once in an MRI scanner and 13 times while reporting their perceptions. The teams tested their methods on fMRI images of the volunteers watching a third set of scenes from the TV show. The goal was to decipher each individual's brain activation patterns and then describe his or her TV-watching experience in a way that would closely match the volunteer's real-time impressions. Winners were announced in June at the Organization for Human Brain Mapping meeting in Florence, Italy.

Overall, predictions were remarkably accurate, Schneider says. The easiest patterns to pick out in the fMRI data were those that occurred when volunteers heard background music. The top group's prediction for music perception was "almost right on top" of the volunteers' own ratings, he says, with an average correlation of 0.84. Patterns for faces, language, and environmental sounds were also generally easy to detect, and some groups excelled at identifying when the volunteers recognized specific actors in the scenes. On the other hand, nearly all groups stumbled at figuring out when food was visible on the screen. Perhaps the mere sight of food doesn't evoke strong signals in the brain, Schneider says, "although one subject did skip lunch, and we got better responses for him."

The top group, led by **Sriharsha Veeramachaneni, PhD**, a researcher at the Center for Scientific and Technological Research at the Istituto Trentino Di Cultura in Italy (ITC-IRST) with a background in computer engineering, built a model with recurrent neural networks. Despite knowing "practically nothing" about analyzing brain images, Veeramachaneni says, the researchers soon realized they could treat these signals as generic data for purposes of this competition.

The second-place team, led by **Denis Chigirev**, a physics doctoral student at Princeton University, concentrated on extensive preprocessing of the data across space and time—an approach that reflects the group's perspective. "Physicists pay careful attention to what is signal and what is noise," Chigirev says. "We wanted to let the signal tell us what to do."

Alexis Battle, a computer science doctoral student at Stanford University, led the third group which explicitly modeled correlations in the dataset. "We thought about the relationships in the data that we could exploit," Battle says. "We chose to encode the relationships in a formal probabilistic framework."

Schneider is already "playing matchmaker" to help facilitate new multidisciplinary collaborations next year. According to **Daphne Koller, PhD**, professor of computer science at Stanford University and principal investigator for Battle's team, "The fMRI field is at the point that genomics was 10 years ago. There's a tremendous opportunity now for us to integrate computational methods with the understanding that's being developed by the brain scientists."

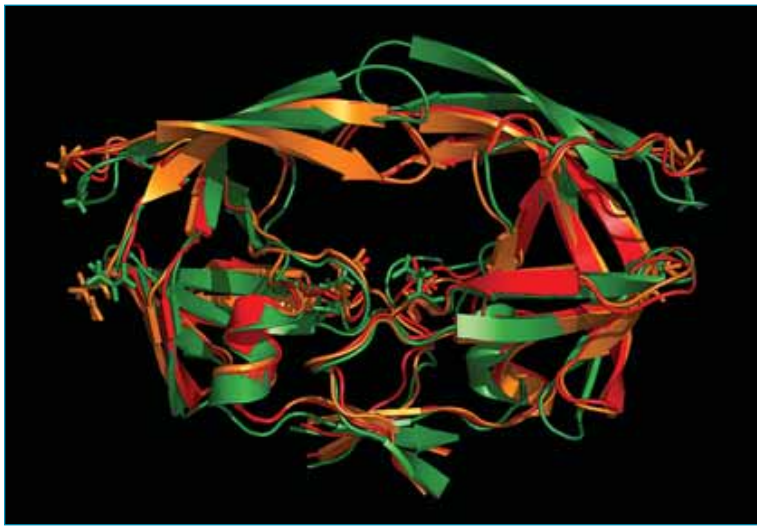
—Regina Nuzzo, PhD

Simulations Find Possible HIV Achilles' Heel

A blindside attack on HIV-1 protease might just combat drug-resistant strains of HIV, according to simulations run by researchers at the University of California, San Diego. When the simulations shut down an exposed movement on the side of the enzyme, the active site shut down as well. The work was published in *Biopolymers* in June 2006.

HIV-1 protease is an indispensable workhorse of the HIV virus: It cuts viral protein chains into building blocks ready for assembly into new virus particles. Many of today's anti-HIV drugs target this enzyme, generally by plugging up its active site and permanently closing two flaps over that area. In HIV strains resistant to these drugs, HIV-1 protease developed flaps

Perryman and his colleagues suggest designing drugs to target flap movement on HIV-1 protease instead of (or in addition to) the protein's active site.



A new target for anti-HIV drugs may be the allosteric grooves on the side of HIV-1 protease (see gaps in the middle of the right and left sides). When those are pinched together (see green protein, right and left sides), the flaps over the active site (top) can open. The flaps remain closed when the groove is propped open (red and orange versions). Courtesy of Alexander Perryman.

that are harder to latch shut. So now some researchers are suggesting targeting flap movement instead of (or in addition to) the active site.

