Solving Nonlinear Poisson-Boltzmann Equation for Biophysical Electrostatic Potential Simulation with Parallel Monotone Iterative Method

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Abstract: - In this paper, a three-dimensional nonlinear the Poisson-Boltzmann equation is solved numerically with parallel finite volume (FV) and monotone iterative (MI) methods. The proposed computational technique has been successfully implemented on a PC-based Linux-cluster with the message passing interface library. First of all, the Poisson-Boltzmann equation is discretized with the FV method. It leads to a system of nonlinear algebraic equations and is directly solved with a global convergent MI algorithm. Based on the strong nonlinear property of the Poisson-Boltzmann equation, our proposed new iterative method does not require accurate initial guess to start the solution procedure and it converges monotonically. This appearing property makes the method is easily implemented on a parallel computing with very good performance. The developed parallel nonlinear Poisson-Boltzmann solver has been tested on a variety of structure problems to show its robustness. Achieved parallel speedup and efficiency are also reported to demonstrate the excellent parallel performance of the method.

Key-Words: - Poisson-Boltzmann Equation, Biophysical Potential, SOD, Parallel Computing Technique, Monotone Iterative Method

1 Introduction

In biology, physics, and chemistry communities, the electrostatic properties and distribution for material, structures, binding phenomena, complex molecules, and proteins have been of great interests and studies in recent years. Modeling and simulation for these interactions play an important role especially in biophysics. Just like various semiconductor device models, such as drift diffusion, hydrodynamic and Boltzmann transport equations require to solve the multi-dimensional Poisson equation for the potential distribution [1-8]; a three-dimensional linear or nonlinear Poisson-Boltzmann equation should be solved numerically for the behavior of electrostatic potential in molecular biophysics [9-19].

In this paper, a 3D nonlinear Poisson-Boltzmann equation is solved numerically with novel parallel finite volume and monotone iterative methods. The proposed computational techniques have been successfully implemented on a 16-PCs based Linux cluster with the message passing interface (MPI) library. First of all, the Poisson-Boltzmann equation is discretized with the FV method [20]. This discretization leads to a system of nonlinear algebraic equations and it is directly solved with a global convergent MI algorithm. The MI solution technique was proposed and applied to semiconductor device simulation successfully by us earlier [1-8]. Based on the strong nonlinear property of Poisson-Boltzmann equation, the proposed new iterative method does not require accurate initial guess to start the solution procedure and it converges monotonically. Furthermore, by comparing with the conventional Newton's iterative method, the new method is easy for implementation, relatively faster with much less computation time, and its algorithm is inherently parallel in large-scale computing [1-8]. The developed parallel nonlinear Poisson-Boltzmann solver has been tested on a variety of structure problems, such as insulin and SOD enzyme to show the efficiency and robustness. Achieved speedup and parallel efficiency are also reported to demonstrate the excellent parallel performance of the method.

The paper is organized as follows. In Sec. 2, we state the numerical modeling for biophysical electrostatic potential simulation. Sec. 3 presents our simulation methodology as well as the parallel algorithm for the model problem. Sec. 4 presents the simulation results and achieved parallel performance. Sec. 5 draws conclusions.

2 Numerical Modeling for Biophysical Electrostatic Potential Problem

In this section, we state the Poisson-Boltzmann equation for biophysical electrostatic potential problem. Continuum models of molecules in ionic solutions, first proposed in 1923 by Debye and Hückel [15], have been an important simulation approach in molecular dynamics [16-17]. Due to the progresses of biotechnologies, this numerical model for studying the electrostatic interactions has been of great interests in recent years. In biophysics, for example, the electrostatic behavior of proteins plays an important role in structure, binding properties, and the kinetics of complex molecules. Modeling of these interactions with macroscopic methodology provides a way in the study of this issue.

We consider the Poisson-Boltzmann equation describing the electrostatic potential around a fixed charge distribution in an ionic solution. The three-dimensional (3D) nonlinear partial differential equation is as follows:

$$\begin{cases} -\nabla\cdot(\varepsilon(r)\nabla u(r)) + \bar{\kappa}^2(r)\sinh(u(r)) = \rho(r), \\ u(\infty) = 0, \end{cases} \quad (1)$$

where the variable u defined as

$$u = \frac{e_c\Phi(r)}{k_B T} \quad (2)$$

represents a dimensionless electrostatic potential as $\Phi(r)$ is the electrostatic potential at a field position r, the permittivity $\varepsilon(r)$ takes the values of the appropriate dielectric constants in the different regions of the model, $\bar{\kappa}^2$ is the Debye-Hückel screening parameter relative with the ionic strength of the solution, and the constants e_c, k_B and T represent the electron charge, Boltzmann constant, and the absolute temperature, respectively.

