

Speaker:
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Date: Tuesday, February 19 2008 at 11am

Venue: E4A, Room 523 (level 5 seminar room)

Title: Identifying the features of co-translational protein folding

Abstract: How does a protein go from an extended chain to a biologically active three-dimensional (3D) configuration? This remains one of the major unanswered questions of biology. Understanding the process would revolutionise the biosciences, opening up the possibility of computationally solving protein structures and advancing structure based drug design. Using the Hydrophobic-Polar (HP) model, we investigate co-translational protein folding as a means of finding the global energy minimum (GEM) structure and show it is a viable mechanism for a significant number of 'protein-like' sequences. Co-translational protein folding is a widely accepted idea in the biosciences. It has received less support in computational studies because attempts to identify co-translational features in solved structures have proved inconclusive. However, these presumed co-translational features have come almost entirely from thought experiments. We circumvent this by using the 2D and 3D HP model, which has been fully enumerated in both sequence and structure space, to exhaustively study co-translational folding to a GEM structure. We subsequently identify the features, in both sequence and structure space, which typify co-translational folding. Counter to expectation we find that cotranslational folders are as compact as global folders and are not enriched in local contacts. We identify a preference for co-translational folders to have previous contacts and a more N-terminal core. We show that cotranslational folding to a GEM structure is characterised by a restriction in N-terminal structure space. We go on to show that solved protein structures are biased towards these features; but these structural features are neither exclusive to nor necessary for co-translational folding. Overall, we find significant evidence to suggest that many proteins may fold co-translationally; and conclude that previous thought experimentation, and therefore the resulting computational studies, into co-translational folding were too simplistic.