nonphotochemical quenching (NPQ), in which excess absorbed light is dissipated safely as heat. The primary, rapidly reversible component of NPQ is energy-dependent quenching (qE), which is induced by a low pH in the thylakoid lumen. Measuring the change in chlorophyll excited state lifetime in PSII due to specific physical processes involved in qE has been difficult because of multiple NPQ components and the difficulty of measuring ultrafast processes on a sample whose photophysical decay pathways change in response to actinic light. Using time-resolved fluorescence, we measured the lifetime of excited chlorophylls in PSII of live cells of the green alga *Chlamydomonas reinhardtii* as they adapted to variable light conditions. The average trajectory to a qE site, τ_{qE}, was measured to be 276 ps for any quenched PSIIs in wild-type cells. This result provides direct evidence that PSII has two primary conformations - unquenched and quenched - and that it switches between these two states based on the pH of the lumen. The appearance of the fast lifetime had a 200 ms delay and 400 ms rise time. We attribute these timescales to changes in the lumen pH, with the first timescale being the time for protons to begin building up in the lumen and the second timescale being the time for the lumen pH to drop to the pK_a of the pH sensing residues of PSII. We anticipate that these methods will be useful for probing the photophysical mechanism of qE quenching and using the dynamics of NPQ induction as a probe of chloroplast dynamics.

832-Pos Board B618
The Retinal Conformation of Metarhodopsin II Elucidated by Molecular Dynamics Simulations
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Rhodopsin is a photo-activated G protein coupled receptor. In dark, rhodopsin consists of apoprotein, opsin, and chromophore, 11-*cis* retinal. After photo absorption, 11-*cis* retinal is isomerized to all-*trans* retinal. Then, the proton of Schiff base transfers to its counter ion and transmembrane helix (TM) 6 moves. In this state, rhodopsin can activate the G protein, transducin, and is called Metarhodopsin II (Meta II).
Activation mechanism of rhodopsin has been focused but the structure of Meta II had not been solved before 2011. In 2011, two crystal structures of active rhodopsin model were solved. In one model, Choe model, the retinal is rotated against that of Lumirhodopsin (Lumi). On the other hand, in another model, Standfuss model, the retinal is not rotated. Here, we addressed which is a good model for Meta II using molecular dynamics (MD) simulations.
In a simulation from the Choe model, the retinal is stable during 100 ns, while in a simulation from the Standfuss model, the polyene chain of retinal is unstable during 100 ns and β-ionone ring of that is rotated during 500 ns. These suggest that Standfuss model is less stable than Choe model and the retinal in Meta II is rotated against that of Lumi. Next, we tried to check how the retinal conformation changes from inactive to active state. We made inactive Meta II from Lumi and performed 1 μs simulation of inactive Meta II. The result of simulation suggests that the retinal has some sub-states, but is not rotated in the inactive Meta II.

833-Pos Board B619
Photochromism in a Flavin Binding Photoreceptor
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We have investigated the photochromic behavior of the LOV protein YtvA using steady state and time-resolved spectroscopies.
Excitation at 475 nm of the dark adapted, fluorescent species converts the chromophore to the nonfluorescent, signalling state. We show that the dark adapted species can be obtained through irradiation with near UV (360 nm) or violet (405 nm) excitation. Under steady state illumination, the spectral overlap between the two species leads to a photoequilibrium, from which the quantum yield for forward and reverse reactions can be obtained. Similar estimates for the quantum yields are obtained form the equilibrium absorption spectra of the mixture, and from the kinetics of the photoconversion.
Switching of the protein between dark and light adapted states can be used to tune fluorescence emission, observed only in the dark adapted state, and may be exploited in super-resolution microscopy applications.

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Computational Methods I

834-Pos Board B620
Prediction of pKa Value of Zinc-Bound Water in Carbonic Anhydrase
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The deprotonation of zinc-bound water in carbonic anhydrase II is the rate-limiting step in the catalytic reaction of CO2-bicarbonate conversion. In order to understand the factors determining the pKa of the zinc bound water at the active site, quantum chemistry calculation together with continuum model is carried out. The pka changes due to the active site mutation are well reproduced. Additionally, the structural analysis and charge/dipole examination provide evidence that the fluctuation of the active site structure and the redistribution of the electrostatics lead to the pKa shift. Also, the distinct pka value of the same type of mutation at different site results from asymmetric ligation and different electronic environment around the zinc ion. This study not only provides insight into the molecular mechanism of the enzyme but also helps design artificial material for CO2 sequestration.

