A novel Brownian-Dynamics algorithm for the simulation of ion conduction through membrane pores

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BROWNIAN DYNAMICS

Brownian-Dynamics (BD) is a powerful approach for the simulation of ion conduction through membrane pores. BD simulations are much less computational demanding than molecular dynamics simulations, thus allowing analyses on the microsecond time scale. Furthermore, compared to other simplified approaches like Poisson-Nernst-Planck equations, BD preserves the discrete nature of the ionic particles, which is particularly important in narrow pores. For these reasons, BD simulations have been widely used to analyze conduction in membrane proteins or carbon nanotubes, obtaining good agreement with experimental data.
In BD simulations the 3D coordinated of the i-th ion ( ) evolves according to:

$$m_i\ddot{X}_i = -m_i\gamma_i\dot{X}_i + ez_iE + R(t)$$

Where m_i, z_i, γ_i are mass, velocity and friction coefficient of the ion; e is the elementary charge; R(t) is the stochastic force, mimicking the effects of the solvent molecules; and E the electric field, which can be expressed as:

$$E = E_{TRANSMEMBRANE} + E_{FIXED\ CHARGES} + E_{INDUCED\ CHARGES} + E_{ION-ION}$$

While the terms due to transmembrane potential and fixed charges are constant in time, and they can be computed at the beginning of the simulation, the terms due to the ion-ion interactions and to the charges induced at the dielectric surface changes at run-time. The electrostatic potential is calculated by solving the Poisson's equation, and with iterative methods this process is too much time-consuming to be performed at every time-step. Thus, the Poisson equation is usually solved in advance on a pre-defined grid for the different ion configurations, and then, the tabulated values are used to calculate the electric field during the simulation. This process, not only introduces a discretization error, but more important, cylindrical symmetry is usually imposed in order to limit the grid size. To overcome these shortcomings, we implemented an ICC (Induced-Charge-Computation) Poisson solver in a BD simulator. The high efficiency of the ICC solver allows the solution of the Poisson equation at run-time.

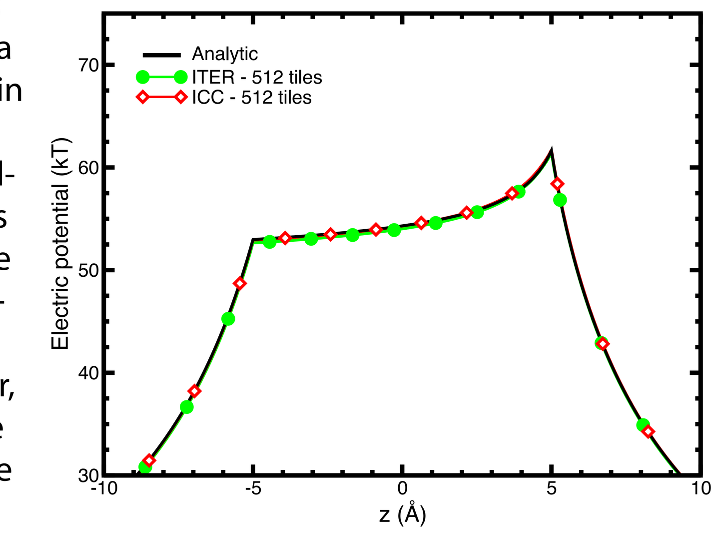
POISSON SOLVER

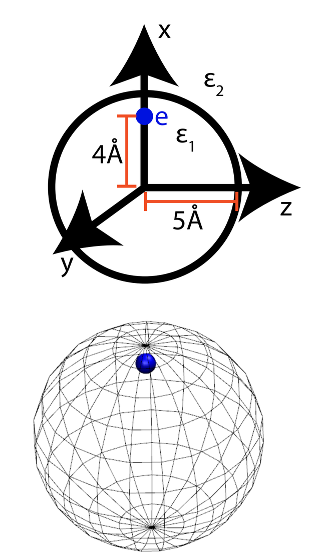
Poisson's equation is the fundamental law that binds the charge density to the spatial distribution of the electrostatic potential.

