Numerical Study of the Poisson-Boltzmann Equation for Biomolecular Electrostatics

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***Abstract* – Electrostatics interaction plays a very important role in almost all biomolecular systems. The Poisson-Boltzmann equation is widely used to treat this electrostatic effect in an ionic solution. In this work, a simple mixed discrete-continuum model is considered and boundary element method is used to solve for the solution.**

Keywords – Boundary Element Method, Biomolecular electrostatics, Poisson-Boltzmann Equation.

1. INTRODUCTION

Electrostatics interaction plays a very important role in almost all biomolecular systems. Some of the areas where electrostatics has been very useful include protein structural stability, enzyme catalysis, biomecular recoginition and biomolecular encounter rates [1]. Thus, there is a need for an accurate modelling and simulation of the biomolecular electrostatiscs.

There are few methods to simulate a biomolecule in an ionic solution. In this paper, a mixed discrete-continuum approach based on combining a continuum description of the macromolecules and solvent with a discrete description of the atomic charges is adopted [2]. Instead of considering the non-linear Poisson-Boltzmann equation, the linearized Poisson-Boltzman equation is considered by assuming that the electrostatic energy of the ions is much lesser than their thermal energy [3].

The boundary element method is used to solve for solution of the equations generated from the above model. It is the preferred method as it treats the infinite domain and point charges more naturally, and is able to reduce the dimensional of the problem by one.

The next section briefly discusses the mixed discrete-continuum model and the boundary integral equations formulation. Then, numerical solutions and some sample 2D computational result are presented. Finally, some of the future investigations are discussed.

2. PROBLEM FORMULATION

2.1 Mixed Discrete-continuum Model

Fig. 1 shows a simplified mixed discrete-continuum model for the problem. Region Ω_1 corresponds to the interior of the molecule and region Ω_2 corresponds to the surrounding solvent.

In region Ω_1, the electrostatic potential is governed by a Poisson equation.

$$\Omega_1 :\ \nabla^2\varphi_1(\vec{r}) = -\sum_{k=1}^{N_c}\frac{q_k}{\varepsilon_1}\delta(\vec{r}-\vec{r}_k) \qquad (1)$$

where φ_1 is the electrostatic potential, $\vec{r}$ is an evaluation position, $\vec{r}_k$ is the location of the point charge, q_k is the strength of the point charge, N_c is the number of point charges, and ε_1 is the dielectric constant in Ω_1.

In region Ω_2, Debye-Hückle theory suggests that the electrostatic potential should satisfy a nonlinear Poisson-Boltzmann equation. This equation can be linearized under the assumption that the electrostatic energy of the ions is much lesser than their thermal energy. The linearized Poisson-Boltzmann is also a Helmholtz equation.

$$\Omega_2 :\ \nabla^2\varphi_2(\vec{r}) - \kappa_D^2\varphi_2(\vec{r}) = 0 \qquad (2)$$

where φ_2 is the electrostatic potential, κ_D is the reciprocal of the Debye length and ε_2 is the dielectric constant in Ω_2.

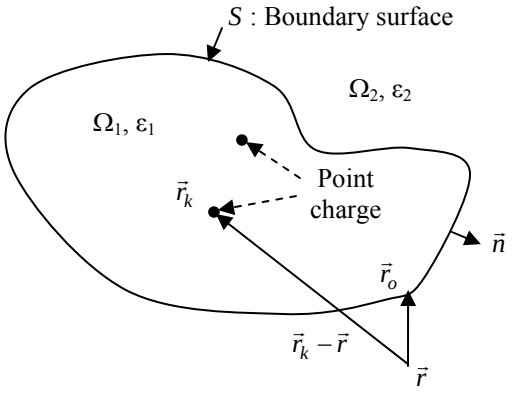


Fig. 1: The mixed discrete-continuum model

2.2 *Boundary Integral Equations Formulation*

The fundamental solution to equations (1) and (2) are

2D: $$G_1(\vec{r},\vec{r}\,') = -\frac{1}{2\pi}\ln(|\vec{r}\,'-\vec{r}|) \quad (3.1)$$

$$G_2(\vec{r},\vec{r}\,') = \frac{i}{4}H_0^{(1)}(i\kappa|\vec{r}\,'-\vec{r}|) \quad (3.2)$$

