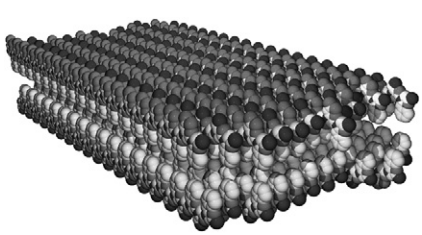
1156-Pos Board B66
Understanding the Effect of Ionic Liquid on the Folding and Conformation of Small Model Peptides
Jia Lin Huang, Karson Schmidt, Leigh Murray, Michael E. Noss, **Michelle R. Bunagan**.
Recent studies have shown that ionic liquids exhibit unusual but useful solvating properties. With regards to proteins, ionic liquids have emerged as a popular solvent for protein storage, as ionic liquids have been shown to stabilize the folded protein conformation when present as an additive, a co-solvent, or the primary solvent. As the overall mechanism of stabilization is not yet fully understood, we have sought to study the effect of neat ionic liquid 1-butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl) imide on small model peptides. Circular dichroism and fluorescence spectroscopy of these peptides in ionic liquid indicate that helical peptides are significantly stabilized, whereas beta-hairpin peptides are destabilized by the ionic liquid solvent. In order to better understand the temperature-dependent conformational dynamics of helical peptides in 1-butyl-1-methylpyrrolidinium bis(trifluoromethylsulfonyl) imide, we have also used Fluorescence Resonance Energy Transfer, to probe the end-to-end distance of a small helical peptide, AKA_2, in the ionic liquid. These results show that the increase in helicity with increasing temperature occurs concomitantly with an increase in peptide length. These results suggest the formation of low-temperature aggregates which dissolve upon heating to yield a highly stable helical structure at high temperature. These results have implication for the proper usage of ionic liquids for biomolecule storage.

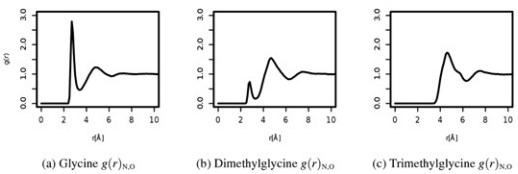
1157-Pos Board B67
Molecular Mechanism of Aβ Amyloid Inhibition by Inositol
Grace Li, Régis Pomès.
Alzheimer's disease (AD) is a severe neurodegenerative disease with no cure. Currently, one method of targeting the underlying disease is to prevent or reverse the amyloid formation of Aβ42, a key pathological hallmark of AD. A novel small-molecule drug candidate, *scyllo*-inositol, is a polyol that exhibits stereochemistry dependent inhibition of the formation of Aβ fibrils *in vitro*. Furthermore, recently completed phase II clinical trials demonstrated that *scyllo*-inositol achieved target drug levels in the cerebral spinal fluid (CSF) of Alzheimer's patients, a main challenge for AD drug candidates to overcome. Despite *scyllo*-inositol's promise as a therapeutic for AD, its mechanism of action at the molecular level is currently not understood. We perform microsecond-timescale atomistic molecular dynamics simulations of the full length Aβ42 protofibril in explicit solvent, successively with and without *scyllo*-inositol and its inactive stereoisomer *chiro*-inositol. From our simulations, we predict binding affinities and characterize the binding modes of inositol and their stereochemistry-dependent effect on the structure of Aβ42 protofibrils. Our results provide molecular insight for the rational design of small-molecule inhibitors of Aβ42 and other amyloid-based diseases.

1158-Pos Board B68
Protein Mimetic Materials from the Self Assembly of Bioinspired Polymers at the Air Water Interface
Ronald Zuckermann.
Peptoids are a class of non-natural biopolymer based on an N-substituted glycine backbone that are ideally suited for protein mimetic research. This bio-inspired material has many unique properties that bridge the gap between proteins and bulk polymers. Like proteins, they are a sequence-specific heteropolymer, capable of folding into specific shapes and exhibiting potent biological activities; and like bulk polymers they are chemically and biologically stable and relatively cheap to make. Peptoids are efficiently assembled via automated solid-phase synthesis from hundreds of chemically diverse building blocks allowing the rapid generation of huge combinatorial libraries. This provides an ideal platform to discover nanostructured materials capable of protein-like structure and function. We have designed a series of amphiphilic peptoid 36mers of specific sequence that self assemble into extremely thin (3 nm) crystalline sheets in aqueous solution. A key intermediate in their formation is an ordered monolayer at the air-water interface. These peptoid nanosheets are one of the thinnest two-dimensional organic crystalline materials known. Because of their atomically defined polar surface, the nanosheets serve as an excellent platform to design chem/bio sensors capable of specific molecular recognition.



