

Effects of (small) permanent charge and channel geometry on ionic flows via classical Poisson-Nernst-Planck models

Shuguan Ji*, Weishi Liu† and Mingji Zhang‡

Abstract

In this work, we examine effects of permanent charges on ionic flows through ion channels via a quasi-one-dimensional classical Poisson-Nernst-Planck (PNP) model. The geometry of the three-dimensional channel is presented in this model to a certain extent, which is crucial for the study in this paper. Two ion species, one positively charged and one negatively charged, are considered with a simple profile of permanent charges: zeros at the two end regions and a constant Q_0 over the middle region. The classical PNP model can be viewed as a boundary value problem (BVP) of a singularly perturbed system. The singular orbit of the BVP depends on Q_0 in a regular way. Assuming $|Q_0|$ is small, a regular perturbation analysis is carried out for the singular orbit. Our analysis indicates that effects of permanent charges depend on a rich interplay between boundary conditions and the channel geometry. Furthermore, interesting common features are revealed: for $Q_0 = 0$, only an average quantity of the channel geometry plays a role; however, for $Q_0 \neq 0$, details of the channel geometry matter, in particular, to optimize effects of a permanent charge, the channel should have a *short* and *narrow* neck within which the permanent charge is confined. The latter is consistent with structures of typical ion channels.

Key Words. Ionic flow, permanent charge, channel geometry

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1 Introduction

In this work, we analyze effects of permanent charges on ionic flows through ion channels, based on a quasi-one-dimensional classical Poisson-Nernst-Planck (PNP) model. The geometry of the three-dimensional channel is presented in this model to a certain extent, which is crucial for the study in this paper. We start with a brief discussion of the biological background of ion channel problems, a quasi-one-dimensional PNP model, and the main concern of our work in this paper.

1.1 Ionic flows and the model

Ion channels provide a major way for cells to communicate with each other and outside world to perform group tasks. They are large proteins embedded in cell membranes that have “holes” open to inside and outside of cells. Once channels open, ions (charged particles) flow from outside to inside of cells and vice versa. The ionic flow produces electric signals that control many biological functions. The study of ion channel properties consists of two related topics: structures of ion channels and ionic flow properties. The key structure of an ion channel is the

*College of Mathematics, Jilin University, 2699 Qianjin Street, Changchun, Jilin 130012, P. R. China, E-mail: jjs@jlu.edu.cn.

†Department of Mathematics, University of Kansas, 1460 Jayhawk Blvd., Room 405, Lawrence, KS 66045, USA, E-mail: wslu@ku.edu.

‡Department of Mathematics, Michigan State University, 619 Red Cedar Road, Room C314, East Lansing, MI 48823, USA, E-mail: mzhang@math.msu.edu, mzhang0129@gmail.com.

channel shape and the *permanent charge*. The shape of a typical ion channel is cylindrical-like with variable cross-section areas along its axis. Within an ion channel, amino acid side chains are distributed, with acidic side chains contributing negative charges and basic side chains contributing positive charges. It is the specific of side chain distributions in an ion channel that is referred to as the permanent charge of the ion channel ([11, 12, 40]).

With a given structure of an ion channel, the main concern is then to understand its electrodiffusion property. The basic continuum model for electrodiffusion is the Poisson-Nernst-Planck (PNP) type systems, which are reduced models that treat the medium (aqueous within which ions are migrating) as dielectric continuum:

$$\begin{aligned}\nabla \cdot (\varepsilon_r(X) \varepsilon_0 \nabla \Phi) &= -e \left(\sum_{s=1}^n z_s c_s + Q(X) \right), \\ \nabla \cdot \mathcal{J}_k &= 0, \quad -\mathcal{J}_k = \frac{1}{k_B T} D_k(X) c_k \nabla \mu_k, \quad k = 1, 2, \dots, n\end{aligned}$$

where $X \in \Omega$ with Ω being a three-dimensional cylindrical-like domain representing the channel, $Q(X)$ is the permanent charge density, $\varepsilon_r(X)$ 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, for the k th ion species, c_k is the concentration, z_k is the valence (the number of charges per particle), μ_k is the electrochemical potential depending on Φ and $\{c_j\}$ (see discussions below), $\mathcal{J}_k$ is the flux density, and $D_k(X)$ is the diffusion coefficient.

PNP systems can be derived as reduced models from molecular dynamic models ([48]), from Boltzmann equations ([4]), and from variational principles ([23, 24, 25]). More sophisticated models have also been developed. Coupling PNP and Navier-Stokes equations for aqueous motions was proposed (see, e.g. [7, 10, 13, 17, 22, 47]). In [13], the coupled system was derived from the energy variational principle. In [10], the coupled system studied numerically for ion channel problems. In [47], the coupled system was studied numerically for electrolyte-osmosis through membranes modeled by capillaries. In [17, 22], Onsager's Reciprocal Law was rigorously established for the relations between the three fluxes (solvent flux, relative solute flux, and electrical current) and the three forces (pressure, osmotic potential, and electrical potential), and the nine coefficients in the relation are explicitly identified. A more fully developed two-fluid model was proposed in [7] which reduces to previously-known models in various simpler situations. Conformations of channel geometries were also incorporated ([53, 54]). Reviews of various models for ion transports and comparisons among the models can be found in [2, 26, 46, 54]. While these sophisticated systems beyond PNP systems can model the physical problem more accurately, it is a great challenge to examine their dynamics analytically and even computationally. Focusing on key features of the biological system, PNP systems represent as appropriate models for analysis and numerical simulations of ionic flows.

Our analysis is based on a further reduction of PNP models. On the basis that ion channels have narrow cross-sections relative to their lengths, PNP systems defined on three-dimensional ion channels are further reduced to quasi-one-dimensional models first proposed in [41] and, for a special case, the reduction is rigorously justified in [37]. For a mixture of n ion species, a quasi-one-dimensional PNP model is

$$\begin{aligned}\frac{1}{h(x)} \frac{d}{dx} \left(\varepsilon_r(x) \varepsilon_0 h(x) \frac{d\Phi}{dx} \right) &= -e \left(\sum_{s=1}^n z_s c_s + Q(x) \right), \\ \frac{d\mathcal{J}_k}{dx} &= 0, \quad -\mathcal{J}_k = \frac{1}{k_B T} D_k(x) h(x) c_k \frac{d\mu_k}{dx}, \quad k = 1, 2, \dots, n\end{aligned}\tag{1.1}$$

where $x \in [0, 1]$ is the coordinate along the axis of the channel that is normalized to $[0, 1]$, $h(x)$ is the area of cross-section of the channel over the location x .

Equipped with system (1.1), we impose the following boundary conditions (see, [14] for a reasoning), for $k = 1, 2, \dots, n$,

$$\Phi(0) = \mathcal{V}, \quad c_k(0) = L_k > 0; \quad \Phi(1) = 0, \quad c_k(1) = R_k > 0. \quad (1.2)$$

For ion channels, an important characteristic is the *I-V (current-voltage) relation*. Given a solution of the boundary value problem (BVP) (1.1) and (1.2), the *current* $\mathcal{I}$ is

$$\mathcal{I} = \sum_{j=1}^n z_j \mathcal{J}_j. \quad (1.3)$$

If boundary concentrations L_k 's and R_k 's are fixed, then $\mathcal{J}_k$'s depend on $\mathcal{V}$ only and formula (1.3) provides a dependence of the current $\mathcal{I}$ on the voltage $\mathcal{V}$.

An important modeling component is the electrochemical potential μ_k . It consists of the ideal component $\mu_k^{id}(x)$ given by

$$\mu_k^{id}(x) = z_k e \Phi(x) + k_B T \ln \frac{c_k(x)}{c_0} \quad (1.4)$$

with some characteristic number density c_0 , and the excess component $\mu_k^{ex}(x)$. The ideal component $\mu_k^{id}(x)$ contains contributions of ion particles as point charges and ignores the ion-to-ion interaction. PNP models including ideal components are referred to as *classical* PNP models. Numerical studies have shown that classical PNP models provide good qualitative agreements with experimental data for I-V relations ([4, 5]). Dynamics of classical PNP models has also been analyzed by using asymptotic expansion methods ([1, 6, 32, 42, 49, 50, 52, 55]) and geometric singular perturbation approaches ([14, 15, 35, 36, 39]).

The excess component $\mu_k^{ex}(x)$ accounts for ion sizes, which is a crucial component for many important properties of ion channels such as selectivity. Modeling of the excess component $\mu_k^{ex}(x)$ is extremely challenging and is not completely understood. A great deal of efforts has been attributed to approximations of $\mu_k^{ex}(x)$ based on mean-spherical approximations, fundamental measure theory, and density functional theory (e.g., [8, 9, 43, 44, 45]). Numerical simulations of PNP with approximated models of $\mu_k^{ex}(x)$ have been conducted for ion channel problems in comparison with experimental data and have shown great successes for properties such as ion permeation and ion selectivity (e.g., [18, 19, 20, 21]). Other important phenomena involving $\mu_k^{ex}(x)$ such as steric effects, layering, charge inversions, and critical potentials have also been studied [3, 16, 23, 24, 25, 27, 30, 31, 33, 34, 38, 56].

In this work, we will take *classical* PNP models that include the ideal component $\mu_k^{id}(x)$ in (1.4) only to examine permanent charge effects on ionic flows.

