



Error Analysis of the Poisson P³M Force Field Scheme for Particle-Based Simulations of Biological Systems

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Abstract. The ability to accurately simulate electrolyte solutions is a strong requirement for the modeling of charge transport in ion channels. In this work, a Particle-Particle-Particle-Mesh (P³M) algorithm is used to model the electrostatic interactions governing the physics of electrolyte solutions. The goal of this study is to define the parameters relevant for this force field, and their respective influence on the accuracy of the simulation. Simulations have been performed for extended ranges of these parameters and the results are compared to theoretical models. Finally, the trade-offs between optimal algorithmic efficiency and accuracy are analyzed.

Keywords: force field scheme, simulation of biological systems, Brownian dynamics

1. Introduction

The systems of interest in this work are aqueous electrolyte solutions. The electrostatic landscape of ion channels require the accurate modeling of these solutions at biologically relevant ionic concentrations, usually less than 1 mole per liter. In those cases, the dynamics of the system can be described by a Brownian dynamics (BD) model [1], in which the ion motion is governed by the full Langevin equation [2]. This model accounts for the water implicitly, while the ions are represented as particles and their trajectories are directly computed. Although the BD model is used in this work, the conclusions drawn here also apply to molecular dynamics (MD) simulative approaches.

The simulation technique studied in this work uses a Poisson Particle-Particle-Particle-Mesh (P³M) force

field scheme [3,4] self-consistently coupled with a Brownian dynamics simulation engine [1] using a Verlet-like integration scheme [5] to model the dynamics of electrolyte solutions.

The purpose of this work is to assess the ability of this method to correctly simulate the behavior and properties of ionic solutions. Indeed, the computer simulation of this physical system is based on a discrete subdivision of both time and space that inevitably affects the accuracy of the simulation results.

2. Simulation Methodology

The P³M force field scheme is based on the separation of the Coulomb interaction into two parts representing the long-range and short-range components of the

force. Specifically, the total force acting on an ion i can be expressed as follows:

$$\vec{F}_i = \vec{F}_i^{LR} + \sum_{j \neq i}^{\Omega_i} [\vec{F}_{ij}^{SR} - \vec{R}_{ij}] \quad (1)$$

where Ω_i is a short-range domain which contains all the particles j within a given cutoff radius of ion i .

The long-range part, symbolized by \vec{F}_i^{LR} in Eq. (1), is computed by a 3D finite difference multi-grid Poisson solver in real space [4]. For each particle i , the force due to the long-range contribution is obtained from the electric field computed as the gradient of the electrostatic potential on the grid points. This long-range component of the total force \vec{F}_i includes the influence of all particles in the system, together with the externally imposed boundary conditions. A triangular shaped cloud is used for the charge assignment and force interpolation, as detailed in [5].

The two terms in the sum of Eq. (1) model the short-range part of the interaction. In particular, \vec{F}_{ij}^{SR} denotes the short-range pair force between two particles, while \vec{R}_{ij} is the so called reference force. The pair force between two particles is given by the sum of the Coulombic interaction and the van der Waals interaction, which is represented by a Lennard-Jones [6] force in this work [5]. The reference force \vec{R}_{ij} is required to compensate for the double counting of the effect of the charges in the short-range domain, which would otherwise be accounted for by both the long-range and the short-range force calculation [3].

The discrepancy between the computer representation and the physical system is related to the discrete subdivision scheme adopted by the model. First, the time is discrete in the simulation: all the properties of the ion trajectories (position, velocity, force) are computed at given time intervals and their effects on the dynamics are updated periodically. The proposed simulation scheme uses two different timesteps: (1) the *free-flight timestep* denoted Δt_{ff} and (2) the *Poisson timestep* denoted Δt_{Poiss} . The time interval between two integrations of the motion equation is Δt_{ff} (on the order of femtoseconds) while Δt_{Poiss} (on the order of picoseconds) is the time between two solutions of Poisson's equation on the real-space grid. The only reason why these intervals are different is computer efficiency: since the system evolves slowly, the time-consuming Poisson solver need not to be run as frequently as the Langevin equation computation. The use of adaptive timesteps could further reduce the computation time

by using a finer time subdivision when the ions are close to the singularity of the Coulombic potential [7].

The spatial subdivision is also a source of error. The bulk electrolyte solution is mapped on a cubic 3D box divided into small cubic cells. This set of grid cells, each of size ΔG along each axis, forms a uniform spatial subdivision, and the potential and electric field accounting for the long-range interaction are assumed constant in each cell. ΔG typically ranges about 1 nm.

3. Benchmarks

A crucial property of the ensemble is its average kinetic energy E_K , and the theoretical value used as a benchmark is the thermal energy for monoatomic particles given by $E_K = \frac{3}{2}k_B T$ [8], where k_B is Boltzmann constant and T is the temperature.

Another structural property of the solution is the Radial Distribution Function (RDF), which is a measure of the average ion density around a given ion in the solution. This function denoted here $g_{ij}(r)$ (density of ions j around an ion i), plays a crucial role in the simulation since many measurable thermodynamic properties of the solution can be derived from it [8].

