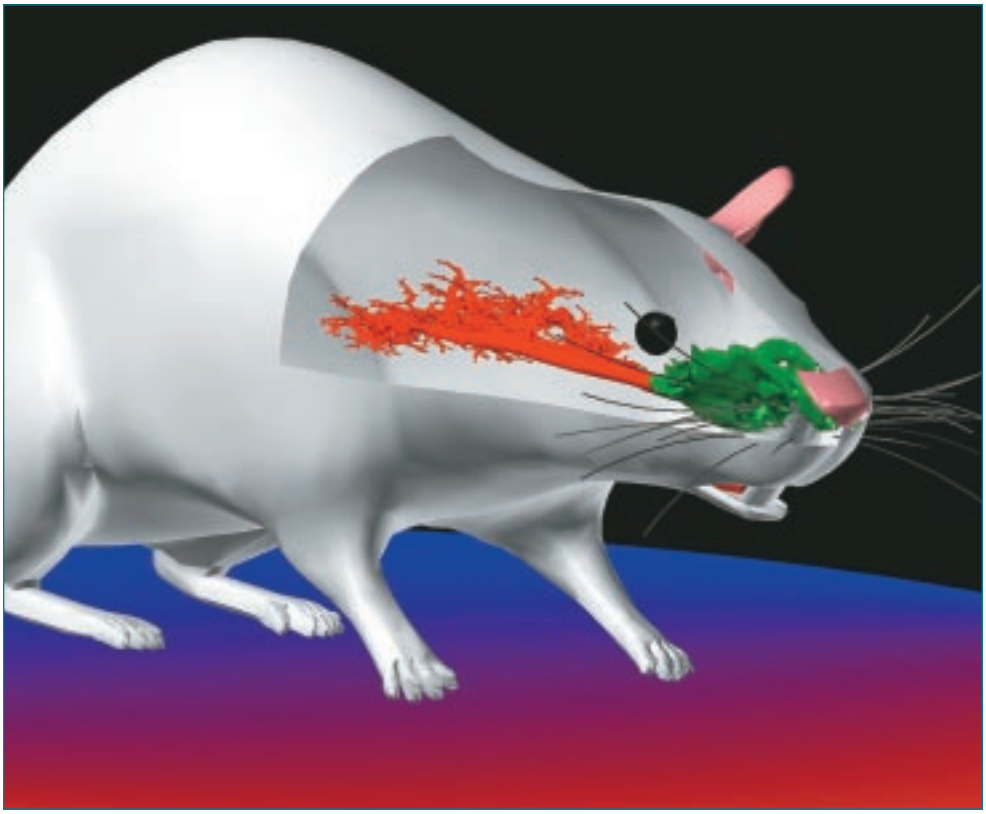


In 2001, Pacific Northwest National Laboratory scientists designed a virtual computer model of the nose, larynx, and lungs of a rat in hopes of better understanding how pollutants affect those systems. Now, they're taking that work further. Courtesy: Pacific Northwest National Laboratory.

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

computationally intensive."

FDTD has been around for a while, but it has been applied to biology only within the last few years. It's a numerical modeling technique that can be applied to interactions between electromagnetic waves and objects whose structural details are small compared to the wavelength of light. "Inside and in the vicinity of the target object, divide your space into a 3-D grid system and divide time into small steps," Lu says. "When the light hits the object, the electric and magnetic field distributions at each point in the grid space are calculated for each time step. Then put everything together to calculate the scattering pattern."

