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Small Permanent Charge Effects on Individual Fluxes via Poisson–Nernst–Planck Models with Multiple Cations

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Abstract

A quasi-one-dimensional Poisson–Nernst–Planck system for ionic flow through a membrane channel is studied. Nonzero but small permanent charge, the major structural quantity of an ion channel, is included in the model. The system includes three ion species, two cations with the same valences and one anion, which provides more correlations/interactions between ions compared to the case included only two oppositely charged particles. The cross-section area of the channel is included in the system, which provides certain information of the geometry of the three-dimensional channel. This is crucial for our analysis. Under the framework of geometric singular perturbation theory, more importantly, the specific structure of the model, the existence and local uniqueness of solutions to the system for small permanent charges is established. Furthermore, treating the permanent charge as a small parameter, through regular perturbation analysis, we are able to derive approximations of the individual fluxes explicitly, and this allows us to examine the small permanent charge effects on ionic flows in detail. Of particular interest is the competition between two cations, which is related to the selectivity phenomena of ion channels. Critical potentials are identified and their roles in characterizing ionic flow properties are studied. Some critical potentials can be estimated experimentally, and this provides an efficient way to

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adjust/control boundary conditions (electric potential and concentrations) to observe distinct qualitative properties of ionic flows. Mathematical analysis further indicates that to optimize the effect of permanent charges, a short and narrow filter, within which the permanent charge is confined, is expected, which is consistent with the typical structure of an ion channel.

Keywords GSPT for PNP · Permanent charges · Channel geometry · Individual fluxes · Electroneutrality conditions

Mathematics Subject Classification 34A26 · 34B16 · 34D15 · 37D10 · 92C35

1 Introduction

Ion channels are large proteins embedded in cell membranes which create openings in the membrane to allow cells to communicate with each other and with the outside to transform signals and to conduct tasks together (Boda et al. 2007; Eisenberg 2011). Ion channels permit the selective passage of charged particles formed from dissolved salts, such as sodium, potassium, calcium and chloride particles which carry electrical current in and out of the cell. The study of ion channels consists of two related major topics: structures of ion channels and ionic flow properties.

The physical structure of ion channels is defined by the channel shape and the spacial distribution of permanent and polarization charge. The shape of a typical ion channel is often approximated as a cylindrical-like domain with a non-uniform cross-section area. Within a large class of ion channels, amino acid side chains are distributed mainly over a "short" and "narrow" portion of the channel, with acidic side chains contributing permanent negative charges and basic side chains contributing permanent positive charges, which is analogous to the doping of semiconductor devices, e.g., bipolar PNP and NPN transistors.

With a given structure of an open channel, the main interest is to understand its electrodiffusion property. Mathematical analysis plays important and unique roles for generalizing and understanding the principles that allow control of electrodiffusion, explaining mechanics of observed biological phenomena and for discovering new ones, assuming a more or less explicit solution of the associated mathematical model can be obtained. However, in general, the latter is too much to expect. Recently, there have been some successes in mathematical analysis of Poisson–Nernst–Planck (PNP) models for ionic flows through membrane channels (Bates et al. 2020, 2017; Eisenberg and Liu 2007; Eisenberg et al. 2015; Ji et al. 2019, 2015; Lin et al. 2013; Liu 2005, 2009; Liu and Xu 2015; Park and Jerome 1997; Wen et al. 2021).

One of the fundamental concerns of physiology is the function of ion channels. The most basic function of ion channels is to regulate the permeability of membranes for a given species of ions and to select the types of ions and to facilitate and modulate the diffusion of ions across cell membrane. Currently, these permeation and selectivity properties of ion channels, actually the most two relevant properties of ion channels, are usually determined from the current–voltage (I–V) relations measured under differing experimental conditions (Eisenberg 2011; Gillespie 2008). The I–V relations define the function of the channel structure, that is, the ionic transport through ion channel, which is governed by fundamental physical laws of electrodiffusion that relate rates of quantities of interest. *However, in terms of applications, it is important to study properties of individual fluxes because most experiments (with some exceptions) can only measure the total current while individual fluxes contain much more information on channel functions* (Hodgkin and Keynes 1955; Ji et al. 2019). The macroscopic properties of ionic flows through ion channels rely further on external driving forces expressed mathematically as boundary conditions (Bates et al. 2017).

In this work, focusing on basic understandings of possible effects of small permanent charges and channel geometry, as a starting point, we will study the qualitative properties of ionic flows through membrane channels via a classical PNP model with multiple cations, a piecewise constant permanent charge (small) and a cylindrical-like channel with variable cross-sectional area. *Of particular interest is permanent charge and channel geometry effects on the individual fluxes, which can be mathematically extracted from solutions of the PNP system; and the competition between cations due to complicated nonlinear interplays among system parameters, which is related to the selectivity phenomena of ion channels*.

1.1 Poisson–Nernst–Planck Models for Ionic Flows

Considering the structural characteristics, the basic continuum model for ionic flows is the Poisson–Nernst–Planck system, which treats the aqueous medium as a dielectric continuum (Eisenberg 2003a, b, 1990, 1996; Gillespie and Eisenberg 2002; Gillespie et al. 2003; Im and Roux 2002; Roux et al. 2004 etc.). The PNP system can be derived as a reduced model from molecular dynamics (Schuss et al. 2001), from Boltzmann equations (Barcilon 1992), and from variational principles (Hyon et al. 2010, 2012, ?). More sophisticated models (Biesheuvel 2011; Chen et al. 1995; Eisenberg et al. 2010; Fair and Osterle 1971; Gross and Osterle 1968; Sasidhar and Ruckenstein 1981; Wei 2010; Wei et al. 2012) have also been developed which can model the physical problem more accurately, however, it is very challenging to examine their dynamics analytically and even computationally. Considering the key feature of the biological system, the PNP system represents an appropriate model for both analysis and numerical simulations of ionic flows.

The simplest PNP system is the *classical* Poisson–Nernst–Planck (cPNP) system that includes the ideal component $\mu_k^{id}(X)$ in (1.4) only. The ideal component μ_k^{id} contains contributions by considering ion particles as point charges and ignoring the ion-to-ion interaction. It has been shown by some numerical studies that classical PNP models provide good qualitative agreement with experimental data for I–V relations (Barcilon 1992; Barcilon et al. 1992). The classical PNP models have been simulated and analyzed extensively (see, e.g., Abaid et al. 2008; Barcilon 1992; Barcilon et al. 1992, 1997; Eisenberg et al. 2015; Lee et al. 2011; Liu and Wang 2010; Liu and Xu 2015; Park and Jerome 1997; Singer and Norbury 2009; Singer et al. 2008; Wang et al. 2014; Zhang 2015, 2018).

For ionic solutions with n ion species, the PNP system reads

$$\begin{aligned}&\nabla\cdot\Big(\varepsilon_r(\mathbf{r})\varepsilon_0\nabla\Phi\Big)=-e\Big(\sum_{s=1}^{n}z_sC_s+\mathcal{Q}(\mathbf{r})\Big),\\&\nabla\cdot\mathcal{J}_k=0,\quad -\mathcal{J}_k=\frac{1}{k_BT}\mathcal{D}_k(\mathbf{r})C_k\nabla\mu_k,\quad k=1,2,\ldots,n,\end{aligned}\tag{1.1}$$

where $\mathbf{r}\in\Omega$ with Ω being a three-dimensional cylindrical-like domain representing the channel, $\mathcal{Q}(\mathbf{r})$ is the permanent charge density, $\varepsilon_r(\mathbf{r})$ is the relative dielectric coefficient, ε_0 is the vacuum permittivity, e is the elementary charge, k_B is the Boltzmann constant, T is the absolute temperature; Φ is the electric potential. Also, for the kth ion species, C_k is the concentration, z_k is the valence, μ_k is the electrochemical potential depending on Φ and $\{C_j\}$, $\mathcal{J}_k$ is the flux density, and $\mathcal{D}_k(\mathbf{r})$ is the diffusion coefficient.

Based on the fact that ion channels have narrow cross-sections relative to their lengths, reduction of the three-dimensional steady-state PNP systems (1.1) to a quasi-one-dimensional models was first proposed in Nonner and Eisenberg (1998) and was rigorously justified in Liu and Wang (2010) for special cases. A quasi-one-dimensional steady-state PNP model takes the form

$$\begin{aligned}&\frac{1}{A(X)}\frac{\mathrm{d}}{\mathrm{d}X}\Big(\varepsilon_r(X)\varepsilon_0A(X)\frac{\mathrm{d}\Phi}{\mathrm{d}X}\Big)=-e\Big(\sum_{s=1}^{n}z_sC_s+Q(X)\Big),\\&\frac{\mathrm{d}\mathcal{J}_k}{\mathrm{d}X}=0,\quad -\mathcal{J}_k=\frac{1}{k_BT}D_k(X)A(X)C_k\frac{\mathrm{d}\mu_k}{\mathrm{d}X},\quad k=1,2,\ldots,n,\end{aligned}\tag{1.2}$$

where $X\in[0,l]$ is the coordinate along the axis of the channel, $A(X)$ is the area of cross-section of the channel over the location X.

Equipped with system (1.2), we impose the following boundary conditions (see, Eisenberg and Liu 2007 for a reasoning), for $k=1,2,\ldots,n$,

$$\Phi(0)=\mathcal{V},\quad C_k(0)=\mathcal{L}_k>0;\quad \Phi(l)=0,\quad C_k(l)=\mathcal{R}_k>0.\tag{1.3}$$

1.1.1 Electrochemical Potential

The electrochemical potential $\mu_k(X)$ for the ith ion species consists of the ideal component $\mu_k^{id}(X)$ and the excess component $\mu_k^{ex}(X)$: $\mu_k(X)=\mu_k^{id}(X)+\mu_k^{ex}(X)$, where

$$\mu_k^{id}(X)=z_ke\Phi(X)+k_BT\ln\frac{C_k(X)}{C_0}\tag{1.4}$$

with some characteristic number density C_0 defined by

$$C_0=\max_{1\le i\le n}\Big\{\mathcal{L}_i,\mathcal{R}_i,\sup_{X\in[0,l]}|Q(X)|\Big\}.$$

The cPNP system takes into consideration of the ideal component $\mu_k^{id}(x)$ only. This component reflects the collision between ion particles and the water molecules. It has been accepted that the cPNP system is a reasonable model in, for example, the dilute case under which the ion particles can be treated as point particles and the ion-to-ion interaction can be more or less ignored. The excess chemical potential $\mu_k^{ex}(x)$ accounts for the finite size effect of ions. We would like to point out that, among many limitations, such as the "gating" phenomena, may not be captured by the simple cPNP model. However, *the basic findings on dynamics of ionic flows and their dependence on the system parameters, in particular, the permanent charges, the channel geometry, the ratios of boundary concentrations of cations, and the ratios of diffusion constants provides important insights into the mechanism of ion channels and better understandings of ionic flow properties. More importantly, some are non-intuitive, and deserve further studies.* More structural detail and more correlations between ions should be taken into considerations in PNP models such as those including various potentials for ion-to-ion interaction accounting for ion size effects (Aitbayev et al. 2019; Bates et al. 2020; Gillespie et al. 2002; Hyon et al. 2010; Ji and Liu 2012; Jia et al. 2016; Kilic et al. 2007; Liu and Eisenberg 2014; Liu et al. 2012; Lu et al. 2018; Lin et al. 2013; Sun and Liu 2018).

1.1.2 Permanent Charge

The spatial distribution of side chains in a specific channel defines the permanent charge of the channel. While some information may be obtained by ignoring the permanent charge and focusing on the effects of boundary conditions, the valences and sizes of ions, etc., we believe that different channel types differ mainly in the distribution of permanent charge (Gillespie 1999). To better understand the importance of the relation of ionic flows and permanent charges, we remark that the role of permanent charges in membrane channels is similar to the role of doping profiles in semiconductor devices. Semiconductor devices are similar to membrane channels in the way that they both use atomic-scale structures to control macroscopic flows from one reservoir to another. Ions move a lot like quasi-particles move in semiconductors. Roughly, holes and electrons are the cations and anions of semiconductors. Semiconductor technology depends on the control of migration and diffusion of quasi-particles of charge in transistors and integrated circuits. Doping is the process of adding impurities into intrinsic semiconductors to modulate its electrical, optical, and structural properties (Rouston 1990; Jr Warner 2001). One may roughly understand in the following sense, doping provides the charges that acid and basic side chains provide in a protein channel. For both ion channels and semiconductors, permanent charges add an additional component−probably the most important one−to their rich behavior. In general, the permanent charge $Q(X)$ is modeled by a piecewise constant function, that is, we assume, for a partition $X_0 = 0 < X_1 < \cdots < X_{m-1} < X_m = l$ of $[0, l]$ into m subintervals, $Q(X) = Q_j$ for $x \in (X_{j-1}, X_j)$ where Q_j's are constants with $Q_1 = Q_m = 0$ (the intervals $[X_0, X_1]$ and $[X_{m-1}, X_m]$ are viewed as the reservoirs where there is no permanent charge).

1.2 Problem Setup

For definiteness, in our later discussion, we assume

(A1). The ionic mixture consists of three ion species ($n = 3$) with $z_1 = z_2 := z > 0$ and $z_3 < 0$.

(A2). The permanent charge is defined by

$$Q(X) = \begin{cases} Q_1, \ X_0 < X < X_1, \\ Q_2, \ X_1 < X < X_2, \\ Q_3, \ X_2 < X < X_3, \end{cases} \tag{1.5}$$

where $X_0 = 0,\ X_3 = l,\ Q_1 = Q_3 = 0$ and Q_2 is some nonzero constant.

(A3). For the electrochemical potential μ_i, we only include the ideal component μ_i^{id} given by (1.4).

(A4). The relative dielectric coefficient and the diffusion coefficient are constants, that is, $\varepsilon_r(X) = \varepsilon_r$ and $D_i(X) = D_i$.

In the sequel, we will assume (A1)–(A4). We first make a dimensionless rescaling following (Gillespie 1999). Let

$$\begin{aligned} \varepsilon^2 =& \frac{\varepsilon_r \varepsilon_0 k_B T}{e^2 l^2 C_0}, \quad x = \frac{X}{l}, \quad h(x) = \frac{A(X)}{l^2}, \quad \mathcal{D}_i = l C_0 D_i; \\ \phi(x) =& \frac{e}{k_B T}\Phi(X), \quad c_i(x) = \frac{C_i(X)}{C_0}, \quad J_i = \frac{\mathcal{J}_i}{D_i}; \\ V =& \frac{e}{k_B T}\mathcal{V}, \quad L_i = \frac{\mathcal{L}_i}{C_0}; \quad R_i = \frac{\mathcal{R}_i}{C_0}. \end{aligned} \tag{1.6}$$

The BVP (1.2)–(1.3) then becomes

$$\begin{aligned} \frac{\varepsilon^2}{h(x)} \frac{\mathrm{d}}{\mathrm{d}x}\left(h(x)\frac{\mathrm{d}}{\mathrm{d}x}\phi\right) &= -\big(z_1 c_1 + z_2 c_2 + z_3 c_3 + Q(x)\big), \\ \frac{\mathrm{d}c_k}{\mathrm{d}x} + z_k c_k \frac{\mathrm{d}\phi}{\mathrm{d}x} &= -\frac{J_k}{h(x)}, \quad \frac{\mathrm{d}J_k}{\mathrm{d}x} = 0, \quad k = 1, 2, 3 \end{aligned} \tag{1.7}$$

with the boundary conditions, for $i = 1, 2, 3$,

$$\phi(0) = V, \ \ c_i(0) = L_i > 0; \ \ \phi(1) = 0, \ \ c_i(1) = R_i > 0. \tag{1.8}$$

Remark 1.1 The dimensionless parameter ε defined in (1.6) as $\varepsilon = \frac{1}{l}\sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{e^2 C_0}}$ is directly related to the ratio κ_D/l, where $\kappa_D = \sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{\sum_j (z_j e)^2 C_j}}$ is the Debye length; in particular, $\varepsilon = \kappa_D/l$ when $z_j^2 = 1$ and $C_j = C_0$. Typically, the parameter ε is small due to the fact that the two variables l, the length of the channel, and C_0, some characteristic number density could be very large. For many cases, the value of ε is of order $O(10^{-3})$ (see Eisenberg and Liu 2017 for a more detailed description).

1.3 Comparison with Some Previous Works

Recently, the classical PNP model has been analyzed under the framework of geometric singular perturbation theory (see Bates et al. 2017; Eisenberg and Liu 2007; Ji et al. 2015; Liu 2005, 2009 for example). For readers' convenience, we would like to briefly discuss the similarities and differences compared to current work.

Our work follows a similar dynamical system framework to establish the existence and uniqueness result of the problem. However, compared to these works, our set-ups are much more challenging and more realistic, more importantly, the specific structure of our model allows us to obtain detailed description of the nonlinear interplay among different system parameters. This is far beyond the existence and uniqueness result. To be specific, our model includes three ion species, two positively charged with *the same valences*, and one negatively charged (in Eisenberg and Liu 2007; Ji et al. 2015; Liu 2005, only two oppositely charged particles are included, selectivity of cations, one of the most relevant biological properties of ion channels cannot be described); and a profile of nonzero but small permanent charges (in Bates et al. 2017, it includes three ion species but with zero permanent charges, the effects on ionic flows from the two key structures of ion channels: channel geometry and distribution of permanent charges, cannot be examined, while this could provide crucial insights for the selectivity of cations through membrane channels). In Liu (2009), the author extended the work in Eisenberg and Liu (2007) and established the existence and local uniqueness of the classical PNP system with n ion species.

Our work, in some sense, is motivated by Ji et al. (2015), and there are some similarities in the treatment. More precisely, both of the works employ regular perturbation analysis to derive the explicit expressions of the individual fluxes up to the first order in the small permanent charge, which is reflected in Sect. 2.4 in current work. However, the derivation is much more challenging due to the nonlinearity of the individual fluxes in the potential V (in Ji et al. 2015, the individual fluxes are linear in the potential V). The nonlinearity of the individual fluxes in the potential provides much more rich dynamics of ionic flows, and more complicated nonlinear interaction among the system parameters, which is addressed in both Sects. 3 and 4. Meanwhile, this indicates that our work provides a better understanding of the mechanism of ionic flows through single ion channels, which is necessary and important for future studies of ion channel problems.

To provide a systematic study of the PNP system, for this more realistic set-up, in Sect. 3, we further verified that (similar treatment as that in Ji et al. (2015) but more challenging due to the nonlinearity)

(I) A small positive permanent charge, depending on other system parameters, cannot enhance the flux of any cation while reduce the flux of the anion. This is consistent with the observation in Ji et al. (2015), and provides complimentary information and better understanding of the phenomena because of the existence of multiple cations (see Remark 3.16 for more details).

(II) To optimize the effect of permanent charges, a short and narrow filter, within which the permanent charge is confined, is expected, which is consistent with the typical structure of an ion channel. This is consistent with the observation obtained in Ji et al. (2015), but much more rich and complicated dynamics are observed (see Remark 3.21 for detailed discussion).

To summarize, most of the results mentioned above mainly focused on the existence and local uniqueness results, and could not provide information for the qualitative properties of ionic flows, especially the selectivity phenomena of ion channels, while the latter is more important for one to understand the internal dynamics of ionic flows, which cannot be detected using current technology. However, in our work for the specific set-up, the qualitative properties of ionic flows, particularly the competition between cations, in terms of the individual fluxes are able to be analyzed in great detail, and the nonlinear interplay among system parameters is characterized almost completely. The mathematical analysis in this work provides deep insights and better understanding of the mechanism of ionic flows through membrane channels, and certain information for the selectivity phenomena of ion channels. This is our main contribution and the novelty.

1.4 Main Results

For convenience, we briefly summarize our main results as follows with $j, k = 1, 2, 3$.

(i) Characterization of boundary/internal layers $\Gamma^{[j-1,r]}$ and $\Gamma^{[j,l]}$, and landing points $\omega(N^{[j-1,r]})$ and $\alpha(N^{[j,l]})$ via the limiting fast system (2.3); see Proposition 2.3 in Sect. 2.1.1.

(ii) Characterization of regular layers Λ_j via the limiting slow system (2.10), and the transversal intersection of $\bar{M}^{[j-1,r]}$, the forward image of $\omega(N^{[j-1,r]})$, and $\bar{M}^{[j,l]}$, the backward image of $\alpha(N^{[j,l]})$, on the slow manifold $\mathcal{Z}_j$; see Lemma 2.4 and Proposition 2.5 in Sect. 2.1.2.

(iii) Establishing the existence and local uniqueness result of the underlying PNP system; see Theorem 2.7 in Sect. 2.3.

(iv) Obtaining the zeroth-order and first-order (in Q_0) solutions of system (2.18)–(2.19), crucial to derive explicit expressions of the individual fluxes up to the first order in Q_0; see Propositions 2.8 and 2.11 in Sect. 2.4.

(v) The sign of M and $1 - N$, critical for our analysis in Sects. 3 and 4; see Lemmas 3.4 and 3.5 in Sect. 3.1.

(vi) Analysis of the small permanent charge effect on the individual fluxes J_k, from three directions

(vi-1) The sign of J_{k1}, the first-order expansions in Q_0; see Theorems 3.10 and 3.13 in Sect. 3.2.1.

(vi-2) Effects on the magnitude of J_k; see Theorem 3.15 in Sect. 3.2.2.

(vi-3) Monotonicity of J_{k1}; see Theorem 3.18 in Sect. 3.2.3.

(vii) Channel geometry effect on the magnitude of J_{k1}; see Theorem 3.20 in Sect. 3.3.

(viii) Study on competition between cations in terms of $\mathcal{J}^1_{1,2} = D_1 J_{11} - D_2 J_{21}$ based on distinct interplays among $\frac{D_1}{D_2}$, $\frac{L_2}{L_1}$ and $\frac{R_2}{R_1}$ consisting of three cases

(viii-1) Case study with $\frac{D_1}{D_2} = \frac{R_2}{R_1}$; see Theorem 4.2 in Sect. 4.1.

(viii-2) Case study with $\frac{D_1}{D_2} > \max\{\frac{L_2}{L_1}, \frac{R_2}{R_1}\}$; see Theorem 4.4 in Sect. 4.2.

(viii-3) Case study with $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$; see Theorem 4.6 in Sect. 4.3.

(ix) Analysis on the magnitude of $\mathcal{J}_{1,2}$, equivalent to examine the sign of $\mathcal{J}^0_{1,2}\mathcal{J}^1_{1,2}$, where $\mathcal{J}^0_{1,2} = D_1 J_{10} - D_2 J_{20}$; see Theorem 4.8 in Sect. 4.4.

Remark 1.2 In (viii), there are actually another three cases: 1) $\frac{D_1}{D_2} = \frac{L_2}{L_1}$; 2) $\frac{D_1}{D_2} < \min\{\frac{L_2}{L_1}, \frac{R_2}{R_1}\}$; and 3) $\frac{R_2}{R_1} < \frac{D_1}{D_2} < \frac{L_2}{L_1}$. The results and arguments are very similar to those corresponding to the case stated in (viii-1)–(viii-3), and are not included in this work. Interested readers can study them following our discussions detailed in Sect. 4.

To end this section, we rewrite the PNP system (1.7) into a standard form of singularly perturbed systems and convert the boundary value problem to a connection problem. Upon introducing $u = \varepsilon\dot{\phi}$ and $\tau = x$, system (1.7) becomes

$$\begin{aligned}
&\varepsilon\dot{\phi} = u, \quad \varepsilon\dot{u} = -z_1c_1 - z_2c_2 - z_3c_3 - Q(\tau) - \varepsilon\frac{h'(\tau)}{h(\tau)}u,\\
&\varepsilon\dot{c}_1 = -z_1uc_1 - \varepsilon\frac{J_1}{h(\tau)}, \quad \varepsilon\dot{c}_2 = -z_2uc_2 - \varepsilon\frac{J_2}{h(\tau)} \quad \varepsilon\dot{c}_3 = -z_3uc_3 - \varepsilon\frac{J_3}{h(\tau)},\\
&\dot{J}_1 = \dot{J}_2 = \dot{J}_3 = 0, \quad \dot{\tau} = 1,
\end{aligned} \tag{1.9}$$

where dot denotes the derivative with respect to x.

System (1.9) will be treated as a dynamical system with the phase space $\mathbb{R}^9$ and the independent variable x is viewed as time. The boundary condition (1.8) becomes

$$\phi(0) = V,\ c_k(0) = L_k,\ \tau(0) = 0; \quad \phi(1) = 0,\ c_k(1) = R_k,\ \tau(1) = 1.$$

Let B_L and B_R be the subsets of the phase space $\mathbb{R}^9$ defined by

$$\begin{aligned}
B_L &= \{(\phi, u, c_1, c_2, c_3, J_1, J_2, J_3, x) : \phi = V, c_1 = L_1, c_2 = L_2, c_3 = L_3, x = 0\},\\
B_R &= \{(\phi, u, c_1, c_2, c_3, J_1, J_2, J_3, x) : \phi = 0, c_1 = R_1, c_2 = R_2, c_3 = R_3, x = 1\}.
\end{aligned} \tag{1.10}$$

Now, the boundary value problem is equivalent to the following connection problem: finding an orbit of (1.9) from B_L to B_R.

The rest of the paper is organized as follows. In Sect. 2, we establish the existence and local uniqueness of solutions to the boundary value problem under the framework of geometric singular perturbation theory, and expand the singular orbit, solutions of the limiting PNP system, in Q_0 near $Q_0 = 0$ to obtain J_{k1}, the leading terms that contain small permanent charge effects. In Sect. 3, we focus on the permanent charge and channel geometry effects on the individual fluxes. Of particular interest is the terms J_{k1}, which are analyzed from different directions, such as the sign of J_{k1}, the monotonicity of J_{k1} and the channel geometry effects on the magnitude of J_{k1} in details. In Sect. 4, we study the competition between the two cations, which further depend on the nonlinear interplays among other system parameters, in addition to small permanent charge and channel geometry, in particular, the interaction between the ratios of diffusion constants and the ratios of boundary concentrations of two cations. Section 5 provides some concluding remarks. Some proofs are provided in Sect. 6.

2 Geometric Singular Perturbation Framework

In this section, we apply a modern invariant manifold theory, geometric singular perturbation theory, to the system (1.7)–(1.8). Together with the specific structure of this concrete model, the existence and local uniqueness of solutions to the boundary value problem is established. Furthermore, the singular orbit of the limiting PNP system ($\varepsilon \to 0$ in (1.7)) depends on the permanent charge Q_j in a regular way, which allows us to further examine the small permanent charge effects on ionic flows via the method of regular perturbations.

To get started, we let M_L^ε be the collection of all forward orbits starting from B_L and M_R^ε be the collection of all backward orbits starting from B_R. Then, for $\varepsilon > 0$ small, the vector field is not tangent to B_L and B_R. Notice that $\dim(B_L) = \dim(B_R) = 4$, which indicates that both M_L^ε and M_R^ε are smooth invariant manifolds of dimension 5. Generically, we expect that M_L^ε and M_R^ε intersect transversally. If this is the case, $\dim(M_L^\varepsilon \cap M_R^\varepsilon) = \dim(M_L^\varepsilon) + \dim(M_R^\varepsilon) - \dim(\mathbb{R}^9) = 5 + 5 - 9 = 1$ and thus, the intersection would consist of a discrete set of orbits. The connection problem then will be solved by proving that the manifold M_L^ε and M_R^ε indeed intersect transversally. The general idea for this process consists of the following two steps:

(i) Constructing a singular orbit, which is a union of fast and slow orbits of different limiting systems of (1.9), where fast orbits represent the boundary/internal layers and slow orbits connect the boundary/internal layers;
(ii) Examining the evolutions of M_L^ε and M_R^ε along the singular orbit for transversality and apply the exchange lemma.

Following the idea in Liu (2009) for $n = 2$ cases, we will first construct orbits on each subinterval $[x_{j-1}, x_j]$ where $Q(x)$ is constant and then match them at jumping points $x = x_j$'s of $Q(x)$. To do so, we will preassign the values of ϕ, c_k's at each x_j for $j = 1, 2$,

$$\phi(x_j) = \phi^{[j]}, \quad c_k(x_j) = c_k^{[j]} \tag{2.1}$$

with given $\phi^{[0]} = V$ and $c_k^{[0]} = L_k$ at $x_0 = 0$, $\phi^{[3]} = 0$ and $c_k^{[3]} = R_k$ at $x_3 = 1$, and introduce the set, for $j = 0, 1, 2, 3$,

$$B_j = \left\{(\phi, u, c_1, c_2, c_3, J_1, J_2, J_3, x) : \phi = \phi^{[j]}, c_1 = c_1^{[j]}, c_2 = c_2^{[j]}, c_3 = c_3^{[j]}, x = x_j\right\}.$$

Notice that $B_0 = B_L$ and $B_3 = B_R$. What follows is to construct singular orbits over each subinterval $[x_{j-1}, x_j]$ for the connection problem from B_{j-1} to B_j. The last step is to match the singular orbits at each x_j to obtain singular orbits over the whole interval [0, 1].

2.1 A Singular Orbit on $[x_{j-1}, x_j]$ with $Q(x) = Q_j$

We now construct singular orbits over the interval $[x_{j-1}, x_j]$, which consists of two boundary layers $\Gamma^{[j-1,r]}$ at $x = x_{j-1}$, $\Gamma^{[j,l]}$ at $x = x_j$ and a regular layer Λ_j over the interval $[x_{j-1}, x_j]$. We would like to point out that the boundary layer at x_j's should be viewed as internal or transition layers relative to the whole interval [0, 1] if x_j is not one of the endpoints.