1.2 Basic concerns and a brief description of main results

As observed in [15], the Nernst-Planck equation in (1.1) for the flux $\mathcal{J}_k$ gives

$$\mathcal{J}_k \int_0^1 \frac{k_B T}{D_k(x) h(x) c_k(x)} dx = \mu_k(0) - \mu_k(1). \quad (1.5)$$

Thus, the *sign* of $\mathcal{J}_k$ is determined by the boundary conditions – *independent* of the permanent charge $Q(x)$. However, *magnitudes* of $\mathcal{J}_k$'s, and hence, the *sign* and the *magnitude* of $\mathcal{I}$ do depend on the permanent charge $Q(x)$ in general. This motivated the following question raised and examined in [15]: *Can permanent charges produce zero current?* For the case $D_k(x) = h(x) = 1$ with a simple profile of a permanent charge

$$Q(x) = \begin{cases} 0, & 0 < x < a, \\ Q_0, & a < x < b, \\ 0, & b < x < 1, \end{cases} \quad (1.6)$$

where Q_0 is a constant, the authors of [15] derived a *single algebraic equation* (equation (3.2) in [15]) that determines the answer; that is, *there is a Q_0 such that $\mathcal{I} = 0$ if and only if the algebraic equation has a real root*. Furthermore, even for simple settings with two oppositely charged ion species, there are extremely rich phenomena for the effects of permanent charges, many are far from intuitive (see Section 4 in [15]).

In this work, we will consider a simple setting with $n = 2$ and $Q(x)$ as in (1.6) with $|Q_0|$ small relative to the boundary concentrations L_k 's and R_k 's. Treating system (1.1) as a singularly perturbed problem (see Section 2 for details), we will apply the geometric singular perturbation method ([14, 36]) to study the BVP (1.1) and (1.2). For the zeroth order approximation of the BVP (1.1) and (1.2), if we consider its dependence on Q_0 and write, particularly,

$$\mathcal{J}_k(Q_0) = \mathcal{J}_{k0} + \mathcal{J}_{k1}Q_0 + O(Q_0^2) \quad \text{and} \quad \mathcal{I}(Q_0) = \mathcal{I}_0 + \mathcal{I}_1Q_0 + O(Q_0^2), \quad (1.7)$$

then $\mathcal{J}_{k1}$'s and $\mathcal{I}_1$ contain the leading information about effects of the permanent charge $Q(x)$ on ionic flows. The main objective of this paper is to study dependences of $\mathcal{J}_{k1}$'s and $\mathcal{I}_1$ on the boundary conditions $\mathcal{V}$, L_k 's, R_k 's, and the channel geometry $h(x)$.

Our analysis indicates that effects of permanent charges depend on a rich interplay between boundary conditions and the channel geometry. Yet, we are able to characterize these complicated interplays in precise terms (see Section 4). Furthermore, interesting common features are revealed: for $Q_0 = 0$, only an average quantity of the channel geometry plays a role; however, for $Q_0 \neq 0$, details of the channel geometry matter, in particular, to optimize effects of a permanent charge, the channel should have a *short* and *narrow* neck within which the permanent charge is confined. We remark that the latter was not anticipated by the authors in the beginning. It is the analysis that leads to this finding, which is consistent with structures of typical ion channels. To the best of the authors' knowledge, this work is the first analysis on roles that channel geometry plays in ionic flows.

The rest of this paper is organized as follows. In Section 2, we provide the setup of our problem, review briefly the geometric singular perturbation theory for classical PNP models, and recall the *governing system* from [14] for singular orbits of the BVP. In Section 3, the singular orbit, determined by the solution of the *governing system*, is expanded in Q_0 near $Q_0 = 0$ to obtain expressions for $\mathcal{J}_{k1}$'s and $\mathcal{I}_1$ defined in (1.7). Section 4 is devoted to a detailed analysis of dependences of $\mathcal{J}_{k1}$'s and $\mathcal{I}_1$ on the boundary conditions $\mathcal{V}$, L_k 's, R_k 's, and the channel geometry $h(x)$. The paper ends with conclusion remarks in Section 5.

2 Problem Setup and the Governing System

Our study of effects of permanent charges on ionic flows starts with an analysis of the BVP (1.1) and (1.2).

2.1 The assumptions

For the BVP (1.1) and (1.2), we will take the same setting as that in [14]; that is,

(A1). We consider two ion species ($n = 2$) with $z_1 > 0 > z_2$.

(A2). For $Q(x)$ in (1.6), we assume $|Q_0|$ is small relative to L_k 's and R_k 's.

(A3). For μ_k , we only include the ideal component μ_k^{id} as in (1.4).

(A4). We assume that $\varepsilon_r(x) = \varepsilon_r$ and $D_k(x) = D_k$ are constants.

In the sequel, we will assume (A1)–(A4). With the re-scaling

$$\phi = \frac{e}{k_B T} \Phi, \quad V = \frac{e}{k_B T} \mathcal{V}, \quad \varepsilon^2 = \frac{\varepsilon_r \varepsilon_0 k_B T}{e^2}, \quad J_k = \frac{\mathcal{J}_k}{D_k},$$

and the expression (1.4) for $\mu_k = \mu_k^{id}(x)$, the BVP (1.1) and (1.2) is, for $k = 1, 2$,

$$\begin{aligned} \frac{\varepsilon^2}{h(x)} \frac{d}{dx} \left(h(x) \frac{d}{dx} \phi \right) &= -z_1 c_1 - z_2 c_2 - Q(x), \\ h(x) \frac{dc_k}{dx} + z_k h(x) c_k \frac{d\phi}{dx} &= -J_k, \quad \frac{dJ_k}{dx} = 0, \end{aligned} \quad (2.1)$$

with the boundary conditions,

$$\phi(0) = V, \quad c_k(0) = L_k; \quad \phi(1) = 0, \quad c_k(1) = R_k. \quad (2.2)$$

We will assume $\varepsilon > 0$ small and treat system (2.1) as a singularly perturbed system and apply the geometric singular perturbation framework from [14] for the BVP (2.1) and (2.2) (see [36] for a general setting with arbitrary n).

2.2 Geometric singular perturbation theory for (2.1)-(2.2)

We will rewrite system (2.1) into a dynamical system of first order ordinary differential equations and convert the BVP (2.1) and (2.2) to a *connecting problem*.

Denote the derivative with respect to x by overdot and introduce $u = \varepsilon \dot{\phi}$ and $\tau = x$. System (2.1) becomes, for $k = 1, 2$,

$$\begin{aligned} \varepsilon \dot{\phi} &= u, \quad \varepsilon \dot{u} = -z_1 c_1 - z_2 c_2 - Q(\tau) - \varepsilon \frac{h_\tau(\tau)}{h(\tau)} u, \\ \varepsilon \dot{c}_k &= -z_k c_k u - \frac{\varepsilon}{h(\tau)} J_k, \quad \dot{J}_k = 0, \quad \dot{\tau} = 1. \end{aligned} \quad (2.3)$$

System (2.3) is a singularly perturbed dynamical system with phase space $\mathbb{R}^7$ and state variables $(\phi, u, c_1, c_2, J_1, J_2, \tau)$. System (2.3) is the so-called *slow system*. The rescaling $x = \varepsilon \xi$ in (2.3) gives rise to the *fast system*, for $k = 1, 2$,

$$\begin{aligned} \phi' &= u, \quad u' = -z_1 c_1 - z_2 c_2 - Q(\tau) - \varepsilon \frac{h_\tau(\tau)}{h(\tau)} u, \\ c'_k &= -z_k c_k u - \frac{\varepsilon}{h(\tau)} J_k, \quad J'_k = 0, \quad \tau' = \varepsilon, \end{aligned} \quad (2.4)$$

where prime denotes the derivative with respect to the variable ξ .

Let B_L and B_R be the subsets of the phase space $\mathbb{R}^7$ defined by

$$\begin{aligned} B_L &= \{(V, u, L_1, L_2, J_1, J_2, 0) \in \mathbb{R}^7 : \text{arbitrary } u, J_1, J_2\}, \\ B_R &= \{(0, u, R_1, R_2, J_1, J_2, 1) \in \mathbb{R}^7 : \text{arbitrary } u, J_1, J_2\}. \end{aligned}$$

Then, the BVP (2.1) and (2.2) is equivalent to a *connecting problem*, namely, finding an orbit of (2.3) or (2.4) from B_L to B_R .

A general approach to the connecting problem: A strategy in analyzing this connecting problem of classical PNP models was developed in [14] (in [36] for a general setting), which has been successfully extended to handle PNP with hard-sphere ions in [27, 34, 38]. The classical PNP system is first reduced to two subsystems: the limiting fast and the limiting slow system. Due to two *special structures* of the classical PNP system, the limiting slow and limiting fast systems can be integrated. A singular orbit, the zeroth order approximation, for the connecting problem is constructed by matching slow orbits (those of the limiting slow system) and fast orbits (those of limiting fast system). The matching leads to a system of algebraic equations, the *governing system* for singular orbits of the connecting problem (see [14, 36]). Once a singular orbit is constructed, under a certain transversality condition, one can apply Exchange Lemmas

(see, e.g., [28, 29, 51]) to show that there is a unique solution of the BVP for small $\varepsilon > 0$ in the vicinity of the singular orbit.

For the present problem with small $|Q_0|$, one can obtain *explicit* expansions in Q_0 of singular slow and fast orbits. Application of the matching to the expansions will lead to an *explicit* expansion of a singular orbit for the connecting problem.

A shortcut based on the governing system: One can also start with the governing system in [14] directly and apply *regular* perturbation theory to obtain the singular orbit for small $|Q_0|$. This will be the approach adopted in this paper to complement the general full procedure described above and developed in other papers mentioned before.

