Accurate calculation of protein folding energetics by difference

Javier Sancho*[1] and Juan José Galano-Frutos[1]

[1]Institute for Biocomputation and Physics of Complex Systems (BIFI) – Spain

Abstract

As proteins perform most cellular functions, quantitative understanding of protein energetics is required to gain control of biological phenomena. Accurate models of native proteins can be obtained experimentally but the lack of equally fine models of unfolded ensembles impedes the calculation of protein folding energetics from first principles. Here we show that an atomistic unfolded ensemble model, consisting on a few dozen conformations built from a protein sequence can be used in conjunction with an X-ray structure of its native state to calculate accurately by difference the changes in enthalpy and in heat capacity of the polypeptide upon folding. The calculation is done using Molecular Dynamics simulations and popular force fields and, for the two model proteins studied (barnase and SNase), the results agree within error or are very close to their experimentally determined properties.

Keywords: Protein stability, enthalpy calculation, heat capacity calculation, unfolded ensemble models, force field, water models, barnase, SNase

*Speaker