2.1.1 Fast Dynamics and Boundary Layers

Setting $\varepsilon = 0$ in (1.9), we have the *slow manifold*

$$\mathcal{Z}_j = \big\{u = 0, z_1c_1 + z_2c_2 + z_3c_3 + Q_j = 0\big\},$$

which is of co-dimension two, i.e., $\dim(\mathcal{Z}_j) = 7$. In terms of the independent variable $\xi = x/\varepsilon$, one obtains the so-called *fast system* of (1.9)

$$\begin{aligned}
\phi' =&u, \quad u' = -z_1c_1 - z_2c_2 - z_3c_3 - Q_j - \varepsilon\frac{h'(\tau)}{h(\tau)}u,\\
c_1' =&- z_1c_1u - \varepsilon\frac{J_1}{h(\tau)}, \quad c_2' = -z_2c_2u - \varepsilon\frac{J_2}{h(\tau)}, \quad c_3' = -z_3c_3u - \varepsilon\frac{J_3}{h(\tau)},\\
J_1' =&J_2' = J_3' = 0, \quad \tau' = \varepsilon,
\end{aligned} \tag{2.2}$$

where prime denotes the derivative about ξ.

The corresponding limiting fast system is

$$\begin{aligned}
\phi' =&u, \quad u' = -z_1c_1 - z_2c_2 - z_3c_3 - Q_j,\\
c_1' =&- z_1c_1u, \quad c_2' = -z_2c_2u, \quad c_3' = -z_3c_3u,\\
J_1' =&J_2' = J_3' = 0, \quad \tau' = 0.
\end{aligned} \tag{2.3}$$

Note that the set of equilibria of (2.3) is exactly $\mathcal{Z}_j$. We have the following result (see also Bates et al. 2017; Lin et al. 2013; Liu 2009).

Lemma 2.1 *For the limiting fast system* (2.3)*, the slow manifold $\mathcal{Z}_j$ is normally hyperbolic.*

Proof The slow manifold $\mathcal{Z}_j$ is precisely the set of equilibria of (2.3). The linearization of (2.3) at each point of $(\phi, 0, c_1, c_2, c_3, J_1, J_2, J_3, \tau) \in \mathcal{Z}_j$ has seven zero eigenvalues whose generalized eigenspace is the tangent space of the seven-dimensional slow manifold $\mathcal{Z}_j$ of equilibria, and the other two eigenvalues are $\pm\sqrt{z_1^2c_1 + z_2^2c_2 + z_3^2c_3}$, whose eigenvectors are not tangent to $\mathcal{Z}_j$ (Recall that c_i's are concentrations and we are only interested in positive ones). Thus, $\mathcal{Z}_j$ is normally hyperbolic. □

The theory of normally hyperbolic invariant manifolds (Fenichel 1979) states that there exists eight-dimensional stable manifold $W^s(\mathcal{Z}_j)$ of $\mathcal{Z}_j$ that consists of points approaching $\mathcal{Z}_j$ in forward time; and there exists eight-dimensional unstable manifold

$W^u(\mathcal{Z}_j)$ of $\mathcal{Z}_j$ that consists of points approaching $\mathcal{Z}_j$ in backward time. Let $M^{[j-1,r]}$ be the collection of all forward orbits from B_{j-1} under the flow of (2.3) and let $M^{[j,l]}$ be the collection of all backward orbits from B_j. Let $N^{[j-1,r]} = M^{[j-1,r]} \cap W^s(\mathcal{Z}_j)$ and $N^{[j,l]} = M^{[j,l]} \cap W^u(\mathcal{Z}_j)$. It then follows from dynamical system theory that $\Gamma^{[j-1,r]} \subset N^{[j-1,r]}$ and $\Gamma^{[j,l]} \subset N^{[j,l]}$.

Now, we introduce our *first specific structure* of the PNP system, which allows us to further examine the ionic flow properties. It can be verified directly.

Proposition 2.2 *System (2.3) has a complete set of eight first integrals given by, for* $k = 1, 2, 3$,

$$H_k = c_k e^{z_k\phi}, \quad H_4 = \frac{1}{2}u^2 - c_1 - c_2 - c_3 + Q_j\phi, \quad H_{4+k} = J_k, \quad H_8 = \tau. \tag{2.4}$$

Under the help of the integrals in Proposition 2.2, we now solve the boundary layer problems from B_{j-1} and B_j to $\mathcal{Z}_j$.

Proposition 2.3 *One has*

(i) *Let* $\Gamma^{[j-1,r]} \subset N^{[j-1,r]}$ *be a boundary layer at* $x = x_{j-1}$. *Suppose* $\Gamma^{[j-1,r]}$ *is the orbit of the solution* $z(\xi) = \big(\phi(\xi), u(\xi), c_1(\xi), c_2(\xi), c_3(\xi), J_1, J_2, J_3, x_{j-1}\big)$ *with* $z(0) \in B_{j-1}$ *and* $\lim_{\xi\to+\infty} z(\xi) = z(+\infty) \in \mathcal{Z}_j$. *Then,*

(i1) $\phi(\xi)$ *is determined by the Hamiltonian system*

$$\phi'' + \sum_{k=1}^{3} z_k c_k^{[j-1]} e^{-z_k\left(\phi - \phi^{[j-1]}\right)} + Q_j = 0,$$

together with the boundary conditions $\phi(0) = \phi^{[j-1]}$ *and* $\phi(+\infty) = \phi^{[j-1,r]}$, *where* $\phi^{[j-1,r]}$ *is the unique solution that satisfies*

$$\sum_{k=1}^{3} z_k c_k^{[j-1]} e^{-z_k\left(\phi - \phi^{[j-1]}\right)} + Q_j = 0;$$

(i2) $u(\xi) = \phi'(\xi)$ *with* $u(0) = u^{[j-1,r]}$ *and* $u(+\infty) = 0$, *where*

$$u^{[j-1,r]} = sgn\big(\phi^{[j-1,r]} - \phi^{[j-1]}\big)\sqrt{\mathcal{K}^{[j-1,r]}}, \tag{2.5}$$

with

$$\mathcal{K}^{[j-1,r]} = \sum_{k=1}^{3} 2c_k^{[j-1]}\left(1 - e^{z_k\left(\phi^{[j-1]} - \phi^{[j-1,r]}\right)}\right) - 2Q_j\left(\phi^{[j-1]} - \phi^{[j-1,r]}\right);$$

(i3) $c_k(\xi) = c_k^{[j-1]} e^{-z_k\left(\phi(\xi)-\phi^{[j-1]}\right)}$ *with*

$$c_k(0) = c_k^{[j-1]} \quad \textit{and} \quad c_k^{[j-1,r]} = c_k(+\infty) = c_k^{[j-1]} e^{-z_k\left(\phi^{[j-1,r]}-\phi^{[j-1]}\right)}.$$

(i4) *The stable manifold $W^s(\mathcal{Z}_j)$ intersects B_{j-1} transversally at points*

$$\left(\phi^{[j-1]}, u^{[j-1,r]}, c_1^{[j-1]}, c_2^{[j-1]}, c_3^{[j-1]}, J_1, J_2, J_3, x_{j-1}\right),$$

and the ω-limit set of $N^{[j-1,r]} = M^{[j-1,r]} \cap W^s(\mathcal{Z}_j)$ is

$$\omega(N^{[j-1,r]}) = \Big\{\left(\phi^{[j-1,r]}, 0, c_1^{[j-1,r]}, c_2^{[j-1,r]}, c_3^{[j-1,r]}, J_1, J_2, J_3, x_{j-1}\right) : \textit{all } J_1, J_2, J_3\Big\}.$$

(ii) *Let $\Gamma^{[j,l]} \subset N^{[j,l]}$ be a boundary layer at $x = x_j$. Suppose $\Gamma^{[j,l]}$ is the orbit of the solution $z(\xi) = \left(\phi(\xi), u(\xi), c_1(\xi), c_2(\xi), c_3(\xi), J_1, J_2, J_3, x_{j-1}\right)$ with $z(0) \in B_j$ and $\lim_{\xi\to-\infty} z(\xi) = z(-\infty) \in \mathcal{Z}_j$. Then,*

(ii1) *$\phi(\xi)$ is determined by the Hamiltonian system*

$$\phi'' + \sum_{k=1}^{3} z_k c_k^{[j]} e^{-z_k\left(\phi-\phi^{[j]}\right)} + Q_j = 0,$$

together with the boundary conditions $\phi(0) = \phi^{[j]}$ and $\phi(-\infty) = \phi^{[j,l]}$, where $\phi^{[j,l]}$ is the unique solution that satisfies

$$\sum_{k=1}^{3} z_k c_k^{[j]} e^{-z_k\left(\phi-\phi^{[j]}\right)} + Q_j = 0;$$

(ii2) $u(\xi) = \phi'(\xi)$ *with* $u(0) = u^{[j,l]}$ *and* $u(-\infty) = 0$, *where*

$$u^{[j,l]} = sgn\left(\phi^{[j,l]} - \phi^{[j]}\right)\sqrt{\mathcal{K}^{[j,l]}}, \tag{2.6}$$

with

$$\mathcal{K}^{[j,l]} = \sum_{k=1}^{3} 2c_k^{[j]}\left(1 - e^{z_k\left(\phi^{[j]}-\phi^{[j,l]}\right)}\right) - 2Q_j\left(\phi^{[j]} - \phi^{[j,l]}\right);$$

(ii3) $c_k(\xi) = c_k^{[j]} e^{-z_k\left(\phi(\xi)-\phi^{[j]}\right)}$ *with*

$$c_k(0) = c_k^{[j]} \quad \textit{and} \quad c_k^{[j,l]} = c_k(-\infty) = c_k^{[j]} e^{-z_k\left(\phi^{[j,l]}-\phi^{[j]}\right)}.$$

(ii4) *The unstable manifold $W^u(\mathcal{Z}_j)$ intersects B_j transversally at points*

$$\big(\phi^{[j]}, u^{[j,l]}, c_1^{[j]}, c_2^{[j]}, c_3^{[j]}, J_1, J_2, J_3, x_j\big),$$

and the α-limit set of $N^{[j,l]} = M^{[j,l]} \cap W^u(\mathcal{Z}_j)$ is

$$\alpha(N^{[j,l]}) = \Big\{\big(\phi^{[j,l]}, 0, c_1^{[j,l]}, c_2^{[j,l]}, c_3^{[j,l]}, J_1, J_2, J_3, x_j\big) : \textit{all } J_1, J_2, J_3\Big\}.$$

Proof We defer the proof to "Appendix Sect. 6". □

To end this section, we comment that the transversality of the intersection $M^{[j-1,r]} \cap W^s(\mathcal{Z}_j)$ indicates that

$$\dim(N^{[j-1,r]}) = \dim(M^{[j-1,r]}) + \dim(W^s(\mathcal{Z}_j)) - 9 = 4.$$

Therefore, $N^{[j-1,r]}$ consists of 3-parameter (with the parameters J_1, J_2 and J_3) family of orbits from B_{j-1} to $\mathcal{Z}_j$. They are the candidates for the boundary layer $\Gamma^{[j-1,r]}$ at x_{j-1}. Similarly, $N^{[j,l]}$ consists of the family with parameter J_1, J_2 and J_3 of candidates for the boundary layer $\Gamma^{[j,l]}$ at x_j. In order to obtain orbits that connect B_{j-1} to B_j, one need construct regular orbits on the slow manifold $\mathcal{Z}_j$ that connect $\omega(N^{[j-1,r]})$ and $\alpha(N^{[j,l]})$, which will be discussed in the next section.

2.1.2 Slow Dynamics and Regular Layers

In this section, we focus on the flow in the vicinity of the slow manifold $\mathcal{Z}_j$ and construct regular layers Λ_j that connect $\omega(N^{[j-1,r]})$ and $\alpha(N^{[j,l]})$. Notice that, restricted onto $\mathcal{Z}_j$, system (1.9) is degenerate in the sense that all dynamical information on the state variable (ϕ, c_1, c_2, c_3) gets lost. To remedy it, we rescale the dependent variables (some other standard approach is introduced in Liu (2009)) by introducing

$$u = \varepsilon p, \quad z_3 c_3 = -z(c_1 + c_2) - Q_j - \varepsilon q. \tag{2.7}$$

With these new variables, the system (1.9) becomes (recall that $z_1 = z_2 := z$)

$$\begin{aligned}
\dot{\phi} =& p,\ \varepsilon \dot{p} = q - \varepsilon \frac{h'(\tau)}{h(\tau)} p, \quad \varepsilon \dot{q} = \big(z(z - z_3)(c_1 + c_2) - z_3 Q_j - \varepsilon z_3 q\big) p + \frac{T^c}{h(\tau)},\\
\dot{c}_1 =& -zpc_1 - \frac{J_1}{h(\tau)}, \quad \dot{c}_2 = -zpc_2 - \frac{J_2}{h(\tau)}, \quad \dot{J}_1 = \dot{J}_2 = \dot{J}_3 = 0, \quad \dot{\tau} = 1,
\end{aligned} \tag{2.8}$$

where $T^c = z(J_1 + J_2) + z_3 J_3$.

The corresponding limiting system of (2.8) reads

$$\begin{aligned}\dot{\phi} =& p,\ 0 = q, \quad 0 = \big(z(z-z_3)(c_1+c_2) - z_3 Q_j\big)p + \frac{T^c}{h(\tau)},\\ \dot{c}_1 =& - zpc_1 - \frac{J_1}{h(\tau)}, \quad \dot{c}_2 = -zpc_2 - \frac{J_2}{h(\tau)}, \quad \dot{J}_1 = \dot{J}_2 = \dot{J}_3 = 0, \quad \dot{\tau} = 1.\end{aligned} \tag{2.9}$$

The slow manifold of this system is given by

$$\mathcal{S}_j = \Big\{ p = -\frac{T^c}{h(\tau)\big(z(z-z_3)(c_1+c_2) - z_3 Q_j\big)}, \quad q = 0 \Big\}.$$

The limiting slow dynamics on $\mathcal{S}_j$ is governed by system (2.9), which now reads

$$\begin{aligned}\dot{\phi} =& - \frac{T^c h^{-1}(\tau)}{z(z-z_3)(c_1+c_2) - z_3 Q_j}, \quad \dot{c}_1 = \frac{T^c h^{-1}(\tau) z c_1}{z(z-z_3)(c_1+c_2) - z_3 Q_j} - \frac{J_1}{h(\tau)},\\ \dot{c}_2 =& \frac{T^c h^{-1}(\tau) z c_2}{z(z-z_3)(c_1+c_2) - z_3 Q_j} - \frac{J_2}{h(\tau)}, \quad \dot{J}_1 = \dot{J}_2 = \dot{J}_3 = 0, \quad \dot{\tau} = 1.\end{aligned} \tag{2.10}$$

Notice that, on $\mathcal{S}_j$ where $q = 0$, from (2.7), one has $z(c_1 + c_2) + Q_j = -z_3 c_3$, and hence, $z(z - z_3)(c_1 + c_2) - z_3 Q_j = z^2(c_1 + c_2) + z_3^2 c_3 > 0$, since c_k's are the concentrations of ion species, and we are only interested in solutions with $c_k > 0$ for $k = 1, 2, 3$.

Note also that since $h(\tau) > 0$ and $z(z - z_3)(c_1 + c_2) - z_3 Q_j > 0$, system (2.10) has the same phase portrait as that of the following system obtained by multiplying $\big(z(z - z_3)(c_1 + c_2) - z_3 Q_j\big)h(\tau)$ on the right-hand side of system (2.10):

$$\begin{aligned}\frac{d\phi}{dy} =& - T^c, \quad \frac{dc_1}{dy} = T^c z c_1 - J_1\big(z(z-z_3)(c_1+c_2) - z_3 Q_j\big),\\ \frac{dc_2}{dy} =& T^c z c_2 - J_2\big(z(z-z_3)(c_1+c_2) - z_3 Q_j\big),\\ \frac{dJ_k}{dy} =& 0, \quad \frac{d\tau}{dy} = h(\tau)\big(z(z-z_3)(c_1+c_2) - z_3 Q_j\big).\end{aligned} \tag{2.11}$$

For convenience in our following discussion, we further introduce, for $j = 1, 2, 3$ and $k = 1, 2$

$$\begin{aligned}T^m =& J_1 + J_2 + J_3,\ C^{[j-1,r]} = c_1^{[j-1,r]} + c_2^{[j-1,r]},\ C^{[j,l]} = c_1^{[j,l]} + c_2^{[j,l]},\\ C^{[k]} =& c_1^{[k]} + c_2^{[k]},\ L = L_1 + L_2,\ R = R_1 + R_2.\end{aligned} \tag{2.12}$$

Lemma 2.4 *There is a unique solution* $(\phi(y), c_1(y), c_2(y), J_1, J_2, J_3, \tau(y))$ *of* (2.11) *such that* $\big(\phi(0), c_1(0), c_2(0), \tau(0)\big) = \big(\phi^{[j-1,r]}, c_1^{[j-1,r]}, c_2^{[j-1,r]}, x_{j-1}\big)$ *and* $\big(\phi(y_j), c_1(y_j), c_2(y_j), \tau(y_j)\big) = \big(\phi^{[j,l]}, c_1^{[j,l]}, c_2^{[j,l]}, x_j\big)$ *for some* $y_j > 0$*, where* $\phi^{[j-1,r]}$*,* $\phi^{[j,l]}$*,* $c_1^{[j-1,r]}$*,* $c_1^{[j,l]}$*,* $c_2^{[j-1,r]}$ *and* $c_2^{[j,l]}$ *are given in* Proposition 2.3*. It is given by*

$$\phi(y) = \phi^{[j-1,r]} - T^c y, \quad c_1(y) = \frac{J_2 c_1^{[j-1,r]} - J_1 c_2^{[j-1,r]}}{J_1 + J_2} e^{zT^c y} - J_1 \cdot \mathcal{A}_j(y),$$
$$c_2(y) = \frac{J_1 c_2^{[j-1,r]} - J_2 c_1^{[j-1,r]}}{J_1 + J_2} e^{zT^c y} - J_2 \cdot \mathcal{A}_j(y),$$
$$\int_{x_{j-1}}^{\tau} \frac{1}{h(s)} \mathrm{d}s = \frac{z - z_3}{z_3 T^m} \left(e^{zz_3 T^m y} - 1\right)\left(C^{[j-1,r]} + \frac{(J_1 + J_2) Q_j}{zT^m}\right) - \frac{T^c}{T^m} Q_j y, \tag{2.13}$$

where $\mathcal{A}_j(y) = \frac{Q_j}{zT^m}\big(1 - e^{zz_3 T^m y}\big) - \frac{C^{[j-1,r]}}{J_1+J_2} e^{zz_3 T^m y}$ *and* $J_1,\ J_2$ *and* J_3 *are uniquely determined as*

$$\phi^{[j,l]} = \phi^{[j-1,r]} - T^c y_j, \quad c_1^{[j,l]} = \frac{J_2 c_1^{[j-1,r]} - J_1 c_2^{[j-1,r]}}{J_1 + J_2} e^{zT^c y_j} - J_1 \cdot \mathcal{A}_j(y_j),$$
$$c_2^{[j,l]} = \frac{J_1 c_2^{[j-1,r]} - J_2 c_1^{[j-1,r]}}{J_1 + J_2} e^{zT^c y_j} - J_2 \cdot \mathcal{A}_j(y_j),$$
$$T^m = \frac{(z - z_3)(C^{[j,l]} - C^{[j-1,r]}) + z_3 Q_j (\phi^{[j,l]} - \phi^{[j-1,r]})}{z_3 (H(x_j) - H(x_{j-1}))}. \tag{2.14}$$

Proof Integrating the $\frac{\mathrm{d}\phi}{\mathrm{d}y}$−equation from 0 to y in (2.11) yields

$$\phi(y) = \phi^{[j-1,r]} - T^c y.$$

Adding the $\frac{\mathrm{d}c_1}{\mathrm{d}y}$−equation and the $\frac{\mathrm{d}c_2}{\mathrm{d}y}$−equations in (2.11) gives

$$\frac{\mathrm{d}(c_1 + c_2)}{\mathrm{d}y} = zz_3 T^m (c_1 + c_2) + z_3 (J_1 + J_2) Q_j,$$

from which, via variation of constant formula, one has

$$c_1(y) + c_2(y) = C^{[j-1,r]} e^{zz_3 T^m y} - \frac{(J_1 + J_2) Q_j}{zT^m} (1 - e^{zz_3 T^m y}). \tag{2.15}$$

Plugging (2.15) into the $\frac{\mathrm{d}c_1}{\mathrm{d}y}$−equation, after regrouping some terms, we have

$$\frac{\mathrm{d}c_1}{\mathrm{d}y} = zT^c c_1 - J_1 \left[z(z - z_3)\left(C^{[j-1,r]} + \frac{J_1 + J_2}{zT^m} Q_j\right) e^{zz_3 T^m y} - \frac{T^c}{T^m} Q_j \right].$$

Again, via the variation of constant formula, after some careful calculations, one has

$$\begin{aligned} c_1(y) =& \frac{J_2c_1^{[j-1,r]} - J_1c_2^{[j-1,r]}}{J_1 + J_2} e^{zT^c y} + J_1\Big[\frac{C^{[j-1,r]}}{J_1 + J_2} e^{zz_3T^m y} + \frac{Q_j}{zT^m}\Big(e^{zz_3T^m y} - 1\Big)\Big] \\ =& \frac{J_2c_1^{[j-1,r]} - J_1c_2^{[j-1,r]}}{J_1 + J_2} e^{zT^c y} - J_1\mathcal{A}_j(y), \end{aligned}$$

where

$$\mathcal{A}_j(y) = \frac{Q_j}{zT^m}\big(1 - e^{zz_3T^m y}\big) - \frac{C^{[j-1,r]}}{J_1 + J_2} e^{zz_3T^m y}.$$

Similarly, one has

$$c_2(y) = \frac{J_1c_2^{[j-1,r]} - J_2c_1^{[j-1,r]}}{J_1 + J_2} e^{zT^c y} - J_2 \cdot \mathcal{A}_j(y).$$

From the last equation in (2.11), one has

$$\frac{\mathrm{d}\tau}{h(\tau)} = \big(z(z - z_3)(c_1 + c_2) - z_3Q_j\big)\mathrm{d}y.$$

Integrating the left hand side from x_{j-1} to τ, and the right hand side from 0 to y, together with (2.15) gives

$$\begin{aligned} \int_{x_{j-1}}^{\tau} \frac{1}{h(s)}\mathrm{d}s =& z(z - z_3)\int_0^y \Big(C^{[j-1,r]}e^{zz_3T^m s} - \frac{(J_1 + J_2)Q_j}{zT^m}(1 - e^{zz_3T^m s})\Big)\mathrm{d}s - z_3Q_j y \\ =& \frac{z - z_3}{z_3T^m}\Big(e^{zz_3T^m y} - 1\Big)\Big(C^{[j-1,r]} + \frac{J_1 + J_2}{zT^m}Q_j\Big) \\ & - \frac{(z - z_3)(J_1 + J_2)}{T^m}Q_j y - z_3Q_j y \\ =& \frac{z - z_3}{z_3T^m}\Big(e^{zz_3T^m y} - 1\Big)\Big(C^{[j-1,r]} + \frac{J_1 + J_2}{zT^m}Q_j\Big) - \frac{T^c}{T^m}Q_j y. \end{aligned}$$

Recall that we seek for solutions to reach $\alpha(N^{[j,l]})$; that is, whenever $\tau(y) = x_j$, we require $\phi(y) = \phi^{[j,l]}$, $c_1(y) = c_1^{[j,l]}$ and $c_2(y) = c_2^{[j,l]}$. Assume $\tau(y_j) = x_j$ for some $y_j > 0$. Then, $\phi(y_j) = \phi^{[j,l]}$, $c_1(y_j) = c_1^{[j,l]}$ and $c_2(y_j) = c_2^{[j,l]}$. Evaluating system (2.13) at $y = y_j$, careful calculation gives system (2.14). This completes the proof. □

We comment that

- In general, the discussion in the proof of Lemma 2.4 does not work if the two cations have distinct ion valences, even for the case with $Q(x) = 0$ over the whole interval [0, 1]. For the case that the cations have distinct valences, some different approach can be employed to obtain implicit solutions of c_k's based on some specific structure of the model. To be specific, with $z_1 \neq z_2$, that is, the two cations have distinct ion valences, the $\frac{dc_k}{dy}-$ equation in (2.11) can be written as

$$\begin{pmatrix} \frac{dc_1}{dy} \\ \frac{dc_2}{dy} \end{pmatrix} = \begin{pmatrix} z_1 T^c + z_1(z_3 - z_1)J_1 & z_2(z_3 - z_2)J_1 \\ z_1(z_3 - z_1)J_2 & z_2 T^c + z_2(z_3 - z_2)J_2 \end{pmatrix} \begin{pmatrix} c_1 \\ c_2 \end{pmatrix} + z_3 Q_j \begin{pmatrix} J_1 \\ J_2 \end{pmatrix} \tag{2.16}$$

a linear system in (c_1, c_2), which can be directly solved via the variation of constant formula (see also Liu 2009).

- There are 4-unknowns (J_1, J_2, J_3) and y_j, and 4 equations. Based on the above analysis, associated to each solution, one is able to construct a singular orbit $\Gamma^{[j-1,r]} \cup \Lambda_j \cup \Gamma^{[j,l]}$ over the interval $[x_{j-1}, x_j]$.

The slow orbit

$$\Lambda_j = \big(\phi(x), c_1(x), c_2(x), J_1, J_2, J_3, \tau(x)\big) \tag{2.17}$$

given in Lemma 2.4 connects $\omega(N^{[j-1,r]})$ and $\alpha(N^{[j,l]})$. Let $\bar{M}^{[j-1,r]}$ (resp. $\bar{M}^{[j,l]}$) be the forward (resp. backward) image of $\omega(N^{[j-1,r]})$ (resp. $\alpha(N^{[j,l]})$) under the slow flow (2.9). One has the following result to be used in the proof of Theorem 2.7 (the proof follows exactly the same line as Proposition 3.7 in Section 3.1.2 of Lin et al. (2013)).

Proposition 2.5 *On the seven-dimensional slow manifold $\mathcal{Z}_j$, $\bar{M}^{[j-1,r]}$ and $\bar{M}^{[j,l]}$ intersect transversally along the unique orbit Λ_j given in* (2.17).

2.2 Singular Orbits over [0, 1]

To have a singular orbit over the whole interval [0, 1], one need to match all the singular orbits $\Gamma^{[j-1,r]} \cup \Lambda_j \cup \Gamma^{[j,l]}$ constructed over each subinterval $[x_{j-1}, x_j]$. For convenience, for each $j = 1, 2, 3$, denote J_k's by $J_k^{[j]}$'s over the interval $[x_{j-1}, x_j]$, and then, the matching conditions are

$$u^{[j,l]} = u^{[j,r]} \text{ at each } x_j \text{ for } j = 1, 2; \text{ and } J_k^{[j]} = J_k^{[j+1]} \text{ for } k = 1, 2;\ j = 1, 2,$$

where $u^{[j,l]}$ and $u^{[j,r]}$ are determined in Proposition 2.3, and $J_k^{[j]}$'s are determined via system (2.14). Notice that the number of matching conditions is 8, which is exactly the number of preassigned unknowns in (2.1).