We comment that, for $Q_0 = 0$, the BVP (1.1) and (1.2) was shown to have a unique solution in [39] for a general n with distinct z_k 's and for $h(x) = 1$; in particular, the transversality condition for an application of the Exchange Lemma is established. This result applies immediately to the present problem for $|Q_0|$ small. We thus will focus on singular orbits in the sequel.

We now summarize the construction of a singular orbit that leads to the governing system derived in [14] and recast in (2.7) and (2.8).

Due to the jumps of the permanent charge $Q(x)$ in (1.6) at $x = a$ and $x = b$, one splits the construction of a singular orbit on the interval $[0, 1]$ into that on three subintervals $[0, a]$, $[a, b]$ and $[b, 1]$ first. For the latter, we preassign (unknown) values of ϕ , c_1 and c_2 at $x = a$ and $x = b$:

$$\phi(a) = \phi^a, \quad c_1(a) = c_1^a, \quad c_2(a) = c_2^a; \quad \phi(b) = \phi^b, \quad c_1(b) = c_1^b, \quad c_2(b) = c_2^b. \quad (2.5)$$

In terms of these *six* unknowns, one can construct singular orbits on each subinterval.

- (i) The singular orbit on $[0, a]$ consists of two boundary layers (fast orbits) Γ_l^0 at $x = 0$, Γ_l^a at $x = a$ and one regular layer (slow orbit) Λ_l over $(0, a)$ with (ϕ, c_1, c_2, τ) being

$$(V, L_1, L_2, 0) \text{ at } x = 0 \text{ and } (\phi^a, c_1^a, c_2^a, a) \text{ at } x = a.$$

In particular, given (ϕ^a, c_1^a, c_2^a) , the scaled flux densities J_1^l, J_2^l and the value $u_l(a)$ are uniquely determined.

- (ii) The singular orbit on $[a, b]$ consists of two boundary layers Γ_m^a at $x = a$, Γ_m^b at $x = b$ and one regular layer Λ_m over (a, b) with (ϕ, c_1, c_2, τ) being

$$(\phi^a, c_1^a, c_2^a, a) \text{ at } x = a \text{ and } (\phi^b, c_1^b, c_2^b, b) \text{ at } x = b.$$

In particular, given (ϕ^a, c_1^a, c_2^a) and (ϕ^b, c_1^b, c_2^b) , the scaled flux densities J_1^m, J_2^m and the values $u_m(a)$ and $u_m(b)$ are uniquely determined.

- (iii) The singular orbit on $[b, 1]$ consists of two boundary layers Γ_r^b at $x = b$, Γ_r^1 at $x = 1$ and one regular layer Λ_r over $(b, 1)$ with (ϕ, c_1, c_2, τ) being

$$(\phi^b, c_1^b, c_2^b, b) \text{ at } x = b \text{ and } (0, R_1, R_2, 1) \text{ at } x = 1.$$

In particular, given (ϕ^b, c_1^b, c_2^b) , the scaled flux densities J_1^r, J_2^r and the value $u_r(b)$ are uniquely determined.

To obtain a singular orbit on $[0, 1]$, one requires the following matching conditions

$$J_1^l = J_1^m = J_1^r, \quad J_2^l = J_2^m = J_2^r, \quad u_l(a) = u_m(a), \quad u_m(b) = u_r(b). \quad (2.6)$$

This consists of *six* conditions, exactly the same as the number of unknowns preassigned in (2.5). The matching conditions (2.6) then reduce the singular connecting problem to the *governing system*, system (43) in [14], recast below (Note that α and β in [14] are related to z_1 and z_2 in this paper as $\alpha = z_1$ and $\beta = -z_2$):

$$\begin{aligned}
& z_1 c_1^a e^{z_1(\phi^a - \phi^{a,m})} + z_2 c_2^a e^{z_2(\phi^a - \phi^{a,m})} + Q_0 = 0, \\
& z_1 c_1^b e^{z_1(\phi^b - \phi^{b,m})} + z_2 c_2^b e^{z_2(\phi^b - \phi^{b,m})} + Q_0 = 0, \\
& \frac{z_2 - z_1}{z_2} c_1^{a,l} = c_1^a e^{z_1(\phi^a - \phi^{a,m})} + c_2^a e^{z_2(\phi^a - \phi^{a,m})} + Q_0(\phi^a - \phi^{a,m}), \\
& \frac{z_2 - z_1}{z_2} c_1^{b,r} = c_1^b e^{z_1(\phi^b - \phi^{b,m})} + c_2^b e^{z_2(\phi^b - \phi^{b,m})} + Q_0(\phi^b - \phi^{b,m}), \\
& J_1 = \frac{c_1^L - c_1^{a,l}}{H(a)} \left(1 + \frac{z_1(\phi^L - \phi^{a,l})}{\ln c_1^L - \ln c_1^{a,l}} \right) = \frac{c_1^{b,r} - c_1^R}{H(1) - H(b)} \left(1 + \frac{z_1(\phi^{b,r} - \phi^R)}{\ln c_1^{b,r} - \ln c_1^R} \right), \\
& J_2 = \frac{c_2^L - c_2^{a,l}}{H(a)} \left(1 + \frac{z_2(\phi^L - \phi^{a,l})}{\ln c_2^L - \ln c_2^{a,l}} \right) = \frac{c_2^{b,r} - c_2^R}{H(1) - H(b)} \left(1 + \frac{z_2(\phi^{b,r} - \phi^R)}{\ln c_2^{b,r} - \ln c_2^R} \right), \\
& \phi^{b,m} = \phi^{a,m} - (z_1 J_1 + z_2 J_2) y, \\
& c_1^{b,m} = e^{z_1 z_2 (J_1 + J_2) y} c_1^{a,m} - \frac{Q_0 J_1}{z_1 (J_1 + J_2)} \left(1 - e^{z_1 z_2 (J_1 + J_2) y} \right), \\
& J_1 + J_2 = - \frac{(z_1 - z_2)(c_1^{a,m} - c_1^{b,m}) + z_2 Q_0(\phi^{a,m} - \phi^{b,m})}{z_2 (H(b) - H(a))},
\end{aligned} \tag{2.7}$$

where $y > 0$ is also unknown, and

$$\begin{aligned}
& \phi^L = V - \frac{1}{z_1 - z_2} \ln \frac{-z_2 L_2}{z_1 L_1}, \quad \phi^R = -\frac{1}{z_1 - z_2} \ln \frac{-z_2 R_2}{z_1 R_1}, \\
& \phi^{a,l} = \phi^a - \frac{1}{z_1 - z_2} \ln \frac{-z_2 c_2^a}{z_1 c_1^a}, \quad \phi^{b,r} = \phi^b - \frac{1}{z_1 - z_2} \ln \frac{-z_2 c_2^b}{z_1 c_1^b}, \\
& c_1^L = \frac{1}{z_1} (z_1 L_1)^{\frac{-z_2}{z_1 - z_2}} (-z_2 L_2)^{\frac{z_1}{z_1 - z_2}}, \quad c_2^L = -\frac{1}{z_2} (z_1 L_1)^{\frac{-z_2}{z_1 - z_2}} (-z_2 L_2)^{\frac{z_1}{z_1 - z_2}}, \\
& c_1^{a,l} = \frac{1}{z_1} (z_1 c_1^a)^{\frac{-z_2}{z_1 - z_2}} (-z_2 c_2^a)^{\frac{z_1}{z_1 - z_2}}, \quad c_2^{a,l} = -\frac{1}{z_2} (z_1 c_1^a)^{\frac{-z_2}{z_1 - z_2}} (-z_2 c_2^a)^{\frac{z_1}{z_1 - z_2}}, \\
& c_1^{b,r} = \frac{1}{z_1} (z_1 c_1^b)^{\frac{-z_2}{z_1 - z_2}} (-z_2 c_2^b)^{\frac{z_1}{z_1 - z_2}}, \quad c_2^{b,r} = -\frac{1}{z_2} (z_1 c_1^b)^{\frac{-z_2}{z_1 - z_2}} (-z_2 c_2^b)^{\frac{z_1}{z_1 - z_2}}, \\
& c_1^{a,m} = e^{z_1(\phi^a - \phi^{a,m})} c_1^a, \quad c_1^{b,m} = e^{z_1(\phi^b - \phi^{b,m})} c_1^b, \\
& c_1^R = \frac{1}{z_1} (z_1 R_1)^{\frac{-z_2}{z_1 - z_2}} (-z_2 R_2)^{\frac{z_1}{z_1 - z_2}}, \quad c_2^R = -\frac{1}{z_2} (z_1 R_1)^{\frac{-z_2}{z_1 - z_2}} (-z_2 R_2)^{\frac{z_1}{z_1 - z_2}}, \\
& H(x) = \int_0^x h^{-1}(s) ds.
\end{aligned} \tag{2.8}$$

Once a solution for (2.7) and (2.8) is obtained, one can determine a singular orbit $(\Gamma_l^0 \cup \Lambda_l \cup \Gamma_l^a) \cup (\Gamma_m^a \cup \Lambda_m \cup \Gamma_m^b) \cup (\Gamma_r^b \cup \Lambda_r \cup \Gamma_r^1)$ to connect B_L and B_R .