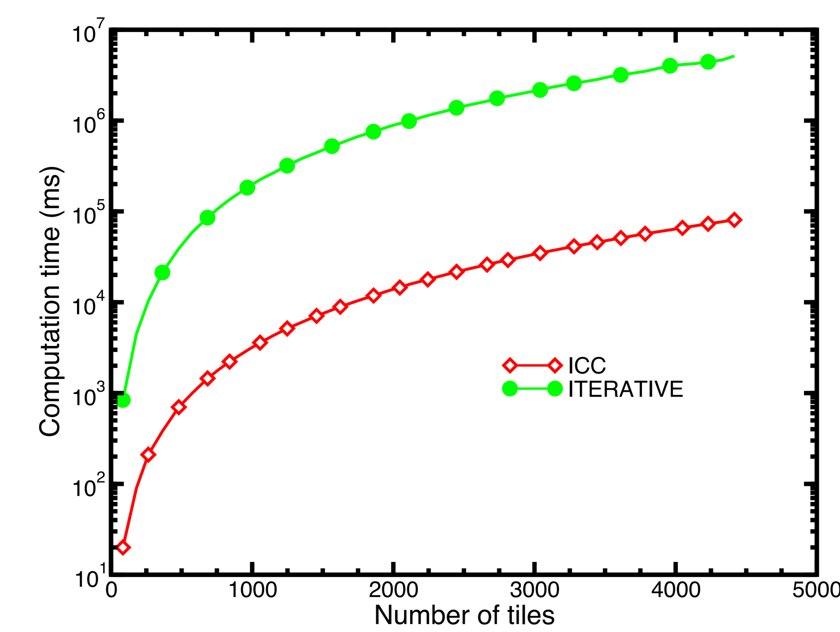
$$-\varepsilon_0\nabla\cdot\left[\varepsilon(r)\nabla\phi(r)\right] = -\rho(r)$$

Where ε_0 is the vacuum permittivity, $\varepsilon(r)$ is the relative permittivity at position r, $\varphi(r)$ is the electrostatic potential, and $\rho(r)$ is the charge density. Induced Charge Computation (ICC) method is a Boundary Element Method (BEM), which can be used to solve the Poisson equation in inhomogeneous dielectric systems. ICC has already been successfully adopted in the Monte Carlo simulation of ion channels.
In BEM, the polarization effects, due to discontinuity in permittivity, are accounted for by adding to the system the polarization charges induced at the boundary surfaces. Within the ICC method, it is not necessary to discretize the whole simulation domain, but only the boundary surfaces. The charges induced on these boundary surfaces are computed by solving a linear system of algebraic equations, obtained directly from the Poisson equation. The solution of Poisson's equation is converted to the solution of the linear equation, Ah=b, where A is a NxN matrix describing the interaction between the surface elements and b is the electric field impinging on each surface element.
Solving for h, the polarization charges induced at the dielectric boundary are found and the electric field in a given point is computed evaluating the Coulomb interactions between all the charges in the systems (source and induced). An analytic description of the boundary surface (tiles), for example with splines, highly improves the accuracy of the solution. Since the dielectric boundary is assumed to be a rigid structure throughout the BD simulation, the matrix A can be computed and inverted just once, at the beginning of the simulation. At run-time, the solution of the Poisson equation requires only the matrix product $A^{-1}b$.

