using the coarse-grained method tCONCOORD and the protein interfaces were identified with the POPSCOMP [1] method and characterized by analyzing the amino acid composition and conservation, the secondary structure content and the promiscuity of binding. A local measure of the interface ''plasticity'' was also obtained using our Structural Alphabet [2].
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924-Pos Board B710
Visualizing Ca^{2+}-Binding Sites using Refined Oxygen and Carbon Clusters
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Identifying Ca2+-binding sites in proteins is the first step towards understanding the molecular basis of diseases related to Ca2+-binding proteins. Currently, these sites are identified in structures either through X-ray crystallography or NMR analysis. However, Ca2+-binding sites are not always visible in X-ray structures due to flexibility in the binding region or low occupancy in a Ca2+-binding site. Similarly, both Ca2+ and its ligand oxygens are not directly observed in NMR structures. To improve our ability to predict Ca2+-binding sites in both X-ray and NMR structures, we report in this paper a new graph theory algorithm (MUGC) to predict Ca2+-binding sites. Using second shell carbon atoms, and without explicit reference to side-chain oxygen ligand coordinates, MUGC is able to achieve 94% sensitivity with 76% selectivity on a dataset of X-ray structures comprised of 43 Ca2+-binding proteins. Additionally, prediction of Ca2+-binding sites in NMR structures were obtained by MUGC using a different set of parameters determined by analysis of both Ca2+-constrained and unconstrained Ca2+-loaded structures derived from NMR data. Based on these more inclusive values, MUGC identified 20 out of 21 Ca2+-binding sites in NMR structures inferred without the use of Ca2+ constraints. MUGC predictions are also highly-selective for Ca2+-binding sites as analyses of binding sites for Mg2+, Zn2+, and Pb2+ were not identified as Ca2+-binding sites. These results indicate that the geometric arrangement of the second-shell carbon cluster is sufficient for both accurate identification of Ca2+-binding sites in NMR and X-ray structures, and for selective differentiation between Ca2+ and other relevant divalent cations. This algorithm has been applied to channels and receptors and proven to be very accurate.

925-Pos Board B711
Efficient Protein Loop Generation using Distance-Guided Sequential Monte Carlo Method
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We have developed a new loop construction method through fast sampling with a knowledge-based energy function. Based on a new sequential Monte Carlo sampling strategy called Distance-guided Sequential Monte Carlo (DSMC), our method efficiently generates accurate loop conformations with low energy. The average CPU time cost for sampling 9 residue loops is 22 minutes, with the average smallest global RMSD of 0.7 A for a set of 40 proteins with a total of 40 loops. After refinement and evaluation using simple knowledge-based scoring function, the average RMSD for lowest energy conformations is 1.7A. Geometric method is incorporated in detecting surface confined feasible region, which accelerated the speed for energy calculation by 3 times. Our approach is especially effective in sampling long loops: The average smallest global RMSD for 12 residue loops is 1.7 A and the CPU time cost in average is only 30 minutes.

926-Pos Board B712
Mapping the Human Single-Span Membrane Proteome for Self-Interacting Transmembrane Domains
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Single-span membrane proteins comprise more than 10% of the human proteome. Most of those integral membrane proteins form non-covalent functional complexes that are frequently supported by sequence-specific interaction of transmembrane domains (TMDs) [1]. It has been suggested that non-covalent membrane protein multimerization may substitute for the frequently observed multi-domain organization of soluble proteins. To date, only a few dimerization motifs such as the GxxxG motif are known. Even those motifs are highly depending on the sequence context.
Here, we investigate biologically relevant sequence similarities of human single-span membrane proteins and use them to construct clusters of homologous TMDs. Using the ToxR system [2] it is possible to experimentally determine the self-interaction of one representative TMD for each group. Amino acids which are conserved in the alignment of each cluster's TMDs were replaced to identify their importance for homotypic interaction.
We are able to group almost half of all bitopic TMD sequences into clusters. Most sequences from large clusters exhibit medium to high self-interaction as shown by the ToxR system. From those findings one can assume specifically interacting TMDs to be highly represented in the human proteome. Almost half of the investigated clusters include a conserved GxxxG or SmallxxxSmall like motif which was found to be important for interaction, if not exclusively. In some cases extracellular domains are by far not as similar as their corresponding TMDs. This raises the question about the origin and development of TMDs by convergent or divergent evolution.
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927-Pos Board B713
Molecular Dynamics Simulations of E. Coli Lipoplysacharide Bilayers
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Lipopolysaccharide (LPS), a component of bacterial outer membranes, is responsible for the toxicity of Gram-negative bacteria. LPS is made up of three regions: the O-antigen, the core, and the innermost lipid A. These three components have been sequenced individually but never as one construct. Utilizing the latest C36 CHARMM lipid and carbohydrate force field, we have constructed a model of an entire E. coli LPS molecule. This strain's LPS contains a bisphosphorylated hexaacyl lipid A bound to an R1-type core. Various explicit bilayers were built of this LPS molecule with varying lengths of 0, 5, 10, and 20 repeating O6 antigen units; a single unit of O6 antigen contains 5 sugars. The simulation results of each system will be discussed in terms of per-lipid surface area, glycosidic angle distribution, O-antigen orientation, and distribution of each system component such as lipid A, R1 core, O6-antigen unit, water, and ions.

928-Pos Board B714
The Molecular Refractive Function of Lens Gamma Crystallins
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Gamma crystallins are the major protein component in the nucleus of the eye lens. Their extraordinary solubility and thermodynamic stability at extremely high protein concentrations help to prevent scattering of light and the formation of cataracts. However, gamma crystallin functions beyond these structural roles have remained mostly unclear. In the present work, we applied a computational approach to predict protein refractive index increments from amino acid composition to all known sequences of the human proteome, and of known members of the beta/gamma crystallin protein family. We show that all lens gamma crystallins have specifically evolved toward a significantly elevated molecular refractive index increment, which is far above those of most proteins, and above non-lens members of the beta-gamma crystallin family from different species. A high refractive index increment can lower the crystallin concentration required to achieve a suitable refractive power of the lens, and thereby reduce the propensity of crystallins to aggregate and form cataract. Thermodynamic consequences of this are demonstrated with a biophysical model of macromolecular crowding. This model can explain the correlation observed by us between the predicted crystallin refractive index increment and lenticular protein concentrations in different species. Independent confirmation of this hypothesis of a molecular refractive index function of crystallins was obtained from the study of squid S crystallins, which have derived from a metabolic enzyme entirely unrelated to beta/gamma crystallins, yet have developed, in parallel evolution, the same trait of an unusually high refractive index increment. To achieve a high protein refractive index increment as observed in these crystallins, a global shift in the amino acid composition is required, which can naturally explain the highly unusual amino acid composition of gamma crystallins and their functional homologues. This function provides a new perspective for interpreting their molecular structure.

929-Pos Board B715
Moonlighting Proteins
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Moonlighting proteins comprise an interesting subset of multifunctional proteins in which the two functions are found in a single polypeptide chain. They do not include proteins that are multifunctional due to gene fusions, families of homologous proteins, splice variants, or promiscuous enzyme activities. Known moonlighting proteins include several different kinds of enzymes and other proteins and different combinations of functions. Recent crystal structures of some moonlighting proteins have provided clues to the molecular mechanisms of one or both