

Spring 2010 CIS Colloquium Series

Protein Intrinsic Disorder and Cell Signaling

Keith Dunker

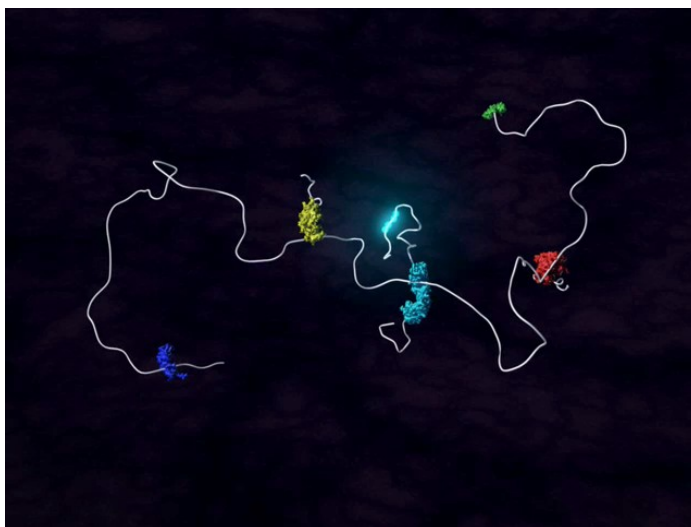
(Indiana University, School of Medicine)

1-2pm, Sunday, April 25

4th Floor Conference Room (Wachman Hall, CC 447)

Abstract: The standard view is that each protein's amino acid sequence provides the information for it to fold into a specific 3D structure, and the active site formed within this structure enables function. Indeed, current biology and biochemical textbooks suggest that virtually all proteins act via this 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 an unregulated bag of enzyme-catalyzed chemical reactions. Biological processes, such as cell division, development of different cell types, etc. require a coordinated regulation and organization of the various cellular components and compartments as well as regulation of the various chemical reactions. These regulatory functions involve proteins that interact with each other and with nucleic acids via complex networks. We have used computational and bioinformatics methods to show that the regulatory signaling interactions in cells depend not only on protein 3D structure, but also depend on lack of 3D structure as well. For signaling proteins, we propose a new general paradigm, given in short as sequence-to-flexible-ensemble-to-function. We will illustrate these ideas by providing a background based on bioinformatics approaches and then by focusing on various signaling proteins and pathways, including those forming the Wnt signaling pathway, a widespread, well studied and exemplary signaling network that is crucial for stem cells and developmental biology in numerous organisms and often is important in cancer.

Bio: Keith Dunker received a broad education, with degrees in chemistry (UC Berkeley, 1965), physics (UW Madison, 1967), and biophysics (UW Madison, 1969), and with postdoctoral training in structural biology (1969-1973, Yale University). After spending a career using biophysics and spectroscopy to study virus and phage structure and assembly especially for the purposes of understanding structures and functions of viral capsid proteins, in the middle 1980s Dr. Dunker realized the coming importance of computational biology and bioinformatics and began to teach, to work and especially to collaborate "on the side" in these newly developing areas. His biophysics work and his computational hobby merged in the mid 1990s with the realization that many proteins lacked 3D structure yet carried out function and could be studied as a group using bioinformatics approaches and methods. His "second career," which focuses on the bioinformatics of intrinsically disordered proteins, is leading to novel ideas regarding protein structure and function, and these will be the topics of his seminar.



Refreshments will be served!