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

As mentioned in the introduction, we will assume that $|Q_0|$ is small. With this assumption, we expand all unknown quantities in the governing system (2.7) and (2.8) in Q_0 ; for example, we write

$$\begin{aligned}
& \phi^a = \phi_0^a + \phi_1^a Q_0 + \phi_2^a Q_0^2 + o(Q_0^2), \quad \phi^b = \phi_0^b + \phi_1^b Q_0 + \phi_2^b Q_0^2 + o(Q_0^2), \\
& c_k^a = c_{k0}^a + c_{k1}^a Q_0 + c_{k2}^a Q_0^2 + o(Q_0^2), \quad c_k^b = c_{k0}^b + c_{k1}^b Q_0 + c_{k2}^b Q_0^2 + o(Q_0^2), \\
& y = y_0 + y_1 Q_0 + y_2 Q_0^2 + o(Q_0^2), \quad J_k = J_{k0} + J_{k1} Q_0 + J_{k2} Q_0^2 + o(Q_0^2).
\end{aligned} \tag{3.1}$$

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

3.1 Zeroth order solution of (2.7) and (2.8)

The problem for $Q_0 = 0$ has been solved in [35] for $h(x) = 1$ and, for a general $h(x)$, it can be solved as in [14] over the interval $[0, a]$. One can also obtain the zeroth order solution directly by substituting (3.1) into (2.7), expanding the identities in Q_0 , and comparing the terms of like-powers in Q_0 . We summarize the result for the zeroth order terms below. Denote

$$\alpha = \frac{H(a)}{H(1)} \quad \text{and} \quad \beta = \frac{H(b)}{H(1)}. \quad (3.2)$$

Proposition 3.1. *The zeroth order solution in Q_0 of (2.7) and (2.8) is given by*

$$\begin{aligned} c_{10}^{a,l} &= c_{10}^{a,m} = c_{10}^a = c_1^L + \alpha(c_1^R - c_1^L), & z_1 c_{10}^a &= -z_2 c_{20}^a, \\ c_{10}^{b,m} &= c_{10}^{b,r} = c_{10}^b = c_1^L + \beta(c_1^R - c_1^L), & z_1 c_{10}^b &= -z_2 c_{20}^b, \\ \phi_0^{a,l} &= \phi_0^{a,m} = \phi_0^a = \frac{\ln c_1^R - \ln c_{10}^a}{\ln c_1^R - \ln c_1^L} \phi^L + \frac{\ln c_{10}^a - \ln c_1^L}{\ln c_1^R - \ln c_1^L} \phi^R, \\ \phi_0^{b,m} &= \phi_0^{b,r} = \phi_0^b = \frac{\ln c_1^R - \ln c_{10}^b}{\ln c_1^R - \ln c_1^L} \phi^L + \frac{\ln c_{10}^b - \ln c_1^L}{\ln c_1^R - \ln c_1^L} \phi^R, \\ y_0 &= \frac{H(1)}{z_1(z_1 - z_2)(c_1^R - c_1^L)} \ln \frac{(1 - \beta)c_1^L + \beta c_1^R}{(1 - \alpha)c_1^L + \alpha c_1^R}, \\ J_{10} &= \frac{c_1^L - c_1^R}{H(1)(\ln c_1^L - \ln c_1^R)} (z_1 V + \ln L_1 - \ln R_1), \\ J_{20} &= \frac{c_2^L - c_2^R}{H(1)(\ln c_2^L - \ln c_2^R)} (z_2 V + \ln L_2 - \ln R_2). \end{aligned}$$

Corollary 3.2. *Under electroneutrality boundary conditions $z_1 L_1 = -z_2 L_2 = L$ and $z_1 R_1 = -z_2 R_2 = R$, one has $c_j^L = L_j$, $c_j^R = R_j$, $\phi^L = V$, $\phi^R = 0$, and*

$$\begin{aligned} z_1 c_{10}^{a,l} &= z_1 c_{10}^{a,m} = z_1 c_{10}^a = (1 - \alpha)L + \alpha R, & z_1 c_{10}^a &= -z_2 c_{20}^a, \\ z_1 c_{10}^{b,m} &= z_1 c_{10}^{b,r} = z_1 c_{10}^b = (1 - \beta)L + \beta R, & z_1 c_{10}^b &= -z_2 c_{20}^b, \end{aligned}$$

$$\begin{aligned} \phi_0^{a,l} &= \phi_0^{a,m} = \phi_0^a = \frac{\ln((1 - \alpha)L + \alpha R) - \ln R}{\ln L - \ln R} V, \\ \phi_0^{b,m} &= \phi_0^{b,r} = \phi_0^b = \frac{\ln((1 - \beta)L + \beta R) - \ln R}{\ln L - \ln R} V, \\ y_0 &= \frac{H(1)}{(z_1 - z_2)(L - R)} \ln \frac{(1 - \alpha)L + \alpha R}{(1 - \beta)L + \beta R}, \\ J_{10} &= \frac{L - R}{z_1 H(1)(\ln L - \ln R)} (z_1 V + \ln L - \ln R), \\ J_{20} &= -\frac{L - R}{z_2 H(1)(\ln L - \ln R)} (z_2 V + \ln L - \ln R). \end{aligned}$$

3.2 First order solution in Q_0 of (2.7) and (2.8)

For the first order terms in Q_0 , we will first express the intermediate variables such as $\phi_1^{a,l}$, $c_{k1}^{a,l}$, etc. in terms of zeroth order terms and ϕ_1^a , c_{k1}^a , etc.

Lemma 3.3. *One has*

$$\begin{aligned} z_1 c_{11}^a + z_2 c_{21}^a &= -\frac{1}{2}, & \phi_1^{a,m} &= \phi_1^a + \frac{1}{2z_1(z_1 - z_2)c_{10}^a}, \\ z_1 c_{11}^b + z_2 c_{21}^b &= -\frac{1}{2}, & \phi_1^{b,m} &= \phi_1^b + \frac{1}{2z_1(z_1 - z_2)c_{10}^b}. \end{aligned}$$

Proof. We will derive the first two identities. Substitute (3.1) into the first equation in (2.7) and expand in Q_0 to get, for the zeroth-order in Q_0 , $z_1 c_{10}^a + z_2 c_{20}^a = 0$ that is stated in Proposition 3.1; for the first order in Q_0 ,

$$\phi_1^a - \phi_1^{a,m} = -\frac{z_1 c_{11}^a + z_2 c_{21}^a + 1}{z_1^2 c_{10}^a + z_2^2 c_{20}^a}. \quad (3.3)$$

Substituting the expression for $c_1^{a,l}$ from (2.8) into the third equation in (2.7) and expanding the resulting equation up to Q_0^2 -order terms, one has that

$$\begin{aligned} -\frac{z_1 - z_2}{z_2} c_{10}^a + (c_{11}^a + c_{21}^a) Q_0 - \frac{(z_1 c_{11}^a + z_2 c_{21}^a)^2}{2(z_1 - z_2)z_1 c_{10}^a} Q_0^2 &= (c_{10}^a + c_{20}^a) + (c_{11}^a + c_{21}^a) Q_0 \\ &+ (z_1 c_{11}^a + z_2 c_{21}^a + 1)(\phi_1^a - \phi_1^{a,m}) Q_0^2 + \frac{z_1^2 c_{10}^a + z_2^2 c_{20}^a}{2} (\phi_1^a - \phi_1^{a,m})^2 Q_0^2. \end{aligned}$$

The zeroth and first order terms on both sides are identical. The Q_0^2 -terms give

$$-\frac{(z_1 c_{11}^a + z_2 c_{21}^a)^2}{2(z_1 - z_2)z_1 c_{10}^a} = (z_1 c_{11}^a + z_2 c_{21}^a + 1)(\phi_1^a - \phi_1^{a,m}) + \frac{z_1^2 c_{10}^a + z_2^2 c_{20}^a}{2} (\phi_1^a - \phi_1^{a,m})^2.$$

Substitute (3.3) for $\phi_1^a - \phi_1^{a,m}$ into above to get

$$\frac{(z_1 c_{11}^a + z_2 c_{21}^a)^2}{(z_1 - z_2)z_1 c_{10}^a} = \frac{(z_1 c_{11}^a + z_2 c_{21}^a + 1)^2}{z_1^2 c_{10}^a + z_2^2 c_{20}^a}.$$

Note that $(z_1 - z_2)z_1 c_{10}^a = z_1^2 c_{10}^a + z_2^2 c_{20}^a$. We thus have $z_1 c_{11}^a + z_2 c_{21}^a = -\frac{1}{2}$. The latter and (3.3) then give the second identity. $\square$

Lemma 3.4. *One has*

$$\begin{aligned} \phi_1^{a,l} &= \phi_1^a - \frac{c_{10}^a c_{21}^a - c_{20}^a c_{11}^a}{(z_1 - z_2)c_{10}^a c_{20}^a}, & c_{11}^{a,l} &= \frac{z_2(c_{11}^a + c_{21}^a)}{z_2 - z_1}, & c_{21}^{a,l} &= \frac{z_1(c_{11}^a + c_{21}^a)}{z_1 - z_2}, \\ c_{11}^{a,m} &= c_{11}^a - \frac{1}{2(z_1 - z_2)}, & c_{11}^{b,m} &= c_{11}^b - \frac{1}{2(z_1 - z_2)}, \\ \phi_1^{b,r} &= \phi_1^b - \frac{c_{10}^b c_{21}^b - c_{20}^b c_{11}^b}{(z_1 - z_2)c_{10}^b c_{20}^b}, & c_{11}^{b,r} &= \frac{z_2(c_{11}^b + c_{21}^b)}{z_2 - z_1}, & c_{21}^{b,r} &= \frac{z_1(c_{11}^b + c_{21}^b)}{z_1 - z_2}. \end{aligned}$$

