

NewsBytes

And the Winner Is... Computer Aided Protein Design

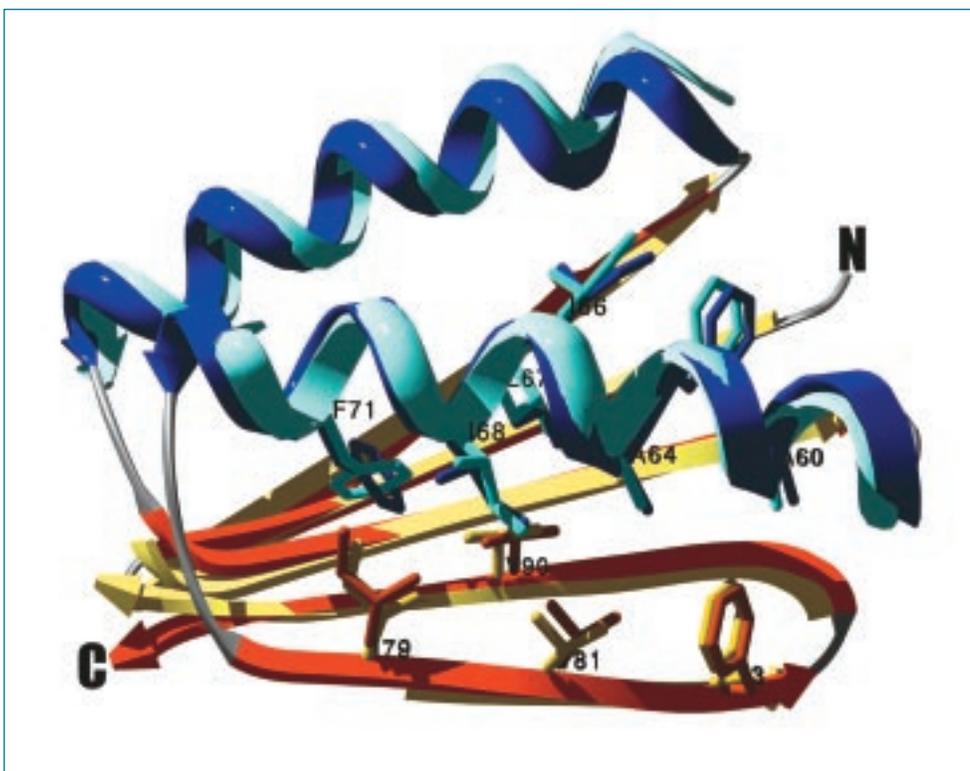
Each year, the American Association for the Advancement of Science (AAAS) gives an award to an outstanding paper that appeared in the pages of *Science*. This year the award—the Newcomb Cleveland Prize—went to researchers who computer-designed and then synthesized a protein that matched the design. The paper was published in the November 2003 issue of *Science*.

and people can make them with very high accuracy.”

Baker and his colleagues designed their novel protein using an iterative process. They started with a three-dimensional cartoon of a structure and used an existing design program to find the lowest energy sequence of amino acids to fit that structure. Like fitting puzzle pieces within an abstract shape, the sequence wasn't a perfect fit for the pre-designed structure. So they perturbed the structure to fit the sequence and then tried again to generate the low-

The work has helped researchers who struggle with the protein structure prediction problem, Baker says. “The prediction and design problems are closely related. The insights from the Top7 design have been helpful in developing methods for prediction, and the reverse is also true.”

Ultimately, Baker hopes to come up with novel protein machines and therapeutics. He's working on making enzymes that will catalyze reactions that aren't catalyzed in nature, and he's also trying to make better vaccines. It's



The Top7 computational model superimposed on the x-ray structure. The backbones are represented as ribbons (computational model: helices - dark blue, strands - red; x-ray structure: helices - light blue, strands - yellow), while selected amino-acid side chains in the protein core are represented as sticks. Courtesy: David Baker

“You see all these marvelous structures in nature and there has always been a question of whether there could be a larger set of proteins that don't exist in nature,” says David Baker, PhD, associate professor of biochemistry at the University of Washington and one of the paper's authors. “This paper showed such proteins do exist

est energy sequence of amino acids to fit the new structure. They went through this process ten times, and ended up with a protein they called Top7.

When they then produced that same protein sequence in the lab, Top7 folded into a shape that very closely matched the computer design. And the shape is unlike anything found in nature.

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an open question whether vaccines might be best designed using a scaffold that doesn't occur in nature, Baker says. “Nature hasn't ever come up with a vaccine on its own.”

Baker foresees a time when computer-designed therapeutics will become a reality, so long as they aren't too immunogenic. The AAAS award suggests that Top7 marks an important step in that direction.

Spaced-Out Neurons

Do neurons need personal space like people in an elevator? Are they influenced by their neighbors or do they randomly find a home in the brain? If the arrangement is patterned, what is the cause of the pattern?

These are all unanswered questions