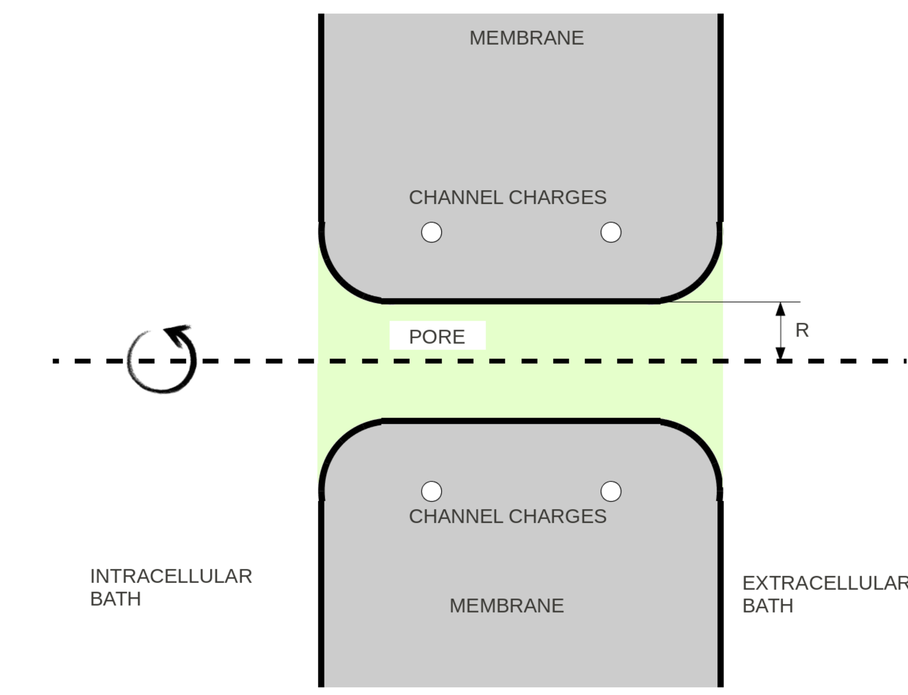
The accuracy of the ICC solver was tested with a known test case, i.e. a high dielectric sphere embedded in a low dielectric space. The sphere, featuring 5 A radius, contains an elementary charge 4 A off-centre. As shown in the figures, both iterative and ICC method can provide accurate solutions, undistinguishable from the analytical curve. However, for a given accuracy threshold, the ICC method is orders of magnitude faster.

