Biomedical and Health Informatics Series

Tuesday, November 6, 2007, Room RR-134, 12:00-12:50

Valerie Daggett, PhD

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"Dynameomics"

The Protein Data Bank (PDB) is a repository of experimentally derived, static protein structures that has stimulated many important scientific discoveries. While the utility of static physical representations of proteins is not in doubt, proteins are dynamic and their mobility is critical to function. Molecular dynamics (MD) simulations provide the unique ability to realistically depict the time-dependent dynamics of biological macromolecules at the atomic level. We have begun an endeavor known as 'Dynameomics' which aims to perform MD simulations (and analyses) of representative proteins from all known folds in their native (i.e., biologically relevant) state and along their unfolding pathways to determine general rules of folding that will allow for improved structure prediction methods and decoding of genomes. Our Dynameomics database currently contains over 2600 simulations of more than 350 proteins, which makes it the largest collection of protein MD simulations in the world, with over 10^3 times more structures than the PDB. As an example of what can be learned from the database, we identified a mechanism of protein stabilization that preserves function while exhibiting significant dynamics. The localized dynamics, in conjunction with a mutation, in another member of the same fold is the cause of a host of disease phenotypes. To encourage similar breakthroughs in the understanding of the relationships between protein dynamics, function and disease by others in the community, we have constructed a web site, complementary to the PDB, which contains the Dynameomics simulations of the top 30 targets and their analyses [http://www.dynameomics.org].

Dr. Daggett has 22 years of experience performing simulations of proteins. She developed the approach of simulating protein unfolding to characterize the folding process. She also was the first to use simulation methods to map conformational changes associated with amyloidosis. At UW she was a founding member, and is now the Director, of the Biomolecular Structure and Design Program. She is PI of NIH, ONR, Microsoft, DOE and other grants. She is a regular study member of the NIH Macromolecular Structure and Function B Study Section. She has also evaluated grants for many other sponsors, including DOE, NAS/NRC, BBSRC, MRC, The Wellcome Trust, the Hereditary Disease Foundation and various NIH projects. Dr. Daggett is the Senior Editor of *Protein Engineering Design and Selection (PEDS)* and she is on several editorial boards: *Biochemistry*, *Structure*, and *Biomedical Computation Review (BCR)*. She is co-editor of the *Current Opinion in Structural Biology* issue on Folding and Binding, published in 2007. She was elected to the Biophysical Society Council (2007-2010), and she has organized several international meetings. Dr. Daggett has published over 125 scientific papers and had two of the 'Top 5' downloaded papers in the *Journal of Molecular Biology* in 2005.
