show that rodlet assembly is possible without additional beta strand formation in the flexible loop regions.
Hydrophobins are small amphipathic proteins characterized by their unique bond pattern of eight Cysteine amino acids and a resulting similar tertiary structure, although only marginal sequence conservation exists within the family. In this work we elucidate the structure of the assembled rodlets in Class-I hydrophobins. The initial model of the EAS mutant is created using homology modeling of the solution structure of EAS allowing for a rigid structure omitting most of the flexible loop regions. A large population of possible docking structures is further generated using a generic protein-protein docking approach and filtered for candidates with distinct amphipathicity to account for the presence of an air-water interface.
The resulting structures are further relaxed in the all-atom-free energy force-field PFF02[1] using the POEM (Protein Optimization using Energy Methods) program package in parallel relaxation runs. Relaxation of the whole population was possible using the distributed volunteer computing platform POEM@HOME (http://boinc.fzk.de/).
[1] A.Verma, W.Wenzel, A Free-Energy Approach for All-Atom Protein Simulation, Biophysical Journal, Volume 96, Issue 9, 2009, P. 3483

3299-Pos
Modeling Protein Stability
Kingshuk Ghosh, Lucas Sawle.
University of Denver, Denver, CO, USA.
We will present our recent model of protein thermodynamics to better understand the role of different forces in determining the origin of protein stability. A long standing question in the field of protein biochemistry has been how does a protein achieve enhanced stability. This has lead to careful thermodynamic studies of several thermophilic proteins to understand the origin of high stability in these proteins. However, conclusions have often been contradictory. Our recent model elucidates thermodynamics of these proteins and comparison of thermophilic and mesophilic protein thermodynamics indicates a possible general strategy that proteins may employ to gain high stability. Our analysis is based on several thermophilic and mesophilic proteins with different fold and sequence. We compare relative roles of enthalpy, entropy and specific heat in stability determination. Our model qualitatively explains experimental data and also provides an explanation for apparently conflicting findings from different experimental studies. Furthermore, we predict stability based on our model and demonstrate quantitative agreement with experimental data.

3300-Pos
A Toy Model for Calculating the Rate and Position of Amyloid Fibril Dissociation
Damien Hall.
University of Tsukuba, Tsukuba-shi, Japan.
In a previous paper we used a statistical model to calculate the form of the dependence of the amyloid association rate constant on the size of an unfolded polypeptide chain (Hall, D and Hirota, N., (2009) *Biophys. Chem.* **140***, 122-128*). In the current work we use a Langevin dynamics based simulation to examine the breakage/dissociation rate of an amyloid fibril in a solution environment. We treat the protein monomers in the amyloid fibril as point particles enclosed by a monomer shell. These encapsulated monomers are joined together by virtual bonds which break when extended beyond a certain limit. The solvent environment is treated as a viscous fluid capable of producing random fluctuating forces that are sensitive to the relative position, but not the velocity of the monomer units making up the amyloid fibril. The simulation results suggest how the rate of fibril breakage /dissociation will alter in response to changes in certain characteristic properties of the amyloid, namely the bonding arrangement, the constituent polypeptide size, the strength of the fibril bond and the existence of bond defects in the fibril. Additionally we use the simulation results to make comment on the likelihood of any position bias with regards to the event of fibril fragmentation - a finding which has important consequences for the 'infectivity'of amyloid fibres *in vivo*.

3301-Pos
Cooperative Folding Kinetics of BBL Protein and Peripheral Subunit-Binding Domain Homologues
Wookyung Yu[1], Kwanghoon Chung[1], Mookyung Cheon[1], Muyoung Heo[1], Kyou-Hoon Han[2], Sihyun Ham[3], **Iksoo Chang[1]**.
[1]Department of Physics, Pusan National University, Pusan, Republic of Korea, [2]Korea Research Institute of Bioscience and Biotechnology, Dae Jeon, Republic of Korea, [3]Department of Chemistry, Sookmyung Women's University, Seoul, Republic of Korea.
Recent experiments claiming that Naf-BBL protein follows a global downhill folding raised an important controversy as to the folding mechanism of fast-folding proteins. Under the global downhill folding scenario, not only do proteins undergo a gradual folding, but folding events along the continuous folding pathway also could be mapped out from the equilibrium denaturation experiment. Based on the exact calculation using a free energy landscape, relaxation eigenmodes from a master equation, and Monte-Carlo simulation of an extended Munoz-Eaton model that incorporates multiscale-heterogeneous pairwise interactions between amino acids, here we show (1) that the very nature of a two-state cooperative transition such as a bimodal distribution from an exact free energy landscape and biphasic relaxation kinetics manifest in the thermodynamics and folding-unfolding kinetics of BBL and peripheral subunit-binding domain homologues. Our results provide an unequivocal resolution to the fundamental controversy related to the global downhill folding scheme, whose applicability to other proteins should be critically reexamined.
(1) Proc. Nat'l. Acad. Sci. (USA), Vol.105, 2397-2402 (2008).

