246-Pos Board B46
Mechanical Properties of a Short Tropocollagen Molecule from a Molecular-Dynamics Simulation
C. Brad Bennett, H.M. Harper, W.G. Matthews, D.A. Rabson, Sagar A. Pandit.
Molecular-dynamics simulations are performed on a model collagen molecule in SPC/E water, with and without 100 mM NaCl. To calculate the persistence length, we find the center of mass of each amino acid. We then group the amino acids into triplets, representing each by the (unweighted) average of the three centers of mass. These center-of-mass positions are used as end points for directors. The time-averaged and spatially averaged cosines between directors are found (by determining the scalar product of the directors) as a function of contour length between them.
Additionally, two-dimensional projections of the three-dimensional images are constructed, in analogy to the experimental deposition of collagen onto a surface. Techniques for measuring and calculating persistence length from AFM images are used on the two-dimensional projection images, and results are compared to the 2D and 3D Flory-model predictions and to actual experimental results. Values for the Young's modulus are also presented and compared to experimental values.

247-Pos Board B47
Improving Accuracy of Functional Surfaces of Protein Structures Modeled From Sequences
Jieling Zhao, Joe Dundas, Sema Kachalo, Zheng Ouyang, Jie Liang.
Accurate models of protein functional surfaces are important for understanding enzyme mechanism, protein function prediction, compound-protein docking, and drug design. As the speed of rapid accumulation of protein sequence information far exceeds that of structures, it is important to construct models of proteins with accurate functional surfaces. A promising approach is to construct comparative models. We built three-dimensional comparative models of proteins using MODELLER and applied the pocket algorithm CASTp based on alpha shapes to compute functional surfaces for the modeled protein structures. To improve the accuracy of modeled functional surfaces, we have developed a new side-chain repacking algorithm based on an approximation algorithm that solves the optimization problem of finding compatible side chain rotamers with lowest energy, which is formulated as an integer programming problem. Our result showed that for 9 challenging modeled proteins (backbone sequence identity less than 40% and pocket fragments sequence identity less than 50%) with functional surface atoms between 60~80, 5 have improved accuracy of functional surfaces after side-chain repacking, with the overall recall increased from 0.193 to 0.203 for all 9 structures.

248-Pos Board B48
Mechanical Properties of Type I Collagen: Insights From Molecular Dynamics Simulations
Paul Tumaneng, Guijun Zhao, Olga Antipova, Joseph P.R.O. Orgel, Sameer Varma, **H. Larry Scott**.
Fibrous collagens are present in all mammalian species where they form the structural basis for connective tissue, including those in the heart, vasculature, skin, cornea, bones, and tendons. While the general features of the structure of type I collagen have been known for a long time, the specific packing arrangement of collagen molecules was identified only recently (Orgel et al., PNAS, 103:9001, 2006). Each collagen molecule is approximately 300 nm long and 1.5 nm in diameter. It is made up of three polypeptide chains, called alpha chains, each containing about 1000 amino acids. These alpha helices are twisted together into a right-handed triple helix, a cooperative quaternary structure presumably stabilized by inter-chain hydrogen bonding and other non-bonded interactions. The individual collagen molecules are then arranged to form a super twisted (discontinuous) right-handed microfibril that interdigitates with neighboring microfibrils. In order to better understand the nature of the intermolecular interactions in collagen at an atomic level, and to understand how observed mechanical properties of collagen emerge from these interactions, we have run a series of molecular dynamics simulations. Our calculations are the first set of atomistic simulations of individual collagen molecules. The data from the simulations provide valuable insights into the origin of the mechanical properties of collagen fibrils, that in some ways are different from those obtained using simulations and experiments of collagen analogues.

249-Pos Board B49
Performance of An All-Atom Free Energy Approach For Protein Structure Prediction
Priya Anand, Timo Strunk, Martin Brieg, Irene Meliciani, Moritz Wolf, Konstantin Klenin, Wolfgang Wenzel.
With the completion of sequencing efforts for many important genomes, protein structure and function prediction, emerge as important challenges. Physics-based or forcefield-based methods, which were initially believed to hold great promise for protein structure prediction, now play only a marginal role in the biannual comparative assessment of methods for protein structure prediction (CASP). Most of the models submitted to this computational experiment presently originate from similarity-based methods however structure prediction for low-homology targets leave significant room for improvement. Here we present some of the results from CASP9, were we combine physics based methods along with homology modeling. However, in case of low homology targets we generated libraries comprising of 10,000-20,000 decoys using the standard ROSETTA fragment assembly protocol and then energy-ranked using the POEM≅HOME, which explores the free-energy surface in many parallel Monte-Carlo random walks, the conformation which is near the native conformations from the large set of decoys was reliably selected.Some experimental structures of CASP9 targets have been released till date and the comparisons of our predictions are encouraging.

250-Pos Board B50
Dxtuber: Detecting Protein Cavities, Tunnels & Surface Clefts Based on Protein & Solvent Dynamics
Martin Raunest, Christian Kandt.
Empty space in a protein structure can provide valuable insight into protein properties such as internal hydration, structure stabilization, substrate translocation, storage compartments or binding sites. This information can be visualized by means of cavity analysis. Numerous tools are available depicting cavities directly or identifying lining residues. So far, all available techniques base on a single conformation neglecting any form of protein and cavity dynamics. Here we report a novel, grid-based cavity detection method that uses protein and solvent dynamics derived from molecular dynamics simulations to identify (I) internal cavities, (II) tunnels or (III) clefts on the protein surface. Driven by graphical user interface, output is written in PDB format where cavities are described as individually selectable groups of adjacent voxels representing regions of high solvent residence probability. Cavities can be analyzed in terms of solvent density, cavity volume and cross-sectional area along a principal axis. Using a set of six example proteins representative of the three main classes of protein cavities, dxTuber was tested and the results compared to SURFNET, CAVER, & PyMOL.

251-Pos Board B51
Evolutionary Connections Between Protein Functions Revealed by the Prototypes of Elementary Functional Loops
Igor N. Berezovsky.
Closed loops are basic structural units of proteins emerged as a consequence of the polymer nature of polypeptide chains. They are also building block of protein functions, delivering residues involved into binding and catalytic transformations into the functional sites of enzymes.
We have derived the prototypes of the elementary functional loops (EFLs), and we use them for dissecting the enzymatic function into its building blocks. As a result, previously uncharted evolutionary connections between seemingly unrelated enzymes become apparent. We show that proteins with different folds performing different biochemical reactions are built from limited set of common elementary functions. These functions are provided by elementary functional loops and they belong to two major types: (i) binding of a particular substrate or cofactor; (ii) providing elementary chemical transformations. We explore the emergence of the most ancient enzymatic domains using the prototypes of the EFLs identified in the Archaea. In particular, we consider the clusters of orthologous genes (COGs) belonging to archaeal core, which represent the most common functions. The connections between core and shell are also delineated using the prototypes of the EFLs. As a results, the picture of new functions emerging as combinations of the prototypes becomes clear. We illustrate it with some of the enzymes from the methanogenic pathway, unique to a group of archaeal species. An example of connections between different methanogenic enzymes sharing a common cofactor-dependent chemical step, as well as example of a function appearing in combination with more generic prototype from the core, are shown.