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Workshop 4: Protein Folding and Stability

2833-Wkshp
Using proteins of reduced complexity to learn about cooperativity in folding
Doug Barrick.
Johns Hopkins University, Baltimore, MD, USA.

2834-Wkshp
Prediction of protein functional states by multi-resolution protein modeling
Cecilia Clementi.
Rice University, Houston, TX, USA.

2835-Wkshp
Alpha-Synuclein Conformation Affects Its Tyrosine Dependent Oxidative Aggregation
Gary J. Pielak, Rebecca A.S. Ruf, Evan A.S. Lutz, Imola G. Zigoneanu.
University of North Carolina at Chapel Hill, Chapel Hill, NC, USA.
Oxidative stress and aggregation of the protein μ-synuclein are thought to be key factors in Parkinson's disease. Previous work shows that cytochrome *c* plus H2O2 causes tyrosine-dependant *in vitro* peroxidative aggregation of proteins, including μ-synuclein. Here, we examine the role of each of α-synuclein's four tyrosine residues and how the protein's conformation affects covalent oxidative aggregation. When μ-synuclein adopts a collapsed conformation, tyrosine 39 is essential for wild-type-like covalent aggregation. This lone N-terminal tyrosine, however, is not required for wild type-like covalent aggregation in the presence of a denaturant or when μ-synuclein is present in non-covalent fibrils. We also show that pre-formed oxidative aggregates are not incorporated into non-covalent fibrils. These data provide insight as to how dityrosine may be formed in Lewy bodies seen in Parkinson's disease.

2836-Wkshp
How Well Evolved Is The Folding Code?
Sheena Radford.
University of Leeds, Leeds, UK.
Proteins are thought to fold on rugged energy landscapes, most proteins folding *via* kinetically trapped intermediates that accumulate as partially folded structures. Whilst such species may form essential stepping stones to the native state, others may allow access to misfolding pathways. Key to understanding the portioning between folding and misfolding, therefore, is to elucidate the structures of partially folded intermediates and to identify features of such species that favour correct folding or promote aberrant folding. Such information is not only of fundamental importance, but underpins our quest to elucidate the mechanism of chaperone action and the events that occur to tip the balance between folding and aggregation. In an attempt to gain high resolution information about the structure of intermediate species, we have used protein engineering, hydrogen exchange and chemical shift analysis, combined with restrained molecular dynamics simulations to derive a model for the structure of an intermediate formed during the folding of the four helical protein, Im7. More recently, we have used these techniques to determine the mechanism for intermediate formation, and hence the very earliest steps in folding wherein the native topology is formed. The data reveal an unusual ruggedness in the folding landscape of this simple protein that we suggest results from the evolutionary pressure to evolve new functions within this simple protein scaffold. In this lecture these results will be described and the influence of functional restraints in determining folding efficiency will be discussed.

2837-Wkshp
Effects Of Sequence And Conformational Contexts In Polyglutamine Aggregation
Rohit Pappu.
Washington University, St. Louis, MO, USA.
Aggregation of proteins with expanded polyglutamine tracts is implicated in the onset and progression of nine different neurodegenerative diseases including Huntington's disease. Recent work from our lab has focused on the driving forces for polyglutamine aggregation. We have shown that water is a poor solvent for polyglutamine. We have also shown that non-specific homotypic associations of collapsed albeit disordered polyglutamine molecules are spontaneous (non-nucleated), chain length dependent, and governed by the intrinsic disorder (spontaneous fluctuations) of these molecules. In addition to a brief overview of previous results, we will present results from recent work that assesses the role of sequence contexts and conformational restraints on the aggregation mechanisms of polyglutamine containing proteins. These results are garnered from a combination of theoretical, computational, and experimental efforts.

Workshop 5: Nanotechnology/Microfluidics

2838-Wkshp
Synthetic biology on the nanoscale
Petra Schwille.
Dresden University of Technology, Dresden, Germany.

2839-Wkshp
Fabrication Of Sealed Nanofluidic Channels Integrated With Surface Electronics
Robert Austin[1], Chih-kuan Tung[2].
[1]Princeton University, Princeton, NJ, USA, [2]Hong Kong Institute of Science and Technology, Hong Kong, Hong Kong.
I will present a method to fabricate nanochannels which are integrated with electronics using entirely room temperature processes. We believe this technology will open the door to integration of many kinds of surface electronics with nanochannel elongated polymer. The nanochannels are capped with a conformal low auto-fluorescence polymer which enables us to perform single-molecule optical imaging in real time with electronic detection.

2840-Wkshp
Nanostructures For Studying The Physics Of Biomolecules And Cells
Cees Dekker.
Delft University of Technology, Delft, Netherlands Antilles.
I will argue that nanostructures open up new opportunities for biophysics and briefly present two examples: 1. We use fabricated nanopores to study DNA and DNA-protein constructs. 2. Micro/nanofabricated chambers and channels are used to study the motility and adaptive behavior of E. coli bacteria. I will report the limits of bacterial penetration through narrow fabricated constrictions.

2841-Wkshp
Dynamic Liquid Film Interfaces
Owe Orwar.
Chalmers University of Technology, Göteborg, Sweden.

2842-Wkshp
Biology in Pico-Liter Droplets
Darren R. Link.
RainDance Technologies, Lexington, MA, USA.
RainDance Technologies is commercializing the use of picoliter droplets in microfluidic channels for applications in the life sciences. In typical applications, cells, nucleic acids, enzymes, or other reagents are encapsulated in aqueous phase droplets dispersed in a fluorinated carrier oil. These droplets range from sub-picoliter to tens of nanoliters in volume, and are manipulated on an individual basis to perform bioassays. Manipulations such as adding reagents or sorting droplets based on their optical properties are achieved solely through the application of external electric fields. Since electric fields can be turned on or off at very high speeds, sorting rates exceeding several thousand per second are readily achieved. We will focus on the techniques used to generate and manipulate droplets and introduce biological applications that are enabled by this technology.