That's why **Alexander Perryman, PhD**, now a postdoctoral fellow at California Institute of Technology, **Andrew McCammon, PhD**, professor of theoretical chemistry and pharmacology at UCSD, and their coworkers were very curious when they noticed an interesting movement on a side surface of HIV-1 protease in molecular dynamics simulations performed in 2004. When the protease closed its flaps across the active site, a groove on the peripheral surface expanded. Conversely, as the active site flaps opened, that same groove, called the allosteric groove, shrunk. It looked as if the movements were directly linked.

So the researchers hypothesized that inhibiting the movement of the allosteric groove would inhibit the movement of the active site flaps as well. In simulations that invoked an imaginary force or drug acting on the allosteric groove, they found their hypothesis was correct. When the allosteric groove is propped open by an imaginary drug, the flaps that guard the active site stay closed. And when the groove is pinched together slightly, these flaps will open.

It is still entirely unknown whether an actual drug exists, or could be created, that would apply the same force as the imaginary drug in the UCSD simulations. **Celia Schiffer, PhD**, associate professor of biochemistry and molecular pharmacology at the University of Massachusetts Medical School, thinks the groove movements are important for protease function, yet she is not convinced that the allosteric groove is a viable drug target. "I think practically that would be a very difficult place for inhibitors to bind in a specific and high-affinity manner."

But **Carlos Simmerling, PhD**, associate professor of chemistry at State University of New York, Stony Brook, is impressed by the UCSD strategy of finding a new drug target by observing enzyme movement. "The idea of targeting the mechanism is a lot more powerful than targeting the shape of the binding pocket, which is what current drugs do," he says.

—Louisa Dalton

Lung Tumors Recap Developmental Patterns

Researchers have long speculated that many of the genetic programs responsible for rapid growth of tumors are also important for the growth that occurs during normal embryonic development.

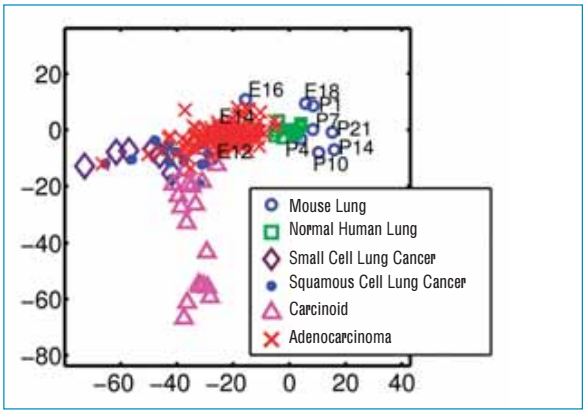
Now, researchers at the Children's Hospital Informatics Program at Harvard have found not only a relationship between tumors and lung development, but also a trend: The tumors with genetic profiles that resemble early lung development are deadlier than those with profiles that resemble later lung development. Separating out the least aggressive tumors from the more dangerous ones might help some lung cancer patients avoid unnecessary toxic chemotherapy. The work was published in *PLoS Medicine* in July 2006.

"Until now, lung cancers were classified through clustering of gene expression data, without seeing the trend from the point of view of development," says **Hongye Liu, PhD**, research fellow in the Children's Hospital Informatics Program at Harvard and MIT. "But we've found that the development trend can predict which cancer is worse."

Earlier work by Liu's co-authors, **Alvin Kho, PhD,** and **Isaac Kohane, MD, PhD**, showed that the gene expression profiles for each of several different types of brain tumors form distinct clusters when projected onto the gene expression profile of mouse genomic cerebellar development. The work by Liu and colleagues confirms these findings in the lung cancer context and takes them one step further by finding a connection between tumors, development and prognosis.

Charles Powell, MD, professor of clinical medicine at Columbia University College of Physicians and Surgeons, says Liu's work is important in emphasizing the link between cancer and development, but prognostic indicators in this paper need to be tested prospectively. More interesting, he says, is the potential

Tumors with genetic profiles that resemble early lung development are deadlier than those with profiles that resemble later lung development.



Principal components of gene expression data for mouse lung and normal human lung compared to that of various types of human lung cancer. The mouse lung development profile (blue dots) marches to the right over time. The most malignant forms of lung cancer (small cell lung cancer) more closely resemble early lung development in the mouse, while the least malignant forms (adenocarcinomas) more closely resemble later lung development in the mouse and normal human lung tissue. Carcinoids (purple triangles) are known to be quite different from the other types of cancers and have a pattern of gene expression that clusters perpendicular to and below the others. Carcinoids can look like small cell lung cancer under a microscope, but the two types of cancer require different treatments. This gene expression tool might help to distinguish them.