For $Q_1 = Q_3 = 0$ and $Q_2 = Q_0$ (correspondingly, y_1 and y_3 will not be needed, and for convenience, we take $y_2 = y_0$ in the following discussion), the above matching conditions give a set of nonlinear algebra equations, the so-called governing system

(noting that $z_1 = z_2 = z$)

$$
\begin{aligned}
0 &= zc_1^{[1]}e^{z\left(\phi^{[1]}-\phi^{[1,r]}\right)} + zc_2^{[1]}e^{z\left(\phi^{[1]}-\phi^{[1,r]}\right)} + z_3c_3^{[1]}e^{z_3\left(\phi^{[1]}-\phi^{[1,r]}\right)} + Q_0,\\
0 &= zc_1^{[2]}e^{z\left(\phi^{[2]}-\phi^{[2,l]}\right)} + zc_2^{[2]}e^{z\left(\phi^{[2]}-\phi^{[2,l]}\right)} + z_3c_3^{[2]}e^{z_3\left(\phi^{[2]}-\phi^{[2,l]}\right)} + Q_0,\\
0 &= C^{[1]}\left(e^{z(\phi^{[1]}-\phi^{[1,r]})} - e^{z(\phi^{[1]}-\phi^{[1,l]})}\right) + c_3^{[1]}\left(e^{z_3(\phi^{[1]}-\phi^{[1,r]})} - e^{z_3(\phi^{[1]}-\phi^{[1,l]})}\right)\\
&\quad + Q_0\left(\phi^{[1]} - \phi^{[1,r]}\right),\\
0 &= C^{[2]}\left(e^{z(\phi^{[2]}-\phi^{[2,r]})} - e^{z(\phi^{[2]}-\phi^{[2,l]})}\right) + c_3^{[2]}\left(e^{z_3(\phi^{[2]}-\phi^{[2,r]})} - e^{z_3(\phi^{[2]}-\phi^{[2,l]})}\right)\\
&\quad - Q_0\left(\phi^{[2]} - \phi^{[2,l]}\right),\\
J_1 &= \frac{C^{[0,r]} - C^{[1,l]}}{\ln C^{[0,r]} - \ln C^{[1,l]}}\,\frac{\ln C^{[0,r]} - \ln C^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}{C^{[0,r]} - C^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}\\
&\quad \times \frac{c_1^{[0,r]} - c_1^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}{H(x_1)}\\
&= \frac{C^{[2,r]} - C^{[3,l]}}{\ln C^{[2,r]} - \ln C^{[3,l]}}\,\frac{\ln C^{[2,r]} - \ln C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}{C^{[2,r]} - C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}\\
&\quad \times \frac{c_1^{[2,r]} - c_1^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}{H(1) - H(x_2)},\\
J_2 &= \frac{C^{[0,r]} - C^{[1,l]}}{\ln C^{[0,r]} - \ln C^{[1,l]}}\,\frac{\ln C^{[0,r]} - \ln C^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}{C^{[0,r]} - C^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}\\
&\quad \times \frac{c_2^{[0,r]} - c_2^{[1,l]}e^{z\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}{H(x_1)}\\
&= \frac{C^{[2,r]} - C^{[3,l]}}{\ln C^{[2,r]} - \ln C^{[3,l]}}\,\frac{\ln C^{[2,r]} - \ln C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}{C^{[2,r]} - C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}\\
&\quad \times \frac{c_2^{[2,r]} - c_2^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}{H(1) - H(x_2)},\\
J_3 &= -\frac{z}{z_3}\,\frac{C^{[0,r]} - C^{[1,l]}}{\ln C^{[0,r]} - \ln C^{[1,l]}}\cdot\frac{\ln C^{[0,r]} - \ln C^{[1,l]}e^{z_3\left(\phi^{[1,l]}-\phi^{[0,r]}\right)}}{H(x_1)}\\
&= -\frac{z}{z_3}\,\frac{C^{[2,r]} - C^{[3,l]}}{\ln C^{[2,r]} - \ln C^{[3,l]}}\cdot\frac{\ln C^{[2,r]} - \ln C^{[3,l]}e^{z_3\left(\phi^{[3,l]}-\phi^{[2,r]}\right)}}{H(1) - H(x_2)},\\
\phi^{[2,l]} &= \phi^{[1,r]} - T^c y_0, \quad c_1^{[2,l]} = \frac{J_2c_1^{[1,r]} - J_1c_2^{[1,r]}}{J_1 + J_2}e^{zT^c y_0} - J_1\cdot\mathcal{A}_2(y_0),\\
c_2^{[2,l]} &= \frac{J_1c_2^{[1,r]} - J_2c_1^{[1,r]}}{J_1 + J_2}e^{zT^c y_0} - J_2\cdot\mathcal{A}_2(y_0),\\
T^m &= \frac{(z - z_3)(C^{[2,l]} - C^{[1,r]}) + z_3Q_0(\phi^{[2,l]} - \phi^{[1,r]})}{z_3(H(x_2) - H(x_1))},
\end{aligned}
\tag{2.18}
$$

where

$$\mathcal{A}_2(y_0)=\frac{Q_0}{zT^m}\left(1-e^{zz_3T^my_0}\right)-\frac{C^{[1,r]}}{J_1+J_2}e^{zz_3T^my_0}$$

and

$$\begin{aligned}
&\phi^{[0,r]}=V-\frac{1}{z-z_3}\ln\frac{-z_3L_3}{zL},\ c_1^{[0,r]}=L_1\Big(\frac{-z_3L_3}{zL}\Big)^{\frac{z}{z-z_3}},\\
&c_2^{[0,r]}=L_2\Big(\frac{-z_3L_3}{zL}\Big)^{\frac{z}{z-z_3}},\\
&c_3^{[0,r]}=L_3\Big(\frac{-z_3L_3}{zL}\Big)^{\frac{z_3}{z-z_3}},\ \phi^{[1,l]}=\phi^{[1]}-\frac{1}{z-z_3}\ln\frac{-z_3c_3^{[1]}}{zC^{[1]}},\\
&c_1^{[1,l]}=c_1^{[1]}\Big(\frac{-z_3c_3^{[1]}}{zC^{[1]}}\Big)^{\frac{z}{z-z_3}},\\
&c_2^{[1,l]}=c_2^{[1]}\Big(\frac{-z_3c_3^{[1]}}{zC^{[1]}}\Big)^{\frac{z}{z-z_3}},\ c_3^{[1,l]}=c_3^{[1]}\Big(\frac{-z_3c_3^{[1]}}{zC^{[1]}}\Big)^{\frac{z_3}{z-z_3}},\\
&\phi^{[2,r]}=\phi^{[2]}-\frac{1}{z-z_3}\ln\frac{-z_3c_3^{[2]}}{zC^{[2]}},\\
&c_1^{[2,r]}=c_1^{[2]}\Big(\frac{-z_3c_3^{[2]}}{zC^{[2]}}\Big)^{\frac{z}{z-z_3}},\ c_2^{[2,r]}=c_2^{[2]}\Big(\frac{-z_3c_3^{[2]}}{zC^{[2]}}\Big)^{\frac{z}{z-z_3}},\\
&c_3^{[2,r]}=c_3^{[2]}\Big(\frac{-z_3c_3^{[2]}}{zC^{[2]}}\Big)^{\frac{z_3}{z-z_3}},\\
&\phi^{[3,l]}=-\frac{1}{z-z_3}\ln\frac{-z_3R_3}{zR},\ c_1^{[3,l]}=R_1\Big(\frac{-z_3R_3}{zR}\Big)^{\frac{z}{z-z_3}},\\
&c_2^{[3,l]}=R_2\Big(\frac{-z_3R_3}{zR}\Big)^{\frac{z}{z-z_3}},\ c_3^{[3,l]}=R_3\Big(\frac{-z_3R_3}{zR}\Big)^{\frac{z_3}{z-z_3}},\\
&c_1^{[1,r]}=c_1^{[1]}e^{z(\phi^{[1]}-\phi^{[1,r]})},\ c_2^{[1,r]}=c_2^{[1]}e^{z(\phi^{[1]}-\phi^{[1,r]})},\ c_3^{[1,r]}=c_3^{[1]}e^{z_3(\phi^{[1]}-\phi^{[1,r]})},\\
&c_1^{[2,l]}=c_1^{[2]}e^{z(\phi^{[2]}-\phi^{[2,l]})},\ c_2^{[2,l]}=c_2^{[2]}e^{z(\phi^{[2]}-\phi^{[2,l]})},\ c_3^{[2,l]}=c_3^{[2]}e^{z_3(\phi^{[2]}-\phi^{[2,l]})}.
\end{aligned}\tag{2.19}$$

Recall that $\big(\phi^{[1]},c_1^{[1]},c_2^{[1]},c_3^{[1]}\big)$ and $\big(\phi^{[2]},c_1^{[2]},c_2^{[2]},c_3^{[2]}\big)$ are the unknown values preassigned at $x=x_1$ and $x=x_2$, J_1, J_2 and J_3 are the unknown values for the flux densities of the three ion species. There are also three auxiliary unknowns $\phi^{[1,r]}$, $\phi^{[2,l]}$ and y_0 in (2.18). The total number of unknowns in (2.18) is fourteen, which matches the total number of equations.

Remark 2.6 A qualitative important question is whether the set of nonlinear equations (2.18) (in general, we call it a *governing system*) has a unique solution. This can be studied through bifurcation analysis and numerical simulations, which is beyond the aim of this work. However, a special case is provided to show that, under some further restrictions, multiple solutions are found.

2.2.1 A Special Case with $z = -z_3 = 1$ and $h(x) = 1$

In this part, we consider a special case with $z = 1$ and $z_3 = -1$ to illustrate the governing system (2.18) actually can have multiple solutions. Further restrictions that $x_1 = 1/3,\ x_2 = 2/3$ and $h(x) = 1$ will be posted later merely for simplicity.

For convenience, we set

$$A = \sqrt{C^{[1]}c_3^{[1]}},\quad B = \sqrt{C^{[2]}c_3^{[2]}}\quad \text{and}\quad Q_0 = 2Q.$$

From the first two equations of (2.18), one has

$$\phi^{[1]} - \phi^{[1,r]} = \ln\frac{\sqrt{Q^2+A^2}-Q}{C^{[1]}},\quad \phi^{[2]} - \phi^{[2,l]} = \ln\frac{\sqrt{Q^2+B^2}-Q}{C^{[2]}}.$$

From the third and fourth equation of (2.18), together with $\phi^{[1]} - \phi^{[1,l]} = \frac{1}{2}\ln\frac{c_3^{[1]}}{C^{[1]}}$ from (2.19), we have

$$\begin{aligned} C^{[1]} =& \left(\sqrt{Q^2+A^2}-Q\right)\exp\left\{\frac{\sqrt{Q^2+A^2}-A}{Q}\right\},\\ C^{[2]} =& \left(\sqrt{Q^2+B^2}-Q\right)\exp\left\{\frac{\sqrt{Q^2+B^2}-B}{Q}\right\}. \end{aligned} \tag{2.20}$$

The rest equations of (2.18) become

$$\begin{aligned} J_1 &= \frac{2(\sqrt{LL_3}-A)}{\ln(LL_3)-\ln A^2}\cdot\frac{V-\phi^{[1]}+\ln L-\ln C^{[1]}}{H(x_1)}\cdot\frac{\frac{L_1}{L}\sqrt{LL_3}-\frac{c_1^{[1]}}{C^{[1]}}Ae^{\delta_1}}{\sqrt{LL_3}-Ae^{\delta_1}}\\ &= \frac{2(B-\sqrt{RR_3})}{\ln B^2-\ln(RR_3)}\frac{\phi^{[2]}-\ln R+\ln C^{[2]}}{H(1)-H(x_2)}\frac{\frac{c_1^{[2]}}{C^{[2]}}B-\frac{R_1}{R}\sqrt{RR_3}e^{\delta_2}}{B-\sqrt{RR_3}e^{\delta_2}},\\ J_2 &= \frac{2(\sqrt{LL_3}-A)}{\ln(LL_3)-\ln A^2}\frac{V-\phi^{[1]}+\ln L-\ln C^{[1]}}{H(x_1)}\frac{\frac{L_2}{L}\sqrt{LL_3}-\frac{c_2^{[1]}}{C^{[1]}}Ae^{\delta_1}}{\sqrt{LL_3}-Ae^{\delta_1}}\\ &= \frac{2(B-\sqrt{RR_3})}{\ln B^2-\ln(RR_3)}\frac{\phi^{[2]}-\ln R+\ln C^{[2]}}{H(1)-H(x_2)}\frac{\frac{c_2^{[2]}}{C^{[2]}}B-\frac{R_2}{R}\sqrt{RR_3}e^{\delta_2}}{B-\sqrt{RR_3}e^{\delta_2}},\\ J_3 &= \frac{2(\sqrt{LL_3}-A)}{\ln(LL_3)-\ln A^2}\frac{\phi^{[1]}-V+\ln L_3-\ln C_3^{[1]}}{H(x_1)}\\ &= \frac{2(B-\sqrt{RR_3})}{\ln B^2-\ln(RR_3)}\frac{\ln C_3^{[2]}-\phi^{[2]}-\ln R_3}{H(1)-H(x_2)},\\ T_s^c y_0 &= \phi^{[1]}-\phi^{[2]}+\ln\frac{C^{[1]}(\sqrt{Q^2+B^2}-Q)}{C^{[2]}(\sqrt{Q^2+A^2}-Q)}, \end{aligned}$$

$$
\begin{aligned}
T_s^m &= \frac{2(\sqrt{Q^2+A^2}-\sqrt{Q^2+B^2})-2QT_s^c y_0}{H(x_2)-H(x_1)},\\
0 &= Q-\sqrt{Q^2+B^2}+\frac{\sqrt{Q^2+A^2}-Q}{e^{T_s^m y_0}}-\frac{2Q(J_1+J_2)}{T_s^m}\left(1-e^{-T_s^m y_0}\right),\\
0 &= J_1\left(\sqrt{Q^2+B^2}-Q-(\sqrt{Q^2+A^2}-Q)e^{T_s^c y_0}\right)\\
&\quad -(J_1+J_2)\left(\frac{c_1^{[2]}}{C^{[2]}}(\sqrt{Q^2+B^2}-Q)-\frac{c_1^{[1]}}{C^{[1]}}(\sqrt{Q^2+A^2}-Q)e^{T_s^c y_0}\right),
\end{aligned}
\tag{2.21}
$$

where

$$
\begin{aligned}
T_s^m &= J_1+J_2+J_3,\quad T_s^c = J_1+J_2-J_3,\\
\delta_1 &= \phi^{[1]}-V+\frac{1}{2}\ln\frac{L_3}{L}-\frac{1}{2}\ln\frac{c_3^{[1]}}{C^{[1]}},\quad \delta_2=\frac{1}{2}\ln\frac{c_3^{[2]}}{C^{[2]}}-\phi^{[2]}-\frac{1}{2}\ln\frac{R_3}{R}.
\end{aligned}
$$

The first three equations in (2.21), together with the $T_s^c y_0$ equation in (2.21), and (2.20), we have

$$
T_s^m = 2\frac{\sqrt{LL_3}-A}{H(x_1)} = 2\frac{B-\sqrt{RR_3}}{H(1)-H(x_2)} = 2\frac{A-B-Q\left(\phi^{[1]}-\phi^{[2]}\right)}{H(x_2)-H(x_1)}. \tag{2.22}
$$

It follows that

$$
\begin{aligned}
T_s^m &= 2\frac{\sqrt{LL_3}-\sqrt{RR_3}-Q\left(\phi^{[1]}-\phi^{[2]}\right)}{H(1)},\\
B &= \frac{H(1)-H(x_2)}{H(x_1)}(\sqrt{LL_3}-A)+\sqrt{RR_3},\\
\phi^{[1]}-\phi^{[2]} &= \frac{(\sqrt{LL_3}-\sqrt{RR_3})H(x_1)-(\sqrt{LL_3}-A)H(1)}{QH(x_1)},\\
T_s^c y_0 &= \frac{\sqrt{Q^2+A^2}-\sqrt{Q^2+B^2}}{Q}+\frac{(A-\sqrt{LL_3})(H(x_2)-H(x_1))}{QH(x_1)}.
\end{aligned}
\tag{2.23}
$$

Adding the first two equations of (2.21), one has

$$
\begin{aligned}
J_1+J_2 &= \frac{2(\sqrt{LL_3}-A)}{H(x_1)}\frac{V-\phi^{[1]}+\ln L-\ln C^{[1]}}{\ln(LL_3)-\ln A^2}\\
&= \frac{2(B-\sqrt{RR_3})}{H(1)-H(x_2)}\frac{\phi^{[2]}-\ln R+\ln C^{[2]}}{\ln B^2-\ln(RR_3)}.
\end{aligned}
$$

Using $\frac{\sqrt{LL_3}-A}{H(x_1)} = \frac{B-\sqrt{RR_3}}{H(1)-H(x_2)}$ from (2.22), we get

$$\frac{V-\phi^{[1]}+\ln L-\ln C^{[1]}}{\ln(LL_3)-\ln A^2} = \frac{\phi^{[2]}-\ln R+\ln C^{[2]}}{\ln B^2-\ln(RR_3)}.$$

Together with (2.23), we obtain

$$\begin{aligned}\phi^{[2]} =& \frac{\ln B^2-\ln(RR_3)}{\ln(LL_3B^2)-\ln(RR_3A^2)}\Bigg(V+\ln\frac{L\big(\sqrt{Q^2+B^2}-Q\big)}{R\big(\sqrt{Q^2+A^2}-Q\big)}\\ &-\frac{\sqrt{Q^2+A^2}-\sqrt{Q^2+B^2}}{Q}-\frac{(A-\sqrt{LL_3})(H(x_2)-H(x_1))}{QH(x_1)}\Bigg)\\ &+\ln R-\ln\big(\sqrt{Q^2+B^2}-Q\big)-\frac{\sqrt{Q^2+B^2}-B}{Q}.\end{aligned}$$

Together with the J_1 equation of (2.21), one has

$$\begin{aligned}\frac{\frac{L_1}{L}\sqrt{LL_3}-\frac{c_1^{[1]}}{C^{[1]}}Ae^{\delta_1}}{\sqrt{LL_3}-Ae^{\delta_1}} &= \frac{\frac{c_1^{[2]}}{C^{[2]}}B-\frac{R_1}{R}\sqrt{RR_3}e^{\delta_2}}{B-\sqrt{RR_3}e^{\delta_2}}\\ &= \frac{\frac{c_1^{[2]}}{C^{[2]}}\big(\sqrt{Q^2+B^2}-Q\big)-\frac{c_1^{[1]}}{C^{[1]}}\big(\sqrt{Q^2+A^2}-Q\big)e^{T_s^c y_0}}{\big(\sqrt{Q^2+B^2}-Q\big)-\big(\sqrt{Q^2+A^2}-Q\big)e^{T_s^c y_0}},\end{aligned} \tag{2.24}$$

and it follows that

$$\frac{\frac{L_1}{L}\sqrt{LL_3}-\frac{c_1^{[1]}}{C^{[1]}}Ae^{\delta_1}}{\sqrt{LL_3}-Ae^{\delta_1}} = \frac{\frac{c_1^{[1]}}{C^{[1]}}\frac{\sqrt{Q^2+A^2}-Q}{\sqrt{Q^2+B^2}-Q}Be^{T_s^c y_0}-\frac{R_1}{R}\sqrt{RR_3}e^{\delta_2}}{\frac{\sqrt{Q^2+A^2}-Q}{\sqrt{Q^2+B^2}-Q}Be^{T_s^c y_0}-\sqrt{RR_3}e^{\delta_2}}.$$

Hence,

$$c_1^{[1]} = \frac{C^{[1]}\left(\frac{\sqrt{Q^2+A^2}-Q}{\sqrt{Q^2+B^2}-Q}\sqrt{LL_3}Be^{T_s^c y_0}-\sqrt{RR_3}Ae^{\delta_1+\delta_2}\right)}{\sqrt{LL_3RR_3}e^{\delta_2}\left(\frac{R_1}{R}-\frac{L_1}{L}\right)+\frac{\sqrt{Q^2+A^2}-Q}{\sqrt{Q^2+B^2}-Q}\frac{L_1}{L}\sqrt{LL_3}Be^{T_s^c y_0}-\frac{R_1}{R}\sqrt{RR_3}Ae^{\delta_1+\delta_2}}.$$

Correspondingly, $c_1^{[2]}$, $c_2^{[1]}$ and $c_2^{[2]}$ can be expressed in terms of A through (2.24), $c_1^{[1]}+c_2^{[1]}=C^{[1]}$ and $c_1^{[2]}+c_2^{[2]}=C^{[2]}$.

Now, all the variables in (2.21) can be expressed in terms of A. Substituting into the last equation in (2.21), we will get an equation $F(A)=0$ in the variable only. The expression of $F(A)$ is complicated but can be given explicitly.

We now assume further that $x_1 = 1/3$, $x_2 = 2/3$ and $h(x) = 1$. Note that $L_3 = L$ and $R_3 = R$ under electroneutrality boundary conditions. Then,

$$
\begin{aligned}
B &= L + R - A, \quad T_s^m = 6(L - A),\\
C^{[1]} &= \big(\sqrt{Q^2 + A^2} - Q\big) \exp\left\{\frac{\sqrt{Q^2 + A^2} - A}{Q}\right\},\\
C^{[2]} &= \big(\sqrt{Q^2 + B^2} - Q\big) \exp\left\{\frac{\sqrt{Q^2 + B^2} - B}{Q}\right\},\\
\phi^{[1]} - \phi^{[2]} &= \frac{3A - 2L - R}{Q},\\
\phi^{[2]} &= \frac{\ln B - \ln R}{\ln(LB) - \ln(RA)}\left(V + \ln\frac{L\big(\sqrt{Q^2 + B^2} - Q\big)}{R\big(\sqrt{Q^2 + A^2} - Q\big)}\right.\\
&\quad \left. + \frac{\sqrt{Q^2 + B^2} - \sqrt{Q^2 + A^2} + L - A}{Q}\right) + \ln\frac{R}{\sqrt{Q^2 + B^2} - Q}\\
&\quad - \frac{\sqrt{Q^2 + B^2} - B}{Q},\\
T_s^c &= \frac{6(L - A)}{\ln(LB) - \ln(RA)}\left(V + \frac{\sqrt{Q^2 + B^2} - \sqrt{Q^2 + A^2} + L - A}{Q}\right.\\
&\quad \left. + \ln\frac{L\big(\sqrt{Q^2 + B^2} - Q\big)}{R\big(\sqrt{Q^2 + A^2} - Q\big)}\right) - 6(L - A),\\
y_0 &= -\frac{\sqrt{Q^2 + B^2} - \sqrt{Q^2 + A^2} + L - A}{QT_s^c},\\
0 &= \left(\sqrt{Q^2 + A^2} + \frac{QT_s^c}{T_s^m}\right) e^{-T_s^m y_0} - \sqrt{Q^2 + B^2} + \frac{QT_s^c}{T_s^m}.
\end{aligned}
\tag{2.25}
$$

The final equation in (2.25) that involves the only unknown A is $F(A) = 0$, where

$$
F(A) = \left(\sqrt{Q^2 + A^2} + \frac{QT_s^c}{6(L - A)}\right) e^{\kappa(A)} - \sqrt{Q^2 + B^2} - \frac{QT_s^c}{6(L - A)}, \tag{2.26}
$$

where

$$
\kappa(A) = -T_s^m y_0 = 6(L - A)\frac{\sqrt{Q^2 + B^2} - \sqrt{Q^2 + A^2} + L - A}{QT_s^c},
$$

$B = L + R - A$, and T_s^c is given above.

In summary, for the special case with

$$
z = -z_3 = 1, \quad x_1 = 1/3, \quad x_2 = 2/3, \quad h(x) = 1,
$$

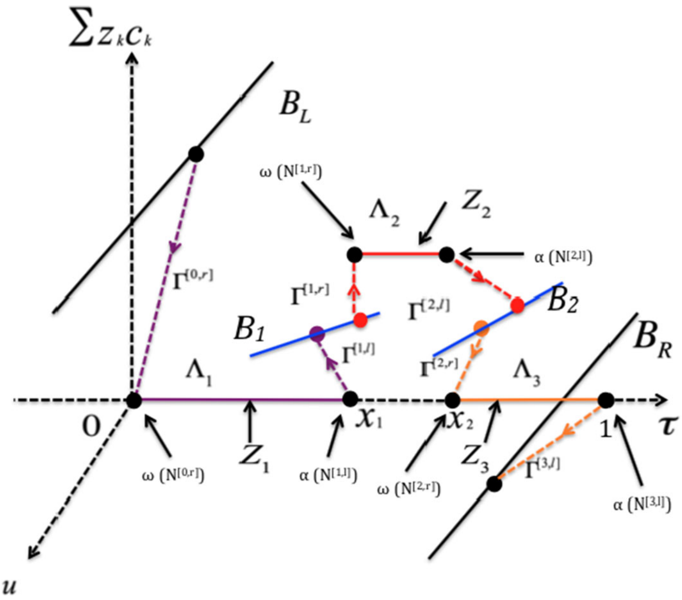

Fig. 1 Schematic picture of a singular orbit projected to the space of $(u, z_1c_z + z_2c_2 + z_3c_3, \tau)$ with $Q_1 = Q_3 = 0$ and $Q_2 = Q_0$. Boundary layers $\Gamma^{[0,r]}$ and $\Gamma^{[3,l]}$ exist if electroneutrality boundary conditions are not assumed

the set of nonlinear algebraic equations is equivalent to $F(A) = 0$, where $F(A)$ is given in (2.26). The expression $F(A)$ involves only one unknown $A = \sqrt{C^{[1]}c_3^{[1]}}$. Other system parameters in $F(A)$ are $L = L_1 + L_2$, L_3, $R = R_1 + R_2$, R_3, V and Q.

In particular, for $L_1 = L_2 = 1$, $L_3 = 2$, $R_1 = 2$, $R_2 = 1$, $R_3 = 3$, $Q_0 = 2Q = 0.02$ and $V = -20$, we find, numerically, two solutions of $F(A) = 0 : A_1 = 2.27130$ and $A_2 = 2$, where the latter is a removable singularity of the functions $F(A)$, J_i's, $\phi^{[1]}$ and $\phi^{[2]}$.

Once the value of A is determined, all the unknowns will be determined. One then obtain a singular orbit consists of nine pieces $\Gamma^{[0,r]} \cup \Lambda_1 \cup \Gamma^{[1,l]} \cup \Gamma^{[1,r]} \cup \Lambda_2 \cup \Gamma^{[2,l]} \cup \Gamma^{[2,r]} \cup \Lambda_3 \cup \Gamma^{[3,l]}$ (see Fig. 1).

2.3 Existence of Solutions Near the Singular Orbit

Note that any solution of the set of algebraic equations determines a singular orbit for the connection problem. Once a singular orbit is constructed, one can apply geometric singular perturbation theory to show that, for $\varepsilon > 0$ small, there is a unique solution that is close to the singular orbit.

For our case, the singular orbit consists of nine pieces: two boundary layers $\Gamma^{[0,r]}$ and $\Gamma^{[3,l]}$; four internal layers $\Gamma^{[1,l]}$, $\Gamma^{[1,r]}$, $\Gamma^{[2,l]}$ and $\Gamma^{[2,r]}$; and three regular layers Λ_1, Λ_2 and Λ_3 (see Fig. 1). More precisely, with $J = (J_1, J_2, J_3)$,

(1) Along the boundary layer $\Gamma^{[0,r]}$: Since $B_0 = B_L$ intersects $W^s(\mathcal{Z}_1)$ transversally, $M^{[0,r]}(\varepsilon)$ will first follow the orbit $\Gamma^{[0,r]}$ towards the vicinity of $\mathcal{Z}_1$ under the inner limit flow (2.3) with $Q(x) = 0$ near $x = x_0 = 0$;
(2) Along regular layer Λ_1: Once $M^{[0,r]}(\varepsilon)$ gets close to $\mathcal{Z}_1$, the outer limit flow (2.10) with $Q(x) = 0$ takes over, and $M^{[0,r]}(\varepsilon)$ will then follow the outer flow on $\mathcal{Z}_1$ or $\mathcal{S}_1$ along the orbit Λ_1 towards the hypersurface $\{x = x_1\}$;
(3) Along the internal layer $\Gamma^{[1,l]}$: Near but before $\{x = x_1\}$, $M^{[0,r]}(\varepsilon)$ will leave the vicinity of $\mathcal{Z}_1$, follow the orbit $\Gamma^{[1,l]}$ under the inner limit flow (2.3) with $Q(x) = 0$ near $x = x_1$, and hit the hypersurface $\{x = x_1\}$;
(4) Along the internal layer $\Gamma^{[1,r]}$: Upon hitting the hypersurface $\{x = x_1\}$, the flow switches to the inner limit flow (2.3) with $Q(x) = Q_0$. $M^{[0,r]}(\varepsilon)$ then follows $\Gamma^{[1,r]}$ towards the vicinity of $\mathcal{Z}_2$;
(5) Along the regular layer Λ_2: Once $M^{[0,r]}(\varepsilon)$ gets close to $\mathcal{Z}_2$, the outer limit flow (2.10) with $Q(x) = Q_0$ takes over, and $M^{[0,r]}(\varepsilon)$ will then follows the outer flow on $\mathcal{Z}_2$ or $\mathcal{S}_2$ along the orbit Λ_2 towards the hypersurface $\{x = x_2\}$;
(6) Along the internal layer $\Gamma^{[2,l]}$: Near but before $\{x = x_2\}$, $M^{[0,r]}(\varepsilon)$ will leave the vicinity of $\mathcal{Z}_2$, follow the orbit $\Gamma^{[2,l]}$ under the inner limit flow (2.3) with $Q(x) = Q_0$ near $x = x_2$, and hit the hypersurface $\{x = x_2\}$;
(7) Along the internal layer $\Gamma^{[2,r]}$: Upon hitting the hypersurface $\{x = x_2\}$, the flow switches to the inner limit flow (2.3) with $Q(x) = 0$. $M^{[0,r]}(\varepsilon)$ then follows $\Gamma^{[2,r]}$ towards the vicinity of $\mathcal{Z}_3$;
(8) Along the regular layer Λ_3: Once $M^{[0,r]}(\varepsilon)$ gets close to $\mathcal{Z}_3$, the outer limit flow (2.10) with $Q(x) = 0$ takes over, and $M^{[0,r]}(\varepsilon)$ will then follows the outer flow on $\mathcal{Z}_3$ or $\mathcal{S}_3$ along the orbit Λ_3 towards the hypersurface $\{x = x_3 = 1\}$;
(9) Along the boundary layer $\Gamma^{[3,l]}$: Near but before $\{x = 1\}$, $M^{[0,r]}(\varepsilon)$ will leave the vicinity of $\mathcal{Z}_3$, follow the orbit $\Gamma^{[3,l]}$ under the inner limit flow (2.3) with $Q(x) = 0$ near $x = 1$. If it hits $B_3 = B_R$, then we get our solution.

The following result can be established by the exchange lemma (see, for example, Jones 1995; Jones and Kopell 1994; Tin et al. 1994) of the geometric singular perturbation theory (see also Eisenberg and Liu 2007; Liu 2005, 2009; Liu and Xu 2015).

Theorem 2.7 *Let* $\Gamma^{[0,r]} \cup \Lambda_1 \cup \Gamma^{[1,l]} \cup \Gamma^{[1,r]} \cup \Lambda_2 \cup \Gamma^{[2,l]} \cup \Gamma^{[2,r]} \cup \Lambda_3 \cup \Gamma^{[3,l]}$ *be the singular orbit of the connecting problem system* (1.9) *associated with* B_L *and* B_R *in system* (1.10). *There exists* $\varepsilon_0 > 0$ *small, so that if* $0 < \varepsilon < \varepsilon_0$, *then the boundary value problem* (1.7)–(1.8) *has a unique solution near the singular orbit* $\Gamma^{[0,r]} \cup \Lambda_1 \cup \Gamma^{[1,l]} \cup \Gamma^{[1,r]} \cup \Lambda_2 \cup \Gamma^{[2,l]} \cup \Gamma^{[2,r]} \cup \Lambda_3 \cup \Gamma^{[3,l]}$.

