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RESEARCH NEWS

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Researchers Launch Online Protein Folding Game

Multiplayer online gaming brings to mind fabulously successful titles, such as World of Warcraft and Ultima. On May 8, Howard Hughes Medical Institute (HHMI) researchers at the University of Washington are bringing the arcane world of protein folding to the online gaming arena with the launch of Foldit, a free game in which players around the world compete to design proteins. The real world benefit: Scientists will test proteins designed by the game's players to see if they make viable candidate compounds for new drugs.

Users can access the game via the web at www.fold.it

The development of the online game is a natural extension of HHMI investigator David Baker's quest to understand how proteins - the building blocks of cells — fold into unique three-dimensional shapes. Over the past decade, Baker and his colleagues have made steady progress in developing computer algorithms to predict how a linear string of amino acids will fold into a given protein's characteristic shape. A detailed understanding of a protein's structure can offer scientists a wealth of information — revealing intricacies about the protein's biological function and suggesting new ideas for drug design.

Predicting the shapes that natural proteins will take is one of the preeminent challenges in biology, and modeling even a small protein requires making trillions of calculations. Over the last three years, volunteers around the globe — now numbering about 200,000— have donated their computer down-time to performing those calculations in a distributed network called *Rosetta@home*. The computing logic behind the network is an algorithm called *Rosetta* that uses the Monte Carlo technique to find the best fit for all of the parts of a given protein.

But as the *Rosetta* volunteers watched their computers blindly trying to work out a solution by methodically testing every possible combination and shape to find the best fit, they began to think that a little human intervention might speed things up. People were writing in, saying, `Hey! The computer is doing silly things! It would be great if we could help guide it,' remembers Baker, who is based at the University of Washington (UW) where he developed the *Rosetta* algorithm and network.

Baker didn't know how he could make that happen until about 18 months ago, when he went hiking on Mt. Rainier with his neighbor David Salesin, a University of Washington computer scientist who also runs a research laboratory at nearby Adobe Systems. Baker and Salesin began discussing ways to make *Rosetta* more interactive. With the inherent fun of competition, Salesin thought a multiplayer online game was the way to go. By the time they got back to the car, they had settled on that idea. Salesin provided Baker with the names of three colleagues, led by UW computer scientist Zoran Popović, who could help Baker create the game.

Over the next few months, doctoral student Seth Cooper and postdoctoral researcher Adrien Treuille, working with Popović and Baker, created the program, and team tested it in small venues. One match between teams from the University of California and the University of Illinois aroused unexpected fervor and cheering among spectators. 30 or 40 people participated, says Baker. The competition was very intense.

Foldit takes players through a series of practice levels designed to teach the basics of protein folding, before turning them loose on real proteins from nature. Our main goal was to make sure that anyone could do it, even if they didn't know what biochemistry or protein folding was, says Popović. At the moment, the game only uses proteins whose three-dimensional structures have been solved by researchers. But, says Popović, soon we'll be introducing puzzles for which we don't know the solution.

Baker has high hopes that the game will speed up the sometimes tedious business of structure prediction. But the part of the game that excites him most is scheduled to debut this fall, when gamers will be able to design all-new proteins. Novel proteins could find use in any number of applications, from pharmaceuticals to industrial chemicals, to pollution clean up. With the ability for any person with a computer and an internet hookup to start building proteins, Baker thinks the pace of discovery could skyrocket. My dream is that a 12-year-old in Indonesia will turn out to be a prodigy, and build a cure for HIV, he says.