Frontiers in Biophysics Jan. 23rd, 2009
Title and Abstract List for Graduate Student Talks

1. **Allard, J.**
   Title: Force generation by a dynamic Z-ring in *Escherichia coli* cell division

   Abstract: Cell division in bacteria requires the formation of a dynamic ring at midcell called the Z-ring, made of FtsZ, a microtubule-like polymer. FtsZ was recently shown to form rings inside tubular liposomes and constrict the liposomes similar to the way bacterial cells constrict, all without other proteins. We propose a mathematical model of the dynamics of the Z-ring and its ability to generate a constriction force. The model resolves the question of how FtsZ accomplishes cell division despite its highly dynamic nature and lack of molecular motors.

2. **Cao, Y.**
   Title: Enhancing mechanical stability of proteins by engineered metal chelation: a general approach in protein mechanics

   Abstract: Mechanical stability is an essential feature shared by elastomeric proteins, which function as molecular springs in a wide variety of biological machinery and biomaterials. Despite the progress in understanding molecular determinants of mechanical stability, it remains challenging to rationally enhancing the mechanical stability of proteins. Here we use single-molecule force spectroscopy and protein engineering techniques to demonstrate that engineered bi-histidine metal chelation can enhance mechanical stability of proteins efficiently and reversibly. This new approach not only opens new avenues towards engineering proteins of tailored nanomechanical properties, but also provides new ways to systematically map the mechanical unfolding pathway of proteins.

3. **Damiani, M.**
   Title: Flavin semiquinone stability in photolyase and cryptochrome: impact of active site Trp/Tyr exchange.

   Abstract: Photolyase (PL) and Cryptochrome (CRY) are a widely-distributed family of light-responsive flavoproteins containing a flavin adenine dinucleotide (FAD) cofactor. PL repair damaged DNA via base-flipping and photo-induced electron transfer. CRY do not repair these DNA substrates and have divergent functions including roles in plant and animal circadian rhythm. PL FAD semiquinone (sq) is exceptionally stable *in vitro*, essential for its high quantum yield of repair (~1). CRY does not posses this sq stability. We define the role of a conserved W/Y in sq stability of PL/CRY by measuring sq formation constants and oxidation kinetics in wild-type and mutant PL and CRY-DASH.

4. **Dennis, M.**
   Title: A nuclear localization signal sequence acts as a secondary membrane binding motif to distinguish the membrane binding affinities of two CCT isoforms

Abstract: CTP: phosphocholine cytidylyltransferase (CCT) is the key regulatory enzyme in the biosynthesis if phosphatidylcholine, the major phospholipid component of most eukaryotic biomembranes. CCT alternates between an active membrane bound form and an inactive soluble form. Despite having very similar amphipathic a-helical membrane binding domains, the CCTα isoform elicits a stronger binding response to lipids than CCTβ. Using biophysical and molecular techniques, we show that the amino-terminal polybasic nuclear localization signal exclusively in CCTα is a novel secondary membrane binding motif which is largely responsible for the differential response between CCT isoforms to anionic membranes *in vitro* and *in vivo*.

5. **Hentrich, T.**
   Title: Engineering nanoscale memory devices to capture transient molecular events in live cells

Abstract: One research branch in the field of biomolecular computing envisions devices that operate in and interact with live cells. These systems sense cellular conditions, process information, and generate molecular outputs, which directly affect cellular behaviour, or that are interpreted by an external observer. Promising progress has been made towards this vision, primarily using DNA to store and proteins to manipulate information. DNA in its organismal role, however,is rather static, and manipulating this molecule usually has severe negative effects. Computation, in contrast, demands the dynamic handling of information.
My research explores the potential of dynamic computation in living organisms, using the natural defense and regulation mechanisms of RNA interference (RNAi). From the viewpoint of my project, RNAi provides a universal protein machinery that allows construction of programmable computational devices on a single-cell scale. My goal is to mathematically describe, analyze, and build devices that are able to capture, count, and visualize transient molecular signals.