Proof Fix $\delta > 0$ small to be determined. Let

$$B_L(\delta) = \left\{(V, u, L_1, L_2, L_3, J_1, J_2, J_3, 0) \in \mathbb{R}^9 : |u - u^{[0,l]}| < \delta, |J_i - J_i^{[0,l]}| < \delta\right\}.$$

For $\varepsilon > 0$, let $M^{[0,r]}(\varepsilon, \delta)$ be the forward trace of $B_L(\delta)$ under the flow of system (1.9) or equivalently of system (2.2) and let $M^{[1,l]}(\varepsilon)$ be the backward trace of B_R. To prove the existence and uniqueness statement, it suffices to show that $M^{[0,r]}(\varepsilon, \delta)$ intersects $M^{[1,l]}(\varepsilon)$ transversally in a neighborhood of the singular orbit $\Gamma^{[0,r]} \cup \Lambda_1 \cup$

$\Gamma^{[1,l]} \cup \Gamma^{[1,r]} \cup \Lambda_2 \cup \Gamma^{[2,l]} \cup \Gamma^{[2,r]} \cup \Lambda_3 \cup \Gamma^{[3,l]}$. This will be established by applying the exchange lemma successively (three times) along the stages described above. The first application of the exchange lemma verifies the descriptions for stages (1), (2), and (3); the second one for stages (4), (5), and (6); and the last application verifies the descriptions for stages (7), (8), and (9). The discussions are similar, and hence, we will just provide detailed argument for the first application that handles stages (1)-(3).

Notice that dim $B_L(\delta)$=4. It is clear that the vector field of the fast system (2.2) is not tangent to $B_L(\delta)$ for $\varepsilon \geq 0$, and hence, dim $M^{[0,r]}(\varepsilon, \delta)$=5. We next apply the Exchange Lemma to track $M^{[0,r]}(\varepsilon, \delta)$ in the vicinity of $\Gamma^{[0,r]} \bigcup \Lambda_1 \bigcup \Gamma^{[1,l]}$. First of all, the transversality of the intersection $B_L(\delta) \bigcap W^s(\mathcal{Z}_1)$ along Γ^0 in Proposition 2.3 implies the transversality of the intersection $M^{[0,r]}(0, \delta) \bigcap W^s(\mathcal{Z}_1)$. Secondly, we have also established that $\dim \omega(N^{[0,r]}) = \dim N^{[0,r]} - 1 = 3$ in Proposition 2.3 and that the limiting slow flow is not tangent to $\omega(N^{[0,r]})$ in Sect. 2.1.2. Under these conditions, the Exchange Lemma (Jones 1995; Jones and Kopell 1994; Tin et al. 1994) states that there exist $\rho > 0$ and $\varepsilon_1 > 0$ so that, if $0 < \varepsilon \leq \varepsilon_1$, then $M^{[0,r]}(\varepsilon, \delta)$ will first follow $\Gamma^{[0,r]}$ toward $\omega(N^{[0,r]}) \subset \mathcal{Z}_1$, then follow the trace of $\omega(N^{[0,r]})$ in the vicinity of Λ_1 towards $\{\tau = x_1\}$, leave the vicinity of $\mathcal{Z}_1$, and, upon exiting, a portion of $M^{[0,r]}(\varepsilon, \delta)$ is C^1 $O(\varepsilon)$-close to $W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1))$ in the vicinity of $\Gamma^{[1,l]}$. Note that $\dim W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1)) = \dim M^{[0,r]}(\varepsilon, \delta) = 5$.

It remains to show that $W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1))$ intersects $M^{[1,l]}(\varepsilon)$ transversally since $M^{[0,r]}(\varepsilon, \delta)$ is C^1 $O(\varepsilon)$-close to $W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1))$. Recall that, for $\varepsilon = 0$, $M^{[1,l]}$ intersects $W^u(\mathcal{Z}_1)$ transversally along $N^{[1,l]}$ (Proposition 2.3); in particular, at $\gamma_1 := \alpha(\Gamma^{[1,l]}) \in \alpha(N^{[1,l]}) \subset \mathcal{Z}_1$, we have

$$T_{\gamma_1} M^{[1,l]} = T_{\gamma_1} \alpha(N^{[1,l]}) \oplus T_{\gamma_1} W^u(\gamma_1) \oplus \text{span}\{V_s\},$$

where, $T_{\gamma_1} W^u(\gamma_1)$ is the tangent space of the one-dimensional unstable fiber $W^u(\gamma_1)$ at γ_1 and the vector $V_s \notin T_{\gamma_1} W^u(\mathcal{Z}_1)$ (the latter follows from the transversality of the intersection of $M^{[1,l]}$ and $W^u(\mathcal{Z}_1)$). Also,

$$T_{\gamma_1} W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1)) = T_{\gamma_1}(\omega(N^{[0,r]}) \cdot x_1) \oplus \text{span}\{V_\tau\} \oplus T_{\gamma_1} W^u(\gamma_1),$$

where the vector V_τ is the tangent vector to the τ-axis as a result of the interval factor $(x_1 - \rho, x_1)$. From Proposition 2.5, $\omega(N^{[0,r]}) \cdot x_1$ and $\alpha(N^{[1,l]})$ are transversal on $\mathcal{Z}_1 \cap \{\tau = x_1\}$. Therefore, at γ_1, the tangent spaces $T_{\gamma_1} M^{[1,l]}$ and $T_{\gamma_1} W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1))$ contain seven linearly independent vectors: V_s, V_τ, $T_{\gamma_1} W^u(\gamma_1)$ and the other four from $T_{\gamma_1}(\omega(N^{[0,r]}) \cdot 1)$ and $T_{\gamma_1} \alpha(N^{[1,l]})$; that is, $M^{[1,l]}$ and $W^u(\omega(N^{[0,r]}) \times (x_1 - \rho, x_1))$ intersect transversally. We thus conclude that, there exists $0 < \varepsilon_0 \leq \varepsilon_1$ such that, if $0 < \varepsilon \leq \varepsilon_0$, then $M^{[0,r]}(\varepsilon, \delta)$ intersects $M^{[1,l]}(\varepsilon)$ transversally.

For uniqueness, note that the transversality of the intersection $M^{[0,r]}(\varepsilon, \delta) \cap M^{[1,l]}(\varepsilon)$ implies $\dim(M^{[0,r]}(\varepsilon, \delta) \cap M^{[1,l]}(\varepsilon)) = \dim M^{[0,r]}(\varepsilon, \delta) + \dim M^{[1,l]}(\varepsilon) - 9 = 1$. Thus, there exists $\delta_0 > 0$ such that, if $0 < \delta \leq \delta_0$, the intersection $M^{[0,r]}(\varepsilon, \delta) \cap M^{[1,l]}(\varepsilon)$ consists of precisely one solution near the singular orbit $\Gamma^{[0,r]} \cup \Lambda_1 \cup \Gamma^{[1,l]}$.

To deal with the stages (4)-(6), one may get start by denoting the intersection of $W^u(N^{[0,r]} \times (x_1 - \rho, x_1))$ with $\{x = x_1\}$ by $I(x_1)$. Then $I(x_1)$ intersects $W^s(\mathcal{Z}_2)$

transversally for the flow (2.10) with $Q = Q_0$. Let $K(x_1)$ be the forward trace of $I(x_1)$ under (1.9) with $Q(x) = Q_0$. The exchange lemma implies that $M^{[0,r]}(\varepsilon)$ will first follow $K(x_1)$ in the vicinity of $\Gamma^{[1,r]}$ towards $\omega(N^{[1,r]}) \subset \mathcal{Z}_2$, then follows the trace of $\omega(N^{[1,r]})$ in the vicinity of Λ_2 towards $\{x = x_2\}$, and leave the vicinity of $\mathcal{Z}_2$. And upon exit, $M^{[0,r]}(\varepsilon)$ is C^1 $O(\varepsilon)-$ close to $W^u(N^{[1,r]} \times (x_2 - \rho_1, x_2))$, for some $\rho_1 > 0$, in the vicinity of $\Gamma^{[2,l]}$.

Similar argument applies to the stage (7)-(9). Eventually, one is able to prove that there exists $\delta_0 > 0$ (may need to be refined) such that, if $0 < \delta \le \delta_0$, the intersection $M^{[0,r]}(\varepsilon, \delta) \cap M^{[3,l]}$ consists of precisely one solution near the singular orbit $\Gamma^{[0,r]} \cup \Lambda_1 \cup \Gamma^{[1,l]} \cup \Gamma^{[1,r]} \cup \Lambda_2 \cup \Gamma^{[2,l]} \cup \Gamma^{[2,r]} \cup \Lambda_3 \cup \Gamma^{[3,l]}(\varepsilon)$. This completes the proof. □

2.4 Expansion of Singular Solutions in Small $|Q_0|$

To get started, we expand all unknown quantities in the governing system (2.18) and (2.19) in Q_0 under the assumption that $|Q_0|$ is small, for example, for $j = 1, 2$ and $k = 1, 2, 3$, we write

$$\begin{aligned} \phi^{[j]} =& \phi_0^{[j]} + \phi_1^{[j]} Q_0 + \phi_2^{[j]} Q_0^2 + o(Q_0^2), \quad c_k^{[j]} = c_{k0}^{[j]} + c_{k1}^{[j]} Q_0 + c_{k2}^{[j]} Q_0^2 + o(Q_0^2), \\ y_0 =& y_{00} + y_{01} Q_0 + y_{02} Q_0^2 + o(Q_0^2), \quad J_k = J_{k0} + J_{k1} Q_0 + J_{k2} Q_0^2 + o(Q_0^2). \end{aligned} \tag{2.27}$$

For the above expansions, we will determine the coefficients of the zeroth-order and first-order terms for dominating effects on ionic flows from the permanent charge. For convenience, we introduce

$$\alpha = \frac{H(x_1)}{H(1)}, \quad \beta = \frac{H(x_2)}{H(1)}, \quad C_i^{[1]} = c_{1i}^{[1]} + c_{2i}^{[1]}, \quad C_i^{[2]} = c_{1i}^{[2]} + c_{2i}^{[2]}, \ i = 0, 1. \tag{2.28}$$

and, corresponding to (2.12), we have $T_0^m = J_{10} + J_{20} + J_{30}$.

Careful calculations lead to the following statements, which are crucial for our later analysis, in particular, the explicit expressions for J_{k0} and J_{k1} obtained in Propositions 2.8 and 2.11.

Proposition 2.8 *The zeroth-order solution in Q_0 of system (2.18)–(2.19), for $k = 1, 2$ is given by*

$$\begin{aligned} \phi_0^{[1,l]} &= \phi_0^{[1,r]} = \phi_0^{[1]} = \frac{\ln C_0^{[1]} - \ln C^{[3,l]}}{\ln C^{[0,r]} - \ln C^{[3,l]}} \phi^{[0,r]} + \frac{\ln C^{[0,r]} - \ln C_0^{[1]}}{\ln C^{[0,r]} - \ln C^{[3,l]}} \phi^{[3,l]}, \\ \phi_0^{[2,l]} &= \phi_0^{[2,r]} = \phi_0^{[2]} = \frac{\ln C_0^{[2]} - \ln C^{[3,l]}}{\ln C^{[0,r]} - \ln C^{[3,l]}} \phi^{[0,r]} + \frac{\ln C^{[0,r]} - \ln C_0^{[2]}}{\ln C^{[0,r]} - \ln C^{[3,l]}} \phi^{[3,l]}, \\ c_{k0}^{[1,l]} &= c_{k0}^{[1,r]} = c_{k0}^{[1]} \end{aligned}$$

$$= \frac{C_0^{[1]}\left(c_k^{[0,r]} - c_k^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}\right) + \left(C^{[0,r]} c_k^{[3,l]} - c_k^{[0,r]} C^{[3,l]}\right) e^{z\left(\phi^{[3,l]}-\phi_0^{[1]}\right)}}{C^{[0,r]} - C^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}},$$

$$c_{k0}^{[2,l]} = c_{k0}^{[2,r]} = c_{k0}^{[2]}$$

$$= \frac{C_0^{[2]}\left(c_k^{[0,r]} - c_k^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}\right) + \left(C^{[0,r]} c_k^{[3,l]} - c_k^{[0,r]} C^{[3,l]}\right) e^{z\left(\phi^{[3,l]}-\phi_0^{[2]}\right)}}{C^{[0,r]} - C^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}},$$

$$y_{00} = \frac{H(1)\left(\ln C_0^{[2]} - \ln C_0^{[1]}\right)}{z(z-z_3)\left(C^{[3,l]} - C^{[0,r]}\right)}, \quad c_{30}^{[1]} = -\frac{z}{z_3} C_0^{[1]}, \quad c_{30}^{[2]} = -\frac{z}{z_3} C_0^{[2]}.$$

In particular,

$$J_{10} = \frac{C^{[0,r]} - C^{[3,l]}}{H(1)\left(\ln C^{[0,r]} - \ln C^{[3,l]}\right)} \frac{\ln C^{[0,r]} - \ln C^{[3,l]} - z(\phi^{[3,l]} - \phi^{[0,r]})}{C^{[0,r]} - C^{[3,l]} e^{z(\phi^{[3,l]}-\phi^{[0,r]})}}$$
$$\times \left(c_1^{[0,r]} - c_1^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}\right),$$

$$J_{20} = \frac{C^{[0,r]} - C^{[3,l]}}{H(1)\left(\ln C^{[0,r]} - \ln C^{[3,l]}\right)} \frac{\ln C^{[0,r]} - \ln C^{[3,l]} - z(\phi^{[3,l]} - \phi^{[0,r]})}{C^{[0,r]} - C^{[3,l]} e^{z(\phi^{[3,l]}-\phi^{[0,r]})}}$$
$$\times \left(c_2^{[0,r]} - c_2^{[3,l]} e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}\right),$$

$$J_{30} = -\frac{z}{z_3} \frac{C^{[0,r]} - C^{[3,l]}}{H(1)\left(\ln C^{[0,r]} - \ln C^{[3,l]}\right)} \left(\ln C^{[0,r]} - \ln C^{[3,l]} - z_3\left(\phi^{[3,l]} - \phi^{[0,r]}\right)\right),$$

where $C_0^{[1]} = (1-\alpha)C^{[0,r]} + \alpha C^{[3,l]}$ *and* $C_0^{[2]} = (1-\beta)C^{[0,r]} + \beta C^{[3,l]}$.

Proof We defer the proof to "Appendix Sect. 6". □

The following result is critical in deriving first-order solutions in small Q_0.

Lemma 2.9 *One has, for* $k = 1, 2$

$$zC_1^{[k]} + z_3 c_{31}^{[k]} = -\frac{1}{2}, \quad \phi_1^{[1,r]} = \phi_1^{[1]} + \frac{1}{2z(z-z_3)C_0^{[1]}}, \quad \phi_1^{[2,l]} = \phi_1^{[2]} + \frac{1}{2z(z-z_3)C_0^{[2]}}.$$

Proof We will provide a detailed proof for the first identity with $k = 1$ and the second identity. Others can be proved similarly. By the first-order expansion in Q_0 of the third equation in (2.18) and the results in Proposition 2.8, we obtain

$$\phi_1^{[1]} - \phi_1^{[1,r]} = -\frac{zC_1^{[1]} + z_3 c_{31}^{[1]} + 1}{z^2 C_0^{[1]} + z_3^2 c_{30}^{[1]}}. \tag{2.29}$$

The second order term in Q_0 of the first equation in (2.18) gives

$$\frac{1}{2}\big(z^2C_0^{[1]}+z_3^2c_{30}^{[1]}\big)\big(\phi_1^{[1]}-\phi_1^{[1,r]}\big)^2-\frac{1}{2}\big(z^2C_0^{[1]}+z_3^2c_{30}^{[1]}\big)\big(\phi_1^{[1]}-\phi_1^{[1,l]}\big)^2 \\ +\big(zC_1^{[1]}+z_3c_{31}^{[1]}\big)\big(\phi_1^{[1]}-\phi_1^{[1,r]}\big)-\big(zC_1^{[1]}+z_3c_{31}^{[1]}\big)\big(\phi_1^{[1]}-\phi_1^{[1,l]}\big) \\ +\phi_1^{[1]}-\phi_1^{[1,r]}=0.$$

Substituting (2.29) into the above equation, together with Proposition 2.8, we have

$$\frac{\big(zC_1^{[1]}+z_3c_{31}^{[1]}\big)^2}{z(z-z_3)C_0^{[1]}}=\frac{\big(zC_1^{[1]}+z_3c_{31}^{[1]}+1\big)^2}{z^2C_0^{[1]}+z_3^2c_{30}^{[1]}}.$$

Note that $z(z-z_3)C_0^{[1]}=z^2C_0^{[1]}+z_3^2c_{30}^{[1]}$. One has $zC_1^{[1]}+z_3c_{31}^{[1]}=-\big(zC_1^{[1]}+z_3c_{31}^{[1]}+1\big)$, which gives the first two identities. □

From (2.19), together with Proposition 2.8 and Lemma 2.9, the following result can be established directly.

Lemma 2.10 *One has, for $k=1,2,3$,*

$$\phi_1^{[1,l]}=\phi_1^{[1]}-\frac{1}{2z(z-z_3)C_0^{[1]}},\quad c_{k1}^{[1,l]}=c_{k1}^{[1]}+\frac{c_{k0}^{[1]}}{2(z-z_3)C_0^{[1]}},\quad c_{k1}^{[1,r]}=c_{k1}^{[1]} \\ -\frac{c_{k0}^{[1]}}{2(z-z_3)C_0^{[1]}},$$

$$\phi_1^{[2,r]}=\phi_1^{[2]}-\frac{1}{2z(z-z_3)C_0^{[2]}},\quad c_{k1}^{[2,r]}=c_{k1}^{[2]}+\frac{c_{k0}^{[2]}}{2(z-z_3)C_0^{[2]}},\quad c_{k1}^{[2,l]}=c_{k1}^{[2]} \\ -\frac{c_{k0}^{[2]}}{2(z-z_3)C_0^{[2]}}.$$

It then follows

Proposition 2.11 *The first-order solutions in Q_0 are given by, for $k=1,2$,*

$$c_{k1}^{[1]}=\frac{1}{C^{[0,r]}-C^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}}\Big[\big(c_k^{[0,r]}-c_k^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big)C_1^{[1]}+C_0^{[1]}\big(c_k^{[0,r]} \\ -c_k^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big)-c_{k0}^{[1]}\big(C^{[0,r]}-C^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big)\Big],$$

$$c_{k1}^{[2]}=\frac{1}{C^{[0,r]}-C^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}}\Big\{\big(c_k^{[0,r]}-c_k^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big)C_1^{[2]} \\ +\left(\frac{1}{2(z-z_3)C_0^{[2]}}+z\phi_1^{[2,r]}\right)\Big[C_0^{[2]}\big(c_k^{[0,r]}-c_k^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big) \\ -c_{k0}^{[2]}\big(C^{[0,r]}-C^{[3,l]}e^{z(\phi^{[3,l]}-\phi^{[0,r]})}\big)\Big]\Big\},$$

$$
\begin{aligned}
\phi_1^{[1]} =& \frac{(1+z\lambda)\,(1+z_3\lambda)\big(C_0^{[1]}-C_0^{[2]}\big)\big(\ln C^{[0,r]}-\ln C_0^{[1]}\big)}{z(z-z_3)C_0^{[1]}C_0^{[2]}\big(\ln C^{[0,r]}-\ln C^{[3,l]}\big)} + \frac{1+2zz_3\alpha\big(\phi_0^{[2]}-\phi_0^{[1]}\big)\lambda}{2z(z-z_3)C_0^{[1]}},\\
\phi_1^{[2]} =& -\frac{(1+z\lambda)\,(1+z_3\lambda)\,\big(C_0^{[1]}-C_0^{[2]}\big)\big(\ln C_0^{[2]}-\ln C^{[3,l]}\big)}{z(z-z_3)C_0^{[1]}C_0^{[2]}\big(\ln C^{[0,r]}-\ln C^{[3,l]}\big)}\\
&+\frac{1+2zz_3(\beta-1)\big(\phi_0^{[2]}-\phi_0^{[1]}\big)\lambda}{2z(z-z_3)C_0^{[2]}},\\
y_{01} =& \frac{\big(C_0^{[1]}(\beta-1)-C_0^{[2]}\alpha\big)\big(\phi_0^{[2]}-\phi_0^{[1]}\big)}{z(z-z_3)C_0^{[1]}C_0^{[2]}T_0^m} + \frac{\big(\ln C_0^{[1]}-\ln C_0^{[2]}\big)\big(\phi_0^{[2]}-\phi_0^{[1]}\big)}{z(z-z_3)\big(C^{[3,l]}-C^{[0,r]}\big)T_0^m}\\
&+\frac{\big(C_0^{[2]}-C_0^{[1]}\big)\,(z_3\,(J_{10}+J_{20})+zJ_{30})}{z^2z_3(z-z_3)C_0^{[1]}C_0^{[2]}\,\big(T_0^m\big)^2}.
\end{aligned}
$$

In particular,

$$
\begin{aligned}
J_{11} =& \frac{c_1^{[0,r]}-c_1^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}}{C^{[0,r]}-C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}}\,\frac{M\,(1+z\lambda)}{(z-z_3)H(1)}\,(z_3(1-N)\lambda+1)\,,\\
J_{21} =& \frac{c_2^{[0,r]}-c_2^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}}{C^{[0,r]}-C^{[3,l]}e^{z\left(\phi^{[3,l]}-\phi^{[0,r]}\right)}}\,\frac{M\,(1+z\lambda)}{(z-z_3)H(1)}\,(z_3(1-N)\lambda+1)\,,\\
J_{31} =& \frac{M\,(1+z_3\lambda)}{(z_3-z)H(1)}\,(z(1-N)\lambda+1)\,,
\end{aligned}
$$

where

$$
\begin{aligned}
C_1^{[1]} =& \frac{z_3\alpha\big(\phi_0^{[2]}-\phi_0^{[1]}\big)}{z-z_3}-\frac{1}{2(z-z_3)},\quad C_1^{[2]} = \frac{z_3(\beta-1)\big(\phi_0^{[2]}-\phi_0^{[1]}\big)}{z-z_3}-\frac{1}{2(z-z_3)},\\
\lambda =& \frac{\phi^{[0,r]}-\phi^{[3,l]}}{\ln C^{[0,r]}-\ln C^{[3,l]}},\quad M = \frac{\big(C^{[3,l]}-C^{[0,r]}\big)\big(C_0^{[1]}-C_0^{[2]}\big)}{C_0^{[1]}C_0^{[2]}\big(\ln C^{[0,r]}-\ln C^{[3,l]}\big)},\\
N =& \frac{\ln C_0^{[2]}-\ln C_0^{[1]}}{M} = \frac{C_0^{[1]}C_0^{[2]}\,\big(\ln C^{[0,r]}-\ln C^{[3,l]}\big)\,\big(\ln C_0^{[2]}-\ln C_0^{[1]}\big)}{\big(C^{[3,l]}-C^{[0,r]}\big)\,\big(C_0^{[1]}-C_0^{[2]}\big)}.
\end{aligned}
$$

Remark 2.12 Following the argument in Bates et al. (2017), we can extend the result to the case with $n-1$ cations having the same valences for arbitrary $n \geq 4$ (n is the total number of ion species involved in the system).

3 Permanent Charge and Channel Geometry Effects on Individual Fluxes

Our focus in this section is to examine the effects on the individual fluxes from small permanent charge and channel geometry in terms of (α, β) defined in (2.28). For convenience, we introduce

$$L_d^- = D_1 L_1 - D_2 L_2,\ R_d^- = D_1 R_1 - D_2 R_2. \tag{3.1}$$

3.1 Some Preparations

Our analysis will be under the so-called electroneutrality boundary conditions. To be specific, from now on, we always assume that

$$zL + z_3 L_3 = 0 \text{ and } zR + z_3 R_3 = 0. \tag{3.2}$$

To get started, we rewrite the zeroth-order and the first-order terms of the individual flux under electroneutrality boundary conditions (3.2).

Lemma 3.1 *Under electroneutrality conditions* (3.2)*, one has* $\phi^{[0,r]} = V,\ c_i^{[0,r]} = L_i,\ \phi^{[3,l]} = 0,\ c_i^{[3,l]} = R_i,\ i = 1, 2, 3$ *and, for* $k = 1, 2$*,*

$$\begin{aligned}
J_{k0} &= \frac{L - R}{H(1)\,(\ln L - \ln R)} \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \left(L_k - R_k e^{-zV}\right), \\
J_{30} &= -\frac{z}{z_3} \frac{L - R}{H(1)\,(\ln L - \ln R)} \left(\ln L - \ln R + z_3 V\right), \\
J_{k1} &= \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \frac{M\,(z_3(1 - N)V + \ln L - \ln R)}{(z - z_3)H(1)\,(\ln L - \ln R)^2} \left(L_k - R_k e^{-zV}\right), \\
J_{31} &= \frac{M\,(z_3 V + \ln L - \ln R)\,(z(1 - N)V + \ln L - \ln R)}{(z_3 - z)H(1)\,(\ln L - \ln R)^2},
\end{aligned} \tag{3.3}$$

where

$$M = \frac{(\beta - \alpha)\,(L - R)^2}{\omega(\alpha)\omega(\beta)\,(\ln R - \ln L)}, \quad N = \frac{\ln \omega(\beta) - \ln \omega(\alpha)}{M}, \tag{3.4}$$

with

$$\omega(x) = (1 - x)L + xR. \tag{3.5}$$

In particular, for $N = 1$*, and* $k = 1, 2$*, one has*

$$\begin{aligned}
J_{k1} &= \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \frac{\left(\ln \omega(\beta) - \ln \omega(\alpha)\right)\left(L_k - R_k e^{-zV}\right)}{(z - z_3)H(1)\,(\ln L - \ln R)}, \\
J_{31} &= \frac{\left(\ln \omega(\beta) - \ln \omega(\alpha)\right)(z_3 V + \ln L - \ln R)}{(z_3 - z)H(1)\,(\ln L - \ln R)}.
\end{aligned} \tag{3.6}$$

Directly, from (3.3) and (3.4), one has the following observation.

Lemma 3.2 *One has*

(i) *The quantities* $M = M(L_1, L_2, R_1, R_2)$ *and* $N = N(L_1, L_2, R_1, R_2)$ *scale invariantly in* (L_1, L_2, R_1, R_2)*, that is, for any* $s > 0$, $M(sL_1, sL_2, sR_1, sR_2) = M(L_1, L_2, R_1, R_2)$ *and* $N(sL_1, sL_2, sR_1, sR_2) = N(L_1, L_2, R_1, R_2)$.

(ii) *The quantities* $J_{k0} = J_{k0}(V; L_1, L_2, R_1, R_2), k = 1, 2, 3$ *scale linearly in* (L_1, L_2, R_1, R_2)*, and* $J_{k1} = J_{k1}(V; L_1, L_2, R_1, R_2), k = 1, 2, 3$ *scale invariantly in* (L_1, L_2, R_1, R_2)*, that is, for any* $s > 0$,

$$J_{k0}(V; sL_1, sL_2, sR_1, sR_2) = sJ_{k0}(V; L_1, L_2, R_1, R_2),$$
$$J_{k1}(V; sL_1, sL_2, sR_1, sR_2) = J_{k1}(V; L_1, L_2, R_1, R_2).$$

For convenience, we introduce a function $\gamma(t)$ for $t > 0$ with

$$\gamma(t) = \begin{cases} \frac{t\ln t - t + 1}{(t-1)\ln t}, & t \neq 1, \\ \frac{1}{2}, & t = 1. \end{cases} \tag{3.7}$$

For $\gamma(t)$, one can easily established the following properties.

Lemma 3.3 *For* $t > 0$*, one has* $0 < \gamma(t) < 1, \gamma'(t) > 0$, $\lim_{t\to 0}\gamma(t) = 0$ *and* $\lim_{t\to\infty}\gamma(t) = 1$.

Lemma 3.4 *Let* $t = L/R$*.* M *has the same sign with that of* $R - L$*, that is, if* $t > 1$ *(resp.* $t < 1$*), then* $M < 0$ *(resp.* $M > 0$*).*

Proof Note that $0 < \alpha < \beta < 1$ from (2.28) and $\omega(\alpha) > 0$ and $\omega(\beta) > 0$ from (3.5). Then, M has the same sign as that of $(\ln R - \ln L)$ from (3.4), and our result follows directly. □

We would like to point out that in our following discussion including the one in Sect. 4, the sign of the term $M(1-N)$ is critical. While the sign of M can be determined by $R - L$ as stated in Lemma 3.4, we now establish the result, which characterizes the sign of $1 - N$. The critical potentials V_1 and V_2 in Lemma 3.5 are defined in Definition 3.7. Throughout the paper, we assume $t = \frac{L}{R} > 1$, similar argument can be applied to the case with $t = \frac{L}{R} < 1$.

Lemma 3.5 *Let* $t = L/R$ *and* $\gamma(t)$ *be as in* (3.7)*. Then,* $N > 0$ *and* $1 - N \to 0$ *as* $t \to 1$*. Furthermore, for* $t > 1$*, one has*

(i) *if* $\alpha \geq \gamma(t)$*, then,* $\frac{z}{z_3} < 0 < 1 - N$ *and* $V_1 < 0 < V_2$*;*

(ii) *if* $\alpha < \gamma(t) < \alpha - \frac{z}{z_3\ln t}$*, then, there exists a unique* $\beta_1 \in (\alpha, 1)$ *such that* $\frac{z}{z_3} < 1 - N < 0$ *and* $V_2 < V_1 < 0$ *for* $\beta \in (\alpha, \beta_1)$*;* $1 - N = 0$ *for* $\beta = \beta_1$*;* $\frac{z}{z_3} < 0 < 1 - N$ *and* $V_1 < 0 < V_2$ *for* $\beta \in (\beta_1, 1)$.

