My research focuses on: (1) Scientific computing and numerical analysis (numerical PDEs, numerical optimization, computational fluid dynamics, and level-set method for interface motion); (2) Applied analysis of partial differential and stochastic differential equations (asymptotic analysis, stability analysis, multiscale analysis, and stochastic analysis); (3) Mathematical modeling (biophysics and colloidal systems); (4) Monte Carlo simulations and Brownian dynamics simulations. I have worked on problems of modeling and computation of charged systems, biomolecular solvation, and stability of fluid-vapor interface.

1. Ionic Size Effects In Charged Systems. Electrostatic interactions between macromolecules and mobile ions in the surrounding solvent play a key role in many important biological processes. In such interactions, ionic sizes or excluded volumes can affect many properties of an underlying biological system. The classical Poisson–Boltzmann (PB) theory is perhaps the most widely used and efficient model of the electrostatics in ionic solutions. Despite its many successful applications, this mean-field theory is known to fail in capturing the ionic size effects. Accurate and efficient modeling and computations of ionic size effects are challenging due to the inhomogeneity, multiple scales, and nature of the many-body interactions. Many groups have been interested in developing an efficient model that takes into account ionic size effects and corresponding computational methods.

My collaborators and I developed a mean-field model that is capable of capturing ionic size effects in charged systems. Central in our mean-field approach is a free-energy functional of ionic concentrations in which the ionic size effects are included through the entropic effect of solvent molecules:

$$F[c] = \int_\Omega \frac{1}{2} \rho \psi dV + \beta^{-1} \sum_{i=0}^{M} \int_\Omega c_i \left[ \ln(v_i c_i) - 1 \right] dV - \int_\Omega \sum_{i=0}^{M} \mu_i c_i dV,$$

where $\psi$ is the electrostatic potential, $\rho$ is the fixed charge density, $\beta = (k_B T)^{-1}$ with $k_B$ the Boltzmann constant and $T$ the temperature, and $v_i$, $N_i$, and $\mu_i$ ($i = 1, \ldots, M$) are the volume, total number, and chemical potential for $i$th species of ions, respectively. Given the volume $v_0$ of a solvent molecule, one can define the solvent concentration by $c_0(x) = v_0^{-1} \left[ 1 - \sum_{i=1}^{M} v_i c_i(x) \right]$. The equilibrium concentrations, $c_i$, are obtained by solving equilibrium conditions $\delta_{c_i} F[c] = 0$, which give generalized Boltzmann distributions that relate equilibrium concentrations to electrostatic potential.

1.1 Mean-field description of ionic sizes. When ionic sizes are different, explicit formulas of the generalized Boltzmann distributions are not available. To overcome this difficulty, I developed a constrained optimization technique to find the equilibrium concentrations [II]. An augmented Lagrange multiplier method is proposed and implemented to numerically solve the constrained optimization problem. Numerical tests demonstrate that the mean-field model and numerical method capture significant ionic size effects, particularly those for multivalent ionic solutions. The first figure in Figure III presents counterion saturations close to a charge surface, rather than unphysical high concentrations predicted by the classical PB theory. Also, size effects lead to multivalent counterions stratification near a charged surface. I found a key physical parameter, the ionic valence-to-volume ratio ($\alpha_i$), to describe the order of stratification of counterions of different species. Remarkably, the order of stratifications is consistent with the order of $\alpha_i$ values, as shown in Figure III (the second to the fourth). Extensive studies show that this key parameter is effective and useful in describing the competitions between counterions of different species.

1.2 Asymptotic analysis of ionic size effects. To confirm the numerical observations above, I study in [5] the equilibrium concentrations in the strong and weak electrostatic potential limits. For a strong electrostatic potential, I prove: (1) Monotonicity of concentrations with the largest and smallest valence-to-volume ratios $\alpha_i$; (2) Asymptotic behavior of concentrations, i.e., saturation of counterions with concentration approaching the reciprocal of its ionic size; (3) Stratification of concentration profiles for different...
values of the electrostatic potential. For a weak electrostatic potential, I obtain a modified (longer) Debye length $\tilde{\lambda}_D$ due to the ionic size effect: $\tilde{\lambda}_D^{-2} = \lambda_D^{-2} - \beta \varepsilon^{-1} \left( \sum_{i=1}^{M} q_i c_i^\infty \right)^2 / \sum_{i=1}^{M} v_i^2 c_i^\infty$, where $\lambda_D$ is the classical Debye length and $v_i$, $c_i^\infty$, and $q_i$ are the volume, bulk concentration, and charge of the $i$th species of ions, respectively. Further, I prove some basic properties of the electrostatic potential for the case of a charged spherical molecule.