1159-Pos Board B69
Origins for the Thermostability of Taq DNA Polymerase: Entropy Versus Heat Capacity
Chin-Chi Liu, **Vince J. LiCata**.
The thermal stability of Taq DNA polymerase is well known, and is the basis for its use in PCR. The free energy versus temperature stability curves of the large fragment domains of Taq (Klentaq) and E. coli (Klenow) DNA polymerases have been compared, and by utilizing the ΔG and ΔCp information obtained from the stability curves, the ΔH and TΔS of folding of each protein as a function of temperature can be calculated directly from the Gibbs-Helmholtz equation. This analysis reveals that Klentaq's extreme stability originates from a significantly decreased entropic folding penalty (TΔS of folding). In contrast, Klentaq's native state enthalpic stabilization (ΔH of folding) is actually considerably less favorable than Klenow's at all temperatures. We have also examined published data on 17 other mesophilic-thermophilic protein pairs using the same approach to calculate ΔH and TΔS as a function of temperature from the stability curves. There are 6 other data sets (7 total including Klenow/Klentaq) with the same thermodynamic pattern, where a reduced entropic penalty is the primary basis for thermostabilization. In contrast, 8 of the 18 total data sets exhibit a highly popularized thermodynamic pattern where a significantly reduced ΔCp of folding is correlated with the enhanced stability of the thermophile. ΔCp has been correlated with changes in accessible surface area during protein folding, so a reduced ΔCp of folding for a thermophilic protein has been suggested to reflect a more compact denatured state of the thermophilic protein, although direct empirical evidence of this is still lacking for any mesophilic-thermophilic protein pair. It is notable that there is minimal overlap between the 8 systems exhibiting a lowered ΔCp of folding and the 7 systems showing a lowered entropic folding penalty.

1160-Pos Board B70
Hydration of Zwitterionic Glycine Betaine and Analogues Through Molecular Simulation
Andrew D. White, Shaoyi Jiang.
We use molecular dynamics simulation to characterize the hydration of 3 molecules important to protein stability: zwitterionic glycine, zwitterionic N,N-dimethylglycine, N,N,N-trimethylglycine (glycine betaine). Both structuring and dynamics of bulk and bound water were examined using a variety of properties and at multiple concentrations. Metrics such as radial distribution functions and residence times were used to characterize hydration. Also, we used more specialized metrics that can discriminate between subtle differences in hydration such as condensed phase order parameters, Voronoi tessellations, and multidimensional pair-pair correlation functions. Trimethylglycine was found to have a unique hydration shell that extends across the entire molecule and has no specific interactions between solute molecules. Glycine was found to aggregate and have a more disjoint hydration shell. Lastly, trimethylglycine is disperse in solution even at very high concentrations and water rapidly moves between trimethylglycine amine groups. The differences in hydration structure between the three zwitterions can be seen in Figure 1, which shows the radial distribution function between the amine and waters. This work has meaningful implications for protein stability where trimethylglycine is known to prevent protein aggregation and interfaces where trimethylglycine prevents protein adsorption.



(a) Glycine $g(r)_{N,O}$ (b) Dimethylglycine $g(r)_{N,O}$ (c) Trimethylglycine $g(r)_{N,O}$

1161-Pos Board B71
Flow and Stop Protocol for the Long-Time Observation of Fluorescence from Free Single Molecules: Application to the Time-Series Analysis of Protein Folding
Kiyoto Kamagata, Akinori Baba, Tamiki Komatsuzaki, Satoshi Takahashi.
A new method was developed to detect fluorescence intensity signals quantitatively from single molecules diffusing freely in a capillary flow cell. A unique optical system based on a spherical mirror was designed so that it enables us to detect the fluorescence intensity quantitatively irrespective of the location of molecules in the capillary. In addition, the ''flow and stop'' control of the sample in the capillary can observe free single molecules for about several seconds, which is more than 1000 times longer than the observation time of a typical confocal method. Here, the method was applied to observe time series traces of the denatured state of iso1-cytochrome *c* labeled with a fluorescent dye. The analysis of the single-molecule traces based on the concept of local equilibrium state (LES) demonstrated that a large fraction of the traces was assigned