MAFELAP 2019 abstracts for the mini-symposium
Numerical Methods for Continuum Solvation

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Continuum models to handle solvent and electrolyte effects in an effective way have a long tradition in quantum-chemistry simulations and are nowadays also being introduced in computational condensed-matter and materials simulations. A key ingredient of continuum models is the choice of the solute cavity, i.e. the definition of the sharp or smooth boundary between the regions of space occupied by the quantum-mechanical (QM) system and the continuum embedding environment. The cavity, which should really reflect the region of space accessible to the degrees of freedom of the environmental components (the solvent), is usually defined by an exclusion approach in terms of the degrees of freedom of the system (the solute), typically the atomic position of the QM system or its electronic density.

While standard approaches to define the cavity lead to comparably high accuracies, some shortcomings are present in most local definitions and limit the transferability of the models to more complex simulations. In particular, local definitions of the interface are often uneffective in characterizing the solvent-excluded regions of space, i.e. regions of space where the solvent molecules would not be able to enter, but the continuum medium can penetrate. Moreover, standard definitions of continuum interfaces require a separate parametrization to handle solvation of charged species, due to the fact that charged solutes more strongly bind the solvent molecules.

In a smooth-interface continuum solvation framework it is possible to capture these additional effects by exploiting non-local definitions of the interface, while keeping the methods computationally inexpensive and without affecting the calculation of derivatives, e.g. as required for running a self-consistent field optimization of the electronic density of a geometry optimization. Here, the solvent-aware and field-aware approaches to continuum interfaces will be presented, the type of parameters involved in these models will be analyzed and the effects of these methods on continuum solvation calculations in condensed-matter simulations will be discussed.
I will present a molecular version of classical DFT (MDFT) at the basic Hyper-Netted-Chain (HNC) level, i.e. second-order Taylor expansion around a fixed homogeneous density, and beyond. The solvent around a molecular solute is represented by a continuous molecular density field depending on positions and orientations (3 + 3 variables discretized on a spatial and angular grid).\cite{1,2,3} Technically, the orientations can be handled efficiently using generalized spherical harmonics expansions and the angular version of FFT’s.\cite{3} The approach is illustrated by a few solvation problems: prediction of solvation free energies and microscopic solvation profiles for organic molecules datasets, identification of water molecules around proteins, electron transfer rates close to surfaces. The necessity of introducing so-called bridge excess functionals beyond the HNC approximation will be discussed.

References


CALCULATION OF THE SOLVENT AND ION ATMOSPHERE OF MACROMOLECULES USING 3D-RISM

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The ionic atmosphere around highly charged molecules, like DNA and other macromolecules, involves a complex interplay of co-ions, counter-ions and water. Rigorously modeling such an environment requires accounting for the discrete molecular nature of the solvent. The reference interaction site model (RISM) uses explicit molecular solvent models to provide a complete equilibrium sampling of bulk solvent and solvent around a solute of arbitrary shape and size.[1] Results are similar to those obtained from explicit solvent molecular dynamics (MD) but at a fraction of the cost. In this talk, I will first introduce RISM theory with special attention for thermodynamic qualities, such as preferential interaction parameters and solvation free energies and entropies. Examples will include the distribution of water and ions around a 24 base pair strand of DNA,[2] and of G-quadruplexes,[3] making comparisons to both experiment and to results from molecular dynamics simulations.

Recent developments allow 3D-RISM calculations to be performed with periodic boundary conditions, opening the way to the description of solvent properties in macromolecular crystals, where the solvent may occupy 50% or less of the volume of the unit cell. Numerical methods akin to the particle-mesh Ewald scheme allow an efficient evaluation of both the potential and the resulting forces on the solute atoms. This opens the way to new models for the “bulk-solvent” contribution to X-ray scattering.

These codes can be obtained as a part of the AmberTools distribution[4] (http://ambermd.org).

References


A new class of Schwarz methods was recently presented in the literature for the solution of solvation models, where the electrostatic energy contribution to the solvation energy can be computed by solving a system of elliptic partial differential equations [1, 2]. Numerical simulations have shown an unusual convergence behavior of Schwarz methods for the solution of this problem, where each atom corresponds to a subdomain: the convergence of the Schwarz methods is independent of the number of atoms [1], even though there is no coarse grid correction. Despite the successful implementation of Schwarz methods for this solvation model, a rigorous analysis for this unusual convergence behavior is required.