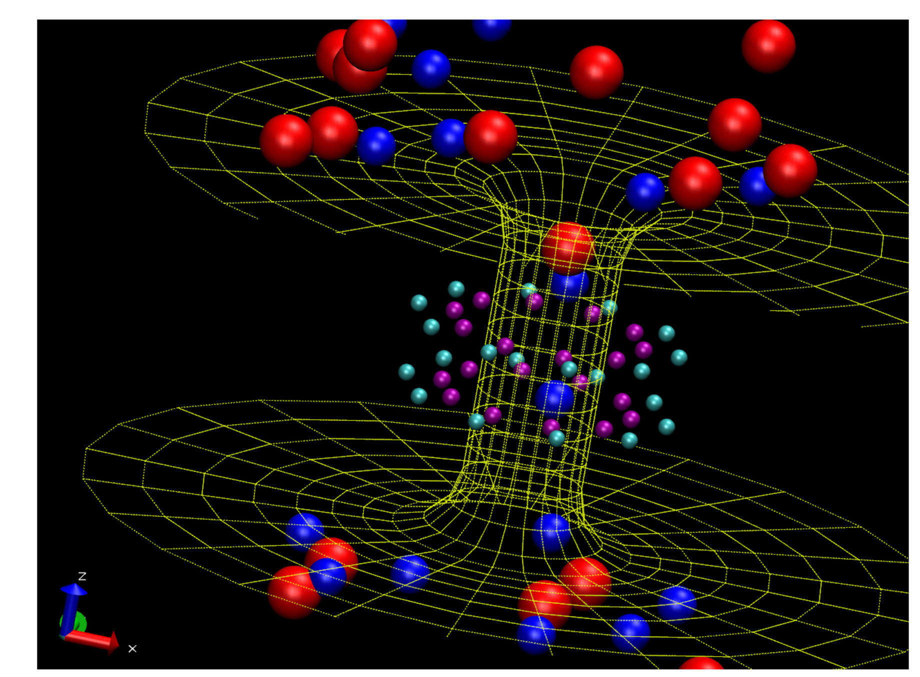






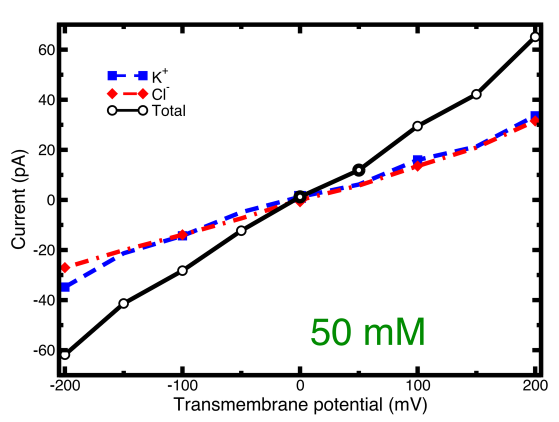
CHANNEL STRUCTURE

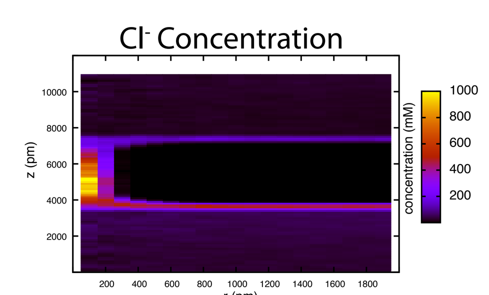


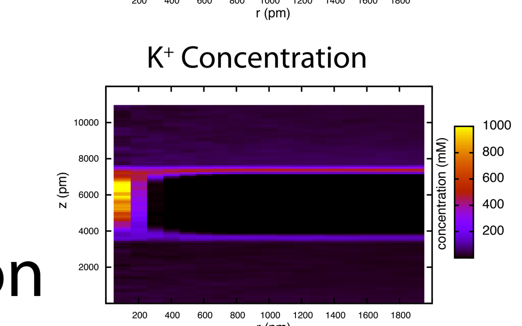


TESTS - UNCHARGED CHANNELS

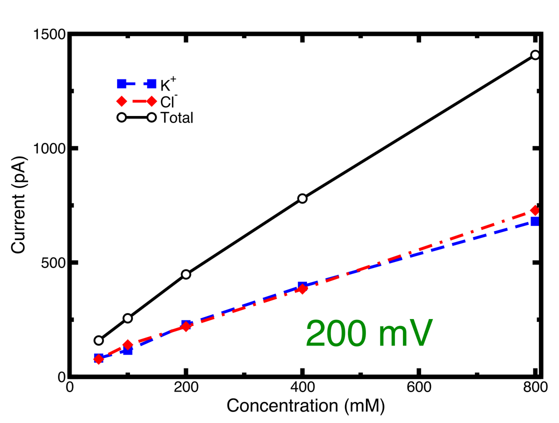
Current-Voltage