The RDF used as a benchmark in this case is computed as a solution of the Ornstein-Zernike equations [9], using the Hypernetted Chain (HNC) approximation [9] as a closure relation. The numerical solution of these HNC equations is done iteratively [10], and the only input is the pair-interaction potential, in this case the exact same potential used in the simulation.

The analytical RDF curve is then used to set two benchmarks: (1) the *RDF peak value* which is the maximum of the RDF between two ions of different types, and (2) the *osmotic coefficient* ϕ of the solution which is derived from the RDF g_{ij} [9]. Comparing the osmotic coefficient is a good complement to the RDF peak value comparison because it permits to estimate how closely the simulated RDF matches the HNC benchmark over the whole ionic separation range.

4. Simulation Results

This section will detail the simulations performed altering each of the three parameters Δt_{ff} , Δt_{Poiss} and ΔG . The test system consists of a cubic simulation box containing a 0.30 M ionic solution of KCl. The size of this box is 20 nm in each dimension. The temperature is set to 298 K and the relative dielectric

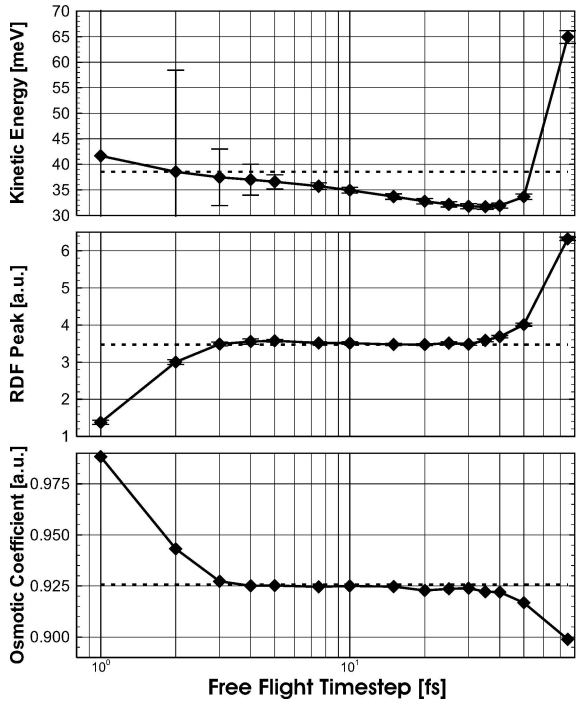


Figure 1. Simulation results for Δt_{ff} ranging between 1 and 75 fs. The dashed lines show the benchmark values.

constant for water is set to 78.0. Two facing sides of the box bear contacts used to apply a bias to the solution to simulate the influence of far, real electrodes. In this work, the voltage bias has been kept null in all cases, since the systems should be in equilibrium to compare the thermodynamics with the HNC results.

The test system has been first simulated for free-flight timesteps Δt_{ff} ranging from 1 to 75 fs. Figure 1 shows the three benchmarks and their evolution for this range of Δt_{ff} values. These results show that over a relatively extended range of Δt_{ff} values (between 3 and 30 fs), the RDF peak and ϕ curves are relatively flat and match the HNC value. Over this range, the kinetic energy is slowly decreasing, but remains within 15% of the theoretical value [5]. When the free-flight is shorter than 3 fs, a significant deviation from the HNC is observed. The fact that the RDF peak decreases is consistent with the increase in the osmotic coefficient ϕ . Conversely, when Δt_{ff} is set above 30 fs, the RDF peak shoots above the HNC results while ϕ starts decreasing. A significant spurious heating is also evident in the population energy.

Simulations for Poisson timesteps ranging from 0.1 to 30 ps have been performed. The results (Fig. 2) show

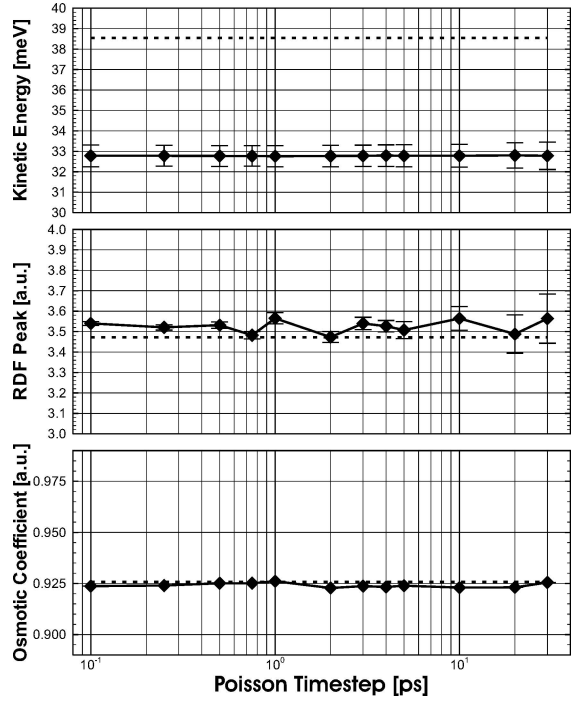


Figure 2. Simulation results for Δt_{Poiss} ranging between 0.1 and 30 ps. The dashed lines show the benchmark values.

little influence of this parameter on the results over the considered range. In particular, the energy remains perfectly stable. The RDF peak shows little error (less than 5% over most of the range) and the osmotic coefficient is within 0.5% of the HNC value.