In this talk, we analyze the behavior of the Schwarz method for the solution of chains of subdomains and show that its convergence does not depend on the number of subdomains in many cases [3, 4]. Moreover, we will present new recent results that study the behavior of the Schwarz method in the cases its convergence depends on the number of subdomains [5].

References


The Poisson-Boltzmann (PB) model is an effective implicit solvent approach for simulating solvated biomolecular systems. By treating the solvent with a mean field approximation and capturing the mobile ions with the Boltzmann distribution, the PB model largely reduces the degree of freedom and computational cost. However, solving the PB equation suffers from many numerical difficulties arising from interface jump conditions, complex geometry, charge singularities, and boundary conditions at infinity. In addressing these difficulties, we recently developed a treecode-accelerated boundary integral (TABI) solver for solving Poisson-Boltzmann (PB) equation. The solver has combined advantages in accuracy, efficiency, memory, and parallelization as it applies a well-posed boundary integral formulation to circumvent many numerical difficulties associated with the PB equation and uses an $O(N \log(N))$ treecode to accelerate the GMRES iterative solver. In this talk, we report our recent improvements to the TABI solver including parallelization, precondition, and surface triangulation. In addition, we provide some biological applications such as the calculation of binding energy and pKa values.
SCALABILITY ANALYSIS OF AN INTEGRAL EQUATION FORMULATION OF THE MANY-BODY DIELECTRIC PROBLEM IN ELECTROSTATICS

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We consider the problem of calculating the electrostatic interaction between dielectric spheres embedded in a polarisable continuum. In order to solve this problem, E. Lindgren and co-workers have proposed in [E. Lindgren et al, An integral equation approach to calculate electrostatic interactions in many-body dielectric systems, Journal of Computational Physics, 2018, pp. 712-731] a numerical method based on a Galerkin discretisation of an integral equation formulation of this problem. The proposed method is general enough to treat any homogeneous dielectric medium containing an arbitrary number of spherical particles of any size, charge, dielectric constant and position in the three-dimensional space. Furthermore, numerical experiments indicate that the algorithmic complexity of the method scales linearly with respect to the number of particles thanks to the use of a modified Fast Multipole Method.

The current talk will present some results on the numerical analysis of this algorithm with a focus on proving that the method is indeed scalable with respect to the number of objects $N$ in the problem. As a first step, we demonstrate that both the infinite-dimensional integral equation formulation and its Galerkin discretisation are well-posed with explicitly characterisable continuity and inf-sup constants. Our main result is to derive error estimates that do not explicitly depend on $N$. We show in addition that under suitable regularity assumptions, the numerical method exhibits exponential convergence. We also obtain an upper bound for the condition number of the stiffness matrix that does not explicitly depend on $N$ and consequently show that under suitable assumptions, a Krylov subspace solver such as GMRES that is used to solve the underlying linear system converges to a given tolerance independent of $N$. We conclude the talk with a brief discussion about the efficient computation of the electrostatic forces.
We have recently developed a multigrid solver for the generalized Poisson equation that can be used for arbitrary solute densities $\rho(r)$ obtained from an electronic structure calculation, by means of which the molecular density $\rho(r)$ and the dielectric polarization $\varphi(r)$ are iterated to mutual self-consistency.\cite{1,2} The generalized Poisson equation may include an arbitrary, spatially-varying dielectric function $\varepsilon(r)$ specified by the user, so that the method can describe anisotropic solvation environments such as the air/water interface. Borrowing ideas from polarizable continuum models, we have implemented nonequilibrium solvation corrections in which the solvent’s optical dielectric constant is used to account for instantaneous re-polarization of the dielectric continuum environment upon vertical excitation or ionization of the solute. We have used this code to compute accurate vertical ionization energies for small ions in bulk water and to examine whether these ionization energies are modified at the air/water interface. Particular attention is paid to whether the solvated electron, $e^{-}(aq)$, is spectroscopically distinguishable at the interface as compared to the same species in bulk water.\cite{1}

References


RECENT WORK ON TREECODES AND APPLICATIONS

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We review a recently developed kernel-independent treecode (KITC) algorithm based on barycentric Lagrange interpolation at Chebyshev points for fast summation of pairwise particle interactions [1]. This is joint work with Lei Wang (University of Wisconsin, Milwaukee) and Svetlana Tlupova (Farmingdale State College, Farmingdale).