Proof. One expands the relevant identities in (2.8) in Q_0 , compares the first order terms in Q_0 and uses the results for the zeroth order terms in Proposition 3.1 and the relation in Lemma 3.3. The relations then follows. The details will be omitted. $\square$

Applying the same procedure as above to the last four identities in (2.7) and using results in Proposition 3.1 and Lemmas 3.3 and 3.4, one obtains directly

$$\begin{aligned}
J_{11} &= -\frac{z_1(c_1^L - c_{10}^a)}{\alpha H(1)(\ln c_1^L - \ln c_{10}^a)} \left(\phi_1^a - \frac{z_2(\phi_0^L - \phi_0^a)(c_{11}^a + c_{21}^a)}{(z_2 - z_1)(\ln c_1^L - \ln c_{10}^a)c_{10}^a} \right. \\
&\quad \left. - \frac{c_{10}^a c_{21}^a - c_{20}^a c_{11}^a}{(z_1 - z_2)c_{10}^a c_{20}^a} \right) - \frac{z_2(c_{11}^a + c_{21}^a)}{(z_2 - z_1)\alpha H(1)} \left(1 + \frac{z_1(\phi_0^L - \phi_0^a)}{\ln c_1^L - \ln c_{10}^a} \right) \\
&= -\frac{z_1(c_{10}^b - c_1^R)}{(1 - \beta)H(1)(\ln c_1^R - \ln c_{10}^b)} \left(\phi_1^b - \frac{z_2(\phi_0^R - \phi_0^b)(c_{11}^b + c_{21}^b)}{(z_2 - z_1)(\ln c_1^R - \ln c_{10}^b)c_{10}^b} \right. \\
&\quad \left. - \frac{c_{10}^b c_{21}^b - c_{20}^b c_{11}^b}{(z_1 - z_2)c_{10}^b c_{20}^b} \right) - \frac{z_2(c_{11}^b + c_{21}^b)}{(z_1 - z_2)(1 - \beta)H(1)} \left(1 + \frac{z_1(\phi_0^R - \phi_0^b)}{\ln c_1^R - \ln c_{10}^b} \right), \\
J_{21} &= -\frac{z_2(c_2^L - c_{20}^a)}{\alpha H(1)(\ln c_2^L - \ln c_{20}^a)} \left(\phi_1^a - \frac{z_1(\phi_0^L - \phi_0^a)(c_{11}^a + c_{21}^a)}{(z_1 - z_2)(\ln c_2^L - \ln c_{20}^a)c_{20}^a} \right. \\
&\quad \left. - \frac{c_{10}^a c_{21}^a - c_{20}^a c_{11}^a}{(z_1 - z_2)c_{10}^a c_{20}^a} \right) - \frac{z_1(c_{11}^a + c_{21}^a)}{(z_1 - z_2)\alpha H(1)} \left(1 + \frac{z_2(\phi_0^L - \phi_0^a)}{\ln c_2^L - \ln c_{20}^a} \right) \\
&= -\frac{z_2(c_{20}^b - c_2^R)}{(1 - \beta)H(1)(\ln c_2^R - \ln c_{20}^b)} \left(\phi_1^b - \frac{z_1(\phi_0^R - \phi_0^b)(c_{11}^b + c_{21}^b)}{(z_1 - z_2)(\ln c_2^R - \ln c_{20}^b)c_{20}^b} \right. \\
&\quad \left. - \frac{c_{10}^b c_{21}^b - c_{20}^b c_{11}^b}{(z_1 - z_2)c_{10}^b c_{20}^b} \right) + \frac{z_1(c_{11}^b + c_{21}^b)}{(z_1 - z_2)(1 - \beta)H(1)} \left(1 + \frac{z_2(\phi_0^R - \phi_0^b)}{\ln c_2^R - \ln c_{20}^b} \right), \\
\phi_1^b &= \phi_1^a + \frac{c_{10}^b - c_{10}^a}{2z_1(z_1 - z_2)c_{10}^a c_{10}^b} - (z_1 J_{10} + z_2 J_{20})y_1 - (z_1 J_{11} + z_2 J_{21})y_0, \\
c_{11}^b &= \left[c_{11}^a - \frac{1}{2(z_1 - z_2)} + \frac{J_{10}}{z_1(J_{10} + J_{20})} \right] \frac{c_{10}^b}{c_{10}^a} + \frac{1}{2(z_1 - z_2)} \\
&\quad + z_1 z_2 c_{10}^b ((J_{10} + J_{20})y_1 + (J_{11} + J_{21})y_0) - \frac{J_{10}}{z_1(J_{10} + J_{20})}, \\
J_{11} + J_{21} &= \frac{(z_2 - z_1)(c_{11}^a - c_{11}^b)}{z_2(\beta - \alpha)H(1)} - \frac{\phi_0^a - \phi_0^b}{(\beta - \alpha)H(1)}.
\end{aligned} \tag{3.4}$$

We are now ready to obtain the first order terms.

Proposition 3.5. *First order terms of the solution in Q_0 to system (2.7) are given by*

$$\begin{aligned}
c_{11}^a &= \frac{z_2 \alpha (\phi_0^b - \phi_0^a)}{z_1 - z_2} - \frac{1}{2(z_1 - z_2)}, \quad c_{21}^a = \frac{z_1 \alpha (\phi_0^b - \phi_0^a)}{z_2 - z_1} - \frac{1}{2(z_2 - z_1)}, \\
c_{11}^b &= \frac{z_2(1 - \beta)(\phi_0^a - \phi_0^b)}{z_1 - z_2} - \frac{1}{2(z_1 - z_2)}, \quad c_{21}^b = \frac{z_1(1 - \beta)(\phi_0^a - \phi_0^b)}{z_2 - z_1} - \frac{1}{2(z_2 - z_1)}, \\
\phi_1^a &= \frac{(1 + z_1 \lambda)(1 + z_2 \lambda)(c_{10}^b - c_{10}^a)(\ln c_1^L - \ln c_{10}^a)}{z_1(z_1 - z_2)c_{10}^a c_{10}^b(\ln c_1^R - \ln c_1^L)} + \frac{1}{2z_1(z_1 - z_2)c_{10}^a} + \frac{z_2 \alpha (\phi_0^b - \phi_0^a)}{(z_1 - z_2)c_{10}^a} \lambda, \\
\phi_1^b &= \frac{(1 + z_1 \lambda)(1 + z_2 \lambda)(c_{10}^b - c_{10}^a)(\ln c_1^R - \ln c_{10}^b)}{z_1(z_1 - z_2)c_{10}^a c_{10}^b(\ln c_1^L - \ln c_1^R)} + \frac{1}{2z_1(z_1 - z_2)c_{10}^b} + \frac{z_2(1 - \beta)(\phi_0^a - \phi_0^b)}{(z_1 - z_2)c_{10}^b} \lambda, \\
y_1 &= \frac{((1 - \beta)c_1^L + \alpha c_1^R)(\phi_0^a - \phi_0^b)}{z_1(z_1 - z_2)(J_{10} + J_{20})c_{10}^a c_{10}^b} + \frac{(\ln c_{10}^a - \ln c_{10}^b)(\phi_0^a - \phi_0^b)}{z_1(z_1 - z_2)(J_{10} + J_{20})(c_1^L - c_1^R)} \\
&\quad - \frac{(z_2 J_{10} + z_1 J_{20})(c_{10}^a - c_{10}^b)}{z_1^2 z_2 (z_1 - z_2)(J_{10} + J_{20})^2 c_{10}^a c_{10}^b},
\end{aligned}$$

$$J_{11} = \frac{A(z_2(1-B)\lambda + 1)}{(z_1 - z_2)H(1)}(z_1\lambda + 1), \quad J_{21} = \frac{A(z_1(1-B)\lambda + 1)}{(z_2 - z_1)H(1)}(z_2\lambda + 1),$$

where

$$\begin{aligned} \lambda &= \frac{\phi^L - \phi^R}{\ln c_1^L - \ln c_1^R}, \quad A = \frac{(c_1^L - c_1^R)(c_{10}^b - c_{10}^a)}{c_{10}^a c_{10}^b (\ln c_1^L - \ln c_1^R)}, \\ B &= \frac{\ln c_{10}^b - \ln c_{10}^a}{A} = \frac{(\ln c_1^L - \ln c_1^R)(\ln c_{10}^b - \ln c_{10}^a)}{(c_1^L - c_1^R)(c_{10}^b - c_{10}^a)} c_{10}^a c_{10}^b. \end{aligned} \quad (3.5)$$

Proof. The two equations $z_1 c_{11}^a + z_2 c_{21}^a = -\frac{1}{2}$ and $z_1 c_{11}^b + z_2 c_{21}^b = -\frac{1}{2}$ in Lemma 3.3 together with the seven equations in (3.4) form a system of nine *linear* equations in the nine first order term variables $(c_{11}^a, c_{21}^a, c_{11}^b, c_{21}^b, \phi_1^a, \phi_1^b, y_1, J_{11}, J_{21})$. Other quantities in the system are zeroth order terms. The solution of this linear system gives rise to the expressions of the first order terms. We omit the details. $\square$

Remark 3.6. In Proposition 3.5, we have expressed the first order quantities ϕ_1^a, ϕ_1^b, y_1 and J_{k1} 's in terms of zeroth order quantities, such as $c_1^L, c_1^R, c_{10}^a, c_{10}^b$, associated to the 1st ion species. Of course, they can all be expressed in terms of zeroth order quantities associated to the 2nd ion species; that is, on the right-hand-sides of the formulas for ϕ_1^a, ϕ_1^b, y_1 and J_{k1} 's, one can interchange the subscripts 1 and 2 to get the same results, after applying the results in Proposition 3.1. There is another symmetry; that is, if one flips the channel with the formal transformation $(V, L_k, 0, R_k; a, b) \rightarrow (0, R_k, V, L_k; b, a)$, then it should result in the change $(\phi_1^a, c_{k1}^a, \phi_1^b, c_{k1}^b, y_1, J_{k1}, \alpha, \beta) \rightarrow (\phi_1^b, c_{k1}^b, \phi_1^a, c_{k1}^a, -y_1, -J_{k1}, 1 - \beta, 1 - \alpha)$. These two symmetries can be verified for the corresponding formulas in Proposition 3.5 easily and we have done so.

