soluble-solute interactions in protein-sucrose mixtures. The results could be satisfactorily accounted for by an effective hard particle model that indicates the nature of the underlying interactions between sucrose and each protein.

2907-Pos  Board B62  
**Stability of Proteins in Cellular Environments**  
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How cellular crowding environment affects protein structures and stability is one of the key issues in molecular and cellular biology. In classical view, volume exclusion effect was emphasized as a major contribution and thus protein is considered to be stabilized under the environment. Atomicistic molecular dynamics with explicit solvent and hydrogen-exchange analysis of NMR spectroscopy show that some proteins are destabilized via protein-protein interaction under the crowded environment. In the current study, two small proteins, stability of protein-G and villin headpiece subdomain are examined and only villin is greatly destabilized when protein volume fraction is greater than around 30%. The denatured structure of villin in crowded environment is totally different from that at high temperature. It is a compact but less hydrophobic packing and secondary structures, showing some similarity with the urea denaturation. NMR measurements show that hydrogen-exchange rates of villin become greater in the residue connecting between helices, suggesting that these regions may interact with other villin or protein-G in crowded environments. Correlation analysis of protein-protein interaction show that protein-protein interaction may change with the protein volume fraction. These results change our views on the cellular crowding effect from entropic-centered volume exclusion to enthalpic-driven protein-protein interactions.

2908-Pos  Board B63  
**Non Linear Effects of Macromolecular Crowding on the Mechanical Unfolding of Proteins**  
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Macromolecules can occupy a large fraction of the volume of the cell and this crowded environment affects many properties of the proteins inside the cell, such as unfolding forces, thermal stability and rates of folding. Although much is known about molecular crowding, it is not well understood how the relative size of the crowder affects the resistance of a protein to mechanical stress. An atomic force microscope-based single molecule method was used to measure the effects of crowding on the mechanical stability of I-27. Crowding was provided by the addition of Dextran of three different molecular weights 6kDa, 10kDa and 40kDa, with concentrations varying from zero to 300 g/L in a pH neutral buffer solution at room temperature. The forces required to unfold biomolecules were found to increase when a high concentration of crowder molecules was added to the buffer solution and the force required to unfold a domain reached a maximum value when the crowder size was comparable to that of the protein. To model the effect of Dextran on the energy barrier Ogston’s Theory as well as Scaled Particle Theory were employed, neither of which was completely satisfactory in describing the results. We hypothesize that the composition of Dextran may play a role in the deviation of the predicted behavior with respect to the experimental data.

2909-Pos  Board B64  
**Sedimentation Velocity Analysis of Polyglutamine Assembly in C. elegans using a Fluorescence Detection System**  
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The presence of different size protein aggregates is a common feature of neurodegenerative diseases and which types of aggregates (whether oligomeric or fibrillar) are toxic is still not well defined. By using expression of various polyQ expression constructs in C. elegans, we apply analytical ultracentrifugation methods with fluorescence detection capability to determine size distribution of protein aggregation. We found that an increase in intermediate size range pools of protein aggregation. We find that an increase in intermediate size range pools of protein expression constructs in fibrillar is toxic are still not well defined.

2910-Pos  Board B65  
**Effect of Hydrophobic Interactions on Volume and Thermal Expansivity as Derived from Micelle Formation**  
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It has long been observed that the net volume change upon protein unfolding is very small. The loss of structural voids and hydration of otherwise shielded charged groups from unfolding contribute negatively to volume change, while expansion persists regarding whether the exposure of hydrophobic groups has a condensing effect or a structure-making effect on water. The development of pressure perturbation calorimetry in recent years has made it possible to determine expansivity directly with great precision. Data obtained for proteins were interpreted in terms of a structure-making effect that expands the water interacting with the solute. We have studied volume and expansivity effects of transfer of alkyl chains into micelles by pressure perturbation calorimetry and isothermal titration calorimetry. The contribution of hydrophobic groups to expansivity upon hydration is positive and independent of temperature, similar to that obtained with hydrophobic amino acids. Our data oppose the widely accepted assumption that water-exposed hydrophobic groups yield a negative contribution to expansivity at low temperatures that would imply a structure-making, water-expanding effect. It is of worth to note that group contributions should be obtained by subtracting molar expansivities, not coefficients of expansion.

2911-Pos  Board B66  
**Simulated Amyloid Fibril Nucleation in Reverse Micelles**  
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A recently published FTIR study has shown that the 40-residue amyloid beta (Abeta) protein forms extended beta-stands in reverse micelles, while an analogue with a scrambled sequence does not. This result suggests that the Abeta sequence is inherently amyloidogenic, and that its amyloidogenicity is enhanced in a crowded confined membrane-like environment of a reverse micelle. This result is significant because it suggests that these factors may nucleate or otherwise promote the formation of amyloid fibrils in the human brain in Alzheimer’s disease. We have conducted molecular dynamics simulations of wild-type and scrambled-sequence Abeta protein in reverse micelles of the same composition studied experimentally to gain insight into the physicochemical factors that promote beta structure in wild type, but not scrambled sequence protein. Preliminary results show that the wild-type sequence does indeed form extended beta structure, while the scrambled sequence does not. The interactions stabilizing beta structure in the wild type sequence appears to be hydrogen bond formation involving amino acid side chains.

**Protein Structure**

2912-Pos  Board B67  
**Crystal Structure of N-Acetylglactosamine-6-Sulfatase: The Molecular Basis for Mucopolysaccharidosis Iva**  
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Lysosomal enzymes catalyze the degradation of macromolecules in the cell. In humans, a deficiency of a single lysosomal enzyme leads to a metabolic defect known as a lysosomal storage disease. Over fifty lysosomal storage diseases are known and have a collective incidence of approximately 1 in 7700 live births. Mucopolysaccharidosides IV A (also known as MPS IV A and Morquio A) is a lysosomal storage disease caused by a deficiency in the human lysosomal enzyme galactosaminase-6-sulfatase (GALNS), also known as N-acetylglactosamine-6-sulfatase and GalNS (E.C. 3.1.6.4). To elucidate the molecular mechanism of this disease, we determined the three-dimensional structure of human GALNS, by x-ray crystallography at 2.2 Å resolution. Enzymatic assays on the insect cell-expressed human GALNS indicate activity against synthetic substrates and inhibition by both substrate and product. Mapping 120 MPS IV A missense mutations onto the structure illustrates that a majority of mutations affect the hydrophobic core of the structure, indicating that most MPS IV A cases result from misfolding of GALNS. The structure of the family, but strict conservation of the catalytic machinery. Overall,