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Permanent Charge Effects on Ionic Flow: A Numerical Study of Flux Ratios and Their Bifurcation

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Abstract. Ionic flow carries electrical signals for cells to communicate with each other. The permanent charge of an ion channel is a crucial protein structure for flow properties while boundary conditions play a role of the driving force. Their effects on flow properties have been analyzed via a quasi-one-dimensional Poisson-Nernst-Planck model for small and relatively large permanent charges. The analytical studies have led to the introduction of flux ratios that reflect permanent charge effects and have a universal property. The studies also show that the flux ratios have different behaviors for small and large permanent charges. However, the existing analytical techniques can reveal neither behaviors of flux ratios nor transitions between small and large permanent charges. In this work we present a numerical investigation on flux ratios to bridge between small and large permanent charges. Numerical results verify the analytical predictions for the two extremal regions. More significantly, emergence of nontrivial behaviors is detected as the permanent charge varies from small to large. In particular, saddle-node bifurcations of flux ratios are revealed, showing rich phenomena of permanent charge effects by the power of combining analytical and numerical techniques. An adaptive moving mesh finite element method is used in the numerical studies.

AMS subject classifications: 65L10, 65L50, 92C35

Key words: Ion channel, permanent charge, flux ratio, bifurcation, finite element method.

1 Introduction

Ion channels are large proteins embedded in membranes of cells. They serve as a major way for cells to communicate and interact with each other and with the outside world. Ion channels may open and close depending on transmembrane voltage, pressure, light, etc. The movement of ions through channels produces electrical signals that control many biological functions. Two key structures of an ion channel are its shape and permanent charge. An ion channel has a varying cross-section area along its longitudinal

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axis and, typically, has a relatively short and narrow neck where the permanent charge is distributed. While the structures are crucial, it is the properties of ionic flows that are the main interest on ion channels. An equally important but sometimes overlooked factor is the boundary conditions – ion concentrations and electric potential on the sides of the ion channel. Their interactions with the channel structures determine specifics of ionic movement. The ultimate goal of ion channel studies is to understand the correspondence from the channel structures and boundary conditions to ionic flow properties. This is a challenging task due to the multi-scale and multi-parameter nature of the problem as well as the fact that present experimental techniques are unable to measure or observe internal (within the channel) behavior of ionic flows. Although it has been known experimentally that ionic flows exhibit extremely rich phenomena, there still lacks so far a good set of mathematical characteristics for ionic flow properties, and thus studies of ion channel problems based on simple models have been playing a unique role in identifying critical characteristics and separatrices among distinct behaviors.

The movement of ion species through membrane channels is affected by multiple physical quantities that interact with each other nonlinearly and non-locally. The basic models for electrodiffusion are self-consistent Poisson-Nernst-Planck (PNP) type models. Those models consider open stage of channels and treat the medium implicitly as dielectric continuum. They are not direct limits of molecular dynamic models as the number of ions approaches infinite. They miss details of motions of individual ions but capture thermodynamic quantities of the ionic flow such as fluxes, pressure, and energy. PNP systems can be viewed as the Fokker-Planck systems of molecular dynamic models [31] coupled with the Poisson equation for the drift (electric field) that is a part of unknown state variables, and they can also be derived from Boltzmann equations [3] or energetic variational principles [19, 20].

Rigorous analysis has the advantage to discover important properties of biological interest and provides detailed classifications of distinct behaviors over different physical domains, in limiting or ideal setups. Numerical simulation has the power to extend the analytical discovery to realistic parameter ranges of physical problems, and often, discover further phenomena along the continuation. This is the methodology of this work. We consider here open channels with fixed shape and permanent charge distribution and combine the advantages of analysis and numerics to examine the effects of permanent charges on individual fluxes. More precisely, previous analysis based on PNP has revealed a number of interesting, some counterintuitive, phenomena of permanent charge effects for small and large permanent charges [23, 36]. For channels with permanent charge density that is small relative to the characteristic concentrations, it has been widely known that the current is increasing with respect to the transmembrane electric potential. The saturation effect due to large permanent charge density has also been established recently [36]. It is still unclear how the flux of each species is influenced by the electrochemical potential interacting with the permanent charge. It seems intuitive that the permanent charge always promotes the fluxes of counter-ion species (those with opposite charge signs as the permanent charge), and reduces the fluxes of co-ion species