3D: $$G_1(\vec{r},\vec{r}\,') = \frac{1}{4\pi|\vec{r}\,'-\vec{r}|} \quad (4.1)$$

$$G_2(\vec{r},\vec{r}\,') == \frac{e^{-\kappa|\vec{r}\,'-\vec{r}|}}{4\pi|\vec{r}\,'-\vec{r}|} \quad (4,2)$$

By applying the direct formulation of the boundary integral equations to equations (1) and (2), we obtain

The integral equation for region Ω_1 is

$$c(\vec{r})\varphi_1(\vec{r}) = \int_S\left[G_1(\vec{r},\vec{r}\,')\frac{\partial\varphi_1(\vec{r}\,')}{\partial n} - \varphi_1(\vec{r}\,')\frac{\partial G_1(\vec{r},\vec{r}\,')}{\partial n}\right]dS + \sum_{k=1}^{N_c}\frac{q_k}{\varepsilon_1}G(\vec{r},\vec{r}_k) \quad (5)$$

The integral equation for region Ω_2 is

$$c(\vec{r})\varphi_2(\vec{r}) = \int_S\left[-G_2(\vec{r},\vec{r}\,')\frac{\partial\varphi_2(\vec{r}\,')}{\partial n} + \varphi_1(\vec{r}\,')\frac{\partial G_2(\vec{r},\vec{r}\,')}{\partial n}\right]dS \quad (6)$$

where $\vec{n}$ is the outward pointing normal as shown in Fig. 1, S is the boundary surface separating Ω_1 and Ω_2, and

$$c(\vec{r}) = \begin{cases} 0.5, & \text{if } \vec{r} = \vec{r}_o \text{ is a point on a smooth boundary} \\ 1, & \text{if } \vec{r} \text{ is a point inside the domain } \Omega \\ 0, & \text{if } \vec{r} \text{ is outside the domain } \Omega \end{cases}$$

The potential φ_1 and φ_2 must satisfy the following boundary conditions.

$$\varphi_1(\vec{r}_o) = \varphi_2(\vec{r}_o) \quad (7)$$

$$\varepsilon_1\frac{\partial\varphi_1(\vec{r}_o)}{\partial n} = \varepsilon_2\frac{\partial\varphi_2(\vec{r}_o)}{\partial n} \quad (8)$$

where $\vec{r}_o \in S$.

Substitute (7) and (8) into (5) and (6), we obtain

$$\frac{1}{2}\varphi_1(\vec{r}) + \int_S\left[\varphi_1(\vec{r}\,')\frac{\partial G_1(\vec{r},\vec{r}\,')}{\partial n} - G_1(\vec{r},\vec{r}\,')\frac{\partial\varphi_1(\vec{r}\,')}{\partial n}\right]dS = \sum_{i=1}^{N_c}\frac{q_i}{\varepsilon_1}G(\vec{r}_o,\vec{r}_i) \quad (9)$$

$$\frac{1}{2}\varphi_2(\vec{r}_o) + \int_S\left[-\varphi_1(\vec{r}_o\,')\frac{\partial G_2(\vec{r}_o,\vec{r}\,')}{\partial n} + G_2(\vec{r}_o,\vec{r}_o)\frac{\varepsilon_1}{\varepsilon_2}\frac{\partial\varphi_2(\vec{r}\,')}{\partial n}\right]dS = 0 \quad (10)$$

Equations (9) and (10) can be used to compute φ_1 and $\frac{\partial\varphi_1}{\partial n}$ on the boundary surface S.