835-Pos Board B621
Dynamic Protonation of Biomolecules in Molecular Simulation
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Using molecular simulation to model a biological phenomenon requires the selection of an assumed static set of ionization states that reflects the experimental conditions. We have developed a general approach to allow for these ionization states to change dynamically during the simulation. Moreover, our framework allows for the theoretical or experimental input of ionization states as the simulation proceeds.

836-Pos Board B622
Charge Burial Energetics and Protein pKa Shifts Modeled with Nonlocal Electrostatics
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Continuum electrostatic theory based on the Poisson equation has proven to be a surprisingly effective simple model for understanding protein function, but it has not enjoyed equal success in every application. In particular, calculations of protein pKa shifts have seemed to require substantially different treatment than other calculations. Many groups have found, independently, that pKa calculations match experimental data much better if one adjusts the protein dielectric constant from experimental estimates (which suggest 2 to 5) up to 10 or even higher; this empirically determined parameter has been justified by various physical arguments including implicit protein flexibility. Here we study protein pKa shifts, and charge burial more generally, using numerical simulation and analytical methods to solve Hildebrandt's ''structured continuum'' formulation of nonlocal electrostatics. Nonlocal solvent response accounts in a simple way for the reduction in dielectric screening that arises at short length scales due to water molecules' finite size and their tendency to form semi-structured networks. We find that the resulting reduction in charge-burial penalties allows the nonlocal model to predict pKa shifts that are comparable in magnitude to shifts computed using the local model with empirically large dielectric constants.

837-Pos Board B623
A Stochastic Technique that Computes Electrostatic Solvation and Binding Free Energies in the Generalized Born Model with Exact Born Radii
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A stochastic generalized Born (GB) solver is presented whose predictions converge to those given by exact GB radii to arbitrary precision. By solving

for the Born radii stochastically, the exact Born radii can be computed without the need for multiple expensive deterministic calculations. In addition, although the proposed method strictly works only on a van der Waals surface, it can be modified to closely match the predictions of the linearized Poisson-Boltzmann equation on a solvent-excluded (SE) surface by determining prior to the calculation which spheres are not solvent exposed in the SE surface and inflating these spheres by the probe radius. Additionally, because the predictions of this method can be made arbitrarily close to those given by exact Born radii, this method can be used to evaluate the ability of the Born approximation to reproduce the electrostatic binding free energy given by the Poisson-Boltzmann equation independently of the approximations usually made to derive the Born radii. This study presents the results of such an investigation for a broad range of biomolecular complexes.

838-Pos Board B624

Accurate Solutions with the Semi-Explicit Assembly Water Model

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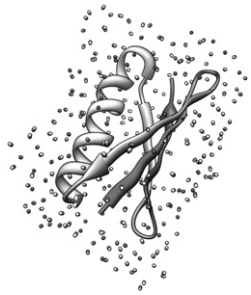
Molecular simulations that are computationally cumbersome using explicit solvent models can be more tractable with implicit solvents. However, such continuum solvent approaches can struggle when the discrete nature of water is needed, often at the solute/solvent interface. We have developed a new solvation method, called Semi-Explicit Assembly (SEA), that merges the best of both routes - the efficiency of an implicit solvent with the microscopic detail and accuracy of an explicit solvent. Here, we give an overview of SEA and highlight some of our recent developments and applications. These include new continuum boundary treatments, application to larger biomolecules, and performance in studies involving blind predictions of solvation free energies.



