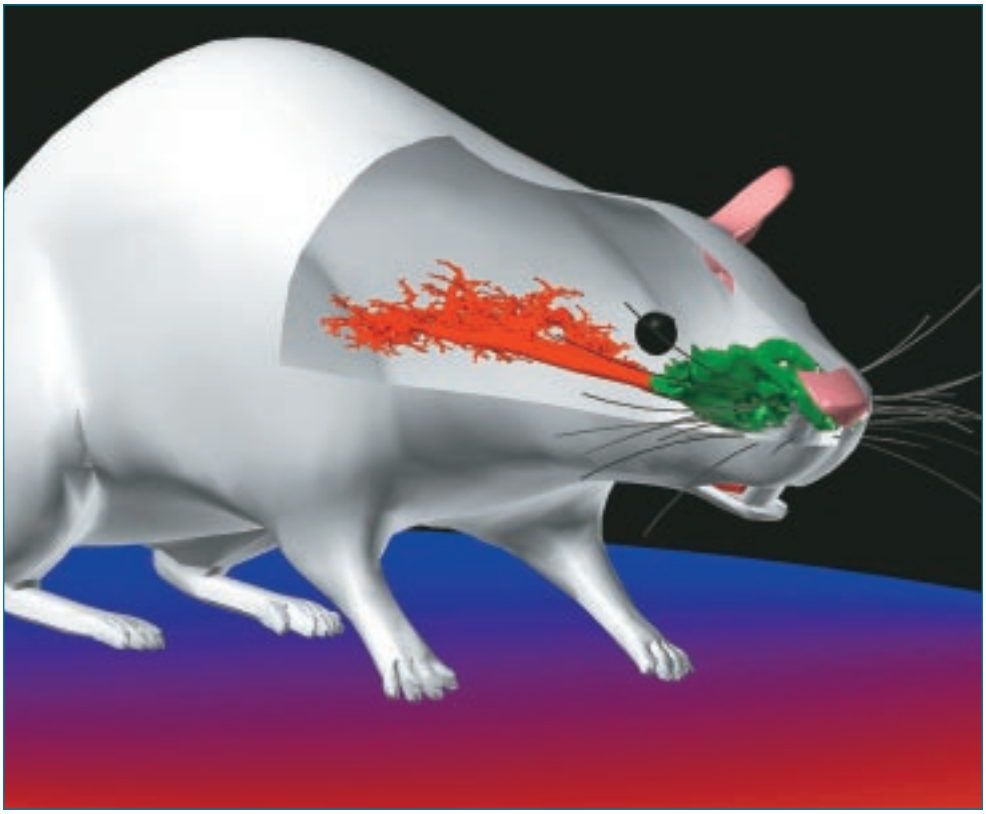
The group plans to make the software available to the public. "By July of 2006, we expect to have a website up and running with both two- and three-dimensional software available for others to download and use," says Reese.

Eventually, Reese would like to understand both cell spacing and its causes: "Is what spaces them apart a diffusible factor emitted by the cells, or is it contact-based, mediated by outgrowing dendrites?" Reese asks.

The understanding of neuron spacing may enlighten us about developmental disorders of the brain, Reese says. Mutations in genes that influence neuronal spacing may, in turn, alter the synaptic connectivity and circuit formation within the nervous system, altering brain function.

Binary Breathing

In September 2004, researchers at Pacific Northwest National Laboratory (PNNL) in Richland, Washington, received a $10 million grant to create a three-dimensional imaging and computer model of how the respiratory tract interacts with particles carried in the air. Ultimately, the researchers hope the effort will lead to a better understanding of what happens when



In 2001, Pacific Northwest National Laboratory scientists designed a virtual computer model of the nose, larynx, and lungs of a rat in hopes of better understanding how pollutants affect those systems. Now, they're taking that work further. Courtesy: Pacific Northwest National Laboratory.

people inhale either toxic substances or medications.

"We hope to develop a good predictive tool for modeling drug delivery or dosimetry," says Richard Corley, PhD, principal investigator and PNNL environmental toxicologist.

Corley and his colleagues have been working in this area for some time. In 2001, they developed a virtual rat lung that breathes on a computer screen. Since then, his collaborators have also been working on virtual models of primate and human lungs—models that integrate movement, as well as cellular information.

At this point, says Corley, "We can go from animal, to image, to a mesh capable of doing air flow simulations within a day or two."

The next step—generating a computational atlas of an animal's respiratory tract—requires that the researchers first determine how variable the animals are. "There's some fundamental biology we're getting out of this," says Corley. "How many animals do we need in order to get an atlas? How variable are we? For the first time, we can get a statistical angle on that."

Another important step is checking the accuracy of the model through lab experiments. "The computational capabilities predict where particles go," Corley says, "but we need to measure it as well, to validate."

While rapidly building up sets of data showing the geometry of the respiratory tract, Corley and his collaborators are also creating function and movement models. And they want to understand what's happening on the cellular level as well—how each of the 40 different types of cells in the respiratory tract interact with particles that land on them.

Eventually, the project will produce a web-based program for interactive simulation modeling. Right now, Corley says, it's important for people doing this work to solve a real medical problem early on. "What's some low-hanging fruit out there for solving? We're looking at drug delivery."

> "We can go from animal, to image, to a mesh capable of doing air flow simulations within a day or two."
>
> **—Richard Corley**

Shining Light on Cells

When light hits an obstacle, its scattering pattern reveals information regarding the internal structure of the obstacle. If that obstacle is a cell, the scattering pattern might indicate whether the cell is healthy or cancerous. But studying and categorizing different cells' light-scattering properties is no small task.

Now, with help from a National Institute of General Medical Sciences grant, Jun Qing Lu, PhD, assistant professor of physics at East Carolina University, and her colleagues are studying cellular light response using a promising mathematical approach called the finite-difference time-domain method (FDTD).

"We're looking inside the cell without opening it. If there are any changes, we should be able to see them from the outside," says Lu.

In the past, researchers used various approximation methods to study how light scatters from cells, but these simplified approaches can only provide limited information about highly-symmetric homogeneous bodies. Since cells are irregular in both shape and contents, a different approach was needed. "FDTD can handle any kind of shape or structure," Lu says. "But it's very