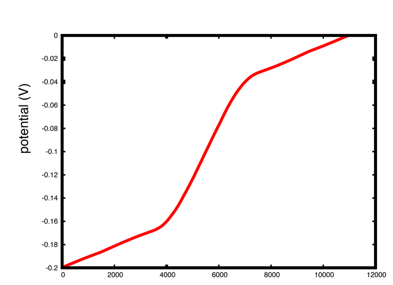


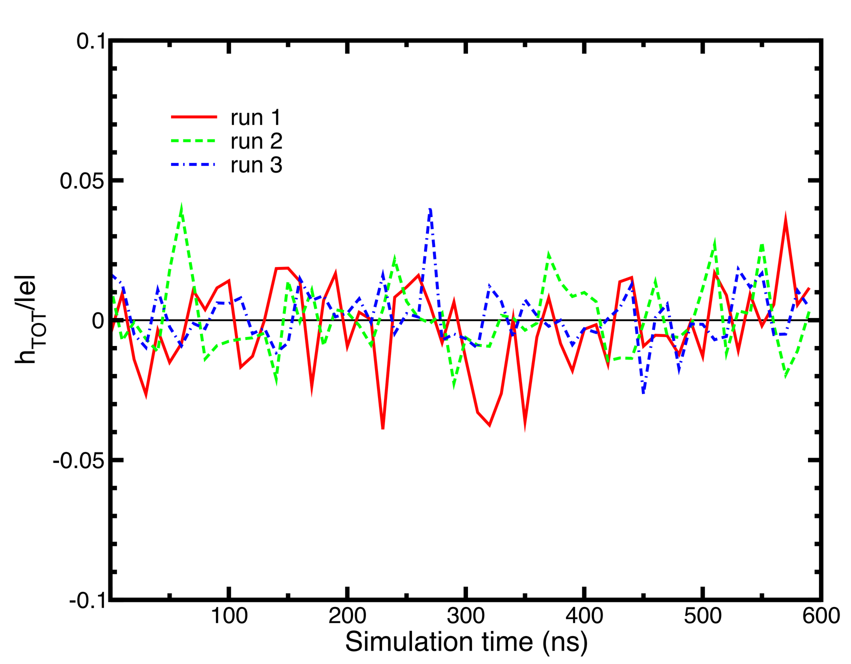




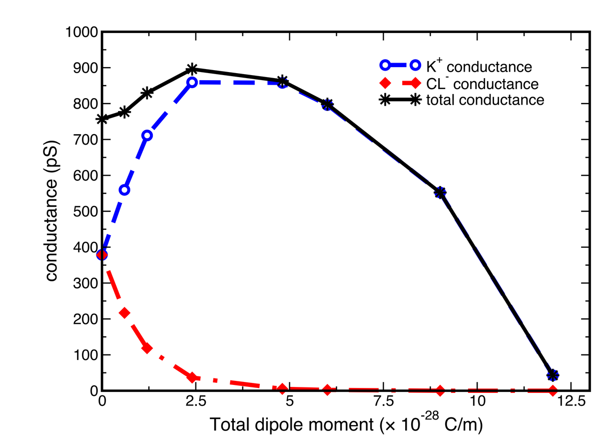
Current-Concentration

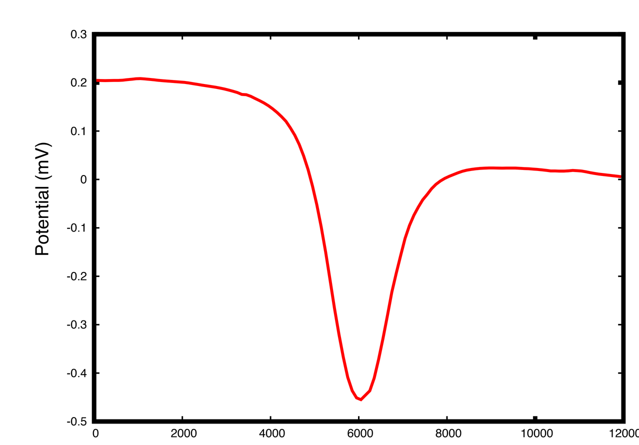


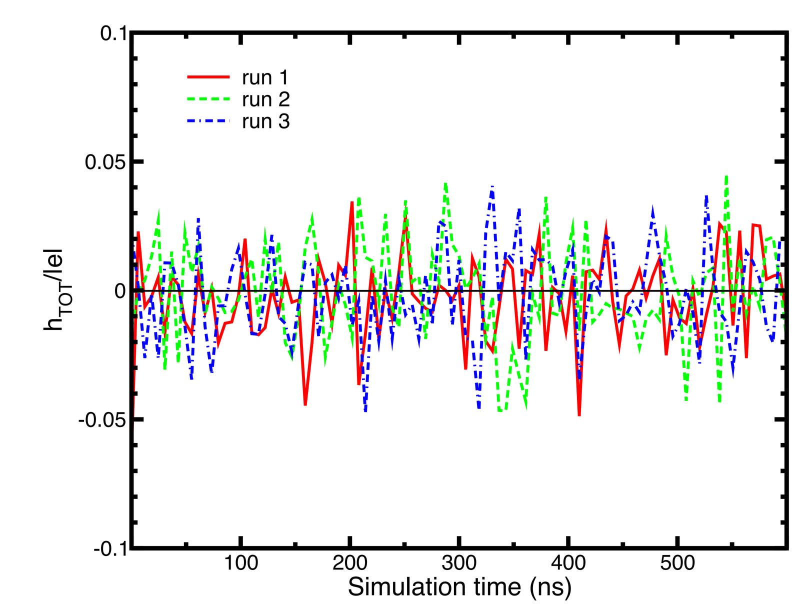




TESTS - CHARGED CHANNELS







CONCLUSIONS