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Flux Ratios for Effects of Permanent Charges on Ionic Flows with Three Ion Species: Case Study (II)

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Abstract. In this paper, we study effects of permanent charges on ion flows through membrane channels via a quasi-one-dimensional classical Poisson-Nernst-Planck system. This system includes three ion species, two cations with different valences and one anion, and permanent charges with a simple structure, zeros at the two end regions and a constant over the middle region. For small permanent charges, our main goal is to analyze the effects of permanent charges on ionic flows, interacting with the boundary conditions and channel structure. Continuing from a previous work, we investigate the problem for a new case toward a more comprehensive understanding about effects of permanent charges on ionic fluxes.

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Key words: Ionic flows, permanent charges, flux ratios.

1 Introduction

Electrodiffusion exhibits rich phenomena and plays a central role for many applications [7,11,12,14,29,30,34]. Ionic flow through ion channels is one of critical topics of physiology. Ion channels are large proteins embedded in cell membranes that provide pathways for electrodiffusion of ions (mainly Na^+, K^+, Ca^{2+} and Cl^-) between inside and outside of cells [21–25,52,60]. Thus, ion channels permit permeation and selectivity, and produce electric signals for cells to communicate with each other.

Ion channels are defined by their structural characteristics, channel shapes and permanent charge distributions, which are responsible for biological functions of ion channels. The shape of a typical channel could be approximated as a cylindrical-like domain,

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with a non-uniform cross-section area. Within an ion channel, amino acid side chains are distributed mainly over a relatively ¡°short¡± and ¡°narrow¡± portion of the channel, with acidic side chains contributing negative charges and basic side chains contributing positive charges. Permanent charges play a major role for controlling ionic flow properties, interacting with other important physical parameters, such as boundary concentrations, boundary potential and ion valences of ionic mixtures [1, 13, 15, 16, 31, 39, 40, 51, 54, 55, 62, 65, 66].

Due to the limitation of present experimental techniques, the most basic functions of ion channels such as permeation and selectivity are mainly extracted from the I-V relation measured experimentally (see, e.g., [4, 6, 9]). The I-V relation defines a functional response of the channel structure and boundary conditions (see display (1.7)) and is an input-output type information of an average effect of the full dynamics of ionic flows. Individual ionic fluxes carry more information than the I-V relation, but it is expensive and challenging to measure them [26, 31, 59]. A point is that it is still not possible to "measure/observe" internal dynamical behaviors of ionic flows, which makes it difficult to understand ion channel properties from experimental data due to extremely rich phenomena that can be created by the multi-scale feature and the nonlinear interplay among those physical parameters.

Mathematical modelings, analyses and numerical simulations of ion channel problems provide an alternative and complementary approach for explaining observed biological phenomena and discovering new ones. Poisson-Nernst-Planck (PNP) systems serve as basic primitive models for ionic flows through ion channels (see, e.g., [2, 3, 15, 18, 28–30, 34, 37, 38, 51, 62]). There have been a great deal successes in analyzing PNP models (see, e.g., [1–4, 17, 27, 28, 43, 45, 46, 48, 57, 61, 65, 66]), particularly, those by geometric singular perturbation (GSP) theory (see, e.g., [10, 16, 17, 31–33, 36, 39–42, 44–46, 56, 64–66]), which makes it possible to explain some effects of different parameters on the physical properties.

For ionic flows involving two ion species (one cation and one anion), effects of permanent charges have been extensively examined and important phenomena, some counter-intuitive, were revealed [27, 33, 41, 65, 66]. In terms of flux ratios introduced in [41], major findings for flows of two ion species are as follows. Depending on boundary conditions, a positive permanent charge can enhance the anion flux while inhibiting that of cation, can enhance the fluxes of both anion and cation, can inhibit the fluxes of both anion and cation, but, cannot enhance the cation flux while inhibiting that of cation; and, independent of boundary conditions, a positive permanent charge always helps the flux of anion more than that of cation.

Recently there are several works on ionic flows with three ion species, two cation species with the same valence and one anion species, and some interesting results are obtained on competition of the two cations (see, e.g., [5, 63, 67]). These results on competition of the two cations are obtained with measurements that are different from flux ratios. However, for three ion species of different valences, the analysis on PNP system is very limited. In [57], the authors started to examine effects of small permanent charges