and their modulation upon adding carbohydrate osmolytes were assessed. Finally, we discuss the effect of these solutes on the conformational landscape, the way they interact with water and effect solution characteristics, and hydrogen bond network restructuring upon adding sugar osmolytes.

2144-Pos Board B130
A Mutant of Atlantic Salmon Fast Muscle Tropomyosin
Korrina R. Fudge, David H. Heeley.
Atlantic salmon fast skeletal muscle alpha-tropomyosin is less conformationally stable than the rabbit counterpart. The two alpha-tropomyosins share a total of twenty substitutions. Every core (''a'' and ''d'') amino acid is conserved with one exception, residue-179 (''d'') Ala (rabbit) to Thr (salmon) which coincides with a region, that in the case of the mammalian protein, is known to be unstable. The effect of this isomorphism has been investigated using far-UV circular dichroism and limited proteolysis. Heat-induced unfolding (1 to 2 mg/mL protein; 5-65 degrees C; Buffer, 0.1M salt + 1mM dithiothreitol, pH 7) of wild type salmon tropomyosin results in two cooperative transitions having Tms of ~38 (main) and ~25 degrees C. The minor transition was less evident in the case of tropomyosins expressed in BL21 and isolated without exposure to elevated temperature or organic solvent. The unfolding profiles of recombinant tropomyosins (temperature ramp, 30 or 60 degrees C per hour; light path, 0.1mm) are dominated by a cooperative transition at ~36 (non-mutated) and ~41 degrees C (single site mutant, Ala-179). The mutant also displays increased resistance to digestion by chymotrypsin which initially cleaves tropomyosin at Leu-169. Thus, the presence of an hydroxyl-containing side-chain at position 179 is concluded to contribute to the reduced conformational stability of Atlantic salmon tropomyosin.

2145-Pos Board B131
The Effect of Protein Stability on Interactions of Apomyoglobin Forms with Phospholipid Membranes
Vitaly A. Balobanov, Nelly B. Ilyina, Natalia S. Katina, Ivan A. Kashparov, **Valentina E. Bychkova**.
The protein structure can be strongly influenced by phospholipid membranes. As it follows from our papers, apomyoglobin structure undergoes a transition from the native to some intermediate state upon interaction with small negatively charged phospholipid vesicles acting as a moderately denaturing agent. In this work, interaction of apomyoglobin and its mutant forms with artificial membranes is studied by tryptophan fluorescence and CD in the far UV-region. It is shown that a negatively charged phospholipid membrane can structure the unfolded protein into the same intermediate state. The nature of this phenomenon consists in selective stabilization of the intermediate state structure. The rate of interactions between apomyoglobin mutant forms and phospholipid membranes depends mainly on the protein molecule stability, as well as on the charge of the membrane surface and the phospholipid vesicles concentration. This rate increases with decreasing protein stability. The importance of the obtained results for the folding of membrane proteins and the choice of the pathway for target delivery of protein drugs are discussed. This work was supported partly by the Howard Hughes Medical Institute Award 55005607 to A.V. Finkelstein, by the RAS Program ''Molecular and Cellular Biology'', by Federal Agency for Science and Innovations 02.740.11.0295, and Program of Scientific Schools 2791.2008.4.

2146-Pos Board B132
An Energetic Representation of Protein Architecture that is Independent of Primary and Secondary Structure
James O. Wrabl, Jason Vertrees, Vincent J. Hilser.
Protein fold classification often assumes that similarity in primary, secondary, or tertiary structure signifies a common evolutionary origin. However, when similarity is not obvious, it is sometimes difficult to conclude that particular proteins are completely unrelated. Clearly, a set of organizing principles that is independent of traditional classification could be valuable in linking different structural motifs and identifying common ancestry from seemingly disparate folds. Here, a four-dimensional ensemble-based energetic space spanned by a diverse set of proteins was defined and its characteristics were contrasted with those of Cartesian coordinate space. Eigenvector decomposition of this energetic space revealed the dominant physical processes contributing to the more or less stable regions of a protein. Unexpectedly, those processes were identical for proteins with different secondary structure content and were also identical among different amino acid types. The implications of these results are twofold. First, it indicates that excited conformational states comprising the protein native state ensemble, largely invisible upon inspection of the high-resolution structure, are the major determinant of the energetic space. Second, it suggests that folds dissimilar in sequence or structure could nonetheless be energetically similar if their respective excited conformational states are considered, one example of which was observed in the N-terminal region of the Arc repressor switch mutant. Taken together, these results provide a surface area-based framework for understanding folds in energetic terms, a framework that may eventually yield a means of identifying common ancestry among structurally dissimilar proteins.

