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THE UNIVERSITY of WISCONSIN MADISON

Department of Physics Colloquium

Friday, October 9, 2009 • 4:00 P.M. • 2241 Chamberlin Hall

cookies & coffee served at 3:30 p.m

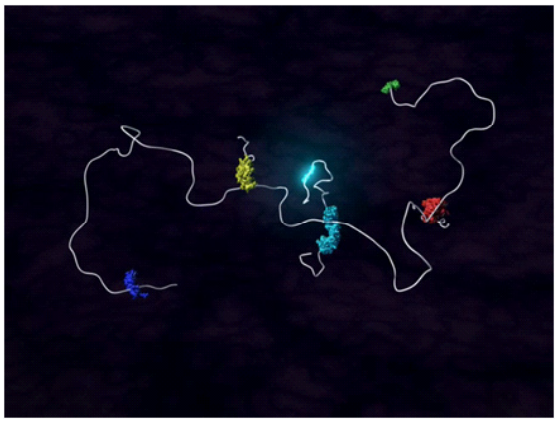
Protein Intrinsic Disorder and Developmental Biology

A. Keith Dunker

Department of Biochemistry and Molecular Biology, Indiana University School of Medicine

Host: McCammon

The standard view is that each protein's amino acid sequence provides the information for it to fold into a specific 3D structure, and this structure is required for its function. Thus, current biology and biochemical textbooks suggest that all proteins act via the sequence-to-structure-to-function paradigm. These views are correct for enzymes, which function as catalysts that accelerate chemical reactions. But a cell is not just a bag of chemical reactions. Biological processes, such as cell division or development of different cell types from a single cell, require regulation and organization of the various chemical reactions. These regulatory functions involve proteins that interact with each other via complex networks. We used computational and bioinformatics methods to show that the regulatory signaling interactions in cells depend not on protein 3D-structure, but rather depend on lack of 3D-structure. For signaling proteins, we propose a new paradigm, given in short as sequence-to-flexible-ensemble-to-function. We will illustrate these ideas using the Wnt signaling pathway, a widespread, well studied and exemplary signaling network that is crucial for developmental biology.



Unstructured Protein and Cell Signaling