In Eq. (1), the source term can be further expressed as a sum of delta functions,

$$\rho(r) = \frac{4\pi e_c^2}{k_B T}\sum_{i=1}^{N} z_i\delta(r - r_i), \quad (3)$$

where N is the number of molecular charges, z_i is the partial charge of each molecular atom, and r_i represents the position of each atom in the molecule. With the Poisson-Boltzmann equation, a system consists of three parts, a solute, such as a protein molecule, ions, and solvent. The dielectric coefficient ε changes by nearly two orders of magnitude across the interface between the protein molecule and the protein-solvent boundary. The Debye-Hückel screening parameter also jumps from zero to a positive value across the interface between the protein molecule and the protein-solvent boundary. The importance of this equation in biomolecular modeling is well known [18,19]. To model this problem we treat it within a finite domain so that it can be solved numerically.

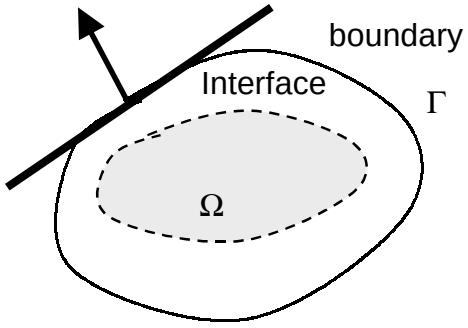

Fig. 1. An illustration for the 3D molecular structure Poisson-Boltzmann problem in a bounded domain.

As shown in Fig. 1, the unbounded domain of Eq. (1) is often truncated into a bounded domain $\Omega\cup\Gamma\subset R^3$, where Ω is an open region and Γ is its boundary. The boundary conditions on Γ are provided by a given analytical expression [17]. The equation in the bounded domain becomes:

$$-\nabla\cdot(\varepsilon\nabla u) + \bar{\kappa}^2\sinh(u) = \rho \quad \text{in} \quad \Omega\subset R^3, \quad (4)$$

and

$$u = g \quad \text{on} \quad \Gamma, \quad (5)$$

where

$$\varepsilon(r) = \begin{cases} 2, \text{inside the molecule} \\ 80, \text{otherwise} \end{cases}, \quad (6)$$

$$\bar{\kappa}^2 = \begin{cases} 0, \text{inside the molecule and interface} \\ 0.8486, \text{otherwise} \end{cases}, \quad (7)$$

and

$$g = \frac{e_c^2}{k_B T \varepsilon(r)} \sum_{i=1}^{N_m} \frac{z_i \exp(-\bar{\kappa}^2 |r - r_i|)}{|r - r_i|}. \quad (8)$$

All above Eqs. (4)-(8) form a 3D nonlinear elliptical PDE and the unknown to be solved is the variable u. We note that the nonlinear term in Eq. (4) is monotone function in u, and it can be further proved that the system has at most one solution. Let the definitions of the spaces $L^2(\Omega)$ and $H^1(\Omega)$ are as usual [21].

Theorem 1 *If the nonlinear terms are estimated with* $L^2(\Omega)$ *functions, then the equation* (4) *has at most one weak solution in* $H^1(\Omega)$.

We proceed with our solution method for the formulated model above. Our approach to the numerical solution of the model consists of the FV and the MI methods. We have utilized this approach successfully for semiconductor devices simulation earlier [1-8].

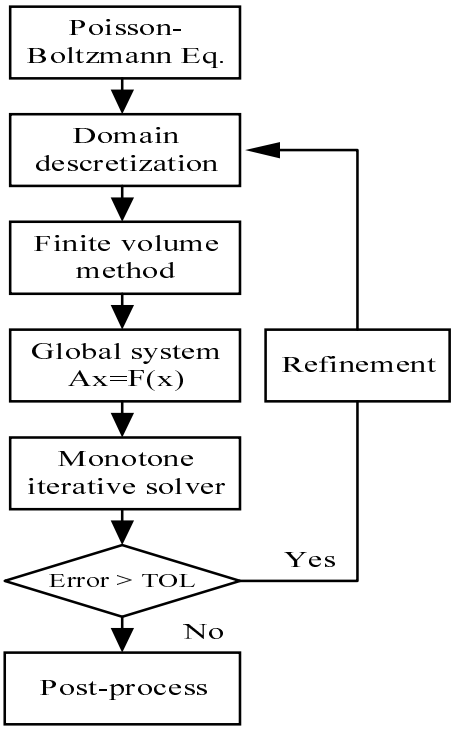

Fig. 2. A computational algorithm for the problem.

