



## **Title: Intrinsically Disordered Proteins Predictions and Applications**

**Keynote Speaker: T. K. Li Distinguished**

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**Abstract:** About 10 years ago we published our first predictor of intrinsically disordered protein residues in another IEEE journal, the Proceedings of the IEEE International Conference on Neural Networks. Others call such proteins "natively unfolded" and "intrinsically unstructured." Since then, we and others have substantially improved the prediction of intrinsically disordered residues. The prediction of protein intrinsic disorder is similar to the prediction of secondary structure in terms of methodology, but, at the structural level, secondary structure (especially random coil) and intrinsic disorder differ completely in their dynamic motion. First, we will briefly describe the prediction of protein disorder, show the progress from  $\sim 70\%$  to  $\sim 85\%$  per residue prediction accuracy, and show that intrinsically disordered proteins are common over the three domains of life, but are especially common among the eukaryotes. Next we will discuss our methods for deducing functions that are associated with disordered rather than structured proteins. In brief, structured proteins have advantages for catalysis while disordered proteins and regions have advantages for the reversible, weak binding often observed in signaling, control, and regulation. After that we will discuss how disorder facilitates binding diversity in protein-protein interaction networks, both for single disordered regions binding to many partners and for many disordered regions with different sequences binding to a common site on the surface of one structured protein. Part three presents data indicating that alternative splicing is more prevalent in regions of RNA that code for disorder than those that code for structure, thus providing a means for evolving tissue-specific signaling networks. Finally, we will present a novel approach to drug discovery based on disordered protein.

This work was jointly with Professors Pedro Romero, Jack Y. Yang, Vladimir N. Uversky, Zoran Obradovic, Jingwei Meng and Christopher J. Oldfield.

**Biography:** T. K. Li Distinguished Professor A. 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 as models for understanding connections between protein conformational changes and function, 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. He is highly regarded in the field as Founder/Father of The Protein Trinity and Intrinsic Disorder concepts, and his work has contributed significantly to increased understanding of the importance of protein disorder. Dr. Dunker's research is supported by NIH and by the Indiana Genomics Initiative, funded in part by the Lilly Endowment. He is currently T. K. Li Distinguished Professor of Medical Research and Director of the Center for Computational Biology and Bioinformatics of Indiana University. The Endowed Professorship title, T. K. Li, honors the current general director of the NIH/NIAAA.