(iii) *if* $\gamma(t) > \alpha - \frac{z}{z_3\ln t}$*, then, there exists a unique* $\beta_1^* \in (\alpha, \beta_1)$ *such that* $1 - N < \frac{z}{z_3} < 0$ *and* $V_1 < V_2 < 0$ *for* $\beta \in (\alpha, \beta_1^*)$*;* $1 - N = \frac{z}{z_3} < 0$ *and* $V_2 = V_1 < 0$ *for* $\beta = \beta_1^*$*;* $\frac{z}{z_3} < 1 - N < 0$ *and* $V_2 < V_1 < 0$ *for* $\beta \in (\beta_1^*, \beta_1)$*;* $1 - N = 0$ *for* $\beta = \beta_1$*,* $\frac{z}{z_3} < 0 < 1 - N$ *and* $V_1 < 0 < V_2$*, for* $\beta \in (\beta_1, 1)$.

Proof We defer the proof to the "Appendix Sect. 6". □

Following from Lemmas 3.4 and 3.5 that

Lemma 3.6 *Let* $t = L/R > 1$ *and* $\gamma(t)$ *be as in* (3.7). *One has*

(i) $N = 1$ *if* $\alpha < \gamma(t)$ *and* $\beta = \beta_1$*;*
(ii) $M(1-N) > 0$ *if* $\alpha < \gamma(t)$ *and* $\beta \in (\alpha, \beta_1)$*;*
(iii) $M(1-N) < 0$ *if* $\alpha < \gamma(t)$ *and* $\beta \in (\beta_1, 1)$.

3.2 Critical Potentials and Analysis of J_{k1}

We are now ready to analyze J_{k1}'s, the leading terms that contains the effects from the small permanent charge, which further depends on complicated nonlinear interplays among other system parameters, especially the channel geometry. It consists of three subsections. More precisely, Sect. 3.2.1 deals with the sign of J_{k1}, which provides important information on whether the small permanent charge reduces or enhances the individual flux J_k; In Sect. 3.2.2, we focus on the effects from small permanent charge on the magnitude of J_k, more precisely, we study the signs of $J_{k0}J_{k1}$; while in Sect. 3.2.3, we consider the monotonicity of J_{k1} to investigate how the boundary potentials will further interact with the small permanent charge.

We first identify some critical potentials that will play crucial roles in our following discussion.

Definition 3.7 We define five critical potentials V_1, V_2, V_3, V_4 and V_5 by

$$\begin{aligned}&L - Re^{-zV_1} = 0, \quad z_3(1-N)V_2 + \ln L - \ln R = 0, \quad L_1 - R_1 e^{-zV_3} = 0,\\ &L_2 - R_2 e^{-zV_4} = 0, \quad L_d^- - R_d^- e^{-zV_5} = 0,\end{aligned}$$

where $L_d^- R_d^- > 0$. Furthermore, for $N \neq 1$, one has

$$V_1 = \frac{1}{z}\ln\frac{R}{L}, \ V_2 = \frac{1}{z_3(1-N)}\ln\frac{R}{L}, \ V_3 = \frac{1}{z}\ln\frac{R_1}{L_1}, \ V_4 = \frac{1}{z}\ln\frac{R_2}{L_2}, \ V_5 = \frac{1}{z}\ln\frac{R_d^-}{L_d^-}.$$

Remark 3.8 Actually, V_2 and V_3 are the zeros of $J_{11}(V)$; V_2 and V_4 are the zeros of $J_{21}(V)$. V_3 is also the zero of $J_{10}(V)$, and V_4 is also the zero of $J_{20}(V)$. $\frac{z}{z_3}V_1$ and $\frac{z_3}{z}V_2$ are the zeros of $J_{31}(V)$. $\frac{z}{z_3}V_1$ is also the zero of $J_{30}(V)$. V_5 is defined for the discussion related to the competition between cations. We would like to further point out that the critical potentials V_2, V_3, V_4, $\frac{z}{z_3}V_1$ and $\frac{z}{z_3}V_2$ could be estimated experimentally. To be precise, taking the potential V_2 and V_3 for example, one can take an experimental individual flux as $J_1(V; Q_0)$ (this may be difficult but possible for some cases) and numerically (or analytically) compute $J_{10}(V; 0)$ for ideal case that allows one to get estimates of V_2 and V_3 by considering the zeros of $J_1(V; Q_0) - J_{10}(V; 0)$. Those critical values play critical roles in characterizing ionic flow properties, they split the potential region into subregions, from which different dynamics of ionic flows are observed. This could provide deep insights into the study of ion channel problems and better understanding of the mechanism of the electrodiffusion phenomena.

3.2.1 Signs of J_{k1}

The study of the sign of J_{k1} consists of two parts: the first part deals with the individual fluxes of the cations, while the second part focuses on the individual flux of the anion. **Small positive permanent charge effects on** J_k **for** $k = 1, 2$**.** We first establish the following result.

Lemma 3.9 *Let* $t = L/R > 1$ *and* $\gamma(t)$ *be as in* (3.7)*. For* $k = 1, 2$*, one has*

(i) $M(1-N) > 0$ *and* $V_2 > V_{2+k}$ *if* $t < L_1/R_1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1^*]$.

(ii) $M(1-N) < 0$ *and* $V_2 > V_{2+k}$ *under one of the following conditions*

- (ii1) $L_k/R_k > 1$ *and* $\alpha \geq \gamma(t)$;
- (ii2) $L_k/R_k > 1$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1, 1)$;
- (ii3) $L_k/R_k > 1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1, 1)$.

(iii) $M(1-N) > 0$ *and* $V_2 < V_{2+k}$ *under one of the following conditions*

- (iii1) $t > 1 > L_k/R_k$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;
- (iii2) $t > L_k/R_k > 1$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;
- (iii3) $t > 1 > L_k/R_k$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;
- (iii4) $t > L_k/R_k > 1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1^*, \beta_1)$.

Proof These statements can be derived directly from Lemmas 3.4 and 3.5. Taking statement (i) with $k = 1$ for example, for $1 < t = \frac{L}{R} < L_1/R_1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ and $\beta \in (\alpha, \beta_1^*]$, one has $M < 0$ from Lemma 3.4 and $1 - N < \frac{z}{z_3} < 0$ from statement (iii) of Lemma 3.5. It follows that $M(1-N) > 0$ and $0 < \frac{1}{z_3(1-N)} < \frac{1}{z}$. Note that $0 < \ln \frac{L}{R} < \ln \frac{L_1}{R_1}$. Then, $\frac{1}{z_3(1-N)} \ln \frac{L}{R} < \frac{1}{z} \ln \frac{L_1}{R_1}$, and further, $-\frac{1}{z_3(1-N)} \ln t > -\frac{1}{z} \ln \frac{L_1}{R_1}$, that is, $V_2 > V_3$. □

As we mentioned earlier (the discussion above Lemma 3.5), the sign of $M(1-N)$ plays critical role in our analysis. Lemma 3.9 further characterizes this key term, and meanwhile provide conditions for the order of some critical potentials identified in Definition 3.7. Following the above argument, together with (3.3), directly, one has

Theorem 3.10 *Suppose that* $N \neq 1$*. For the term* J_{k1} *with* $k = 1, 2$*, one has*

(i) *Under the condition stated in the statement (i) of* Lemma 3.9*, one has,* $J_{k1} < 0$ *if* $V < V_{2+k}$ *or* $V > V_2$*, and* $J_{k1} > 0$ *if* $V_{2+k} < V < V_2$*, that is, (small) positive permanent charge reduces the individual flux* J_k *if* $V < V_{2+k}$ *or* $V > V_2$*, and enhances* J_k *if* $V_{2+k} < V < V_2$*;*

(ii) *Under one of the conditions stated in the statement (ii) of* Lemma 3.9*, one has,* $J_{k1} > 0$ *if* $V < V_{2+k}$ *or* $V > V_2$*, and* $J_{k1} < 0$ *if* $V_{2+k} < V < V_2$*, that is, (small) positive permanent charge enhances the individual flux* J_k *if* $V < V_{2+k}$ *or* $V > V_2$*, and reduces* J_k *if* $V_{2+k} < V < V_2$*;*

(iii) *Under one of the conditions stated in the statement (iii) of* Lemma 3.9*, one has,* $J_{k1} < 0$ *if* $V < V_2$ *or* $V > V_{2+k}$*, and* $J_{k1} > 0$ *if* $V_2 < V < V_{2+k}$*, that is, (small) positive permanent charge reduces the individual flux* J_k *if* $V < V_2$ *or* $V > V_{2+k}$*, and enhances* J_k *if* $V_2 < V < V_{2+k}$*.*

In particular, for $N = 1$, one has, $J_{k1} > 0$ (resp. $J_{k1} < 0$) if $V < V_{2+k}$ (resp. $V > V_{2+k}$), that is, (small) positive permanent charge enhances (resp. reduces) the individual flux J_k if $V < V_{2+k}$ (resp. $V > V_{2+k}$).

Small positive permanent charge effects on J_3. For the individual flux J_3. We first establish the following result, which will be important to study the sign of J_{31}.

Lemma 3.11 *Set $t = L/R > 1$ and $\gamma(t)$ be as in (3.7). One has*

(i) *if $\alpha \geq \gamma(t)$, then $\frac{z_3}{z} < 0 < 1 - N$ and $\frac{z}{z_3}V_1 > 0 > \frac{z_3}{z}V_2$.*
(ii) *if $\alpha < \gamma(t) < \alpha - \frac{z_3}{z\ln t}$, then then, there exists a unique $\beta_1 \in (\alpha, 1)$ such that $\frac{z_3}{z} < 1 - N < 0$ and $\frac{z_3}{z}V_2 > \frac{z}{z_3}V_1 > 0$ for $\beta \in (\alpha, \beta_1)$; $\frac{z_3}{z} < 1 - N = 0$ for $\beta = \beta_1$; $\frac{z_3}{z} < 0 < 1 - N$ and $\frac{z}{z_3}V_1 > 0 > \frac{z_3}{z}V_2$ for $\beta \in (\beta_1, 1)$.*
(iii) *if $\gamma(t) > \alpha - \frac{z_3}{z\ln t}$, then, there exists a unique $\beta_{11}^* \in (\alpha, \beta_1)$ such that $1 - N < \frac{z_3}{z} < 0$ and $\frac{z}{z_3}V_1 > \frac{z_3}{z}V_2 > 0$ for $\beta \in (\alpha, \beta_{11}^*)$; $1 - N = \frac{z_3}{z} < 0$ and $\frac{z_3}{z}V_2 = \frac{z}{z_3}V_1 < 0$ for $\beta = \beta_{11}^*$; $\frac{z_3}{z} < 1 - N < 0$ and $\frac{z_3}{z}V_2 > \frac{z}{z_3}V_1 > 0$ for $\beta \in (\beta_{11}^*, \beta_1)$; $\frac{z_3}{z} < 1 - N = 0$ for $\beta = \beta_1$; $\frac{z_3}{z} < 0 < 1 - N$ and $\frac{z}{z_3}V_1 > 0 > \frac{z_3}{z}V_2$ for $\beta \in (\beta_1, 1)$.*

To further examine the small permanent charge effects on the individual flux J_3, we establish the following result, which can be verified easily based on Lemmas 3.4 and 3.11.

Lemma 3.12 *Set $t = L/R > 1$ and $\gamma(t)$ be as in (3.7). One has*

(i) *$M(1 - N) < 0$ and $\frac{z_3}{z}V_2 < \frac{z}{z_3}V_1$ under one of the following conditions*
   (i1) *$\alpha \geq \gamma(t)$;*
   (i2) *$\alpha < \gamma(t) < \alpha - \frac{z_3}{z\ln t}$ and $\beta \in (\beta_1, 1)$;*
   (i3) *$\gamma(t) > \alpha - \frac{z_3}{z\ln t}$ and $\beta \in (\beta_1, 1)$.*
(ii) *$M(1 - N) > 0$ and $\frac{z_3}{z}V_2 < \frac{z}{z_3}V_1$ if $\gamma(t) > \alpha - \frac{z_3}{z\ln t}$ and $\beta \in (\alpha, \beta_{11}^*)$.*
(iii) *$M(1 - N) > 0$ and $\frac{z_3}{z}V_2 > \frac{z}{z_3}V_1$ under one of the following conditions*
   (iii1) *$\alpha < \gamma(t) < \alpha - \frac{z_3}{z\ln t}$ and $\beta \in (\alpha, \beta_1)$;*
   (iii2) *$\gamma(t) > \alpha - \frac{z_3}{z\ln t}$ and $\beta \in (\beta_{11}^*, \beta_1)$.*

Directly from Lemma 3.12 and (3.3), one has

Theorem 3.13 *Suppose $N \neq 1$. For the term J_{31}, one has*

(i) *Under one of the conditions stated in the first statement (i) of* Lemma 3.12*, one has, $J_{31} < 0$ if $V < \frac{z}{z_3}V_2$ or $V > \frac{z_3}{z}V_1$, and $J_{31} > 0$ if $\frac{z}{z_3}V_2 < V < \frac{z_3}{z}V_1$, that is, (small) positive permanent charge reduces the individual flux J_3 if $V < \frac{z}{z_3}V_2$ or $V > \frac{z_3}{z}V_1$, and enhances J_3 if $\frac{z}{z_3}V_2 < V < \frac{z_3}{z}V_1$;*
(ii) *Under the condition stated in the second statement (ii) of* Lemma 3.12*, one has, $J_{31} > 0$ if $V < \frac{z}{z_3}V_2$ or $V > \frac{z_3}{z}V_1$, and $J_{31} < 0$ if $\frac{z}{z_3}V_2 < V < \frac{z_3}{z}V_1$, that is, (small) positive permanent charge enhances the individual flux J_3 if $V < \frac{z}{z_3}V_2$ or $V > \frac{z_3}{z}V_1$, and reduces J_3 if $\frac{z}{z_3}V_2 < V < \frac{z_3}{z}V_1$;*

(iii) *Under one of the conditions stated in the third statement (iii) of* Lemma 3.12, *one has,* $J_{31} > 0$ *if* $V < \frac{z_3}{z}V_1$ *or* $V > \frac{z}{z_3}V_2$*, and* $J_{31} < 0$ *if* $\frac{z_3}{z}V_1 < V < \frac{z}{z_3}V_2$*, that is, (small) positive permanent charge enhances the individual flux* J_3 *if* $V < \frac{z_3}{z}V_1$ *or* $V > \frac{z}{z_3}V_2$*, and reduces* J_3 *if* $\frac{z_3}{z}V_1 < V < \frac{z}{z_3}V_2$.

In particular, for $N = 1$*, one has,* $J_{31} > 0$ *(resp.* $J_{31} < 0$*) if* $V > \frac{z}{z_3}V_1$ *(resp.* $V < \frac{z}{z_3}V_2$*), that is, small positive permanent charge enhances (resp. reduces) the individual flux* J_3 *if* $V > \frac{z}{z_3}V_1$ *(resp.* $V < \frac{z}{z_3}V_1$*).*

Remark 3.14 In this part, we examine the sign of J_{k1}, the first-order term containing small permanent charge effects. The sign of J_{k1} is critical, which determines whether the small positive permanent charge enhances or reduces the individual flux J_k. More precisely, based on the expansion $J_k = J_{k0} + Q_0 J_{k1} + o(Q_0)$ with $Q_0 > 0$, if $J_{k1} > 0$, then, clearly, the term J_{k1} will enhance the individual flux J_k, otherwise, it will reduce the individual flux J_k. Critical potentials identified in Definition 3.7 play very important roles in our study. Our analysis indicates that the sign of J_{k1} sensitively depend on other physical parameters involved in the system, especially, the ratio $\frac{L}{R}$ with $L = L_1 + L_2$ and $R = R_1 + R_2$ and the channel geometry in terms of (α, β), where $\alpha = \frac{H(x_1)}{H(1)}$ and $\beta = \frac{H(x_2)}{H(1)}$. Meanwhile, the analysis, especially the nonlinear interplays among those system parameters help one better understand the internal dynamics of the ionic flows through membrane channels, which cannot be observed with present technique. Moreover, the interactions among those system parameters are not intuitive, such as the interplays among α, $\gamma(t)$ and $\alpha - \frac{z_3}{z\ln t}$ with $t = \frac{L}{R}$ in Lemma 3.12, and mathematical analysis is necessary.

3.2.2 Effects on the Magnitude of J_k

We study the effects on the magnitude of the individual fluxes from the small positive permanent charges. Based on the discussion from the previous sections, particularly Lemma 3.4, the following results can be established.

Theorem 3.15 *Suppose that* $N \neq 1$*. For* $t = L/R > 1$*, one has*

(i) *if either* $\alpha \geq \gamma(t)$*, or* $\alpha < \gamma(t)$ *and* $\beta \in (\beta_1, 1)$*, then,* $\frac{z_3}{z}V_2 < 0 < V_2$ *and*

(i1) *for* $V \in (\frac{z_3}{z}V_2, V_2)$*,* $J_{10}J_{11} < 0$*,* $J_{20}J_{21} < 0$ *and* $J_{30}J_{31} > 0$*, that is, (small) positive permanent charge reduces both* $|J_1|$ *and* $|J_2|$ *while enhances* $|J_3|$*;*

(i2) *for* $V > V_2$*,* $J_{10}J_{11} > 0$*,* $J_{20}J_{21} > 0$ *and* $J_{30}J_{31} > 0$*, that is, (small) positive permanent charge enhances* $|J_1|$*,* $|J_2|$ *and* $|J_3|$*;*

(i3) *for* $V < \frac{z_3}{z}V_2$*,* $J_{10}J_{11} < 0$*,* $J_{20}J_{21} < 0$ *and* $J_{30}J_{31} < 0$*, that is, (small) positive permanent charge reduces* $|J_1|$*,* $|J_2|$ *and* $|J_3|$.

(ii) *if* $\alpha < \gamma(t)$ *and* $\beta \in (\alpha, \beta_1)$*, then,* $V_2 < 0 < \frac{z_3}{z}V_2$ *and*

(ii1) *for* $V \in (V_2, \frac{z_3}{z}V_2)$*,* $J_{10}J_{11} < 0$*,* $J_{20}J_{21} < 0$ *and* $J_{30}J_{31} > 0$*, that is, (small) positive permanent charge reduces* $|J_1|$ *and* $|J_2|$ *while enhances* $|J_3|$*;*

(ii2) *for* $V < V_2$*,* $J_{10}J_{11} > 0$*,* $J_{20}J_{21} > 0$ *and* $J_{30}J_{31} > 0$*, that is, (small) positive permanent charge enhances* $|J_1|$*,* $|J_2|$ *and* $|J_3|$*;*

(ii3) *for* $V > \frac{z_3}{z}V_2$, $J_{10}J_{11} < 0$, $J_{20}J_{21} < 0$ *and* $J_{30}J_{31} < 0$, *that is, (small) positive permanent charge reduces* $|J_1|$, $|J_2|$ *and* $|J_3|$.

In particular, for $N = 1$, *one has* $J_{10}J_{11} < 0$, $J_{20}J_{21} < 0$ *and* $J_{30}J_{31} > 0$, *that is, (small) positive permanent charge reduces both* $|J_1|$ *and* $|J_2|$ *while enhances* $|J_3|$.

Proof From (3.3), it is easy to see that the sign of $J_{10}J_{11}$ (resp. $J_{20}J_{21}$) is determined by that of $z_3M(1-N)(V-V_2)$, while the sign of $J_{30}J_{31}$ is determined by the sign of $\frac{1}{z_3-z}M(1-N)(V-\frac{z_3}{z}V_2)$. Together with Lemmas 3.4 and 3.5, one can easily established the results. □

Remark 3.16 From Theorem 3.15, we observe that, depending on the boundary conditions and channel geometry, in terms of (α, β), a small positive permanent charge

(i) can reduce the fluxes of both cations and enhance that of anion;
(ii) can enhance the fluxes of both cations and anion;
(iii) can reduce the fluxes of both cations and anion;
(iv) but cannot enhance the flux of any cation while reduce that of anion.

This observation is consistent with the result obtained in Ji et al. (2015) (Theorems 4.7 and 4.8) for the PNP system with just one cation and one onion. A conjecture we would like to make here is that for the classical PNP model, the small positive permanent charge cannot enhance the flux of any cation while reduce that of anion assuming only one type of anion included!

3.2.3 Monotonicity of J_{k1}

In this section, we focus on the monotonicity of the leading terms J_{k1} as functions of the potential V for fixed boundary concentrations.

To get started, we point out that a similar argument as that in the proof of lemma 3.5 provides sufficient conditions to determine the sign of the quantity C defined by

$$C = \frac{1}{1-N}\Big(\frac{z}{z_3}\ln t - (\ln t + 2)(1-N)\Big), \tag{3.8}$$

which will be used in the proof of Theorem 3.18.

Lemma 3.17 *Set* $t = L/R > 1$ *with* $\gamma(t)$ *being as in* (3.7). *One has*

(i) *if* $\alpha \geq \gamma(t)$, *then,* $C < 0$ *for* $\beta \in (\alpha, 1)$;
(ii) *if* $\alpha < \gamma(t) < \alpha - \frac{z}{z_3(\ln t+2)}$, *then,* $C > 0$ *for* $\beta \in (\alpha, \beta_1)$ *and* $C < 0$ *for* $\beta \in (\beta_1, 1)$.
(iii) *if* $\gamma(t) > \alpha - \frac{z}{z_3(\ln t+2)}$, *then, there exists a unique* $\bar{\beta}_1 \in (\alpha, \beta_1)$ *such that* $C < 0$ *for* $\beta \in (\alpha, \bar{\beta}_1)$; $C = 0$ *for* $\beta = \bar{\beta}_1$; $C > 0$ *for* $\beta \in (\bar{\beta}_1, \beta_1)$ *and* $C < 0$ *for* $\beta \in (\beta_1, 1)$.

Theorem 3.18 *Suppose that* $N \neq 1$. *For* $k = 1, 2$, *one has,*

(i) *for* J_{k1},

(i1) *if* $M(1-N) < 0$*, then, there exists a critical* V_{k1}^1 *between* V_2 *and* V_{k+2} *such that* $J_{k1}(V)$ *decreases on* $(-\infty, V_{k1}^1)$ *and increases on* $(V_{k1}^1, +\infty)$*;*
(i2) *if* $M(1-N) > 0$*, then, there exists a critical* V_{k1}^2 *between* V_2 *and* V_{k+2} *such that* $J_{k1}(V)$ *increases on* $(-\infty, V_{k1}^2)$ *and decreases on* $(V_{k1}^2, +\infty)$.

(ii) *for* J_{31},

(ii1) *if* $M(1-N) < 0$*, then, there exists a critical* $V_{31}^1 = \frac{1}{2}\left(\frac{z}{z_3}V_1 + \frac{z_3}{z}V_2\right)$ *between* $\frac{z}{z_3}V_1$ *and* $\frac{z_3}{z}V_2$ *such that* $J_{31}(V)$ *increases on* $(-\infty, V_{31}^1)$ *and decreases on* $(V_{31}^1, +\infty)$*;*
(ii2) *if* $M(1-N) > 0$*, then, there exists a critical* $V_{31}^2 = \frac{1}{2}\left(\frac{z}{z_3}V_1 + \frac{z_3}{z}V_2\right)$ *between* $\frac{z}{z_3}V_1$ *and* $\frac{z_3}{z}V_2$ *such that* $J_{31}(V)$ *decreases on* $(-\infty, V_{31}^2)$ *and increases on* $(V_{31}^2, +\infty)$.

In particular, for $N = 1$*, one has,* $J_{11}(V)$*,* $J_{21}(V)$ *and* $J_{31}(V)$ *decrease in* V.

Proof We defer the proof to the "Appendix Sect. 6". □

3.3 Effect of Channel Geometry on Magnitudes of J_{k1}

Recall that $0 \le \alpha \le \beta \le 1$. Rewrite J_{k1}, $k = 1, 2$ and J_{31} as

$$\begin{aligned} J_{k1} =& \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \frac{p_1(\alpha,\beta)\left(L_k - R_k e^{-zV}\right)}{(z - z_3)H(1)\,(\ln L - \ln R)^2}, \\ J_{31} =& \frac{(z_3V + \ln L - \ln R)\; p_2(\alpha,\beta)}{(z_3 - z)H(1)\,(\ln L - \ln R)^2}, \end{aligned}$$

where

$$\begin{aligned} p_1(\alpha,\beta) &= \frac{(\alpha-\beta)\,(L-R)^2\,(\ln L - \ln R + z_3V)}{\omega(\alpha)\omega(\beta)\,(\ln L - \ln R)} - z_3V\ln\frac{\omega(\beta)}{\omega(\alpha)}, \\ p_2(\alpha,\beta) &= \frac{(\alpha-\beta)\,(L-R)^2\,(\ln L - \ln R + zV)}{\omega(\alpha)\omega(\beta)\,(\ln L - \ln R)} - zV\ln\frac{\omega(\beta)}{\omega(\alpha)}. \end{aligned}$$

Lemma 3.19 *Set* $t = L/R$*. One has*

(i) *If* $\gamma_1^* = \gamma(t) - \frac{1}{z_3V} \in (0,1)$*, then, the maximum of* $|p_1(\alpha,\beta)|$ *occurs when either* $(\alpha,\beta) = (0,\gamma_1^*)$ *or* $(\alpha,\beta) = (\gamma_1^*, 1)$*. Otherwise, the maximum of* $|p_1(\alpha,\beta)|$ *occurs when* $(\alpha,\beta) = (0,1)$.
(ii) *If* $\gamma_2^* = \gamma(t) - \frac{1}{zV} \in (0,1)$*, then, the maximum of* $|p_2(\alpha,\beta)|$ *occurs when either* $(\alpha,\beta) = (0,\gamma_2^*)$ *or* $(\alpha,\beta) = (\gamma_2^*, 1)$*. Otherwise, the maximum of* $|p_2(\alpha,\beta)|$ *occurs when* $(\alpha,\beta) = (0,1)$.

Proof We just prove the first statement for $p_1(\alpha, \beta)$ and the statement for $p_2(\alpha, \beta)$ can be argued similarly. Direct computation gives

$$\partial_\alpha p_1(\alpha, \beta) = \frac{(L-R)^2(\ln L - \ln R + z_3 V)}{\omega(\alpha)^2(\ln L - \ln R)} - \frac{z_3 V(L-R)}{\omega(\alpha)},$$
$$\partial_\beta p_1(\alpha, \beta) = -\frac{(L-R)^2(\ln L - \ln R + z_3 V)}{\omega(\beta)^2(\ln L - \ln R)} + \frac{z_3 V(L-R)}{\omega(\beta)}.$$

It follows that any critical point (α, β) satisfies $\alpha = \beta$, where p_1 vanishes. Since $p_1(\alpha, \alpha) = 0$ is the minimum of $|p_1(\alpha, \beta)|$. Therefore, $|p_1(\alpha, \beta)|$ must attain its maximum on the boundary of Ω,

$$\big\{\alpha = 0, \beta \in [0, 1]\} \cup \{\alpha \in [0, 1], \beta = 1\big\}.$$

Careful calculation shows that the critical point of $p_1(0, \beta)$ is $\beta = \gamma_1^*$, and the critical point of $p_1(\alpha, 1)$ is $\alpha = \gamma_1^*$, where $\gamma_1^* = \gamma(t) - \frac{1}{z_3 V}$. Obviously, if $\gamma(t) - 1 < \frac{1}{z_3 V} < \gamma(t)$, then $\gamma_1^* \in (0, 1)$, where $t = L/R$ and $\gamma(t) \in (0, 1)$ is given in (3.7).

Now we compare $p_1(0, \gamma_1^*)$, $p_1(\gamma_1^*, 1)$ and $p_1(0, 1)$ to determine the maximum value of $|p_1(\alpha, \beta)|$.

Direct calculation gives

$$p_1(0, \gamma_1^*) = -\Big(1 - \frac{\omega_1}{L} + \ln\frac{\omega_1}{L}\Big)z_3 V, \quad p_1(\gamma_1^*, 1) = \Big(1 - \frac{\omega_1}{R} + \ln\frac{\omega_1}{R}\Big)z_3 V,$$

where

$$\omega_1 = (1 - \gamma_1^*)L + \gamma_1^* R = \frac{(L-R)(\ln L - \ln R + z_3 V)}{(\ln L - \ln R)z_3 V}.$$

Note that $1 - x + \ln x \le 0$ for any $x > 0$ and $\omega_1 = (1 - \gamma^*)L + \gamma^* R > 0$, since $0 < \gamma_1^* < 1$, which indicates that $p_1(0, \gamma_1^*)$ and $p_1(\gamma_1^*, 1)$ have opposite signs. Note also that $p_1(0, \gamma_{p_1}^*) + p_1(\gamma_1^*, 1) = p_1(0, 1)$. Therefore, for the case $\gamma^* \in (0, 1)$, $|p_1(\alpha, \beta)|$ attains its maximum at either $(0, \gamma_1^*)$ or $(\gamma_1^*, 1)$; otherwise, $|p_1(\alpha, \beta)|$ attains its maximum at $(0, 1)$. □

From Lemma 3.19, one has

Theorem 3.20 *If* $\gamma_1^* \notin (0, 1)$*, then,* $|J_{11}|$ *and* $|J_{21}|$ *attain their maximums at* $(0, 1)$*. If* $\gamma_1^* \notin (0, 1)$*, then,* $|J_{11}|$ *and* $|J_{21}|$ *attain their maximums at either* $(0, \gamma_1^*)$ *or* $(\gamma_1^*, 1)$.

