

measurements. Finally, the results of the application of the modified PHS method to simulating the cytoplasmic region of the transmembrane protein Plexin B1, and its interaction with the membrane are discussed.

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Image Charge Methods for a Hybrid Solvation Model with Transition Layer

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We present a novel three dielectric layer hybrid solvation model for treating electrostatic interactions of biomolecules in solvents using the Poisson-Boltzmann equation. In this model, the interior spherical cavity contains the solute and explicit solvent molecules. An intermediate buffer layer is introduced, which also contains solvent molecules. Outside the spherical shell defines the exterior layer, where bulk solvent is modeled implicitly and characterized by a dielectric constant. Within the intermediate layer, a special dielectric permittivity profile is constructed to give a continuous transition from the interior cavity to the exterior layer. The selection of this special profile using a harmonic interpolation allows an analytical solution of the model by generalizing the classical Kirkwood series expansion. To speed up numerical calculations of the electrostatic potential solutions, discrete image charges are employed following previous work [1]. Two approaches for constructing discrete image approximations to the potentials are considered: Semi-analytical and least square methods. Both methods are employed for the reaction field of solvents without and with finite ionic strength. Numerical results are presented to validate the accuracy and effectiveness of the image charge methods. This work is supported by NIH 1R01 GM083600-02. Z. Xu is also partially supported by the Charlotte Research Institute through a Duke Postdoctoral Fellowship.

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Molecular versus van der Waals-like Surfaces: Revisiting The Choice Of Solute-solvent Boundary Definition In Implicit Solvent

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Implicit treatment of the solvent environment offers an optimal balance between efficiency and accuracy that greatly extends our ability to simulate protein structures and conformational transitions. The most accurate description so far is achieved by continuum dielectric solvation models, including generalized Born (GB) and Poisson-Boltzmann (PB) theories. The precise definition of the solute-solvent boundary is one of the most important features in continuum dielectric models. While it is believed that so-called molecular surfaces (MS) should provide the most physical description, most existing GB models are based on van der Waals-like (VDW) surfaces for computational simplicity and efficiency. VDW surfaces do not capture so-called reentrant surface. While it has been pointed out that VDW surface definition leads to small, solvent-inaccessible (and thus unphysical) high dielectric pockets in large proteins, the precise consequences of using VDW surfaces in simulation of smaller peptides are not well understood. In particular, it is believed by many that one might be able to compensate for drawbacks of VDW surfaces through optimization of certain parameters such as intrinsic radii of atoms. Here, we first demonstrate that such optimization has limited capability to compensate for systematic errors of VDW surfaces, which is particularly problematic for describing charged side chains and has important implications in conformational equilibrium of even small peptides. We then describe an efficient approximation of MS within the frame work the generalized Born with a simple switching (GBSW) model. The new model is as efficient as the original VDW surface based GBSW model, but is able to reproduce the Born radii calculated from the MS PB theory with a correlation of 0.98. Preliminary results of optimization of the new model on peptide simulations will also be discussed.

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Introducing A Software Package For The Simulation Of Biomacromolecules Using The ABSINTH Implicit Solvation Model

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Computer simulations of biomolecules offer detailed insight into the molecular driving forces and mechanisms of fundamental biological processes such as protein folding or aggregation. This insight is accompanied by two major caveats, i) how authentic is the description of the system by the chosen model, and ii) how reliable are the data obtained in a statistical sense, i.e., what is the quality of sampling.

The ABSINTH model, published recently (Vitalis & Pappu, *J. Comput. Chem.*, 2008, DOI 10.1.1002/jcc.21005) tries to satisfy the second concern by coarse-graining of the solvent degrees of freedom. This leads to considerable speed-up of the simulations and allows for the study of hitherto inaccessible length and timescales *in silico*. Furthermore, ABSINTH has been shown to satisfy the first concern well, as a careful calibration with respect to various pieces of experimental data on relevant systems has been carried out.

Here, we present the software package our laboratory has developed to study biological systems using the ABSINTH model primarily via a Monte Carlo sampling approach. We lay out the strategies employed to achieve maximal sampling quality given the challenging nature of the systems we study with finite computational resources. In addition, we provide a brief overview of the many options the program offers, which will make it a user-friendly and flexible tool that could become an important addition to the existing suite of packages and tools for the molecular simulation community. The software package will be freely available under a public license (open-source) and is not tied to any commercial interests whatsoever. To further make the case for ABSINTH, we will present new calibration results on a range of complex systems obtained using the ABSINTH paradigm.

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The Rankwise Distributed Multipole Analysis (RWDMA) of the Electrostatic Field of Large Biomolecules

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Electrostatic interactions play an essential role in many molecular processes in living organisms. However, given the large size of the macromolecules typically involved in such processes, the accurate representation of the electrostatic potential is difficult to achieve in simple and computationally efficient ways. Among the methods used to reduce the complexity of such models, the multipolar expansions provide a systematic method to separate essential features of the electrostatic field according to spatial scale. Yet, the dependence of the multipole moments on the center of expansion makes the method ambiguous and the accuracy unreliable. We present the Rankwise Distributed Multipole Analysis (RWDMA) method, which removes the ambiguity associated with the center of expansion and, at the same time, provides a recursive minimization of the truncation error of the multipole expansion. We illustrate the method with the example of the electrostatic potential generated by the histone core of a nucleosome complex.

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Cooperative Sucrose Metabolism In Yeast Is A Snowdrift Game

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Understanding the conditions required for the initiation and maintenance of cooperation is a classic problem in evolutionary biology. In order for the budding yeast *S. cerevisiae* to grow on sucrose the disaccharide must first be hydrolyzed by the enzyme invertase. This hydrolysis reaction is performed outside of the cell, in the periplasmic space between the plasma membrane and the cell wall, suggesting that invertase production may represent a cooperative behavior. Here we demonstrate that the vast majority (~99%) of the monosaccharides created by sucrose hydrolysis diffuse away before they can be imported, thus making invertase production and secretion a cooperative behavior. In competition experiments we find coexistence between the wildtype cooperator strain and a mutant cheater strain that does not produce invertase, implying that the interaction is governed by the snowdrift game in which the optimal strategy is the opposite of one's opponents. A simple model of the cooperative interaction incorporating nonlinear benefits is able to explain this coexistence and also produces a phase diagram predicting that the outcome of the competition can be altered by varying either the cost of cooperation or the glucose concentration in the media. We are able to confirm the predictions of this phase diagram and also find that increasing the availability of glucose can have the surprising effect of decreasing the growth rate of the culture. Finally, we have characterized the wildtype invertase production strategy and find that the response is appropriate for the snowdrift game—wildtype cells cooperate when competing against cheater cells but cheat when competing against cells that always cooperate.

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Sensing and uptake of glucose in *Saccharomyces cerevisiae*

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Maintaining diverse cellular activities while consuming enough nutrients to sustain them is an essential task for all organisms. For the budding yeast