4 Effects of Permanent Charge and Channel Geometry

In this section, we study effects of permanent charges and channel geometry on individual fluxes and on I-V relations under electroneutrality conditions

$$z_1 L_1 = -z_2 L_2 = L \quad \text{and} \quad z_1 R_1 = -z_2 R_2 = R. \quad (4.1)$$

This will be based on the singular orbit of the BVP constructed in the previous section.

For $|Q_0|$ small, the flux $\mathcal{J}_k$ of the k th ion species and the current $\mathcal{I}$ are

$$\mathcal{J}_k = D_k J_{k0} + D_k J_{k1} Q_0 + O(Q_0^2), \quad \mathcal{I} = \mathcal{I}_0 + \mathcal{I}_1 Q_0 + O(Q_0^2),$$

where

$$\mathcal{I}_0 = z_1 D_1 J_{10} + z_2 D_2 J_{20} \quad \text{and} \quad \mathcal{I}_1 = z_1 D_1 J_{11} + z_2 D_2 J_{21}. \quad (4.2)$$

The quantities J_{11} and J_{21} encode the leading effects of permanent charges and channel geometry on the ionic flow and will be analyzed for this purpose.

4.1 A comparison between zeroth order and first order in Q_0

For the k th ion species, denote the difference of its electrochemical potentials at the two boundaries by

$$\mu_k^\delta := \mu_k^\delta(V; L_k, R_k) = \mu_k(0) - \mu_k(1) = k_B T (z_k V + \ln L_k - \ln R_k). \quad (4.3)$$

Under the electroneutrality conditions (4.1), from Corollary 3.2,

$$\begin{aligned} J_{10} &= \frac{L - R}{z_1 H(1)(\ln L - \ln R)} \frac{\mu_1^\delta}{k_B T} = \frac{L_1 - R_1}{H(1)(\ln L_1 - \ln R_1)} \frac{\mu_1^\delta}{k_B T}, \\ J_{20} &= \frac{R - L}{z_2 H(1)(\ln L - \ln R)} \frac{\mu_2^\delta}{k_B T} = \frac{L_2 - R_2}{H(1)(\ln L_2 - \ln R_2)} \frac{\mu_2^\delta}{k_B T}. \end{aligned} \quad (4.4)$$

Also, it follows from Proposition 3.5 that

$$\begin{aligned} J_{11} &= \frac{A(z_2(1 - B)V + \ln L - \ln R)}{(z_1 - z_2)H(1)(\ln L - \ln R)^2} \frac{\mu_1^\delta}{k_B T}, \\ J_{21} &= \frac{A(z_1(1 - B)V + \ln L - \ln R)}{(z_2 - z_1)H(1)(\ln L - \ln R)^2} \frac{\mu_2^\delta}{k_B T}, \end{aligned} \quad (4.5)$$

where, in terms of α and β defined in (3.2), A and B defined in (3.5) become

$$\begin{aligned} A &= A(L, R) = -\frac{(\beta - \alpha)(L - R)^2}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)}, \\ B &= B(L, R) = \frac{\ln((1 - \beta)L + \beta R) - \ln((1 - \alpha)L + \alpha R)}{A}. \end{aligned} \quad (4.6)$$

Lemma 4.1. *The quantities $A = A(L, R)$, $B = B(L, R)$ and $\mu_k^\delta(V; L, R)$ scale invariantly in (L, R) ; that is, for any $s > 0$,*

$$A(sL, sR) = A(L, R), \quad B(sL, sR) = B(L, R), \quad \text{and} \quad \mu_k^\delta(V; sL, sR) = \mu_k^\delta(V; L, R).$$

Proof. It follows directly from the expressions for A, B in (4.6) and μ_k^δ in (4.3). $\square$

Proposition 4.2. *The quantities $J_{k0}(V; L, R)$ and $\mathcal{I}_0(V; L, R)$ scale linearly in (L, R) , and $J_{k1}(V; L, R)$ and $\mathcal{I}_1(V; L, R)$ scale invariantly in (L, R) ; that is, for any $s > 0$,*

$$\begin{aligned} J_{k0}(V; sL, sR) &= sJ_{k0}(V; L, R), \quad \mathcal{I}_0(V; sL, sR) = s\mathcal{I}_0(V; L, R), \\ J_{k1}(V; sL, sR) &= J_{k1}(V; L, R), \quad \mathcal{I}_1(V; sL, sR) = \mathcal{I}_1(V; L, R). \end{aligned}$$

Proof. The statements follow directly from (4.2), (4.4), (4.5), and Lemma 4.1. $\square$

Remark 4.3. (i) Formulas (4.4) and (4.5) for the approximations up to order $O(Q_0)$ of J_{k0} 's and J_{k1} 's are consistent with the formulas in (1.5), that is, for $|Q_0|$ small, $\mathcal{J}_k = D_k J_{k0} + D_k J_{k1} Q_0$ is positively proportional to $\mu_k^\delta = \mu_k(0) - \mu_k(1)$.

(ii) Note that J_{10} is independent of the other type of ion species; that is, for different values of z_2 , J_{10} stays the same as long as the electroneutrality conditions hold. Likewise, J_{20} is independent of z_1 in the same sense. However, J_{11} does depend on z_2 and J_{21} does depend on z_1 . This is expected since a permanent charge $Q(x)$ provides an agency for one ion species to interact with the other through electric field.

(iii) The channel geometry does have effects on J_{10} and J_{20} but in a simpler way through the average quantity $H(1)$ on the denominator in (4.4). More details of the channel geometry through α and β in addition to $H(1)$ are involved in (4.5) for J_{11} and J_{21} . We will examine the roles of channel geometry on the signs of J_{k1} and on the magnitudes of J_{k1} in the next part.

To end this part, we introduce a function that will be used in a number of places below. For $t > 0$, set

$$\gamma(t) = \frac{t \ln t - t + 1}{(t - 1) \ln t} \quad \text{for } t \neq 1 \quad \text{and} \quad \gamma(1) = \frac{1}{2}. \quad (4.7)$$

One establishes easily that

Lemma 4.4. *For $t > 0$, $0 < \gamma(t) < 1$, $\gamma'(t) > 0$, $\lim_{t \rightarrow 0} \gamma(t) = 0$, $\lim_{t \rightarrow \infty} \gamma(t) = 1$.*

4.2 Dependence of signs of J_{k1} on channel geometry

In this part, we will determine the signs of J_{k1} 's relative to those of J_{k0} 's in terms of the channel geometry (α, β) and the boundary condition (V, L, R) .

Lemma 4.5. *Assume $z_1 > 0 > z_2$. Then, A and $R - L$ have the same sign.*

Proof. This follows from the expression for A in (4.6). □

Lemma 4.6. *Set $t = L/R$ and let $\gamma(t)$ be as in (4.7). Then, $B > 0$ and $\lim_{t \rightarrow 1} B = 1$.*

For $t > 1$, one has

(i) *if $\alpha < \gamma(t)$, then there exists a unique $\beta_1 \in (\alpha, 1)$ such that*

$$1 - B < 0 \text{ for } \beta \in (\alpha, \beta_1) \text{ and } 1 - B > 0 \text{ for } \beta \in (\beta_1, 1);$$

(ii) *if $\alpha \geq \gamma(t)$, then $1 - B > 0$.*

For $t < 1$, one has

(iii) *if $1 - \beta < \gamma(1/t)$, then there exists a unique $\alpha_1 \in (0, \beta)$ such that*

$$1 - B < 0 \text{ for } \alpha \in (\alpha_1, \beta) \text{ and } 1 - B > 0 \text{ for } \alpha \in (0, \alpha_1);$$

(iv) *if $1 - \beta \geq \gamma(1/t)$, then $1 - B > 0$.*

Proof. Since both A and $\ln((1 - \beta)L + \beta R) - \ln((1 - \alpha)L + \alpha R)$ have the opposite sign as that of $L - R$, it yields that $B > 0$. With $t = L/R$,

$$1 - B = \frac{g(\beta)}{(\beta - \alpha)(t - 1)^2},$$

where

$$g(\beta) = ((1 - \alpha)t + \alpha)((1 - \beta)t + \beta) \ln t \ln \frac{(1 - \beta)t + \beta}{(1 - \alpha)t + \alpha} + (\beta - \alpha)(t - 1)^2.$$

With a direct application of l'Hospital's rule, one has $\lim_{t \rightarrow 1} (1 - B) = 0$.

For the other statements, we will establish (i) and (ii) for $t > 1$. Those for $t < 1$ can be established in a similar way.