3302-Pos
Fast Prediction of Protein Thermodynamics
Hui Wang, Chuanbin Du, Dennis R. Livesay, Donald J. Jacobs.
University of North Carolina at Charlotte, Charlotte, NC, USA.
A computational method for a Flexibility And Stability Test (FAST) on three-dimensional protein structure is described. A four-dimensional free energy landscape defined by temperature and three order parameters is calculated in matter of minutes. The order parameters characterize structure and solvent properties. Specifically, they depict the number of native vs. disordered residues that are within a particular solvent state. Thermodynamic properties are derived from the free energy landscape, including stability curves and heat capacity over all experimentally accessible temperatures. Protein flexibility and correlated motions for a given thermodynamic and solvent condition are also calculated to highlight structural mechanisms. A Free Energy Decomposition (FED) is employed to account for essential enthalpy-entropy compensation mechanisms that include: hydrogen bonding, chemical diversity among residues, atomic packing, strain and vibration energy, pH effects, solvation effects such as clathrate water interacting with residues, hydrophobic effects due to water transfer from buried regions to bulk solvent, and network rigidity. Network rigidity is a long-range underlying mechanical interaction that accounts for conformational entropy nonadditivity during Free Energy Reconstitution (FER). In contrast to molecular simulation, FAST is based on a free energy functional that is solved using self-consistent mean field theory. Individual free energy components come from molecular partition functions that are parameterized from a combination of long all-atom molecular dynamics simulations in explicit solvent, and empirical fitting to experimental data. FAST is a unified model that accounts for several modes of protein denaturation driven by extreme: temperature, pH, and concentration of co-solute. Pressure dependence will also be incorporated in future work. Because of its computational efficiency, FAST can be used in high throughput applications (i.e., design) to assess the consequences of all FED components on the free energy. This work is supported by NIH grant R01-GM073082.

3303-Pos
Non-Covalent Interactions Involving Aromatic Residues in Protein Structures: Stability and Dynamics in Membrane and Globular Proteins using Molecular Dynamics Simulations
Alok Jain, Ramasubbu Sankararamakrishnan.
Indian Institute of Technology Kanpur, Kanpur, India.
Recent studies have revealed the importance of non-covalent interactions in proteins viz. conventional & non-conventional H-bonds. Importance of interactions involving π electron cloud of aromatic residues namely C-H $\cdots\pi$, D-H$\cdots\pi$, lone-pair$\cdots\pi$ and cation$\cdots\pi$ have recently been recognized. Most of the studies involved crystal structure analysis of proteins or ab-initio calculations. However, the dynamic properties such as stability and life time of these interactions through experimental studies have not been investigated due to difficulties in carrying out such experiments.
In this study, we carried out simulations on four globular and two membrane proteins with different secondary structural contents. The dynamic nature of six different non-covalent interactions was analyzed to identify their behavior over time within and across the different classes (all-α versus all-β) and different types (globular versus membrane) of proteins. Some of the properties analyzed were, fraction of each type of interaction that was maintained throughout the simulation, maximum residence time (MRT) and the life time of the interactions. Our preliminary investigation reveals that conventional H-bonds are dominant (~60%) interactions and is mostly due to main-chain functional groups. They are predominantly stable with a MRT of at least 10 ns, owing to their role in maintaining the secondary structure of proteins. Our analysis reveals that C-H$\cdots$O interactions involving the main-chain Cα and main-chain carbonyl oxygen atoms are the second most dominant interactions in the all-β-proteins. Large proportion of them is relatively more stable. Cation$\cdots\pi$ interactions are