Next we present an application of the KITC to accelerate the evaluation of the asymptotic correlation functions in 3D-RISM (Reference Interaction Site Model) for computation of thermodynamic properties and solvent structure of solvated biomolecules [2]. The 3D-RISM/KITC is demonstrated for a solvated tubulin (1TVK) with 13456 atoms on a grid of dimensions $320 \times 256 \times 256$ computed on 64 cores. This is joint work with Leighton Wilson (University of Michigan, Ann Arbor) and Tyler Luchko (California State University, Northridge).

Finally we present a boundary element method for the interaction energy of charged dielectric spheres immersed in solvent. Accuracy is improved by singularity subtraction and Richardson extrapolation, and the BEM is applied to demonstrate the like-charge attraction of asymmetric dielectric spheres. This is joint work with Zecheng Gan (University of Michigan, Ann Arbor) and Weihua Geng (Southern Methodist University, Dallas).

References


Polarizable continuum solvation models (PCSM) nowadays have become a standard tool in computational chemistry to include solvation in a wide range of applications, usually coupled with quantum mechanical (QM) methods.\cite{3} However, recent developments in algorithms made QM methods applicable to systems large enough that the cost associated with solving the PCSM equations can become the computational bottleneck.

In order for PCSM to be applicable to large and very large molecular problems, an efficient and robust numerical strategy has to be devised. In recent years, we have proposed a completely new formulation of PCSM that is not based on the numerical solution of an integral equation as in traditional methods, but on a domain-decomposition (dd) strategy. This new formulation has been applied first to PCSM in the conductor-like approximation (ddCOSMO)\cite{1} and then to the dielectric scheme (ddPCM).\cite{2}

In this work, we present the first implementation of ddPCM for a solute described at a quantum mechanical level of theory. We start by discussing the ideas behind the ddPCM method and then how it is coupled to Hartree-Fock, Density Functional Theory and semi-empirical methods. In particular, we discuss how to compute the solvation effect on properties and excitation energies of the solute. Finally, we discuss the timings and scaling of the new implementation and we compare it with a previous, state-of-the-art, implementation of a PCSM.

References


A particular domain decomposition method, called ddLPB, is developed for solving the Poisson–Boltzmann solvation model in quantum chemistry. In this method, the domain (solute molecule) is decomposed into (atomic) balls and the global Poisson–Boltzmann equation is transformed into a system of coupled subequations restricted in these balls. As a consequence, each local subequation can be solved explicitly, using the Galerkin spectral method with spherical harmonics as basis functions. Based on the local solvers, the coupling conditions among the subequations are then discretized, which derives a global linear system that can be solved by linear solvers. A series of numerical experiments will be presented to show the robustness and the efficiency of this new method.
EFFICIENT MOLECULAR SURFACE CONSTRUCTION WITHIN
AND BEYOND THE CONTINUUM SOLVATION FRAMEWORK:
THE NANOSHAPER EXAMPLE

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The progress of powerful experimental techniques such as Cryo-Electron Microscopy represents a remarkable opportunity but also a significant challenge for computational techniques, which aim at extracting useful information and predicting the behavior of biomolecular systems. While pioneering attempts to perform molecular dynamics simulation at this scale by means of super-computers have been made, there still is the compelling need for enabling tools and approaches able to routinely analyze this kind of structures, identifying, for instance, interaction hot spots or new target regions for next generation drug discovery. In this context, the construction and analysis of the Molecular Surface (MS) can play a significant role. MS, in the Solvent Excluded Surface definition, has been widely used as a separation between high from low dielectric regions preliminary to the solution of the Poisson-Boltzmann equation. However, the range of its application is significantly larger. Here, I will describe the development of NanoShaper,[1] a tool for building and analyzing the molecular surface of systems at the nanoscale, as well as a number of its applications, ranging from pocket identification to hydration analysis in molecular dynamics trajectories, until its integration with the widely used VMD software utility [2].

2. S. Decherchi, A. Spitaleri, J. Stone, and W. Rocchia ”NanoShaper-VMD interface: computing and visualizing surfaces, pockets and channels in molecular systems” Bioinformatics, bty761, 2018