> "We're looking inside the cell without opening it." —**Jun Qing Lu**

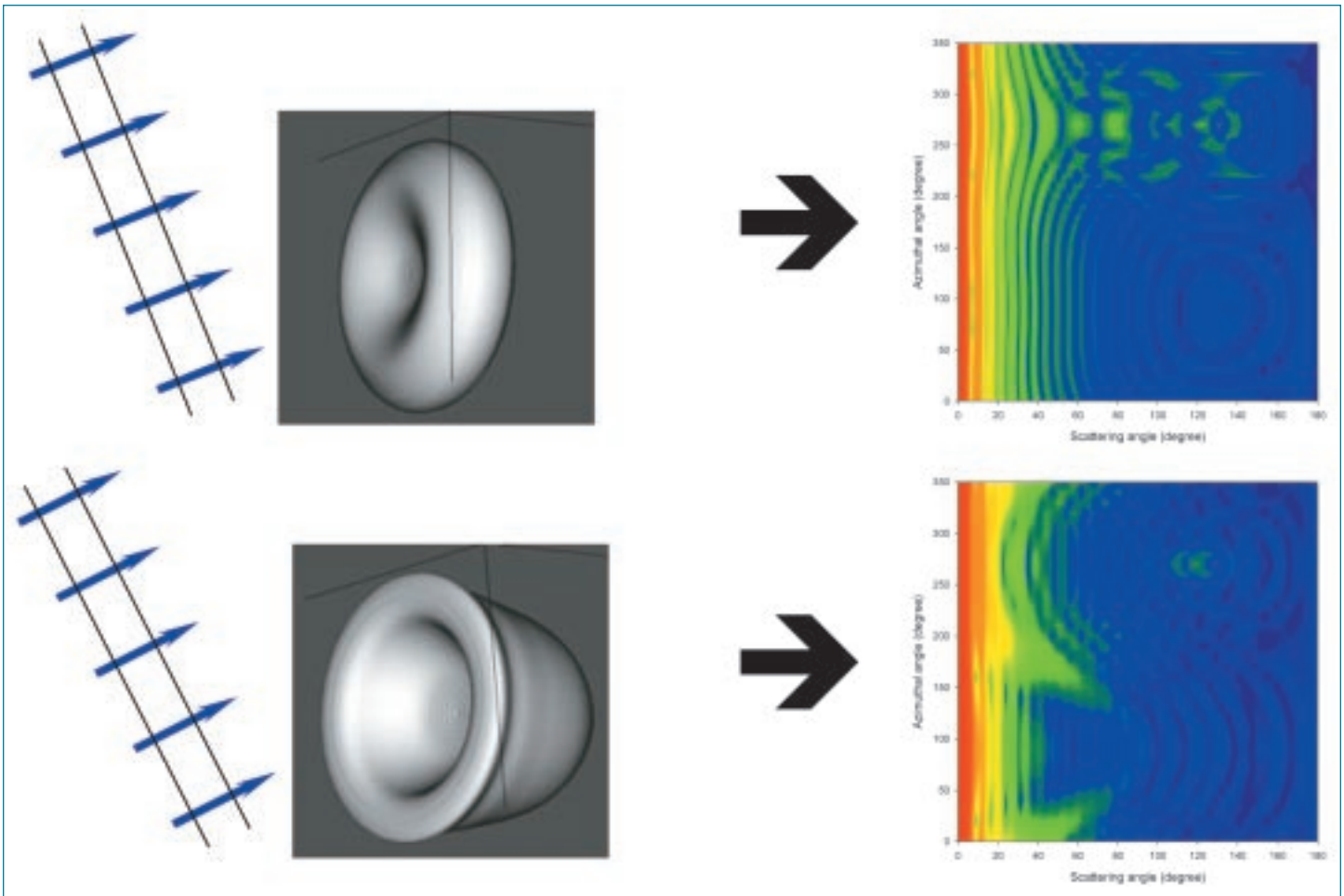
With about a million grid points, about two thousand time steps, and six finite difference equations for each grid point, it's clear why the process requires lots of computational power. If you also want to see how the light scattering changes with different cell types or the same cell in a different life stage, that requires even more power. "Parallel computing makes it faster," Lu says.

Lu and her colleagues work side by side doing computational modeling and experimental work. "I'm a theoretician," Lu says. "But I have scientists by my side doing experiments. So far, the models match reality pretty well."

Thus far, Lu's group has been studying light scattering by individual cells. Eventually, they will use the FDTD technique to do tissue studies—with hopes of distinguishing tumor from non-tumor. "People are showing lots of interest in this method," says Lu. "It's the right direction to pursue."

Integrative Cancer Biology Program is Born

The National Cancer Institute launched the Integrative Cancer Biology Program (ICBP) in October 2004, providing a total of $15 million to nine multidisciplinary centers. The goal: to use predictive cancer modeling to better understand how the disease



Light scatters differently from normal and deformed red blood cells.