Quantitative Prediction of Protein Folding Behaviors from a Simple Statistical Model

The paper has been elaborated by Athi N.Naganathan, from the Joint Research Program in Computational Biology between BSC and IRB, and Pierpaolo Bruscolini, from BIFI (Institute for Biocomputation and Physics of Complex Systems of the University of Zaragoza) and represents another step forward in the field of protein folding

Barcelona, 4th April 2011.- The prestigious journal JACS (Journal of the American Chemical Society) has published the study *Quantitative Prediction of Protein Folding Behaviors from a Simple Statistical Model* carried out by the researchers Athi N. Naganathan and Pierpaolo Bruscolini.

"A key issue emerging from this study is that the WSME-S model, which is really a simple statistical-mechanical model neglecting non-native interactions, is able to quantitatively reproduce the folding equilibrium and kinetics, at least for the two small proteins considered", say the authors.

Protein folding concerns the re-arrangement of different segments of a linearly and minimally structured polymer chain (unfolded state) to typically a specific well-defined three-dimensional structure (folded state). From a computational viewpoint, studying this process is quite challenging as it involves several hundred atoms requiring years of simulation time to obtain good statistics at the atomic-level while it is almost impossible to reproduce experimental probes quantitatively. An alternative is to employ simple statistical-mechanical models parameterized at the residue-level, such as the Wako-Saitô-Muñoz-Eaton model. Here, every residue is assumed to access just two conformations, resulting in a total of 2^N configurations for an N-residue protein. In this project, the researchers develop a simple methodology (WSME-S) to access the exact energetics of all the configurations that is solely dependent on the distribution of contacts in the native state and the degree of exposure to the solvent. The team proceeded to study the folding behaviors of two different proteins with this model: one that folds in the microsecond time-scale (gpW) and other that folds in milliseconds (SH3). By tuning the model to reproduce one experiment, they reproduce other equilibrium and kinetic probes quantitatively highlighting the strength of the model. An added and a crucial advantage is the speed at which equilibrium predictions can be obtained – in just about a few seconds.

The authors also add that "the quality of the prediction is certified not only by the goodness of the fit to the calorimetric signals, but, most importantly, by the fact that adjusting the model parameters to reproduce the former, we also obtain accurate predictions for other equilibrium and kinetics observables. The model, therefore, appears to grasp all the important aspects of protein energetics. Even if we do not expect such good agreement to extend generically to all proteins, the model appears as a powerful candidate tool to interpret experimental data and to provide useful insights in designing new experiments".

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