1.3 Monte Carlo simulations of charged systems. To further test the phenomena predicted by our size-modified model, I conduct canonical ensemble Monte Carlo (MC) simulations with the Metropolis criterion [2] to study the ionic distribution in a charged system, cf. a snapshot of MC simulations shown in the first figure of Figure 2. For a highly charged surface, both of the size-modified model and MC simulations demonstrate that the counterions bind tightly around the charged surface, resulting in a stratification of counterions of different species. The competition between mixed entropy and electrostatic energetics leads to a compromise that the ionic species with a higher valence-to-volume ratio distributes closer to the charged surface, cf. Figure 2. This is consistent with the results predicted by the size-modified model.

2. Variational implicit-solvent modeling and numerical methods for biomolecular interactions. Aqueous solvent plays a significant role in dynamical processes of biological molecules, such as molecular recognition and molecular assembly. Implicit-solvent models are efficient descriptions of biomolecular interactions in an aqueous environment. In such a model, the solvent is treated implicitly as a continuum and the effect of individual solvent molecules are coarse grained. With an implicit solvent, dielectric solute-solvent interfaces are fundamental in the accurate and efficient prediction of biomolecular interfacial properties, electrostatic interactions, and solvation free energies. Recently, Dzubiella et al. (Phys. Rev. Lett., 96, 087802, 2006; J. Chem. Phys., 124, 084905, 2006) proposed a variational implicit-solvent model (VISM). In this formulation, the solvation free energy and equilibrium solute-solvent interfaces are obtained by minimizing a solvation free-energy functional of all possible surfaces $\Gamma$ that surround all the fixed solute atoms
\[ x_1, \ldots, x_N \text{ (cf. Figure 4):} \]

\[ G[\Gamma] = P \text{vol}(\Omega_m) + \int_{\Gamma} \gamma dS + \rho_w \sum_{i=1}^{N} \int_{\Omega_w} U_i(|x-x_i|) dV + G_{\text{elec}}[\Gamma]. \]  \hspace{1cm} (1)

Here, \( P \) is the pressure difference, \( \gamma \) is the surface tension, \( H \) is the mean curvature, \( \rho_w \) is the bulk solvent density, and \( U_i \) is the Lennard-Jones potential for the \( i \)th solute atom, and \( \Omega_m \) and \( \Omega_w \) are the solute (molecule) region and solvent region, respectively.

2.1 VISM with Poisson–Boltzmann theory. The Poisson–Boltzmann theory is a well-established continuum description of electrostatic interactions of biomolecules in an aqueous solvent. In [6], I incorporate the classical PB theory of continuum electrostatics into our VISM formulation of the solvation free energy. The solute-solvent interface \( \Gamma \) is relaxed in the steepest descent direction of the VISM functional (11) by using the level-set method. I develop a robust and highly accurate compact coupling interface method (CCIM) for the nonlinear PB equation with complex interface geometry, and evaluate the dielectric boundary force with high-order interpolation schemes. The newly developed VISM-PB theory is applied to analyze the solvent potentials of mean force and hydrophobic hydration for some molecular systems. As shown Figure 4, the PB-VISM theory successfully predicts the following phenomena.

1. The PB description is able to capture the desolvation effect when two particles merge together.
2. The electrostatic interaction between two particles is greatly screened by the solvent and ionic solutions with different bulk concentrations.
3. The change of the shape of two particles as the distance varies demonstrates that the theory inherently couples the nonpolar and polar contributions into the free energy.
4. The equilibrium surfaces show remarkable stepwise dewetting transitions due to the heterogeneously charged pattern in two plates. This is a significant achievement for an implicit-solvent model to capture the effect of electrostatics on the hydrophobic interactions between two plates.

I also work on a software package for the analysis of biomolecular solvation by assembling the numerical codes developed in the PB-VISM theory [11].