If $\gamma_2^* \notin (0, 1)$*, then,* $|J_{31}|$ *attains its maximum at* $(0, 1)$*. If* $\gamma_2^* \notin (0, 1)$*, then,* $|J_{31}|$ *attains its maximum at either* $(0, \gamma_2^*)$ *or* $(\gamma_2^*, 1)$.

To further understand the above result, we add the following remark first mentioned in Ji et al. (2015) for a simpler setups.

Remark 3.21 Recall from (3.5) that $\alpha = H(a)/H(1)$ and $\beta = H(b)/H(1)$. One can easily see that $\alpha \approx 0$ and $\beta \approx 1$ could be realized in the following two ways:

(I) $(a, b) \approx (0, 1)$ and $h(x)$ is uniform for $x \in (0, 1)$;
(II) $b - a \ll 1$ and $h(x)$ for $x \in (a, b)$ is much smaller than $h(x)$ for $x \notin [a, b]$.

Obviously, setting (II) indicates that the filter of the channel to which the permanent charge is distributed is short and narrow. Notice that, to produce the same permanent charge *density* Q_0, it requires much more *numbers* of charges for setting (I) compared to setting (II). In this sense, for ion channels, setting (II) is optimal for effects on ionic flows from permanent charges.

One can also check that, if $\gamma^* \in [0, 1]$, then the "optimal" setting is as follows (we take J_{11} for example):

(i) If $(\alpha, \beta) = (\gamma^*, 1)$ provides the maximum of $|J_{11}|$, then, there exists some parameter $c \in (0, a)$ such that $b - c \ll 1$, and $h(x)$ is small for $x \in [c, b]$ (in particular, for $x \in [a, b]$) and large otherwise;
(ii) If $(\alpha, \beta) = (0, \gamma^*)$ provides the maximum of $|J_{11}|$, then, there exists some parameter $c \in (b, 1)$ such that $c - a \ll 1$, and $h(x)$ is small for $x \in [a, c]$ and large otherwise.

It turns out that for all cases, $h(x)$ should be small for $x \in [a, b]$ and $b - a \ll 1$, in other words, the channel filter to which the permanent charge is distributed should be short and narrow. This is consistent with the typical structure of an ion channel.

We finally comment that for both the simpler case studied in Ji et al. (2015) and the more realistic and complicated one considered in this work, a stable structure of an ion channel is observed through rigorous mathematical analysis, that is, the filter of the ion channel, where the permanent charge is distributed, should be "narrow" and "short" in order to optimize the effect of permanent charges. This is consistent with the typical structure of an ion channel.

4 Competitions Between Cations

We focus on the competition between two positively charged ion species that depends on the nonlinear interplays among system parameters, particularly, permanent charges (Q_0), channel geometry (α, β), diffusion coefficients (D_1, D_2) and boundary conditions $(L_1, L_2, L_3, R_1, R_2, R_3; V)$, which is closely related to the selectivity phenomena of ion channels.

We first define $\mathcal{J}_{1,2}(V)$ as

$$\mathcal{J}_{1,2}(V) = D_1 J_1(V) - D_2 J_2(V) = \mathcal{J}^0_{1,2}(V) + \mathcal{J}^1_{1,2}(V) Q + O(Q^2), \tag{4.1}$$

where, for $N \neq 1$,

$$\begin{aligned}
\mathcal{J}^0_{1,2}(V) =& D_1 J_{10}(V) - D_2 J_{20}(V) \\
=& \frac{L - R}{H(1)\,(\ln L - \ln R)} \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \left(L^-_d - R^-_d e^{-zV} \right), \\
\mathcal{J}^1_{1,2}(V) =& D_1 J_{11}(V) - D_2 J_{21}(V)
\end{aligned}$$

$$
= \frac{Mzz_3(1-N)}{(z-z_3)H(1)\,(\ln L - \ln R)^2} \frac{(V-V_1)\,(V-V_2)}{L-Re^{-zV}} \Big(L_d^- - R_d^- e^{-zV} \Big). \tag{4.2}
$$

In particular, for $N=1$, one has

$$
\mathcal{J}_{1,2}^1(V) = \frac{\ln L - \ln R + zV}{L - Re^{-zV}} \frac{\big(\ln\omega(\beta) - \ln\omega(\alpha)\big)\big(L_d^- - R_d^- e^{-zV}\big)}{(z-z_3)H(1)\,(\ln L - \ln R)}. \tag{4.3}
$$

This section consists of four parts based on the distinct interplays among $\frac{D_1}{D_2}$, $\frac{L_2}{L_1}$ and $\frac{R_2}{R_1}$, which strongly indicates the complexity and the rich dynamics of ionic flows through membrane channels. In the first three parts, our analysis will focus on the sign of $\mathcal{J}_{1,2}^1(V)$ as a function of the potential V, which provides important information of the preference of the ion channel over different cations; and the monotonicity of $\mathcal{J}_{1,2}^1(V)$, which provides insights into the control/adjustment of system parameters to enhance/reduce the preference. Meanwhile, they reflect the effect from positive small permanent changes on ionic flows. The fourth part focus on the magnitude of $\mathcal{J}_{1,2}(V)$, which is equivalent to studying the sign of $\mathcal{J}_{1,2}^0(V)\mathcal{J}_{1,2}^1(V)$.

4.1 Case Study with $\frac{D_1}{D_2} = \frac{R_2}{R_1}$

We analyze the term $\mathcal{J}_{1,2}^1$, which reflects the preference of the ion channel over different cation under the condition $\frac{D_1}{D_2} = \frac{R_2}{R_1}$.

We first give the sufficient conditions to determine the sign of $2+z\,(V_1-V_2)$ which will be used in the proof of Theorem 4.2. Note that, for $N \neq 1$,

$$
2 + z\,(V_1 - V_2) = \frac{1}{1-N}\Big((2-\ln t)(1-N) + \frac{z}{z_3}\ln t\Big).
$$

The following result can be directly established.

Lemma 4.1 *Set $t = L/R$ and $\gamma(t)$ be as in (3.7). One has*

(i) *For $t > e^2$,*

- (i1) *if $\alpha \ge \gamma(t)$, then, $2 + z\,(V_1 - V_2) < 0$, for $\beta \in (\alpha, 1)$;*
- (i2) *if $\alpha < \gamma(t) < \alpha - \frac{z}{z_3(\ln t - 2)}$, then, $2 + z\,(V_1 - V_2) > 0$, for $\beta \in (\alpha, \beta_1)$, $2 + z\,(V_1 - V_2) < 0$, for $\beta \in (\beta_1, 1)$.*
- (i3) *if $\gamma(t) > \alpha - \frac{z}{z_3(\ln t - 2)}$, then, there exists a unique $\tilde{\beta}_1 \in (\alpha, \beta_1)$ such that $2 + z\,(V_1 - V_2) < 0$ for $\beta \in (\alpha, \tilde{\beta}_1)$, $2 + z\,(V_1 - V_2) = 0$ for $\beta = \tilde{\beta}_1$, $2 + z\,(V_1 - V_2) > 0$ for $\beta \in (\tilde{\beta}_1, \beta_1)$, $2 + z\,(V_1 - V_2) < 0$ for $\beta \in (\beta_1, 1)$.*

(ii) *For $t = e^2$,*

- (ii1) *if $\alpha \ge \gamma(t)$, then, $2 + z\,(V_1 - V_2) < 0$ for $\beta \in (\alpha, 1)$;*
- (ii2) *if $\alpha < \gamma(t)$, then, $2 + z\,(V_1 - V_2) > 0$ for $\beta \in (\alpha, \beta_1)$; $2 + z\,(V_1 - V_2) < 0$ for $\beta \in (\beta_1, 1)$.*

(iii) *For* $1 < t < e^2$,

(iii1) *if* $\alpha \geq \gamma(t)$ *and* $e^{\frac{2z_3}{z_3-z}} < t < e^2$, *then,* $2 + z(V_1 - V_2) < 0$ *for* $\beta \in (\alpha, 1)$*;*

(iii2) *if* $\alpha - \frac{z}{z_3(\ln t - 2)} < \gamma(t) \leq \alpha$ *and* $1 < t < e^{\frac{2z_3}{z_3-z}}$, *then, there exists a unique* $\tilde{\beta}_2 \in (\alpha, 1)$ *such that* $2 + z(V_1 - V_2) < 0$ *for* $\beta \in (\alpha, \tilde{\beta}_2)$*;* $2 + z(V_1 - V_2) = 0$ *for* $\beta = \tilde{\beta}_2$*;* $2 + z(V_1 - V_2) > 0$ *for* $\beta \in (\tilde{\beta}_2, 1)$.

(iii3) *if* $\gamma(t) < \alpha - \frac{z}{z_3(\ln t - 2)}$, *then,* $2 + z(V_1 - V_2) > 0$ *for* $\beta \in (\alpha, 1)$*;*

(iii4) *if* $\alpha < \gamma(t)$ *and* $e^{\frac{2z_3}{z_3-z}} < t < e^2$, *then,* $2 + z(V_1 - V_2) > 0$ *for* $\beta \in (\alpha, \beta_1)$*; and* $2 + z(V_1 - V_2) < 0$ *for* $\beta \in (\beta_1, 1)$*;*

(iii5) *if* $\gamma(t) > \alpha$ *and* $1 < t < e^{\frac{2z_3}{z_3-z}}$, *then, there exists a unique* $\tilde{\beta}_3 \in (\beta_1, 1)$ *such that* $2 + z(V_1 - V_2) > 0$ *for* $\beta \in (\alpha, \beta_1)$*;* $2 + z(V_1 - V_2) < 0$ *for* $\beta \in (\beta_1, \tilde{\beta}_3)$*;* $2 + z(V_1 - V_2) = 0$ *for* $\beta = \tilde{\beta}_3$*; and* $2 + z(V_1 - V_2) > 0$ *for* $\beta \in (\tilde{\beta}_3, 1)$.

Theorem 4.2 *Assume* $N \neq 1$ *and* $\frac{D_1}{D_2} = \frac{R_2}{R_1}$. *One has*

(i) *if* $M(1 - N)L_d^- < 0$, *then, there exists a critical* V_c^{11} *with* $V_c^{11} < V_2$ *such that* $\mathcal{J}_{1,2}^1$ *decreases on* $(-\infty, V_c^{11})$ *and increases on* (V_c^{11}, ∞). *Additionally,* $\mathcal{J}_{1,2}^1 < 0$ *for* $V < V_2$*;* $\mathcal{J}_{1,2}^1 = 0$ *for* $V = V_2$*; and* $\mathcal{J}_{1,2}^1 > 0$, *for* $V > V_2$*; that is, (small) positive permanent charge reduces* $\mathcal{J}_{1,2}$ *for* $V < V_2$ *while enhances* $J_{1,2}$ *for* $V > V_2$*, and the effect is balanced for* $V = V_2$.

(ii) *if* $M(1 - N)L_d^- > 0$, *then, there exists a critical* V_c^{12} *with* $V_c^{12} < V_2$ *such that* $\mathcal{J}_{1,2}^1$ *increases on* $(-\infty, V_c^{12})$ *and decreases on* (V_c^{12}, ∞). *Additionally,* $\mathcal{J}_{1,2}^1 > 0$ *for* $V < V_2$*;* $\mathcal{J}_{1,2}^1 = 0$ *for* $V = V_2$*; and* $\mathcal{J}_{1,2}^1 < 0$ *for* $V > V_2$*; that is, (small) positive permanent charge enhances* $\mathcal{J}_{1,2}$ *for* $V < V_2$ *while reduces* $J_{1,2}$ *for* $V > V_2$*, and the effect is balanced for* $V = V_2$.

In particular, for $N = 1$, *one has, if* $\frac{D_1}{D_2} < \frac{L_2}{L_1}$ *(resp.* $\frac{D_1}{D_2} > \frac{L_2}{L_1}$*), then,* $\mathcal{J}_{1,2}^1(V)$ *increases (resp. decreases) in the potential* V*; and* $\mathcal{J}_{1,2}^1(V) > 0$ *(resp.* $\mathcal{J}_{1,2}^1(V) < 0$*), that is, (small) positive permanent charge enhances (resp. reduces)* $\mathcal{J}_{1,2}$.

Proof We just prove the first statement with $N \neq 1$ here, and the second one can be proved by a similar argument. The case with $N = 1$ can be verified directly from (4.3). For $\frac{D_1}{D_2} = \frac{R_2}{R_1}$, one has, from (4.2),

$$\mathcal{J}_{1,2}^1(V) = D_1 J_{11} - D_2 J_{21} = \frac{Mzz_3(1-N)L_d^-}{(z - z_3)H(1)(\ln L - \ln R)^2} \frac{(V - V_1)(V - V_2)}{L - Re^{-zV}}.$$

It follows that

$$\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} = \frac{Mzz_3(1-N)L_d^-}{(z - z_3)H(1)(\ln L - \ln R)^2} \frac{e^{-zV}}{\left(L - Re^{-zV}\right)^2} f_{d1}(V),$$

where

$$f_{d1}(V) = (2V - V_1 - V_2)\left(Le^{zV} - R\right) - z(R_1 + R_2)(V - V_1)(V - V_2),$$

and further

$$f'_{d1}(V) = \frac{\mathrm{d}f_{d1}}{\mathrm{d}V} = \left(Le^{zV} - R\right)\left(2 + z\left(2V - V_1 - V_2\right)\right). \tag{4.4}$$

From (4.4), $f'_{d1}(V)$ has two zeros V_1 and $V_{d1} = \frac{1}{2}\left(V_1 + V_2 - \frac{2}{z}\right)$. To determine the order of V_1 and V_{d1}, one just need to study the sign of $2 + z\,(V_1 - V_2)$. In fact, if $2 + z\,(V_1 - V_2) > 0$, then $V_1 > V_{d1}$, if $2 + z\,(V_1 - V_2) = 0$, then $V_1 = V_{d1}$, if $2 + z\,(V_1 - V_2) < 0$, then $V_1 < V_{d1}$.

Lemma 4.1 show the sufficient conditions to determine the sign of $2+z\,(V_1 - V_2)$, and hence further determine the order of V_1 and V_{d1}.

If $V_1 < V_{d1}$, then $f_{d1}(V)$ increases on $(-\infty, V_1)$, decreases on (V_1, V_{d1}), and increases on (V_{d1}, ∞). Note that $f_{d1}(V_1) = 0$, which is a local maximum of f_{d1}, $\lim\limits_{V\to-\infty} f_{d1} = -\infty$ and $\lim\limits_{V\to\infty} f_{d1} = \infty$, f_{d1} has the other zero V_c^{11} with $V_c^{11} > V_1$. Furthermore, if $M(1 - N)L_d^- < 0$, then

$$\lim_{V\to V_1} \frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} = \frac{Mz_3(1 - N)L_d^-\,(2 + z\,(V_1 - V_2))}{2(z - z_3)H(1)\,(\ln L - \ln R)^2\,L} < 0,$$

since $2 + z\,(V_1 - V_2) < 2 + z\,(2V_{d1} - V_1 - V_2) = 0$, which can be obtained from the fact that $2+z\,(2V - V_1 - V_2)$ increases on $(-\infty, V_{d1})$ and $V_1 < V_{d1}$. Therefore, $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} > 0$ if $V > V_c^{11}$ and $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} < 0$ if $V < V_c^{11}$ (also true for $V_1 \geq V_{d1}$, which can be proved similarly). Statement (i) follows from $\lim\limits_{V\to\infty} \mathcal{J}_{1,2}^1 = \infty$ and $\lim\limits_{V\to-\infty} \mathcal{J}_{1,2}^1 = 0$. □

4.2 Case Study with $\frac{D_1}{D_2} > \max\left\{\frac{L_2}{L_1}, \frac{R_2}{R_1}\right\}$

We study the term $\mathcal{J}_{1,2}^1$, which provides information of the preference of the ion channel over different cation under the condition $\frac{D_1}{D_2} > \max\left\{\frac{L_2}{L_1}, \frac{R_2}{R_1}\right\}$.

To get started, we introduce the following result, which is crucial to study the sign of the term $\mathcal{J}_{1,2}^1$ as a function of the potential V.

Lemma 4.3 *Set $t = L/R > 1$ and $\gamma(t)$ be as in (3.7). Suppose that $L_d^- R_d^- > 0$. One has*

(i) $M(1 - N) > 0$ *and* $V_2 < V_5$ *under one of the following conditions*

(i1) $t > 1 > L_d^-/R_d^-$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;

(i2) $t > L_d^-/R_d^- > 1$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;

(i3) $t > 1 > L_d^-/R_d^-$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1)$;

(i4) $t > L_d^-/R_d^- > 1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1^*, \beta_1)$.

(ii) $M(1-N) > 0$ *and* $V_2 > V_5$ *if* $t < L_d^-/R_d^-$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\alpha, \beta_1^*]$.

(iii) $M(1 - N) < 0$ *and* $V_2 > V_5$ *under one of the following conditions*

(iii1) $L_d^-/R_d^- > 1$ *and* $\alpha \geq \gamma(t)$*;*
(iii2) $L_d^-/R_d^- > 1$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1, 1)$*;*
(iii3) $L_d^-/R_d^- > 1$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ *and* $\beta \in (\beta_1, 1)$.

Proof We only prove case (i), other cases can be proved similarly. Now we prove (i1)–(i4) one by one.

(i1) If $t > 1 > L_d^-/R_d^-$, $\alpha < \gamma(t) < \alpha - \frac{z}{z_3 \ln t}$ and $\beta \in (\alpha, \beta_1)$, then, $M < 0$ from Lemma 3.4 and $\frac{z}{z_3} < 1 - N < 0$ from the statement (ii) of Lemma 3.5. Thus, $M(1-N) > 0$ and $\frac{1}{z_3(1-N)} > \frac{1}{z} > 0$. Note that $\ln \frac{L}{R} > 0 > \ln \frac{L_d^-}{R_d^-}$. We have $\frac{1}{z_3(1-N)} \ln \frac{L}{R} > 0 > \frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, and further, $-\frac{1}{z_3(1-N)} \ln t < 0 < -\frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, that is, $V_2 < 0 < V_5$.

(i2) A similar argument as that in (i1) yields $M(1-N) > 0$ and $\frac{1}{z_3(1-N)} > \frac{1}{z} > 0$. Note that $\ln \frac{L}{R} > \ln \frac{L_d^-}{R_d^-} > 0$. We have $\frac{1}{z_3(1-N)} \ln \frac{L}{R} > \frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, and further, $-\frac{1}{z_3(1-N)} \ln t < -\frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, that is, $V_2 < V_5$.

(i3) If $t > 1 > L_d^-/R_d^-$, $\gamma(t) > \alpha - \frac{z}{z_3 \ln t}$ and $\beta \in (\alpha, \beta_1)$, then, $M < 0$ from Lemma 3.4 and $1 - N < 0$ from statement (iii) of Lemma 3.5. Thus, $M(1-N) > 0$ and $\frac{1}{z_3(1-N)} > 0$. Note that $\frac{1}{z} > 0$ and $\ln \frac{L}{R} > 0 > \ln \frac{L_d^-}{R_d^-}$. One has $\frac{1}{z_3(1-N)} \ln \frac{L}{R} > 0 > \frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, and further, $-\frac{1}{z_3(1-N)} \ln t < 0 < -\frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, that is, $V_2 < 0 < V_5$.

(i4) A similar argument as that in (i3) gives $M(1-N) > 0$ and $\frac{1}{z_3(1-N)} > \frac{1}{z} > 0$. Note that $\ln \frac{L}{R} > \ln \frac{L_d^-}{R_d^-} > 0$. We have $\frac{1}{z_3(1-N)} \ln \frac{L}{R} > \frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, and further, $-\frac{1}{z_3(1-N)} \ln t < -\frac{1}{z} \ln \frac{L_d^-}{R_d^-}$, that is, $V_2 < V_5$.

□

It follows from Lemma 4.3 that

Theorem 4.4 *Assume* $N \neq 1$ *and* $\frac{D_1}{D_2} > \max\left\{\frac{L_2}{L_1}, \frac{R_2}{R_1}\right\}$*. Then,*

(i) *For* $M(1-N) < 0$ *and* $V_2 > V_5$*, one has,* $\mathcal{J}_{1,2}^1(V) > 0$ *if* $V < V_5$ *or* $V > V_2$*;* $\mathcal{J}_{1,2}^1(V) < 0$ *if* $V_5 < V < V_2$*, that is, (small) positive permanent charge enhances* $\mathcal{J}_{1,2}(V)$ *if* $V < V_5$ *or* $V > V_2$*, and reduces* $\mathcal{J}_{1,2}(V)$ *if* $V_5 < V < V_2$*. Furthermore, there exists a critical potential* V_c^{31} *between* V_2 *and* V_5 *such that* $\mathcal{J}_{1,2}^1(V)$ *decreases on* $(-\infty, V_c^{31})$ *and increases on* $(V_c^{31}, +\infty)$*.*

(ii) *For* $M(1-N) > 0$*,*

(ii1) *For* $V_2 > V_5$*, one has,* $\mathcal{J}_{1,2}^1(V) < 0$ *if* $V < V_5$ *or* $V > V_2$*;* $\mathcal{J}_{1,2}^1(V) > 0$ *if* $V_5 < V < V_2$*, that is, (small) positive permanent charge reduces* $\mathcal{J}_{1,2}(V)$ *if* $V < V_5$ *or* $V > V_2$*, and enhances* $\mathcal{J}_{1,2}(V)$ *if* $V_5 < V < V_2$*;*

(ii2) *For* $V_2 < V_5$*, one has,* $\mathcal{J}_{1,2}^1(V) < 0$ *if* $V < V_2$ *or* $V > V_5$*;* $\mathcal{J}_{1,2}^1(V) > 0$ *if* $V_2 < V < V_5$*, that is, (small) positive permanent charge reduces* $\mathcal{J}_{1,2}(V)$ *if* $V < V_2$ *or* $V > V_5$*, and enhances* $\mathcal{J}_{1,2}(V)$ *if* $V_2 < V < V_5$*.*

Furthermore, there exists a critical potential V_c^{32} between V_2 and V_5 such that $\mathcal{J}_{1,2}^1(V)$ increases on $(-\infty, V_c^{32})$ and decreases on $(V_c^{32}, +\infty)$.

In particular, for $N = 1$, one has $\mathcal{J}_{1,2}^1(V) > 0$ (resp. $\mathcal{J}_{1,2}^1(V) < 0$) if $V < V_5$ (resp. $V > V_5$), that is, (small) positive permanent charge enhances (resp. reduces) $\mathcal{J}_{1,2}(V)$ if $V < V_5$ (resp. $V > V_5$). Additionally, $\mathcal{J}_{1,2}^1$ decreases in the potential V.

4.3 Case Study with $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$

We study the term $\mathcal{J}_{1,2}^1(V)$, which provides information of the preference of the ion channel over different cation under the condition $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$.

For $N \neq 1$, we first define a function $h(V)$ by

$$h(V) = -4L_d^- R_d^- - (L_d^-)^2 e^{zV} - (R_d^-)^2 e^{-zV}.$$

The following result can be easily established, and will be used in the proof of Theorem 4.6.

Lemma 4.5 *Assume $N \neq 1$ and $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$. There exists two zeroes of $h(V)$, V_z^1 and V_z^2 with $V_z^1 < V_z^2$ such that $h(V) > 0$, for $V_z^1 < V < V_z^2$, and $h(V) < 0$, for $V < V_z^1$ or $V > V_z^2$.*

Theorem 4.6 *Assume $N \neq 1$ and $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$. One has*

(i) *For $M(1-N) < 0$, if $g_{d3}(V_{d3}) \geq 0$ (or $g_{d3}(V_{d3}) < 0$), $f_{d3}(V_z^3) > 0$ and $f_{d3}(V_z^4) > 0$, then, $\mathcal{J}_{1,2}^1(V)$ always increases; if $g_{d3}(V_{d3}) < 0$, and $f_{d3}(V_z^3) < 0$ (or $f_{d3}(V_z^4) < 0$), then, there exists two critical potentials V_c^{51} and V_c^{52} with $V_c^{51} < V_c^{52}$ such that $\mathcal{J}_{1,2}^1(V)$ increases on $(-\infty, V_c^{51})$, decreases on (V_c^{51}, V_c^{52}) and increases on (V_c^{52}, ∞). Furthermore, $\mathcal{J}_{1,2}^1(V) < 0$ for $V < V_2$; $\mathcal{J}_{1,2}^1(V_2) = 0$; and $\mathcal{J}_{1,2}^1(V) > 0$ for $V > V_2$; that is, (small) positive permanent charge reduces $\mathcal{J}_{1,2}$ for $V < V_2$ while enhances $J_{1,2}$ for $V > V_2$, and the effect is balanced for $V = V_2$.*

(ii) *For $M(1-N) > 0$, if $g_{d3}(V_{d3}) \geq 0$ (or $g_{d3}(V_{d3}) < 0$), $f_{d3}(V_z^3) > 0$ and $f_{d3}(V_z^4) > 0$, then, $\mathcal{J}_{1,2}^1(V)$ always decreases; if $g_{d3}(V_{d3}) < 0$, and $f_{d3}(V_z^3) < 0$ (or $f_{d3}(V_z^4) < 0$), then, there exists two critical potentials V_c^{61} and V_c^{62} with $V_c^{61} < V_c^{62}$ such that $\mathcal{J}_{1,2}^1(V)$ decreases on $(-\infty, V_c^{61})$, increases on (V_c^{61}, V_c^{62}) and decreases on (V_c^{62}, ∞). Furthermore, $\mathcal{J}_{1,2}^1(V) > 0$ for $V < V_2$; $\mathcal{J}_{1,2}^1(V_2) = 0$; and $\mathcal{J}_{1,2}^1(V) < 0$ for $V > V_2$; that is, (small) positive permanent charge enhances $\mathcal{J}_{1,2}$ for $V < V_2$ while reduces $J_{1,2}$ for $V > V_2$, and the effect is balanced for $V = V_2$.*

Here,

$$
\begin{aligned}
f_{d3}(V) =& (2V - V_1 - V_2)\left(L - Re^{-zV}\right)\left(L_d^- - R_d^- e^{-zV}\right)e^{zV} \\
&+ z\left(R_d^- L - L_d^- R\right)(V - V_1)(V - V_2), \qquad (4.5)\\
g_{d3}(V) =& 2\left(L_d^- - R_d^- e^{-zV}\right) + z(2V - V_1 - V_2)\left(L_d^- + R_d^- e^{-zV}\right).
\end{aligned}
$$

V_{d3} is the unique critical point of $g'_{d3}(V)$. V_z^3 and V_z^4 are two zeros of $g_{d3}(V)$ under the condition that $g_{d3}(V_{d3}) < 0$.

In particular, for $N = 1$, One has $\mathcal{J}_{1,2}^1(V) < 0$, that is, (small) positive permanent charge reduces $\mathcal{J}_{1,2}(V)$. Furthermore, there exists a critical V_c^5 such that $\mathcal{J}_{1,2}^1(V)$ increases on $(-\infty, V_c^5)$, and decreases on (V_c^5, ∞).

Proof We defer the proof to the “Appendix Sect. 6”. □

Remark 4.7 Recall that, with $Q_0 > 0$ small, one has $\mathcal{J}_{1,2}(V, Q_0) = \mathcal{J}_{1,2}^0(V) + Q_0\mathcal{J}_{1,2}^1(V) + o(Q_0)$. Further depending on the interaction among $\frac{D_1}{D_2}, \frac{R_2}{R_1}, \frac{L_2}{L_1}$, we analyze the leading term $\mathcal{J}_{1,2}^1(V)$, in particular, the sign of $\mathcal{J}_{1,2}^1(V)$, which characterizes the small positive permanent charge effects on the competition between two cations. To be specific, if $\mathcal{J}_{1,2}^1(V) > 0$ (resp. $\mathcal{J}_{1,2}^1(V) < 0$), then, the small positive permanent charge enhances (resp. reduces) $\mathcal{J}_{1,2}(V; Q_0)$, and in either way, it affects the preference of the ion channel over different cation. In other words, the sign of $\mathcal{J}_{1,2}^1(V)$ has impact on the selectivity of the ion channel. On the other hand, $\mathcal{J}_{1,2}^1(V) > 0$ (resp. $\mathcal{J}_{1,2}^1(V) < 0$), indicates $\mathcal{J}_{1,2}(V, Q_0) > \mathcal{J}_{1,2}(V; 0)$ (resp. $\mathcal{J}_{1,2}(V, Q_0) < \mathcal{J}_{1,2}(V; 0)$), but it does not provide any information on the relation of $|\mathcal{J}_{1,2}(V; Q_0)|$ and $|\mathcal{J}_{1,2}(V, 0)|$, which contains even more important information for the competition, and further depends on the sign of $\mathcal{J}_{1,2}^0(V)$. This is discussed in the next section.

4.4 Study on the Magnitude of $\mathcal{J}_{1,2}$

To end this section, we examine the effects from the small permanent charge on the magnitude of $\mathcal{J}_{1,2}(V; Q_0)$, which is equivalent to studying the sign of $\mathcal{J}_{1,2}^0(V)\mathcal{J}_{1,2}^1(V)$.

