Contribution ID: **614** Type: **Invited Speaker / Conférencier invité**

Watching proteins fold: capturing the conformational diffusion of single molecules during structural self-assembly

Tuesday 16 June 2015 15:45 (30 minutes)

The self-assembly of intricate structures by proteins is a complex process involving myriad degrees of freedom. Such "folding"is usually described in terms of a diffusive search over a multi-dimensional energy landscape in conformational space for the lowest-energy structure. The diffusion coefficient, *D*, encodes the rates at which microscopic motions occur during folding and is thus of fundamental interest, but it is very difficult to measure. I show how *D* can be determined from measurements of single proteins folding and unfolding under tension in optical tweezers. By reconstructing the energy landscape for folding from the statistics of the single-molecule trajectories, *D* can be found using classic kinetic rate theories. More sensitive measures of *D* can be obtained by measuring the "transition time"required for the molecule to transit the energy barrier separating two structures. Using the folding of the protein PrP, which forms incorrect structures that lead to "mad cow"disease, as an example, *D* is seen to be orders of magnitude faster for the correct structure of the protein than for incorrect structures. Indeed, the incorrect structures form sufficiently slowly that the path the protein follows during the structural change—never before observed directly for any protein—can now be seen. Finally, I discuss how the properties of such transition paths can be used to show that the multi-dimensional problem of protein folding can be reduced quantitatively to one-dimensional diffusion.

Author: WOODSIDE, Michael (University of Alberta)

Presenter: WOODSIDE, Michael (University of Alberta)

Session Classification: T3-9 Molecular Biophysics (DMBP) / Biophysique moléculaire (DPMB)

Track Classification: Medical and Biological Physics / Physique médicale et biologique (DMBP-DPMB)