Research Interest

The research in my lab investigates the relationship between the 3D structures of proteins and how a sampled conformation imparts function. The protein conformation is influenced by local solvent conditions such as dielectric constant, pH, ligand binding, molecular crowding and small molecules, which has an effect on the protein’s function. Therefore, a detailed understanding of how changes in solvent conditions affect a change in 3D structure is important for relating the protein’s capacity to function under a variety of physiological conditions that are stimulated during processes relevant to signaling cascades from the membrane to the nucleus. The structure-function paradigm is also an important consideration for fabrication and characterization of smart material/polymer conjugates, tailored for a specific function in distinct micro-environments in cells or on the surface of synthetic materials. High resolution NMR spectroscopy and spectroscopic methods such as CD, UV-Vis and Fluorescence will be used to shed light on the structural perturbations of proteins in distinct solvents. A brief description of the current projects under investigation in the lab follows below.

Hydration, high concentration of salts and small molecules, dehydrated solvent conditions and pressure are physiological parameters that are imposed on pre-spun silks by spiders to produce high quality and robust, properly folded silk-fibers. We are interested in obtaining structural information, at atomic level resolution, (the conformation) of engineered spider-silk mimetics under similar solution conditions and in the solid state to determine the effects of the transient chemical treatment on the conformation of the silk protein-polymer. This information will lead to improvements in the material properties of synthetically produced fibers in terms of aggregation state and the design of new silk inspired block co-polymers with novel functions.

Cytochrome C is a 12 kDa, water soluble heam protein that is an important component of mitochondrial electron transport and oxidative phosphorylation, and also functions as an activator of apoptosis. Mitochondrial membrane associated cytochrome C shuttles electrons between complex 3 and complex 4 (Cyto C oxidase and Cyto C reductase), by performing redox chemistry at the surface of the inner mitochondrial membrane in the production of ATP and water. And cytoplasmic cytochrome C is an initiator of cellular apoptosis. Recently, it was discovered that a small tetra-peptide, termed SS31 for Schilling and Szeto, co-localized with cytochrome C in the mitochondria, and this resulted in increased electron transport. We are investigating the structural alterations induced in cytochrome C in complex with the SS31 peptide to determine how this small tetra-peptide facilitates accelerated electron transport and other therapeutic...

Actin cytoskeleton dynamics are important for cytokinesis, cell motility, cell shape and pathological processes such as tumor growth and metastasis. The profilins are ubiquitous actin monomer binding proteins that regulate actin based processes invivo by localizing ATP-G-actin monomers in regions undergoing dynamic filament assembly. The molecular features of profilin
in complex with G-actin and various ligands have been determined by high resolution X-ray crystallography, however the mechanism by which profilin releases the actin monomer for filament formation is not yet clear. Understanding the differential, isoform specific mechanism for regulation of profiling mediated actin polymerization might provide alternative therapeutic approaches to a number of pathological processes.

**Lab members:** At various times the lab has been populated by students at the high school level, undergrads and graduate students. Lab members for 2011 are shown below.

**Relevant publications:**
High-resolution NMR Characterization of a Spider-Silk Mimetic Composed of 15 Tandem Repeats and a CRGD Motif; Protein Science 2009, 18, 206-216
GD McLachlan, J Slocik, R Mantz, D Kaplan, S Cahill, M Girvin and SG Greenbaum

Acid-Induced Equilibrium Unfolding Intermediate of Human Platelet Profilin; Biochemistry 2007, 46, 6931 -6943
GD McLachlan, S Cahill, M Girvin and SC Almo

Solid State NMR Characterization of Electrolyte Breakdown Products in Nonaqueous Asymmetric Hybrid Supercapacitors; Electrochemical and Solid State Letters 2007, 10, A5-A8
I Nicotera, GD McLachlan, GD Bennett, I Plitz, F Badway, GG Amatucci, and SG Greenbaum