

versions of PGxPipeline predicted with similar accuracy a test set of 682 drug-gene interactions. And the text-mining-based version was slightly better at identifying genes that play the largest roles in response to a specific drug.

Garten hopes to use the revised PGxPipeline to parse all relevant scientific literature for drug-gene relationships. Better predictions will save researchers time in deciding which of the possible interactions to test in the lab and eventually influence how doctors prescribe drugs, she maintains.

“There is an emerging trend in bioinformatics to combine information from curated databases with information extracted from text,” says **Tom Rindfleisch, PhD**, principal investigator for the semantic knowledge representation project at the National Institutes of Health in Bethesda, Maryland. “This is an excellent example.”

—By *Olga Kuchment, PhD*

Scientific Discovery Through Video Games

When it comes to folding proteins, even modern supercomputers don't always get things exactly right. Enter

FoldIt, an online video game that harnesses the human brain's natural pattern-recognition abilities to tweak computer oversights. Since its release in May 2008, FoldIt has captivated a core group of several thousand dedicated players. Contestants manipulate three-dimensional protein chains into the best configuration they can find, exposing effective and previously unknown algorithms. In recent months, the puzzles have focused on medical applications. For example, a puzzle released in October called “Finding Home” asks players to bind a potential gene therapy tool—a homing endonuclease—to DNA. In another, called “Pack the Holes and Fight Cancer,” gamers will help design a protein that could activate a new kind of cancer drug.

“The players, most of whom are non-experts, have sort of become protein scientists,” says **Adrien Treuille, PhD**, assistant professor of computer science at Carnegie Mellon University. Treuille helped create FoldIt with a team at the University of Washington led by graduate student **Seth Cooper**, computer scientist **Zoran Popović, PhD**, and biochemist **David Baker, PhD**.

Researchers often must correct obvious errors in computer-folded proteins. FoldIt was developed to allow amateurs to spot and fix these computer inaccuracies. Players rack up points by pulling, wiggling, and tweaking a polypeptide sequence into the most chemically and physically accurate orientation. Most gameplay has concentrated on uncovering new folding algorithms, but FoldIt's current focus is producing player-designed proteins that can interact with particular biological targets, such as a small DNA strand. The game's creators recently released a puzzle asking players to generate a better design for human fibronectin, a protein used to mimic antibodies. One player modified fibronectin's peptide chain in a way that may turn out to be more stable than the original. Chemists at the University of Southern California are currently fabricating the novel structure for testing.

“FoldIt is a seminal and important project,” says **David P. Anderson, PhD**, research scientist at the University of California, Berkeley Space Sciences Laboratory who created an online astronomy volunteer project called Stardust@home. But he encourages the team to focus more on hard scientific data in the future. “I hope they are able to quantify what they've actually done,” he says.

Despite such concerns, Treuille thinks other researchers might imitate FoldIt's approach to computational analysis. “Everywhere you look in science there's labor that could use many people,” he says. Treuille believes that similar projects could draw on the power of crowds while entertaining and educating the public.

—By *Adam Mann* □

A team at the University of Washington designed the online game FoldIt to improve protein-folding algorithms. Players maneuver polypeptide chains, such as this 2HSH sequence, into their lowest energy configuration to get the highest score. Image courtesy of Seth Cooper at the University of Washington.