It's clear that $(1 - B)$ has the same sign as that of $g(\beta)$. Note that,

$$g'(\beta) = ((1 - \alpha)t + \alpha)(1 - t) \ln t \ln \frac{(1 - \beta)t + \beta}{(1 - \alpha)t + \alpha} + (\alpha - \gamma(t))(t - 1)^2 \ln t,$$

$$g''(\beta) = \frac{(1 - \alpha)t + \alpha}{(1 - \beta)t + \beta} (1 - t)^2 \ln t,$$

where $\gamma(t)$ is defined in (4.7). Therefore, for $t > 1$, $g(\beta)$ is concave upward. Furthermore, since $\lim_{\beta \rightarrow \alpha} g(\beta) = 0$, one has, for $t > 1$,

(i) *if $\alpha < \gamma(t)$, then $\lim_{\beta \rightarrow \alpha} g'(\beta) < 0$, and hence, there exists a unique $\beta_1 > \alpha$ such that $g(\beta) < 0$ for $\beta \in (\alpha, \beta_1)$ and $g(\beta) > 0$ for $\beta > \beta_1$;*

(ii) *if $\alpha \geq \gamma(t)$, then $\lim_{\beta \rightarrow \alpha} g'(\beta) \geq 0$, and hence, $g(\beta) > 0$ for $\beta > \alpha$.*

It remains to show that $\beta_1 < 1$, which is implied by $g(1) > 0$. For $t > 1$, set

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

It follows from $f''(\alpha) = -\frac{(1-t)^2 \ln t}{(1-\alpha)t + \alpha} < 0$ that $f(\alpha)$ is concave downward for $t > 1$. Note that $f(1) = 0$. Thus, $g(1) > 0$ is implied by $f(0) \geq 0$. Set now $\rho(t) := f(0) = -t(\ln t)^2 + (t-1)^2$. Then,

$$\rho'(t) = -(\ln t)^2 - 2 \ln t + 2(t-1) \quad \text{and} \quad \rho''(t) = \frac{2}{t}(t-1 - \ln t) > 0.$$

Since $\rho(1) = \rho'(1) = 0$ and $\rho''(t) > 0$ for $t > 1$, one concludes that $\rho(t) = f(0) > 0$. $\square$

Theorem 4.7. *Suppose $B = 1$ where B is in (4.6). Then, $J_{10}J_{11} < 0$ and $J_{20}J_{21} > 0$.*

Proof. It follows from the formulas (4.4) for J_{k0} 's, (4.5) for J_{k1} 's and Lemma 4.5. $\square$

Theorem 4.8. *Suppose $B \neq 1$ where B is in (4.6). Let V_q^1 and V_q^2 be as*

$$V_q^1 = V_q^1(L, R) = -\frac{\ln L - \ln R}{z_2(1-B)} \quad \text{and} \quad V_q^2 = V_q^2(L, R) = -\frac{\ln L - \ln R}{z_1(1-B)}; \quad (4.8)$$

that is, $z_2(1-B)V_q^1 + \ln L - \ln R = 0$ and $z_1(1-B)V_q^2 + \ln L - \ln R = 0$.

Then, for $t = L/R > 1$, $A < 0$ where A is in (4.6), and

(i) if $\alpha < \gamma(t)$ where $\gamma(t)$ is in (4.7) and $\beta \in (\alpha, \beta_1)$, then $V_q^1 < 0 < V_q^2$; and,

(i1) for $V \in (V_q^1, V_q^2)$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} > 0$;

(i2) for $V < V_q^1$, $J_{10}J_{11} > 0$ and $J_{20}J_{21} > 0$;

(i3) for $V > V_q^2$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} < 0$;

or equivalently, for $V > V_q^1$, (small) positive Q_0 reduces $|J_1|$ and, for $V < V_q^1$, (small) positive Q_0 strengthens $|J_1|$; and for $V > V_q^2$, (small) positive Q_0 reduces $|J_2|$ and, for $V < V_q^2$, (small) positive Q_0 strengthens $|J_2|$;

(ii) if either $\alpha < \gamma(t)$ and $\beta \in (\beta_1, 1)$ or $\alpha \geq \gamma(t)$, then $V_q^1 > 0 > V_q^2$; and,

(ii1) for $V \in (V_q^2, V_q^1)$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} > 0$;

(ii2) for $V > V_q^1$, $J_{10}J_{11} > 0$ and $J_{20}J_{21} > 0$;

(ii3) for $V < V_q^2$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} < 0$;

or equivalently, for $V < V_q^1$, (small) positive Q_0 reduces $|J_1|$ and, for $V > V_q^1$, (small) positive Q_0 strengthens $|J_1|$; and for $V < V_q^2$, (small) positive Q_0 reduces $|J_2|$ and, for $V > V_q^2$, (small) positive Q_0 strengthens $|J_2|$;

For $t = L/R < 1$, $A > 0$, and

(iii) if $1 - \beta < \gamma(1/t)$ and $\alpha \in (\alpha_1, \beta)$, then $V_q^1 > 0 > V_q^2$; and,

(iii1) for $V \in (V_q^2, V_q^1)$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} > 0$;

(iii2) for $V > V_q^1$, $J_{10}J_{11} > 0$ and $J_{20}J_{21} > 0$;

(iii3) for $V < V_q^2$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} < 0$;

or equivalently, for $V < V_q^1$, (small) positive Q_0 reduces $|J_1|$ and, for $V > V_q^1$, (small) positive Q_0 strengthens $|J_1|$; and for $V < V_q^2$, (small) positive Q_0 reduces $|J_2|$ and, for $V > V_q^2$, (small) positive Q_0 strengthens $|J_2|$;

(iv) if either $1 - \beta < \gamma(1/t)$ and $\alpha \in (0, \alpha_1)$ or $1 - \beta \geq \gamma(1/t)$, then $V_q^1 < 0 < V_q^2$; and,

(iv1) for $V \in (V_q^1, V_q^2)$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} > 0$;

(iv2) for $V < V_q^1$, $J_{10}J_{11} > 0$ and $J_{20}J_{21} > 0$;

(iv3) for $V > V_q^2$, $J_{10}J_{11} < 0$ and $J_{20}J_{21} < 0$;

or equivalently, for $V > V_q^1$, (small) positive Q_0 reduces $|J_1|$ and, for $V < V_q^1$, (small) positive Q_0 strengthens $|J_1|$; and for $V > V_q^2$, (small) positive Q_0 reduces $|J_2|$ and, for $V < V_q^2$, (small) positive Q_0 strengthens $|J_2|$.

Proof. We will establish the statement for case (i1) with $t = L/R > 1$. The others can be established in the similar way.

It follows from Lemma 4.6 and $z_1 > 0 > z_2$ that, for this case, $z_2(1 - B) > 0 > z_1(1 - B)$. Thus, from (4.8), one gets $V_q^1 < 0 < V_q^2$. Furthermore, for $V \in (V_q^1, V_q^2)$, one has $z_2(1 - B)V + \ln L - \ln R > 0$ and $z_1(1 - B)V + \ln L - \ln R > 0$. Since $A < 0$, one concludes that

$$\frac{A(z_2(1 - B)V + \ln L - \ln R)}{(z_1 - z_2)H(1)(\ln L - \ln R)^2} < 0 \quad \text{and} \quad \frac{A(z_1(1 - B)V + \ln L - \ln R)}{(z_2 - z_1)H(1)(\ln L - \ln R)^2} > 0. \quad (4.9)$$

Note that, from (4.4), J_{k0} is a scalar multiple of μ_k^δ with positive multiplier. The claim in (i1) then follows from (4.5) and (4.9). $\square$

Proposition 4.9. *The potentials $V_q^1(L, R)$ and $V_q^2(L, R)$ scale invariantly in (L, R) .*

Proof. This follows from the expressions (4.8) for V_q^1 and V_q^2 and that $B = B(L, R)$ scales invariantly in (L, R) as in Lemma 4.1. $\square$

4.3 Dependence of magnitudes of J_{k1} on channel geometry

We now analyze how magnitudes of J_{k1} depend on the channel geometry (α, β) and the boundary condition (V, L, R) . It turns out that there is a common feature that is essentially independent of the boundary condition (V, L, R) .

Recall that $(\alpha, \beta) \in \Omega := \{0 \leq \alpha \leq \beta \leq 1\}$. Write

$$J_{11} = \frac{p_1(\alpha, \beta)\mu_1^\delta(V; L, R)}{k_B T(z_1 - z_2)H(1)(\ln L - \ln R)^2} \quad \text{and} \quad J_{21} = \frac{p_2(\alpha, \beta)\mu_2^\delta(V; L, R)}{k_B T(z_2 - z_1)H(1)(\ln L - \ln R)^2}$$

where

$$p_1(\alpha, \beta) = \frac{(\alpha - \beta)(L - R)^2(z_2V + \ln L - \ln R)}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)} - z_2V \ln \frac{(1 - \beta)L + \beta R}{(1 - \alpha)L + \alpha R},$$

$$p_2(\alpha, \beta) = \frac{(\alpha - \beta)(L - R)^2(z_1V + \ln L - \ln R)}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)} - z_1V \ln \frac{(1 - \beta)L + \beta R}{(1 - \alpha)L + \alpha R}.$$

Lemma 4.10. *If $\gamma_1^* = \gamma(L/R) - \frac{1}{z_2V} \in (0, 1)$ where $\gamma(t) \in (0, 1)$ is defined in (4.7), then $|p_1(\alpha, \beta)|$ attains its maximum at either $(0, \gamma_1^*)$ or $(\gamma_1^*, 1)$. Otherwise, $|p_1(\alpha, \beta)|$ attains its maximum at $(0, 1)$.*

