Researchers shed light on how proteins find their shapes

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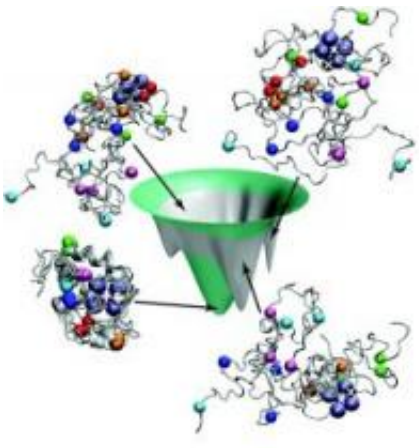

The UCSD model of the folding energy landscape for cytochrome c. The landscape was probed experimentally at Caltech, using time-resolved fluorescence energy transfer from six donor labels (represented as single spheres of differing colors) to the heme acceptor. [Credit: Peter Weinkam, UCSD]

(PhysOrg.com) -- Researchers from the California Institute of Technology (Caltech) and the University of California at San Diego (UCSD) have brought together UCSD theoretical modeling and Caltech experimental data to show just how amino-acid chains might fold up into unique, three-dimensional functional proteins.

Their insights were recently published in the February 10 issue of the *Proceedings of the National Academy of Sciences* (PNAS).

The paper details the matching of a series of protein-folding models created by the UCSD team (led by Peter Wolynes, UCSD professor of chemistry and biochemistry and physics) with experimental data gathered using a novel technique created by the Caltech team (led by Faculty Associate in Chemistry Jay Winkler and Harry Gray, Caltech's Arnold O. Beckman Professor of Chemistry and founding director of the Beckman Institute).

The Winkler-Gray method of watching proteins as they crumple and fold involves the use of a picosecond camera that captures fluorescent flashes as a laser pulse excites a donor probe, which emits light and transfers that light to an acceptor probe. The distance between the donor and acceptor change as the amino-acid chain transforms itself into a three-dimensional protein.

In the PNAS paper, the two groups combined the Caltech experimental technique--first described in a 2002 paper published in the *Journal of the American Chemical Society*--with Wolynes's protein-folding models to see if they could come up with the precise folding pattern of cytochrome c, a protein that is part of the mitochondrial electron-transfer chain that turns food into cellular energy.

At first the models and the experimental data seemed to be describing two entirely different things, according to Winkler. "The researchers had to account for charge-charge interactions between amino acids that appear to be important--the way that like charges repel and opposite charges attract," he explains. "And they had to consider the hydrophobic interactions--the way that oily parts of the proteins like to stick together but are repelled by the watery parts. When their models took account of these interactions, it fit the experimental data."

"It was the first time anyone has been able to develop a theoretical model able to account for the results we've been getting with our time-resolved

energy-transfer experiments," adds Gray.

Other coauthors on the PNAS paper, entitled "Electrostatic effects on funneled landscapes and structural diversity in denatured protein ensembles," are Patrick Weinkam from UCSD and Ekaterina Pletneva, formerly at Caltech and now at Dartmouth College.

Source: California Institute of Technology