reference to the experimental data, under the so-called maximum entropy principle. Recent practical formulations of this approach involve simulations carried out over multiple replicas or iterative ensemble-correction procedures based on the determination of several (Lagrange) parameters. Here, we present an alternative, self-learning approach to sample molecular ensembles compatible with experimental data with the minimal possible bias on the simulation trajectories. The method does not require multiple replicas and is based on adding an adaptive bias potential during the simulation that discourages the sampling of conformations that are not consistent with the experimental measurements. To illustrate this approach, we applied this novel simulation technique to spin-labeled T4-lysozyme, targeting a set of spin-spin distance distributions measured by DEER/EPR spectroscopy. We show how the proposed method is able to efficiently sample the experimental distance distributions without altering uncorrelated degrees of freedom. We anticipate that this new simulation approach will be widely useful to obtain conformational ensembles compatible with diverse types of experimental measurements of biomolecular dynamics.

792-Pos Board B572
Efficient High Accuracy Non-Bonded Interactions in the CHARMM Simulation Package
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Most molecular dynamics simulations are carried out using isotropic atom-atom potentials to model non-bonded interactions. Such potentials can be insufficient to accurately model a variety of physical properties present in biologically relevant molecules. A proper description of the anisotropy of the electrostatic interactions is of particular importance, as it directly affects a variety of structural and transport properties such as hydrogen bonding and diffusion. We have recently developed a novel, algorithm to efficiently calculate coulombic forces in the CHARMM simulation package using an arbitrary order multipole expansion. Further work has extended this algorithm to efficiently account for dipolar polarization and dispersion. We present details of the algorithm, its implementation and initial calculations on condensed phase water enabled by this work.

793-Pos Board B573
Towards a Polarizable Force Field for RNA based on the Classical Drude Oscillator
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RNA plays many important roles in the cell, including information transfer, gene regulation, protein synthesis, and catalysis. This diversity in function arises in part from the adoption of complex tertiary structures and interconversion between multiple conformational states in response to bound metabolites or changes in other cellular conditions. Modeling RNA with atomistic resolution using molecular dynamics (MD) simulations requires a high-quality empirical force field that can adequately describe the properties of both canonical and non-canonical structures and is sensitive to environmental conditions. To this end, we are developing a force field for RNA that includes the explicit treatment of electronic polarization using the classical Drude Oscillator model. Optimization is focused on the RNA 2′-hydroxyl group and the phosphodiester backbone targeting 2-D quantum mechanical (QM) potential energy and dipole moment surfaces in combination with condensed phase MD simulations of both canonical and non-canonical RNA structures. Parameter validation involves conducting MD simulations of various RNAs not included in the training set.

794-Pos Board B574
Implementation of Replica-Exchange Umbrella Sampling to the DFTB+ Simulation Package
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We have investigated the computational methods which combined the self-consistent-charge Density Functional based Tight Binding (DFTB) method [1] for fast calculations of quantum effects and the Replica-Exchange Umbrella Sampling (REUS)[2] for enhanced conformational sampling. One of the excellent QM-MD simulation package named DFTB+ does not have REUS method incorporated. We thus modified DFTB+ to include the REUS method. We will compare the results of DFTB+ calculations with those by another simulation package. We will present the two comparative results for proton transfer reactions in small molecules.
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[2] Y. Sugita, A. Kitao, and Y. Okamoto, J. Chem. Phys. 113, 6042 (2000).

795-Pos Board B575
CHARMM Gui Membrane Builder Updates
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CHARMM-GUI, http://www.charmm-gui.org, is a web-based user interface designed to generate various molecular simulation systems and input files to facilitate and standardize the usage of common and advanced simulation through an automated optimized process. We have made a significant amount of efforts to implement basic and common molecular dynamics simulation techniques into web interface and the web interface has generated a multitude of positive feedback from our users. In this work, we describe our latest efforts to bringing more advanced molecular modeling and simulation techniques to the web interface, including (1) HMMM builder establishing the high mobile membrane-mimetic model, (2) martini maker building coarse-grain models in Martini force fields, (3) NAMD, GROMACS, OpenMM equilibration and production inputs.

796-Pos Board B576
Experimental and Theoretical Approaches to the Study of Probe Diffusion in Macromolecular Solutions
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Diffusion in macromolecular solutions and networks is a topic of vast importance in many fields related to medical devices, biotechnology, tissue engineering, or drug delivery. Thus, effort has been devoted to developing techniques for measuring and models for predicting diffusion in macromolecular solutions and networks. However, very few techniques are capable of probing diffusion *in situ*, real time, and non-invasively and while many models of diffusion exist, all of them have their drawbacks. Ideally a model starting from basic physics using rigorous mathematical principles should be developed that is also supported by experimental findings.
First, we present measurements of probe diffusion in polymeric solutions conducted by Fluorescence Correlation Spectroscopy (FCS). We have shown that FCS is an excellent tool for real time, non-invasive study of diffusion in complex media. Here, we present studies identifying several transport regimes – without interaction, and with interaction between the probe and the macromolecule. In the latter regime the nature of the interaction determines the specifics of the sub-diffusional process. We discuss two interaction examples – one where a ''permanent'' polymer/probe complex is formed, and one where ionic interaction is responsible for the decrease in probe diffusivity.
We have also developed a novel mathematical model based on homogenization theory, to describe the effective diffusion process. To the best of our knowledge, homogenization theory, has not been used previously to describe the diffusion of probes in macromolecular solutions. The homogenization theory was confirmed by Monte Carlo simulations. An excellent agreement between the homogenization theory and Monte Carlo simulations as well as comparison to experimental data provided evidence for the utility of the homogenization theory for predicting diffusion in macromolecular solutions.

797-Pos Board B577
A Coupled Two-Dimensional Main Chain Torsional Potential for Protein Dynamics
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A new AMBER compatible force field is proposed for balanced representation of secondary structures. In this modified AMBER force field (AMBER^{2D}), the main chain torsion energy is represented by 2-dimensional Fourier expansions with parameters fitted to the potential energy surface generated by quantum mechanical calculations of small peptides in solution at M06 2X/aug-cc-pvtz//HF/6-31G** level. Solvation model based on solute electron density (SMD) developed in Truhlar's group was considered. The benchmark systems used in the validation of this force field include capped dipeptides (Ace-X-NME, XP), tripeptides (XXX, XA, G, V}; GYG, Y {A, V, F, L, S, E, K, M}), alanine tetrapeptide, Ac-(AAQAA)$_3$ -NH2, and ubiquitin. Besides, we also investigate the folding of two representative proteins (PDB ID 2I9M and 1LE1). The results demonstrated that this 2D main chain torsion is effective in delineating the energy variation associated with main chain torsions. Furthermore, the electrostatic polarization effect is very important for long peptides or proteins. This work also serves as an implication for the necessity of