2.2 Variational implicit-solvent modeling of host-guest binding. The host-guest system CB[7]-B2 has attracted much attention due to its ultra-high binding affinity. In [4], I apply the VISM to study hydration effects on the high-affinity binding of the system. Figure 5 shows the equilibrium surfaces for the binding process of the CB[7]-B2 system. I analyze the potential of mean force versus the distance between the host and the guest and the evolution of the geometric part, vdW part, and the electrostatic part of the VISM solvation free energy (11), during the binding process. Results show that the major driving forces of the binding are water-mediated hydrophobic interactions and the intrinsic host-guest vdW interactions. The binding affinities predicted by the VISM are in line with recent experiments and molecular dynamics simulations with explicit solvent. It is expected that the level-set VISM can efficiently predict molecular binding and recognition in a wide range of future applications.
3. Stability analysis of solute-solvent interface

3.1 Motion of a cylindrical dielectric boundary. The interplay between geometry and electrostatics contributes significantly to hydrophobic interactions of biomolecules in an aqueous solution. In [3], my collaborators and I study the motion of a cylindrical dielectric boundary $\Gamma$ as the steepest descent of a free-energy functional

$$F[\Gamma] = \gamma_0 \text{Area}(\Gamma) + \int_\Omega \frac{1}{2} \rho \psi_F dV,$$  

(2)

where the electrostatic potential $\psi_F$ satisfies the Poisson’s equation with a dielectric jump from solute region to solvent region, cf. the first figure in Figure 6. Here, $\gamma_0$ is the surface tension and $\rho$ is the charge density. The motion of $\Gamma$ is governed by $V_n = -M \delta_\Gamma F[\Gamma]$. We derive an explicit formula for the effective dielectric boundary force, which always points from the solvent region to solute region. In the case that the interior of a cylinder is of a higher dielectric, the competition between the geometrical and electrostatic contributions leads to the existence of equilibrium boundaries. Linear stability analysis is presented to show that such an equilibrium is only stable for a perturbation with a wavenumber larger than a critical value. See the second figure in Figure 6 for the dispersion relation $\omega(k)$. Numerical simulations are reported to confirm the analysis on the role of each component of the driving force. Implications of the mathematical findings to the understanding of charged molecular systems are discussed.

3.2 Effects of the hydrodynamics on the stability of the solute-solvent interface. Along the line of the work described above, my collaborators and I study in [7] the stability of a cylindrical solute-solvent interface under the influence of the vdW interactions, interfacial surface energy, electrostatics, and solvent fluid motion. We construct a solvent fluid dielectric boundary model for the solvation of charged molecules. The motion of the solute-solvent interface is defined to be the same as that of solvent fluid at the interface. The solvent fluid is assumed to be incompressible and is described by Stokes’ equation. The solute is modeled simply by the ideal-gas law. All the viscous force, hydrostatic pressure, solute-solvent van der Waals interaction, surface tension, and electrostatic force are balanced at the solute-solvent interface. For a cylindrical geometry, we find circularly cylindrical equilibrium solute-solvent interfaces. For their linearized systems, we use the projection method to solve the fluid equation and find the dispersion relation. We find that the steady state solutions exhibit bifurcation behaviors with respect to charge strength in the system. Our asymptotic analysis shows that the dispersion relation for large wavenumbers is given by $\omega(k) = -\frac{\gamma_0}{2\mu_\omega} k$ for $k \gg 1$, where $\mu_\omega$ is the fluid viscosity. This indicates that the solvent viscosity does affect the stability of a solute-solvent interface.

4. Future research

(1) The classical PB theory fails to predict the phenomenon of charge inversion due to the ignored ion-ion correlation. I am working to incorporate the ion-ion correlation into our size-modified model. Also, I am working on mean-field models and Monte Carlo simulations that are able to consider electrostatic interactions in an inhomogeneous dielectric environment.

(2) To get a better estimate of the electrostatic solvation energy, I am working on incorporating the charge asymmetry effect of water molecules into the VISM. Also, I am working on modeling the solvent effect by Stokes’ equation and fast, accurate numerical methods for fluid-solute interface with traction boundary conditions. Incorporation of fluctuations into VISM through binary level-set method will also be my future work.
(3) Also, I am working on a hybrid diffusion model interfacing the Brownian dynamics and a continuum description. Multiscale modeling and mathematical analysis of the hybrid model will be our future work.

Besides my research mentioned above, I am also open to the possibility of exploring exciting interdisciplinary research topics such as inverse problems, image processing, data science, etc. After years of rigorous training in mathematics and computation, especially in numerical PDEs, optimization, deterministic and stochastic modeling, and the numerical simulations of various problems in science and engineering, I am confident to conduct new research subjects of applied mathematics and work with scientists in different fields.

References