3 Computational Techniques

We now introduce our monotone iterative finite volume [1-8,20] and parallel domain decomposition computational algorithms for the numerical solution of the above model introduced in Sec. 2. As shown in Fig. 2, we outline the solution procedure; first of all the model is transformed into the FV weak formulation, the corresponding nonlinear system is solve directly with MI method, if the solution error does not meet the stopping criterion we refine the nonuniform mesh automatically.

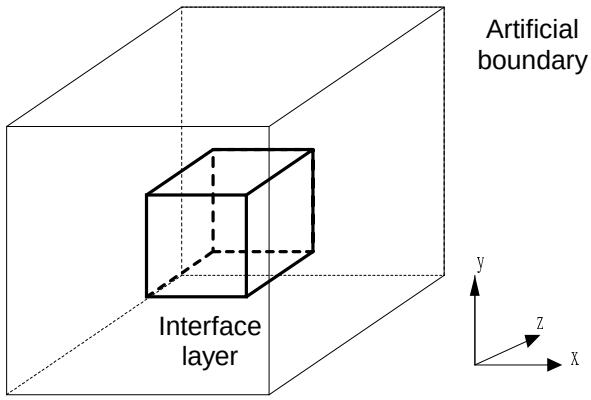

Fig. 3. An illustration of the bounded domain for the molecular structure simulation.

Fig 3 shows the bounded 3D domain for molecular structure Poisson-Boltzmann model simulation. The artificial boundary is taken far away enough so that it does not affect the final solution of the problem. The form of Eq. (1) is sometimes referred to as the strong form. For FV formulation we first choose a test function, multiply the equation by this test function v, and then obtain the weak form as

$$\int_\Omega (-\nabla \cdot (\varepsilon \nabla u) + \bar{\kappa}^2 \sinh(u)) v dr = \int_\Omega \rho(r) v dr . \quad (9)$$

By using divergence theorem (integration by parts), then we can construct the corresponding system of nonlinear algebraic equations:

$$\mathbf{Ax} = \mathbf{-F(x)}, \quad (10)$$

where **F** and **x** are column vectors, **A** is a $n \times n$ matrix, and n is the number of nodes after FV discretization in the simulation domain. The volume integrals in this formulation are approximated with the quadrature rule [20]. The FV method (so-called finite box method) has been one of the standard approaches for discretizing many engineering and science problems that involve interface layers, such as in fluid dynamics and semiconductor device simulation [1-8,20]. It can be shown that the matrix **A** is a symmetric M-matrix. Therefore we have the following theorem for the FV discretized nonlinear Poisson-Boltzmann equation with tensor-product hexahedral elements.

Theorem 2 *The finite volume discretized nonlinear Poisson-Boltzmann equation leads to a system of nonlinear algebraic equations and the equation* (10) *is well-posed.*

We solve the FV discretized nonlinear system by using the MI method. We have successfully applied this solution technique to various semiconductor device simulations earlier [1-8]. The MI algorithm corresponding to the system of nonlinear algebraic equations is

$$(D + \lambda I)\mathbf{x}^{(m+1)} = (L + U)^{(m)} - \mathbf{F}(\mathbf{x}^{(m)}) + \lambda \mathbf{I}\mathbf{x}^{(m)}, \quad (11)$$

where **x** is the unknown vector, **F** is the nonlinear vector form, and D, L, U, and I are diagonal, lower triangular, upper triangular, and identity matrices, respectively. The m is iteration loop index and parameter λ is determined node-by-node depending on 3D structure and nonlinear property of equation. With the similar arguments [2,7], we can prove the solutions of Eq. (11) converge to the solution of Eq. (10) monotonically.