3. NUMERICAL SOLUTION

3.1 *Discretization Method*

A standard piecewise-constant centroid collocation scheme is used to discretize (9) and (10). The boundary surface S is discretized into N elements S_j and the midpoint of each element $\vec{r}_i$ is chosen as the collocation point. This results in the following 2N system of equations.

$$\begin{bmatrix} \frac{1}{2}I + \int_{S_j}\frac{\partial G_1}{\partial n}dS_j & -\int_{S_j}G_1 dS_j \\ \frac{1}{2}I - \int_{S_j}\frac{\partial G_2}{\partial n}dS_j & \frac{\varepsilon_1}{\varepsilon_2}\int_{S_j}G_2 dS_j \end{bmatrix}\begin{bmatrix} \varphi \\ \frac{\partial\varphi}{\partial n} \end{bmatrix} = \begin{bmatrix} \sum_{k=1}^{N_c}\frac{q_k}{\varepsilon_1}G_1(\vec{r}_i,\vec{r}_k) \\ 0 \end{bmatrix} \quad (11)$$

where $\int_{S_j}$ corresponds to an integration over j[th] element.

4. COMPUTATIONAL RESULTS

In this paper, the problem being considered has a cylindrical geometry. Therefore, the original 3D problem can be simplified into a 2D problem. The simulation results for 2 test cases are presented below. First, a hypothetical cylindrical molecule with a unit charge at the centre of the molecule is considered. It is then followed by considering a hypothetical cylindrical molecule with a unit dipole around the centre of the molecule.

4.1 *Potential of a hypothetical cylindrical molecule with a unit charge*

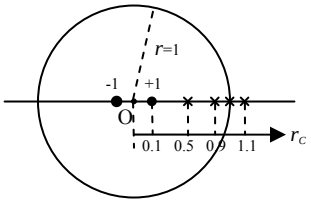
A hypothetical cylindrical molecule of radius a with a unit charge located at the centre of the molecule in a solution is simulated. The case where $\varepsilon_1 = 1$, $\varepsilon_2 = 20$ and $\kappa_D = 1/a$ is considered. The potential at the radial distance $r_C = 0.5a$, $r_C = 0.9a$, $r_C = a$ and $r_C = 1.1a$ is tabulated in Table 1.

4.2 *Potential of a hypothetical cylindrical molecule with a unit dipole*

A hypothetical cylindrical molecule of radius a with a unit dipole around the centre of the molecule in a solution is simulated. The case where $\varepsilon_1 = 1$, $\varepsilon_2 = 20$ and $\kappa_D = 1/a$ is considered. The locations of the unit dipole and the locations of the point where the potential is to be evaluated is shown in Fig. 2. The values of these potentials are tabulated in Table 2.

Potential	N (Number of elements)		
	50	100	200
$r_C = 0.5a$	0.1168367	0.1169774	0.1170018
$r_C = 0.9a$	0.0232880	0.0234282	0.0234527
$r_C = a$	0.0096749	0.0096089	0.0095776
$r_C = 1.1a$	0.0058682	0.0058344	0.0058170

Table 1: Potential of a hypothetical cylindrical molecule with a unit charge



● : Location of the dipole

× : Locations of the point where potential is to be evaluated

Fig. 2: Location of the unit dipoles and the points where the potential is to be evaluated

Potential	N (Number of elements)		
	50	100	200
$r_C = 0.5a$	0.0494663	0.0495021	0.0495109
$r_C = 0.9a$	0.0083473	0.0084118	0.0084278
$r_C = a$	0.0031264	0.0031237	0.0031231
$r_C = 1.1a$	0.0015498	0.0015483	0.0015480

Table 2: Potential of a hypothetical cylindrical molecule with a unit dipole

5. CONCLUSION

In this paper, a 2D numerical simulation to the mixed discrete-continuum model of the biomolecular electrostatics based on boundary integral equation approach is presented. Some computational results are presented to show the effectiveness of such model. More work is required to extend the simulation to the 3D case which allows the simulation of a real biomolecular structure. However, the tradeoff is that the problem size will become much larger. Thus, it is necessary to develop a faster and more memory-efficient numerical algorithm.

6. REFERENCES

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