6. **Jetha, N.**
   Title: Probing the energy landscape associated with prion protein conversion via single molecule nanopore force spectroscopy

Abstract: Single molecule force spectroscopy using nanopores provides an excellent means to probe the energy landscapes associated with structural transitions in prion protein conversion (PrP^{C} to PrP^{SC}) taking place in prion diseases such as variant Creutzfeldt-Jakob disease. The technique is based on electrophoretically driving a single prion protein (immersed in an ionic solution) into a nanometer-scale pore, and observing the modulation of ionic current through the pore as structural domains fold and unfold due to the applied electrostatic force. We present preliminary results, showing voltage dependent structural transitions, which we associate with the melting and annealing of the β-sheet adjacent to the unstructured N-terminus of PrP^{C}. By measuring the rate of folding & unfolding over a range of applied forces and temperatures the energy landscape associated with these structural transitions can be reconstructed according to a modified Arrhenius relationship.

7. **Pel, J.**
   Title: A new method for biomolecule concentration

Abstract: We have developed a technology based on SCODA, a novel dynamic electrophoretic concentration mechanism, for efficiently purifying and concentrating biomolecules from challenging samples. SCODA offers unique advantages in biomolecule concentration including rejection of PCR inhibitors, an ability to enrich for low abundance nucleic acids, and ability to length-select nucleic acid fragments.
We present the fundamentals of the technology and examples of performance. This includes reduction of sample processing times to < 10 min, contaminant rejection, low level detection, concentration of proteins, and length selection of purified molecules.

8. **Peng, Q.**
Title: Single molecule force spectroscopy and steered molecular dynamics simulations reveal the mechanical design of the third FnIII domain of tenascin-C

Abstract: By combining single molecule AFM, proline mutagenesis and steered molecular dynamics simulations, we investigate the mechanical unfolding dynamics and mechanical design of the third FnIII domain of tenascin-C (TNfn3) in detail. Employing proline mutagenesis, we showed that the mechanical design of TNfn3 is very robust, and not only hydrophobic core packing plays important roles in determining the mechanical stability of TNfn3, backbone hydrogen bonds in β hairpins are also responsible for the overall mechanical stability of TNfn3. We also compare the AFM results with those of SMD simulations to understand the molecular details underlying the mechanical unfolding of TNfn3.

9. **Sadeghi, S.**
Title: The dependence of coiled-coil chirality on elastic energy

Abstract: Coiled coils are proteins that consist of two or more alpha-helices that wrap around each other to form a super-helical structure. Using a continuum elastic model, a recent paper[1] has shown that the chirality of the superhelical twist is dictated by the chirality of the pattern of hydrophobic residues on each helix only when the bending and twisting energy of each helix is considered. In the absence of any energy cost due to the flexible motions of each helix, they showed that there is a family of structures which are consistent with the hydrophobic pattern. Using a coarse-grained atomistic model for coiled coils that includes the flexible degrees of freedom for each helix, we have carried out monte-carlo simulations to examine how the energy and chirality of coiled coils depends on the strength of the elastic energy. We find that there is an optimal weighting of the elastic energy that leads to the coiled coils adopting the same chirality as the hydrophobic pattern on each helix. We then explored how the chirality of the coiled coil changed under the application of an applied force or an applied torque. Our findings are compared to recent measurements on the mechanics of coiled-coils from single-molecule studies.
[1] S.Neukirch, A.Goriely and A.C.Hausrath,PRL, 100, 038105 (2008)

10. **Tait, A.**
Title: Efficient high yield expression of novel membrane proteins

Abstract: Membrane proteins constitute about 70 percent of all drug targets and represent one

third of the human genome. However, only one percent of the protein structures that are known are for membrane proteins. One major reason for the lack of structural information is that membrane proteins are notoriously difficult to produce in sufficiently high enough and pure enough yields. Using a combination of approaches that have been previously established for globular proteins, we provide a novel method which will likely help to make available certain hard to obtain membrane proteins. Our case example is U24, a membrane protein from Human Herpesvirus Type 6, and implicated in the pathology of multiple sclerosis.