Theorem 3 *Let* $\mathbf{x}^{(0)} = x_n^{(0)}$ *be an arbitrary vector and* $\mathbf{x}^{(m)}$, $m \geq 1$, *be the solution of Eq.* (11). *Let* $\mathbf{x}^* = x_n^{(*)}$ *be the solution of Eq.* (10). *Then* $\mathbf{x}^{(m)} \longrightarrow \mathbf{x}^*$, *as* $m \to \infty$.

Note that the Eq. (11) is of the Jacobi type and hence is highly parallel. Based on constructive convergence property of the MI method, we further propose here a parallel domain decomposition algorithm for 3D Poisson-Boltzmann simulation. As shown in Fig. 4, we perform error estimation for all the computed approximation solutions.

```
For e=1 to (total number of all Cubes)
   If (abs(Error1, Error2, Error3)> tolerance error)
      Cube[e] needs to be refined.
   End If
End For Loop

If (Cube[e] needs to be refined)
   For neighbor_i =1 to 6
      If (the level of Cube[e]>the level of neighbor_i)
         Refine neighbor_i
      End If
   End For Loop
   Divide the Cube[e]
End If
```

Cubic cell in the 3D mesh

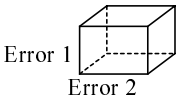

Fig. 4. Error estimation and mesh refinement for 3D molecular structure potential problem.

For more accurate solution, we have to perform the simulation with very fine nonuniform mesh automatically. However the fine mesh leads to a time-consuming simulation. We now state the parallel algorithm for the fast simulation of the model. According to 3D molecular structure, the simulation domain is partitioned into disjoint sub-domains. A geometric dynamic graph partitioning method in x-, y-, or z- direction is applied to partition the total number of nodes and assign those partitioned nodes to each processor. Each partitioned sub-domain is solved with Eq. (11).

The proposed procedure for parallel domain decomposition is as follows:

(p1) initialize the MPI computing environment and the configuration of the necessary parameters;
(p2) based on the nonuniform meshing rule, a tree structure and mesh are established;
(p3) count the number of nodes and applies an *empirical partition algorithm* to determinate how many processors are necessary for the simulation;
(p4) all assigned jobs are solved with Eq. (11) independently;
(p5) all the computed data communicates under the MPI protocol;
(p6) perform error estimation for all elements and run the mesh refinement for those elements having larger errors;
(p7) repeats steps (p3)-(p6) until the error of all elements is less than a specified error bound; and
(p8) host collects all computed results and stops the MPI environment.

Fig. 5 presents a load balancing parallel dynamic partition algorithm that implemented in this parallel domain decomposition above.

```
For (all elements)
   Count number of nodes
End For Loop
Decide optimal number of processors (N) with the node numbers
The number of jobs of each processor (M) = total nodes/N
For ( i = 1 to N )
   Assign M nodes to processor_i
End For Loop
```

Fig. 5. A pseudo code for the dynamic partition.

The constructed Linux-cluster contains 16 PCs in this work (Fig. 6); files access and share are through network file system and network information system. The user datagram protocol controlled by MPI is applied to short distance fast communication.

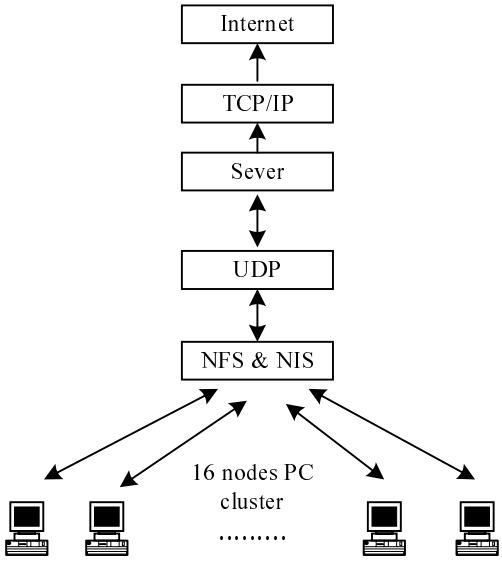

Fig. 6. The constructed 16 nodes PC cluster.

4 Results and Discussion

As shown in Fig. 7, the proposed solution technique for an insulin test example has a good convergence behavior. The initial guess in this simulation example is straightforwardly set to be zero.