Recall from Lemma 3.4 that $M < 0$ if $L > R$. Together with (3.6), we have

Theorem 4.8 *Assume $t = L/R > 1$ and $N \neq 1$. One has*

(i) *if either $\alpha \geq \gamma(t)$, or $\alpha < \gamma(t)$ and $\beta \in (\beta_1, 1)$, then, $1 - N > 0$ and*

  (i1) *$\mathcal{J}_{1,2}^0(V)\mathcal{J}_{1,2}^1(V) > 0$ if $V > V_2$, that is, (small) positive permanent charge enhances $|\mathcal{J}_{1,2}(V)|$;*

  (i2) *$\mathcal{J}_{1,2}^0(V)\mathcal{J}_{1,2}^1(V) < 0$ if $V < V_2$, that is, (small) positive permanent charge reduces $|\mathcal{J}_{1,2}(V)|$.*

(ii) *if $\alpha < \gamma(t)$ and $\beta \in (\alpha, \beta_1)$, then, $1 - N < 0$ and* (ii1) $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V) > 0$ *if* $V < V_2$*, that is, (small) positive permanent charge enhances* $|\mathcal{J}_{1,2}(V)|$*;*

(ii2) $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V) < 0$ *if* $V > V_2$*, that is, (small) positive permanent charge reduces* $|\mathcal{J}_{1,2}(V)|$.

In particular, for $N = 1$*, one has* $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V) < 0$*, that is, (small) positive permanent charge reduces* $|\mathcal{J}_{1,2}(V)|$.

Proof From (4.2), the sign of $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V)$ is determined by the sign of $z_3M(1-N)(V-V_2)$. Together with Lemmas 3.4 and 3.5, one can easily establish the result. □

We point out that the study in this part further provides information of the preference of the ion channel over distinct cations. For convenience in the argument, we let S_1 represent the first cation corresponding to the flux $\mathcal{J}_1$ and S_2 be the cation corresponding to the flux $\mathcal{J}_2$.

For $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V) > 0$,

- if $\mathcal{J}_{1,2}^{0}(V) > 0$ and $\mathcal{J}_{1,2}^{1}(V) > 0$, then, the ion channel prefers the cation S_1 over the cation S_2, and the small positive permanent charge further enhances this preference;
- if $\mathcal{J}_{1,2}^{0}(V) < 0$ and $\mathcal{J}_{1,2}^{1}(V) < 0$, then, the ion channel prefers the cation S_2 over the cation S_1, and the small positive permanent charge further enhances this preference.

For $\mathcal{J}_{1,2}^{0}(V)\mathcal{J}_{1,2}^{1}(V) < 0$,

- if $\mathcal{J}_{1,2}^{0}(V) > 0$ and $\mathcal{J}_{1,2}^{1}(V) < 0$, then, the ion channel prefers the cation S_1 over the cation S_2, but the small positive permanent charge reduces this preference;
- if $\mathcal{J}_{1,2}^{0}(V) < 0$ and $\mathcal{J}_{1,2}^{1}(V) > 0$, then, the ion channel prefers the cation S_2 over the cation S_1, but the small positive permanent charge reduces this preference.

Our analysis for this concrete model provides some efficient way to adjust the boundary conditions (potential and concentration) to affect the preference of ion channels over distinct cations.

5 Concluding Remarks

In this work, we analyzed the small permanent charge effect on the individual fluxes for biological channels via a one-dimensional steady-state Poisson–Nernst–Planck system. Two specific structures of the PNP model mentioned in Sect. 2.1.1 (Proposition 2.2) and Sect. 2.1.2 (Eq. (2.16)), allows one to reduce the singularly perturbed boundary value problem to an algebraic system-the governing system (2.18). The significance of the governing system is: (i) it includes almost all relevant physical parameters, and (ii) once a solution of the governing system is obtained, the singular orbit (the zeroth-order approximation (in ε) solution of the boundary value problem) can be readily determined. Based on these specific structures of this concrete model, under the framework of the geometric singular perturbation theory, a singular orbit is obtained, from which explicit expressions of J_{k0} and J_{k1} are extracted. This makes it possible for one to further examine the dynamics of ionic flows.

Of particular interest are (i) the leading terms J_{k1} that contains small permanent charge effects, and (ii) competitions between cations, which depend on the complicated nonlinear interplays among system parameters, such as the diffusion coefficients (D_1, D_2), the channel geometry in terms of (α, β), the boundary conditions $(L_k, R_k; V),\ k = 1, 2, 3$ and so on. Among others, we find

- To optimize the permanent charge effects, a short and narrow filter, within which the permanent charge is confined, is expected (Theorem 3.20 and Remark 3.21);
- The small positive permanent charge cannot enhance the flux of any cation while reduce that of anion (Theorem 3.15 and Remark 3.16);
- The interaction among $\frac{D_1}{D_2}$, $\frac{R_2}{R_1}$ and $\frac{L_2}{L_1}$ plays a critical role in characterizing the competition between cations (Sects. 4.1–4.3).

Finally, we comment that the setup in this work is relatively simple, and may raise the concern about the feasibility. Indeed, cPNP is known to be reliable when the ionic mixture is dilute, but with more ion species and nonzero permanent charges included, the ionic mixture would be crowded. On the other hand, the setup is reasonable for semi-conductor problems and for synthetic channels. Furthermore, the study in this work is the first step for analysis of more realistic models. The simple model considered in this work allows us to obtain more explicit expressions of the ionic fluxes in terms of physical parameters of the problem so that we are able to extract concrete information on small permanent charge effects. Moreover, the analysis in this simpler setting provides important insights for the analysis and numerical studies of more realistic models.

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6 Appendix: Proofs of Some Results

6.1 Proof of Proposition 2.3

We will provide a detailed proof for statement (i), and the second statement can be argued in a similar way. To get started, we assume

$$z(\xi) = (\phi(\xi), u(\xi), c_1(\xi), c_2(\xi), c_3(\xi), J_1(\xi), J_2(\xi), J_3(\xi), \tau(\xi))$$

is a solution of the limiting fast system (2.3) from B_{j-1} to $\mathcal{Z}_j$; namely, $z(\xi) \in N^{[j-1,r]} = M^{[j-1,r]} \cap W^s(\mathcal{Z}_j)$. It follows that $J_1(\xi), J_2(\xi), J_3(\xi)$ are constants and $\tau(\xi) = x_{j-1}$. Notice that $z(0) \in B_{j-1}$ and $\lim_{\xi\to+\infty} z(\xi) = z(+\infty) \in \mathcal{Z}_j$. One has $\phi(0) = \phi^{[j-1]},\ c_k(0) = c_k^{[j-1]},\ u(+\infty) = 0$, and $z_1c_1(+\infty) + z_2c_2(+\infty) + z_3c_3(+\infty) + Q_j = 0$. Define $u(0) = u^{[j-1,r]}$. By the integrals in Proposition 2.2, we get

$$\ln c_k(\xi) + z_k\phi(\xi) = \ln c_k^{[j-1]} + z_k\phi^{[j-1]}.$$

Hence,

$$c_k(\xi) = c_k^{[j-1]} e^{-z_k\left(\phi(\xi)-\phi^{[j-1]}\right)}. \tag{6.1}$$

Now the first two equations in the limiting fast system (2.3) read

$$\phi' = u, \quad u' = -\sum_{k=1}^{3} z_k c_k^{[j-1]} e^{-z_k\left(\phi-\phi^{[j-1]}\right)} - Q_j, \tag{6.2}$$

which is a Hamiltonian system with a Hamiltonian function given by

$$H(\phi, u) = \frac{1}{2}u^2 - \sum_{k=1}^{3} c_k^{[j-1]} e^{-z_k\left(\phi-\phi^{[j-1]}\right)} + Q_j\phi.$$

Not difficult to see that the above Hamiltonian function is exactly the integral H_4 in Proposition 2.2 with the relation (6.1). The equilibria of (6.2) are given by

$$u = 0, \quad \sum_{k=1}^{3} z_k c_k^{[j-1]} e^{-z_k\left(\phi-\phi^{[j-1]}\right)} + Q_j = 0. \tag{6.3}$$

We now claim that $\phi^{[j-1,r]}$ is the unique solution of the second equation in (6.3). To get started, we let

$$f(\phi) = \sum_{k=1}^{3} z_k c_k^{[j-1]} e^{z_k\left(\phi^{[j-1]}-\phi\right)} + Q_j. \tag{6.4}$$

It is easy to see that $f'(\phi) = -\sum_{k=1}^{3} z_k^2 c_k^{[j-1]} e^{z_k\left(\phi^{[j-1]}-\phi\right)} < 0$, which implies that $f(\phi)$ is a decreasing function. Note that in our set-up, $z_1 > 0,\ z_2 > 0,\ z_3 < 0$ and $c_k^{[j-1]}$'s are positive, one has $f(\phi) \to -\infty$ as $\phi \to +\infty$ and $f(\phi) \to +\infty$ as $\phi \to -\infty$. Correspondingly, (6.3) has a unique solution.

Let $c_k(+\infty) = c_k^{[j-1,r]}$, then, from (6.1), one has $c_k^{[j-1,r]} = c_k^{[j-1]} e^{-z_k\left(\phi^{[j-1,r]}-\phi^{[j-1]}\right)}$. Evaluating the integral H_4 in Proposition 2.2 at $\xi = 0$ and $\xi \to +\infty$, we have

$$\frac{1}{2}u^2(0) - \sum_{k=1}^{3} c_k^{[j-1]} + Q_j\phi^{[j-1]} = -\sum_{k=1}^{3} c_k^{[j-1]} e^{-z_k\left(\phi^{[j-1,r]}-\phi^{[j-1]}\right)} + Q_j\phi^{[j-1,r]},$$

which gives the expression for $u^{[j-1,r]}$. The choice of the sign can be determined from the phase portrait sketched in Fig. 2.

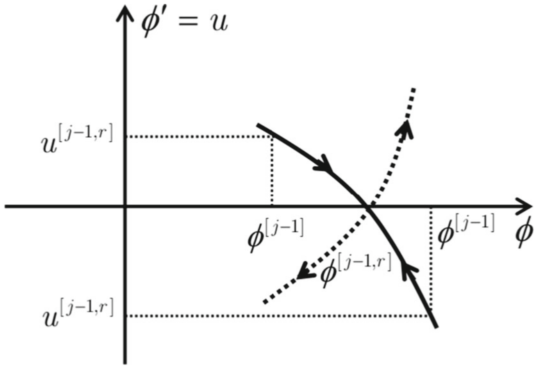

Fig. 2 The phase portrait for the Hamiltonian system (6.2). The sign of $u^{[j-1,r]}$ agrees with the sign of $\phi^{[j-1,r]} - \phi^{[j-1]}$

We now claim that the expressions under the square root in $u^{[j-1,r]}$ and $u^{[j,l]}$ are non-negative. We just provide the proof for the expression in $u^{[j-1,r]}$. Let

$$F(\phi) = \sum_{k=1}^{3} c_k^{[j-1]}\big(1 - e^{z_k(\phi^{[j-1]}-\phi)}\big) - Q_j\big(\phi^{[j-1]} - \phi\big).$$

Notice that $F'(\phi) = f(\phi)$ and $F''(\phi) = f'(\phi)$ where $f(\phi)$ is defined in (6.4). Since $f'(\phi) < 0$, one has $F(\phi)$ is concave down. Together with $F'(\phi^{[j-1,r]}) = f(\phi^{[j-1,r]}) = 0$, one has $F(\phi^{[j-1,r]})$ is the unique maximal value of $F(\phi)$, and in particular, $F(\phi^{[j-1,r]}) \geq F(\phi^{[j-1]}) = 0$.

Finally, we consider the transversal intersection of the stable manifold $W^s(\mathcal{Z}_j)$ and B_{j-1} at points $\big(\phi^{[j-1]}, u^{[j-1,r]}, c_1^{[j-1]}, c_2^{[j-1]}, c_3^{[j-1]}, J_1, J_2, J_3, x_{j-1}\big)$. From the above argument, they do intersect at the specified points, and one only need to verify the intersection is transversal. Since the stable manifold is completely characterized, one can compute its tangent space at each intersection point (via the complete set of first integrals obtained in Proposition 2.2) to verify the transversality of the intersection. It is slightly complicated but straightforward. We would like to omit the detail here. This completes the proof.

6.2 Proof of Proposition 2.8

Plugging (2.27) into (2.18), the zeroth-order system in Q_0 reads

$$\begin{aligned}
0 &= zc_{10}^{[1]} e^{z(\phi_0^{[1]}-\phi_0^{[1,r]})} + zc_{20}^{[1]} e^{z(\phi_0^{[1]}-\phi_0^{[1,r]})} + z_3 c_{30}^{[1]} e^{z_3(\phi_0^{[1]}-\phi_0^{[1,r]})},\\
0 &= zc_{10}^{[2]} e^{z(\phi_0^{[2]}-\phi_0^{[2,l]})} + zc_{20}^{[2]} e^{z(\phi_0^{[2]}-\phi_0^{[2,l]})} + z_3 c_{30}^{[2]} e^{z_3(\phi_0^{[2]}-\phi_0^{[2,l]})},\\
0 &= C_0^{[1]}\Big(e^{z(\phi_0^{[1]}-\phi_0^{[1,r]})} - e^{z(\phi_0^{[1]}-\phi_0^{[1,l]})}\Big) + c_{30}^{[1]}\Big(e^{z_3(\phi_0^{[1]}-\phi_0^{[1,r]})} - e^{z_3(\phi_0^{[1]}-\phi_0^{[1,l]})}\Big),\\
0 &= C_0^{[2]}\Big(e^{z(\phi_0^{[2]}-\phi_0^{[2,r]})} - e^{z(\phi_0^{[2]}-\phi_0^{[2,l]})}\Big) + c_{30}^{[2]}\Big(e^{z_3(\phi_0^{[2]}-\phi_0^{[2,r]})} - e^{z_3(\phi_0^{[2]}-\phi_0^{[2,l]})}\Big),
\end{aligned}$$

$$
\begin{aligned}
J_{10} =& \frac{C^{[0,r]} - C_0^{[1,l]}}{\ln C^{[0,r]} - \ln C_0^{[1,l]}} \cdot \frac{\ln C^{[0,r]} - \ln C_0^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}}{C^{[0,r]} - C_0^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}} \\
&\cdot \frac{c_1^{[0,r]} - c_{10}^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}}{H(x_1)} \\
=& \frac{C_0^{[2,r]} - C^{[3,l]}}{\ln C_0^{[2,r]} - \ln C^{[3,l]}} \cdot \frac{\ln C_0^{[2,r]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}}{C_0^{[2,r]} - C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}} \\
&\cdot \frac{c_{10}^{[2,r]} - c_1^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}}{H(1) - H(x_2)}, \\
J_{20} =& \frac{C^{[0,r]} - C_0^{[1,l]}}{\ln C^{[0,r]} - \ln C_0^{[1,l]}} \cdot \frac{\ln C^{[0,r]} - \ln C_0^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}}{C^{[0,r]} - C_0^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}} \\
&\cdot \frac{c_2^{[0,r]} - c_{20}^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}}{H(x_1)} \\
=& \frac{C_0^{[2,r]} - C^{[3,l]}}{\ln C_0^{[2,r]} - \ln C^{[3,l]}} \cdot \frac{\ln C_0^{[2,r]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}}{C_0^{[2,r]} - C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}} \\
&\cdot \frac{c_{20}^{[2,r]} - c_2^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}}{H(1) - H(x_2)}, \\
J_{30} =& -\frac{z}{z_3} \frac{C^{[0,r]} - C_0^{[1,l]}}{\ln C^{[0,r]} - \ln C_0^{[1,l]}} \frac{\ln C^{[0,r]} - \ln C_0^{[1,l]} e^{z(\phi_0^{[1,l]} - \phi^{[0,r]})}}{H(x_1)} \\
=& -\frac{z}{z_3} \frac{C_0^{[2,r]} - C^{[3,l]}}{\ln C_0^{[2,r]} - \ln C^{[3,l]}} \frac{\ln C_0^{[2,r]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2,r]})}}{H(1) - H(x_2)}, \\
\phi_0^{[2]} =& \phi_0^{[1]} - T_0^c y_{00}, \quad c_{10}^{[2,l]} = \frac{J_{20} c_{10}^{[1,r]} - J_{10} c_{20}^{[1,r]}}{J_{10} + J_{20}} e^{z T_0^c y_{00}} + \frac{J_{10} C_0^{[1,r]}}{J_{10} + J_{20}} e^{z z_3 T_0^m y_{00}}, \\
c_{20}^{[2,l]} =& \frac{J_{10} c_{20}^{[1,r]} - J_{20} c_{10}^{[1,r]}}{J_{10} + J_{20}} e^{z T_0^c y_{00}} + \frac{J_{20} C_0^{[1,r]}}{J_{10} + J_{20}} e^{z z_3 T_0^m y_{00}}, \\
T_0^m =& \frac{z_3 - z}{z_3} \frac{C_0^{[1]} - C_0^{[2]}}{H(x_2) - H(x_1)}.
\end{aligned} \tag{6.5}
$$

Recall that on $\mathcal{Z}_j$, one has $z_1 c_1 + z_2 c_2 + z_3 c_3 + Q_j = 0$. Plugging (2.27) into it, the zeroth-order terms in Q_0 gives

$$
c_{30}^{[1]} = -\frac{z}{z_3} C_0^{[1]}, \quad c_{30}^{[2]} = -\frac{z}{z_3} C_0^{[2]}. \tag{6.6}
$$

Plugging (6.6) into the first two equations of (6.5) gives

$$
\phi_0^{[1]} = \phi_0^{[1,r]} \quad \text{and} \quad \phi_0^{[2]} = \phi_0^{[2,l]}.
$$

From (2.19), one then has

$$\phi^{[0,r]} = V - \frac{1}{z - z_3} \ln \frac{-z_3 L_3}{zL},\ c_1^{[0,r]} = L_1\Big(\frac{-z_3 L_3}{zL}\Big)^{\frac{z}{z-z_3}},\ c_2^{[0,r]} = L_2\Big(\frac{-z_3 L_3}{zL}\Big)^{\frac{z}{z-z_3}},$$
$$c_3^{[0,r]} = L_3\Big(\frac{-z_3 L_3}{zL}\Big)^{\frac{z_3}{z-z_3}},\ \phi^{[3,l]} = -\frac{1}{z - z_3} \ln \frac{-z_3 R_3}{zR},\ c_1^{[3,l]} = R_1\Big(\frac{-z_3 R_3}{zR}\Big)^{\frac{z}{z-z_3}},$$
$$c_2^{[3,l]} = R_2\Big(\frac{-z_3 R_3}{zR}\Big)^{\frac{z}{z-z_3}},\ c_3^{[3,l]} = R_3\Big(\frac{-z_3 R_3}{zR}\Big)^{\frac{z_3}{z-z_3}},$$
$$\phi_0^{[1,l]} = \phi_0^{[1,r]} = \phi_0^{[1]},\ \phi_0^{[2,l]} = \phi_0^{[2,r]} = \phi_0^{[2]},\ c_{k0}^{[1,l]} = c_{k0}^{[1,r]} = c_{k0}^{[1]},\ c_{k0}^{[2,l]} = c_{k0}^{[2,r]} = c_{k0}^{[2]},$$

for $k = 1, 2, 3$, and further, from (6.5), we have

$$\begin{aligned}
J_{10} &= \frac{C^{[0,r]} - C_0^{[1]}}{\ln C^{[0,r]} - \ln C_0^{[1]}} \frac{\ln C^{[0,r]} - \ln C_0^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}}{C^{[0,r]} - C_0^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}} \frac{c_1^{[0,r]} - c_{10}^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}}{H(x_1)} \\
&= \frac{C_0^{[2]} - C^{[3,l]}}{\ln C_0^{[2]} - \ln C^{[3,l]}} \frac{\ln C_0^{[2]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}}{C_0^{[2]} - C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}} \frac{c_{10}^{[2]} - c_1^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}}{H(1) - H(x_2)}, \\
J_{20} &= \frac{C^{[0,r]} - C_0^{[1]}}{\ln C^{[0,r]} - \ln C_0^{[1]}} \frac{\ln C^{[0,r]} - \ln C_0^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}}{C^{[0,r]} - C_0^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}} \frac{c_2^{[0,r]} - c_{20}^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}}{H(x_1)} \\
&= \frac{C_0^{[2]} - C^{[3,l]}}{\ln C_0^{[2]} - \ln C^{[3,l]}} \frac{\ln C_0^{[2]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}}{C_0^{[2]} - C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}} \frac{c_{20}^{[2]} - c_2^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}}{H(1) - H(x_2)}, \\
J_{30} &= -\frac{z}{z_3} \frac{C^{[0,r]} - C_0^{[1]}}{\ln C^{[0,r]} - \ln C_0^{[1]}} \frac{\ln C^{[0,r]} - \ln C_0^{[1]} e^{z(\phi_0^{[1]} - \phi^{[0,r]})}}{H(x_1)} \\
&= -\frac{z}{z_3} \frac{C_0^{[2]} - C^{[3,l]}}{\ln C_0^{[2]} - \ln C^{[3,l]}} \frac{\ln C_0^{[2]} - \ln C^{[3,l]} e^{z(\phi^{[3,l]} - \phi_0^{[2]})}}{H(1) - H(x_2)}, \\
\phi_0^{[2]} &= \phi_0^{[1]} - T_0^c y_{00}, \quad C_0^{[2]} = C_0^{[1]} e^{z z_3 T_0^m y_{00}}, \\
& J_{10}\left(C_0^{[2]} - C_0^{[1]} e^{z T_0^c y_{00}}\right) = (J_{10} + J_{20})\left(c_{10}^{[2]} - c_{10}^{[1]} e^{z T_0^c y_{00}}\right), \\
T_0^m &= \frac{z_3 - z}{z_3} \frac{C_0^{[1]} - C_0^{[2]}}{H(x_2) - H(x_1)}.
\end{aligned} \tag{6.7}$$

Adding J_{10}, J_{20} and J_{30} in (6.7), together with the last equation in (6.7), one has

$$T_0^m = \frac{z_3 - z}{z_3} \frac{C^{[0,r]} - C_0^{[1]}}{H(x_1)} = \frac{z_3 - z}{z_3} \frac{C_0^{[2]} - C^{[3,l]}}{H(x_2) - H(x_1)} = \frac{z_3 - z}{z_3} \frac{C_0^{[1]} - C_0^{[2]}}{H(x_2) - H(x_1)}, \tag{6.8}$$

from which

$$\frac{C^{[0,r]} - C_0^{[1]}}{H(x_1)} = \frac{C_0^{[2]} - C^{[3,l]}}{H(x_2) - H(x_1)} = \frac{C_0^{[1]} - C_0^{[2]}}{H(x_2) - H(x_1)} = \frac{C^{[0,r]} - C^{[3,l]}}{H(1)}, \tag{6.9}$$

which implies

$$C_0^{[1]} = (1-\alpha)C^{[0,r]} + \alpha C^{[3,l]}, \; C_0^{[2]} = (1-\beta)C^{[0,r]} + \beta C^{[3,l]}$$

and

$$T_0^m = \frac{z_3 - z}{z_3} \frac{C^{[0,r]} - C^{[3,l]}}{H(1)}.$$

It follows from the fifth equation in (6.7) that

$$y_{00} = \frac{H(1)\big(\ln C_0^{[2]} - \ln C_0^{[1]}\big)}{z(z-z_3)\left(C^{[0,r]} - C^{[3,l]}\right)}. \tag{6.10}$$

Adding the first two equations in (6.7), one has

$$\begin{aligned} J_{10} + J_{20} =& \frac{C^{[0,r]} - C_0^{[1]}}{H(x_1)}\left(1 - \frac{z(\phi_0^{[1]} - \phi_0^{[0]})}{\ln C^{[0,r]} - \ln C_0^{[1]}}\right) \\ =& \frac{C_0^{[2]} - C^{[3,l]}}{H(1) - H(x_2)}\left(1 - \frac{z(\phi^{[3,l]} - \phi_0^{[2]})}{\ln C_0^{[2]} - \ln C^{[3,l]}}\right). \end{aligned} \tag{6.11}$$

Equations (6.9), (6.10), (6.11), together with the fourth equation in (6.7) yield

$$\frac{\phi_0^{[1]} - \phi_0^{[0]}}{\ln C_0^{[1]} - \ln C^{[0,r]}} = \frac{\phi^{[3,l]} - \phi_0^{[2]}}{\ln C^{[3,l]} - \ln C_0^{[2]}} = \frac{\phi_0^{[2]} - \phi_0^{[1]}}{\ln C_0^{[2]} - \ln C_0^{[1]}} = \frac{\phi^{[3,l]} - \phi_0^{[0]}}{\ln C^{[3,l]} - \ln C^{[0,r]}}. \tag{6.12}$$

It now follows that

$$\begin{aligned} \phi_0^{[1]} &= \frac{\ln C_0^{[1]} - \ln C^{[3,l]}}{\ln C^{[0,r]} - \ln C^{[3,l]}}\phi^{[0,r]} + \frac{\ln C^{[0,r]} - \ln C_0^{[1]}}{\ln C^{[0,r]} - \ln C^{[3,l]}}\phi^{[3,l]}, \\ \phi_0^{[2]} &= \frac{\ln C_0^{[2]} - \ln C^{[3,l]}}{\ln C^{[0,r]} - \ln C^{[3,l]}}\phi^{[0,r]} + \frac{\ln C^{[0,r]} - \ln C_0^{[2]}}{\ln C^{[0,r]} - \ln C^{[3,l]}}\phi^{[3,l]}. \end{aligned}$$

From the first two equations and the penultimate equation in (6.7), one has

$$\frac{J_{10}}{J_{10}+J_{20}} = \frac{c_1^{[0,r]} - c_{10}^{[1]} e^{z(\phi_0^{[1]}-\phi^{[0,r]})}}{C^{[0,r]} - C_0^{[1]} e^{z(\phi_0^{[1]}-\phi^{[0,r]})}} = \frac{c_{10}^{[2]} - c_1^{[3,l]} e^{z(\phi^{[3,l]}-\phi_0^{[2]})}}{C_0^{[2]} - C^{[3,l]} e^{z(\phi^{[3,l]}-\phi_0^{[2]})}}$$
$$= \frac{c_{10}^{[2]} - c_{10}^{[1]} e^{z(\phi_0^{[1]}-\phi_0^{[2]})}}{C_0^{[2]} - C_0^{[1]} e^{z(\phi_0^{[1]}-\phi_0^{[2]})}},$$

from which, one obtains the expressions of $c_{10}^{[1]}$, $c_{20}^{[1]}$, $c_{10}^{[2]}$ and $c_{20}^{[2]}$. The expressions for J_{10} and J_{20} then follow. This completes the proof.

6.3 Proof of Lemma 3.5

$N > 0$ follows from the fact that both M and $\ln \frac{\omega(\beta)}{\omega(\alpha)}$ have the same sign with that of $R - L$. Rewrite $1 - N$ as

$$1 - N = \frac{g(\beta)}{(\beta-\alpha)(t-1)^2}, \quad \text{where } g(\beta) = \omega(\alpha)\omega(\beta) \ln t \ln \frac{\omega(\beta)}{\omega(\alpha)} + (\beta-\alpha)(t-1)^2.$$

One then can easily obtain $\lim_{t\to 1}(1 - N) = 0$.

For the other statements, we just established statement (i) for $t > 1$, and those for $t < 1$ can be proved similarly. Direct computation yields $\frac{\mathrm{d}(1-N)}{\mathrm{d}\beta} = \frac{g_1(\beta)}{(\beta-\alpha)^2(t-1)^2}$, where $g_1(\beta) = -\omega^2(\alpha) \ln t \ln \frac{\omega(\beta)}{\omega(\alpha)} + (\beta-\alpha)(t-1)^2 \left((\alpha-\gamma(t))\ln t - 1\right)$, and further

$$g_1'(\beta) = \omega^2(\alpha)\frac{t-1}{\omega(\beta)} \ln t + (t-1)^2 \left((\alpha-\gamma(t))\ln t - 1\right), \quad g_1''(\beta) = \frac{\omega^2(\alpha)}{\omega^2(\beta)}(1-t)^2 \ln t.$$

It then follows that for $t > 1$, $g_1(\beta)$ is concave upward. Furthermore, one has

$$\lim_{\beta\to\alpha} g_1(\beta) = 0 \text{ and } \lim_{\beta\to\alpha} g_1'(\beta) = 0,$$

which implies $g_1(\beta) > 0$ for $\beta > \alpha$. Note that $\lim_{\beta\to\alpha} \dfrac{\mathrm{d}(1-N)}{\mathrm{d}\beta} = \ln \dfrac{t}{2} > 0$ for $t > 1$. We have $\frac{\mathrm{d}(1-N)}{\mathrm{d}\beta} > 0$ for $\beta > \alpha$, and $1 - N$ is strictly increasing on $(\alpha, +\infty)$. Additionally, since $\lim_{\beta\to\alpha}(1 - N) = (\alpha - \gamma(t)) \ln t$, one has, for $t > 1$,

(i1) if $\alpha \geq \gamma(t)$, then $\frac{z}{z_3} < 0 < 1 - N$, which yields $V_1 < 0 < V_2$;
(i2) For $\alpha < \gamma(t)$, we first claim that there exists a unique $\beta_1 \in (\alpha, 1)$ such that $1 - N = 0$ for $\beta = \beta_1$. In fact, based on the facts that

$$\lim_{\beta\to\alpha}(1 - N) = (\alpha - \gamma(t)) \ln t < 0$$

and $1-N$ is strictly increasing on $(\alpha, +\infty)$, one just need to show that $1-N > 0$ for $\beta = 1$, which is yielded by $g(1) > 0$. For convenience, for $t > 1$, we set

$$g_2(\alpha) := g(1) = -\omega(\alpha)\ln t \ln\omega(\alpha) + (1-\alpha)(t-1)^2.$$

Note that $g_2''(\alpha) = -\frac{(1-t)^2\ln t}{\omega(\alpha)} < 0$, which indicates that $g_2(\alpha)$ is concave downward for $t > 1$. Note also that $g_2(1) = 0$. To show that $g(1) > 0$, we claim $g_2(0) \geq 0$. To get started, we set

$$g_3(t) := g_2(0) = -t(\ln t)^2 + (t-1)^2.$$

Direct calculation gives $g_3'(t) = -(\ln t)^2 - 2\ln t + 2(t-1)$ and $g_3''(t) = \frac{2}{t}(t-1-\ln t) > 0$ for all $t > 1$. Together with $g_3(1) = g_3'(1) = 0$, one has $g_3(t) = g_2(0) > 0$.
If $\alpha < \gamma(t)$ and $\frac{z}{z_3} < (\alpha - \gamma(t))\ln t$, which is equivalent to $\alpha < \gamma(t) < \alpha - \frac{z}{z_3\ln t}$, then, one has $\frac{z}{z_3} < 1-B$ for all $\beta > \alpha$, and more specifically, $\frac{z}{z_3} < 1-N < 0$, which implies $V_2 < V_1 < 0$ for $\beta \in (\alpha, \beta_1)$; $\frac{z}{z_3} < 1-N = 0$ for $\beta = \beta_1$; $\frac{z}{z_3} < 0 < 1-N$, which indicates $V_1 < 0 < V_2$, for $\beta \in (\beta_1, 1)$.