2147-Pos Board B133
Effects of Ionic Salts in Aqueous Environments on the Folding Dynamics of the 21-30 Fragment of the Amyloid Beta-Protein
Micholas D. Smith, Luis Cruz.
The amyloid β-protein (Aβ) has been implicated in the pathogenesis of Alzheimer's disease. Although little is known about the initial deleterious misfolding of the full-length Aβ, in vitro experiments have shown that a 21 through 30 fragment of Aβ, the Aβ(21-30), may be the folding nucleus of the full-length protein. Our previous all-atom molecular dynamics work shed light on the behavior of the Aβ(21-30) in bulk water. Here, we explore the effects on the folding dynamics of the Aβ(21-30) of dissolved ionic salts (NaCl, CaCl2, and KCl) that are common to the cellular environment. Using microsecond-long all-atom molecular dynamics we find that previously found extended beta secondary structures are suppressed by KCl, promoted by CaCl2, and slightly promoted by NaCl. Measurements of distances, radial distributions, and contacts of ions surrounding the Aβ(21-30) are also analyzed. Our results suggest that electrostatic interactions between the ions and residues play a less significant role than interactions between solvent and residues due to structure ordering of solvent molecules by local ions.

2148-Pos Board B134
Molecular Basis for the Solvation and Reconstructive Denaturation of Proteins by Detergents
John C. Holyoake, Gil Privé, Régis Pomès.
Detergents are widely used for the biochemical and structural study of proteins. Non-ionic and zwitterionic detergents are used as membrane mimetics, where they solvate the hydrophobic regions of integral membrane proteins. In contrast, ionic detergents such as anionic sodium dodecyl sulfate (SDS) and cationic lauryl trimethylammonium chloride (LTAC) are strong protein denaturants that unfold both soluble and membrane proteins. Not only does the SDS-unfolded state have high α-helix content, but SDS also induces α-helix formation irrespective of the intrinsic native secondary structure, a process known as ''reconstructive denaturation.'' Although this latter phenomenon underpins the ubiquitous technique SDS-PAGE, the mechanism of SDS denaturation and the molecular nature of the SDS denatured state are not known. We use a combined biophysical and computational approach to elucidate the molecular basis of protein denaturation by ionic detergents, with a special focus on the mechanism of reconstructive denaturation by SDS.
Specifically, biophysical techniques, including CD and ITC, are used to study the interaction of a set of detergents with model systems that build in complexity from model peptides to full proteins. In the first case, peptide sequence design is used to explore the specific features determining interactions with ionic detergents, while in the latter, chemical modification of residue side chains is used to explore the determinants of detergent interactions in the complex background of a biological protein sequence. In parallel with the biophysical studies, molecular dynamics simulations of the same systems are used to provide atomic resolution detail of the results from the biophysical experiments, and to determine the modes of detergent micelle-protein interaction. Together, these results suggest a consistent mechanism for the reconstructive denaturation phenomenon, for sequence based specificity of ionic detergent interactions, and ultimately, for SDS's universal protein denaturing action.

2149-Pos Board B135
Investigating Domain-Swapped Proteins by 19F NMR
Lin Liu, In-Ja Byeon, Ivet Bahar, Angela M. Gronenborn.
For most proteins under physiological conditions, the native functional state is a single, stable structure. However, certain circumstances may push protein folding into distinctly different structures. The most common alternative structures comprise different multimeric assemblies of identical polypeptide chains. Among thousands of homo-oligomeric protein structures, there is a small, but growing subset of 'domain-swapped' proteins[1], in which the exchanged subunit in the oligomer is identical to the one in the corresponding monomer. For domain-swapped structures, the only structural difference between the monomer and the pseudo-monomeric unit in the multimer is the region that links the exchanging domains. Although no unifying molecular mechanism of domain swapping has been elucidated, it appears that domain swapping is closely associated with the unfolding/folding process of proteins. For some proteins, distinct intermediates may exist, while for others, complete un/folding may occur. We are studying the dynamics and conformational behavior of specific domain-swapped systems by ^{19}F-NMR in order to gain a better mechanistic understanding of domain swapping.