A novel Brownian-Dynamics algorithm for the simulation of ion conduction through membrane pores
Claudio Berti, Dirk Gillespie, Bob Eisenberg, Simone Furini and Claudio Fiegna
ARCES, University of Bologna, Italy

BROWNION 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 coordinate of the i-th ion evolves according to:

\[ m_i \ddot{X}_i = -m_i \gamma_i X_i + c_i E + R(t) \]

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

\[ E = E_{\text{membrane}} + E_{\text{fixed charges}} + E_{\text{induced charges}} + E_{\text{dielectric}} \]

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 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's 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 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-Computing) Poisson solver in a BD simulator. The 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.

\[ \nabla \cdot (\varepsilon \nabla \phi) = -\rho \]

where \( \varepsilon \) is the vacuum permittivity, \( c_i \) is the relative permittivity at position \( c \), \( \phi \) is the electrostatic potential, and \( \rho \) 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: \( Ax = b \), where \( A \) is a \( N \times N \) 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 is given point by point. The Coulomb interactions between all the charges in the system (source and induced) are taken into account.

An analytic description of the boundary surface (tiles), for example with splines, 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 is given point by point. The Coulomb interactions between all the charges in the system (source and induced) are taken into account.

Solving for \( h \), the polarization charges induced at the dielectric boundary are found and the electric field is given point by point. The Coulomb interactions between all the charges in the system (source and induced) are taken into account.

CONCLUSIONS
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 3 Å radius, contains an elementary charge 4 Å 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.

TESTS - UNCHARGED CHANNELS

TESTS - CHARGED CHANNELS

Alma Mater Studiorum - University of Bologna