839-Pos Board B625

Improving Implicit Solvent Models with Differential Geometry

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Implicit solvent models are popular for their high computational efficiency and simplicity over explicit solvent models. Hence, there has been significant interest in testing and improving these models for their ability to accurately compute the thermodynamic properties of a wide range of chemicals and macromolecules. One such model is a differential geometry-based solvation model where a generalized geometric flow (GF) equation and a generalized Poisson-Boltzmann (PB) equation are self-consistently solved to compute a smooth dielectric profile, and the polar and non-polar solvation free energies. The GF equation contains the polar energetic terms defined by the PB equation, and non-polar energetic terms describing the pressure-volume work to create a cavity in the solvent, energy to create a solute-solvent interface, and solute-solvent attractive dispersion interactions. The solution to the GF equation is a characteristic function that describes a smooth solute-solvent boundary. This function defines the smooth dielectric profile used in the PB equation to compute the electrostatic potential. Therefore, the main parameters of the model are the solute/solvent dielectric, solvent pressure, surface tension, solvent density, and molecular force-field parameters. As for other solvation models, these parameters have to be determined by experimental conditions or optimized against experimental solvation energy data before the model can be applied for new molecules. However, it is not clearly understood how different choices of the model parameters are coupled with force field choice to affect the computed results. In this work, we have performed a parametric study on the GF-based solvation model to investigate how changes in the pressure, surface tension and use of different force fields affect the optimal solutions to the solvation free energies of small organic molecules. Results of this model will be presented for a set of 17 small organic molecules using three different force fields.

840-Pos Board B626

Coarse Grained Ion-Ion and Ion-Water Interactions

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A detailed knowledge of ion transfer mechanisms between water and low-polarity media is crucial for many areas of chemistry and biochemistry such as phase transfer catalysis, separations, and biomembranes. [1,2] It has become clear from experiments [3] and simulations[4] that the transfer of small hydrophilic ions from water to an immiscible organic liquid is typically accompanied by the co-transfer of several water molecules. As a result, the ion exists in the organic phase as a hydrated cluster. To properly simulate biological phenomena at the coarse grained (CG) level, a proper treatment of the hydrated ions and solvent is crucial and is nontrivial. We have recently parameterized an uncharged and 4:1 mapped CG water with 3 interaction sites based on a generalized Morse -like potential which has greater flexibility in tuning the landscapes of CG effective pairwise potentials. [5] This new CG water becomes polarizable when it interacts with ions (Na+, Cl-) and or any other charged sites but not among its own species. The Morse interaction parameters for the CG ion-ion, ion-water, and ion-alkane are to be parameterized against the free energy of transfer of ions between water and liquid alkanes as well as radial distributions of ion-ion and ion-water. The target data are to be derived from atomic simulations.

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841-Pos Board B627

Predicting Bound Ions on the Protein Surface

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Biological macromolecules exist in the complex environment of the cell, constantly interacting with other molecules and ions. Some of the ions may bind directly to proteins affecting their structure and thus altering their function. Though the X-ray crystallography remains to be one of the most popular methods of proteins structure determination, typically the positions of bound ions are not routinely revealed. Here we report a development of an approach, based on numerical solutions of the Poisson-Boltzmann equation (PBE) as implemented in DelPhi, which predicts the positions of surface bound ions taking into account geometrical considerations as well. The method is tested against existing experimental data of proteins with different types of ions on the surface and it is shown that it the electrostatic potential is the dominant factor for ion binding not involving chemical interactions. We further outline the importance of such an approach with respect to relaxing the limits of Poisson-Boltzmann formalism in describing the perturbation of ion's concentration in the space regions with large local electrostatic potential. The work is supported by NIH, NIGMS, grant number 1R01GM093937-01.

842-Pos Board B628

Towards Fast and Accurate Calculation of Protein pKa Values Exploiting Various Degrees of Conformational Flexibility

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Virtually every biological process is pH dependent. Many fundamental biological phenomena including protein folding, enzyme catalysis, protein-protein interactions and pathological conditions are profoundly influenced by the pH of their environment. Accurate prediction of the pKa values of residues that can adopt variable protonation states would be a significant step towards probing the effects of pH on proteins. Despite the progress in pKa prediction algorithms, developing a method that can incorporate extensive protein conformational flexibility while retaining a relatively small computational resource footprint remains a significant challenge. We developed a fast and accurate method to predict pKas of residues that commonly exhibit variable protonation states in proteins. The algorithm