webserver which requires only coordinate file to be inputted and the user is provided with various, but easy to navigate, options. The output information including the change in hydrogen bonds network and binding energy due to amino acid substitution is displayed on the output and is available for download.

**786-Pos Board B566**
**Bio.B-Gen: An Initial System Generator for Biological Molecular Simulations**
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Atomistic and coarse-grained simulations can be a great help in uncovering the mechanisms of physical processes at microscopic and mesoscopic levels at time scales ranging from femtoseconds to milliseconds.
Any simulation study involves (1) setting up an appropriate simulation system representing the physical problem, (2) running the simulation and collecting information about the system, and (3) analyzing the collected data. The last step eventually leads to final conclusions about the system. Software for molecular simulation has been in development for many years and a number of high quality freely distributed general purpose simulation packages is available for researchers. Data analysis tools are usually less general as they often depend on a specific research project and the system under investigation. While many simulation packages come with a set of some general data analysis utilities, it is not unusual for such analysis tools to be developed on a per project basis inside research groups. Interestingly, there is a very limited set of available tools for setting up simulation systems, even though this is the very first and vital step of every simulation study. This lack of convenient general simulation system generators sometimes may even dictate the kind of simulations done based on the available initial systems rather than on the system being the best for a particular problem.
In this work we describe a general software tool, bio.b-gen, for the creation of initial systems for biological molecular simulations. A number of case systems are demonstrated using an atomistic force field as well as the coarse grained MARTINI force field. The tool is designed to generate initial systems for the GROMACS general simulation package.

**787-Pos Board B567**
**Validation and Development of the Force Field Parameters for Drug and Drug-Like Molecules**
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Highly optimized and well-validated parameters have been developed for structure refinement and computer simulation of biomolecules. However, the force fields for most drug and drug-like ligand molecules are not properly validated. Out of ~100,000 X-ray crystal structures in the Protein Data Bank (2014), >25,000 structures contain at least one of >17,000 chemically diverse ligand molecules. In addition, there is over a million ligand molecules of interest in databases such as NCI and Pubchem. Understanding interatomic interactions of a given ligand with its target acceptor is crucial in molecular modelling and the lack of precise force field parameters for small heteromolecules may result in failure of drug design efforts.
A web accessible Automated force field Topology Builder (ATB; http://compbio.biosci.uq.edu.au/atb/) and Repository was developed to facilitate the generation of force field parameters for chemically diverse ligand molecules. The ATB performs quantum mechanical calculations combined with a knowledge-based approach to ensure compatibility with a biomolecular force field. The topologies and parameters created can be used in simulations, computational drug design and X-ray refinement.
Most importantly, a fully automated validation of the force field parameters has been incorporated into the ATB methodology. Recent work on the validation of parameters against structural and thermodynamic data as well as the outcome of participating in the SAMPL4 community challenge for the prediction of hydration free energy of drug-like molecules will be presented. Further refinement strategies to improve the parameters by scaling of the van der Waals and electrostatic interactions will be discussed as well.

**788-Pos Board B568**
**A Novel Method for Force-Field Calibration Based on Maximum-Likelihood Approach and Thermal Unfolding Data**
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Calibration is the final and critical stage of the design of the force fields for proteins and other biological macromolecules. For proteins, the usual goal of this procedure is to optimize the force-field parameters to reproduce the native structures of selected training proteins. However, the resulting force fields are usually not sufficiently predictive, because only the structures of folded proteins are used. Thus, a force field is not sufficiently trained to distinguish folded structures from misfolded ones. In this work, we propose a novel approach, in which a force field is calibrated with the ensembles of structures determined by NMR at various temperatures that encompass the region of thermal unfolding. The method is based on applying the maximum-likelihood principle. Each conformation of the NMR-determined ensemble at a given temperature is an experimental point and the theoretical probability-density function is represented by a sum of Gaussians centred at the decoys from the corresponding ensembles generated by simulations; in this work the replica exchange molecular dynamics procedure was used. The maximum-likelihood function (-logL) is minimized using the current decoy set, then new decoys are generated with the optimized force-field parameters. The procedure is iterated until convergence. The method was applied to the physics-based coarse-grained UNRES force field developed in our laboratory. On the first attempt, NMR structures of a small alpha-helical protein, the tryptophan cage, were used. The resulting force field predicted correctly the structures of 13 out of 14 alpha-helical proteins with different helix-packing topology and size from 36 to 104 amino-acid residues. Results of the calibration of the UNRES force field with more proteins, including villin headpiece (alpha), the C-terminal fragment of the IGG protein (beta), and full-sequence design 1 (alpha+beta), will be presented.

**789-Pos Board B569**
**Quantum Mechanical Molecular Mechanical Calculations using AMOEBA Force Fields**
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We report an implementation of quantum mechanical molecular mechanical (QM/MM) calculations with AMOEBA force field applied to water molecules in the molecular mechanics region. Three AMOEBA parameter sets (AMOEBA03, iAMOEBA, and AMOEBA14) are employed, and compared to TIP3P and other water models in terms of their performance in QM/MM calculations. The effect of the MM polarization (MM induced dipoles due to QM electron density) will also be discussed.

**790-Pos Board B570**
**The Do's and Do Not's of a 100 Million Atom Molecular Dynamics Simulation**
**Abhishek Singharoy**[1], Danielle Chandler[1], Jacob Durrant[2], Melih Sener[1], Rommie Amaro[2], Klaus Schulten[1].
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The ever so growing prowess of petascale computing resources has pushed the envelope of biomolecular modeling, simulation, and analysis into the regime of hundred million atom systems. To bring a very challenging organelle-scale system under simulation control often involves substantial modifications of existing computational tools. Using two ongoing simulations of a bacterial chromatophore and the influenza virion coat, we demonstrate VMD-, NAMD-, MDFF-, and python-based innovations that enable large-scale biomolecular simulations. The protocol involves new semi-automated, yet high throughput, ways of large-scale atomic model construction, including in disordered membrane environments, their solvation, ionization, and equilibration, particularly for system sizes in excess of tens of million atoms. Discussions will extend to tools for characterizing the physical properties of a hundred million atom system, such as long-range electrostatics. Finally, the scientific purpose of performing such simulations will be justified in the light of results obtained from whole-chromatophore and whole-virion-coat simulations.

**791-Pos Board B571**
**Minimally-Biased Metadynamics Method to Sample Conformational Ensembles Compatible with Experimental Measurements**
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A primary goal in computational biophysics is to harness experimental measurements to obtain information on the structure and dynamics of biomolecules. However, most biophysical techniques such as NMR and EPR spectroscopy provide signals that arise from an ensemble of multiple molecular conformations. Thus, it is typically not straightforward to extract detailed structural information from the experimental data. A possible strategy is to bias the conformational sampling obtained in a molecular dynamics simulations in