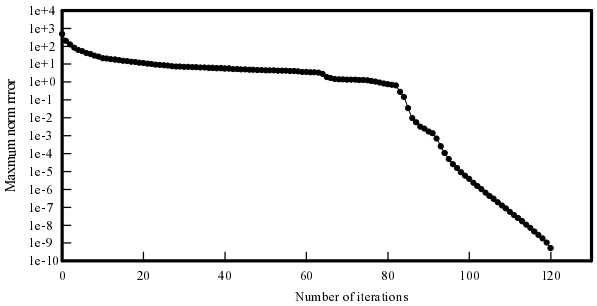

Fig. 7. A plot of the convergence behavior for the numerical solution of the three-dimensional Poisson-Boltzmann model.

The test molecules chosen for our study of the nonlinear Poisson-Boltzmann equation are insulin at 0.1 molar, a medium size molecule and SOD at 0.1 molar, a large enzyme. These related problems, in biophysics community, have been of great interests and received intensive studies, recently. The convergence behavior for the insulin simulation is shown in Fig. 7. It takes about 120 iterations for maximum norm error 10^{-9}. A plot of a cross section (along x = 10) for the simulated 3D structure is illustrated in Fig. 8. The nonuniform hexahedral mesh is applied to simulate this 3D structure.

In addition, for a larger test example, SOD at 0.1 molar, achieved parallel speedup and efficiency are shown in Fig. 9 to demonstrate the parallel performance of the method. In this test, we use very fine nonuniform mesh (400^3) to locate the sharp variation of electrostatic potential near the interface.

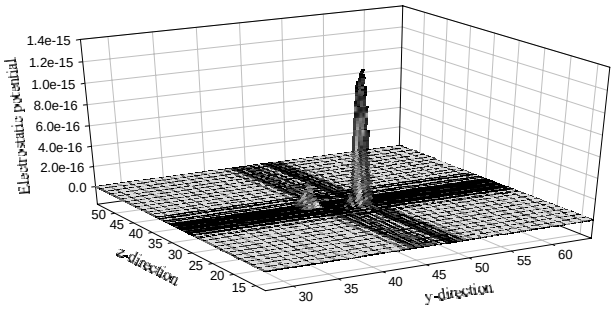

Fig. 8. A cross section plot for the simulated result.

The definition of speedup is the ratio of simulation time on a processor to that on multiple processors. Efficiency equals to speedup divided by number of processors. We found there is 11.8 speedup with respect to 16 processors and the efficiency is about 74% in this test example. The parallel efficiency is less than 80%; based on our simulation experiences, to improve the parallel performance, a faster network connector should be considered in the future work.

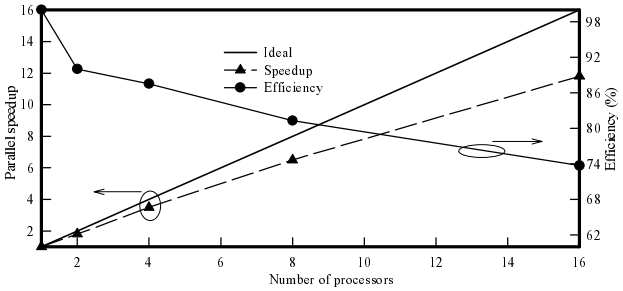

Fig. 9. Speedup and parallel efficiency for the SOD simulation.

5 Conclusion

In this paper, a 3D nonlinear Poisson-Boltzmann equation for biophysical electrostatic potential simulation is formulated and solved numerically. The nonlinear PDE has a weak solution and its corresponding nonlinear algebraic system arising from the finite volume discretized has a unique solution. We solve this finite volume discretized 3D nonlinear Poisson-Boltzmann equation numerically with the proposed parallel monotone iterative method. This computational technique has been successfully implemented on a 16-PC Linux cluster with the MPI library. In our simulation experience, due to the strong nonlinear property of the Poisson-Boltzmann equation, this parallel iterative

solution method converges monotonically and has very good parallel performance. The developed parallel nonlinear Poisson-Boltzmann solver has been tested on a variety of molecular structure problems to show its primary robustness and future applications. Achieved speedup and parallel efficiency also reported to demonstrate its parallel performance.

Acknowledgements

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References:

[1] Y. Li, et al., "A new parallel adaptive finite volume method for the numerical simulation of semiconductor devices," *Comput. Phys. Comm.*, 142, 1-3, 2001, pp. 285-289.

