# Multiscale Quantum Dynamics in Continuum Model and Simulations for Proton Transport

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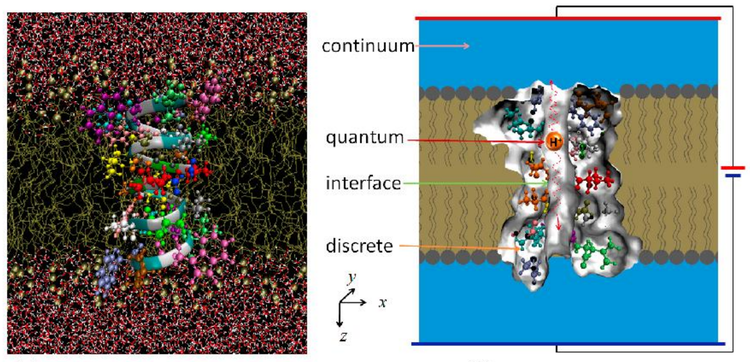
## Proton transport in membrane proteins

Proton transport is of central importance and plays a major role in many biochemical processes, such as cellular respiration, ATP synthase, photosynthesis and denitrification. Proton transport in membrane proteins distinguishes itself from permeation of regular cations through ion channels by special physical properties and translocation mechanism of protons. The objective of present work is to develop a multiscale/multiphysics model and numerical algorithms to study proton transport through membrane proteins.

Figure 1: The Grotthuss mechanism of proton translocation along water molecule chain

Membrane proteins that form water-filled channel pores provide one of the pathways for proton to permeate lipid bilayers. The following graph shows a specific example of channel protein and our general modeling strategy:




(a) Gramicidin A (GA) in membrane (b) Model setup

Figure 2: GA as a channel pore for proton transport and the corresponding simulation setup

The proton is modeled *quantum mechanically* while the rest of the system is treated in a classical sense; atomic details are accounted for the membrane protein but the solvent is modeled implicitly. Solvent and solute regions are separated by the variational solute-solvent interface.

## Model: framework of total free energy functional

The system is described by a total free energy functional:

$$\begin{aligned} G_{\text{Total}}[S,\Phi,n] = & \int \Big\{ \gamma \|\nabla S(\mathbf{r})\| + pS(\mathbf{r}) + \rho_0(1-S(\mathbf{r}))U_{ss} + S(\mathbf{r}) \left[ -\frac{\epsilon_m}{2}|\nabla\Phi|^2 + \Phi\rho_f \right] \\ & + (1-S(\mathbf{r})) \left[ -\frac{\epsilon_s(\mathbf{r})}{2}|\nabla\Phi|^2 + \Phi(\mathbf{r})n(\mathbf{r}) - k_BT\sum_j^{N_c'} n_j^0 \left( e^{-\frac{q_j\Phi - V_{\text{Chem}}^j}{k_BT}} - 1 \right) \right] \\ & + (1-S(\mathbf{r})) \left[ \int \frac{\hbar^2 e^{-(E-E_{\text{ext}})/k_BT}}{2m(\mathbf{r})} |\nabla\Psi_E(\mathbf{r})|^2 dE + U_{\text{GC}}[n] + U_{\text{Exter}}[n] \right] \\ & + (1-S(\mathbf{r}))\lambda \left[ \frac{N_p}{V_\Omega} - \int e^{-(E-E_{\text{ext}})/k_BT} |\Psi_E(\mathbf{r})|^2(\mathbf{r}) dE \right] \Big\} d\mathbf{r}. \end{aligned} \tag{1}$$

which consists of kinetic and potential energies of protons, free energy of other solvent ions and polar/nonpolar system energies on an equal footing. Variables $S(\mathbf{r})$, $\Phi(\mathbf{r})$ are $n(\mathbf{r})$ are the solute-solvent characteristics function, electrostatics and proton number density, respectively.

The proton current is defined as the transmission probability

$$I = q\text{Tr}\frac{1}{2}\left( n_H v^\dagger + v n_H \right) \tag{2}$$

where $v$ and $n_H$ are the velocity and density operators of the proton, respectively.

## Coupled governing equations

- **Generalized Laplace-Beltrami Equation** for solute-solvent characteristics function $S(\mathbf{r})$

$$-\nabla\cdot\left(\gamma\frac{\nabla S}{\|\nabla S\|}\right) - V_{\text{LB}} = 0 \tag{3}$$

- **Generalized Poisson-Boltzmann Equation** gives the electrostatics $\Phi(\mathbf{r})$:

$$-\nabla\cdot(\epsilon(S)\nabla\Phi(\mathbf{r})) - (1-S)\sum_{j=1}^{N_c'} q_j n_j^0 e^{-\frac{q_j\Phi - V_{\text{Chem}}^j}{k_BT}} = (1-S)qn(\mathbf{r}) + S\sum_{i=1}^{N_a} Q_i\delta(\mathbf{r}-\mathbf{r}_i) \tag{4}$$

- **Generalized Kohn-Sham equation** describes the proton distribution:

$$H\Psi_E(\mathbf{r}) = -\nabla\cdot\frac{\hbar^2}{2m(\mathbf{r})}\nabla\Psi_E(\mathbf{r}) + V(\mathbf{r})\Psi_E(\mathbf{r}) = E\Psi_E(\mathbf{r}) \tag{5}$$

- **The Self-consistent system:** Equations (3), (4) and (5) are coupled together by relations:

$$V_{\text{LB}} = \mathscr{F}(\Phi(\mathbf{r}), \Psi_E(\mathbf{r})) \tag{6}$$

$$n(\mathbf{r}) = <\mathbf{r}|e^{-(H-E_{\text{ext}})/k_BT}|\mathbf{r}> = \sum_E |\Psi_E(\mathbf{r})|^2 e^{-(E-E_{\text{ext}})/k_BT} \tag{7}$$

$$V(\mathbf{r}) = q\Phi(\mathbf{r}) + V_{\text{GC}}[n] + V_{\text{Exter}}(\mathbf{r}) \tag{8}$$