(i3) if $\gamma(t) > \alpha - \frac{z}{z_3\ln t}$, then, the straight line $w = \frac{z}{z_3}$ and $w = 1-N$ have a unique intersection point $(\beta_1^*, w(\beta_1^*))$, which indicates that there exists a unique $\beta_1^* \in (\alpha, \beta_1)$ such that $1-N < \frac{z}{z_3} < 0$, which suggests $V_1 < V_2 < 0$ for $\beta \in (\alpha, \beta_1^*)$; $1-N = \frac{z}{z_3} < 0$ and further $V_2 = V_1 < 0$ for $\beta = \beta_1^*$; $\frac{z}{z_3} < 1-N < 0$, which yields $V_2 < V_1 < 0$ for $\beta \in (\beta_1^*, \beta_1)$; $\frac{z}{z_3} < 1-N = 0$ for $\beta = \beta_1$; and $\frac{z}{z_3} < 0 < 1-N$, which indicates $V_1 < 0 < V_2$ for $\beta \in (\beta_1, 1)$.

6.4 Proof of Theorem 3.18

Rewrite J_{11} as J_{11}

$$= \frac{Mzz_3(1-N)}{(z-z_3)H(1)(\ln L - \ln R)^2}\frac{(V-V_1)(V-V_2)}{L-Re^{-zV}}\left(L_1 - R_1e^{-zV}\right).$$

Direct calculation yields $\frac{\mathrm{d}J_{11}}{\mathrm{d}V}$

$$= \frac{Mzz_3(1-N)}{(z-z_3)H(1)(\ln L - \ln R)^2}\frac{e^{-zV}}{\left(L-Re^{-zV}\right)^2}f_{11}(V),$$

where

$$f_{11}(V) = (2V - V_1 - V_2)\left(L - Re^{-zV}\right)\left(L_1 - R_1e^{-zV}\right) + z\left(R_1L - L_1R\right)(V-V_1)(V-V_2).$$

It follows that

$$f_{11}'(V) = \frac{\mathrm{d}f_{11}}{\mathrm{d}V} = e^{zV}\left(L - Re^{-zV}\right)g_{11}(V),$$

where $g_{11}(V) = 2\left(L_1 - R_1e^{-zV}\right) + z\left(2V - V_1 - V_2\right)\left(L_1 + R_1e^{-zV}\right)$. For $g_{11}(V)$, one has

$$\begin{aligned} g_{11}'(V) &= \frac{\mathrm{d}g_{11}}{\mathrm{d}V} = 4zR_1e^{-zV} + 2zL_1 - z^2R_1e^{-zV}\left(2V - V_1 - V_2\right), \\ g_{11}''(V) &= \frac{\mathrm{d}^2g_{11}}{\mathrm{d}V^2} = z^2R_1e^{-zV}\left(z\left(2V - V_1 - V_2\right) - 6\right). \end{aligned} \tag{6.13}$$

From (6.13), we obtain a unique zero of $g_{11}''(V)$ given by $V_0 = \frac{1}{2}\left(\frac{6}{z} + V_1 + V_2\right)$, which is the minimum point of $g_{11}'(V)$. Note that $\lim\limits_{V\to+\infty} g_{11}'(V) = 2zL_1 > 0$ and $\lim\limits_{V\to-\infty} g_{11}'(V) = +\infty$. If the minimal value $g_{11}'(V_0) = 2z\left(L_1 - R_1e^{-zV_0}\right) \geq 0$, i.e., $V_0 \leq V_3$, then, $g_{11}'(V) \leq 0$ for all V. In this case, $g_{11}(V)$ has a unique zero, since $\lim\limits_{V\to+\infty} g_{11}(V) = +\infty$ and $\lim\limits_{V\to-\infty} g_{11} = -\infty$. If the minimal value $g_{11}'(V_0) = 2z\left(L_1 - R_1e^{-zV_0}\right) < 0$ i.e., $V_0 < V_3$, then $g_{11}'(V)$ has two zeros. Suppose V_e is a zero point of $g_{11}'(V)$, one has $2V_e - V_1 - V_2 = \frac{4R_1+2L_1e^{zV_e}}{zR_1}$ and the extreme value of $g_{11}(V)$ given by $g_{11}(V_e) = \frac{2}{R_1}\left(L_1^2e^{zV_e} + R_1^2e^{-zV_e} + 4L_1R_1\right) > 0$, which indicates that $g_{11}(V)$ has a unique zero point. Therefore, no matter $V_0 \leq V_3$ or $V_0 < V_3$, $g_{11}(V)$ always has a unique zero denoted by V_z. Furthermore, $f_{11}'(V)$ has two zeros V_1 and V_z. To determine the order of V_1 and V_z, one just need to determine the sign of $g_{11}(V_1)$. In fact, if $g_{11}(V_1) > 0$, then $V_1 > V_z$, if $g_{11}(V_1) = 0$, then $V_1 = V_z$, if $g_{11}(V_1) < 0$, then $V_1 < V_z$.

Note that $g_{11}(V_1) = \frac{1}{zL_1LR}\left[C\frac{R_1}{L_1} + \frac{1}{(1-N)t}\left(\frac{z}{z_3}\ln t - (\ln t - 2)(1 - N)\right)\right]$, where C is defined in (3.8) and the sign of the quantity C has been studied in Lemma 3.17. It then follows that , with $\Delta = \frac{\frac{z}{z_3}\ln t - (\ln t - 2)(1-N)}{\frac{z}{z_3}\ln t - (\ln t + 2)(1-N)}$,

- for $C > 0$, one has $g_{11}(V_1) > 0$ if $\frac{R_1}{L_1} > -\frac{\Delta}{t}$, and $g_{11}(V_1) < 0$ if $\frac{R_1}{L_1} < -\frac{\Delta}{t}$.
- for $C < 0$, one has $g_{11}(V_1) > 0$ if $\frac{R_1}{L_1} < -\frac{\Delta}{t}$, and $g_{11}(V_1) < 0$ if $\frac{R_1}{L_1} > -\frac{\Delta}{t}$.
- for $C = 0$, one has $g_{11}(V_1) > 0$.

In particular, $g_{11}(V_1) = 0$ if $\frac{R_1}{L_1} = -\frac{\Delta}{t}$ with $C \neq 0$.

If $V_1 < V_z$, then f_{11} is increasing on $(-\infty, V_1)$, decreasing on (V_1, V_2), and increasing on (V_2, ∞). Note that $f_{11}(V_1) = 0$, which is a local maximum of f_{11}, $\lim_{V\to-\infty} f_{11} = -\infty$ and $\lim_{V\to\infty} f_{11} = \infty$, f_{11} has the other zero V_{11}^1 with $V_{11}^1 > V_1$. Furthermore, $\lim\limits_{V\to V_1} \frac{\mathrm{d}J_{11}}{\mathrm{d}V} = \frac{Mz_3(1-N)e^{zV_1}}{2(z - z_3)H(1)\left(\ln L - \ln R\right)^2 R} g_{11}(V_1) < 0$, since $g_{11}(V_1) < g_{11}(V_z) = 0$, which can be obtained from the fact that g_{11} is increasing on $(-\infty, V_z)$ and $V_1 < V_z$. Therefore, when $V > V_{11}^1$, $\frac{\mathrm{d}J_{11}}{\mathrm{d}V} > 0$, and when $V < V_{11}^1$,

$\frac{dJ_{11}}{dV} < 0$. This result also hold for the case when $V_1 \geq V_z$, which can be proved in a similar way. Consequently the statement (i) follows.

The statements for J_{21} and J_{31} can be proved similarly.

6.5 Proof of Theorem 4.6

We will just prove the first statement. Statement (ii) can be proved by a similar argument. For $\frac{L_2}{L_1} < \frac{D_1}{D_2} < \frac{R_2}{R_1}$, one has

$$\mathcal{J}_{1,2}^1 = \frac{Mzz_3(1-N)}{(z-z_3)H(1)\,(\ln L - \ln R)^2}\frac{(V-V_1)\,(V-V_2)}{L-Re^{-zV}}\left(L_d^- - R_d^- e^{-zV}\right).$$

Direct calculation yields

$$\frac{d\mathcal{J}_{1,2}^1}{dV} = \frac{Mzz_3(1-N)}{(z-z_3)H(1)\,(\ln L - \ln R)^2}\frac{e^{-zV}}{\left(L-Re^{-zV}\right)^2} f_{d3}(V),$$

and further

$$f_{d3}'(V) = e^{zV}\left(L-Re^{-zV}\right) g_{d3}(V), \tag{6.14}$$

where $f_{d3}(V)$ and $g_{d3}(V)$ are given in (4.5).

For $g_{d3}(V)$, we have

$$\begin{aligned} g_{d3}'(V) =& 2zL_d^- + 4zR_d^- e^{-zV} - z^2R_d^- e^{-zV}\,(2V - V_1 - V_2)\,, \\ g_{d3}''(V) =& -z^2R_d^- e^{-zV}\,(6 - z\,(2V - V_1 - V_2))\,. \end{aligned} \tag{6.15}$$

From (6.15), we obtain a unique zero of $g_{d3}''(V)$ given by $V_0 = \frac{1}{2}\left(\frac{6}{z} + V_1 + V_2\right)$, which actually is the maximum value point of $g_{d3}'(V)$. Note that

$$\lim_{V\to+\infty} g_{d3}'(V) = 2zL_d^- > 0, \quad \lim_{V\to-\infty} g_{d3}'(V) = -\infty,$$

and the maximal value $g_{d3}'(V_0) = 2z\left(L_d^- - R_d^- e^{-zV_0}\right) > 0$. Hence, $g_{d3}'(V)$ has a unique zero denoted by V_{d3} and V_{d3} is actually the minimum value point of $g_{d3}(V)$. From $g_{d3}'(V) = 0$, one immediately has $2V_{d3} - V_1 - V_2 = \frac{4R_d^- + 2L_d^- e^{zV_{d3}}}{zR_d^-}$ and the corresponding extreme value of $g_{d3}(V)$, i.e., $g_{d3}(V_{d3}) = -\frac{2}{R_d^-}h(V_{d3})$. From lemma 4.5, $g_{d3}(V_{d3}) > 0$ for $V_z^1 < V_{d3} < V_z^2$, $g_{d3}(V_{d3}) = 0$ for $V_{d3} = V_z^1$ or $V_{d3} = V_z^2$, and $g_{d3}(V_{d3}) < 0$ for $V_{d3} < V_z^1$ or $V_{d3} > V_z^2$.

If $g_{d3}(V_{d3}) > 0$, then, $g_{d3}(V) > 0$ for all V. It follows that $f_{d3}'(V)$ has a unique zero V_1, $f_{d3}'(V) > 0$ for $V > V_1$, and $f_{d3}'(V) < 0$ for $V < V_1$. Therefore, the minimal value of $f_{d3}(V)$ is $f_{d3}(V_1) = 0$. Note that

$\lim\limits_{V\to V_1} \dfrac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} = \dfrac{Mz_3(1-N)g_{d3}(V_1)}{2(z-z_3)H(1)\,(\ln L-\ln R)^2\,L} > 0$. Then, $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} > 0$ follows, which yields $\mathcal{J}_{1,2}^1(V)$ always increases.

If $g_{d3}(V_{d3}) = 0$, then $g_{d3}(V)$ has the unique zero V_{d3}. From (6.14), $f_{d3}'(V)$ has two zeros V_1 and V_{d3}. To determine the position relation of V_1 and V_{d3}, one just need to determine the sign of $g_{d3}'(V_1) = 2zR_d^-\left(\frac{L_d^-}{R_d^-} + \frac{t\left((4+\ln t)(1-N)-\frac{z}{z_3}\ln t\right)}{2(1-N)}\right)$. In fact, if $g_{d3}'(V_1) < 0$, then $V_1 < V_{d3}$, if $g_{d3}'(V_1) = 0$, then $V_1 = V_{d3}$, if $g_{d3}'(V_1) > 0$, then $V_1 > V_{d3}$. However, no matter $V_1 < V_{d3}$ or $V_1 \geq V_{d3}$, from (6.14), one always has $f_{d3}' \leq 0$ for $V < V_1$ and $f_{d3}' \geq 0$ for $V > V_1$. Hence, the minimal value of f_{d3} is $f_{d3}(V_1) = 0$. Note that $\lim\limits_{V\to V_1} \dfrac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} = \dfrac{Mz_3(1-N)g_{d3}(V_1)}{2(z-z_3)H(1)\,(\ln L-\ln R)^2\,L} > 0$. Then, $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} > 0$ follows, and hence, $\mathcal{J}_{1,2}^1(V)$ always increases.

If $g_{d3}(V_{d3}) < 0$, then, $g_{d3}(V)$ has two zeros denoted by V_z^3 and V_z^4 with $V_z^3 < V_z^4$, since $\lim\limits_{V\to\pm\infty} g_{d3} = +\infty$. It follows that $f_{d3}'(V)$ has three zeros V_1, V_z^3 and V_z^4. To determine the position relation of V_1, V_z^3 and V_z^4, one just need to determine the sign of $g_{d3}(V_1)$ and $g_{d3}'(V_1)$. In fact, if $g_{d3}(V_1) < 0$, then $V_z^3 < V_1 < V_z^4$, if $g_{d3}(V_1) > 0$ and $g_{d3}'(V_1) < 0$, then $V_1 < V_z^3 < V_z^4$, and if $g_{d3}(V_1) > 0$ and $g_{d3}'(V_1) > 0$, then $V_z^3 < V_z^4 < V_1$.

Note that $g_{d3}(V_1) = \frac{\frac{z}{z_3}\ln t-(\ln t-2)(1-N)}{(1-N)R_d^-}\left(\frac{L_d^-}{R_d^-} + \frac{1}{t\Delta}\right)$. It follows that

- For $\frac{1}{1-N}\left(\frac{z}{z_3}\ln t-(\ln t-2)(1-N)\right) > 0$, one has $g_{d3}(V_1) > 0$ (resp. $g_{d3}(V_1) < 0$) if $\frac{L_d^-}{R_d^-} < -\frac{1}{t\Delta}$ (resp. $\frac{L_d^-}{R_d^-} > -\frac{1}{t\Delta}$);
- For $\frac{1}{1-N}\left(\frac{z}{z_3}\ln t-(\ln t-2)(1-N)\right) < 0$, one has $g_{d3}(V_1) > 0$ (resp. $g_{d3}(V_1) < 0$) if $\frac{L_d^-}{R_d^-} > -\frac{1}{t\Delta}$ (resp. $\frac{L_d^-}{R_d^-} < -\frac{1}{t\Delta}$);
- For $\frac{1}{1-N}\left(\frac{z}{z_3}\ln t-(\ln t-2)(1-N)\right) \neq 0$, one has $g_{d3}(V_1) = 0$ if $\frac{L_d^-}{R_d^-} = -\frac{1}{t\Delta}$;
- For $\frac{1}{1-N}\left(\frac{z}{z_3}\ln t-(\ln t-2)(1-N)\right) = 0$, one has $g_{d3}(V_1) > 0$.

If $V_z^3 < V_1 < V_z^4$, then, $f_{d3}(V)$ decreases on $(-\infty, V_z^3)$, increases on (V_z^3, V_1), decreases on (V_1, V_z^4), and increases on (V_z^4, ∞). Note that $f_{d3}(V_1) = 0$, which is a local maximum of $f_{d3}(V)$, one has $f_{d3}(V_z^3) < 0$ and $f_{d3}(V_z^4) < 0$. Since

$$\lim_{V\to V_1} \frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} = \frac{Mz_3(1-N)g_{d3}(V_1)}{2(z-z_3)H(1)\,(\ln L-\ln R)^2\,L} < 0,$$

$\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V}$ has two zeros denoted by V_c^{51} and V_c^{52} with $V_c^{51} < V_c^{52}$ such that $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} > 0$ for $V < V_c^{51}$ or $V > V_c^{52}$, and $\frac{\mathrm{d}\mathcal{J}_{1,2}^1}{\mathrm{d}V} < 0$ for $V_c^{51} < V < V_c^{52}$, that is, $\mathcal{J}_{1,2}^1$ increases on $(-\infty, V_c^{51})$, decreases on (V_c^{51}, V_c^{52}), and increases on (V_c^{52}, ∞).

Similar discussions can be applied to the cases with $V_1 < V_z^3 < V_z^4$ and $V_z^3 < V_z^4 < V_1$, respectively. This completes the proof of the first statement.

References

Abaid, N., Eisenberg, R.S., Liu, W.: Asymptotic expansions of I–V relations via a Poisson–Nernst–Planck system. SIAM J. Appl. Dyn. Syst. **7**, 1507–1526 (2008)

Aitbayev, R., Bates, P.W., Lu, H., Zhang, L., Zhang, M.: Mathematical studies of Poisson–Nernst–Planck systems: dynamics of ionic flows without electroneutrality conditions. J. Comput. Appl. Math. **362**, 510–527 (2019)

Barcilon, V.: Ion flow through narrow membrane channels: part I. SIAM J. Appl. Math. **52**, 1391–1404 (1992)

Barcilon, V., Chen, D.-P., Eisenberg, R.S.: Ion flow through narrow membrane channels: part II. SIAM J. Appl. Math. **52**, 1405–1425 (1992)

Barcilon, V., Chen, D.-P., Eisenberg, R.S., Jerome, J.W.: Qualitative properties of steady-state Poisson–Nernst–Planck systems: perturbation and simulation study. SIAM J. Appl. Math. **57**, 631–648 (1997)

Bates, P.W., Chen, J., Zhang, M.: Dynamics of ionic flows via Poisson–Nernst–Planck systems with local hard-sphere potentials: competition between cations. Math. Biosci. Eng. **17**, 3736–3766 (2020)

Bates, P.W., Jia, Y., Lin, G., Lu, H., Zhang, M.: Individual flux study via steady-state Poisson–Nernst–Planck systems: effects from boundary conditions. SIAM J. Appl. Dyn. Syst. **16**(1), 410–430 (2017)

Biesheuvel, P.M.: Two-fluid model for the simultaneous flow of colloids and fluids in porous media. J. Colloid Interface Sci. **355**, 389–395 (2011)

Boda, D., Nonner, W., Valisko, M., Henderson, D., Eisenberg, B., Gillespie, D.: Steric selectivity in Na channels arising from protein polarization and mobile side chains. Biophys. J. **93**, 1960–1980 (2007)

Chen, D., Eisenberg, R., Jerome, J., Shu, C.: Hydrodynamic model of temperature change in open ionic channels. Biophys. J. **69**, 2304–2322 (1995)

Eisenberg, B.: Ion channels as devices. J. Comp. Electron. **2**, 245–249 (2003)

Eisenberg, B.: Proteins, channels, and crowded ions. Biophys. Chem. **100**, 507–517 (2003)

Eisenberg, R.S.: Channels as enzymes. J. Memb. Biol. **115**, 1–12 (1990)

Eisenberg, R.S.: Atomic biology, electrostatics and ionic channels. In: Elber, R. (ed.) New Developments and Theoretical Studies of Proteins, pp. 269–357. World Scientific, Philadelphia (1996)

Eisenberg, B.: Crowded charges in ion channels. In: Rice, S.A. (ed.) Advances in Chemical Physics, pp. 77–223. Wiley, Hoboken (2011)

Eisenberg, B., Hyon, Y., Liu, C.: Energy variational analysis of ions in water and channels: field theory for primitive models of complex ionic fluids. J. Chem. Phys. **133**(104104), 1–23 (2010)

Eisenberg, B., Liu, W.: Poisson-Nernst-Planck systems for ion channels with permanent charges. SIAM J. Math. Anal. **38**, 1932–1966 (2007)

Eisenberg, B., Liu, W.: Relative dielectric constants and selectivity ratios in open ionic channels. Mol. Based Math. Biol. **5**, 125–137 (2017)

Eisenberg, B., Liu, W., Xu, H.: Reversal charge and reversal potential: case studies via classical Poisson–Nernst–Planck models. Nonlinearity **28**, 103–128 (2015)

Fair, J.C., Osterle, J.F.: Reverse Electrodialysis in charged capillary membranes. J. Chem. Phys. **54**, 3307–3316 (1971)

Fenichel, N.: Geometric singular perturbation theory for ordinary differential equations. J. Differ. Equ. **31**, 53–98 (1979)

Gillespie, D.: Energetics of divalent selectivity in a calcium channel: the Ryanodine receptor case study. Biophys. J. **94**, 1169–1184 (2008)

Gillespie, D., Eisenberg, R.S.: Physical descriptions of experimental selectivity measurements in ion channels. Eur. Biophys. J. **31**, 454–466 (2002)

Gillespie, D.: A singular perturbation analysis of the Poisson-Nernst-Planck system: Applications to Ionic Channels. Ph.D Dissertation, Rush University at Chicago (1999)

Gillespie, D., Nonner, W., Eisenberg, R.S.: Coupling Poisson–Nernst–Planck and density functional theory to calculate ion flux. J. Phys. Condens. Matter **14**, 12129–12145 (2002)

Gillespie, D., Nonner, W., Eisenberg, R.S.: Crowded charge in biological ion channels. Nanotechnology **3**, 435–438 (2003)

Gross, R.J., Osterle, J.F.: Membrane transport characteristics of ultra fine capillary. J. Chem. Phys. **49**, 228–234 (1968)
Hodgkin, A.L., Keynes, R.D.: The potassium permeability of a giant nerve fibre. J. Physiol. **128**, 61–88 (1955)
Hyon, Y., Eisenberg, B., Liu, C.: A mathematical model for the hard sphere repulsion in ionic solutions. Commun. Math. Sci. **9**, 459–475 (2010)
Hyon, Y., Fonseca, J., Eisenberg, B., Liu, C.: Energy variational approach to study charge inversion (layering) near charged walls. Discrete Contin. Dyn. Syst. Ser. B **17**, 2725–2743 (2012)
Hyon, Y., Liu, C., Eisenberg, B.: PNP equations with steric effects: a model of ion flow through channels. J. Phys. Chem. B **116**, 11422–11441 (2012)
Im, W., Roux, B.: Ion permeation and selectivity of OmpF porin: a theoretical study based on molecular dynamics, Brownian dynamics, and continuum electrodiffusion theory. J. Mol. Biol. **322**, 851–869 (2002)
Ji, S., Eisenberg, B., Liu, W.: Flux ratios and channel structures. J. Dyn. Differ. Equ. **31**, 1141–1183 (2019)
Ji, S., Liu, W.: Poisson–Nernst–Planck systems for ion flow with density functional theory for hard-sphere potential: I–V relations and critical potentials: part I: analysis. J. Dyn. Differ. Equ. **24**, 955–983 (2012)
Ji, S., Liu, W., Zhang, M.: Effects of (small) permanent charges and channel geometry on ionic flows via classical Poisson–Nernst–Planck models. SIAM J. Appl. Math. **75**, 114–135 (2015)
Jia, Y., Liu, W., Zhang, M.: Qualitative properties of ionic flows via Poisson–Nernst–Planck systems with Bikerman's local hard-sphere potential: ion size effects. Discrete Contin. Dyn. Syst. Ser. B **21**, 1775–1802 (2016)
Jones, C.: Geometric singular perturbation theory. Dynamical systems (Montecatini Terme, 1994), pp. 44–118. Lect. Notes in Math. **1609**, Springer, Berlin (1995)
Jones, C., Kopell, N.: Tracking invariant manifolds with differential forms in singularly perturbed systems. J. Differ. Equ. **108**, 64–88 (1994)
Kilic, M.S., Bazant, M.Z., Ajdari, A.: Steric effects in the dynamics of electrolytes at large applied voltages: II: modified Poisson–Nernst–Planck equations. Phys. Rev. E **75**, 021503 (2007)
Liu, J.L., Eisenberg, B.: Poisson–Nernst–Planck–Fermi theory for modeling biological ion channels. J. Chem. Phys. **141**, 12B640 (2014)
Lee, C.-C., Lee, H., Hyon, Y., Lin, T.-C., Liu, C.: New Poisson–Boltzmann type equations: one-dimensional solutions. Nonlinearity **24**, 431–458 (2011)
Lin, G., Liu, W., Yi, Y., Zhang, M.: Poisson–Nernst–Planck systems for ion flow with density functional theory for local hard-sphere potential. SIAM J. Appl. Dyn. Syst. **12**, 1613–1648 (2013)
Liu, W.: Geometric singular perturbation approach to steady-state Poisson–Nernst–Planck systems. SIAM J. Appl. Math. **65**, 754–766 (2005)
Liu, W.: One-dimensional steady-state Poisson–Nernst–Planck systems for ion channels with multiple ion species. J. Differ. Equ. **246**, 428–451 (2009)
Liu, W., Wang, B.: Poisson–Nernst–Planck systems for narrow tubular-like membrane channels. J. Dyn. Differ. Equ. **22**, 413–437 (2010)
Liu, W., Tu, X., Zhang, M.: Poisson–Nernst–Planck systems for ion flow with density functional theory for hard-sphere potential: I–V relations and critical potentials: part II: Numerics. J. Dyn. Differ. Equ. **24**, 985–1004 (2012)
Liu, W., Xu, H.: A complete analysis of a classical Poisson–Nernst–Planck model for ionic flow. J. Differ. Equ. **258**, 1192–1228 (2015)
Lu, H., Li, J., Shackelford, J., Vorenberg, J., Zhang, M.: Ion size effects on individual fluxes via Poisson–Nernst–Planck systems with Bikerman's local hard-sphere potential: analysis without electroneutrality boundary conditions. Discrete Contin. Dyn. Syst. Ser. B **23**, 1623–1643 (2018)
Nonner, W., Eisenberg, R.S.: Ion permeation and glutamate residues linked by Poisson–Nernst–Planck theory in L-type Calcium channels. Biophys. J. **75**, 1287–1305 (1998)
Park, J.-K., Jerome, J.W.: Qualitative properties of steady-state Poisson–Nernst–Planck systems: mathematical study. SIAM J. Appl. Math. **57**, 609–630 (1997)
Rouston, D.J.: Bipolar Semiconductor Devices. McGraw-Hill, New York (1990)
Roux, B., Allen, T.W., Berneche, S., Im, W.: Theoretical and computational models of biological ion channels. Q. Rev. Biophys. **37**, 15–103 (2004)
Sasidhar, V., Ruckenstein, E.: Electrolyte osmosis through capillaries. J. Colloid Interface Sci. **82**, 439–457 (1981)

Schuss, Z., Nadler, B., Eisenberg, R.S.: Derivation of Poisson and Nernst–Planck equations in a bath and channel from a molecular model. Phys. Rev. E **64**, 1–14 (2001)
Singer, A., Norbury, J.: A Poisson–Nernst–Planck model for biological ion channels-an asymptotic analysis in a three-dimensional narrow funnel. SIAM J. Appl. Math. **70**, 949–968 (2009)
Singer, A., Gillespie, D., Norbury, J., Eisenberg, R.S.: Singular perturbation analysis of the steady-state Poisson–Nernst–Planck system: applications to ion channels. Eur. J. Appl. Math. **19**, 541–560 (2008)
Sun, L., Liu, W.: Non-localness of excess potentials and boundary value problems of Poisson–Nernst–Planck systems for ionic flow: a case study. J. Dyn. Differ. Equ. **30**, 779–797 (2018)
Tin, S.-K., Kopell, N., Jones, C.: Invariant manifolds and singularly perturbed boundary value problems. SIAM J. Numer. Anal. **31**, 1558–1576 (1994)
Warner, R.M., Jr.: Microelectronics: its unusual origin and personality. IEEE Trans. Electron. Dev. **48**, 2457–2467 (2001)
Wang, X.-S., He, D., Wylie, J., Huang, H.: Singular perturbation solutions of steady-state Poisson–Nernst–Planck systems. Phys. Rev. E **89**(022722), 1–14 (2014)
Wei, G.W.: Differential geometry based multiscale models. Bull. Math. Biol. **72**, 1562–1622 (2010)
Wei, G.W., Zheng, Q., Chen, Z., Xia, K.: Variational multiscale models for charge transport. SIAM Rev. **54**, 699–754 (2012)
Wen, Z., Zhang, L., Zhang, M.: Dynamics of classical Poisson–Nernst–Planck systems with multiple cations and boundary layers. J. Dyn. Differ. Equ. **33**, 211–234 (2021)
Zhang, M.: Asymptotic expansions and numerical simulations of I–V relations via a steady-state Poisson–Nernst–Planck system. Rocky Mountain J. Math. **45**, 1681–1708 (2015)
Zhang, M.: Boundary layer effects on ionic flows via classical Poisson–Nernst–Planck systems. Comput. Math. Biophys. **6**, 14–27 (2018)