[2] Y. Li, et al., "Monotone Iterative Method for Parallel Numerical Solution of 3D Semiconductor Poisson Equation," in "*Advances in Scientific Computing, Computational Intelligence and Applications*" Edited by N. Mastorakis, et al., WSES Press, 2001, pp. 54-59.

[3] Y. Li, et al., "Parallel Dynamic Load Balancing for Semiconductor Device Simulations on a Linux Cluster," *Technical Proceedings of 4th ACR/IEEE International Conference on Modeling and Simulation of Microsystem* (*MSM 2001*), South Carolina, March 2001, pp. 562-566.

[4] Y. Li, et al., "Adaptive finite volume simulation of semiconductor devices on cluster architecture," in "*Recent Advances in Applied and Theoretical Mathematics*" Ed. by N. Mastorakis, WSES Press, 2000, pp. 107-113.

[5] Y. Li, et al., "A novel approach for the two-dimensional simulation of submicron MOSFET's using monotone iterative method," *Proceedings of IEEE International Symposium of VLSI Technology, Systems, and Applications*, Taipei, June 1999, pp. 27-30.

[6] Y. Li, et al., "Monotone Iterative Method and Adaptive Finite Volume Method for Parallel Numerical Simulation of Submicron MOSFET Devices," in "*Topics in Applied and Theoretical Mathematics and Computer Science*" Ed. by V. V. Kluev, et al., WSEAS Press, 2001, pp. 25-30.

[7] Y. Li, "A Monotone Iterative Method for Semiconductor Device Drift Diffusion Equations," *WSEAS TRANSACTIONS ON SYSTEMS*, Vol. 1, No. 1, Jan. 2002, pp. 68-73.

[8] Y. Li, et al., "A Domain Partition Approach to Parallel Adaptive Simulation of Dynamic Threshold Voltage MOSFET," accepted for publication in *Comput. Phys. Comm.* to appear in 2002.

[9] B. Honig and A. Nicholls, "Classical Electrostatics in Biology and Chemistry," *Science*, 268, 1995, pp. 1144-1149.

[10] A. Neumaier, "Molecular Modeling of Proteins and Mathematical Prediction of Protein Structure," *SIAM Rev.*, 39, 1997, pp. 407-460.

[11] V. K. Misra and David E. Draper, "Mg^{2+} Binding to tRNA Revisited: The Nonlinear Poisson-Boltzmann Model," *J. Mol. Biol.*, 299, 2000, pp. 813-825.

[12] M. J. Kim and Byung Jun Yoon, "Iterative Solution Method for the Linearized Poisson-Boltzmann Equation: Indirect Boundary Integral Equation Approach," *J. Coll. Inter. Sci.*, 236, 2001, pp. 173-179.

[13] M. Holst, N. Baker, and F. Wang, "Adaptive Multilevel Finite Element Solution on the Poisson-Boltzmann Equation II: Algorithms and Examples," *J. Comp. Chem.*, 21, 2000, pp. 1319-1342.

[14] N. Baker, M. Holst, and F. Wang, "Adaptive Multilevel Finite Element Solution on the Poisson-Boltzmann Equation II: Refinement at Solvent Accessible Surfaces in Biomolecular Systems," *J. Comput. Chem.*, 21, 2000, pp. 1343-1352.

[15] P. Debye and E. Hückel, "Zur Theorie der Elektrolyte I.," *Physik. Z.*, 24, 1923, pp.185-206.

[16] M. E. Davis, J. D. Madura, B. A. Luty, and J. A. McCammon, "Electrostatics and Diffusion of Molecules in solution: Simulation with the University of Houston Brownian Dynamics Program," *Comput. Phys. Comm.*, 62, 1990, pp. 187-197.

[17] C. Tanford, *Physical Chemistry of Macromolecules*, John Wiley & Sons, 1961.

[18] J. M. Briggs and J. A. McCammon, "Computation Unravels Mysteries of Molecular Biophysics," *Comput. in Phys.*, 6, 1990, pp. 238-243.

[19] K. A. Sharp and B. Honing, "Electrostatics interactions in macromolecules: Theory and Applications," *Annu. Rev. Biophys. Chem.*, 19, 1990, pp. 301-332.

[20] R. S. Varga, *Matrix Iterative Analysis*, Prentice-Hall, 2000.

[21] R. A. Adams, *Sobolev Spaces*, Academic Press, New Work, 1975.