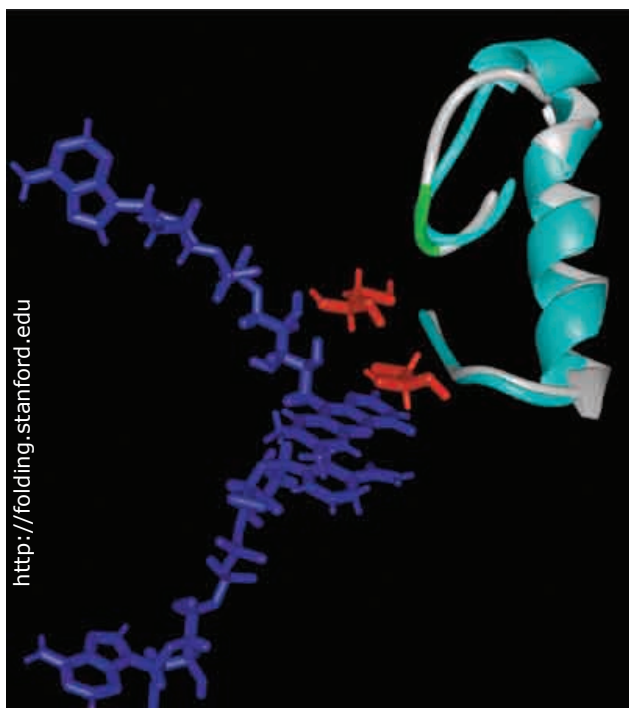


Folding Proteins at Home

by Ryan Propper

Computer users unlock medical miracles

Folding@Home, a leading research group at the James H. Clark Center, exemplifies the interdisciplinary vision and collaboration of the new Bio-X program through their integration of biomedical science and computer technology. This pioneering team in the field of biomedical computation is offering anyone who owns a computer the opportunity to contribute to their innovative work in the field of biomedical computation. People can take part in solving today's medical mysteries – and developing tomorrow's medical miracles – every time they turn on their computer.



Computer simulations of protein folding are helping research to unlock the structure of molecules such as these. Their insights may ultimately lead to new drugs and treatments for a variety of human disease.

Understanding Protein Folding

Folding@Home is an effort to better understand how many different classes of biological molecules “fold,” or assemble themselves into their final molecular form, before they assume their normal biochemical functions. The project, pioneered by Professor Vijay Pande and a team of 16 graduate students, employs novel computational

algorithms to bring previously impossible problems into the realm of feasibility. Their broad interest is to understand the fundamentals of biochemical interactions, not just the dynamics of proteins but also of nucleic acids, amino acids, and other biological molecules.

Understanding Protein Misfolding

Pande's group is seeking to understand biochemical questions which, although crucial to human life and health, are enormously complex and poorly understood. Protein misfolding is thought to be the cause of many serious diseases, such as Alzheimer's, cystic fibrosis, and some forms of cancer. Misfolded proteins form insoluble chemical masses which impede biological processes and can even poison neighboring tissue. For example, Alzheimer's disease results from tangles of neurofibrillary proteins blocking neural pathways in the brain. Unfortunately, these errors in protein folding are nearly impossible for other molecules to correct, just as it is extremely difficult to untangle a shoelace which has been knotted hundreds or thousands of times.

At the same time, however, the process of protein folding occurs so quickly that even today's fastest supercomputers cannot model the molecular interactions. A typical desktop computer today can simulate a nanosecond – one billionth of a second – in about a day, assuming the fastest known algorithms are used. But proteins can take 10,000 nanoseconds or more to “fold,” meaning a single computer would need 10,000 days -- 30 years -- to complete the calculations necessary for one result!

The Solution: Distributed Computing

The Folding@Home team turned instead to “distributed computing,” a term signifying the allocation of work in a single, large computing project among many separate computers. They rely on the more than 500,000 users who have downloaded and installed the Folding@Home client program from their website (<http://folding.stanford.edu>), allowing their computers to take part in the university's research efforts. The software only



performs its calculations using a computer's "idle cycles," time when it is not completing any other processor-intensive tasks, and can be configured to display its progress in a graphical screensaver. Pande encourages as many people as possible to download the client, which is designed to provide a linear speed increase as each new computer joins the network. Folding@Home allows anybody from any community – local, national, or global – to take part in cutting-edge biomedical research. Many of the most active participants are technology enthusiasts who form teams by school, state, country, or even an alliance to a particular magazine or website.

The Folding Problem

The distributed approach to the "folding problem" necessitated the formulation of complicated new computer algorithms to effectively share the calculations among hundreds of thousands of computers. Although these computational techniques are difficult to describe, Pande offers an analogy to help envision their complexity. Suppose that a math professor, with a class of 60 students, chose not to give each student an hour-long exam, but

instead to allow the entire class to work together on a one-minute exam. How would you design an algorithm which enabled the entire class to successfully complete the test? Or, in the most extreme case, how would you coordinate a class of 500,000 students in a group test lasting only one hundred thousandth of a second? As part of their solution, Pande's group has drawn on collaboration with other researchers from the biology, chemistry, and computer science departments. The team's offices, located in the Clark Center, serve as a hub for communication and facilitate associations with similarly interested groups.

Expanding the Project

Now in its third year as an active research endeavor, the Folding@Home group has published about one dozen papers. Their research results have been featured in prestigious scientific journals such as *Nature* and the team has enjoyed publicity through CNN, the New York Times, and Wired Magazine. Also, their client software has been integrated into the Google toolbar application (which integrates the Google search engine into the web browser). Most importantly, Pande's group has successfully simulated the folding of several simple proteins, and their results were validated experimentally in the laboratory. This has vindicated Folding@Home's efforts by demonstrating that it is, in fact, possible to bridge the gap between simulation and experimentation. Pande's unique approach of drawing from the vast computational power of hundreds of thousands of computers has enabled significant progress in the field of biochemistry.

While the Pande group continually refines and improves their computational algorithms and acquires a larger user base, they are also striking out in new directions in biomedical computation. Currently, the team is looking at medically important molecules and structures such as collagen, one of the most important proteins in the human body. Understanding the misfolding of collagen could result in earlier detection and drug treatment of various diseases, including osteogenesis imperfecta, scurvy, and Ehlers-Danlos syndrome.

As the Folding@Home team continues to explore the building blocks of human life, they depend on the enormous potential of distributed computing and the power of Internet users' volunteerism. Anyone can support their research by downloading Folding@Home's client program from <http://folding.stanford.edu>. Your computer could be the key to unlocking the next medical miracles. **S**



Vijay S. Pande, leader of the Folding@Home team.