## Surface driven dynamical iteration

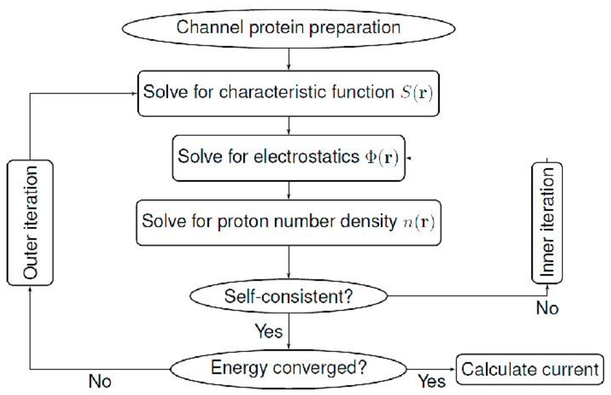



Figure 3: Flowchart of iteration that solves Eqs. (3), (4) and (5)

## Conclusion

A general multiscale quantum dynamics in continuum model is proposed to simulate the protons transport. Several associated numerical schemes are employed to solve the model numerically with high accuracy and efficiency. The validity of this model is tested through the Gramicidin A, by studying solute-solvent surface generation, channel electrostatic profile and proton conductance.

## References

- 1. Duan Chen and Guo-Wei Wei, Quantum dynamics in continuum for proton transport I: Basic formulation, submitted;
- 2. Duan Chen, Zhan Chen and Guo-Wei Wei, Quantum dynamics in continuum for proton transport II: Variational solvent-solute interface, submitted.

## Acknowledgement

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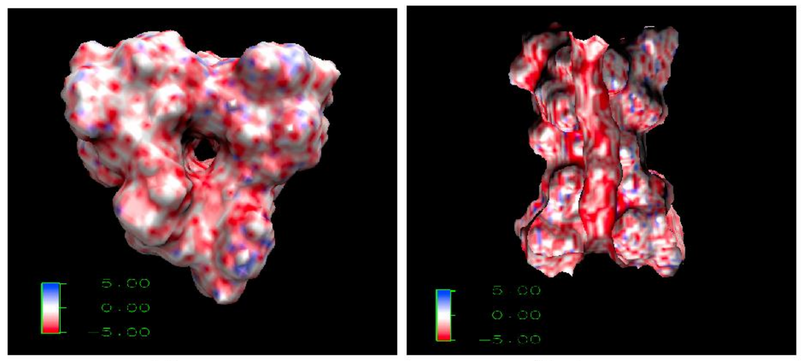
## Simulation Results

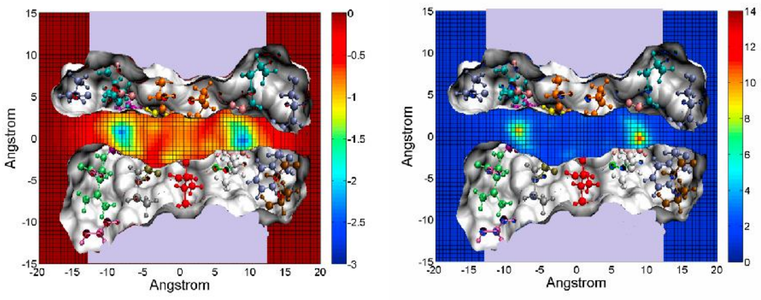
Model and algorithms are validated through a specific channel protein, the Gramicidin A (PDB code: 1MAG). The variational solvent-solute interface (VSI), solution of Eq. (3), is visualized in the following two graphs with a proper surface isovalue. The intensive red color represents the negative electrostatics, which indicates the selectivity of the GA to monovalent cations.



(a) Top view (b) Channel view

Figure 4: Visualization of the GA solute-solvent interface with surface electrostatics

The solution of Eq. (4) and the corresponding density of monovalent cations by the Boltzmann distribution are displayed in the next two graphs. The quantities are presented in the middle cross-section of the *xy* confined direction.




(a) Electrostatics (b) Cation density

Figure 5: Electrostatics and cation density profile in the GA channel

Equation (5) is solved for the proton density quantum mechanically and formula (2) is utilized to calculate the proton current. The proton conductance of GA channel is then simulated and compared with corresponding experimental data

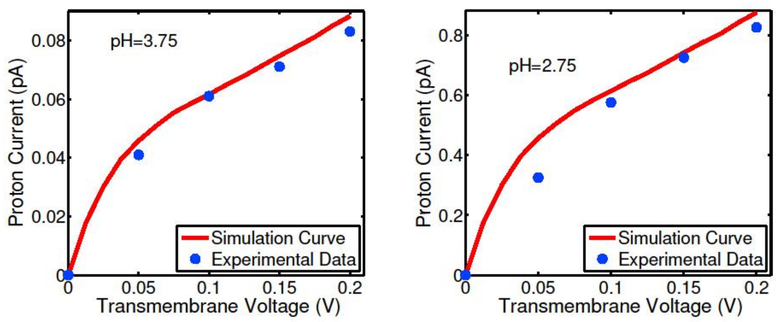



Figure 6: simulation-experiment comparisons of the current-voltage (I-V) curves. All experimental data are from G. Eiseman et al., 1980, *Ann. N.Y. Acad. Sci.*, 339:8-20, 1980

Parameters in the simulation are all taken in the biological and physiological range.

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