

Researcher among best in protein modeling contests

March 30 2015, by Elizabeth K. Gardner



Daisuke Kihara, a Purdue University professor of biological sciences and computer science, sits at his desk with the illustration of a protein model on his computer screen. Kihara led teams that ranked among the top in the world in protein structure prediction competitions. Credit: Purdue University photo/Charles Jischke

A Purdue University researcher ranks among the best in the world in bioinformatics competitions to predict protein structure, docking and function, making him a triple threat in the world of protein modeling.



Daisuke Kihara, a professor of biological sciences and computer science, developed computer programs that predict the structures and functions of proteins for which this information is unknown.

"It is very difficult to capture the structure of some proteins through the standard experimental methods such as X-ray crystallography and electron microscopy," he said. "It is usually a long and difficult process."

Kihara's work, called <u>protein</u> structure prediction, could shave years off of drug development and other work that depends on understanding protein structure and function. It also plays into the field of artificial protein design, where the future may hold proteins created and programmed to carry out tasks like degrading harmful compounds in soil or fixing malfunctions and repairing injuries within a cell.

"Proteins are active, working machines involved in all of the processes of life," Kihara said. "Researchers are already synthesizing artificial proteins that have new structures, new assemblies and different functions from natural proteins, but they are capable of so much more. The key is gaining the ability to control a protein's assembly, or folding into its final shape, and structure prediction is a foundation of this."

Kihara led teams that earned among the top ranks in CASP, CAPRI and CAFA. CASP, or Community Wide Experiment on the Critical Assessment of Techniques for Protein Structure Prediction, is an international protein structure prediction contest. CAPRI, or Critical Assessment of Prediction of Interactions, is an international test of protein-protein docking predictions. CAFA, or Critical Assessment of Function Annotation experiment, is an international protein function prediction contest.

In CASP the participants are given the protein sequences of target proteins for which the structures are not known, but are soon to be



discovered through traditional research methods. By the end of the contests researchers outside the protein modeling field, including crystallographers and NMR spectroscopists, have determined the structures, which can be compared to the predictions, Kihara said.

There are two main approaches to protein <u>structure prediction</u>: templatebased modeling and free modeling. Template-based models use an existing known structure from a similar protein as a template that is built upon or modified. However, many proteins have no such templates available, and then free modeling must be used.

Kihara and his team created a free modeling method that searches existing databases for clues that can be used to build a model from scratch. The method is able to identify what information among the massive amounts collected in databases is useful. Known fragments of structures, super secondary structures and structures known to correspond to certain protein sequence patterns can be used as building units for the model, he said.

The model submitted by Kihara's team in the CASP free modeling category received the top ranking among more than 200 groups that participated. Hyung-Rae Kim, a postdoctoral researcher in Kihara's laboratory, led the work to the top-ranked prediction.

While Kihara and his team are very good at identifying clues to a target protein's structure, the key to their success is a scoring method to evaluate existing models of a <u>target protein</u>, he said. Kim and Kihara developed the procedure named Protein Residue Environment Score, or PRESCO. PRESCO looks at the atomic environment surrounding an amino acid residue. Amino acid residues are the building blocks of the protein molecule and PRESCO provides a larger view than commonly used scoring functions that focus on physical interactions within a single atom, Kihara said.



"This approach goes beyond the pair interactions within an atom and shows how several atoms are oriented in relationship to each other," he said. "It is like looking at a neighborhood instead of a single house within a city."

Free modeling is not yet at the stage where it can be used routinely to aid research, he said. A structure must be known to a resolution of at least 2 angstroms to be useful, and X-ray crystallography achieves a resolution of 1.5 angstroms or better, he said. Free modeling cannot yet consistently achieve this level of resolution, but the methods continue to improve.

"These competitions provide the opportunity to work on a variety of target proteins and to identify our strengths and weaknesses, and the circumstances that lead to the best results from our methods," Kihara said. "They also are a time when we get to speak with experimentalists and find out what they want from us and if there are certain regions of proteins that are of special interest."

In the model refinement category of CASP, in which participants refine close-to-correct models, Kihara's team ranked within the top 10. Amit Roy, a postdoctoral researcher in Kihara's group at the time, led the refinement work.

In round 30 of the CAPRI protein docking prediction competition Kihara's team was often ranked among the top five when evaluated in several different ways. In addition to Kihara, Kim and Roy, Kihara's CAPRI team included graduate students Lenna Peterson, Juan Esquivel-Rodriguez, and Xusi Han. CAPRI is intermittently held throughout one year and the current team includes post-doctoral researchers Jian Zhang and Woong-Hee Shin.

In the CAFA competition, where participants predict the function of



proteins, Kihara's team ranked within the top five in 2014. Ishita Khan, a graduate student in Kihara's research group led this work.

The CASP and CAPRI results were presented at the assessment meeting in December and are now available online. The CAFA results were presented in a paper published in the journal *Nature Methods*.

"Computational prediction can make significant contributions to experimental research by providing testable hypotheses and aiding in interpretation of experimental data," Kihara said. "These competitions have shown we are among the top teams working on prediction of <u>protein structure</u>, docking and function. However, more improvements are needed to achieve our goals and realize the potential of the field."

Provided by Purdue University

Citation: Researcher among best in protein modeling contests (2015, March 30) retrieved 28 April 2024 from <u>https://phys.org/news/2015-03-protein-contests.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.