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Quantum Dynamics in Continuum for Proton Transport I: Basic Formulation

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Abstract. Proton transport is one of the most important and interesting phenomena in living cells. The present work proposes a multiscale/multiphysics model for the understanding of the molecular mechanism of proton transport in transmembrane proteins. We describe proton dynamics quantum mechanically via a density functional approach while implicitly model other solvent ions as a dielectric continuum to reduce the number of degrees of freedom. The densities of all other ions in the solvent are assumed to obey the Boltzmann distribution. The impact of protein molecular structure and its charge polarization on the proton transport is considered explicitly at the atomic level. We formulate a total free energy functional to put proton kinetic and potential energies as well as electrostatic energy of all ions on an equal footing. The variational principle is employed to derive nonlinear governing equations for the proton transport system. Generalized Poisson-Boltzmann equation and Kohn-Sham equation are obtained from the variational framework. Theoretical formulations for the proton density and proton conductance are constructed based on fundamental principles. The molecular surface of the channel protein is utilized to split the discrete protein domain and the continuum solvent domain, and facilitate the multiscale discrete/continuum/quantum descriptions. A number of mathematical algorithms, including the Dirichlet to Neumann mapping, matched interface and boundary method, Gummel iteration, and Krylov space techniques are utilized to implement the proposed model in a computationally efficient manner. The Gramicidin A (GA) channel is used to demonstrate the performance of the proposed proton transport model and validate the efficiency of proposed mathematical algorithms. The electrostatic characteristics of the GA channel is analyzed with a wide range of model parameters. The proton conductances are studied over a number of applied voltages and reference concentrations. A comparison with experimental data verifies the present model predictions and validates the proposed model.

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1 Introduction

Proton transport is of central importance and plays a major role in many biochemical processes, such as cellular respiration, ATP synthase, photosynthesis and denitrification [28]. Energy transduction in a bioenergetic system requires the generation of large proton concentration gradients. For example, the chemical energy is stored as proton gradient that drives the ATP generation in mitochondria. For plants, sunlight energy is transduced into a proton gradient to create ATP in chloroplasts [20]. Another important function of voltage-gated proton channels occur in phagocytes, such as human neutrophils, during the respiratory burst process. The proton efflux through the proton channels balances the electron movement generated by the NADPH oxidase and assists the production of extracellular reactive oxygen species that kill bacteria. However, main mechanism of proton transport is not fully understood yet [42], with the belief that the proton has distinguished properties from those of other cations and has significantly different conductivity. The motion of regular ions in solvent is usually described as diffusion, while the proton is interchangeable with protons that form water molecules, then it may translocate through a succession of hops in the hydrogen-bond network as indicated by the Grotthuss theory [33]. The proton has the lightest mass among all ions and an effective radius that is at least 10^5 smaller than other ions because the H^+ has no electron [20]. The light mass and tiny size greatly facilitate proton transfer reaction and electrostatic interactions with surrounding molecules [32]. Due to these unique physical properties, the mobility of protons in bulk solution is about fivefold higher than that of other cations [2]. The proton permeation across the membrane is also quite different. Regular ions are prohibited to permeate the membrane because of the huge energy barrier formed by the bilayer. They can only transport through the membrane with the assistance of ion channels, which form water pores and guide ions by diffusion and electrostatic potentials.

Transport pathways of proton across the membrane can have various mechanisms. Protons can achieve the translocation by means of hydrogen-bonded chain (HBC) [22], which may consist not only water molecules, but also side groups of amino acids capable of forming hydrogen bonds. In this sense, proton can transport through the membrane when the row of water molecules is not continuous, since the HBC can be connected by the one from side chains of amino acids of membrane proteins. Moreover, proton may permeate phospholipid membrane even when membrane proteins are absent. For example, a chain of water molecules could happen to line up across the membrane due to thermal fluctuations [23] and provide the HBC to conduct protons. Naturally, protons can transport in water-filled channel pores as well, such as the Gramicidin A (GA) and other "normal" cation-selective channels. However, transport motion of protons in the narrow channel pore is quite different from that in the bulk solvent. Since the length