Finally, the simulation for a range of grid spacing ΔG has been performed for values between 0.30 and 5.0 nm, as can be seen on Fig. 3. Again, the kinetic energy curve is flat and constant over the whole range. The other two benchmarks show a very good agreement with HNC for grid spacings above about 0.7 nm, but depart significantly from it below this value.

5. Discussion

The first breakpoint seen for values of Δt_{ff} above 50 fs is due to a lack of precision in the time evolution of the ion trajectories. The mean time between collisions for the test system at this temperature is about 5 ps, and Δt_{ff} has to be much smaller. However, because of the sharp increase in the force when the distance between ions gets small, an appreciable deviation starts to appear at only 50 fs. Actually, even a small error in the particle position can significantly impact the results.

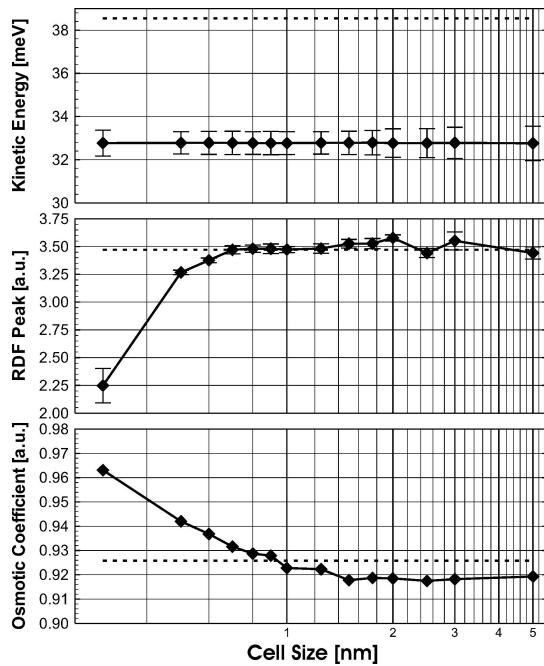


Figure 3. Simulation results for ΔG ranging between 0.30 and 5.0 nm. The dashed lines show the benchmark values.

The second breakpoint appears when Δt_{ff} falls below 3 fs, due to computational instability of the algorithm. Numerical errors (very large error bars in Fig. 1) tend to accumulate rather than cancel when the motion equation is computed too often.

The results for variations of the Poisson timestep show that the three benchmarks are almost constant over the whole range. Since Δt_{ff} for this set of simulations is kept constant at 20 fs, the kinetic energy is consistent with the other set (Fig. 1) and is actually independent of Δt_{Pois} . However, some instability is visible for values of Δt_{Pois} above about 5 ps. These effects are not very pronounced in this homogeneous system, but would be much more important in the case of real ion channel simulations. This can be explained by the fact that the plasma frequency (frequency of collective ion oscillations, [3]) for this system is about 3 ps. This is not exactly applicable to our system since an ionic solution is not fully representable as a plasma, but it gives an estimate for the range of Δt_{Pois} .

The result for the grid spacing sweep shows only one major breakpoint, when the grid size falls below 0.7 nm. The energy is again independent of ΔG and matches the expected value for $\Delta t_{\text{ff}} = 20$ fs. The breakdown in RDF peak and the consistent increase in the osmotic coefficient are the result of several aspects of

the simulation setup: (1) The Debye length [3] (about 0.8 nm in this case) which sets a maximal value for the grid spacing in order to resolve the spatial variations of the charge distribution. (2) Since the simulated solution is very diluted, for a grid spacing of 0.8 nm the number of particles per cell is less than 0.2. The Poisson solver gives very irregular and inaccurate field distributions under these conditions, and the reference force does not fully compensate for it. Using larger values for ΔG improves the accuracy for two reasons: (1) the number of particles per cell is larger and (2) the error becomes less significant in the short-range (RDF, and ϕ are computed only for ion separations up to 2 nm). The osmotic coefficient ϕ stabilizes to a value which is about 0.8% off the benchmark, due to a slight residual discrepancy between the Poisson solution and the reference force.

It is worth noting that the use of smaller timesteps significantly impacts the computer time required to perform the simulations, and a trade-off exists between accuracy and computational cost. We found that for the simulated solutions, values of Δt_{ff} between 20 and 30 fs and Δt_{Pois} around 5 ps are a good compromise. Concerning the grid spacing, decreasing ΔG significantly increases the time needed for the Poisson solver, while an increase overloads the short-range particle-particle force computation. Values in the range of 1 nm for the grid spacing have been found adequate for the studied system.

6. Conclusions

The error analysis of the Poisson P³M force field scheme has been performed for the simulation of biologically relevant ionic solutions. Benchmark models for simulation error measurement have been presented, and the simulation results for the P³M parameters are discussed. Theoretical interpretation and computer efficiency trade-offs have been proposed.

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