calculates the binding affinity of a solute molecule, its preferred spatial arrangement, lowest energy path and energy barriers along the membrane normal using solute 3D structure and pKa together with parameters of the membrane, such as surface, transmembrane potentials and pH values on both sides of the membrane. The method was tested for series of peripheral proteins, peptides and small molecules experimentally studied in lipid bilayers. Some of the results have been deposited in the Orientations of Proteins in Membranes database (http://opm.phar.umich.edu). The predicted membrane permeability of potential anticancer drugs, proapoptotic peptidomimetics correlates with their cellular activities.

2083-Pos Board B53
Generic Coarse-Grained Model for Protein Folding and Aggregation
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The complexity involved in protein structure is not only due to the rich variety of amino acids, consistent with the random heteropolymer picture, but also the weak interactions involved, comparable to thermal energy, and important cooperative phenomena. This presents a challenge in computer simulations, as it is associated with high-dimensionality and ruggedness of the free energy landscape as well as long equilibration times, frequently exceeding what can be handled in atomistic studies. We have recently developed a coarse-grained (CG) implicit solvent peptide model which has been designed to reproduce key consequences of the abovementioned weak interactions. Its intermediate level of resolution, four beads per amino acid, allows for accurate sampling of local conformations, in particular secondary structure, by designing a force field that relies on simple interactions (e.g. hydrogen bonds, hydrophobicity). A realistic ratio of alpha-helix to beta-sheet content is achieved by mimicking a nearest-neighbor dipolar interaction.
In the present study, we tune the model in order to fold helical proteins while systematically comparing the structure with NMR data. Very good agreement is achieved for proteins that have simple tertiary structures, which implies that the force field is able to reproduce important cooperativity features between amino acids. We further probe these effects by looking at peptide aggregation scenarios. Hydrophobic peptide fragments cooperatively form largescale beta-sheet structures. The model is able to reproduce features from atomistic simulations on a qualitative basis. The large-scale and long-term regime that this CG model offers, coupled with our design criteria (folding and realistic alpha/beta content), make it very suitable for many biological processes, such as misfolding and oligomerization involved in neurodegenerative diseases.

2084-Pos Board B54
Martini Force Field: Extension To Carbohydrates
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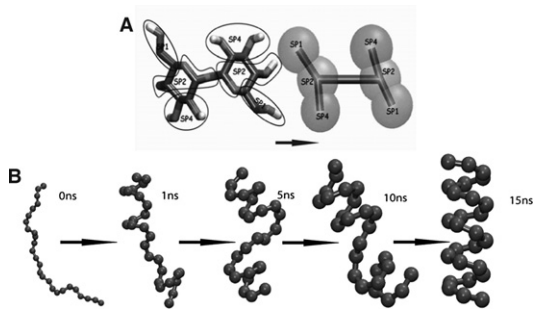
MARTINI force field: extension to carbohydrates
We present an extension of the coarse grained (CG) MARTINI force field (1) to carbohydrates. In line with the MARTINI force field development, the coarse grained model for carbohydrates has been systematically parameterized based on reproduction of experimental partitioning free energies in combination with mimicking the behaviour seen in atomistic simulations. Parameters were derived for all common mono- and disaccharides, considering the different ways of linking for monosaccharide units. The model has been tested on a number of small polysaccharides. For instance, the folding of a 26 (α 1-4) D-glucopyranose amylose chain was simulated both in a non-polar (nonane) and polar (water) environment. The folded structure is found to be similar for the CG and the all-atom model.



Coarse grain mapping of trehalose (A) and simulation of the folding of a CG 26-glucose amylose chain in nonane (B). For representation just the backbone beads are shown
The CG carbohydrate model is fully compatible with the previously parameterized lipid and protein models, and opens up the way to study a large variety of biological systems in which carbohydrates are important.
(1) S.J. Marrink, H.J. et al, JPC-B, 111:7812-7824, 2007.

2085-Pos Board B55
Scaal: A Robust, Accurate, And High-efficient All-atomistic Protein Reconstruction Method From Low-resolution Protein Models
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In the quest to develop multiscale molecular simulation methods for complex protein dynamics that fuse high-resolution and low-resolution protein representations, it is important to investigate the required information of reconstruction of all-atomistic proteins from low resolution ones with manageable uncertainly. In this paper, we introduce a robust, accurate, and fast reconstruction method (SCAAL) that produces reliable all-atomistic protein structure by taking few beads from a coarse-grained model with at least one side chain bead and one Cα bead in the backbone (Side chain-Cα Model, SCM) into accounts. Our algorithm (SCAAL) is compared with SCWRL3.0 and it excels in robustness and is more accurate in the reconstruction of large amino acids. In addition, we further test SCAAL in the reconstruction of a complete protein folding trajectory from SCM coarse-grained models. We show that the efficiency, accuracy, and robustness of SCAAL as leverage for multi-scale simulations are excellent in terms of low root mean square deviations that lie within 1Å resolution.

2086-Pos Board B56
Self-Learning Multiscale Simulation
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Molecular dynamics (MD) simulation plays more and more crucial roles in understanding the underlying molecular mechanisms of many biological processes. Unfortunately, due to the large number of degrees of freedom involved and inherently rugged energy surface, the time scale currently reachable by accurate all-atom (AA) simulation is far below typical biologically relevant time scale. Coarse graining the molecular representation can accelerate sampling, but the coarse grained (CG) simulation is unavoidably less accurate in energy estimate. To surmount these problems, a number of strategies have been proposed to integrate the AA and CG simulations, which is often called multiscale simulations. However, traditional multiscale methods heavily rely on the accuracy of the CG model. If the CG potential has its major basins different from those of AA potential, the multiscale simulation is not efficient and sometimes even bias the sampling. Here, we propose a new multiscale simulation method, self-learning multiscale molecular dynamics (SLMS-MD), which can achieve high accuracy and high sampling efficiency simultaneously. Based on the resolution exchange MD between atomistic and CG replicas, a self-learning strategy is introduced to progressively improve the initial CG potential by an iterative way based on the previously sampled CG conformations and their corresponding AA energies. The CG simulation ensures the efficient and broad sampling, and simultaneously the AA energies shape up the accuracy of the CG potential. Testing results show that the SLMS-MD can optimally combine the advantages of the AA and CG simulations, and achieve accurate and efficient multiscale simulations even when the initial CG potential is very poor. The resulting free energy converged to the exact result much faster than that by the replica exchange method. This method is generic and can be applied to many biological as well as non-biological problems.

2087-Pos Board B57
Simultaneous Use Of Class-i And Class-ii Force Fields In CHARMM For Solid-liquid Multiphase Simulation Of Protein-surface Interaction
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An appropriate understanding of conformational and behavioral changes of proteins upon their adsorption to synthetic surfaces is of crucial importance in the development of biomaterials because the changes play a governing role in determining cellular responses to implanted materials and substrates for tissue engineering. A detailed analysis of molecular behavior is key to such an understanding, and classical molecular dynamic (MD) simulation is one of the direct methods of addressing this issue. However, one of the challenges in using MD simulation is that class-I force fields (CHARMM, AMBER, OPLS, etc.) that have been parameterized for proteins are not suitable for