Similarly, if $\gamma_2^ = \gamma(L/R) - \frac{1}{z_1V} \in (0, 1)$, then $|p_2(\alpha, \beta)|$ attains its maximum at either $(0, \gamma_1^*)$ or $(\gamma_1^*, 1)$. Otherwise, $|p_2(\alpha, \beta)|$ attains its maximum at $(0, 1)$.*

Proof. We prove the statement for $p_1(\alpha, \beta)$. Note that $p_1(\alpha, \alpha) = 0$.

$$\partial_\alpha p_1(\alpha, \beta) = \frac{(L - R)^2(z_2V + \ln L - \ln R)}{((1 - \alpha)L + \alpha R)^2(\ln L - \ln R)} + z_2V \frac{R - L}{(1 - \alpha)L + \alpha R},$$

$$\partial_\beta p_1(\alpha, \beta) = - \frac{(L - R)^2(z_2V + \ln L - \ln R)}{((1 - \beta)L + \beta R)^2(\ln L - \ln R)} - z_2V \frac{R - L}{(1 - \beta)L + \beta R}.$$

Therefore, any critical point (α, β) satisfies $\alpha = \beta$ where p_1 vanishes. Hence, the maximum of $|p_1(\alpha, \beta)|$ on Ω attains on the boundary

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

On the portion of the boundary $\{\alpha = 0, \beta \in [0, 1]\}$,

$$\begin{aligned} p_1(0, \beta) &= -\frac{\beta(L-R)^2(z_2V + \ln L - \ln R)}{L((1-\beta)L + \beta R)(\ln L - \ln R)} - z_2V \ln \frac{(1-\beta)L + \beta R}{L}, \\ \partial_\beta p_1(0, \beta) &= -\frac{(L-R)^2(z_2V + \ln L - \ln R)}{((1-\beta)L + \beta R)^2(\ln L - \ln R)} - z_2V \frac{R-L}{(1-\beta)L + \beta R}. \end{aligned}$$

The critical point of $p_1(0, \beta)$ is

$$\beta = \gamma_1^* = \frac{L}{L-R} - \frac{1}{\ln L - \ln R} - \frac{1}{z_2V}.$$

To have $\gamma_1^* \in (0, 1)$, necessarily,

$$-\gamma(t) < -\frac{1}{z_2V} < 1 - \gamma(t) \quad \text{or} \quad \gamma(t) - 1 < \frac{1}{z_2V} < \gamma(t)$$

where $t = L/R$ and $\gamma(t) \in (0, 1)$ is defined in (4.7).

On the boundary $\{\alpha \in [0, 1], \beta = 1\}$,

$$\begin{aligned} p_1(\alpha, 1) &= \frac{(\alpha-1)(L-R)^2(z_2V + \ln L - \ln R)}{R((1-\alpha)L + \alpha R)(\ln L - \ln R)} - z_2V \ln \frac{R}{(1-\alpha)L + \alpha R}, \\ \partial_\alpha p_1(\alpha, 1) &= \frac{(L-R)^2(z_2V + \ln L - \ln R)}{((1-\alpha)L + \alpha R)^2(\ln L - \ln R)} + z_2V \frac{R-L}{(1-\alpha)L + \alpha R}. \end{aligned}$$

The critical point of $p_1(\alpha, 1)$ is clearly $\alpha = \gamma_1^*$.

It remains to compare $p_1(0, \gamma_1^*)$, $p_1(\gamma_1^*, 1)$ and $p_1(0, 1)$ for extrema of $p_1(\alpha, \beta)$.

Direct computation gives

$$p_1(0, \gamma_1^*) = -(1 - w_L + \ln w_L) z_2V, \quad p_1(\gamma_1^*, 1) = (1 - w_R + \ln w_R) z_2V,$$

where

$$w_L = \frac{(L-R)(z_2V + \ln L - \ln R)}{z_2V(\ln L - \ln R)L} \quad \text{and} \quad w_R = \frac{(L-R)(z_2V + \ln L - \ln R)}{z_2V(\ln L - \ln R)R}.$$

It is easy to check that $1 - w + \ln w \leq 0$ for any $w > 0$. Therefore, $p_1(0, \gamma_1^*)$ and $p_1(\gamma_1^*, 1)$ have opposite signs. Note also that, for any $\gamma \in [0, 1]$, $p_1(0, \gamma) + p_1(\gamma, 1) = p_1(0, 1)$. We thus conclude that, in the case that $\gamma_1^* \in (0, 1)$, $|p_1(\alpha, \beta)|$ attains its maximum at either $(0, \gamma_1^*)$ or $(\gamma_1^*, 1)$; otherwise, $|p_1(\alpha, \beta)|$ attains its maximum at $(0, 1)$. $\square$

In summary, one has

Proposition 4.11. *If $\gamma_1^* \notin [0, 1]$, then the maximum of $|J_{11}|$ occurs when $(\alpha, \beta) = (0, 1)$. If $\gamma_1^* \in [0, 1]$, then the maximum of $|J_{11}|$ occurs when either $(\alpha, \beta) = (0, \gamma_1^*)$ or $(\alpha, \beta) = (\gamma_1^*, 1)$.*

If $\gamma_2^ \notin [0, 1]$, then the maximum of $|J_{21}|$ occurs when $(\alpha, \beta) = (0, 1)$. If $\gamma_2^* \in [0, 1]$, then the maximum of $|J_{21}|$ occurs when either $(\alpha, \beta) = (0, \gamma_2^*)$ or $(\alpha, \beta) = (\gamma_2^*, 1)$.*

Recall that $\alpha = H(a)/H(1)$ and $\beta = H(b)/H(1)$. It is easy to see that $\alpha \approx 0$ and $\beta \approx 1$ can be realized in 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 $x \notin [a, b]$. The latter means that the neck of the

channel to which the permanent charge is confined is *short* and *narrow*. Note that, in order to produce the same permanent charge *density* Q_0 , it requires much more *numbers* of charges for setting (i) than for setting (ii). In this sense, setting (ii) for ion channels is optimal for effects of permanent charges on ionic flows.

One can also check that, if $\gamma_k^* \in [0, 1]$, then the “optimal” setting is as follows:

- If $(\alpha, \beta) = (\gamma_k^*, 1)$ provides the maximum of $|J_{k1}|$, then there exists $0 < c < a$ 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;
- If $(\alpha, \beta) = (0, \gamma_k^*)$ provides the maximum of $|J_{k1}|$, then there exists $b < c < 1$ such that $c - a \ll 1$, and $h(x)$ is small for $x \in [a, c]$ and large otherwise.

Remark 4.12. In all cases, $h(x)$ should be small for $x \in [a, b]$ and $b - a \ll 1$; that is, the channel neck to which the permanent charge is confined should be short and narrow.

4.4 Permanent charge effects on I-V relation

It follows from (4.4) and (4.5) that

$$\mathcal{I}_0 = \frac{L - R}{H(1)(\ln L - \ln R)} \left(D_1 \frac{\mu_1^\delta}{k_B T} - D_2 \frac{\mu_2^\delta}{k_B T} \right), \quad \mathcal{I}_1 = \frac{A}{(z_1 - z_2)H(1)} P(V; L, R), \quad (4.10)$$

where, with $\lambda = V/(\ln L - \ln R)$,

$$P = P(V; L, R) = z_1 z_2 (z_1 D_1 - z_2 D_2) (1 - B) \lambda^2 + (z_1^2 D_1 - z_2^2 D_2 + z_1 z_2 (D_1 - D_2) (1 - B)) \lambda + (z_1 D_1 - z_2 D_2), \quad (4.11)$$

and A and B are defined in (4.6).

Theorem 4.13. For $Q_0 = 0$, the zeroth order in ε approximation of the reversal potential V_{rev} is given by

$$V_{rev} = - \frac{D_1 - D_2}{z_1 D_1 - z_2 D_2} (\ln L - \ln R).$$

Hence, $\mathcal{I}_0 > 0$ if $V > V_{rev}$ and $\mathcal{I}_0 < 0$ if $V < V_{rev}$.

Proof. Recall that $V = V_{rev}$ is such that $\mathcal{I}_0 = 0$. The latter is equivalent to, from (4.10),

$$D_1 \frac{\mu_1^\delta}{k_B T} - D_2 \frac{\mu_2^\delta}{k_B T} = (z_1 D_1 - z_2 D_2) V_{rev} + (D_1 - D_2) (\ln L - \ln R) = 0.$$

The formula for V_{rev} then follows. $\square$

We now examine the sign of $\mathcal{I}_1$ to determine the leading effects of the permanent charge on the current. Note that, if $B = 1$, then

$$\mathcal{I}_1 = \frac{A}{(z_1 - z_2)H(1)(\ln L - \ln R)} \left((z_1^2 D_1 - z_2^2 D_2) V + (z_1 D_1 - z_2 D_2) (\ln L - \ln R) \right).$$

For $z_1^2 D_1 - z_2^2 D_2 \neq 0$, let

$$V^0 = - \frac{z_1 D_1 - z_2 D_2}{z_1^2 D_1 - z_2^2 D_2} (\ln L - \ln R).$$

Theorem 4.14. Suppose $B = 1$.

- If $z_1^2 D_1 - z_2^2 D_2 = 0$, then $\mathcal{I}_1 > 0$ for $L < R$ and $\mathcal{I}_1 < 0$ for $L > R$.
- If $z_1^2 D_1 - z_2^2 D_2 < 0$, then $\mathcal{I}_1 > 0$ for $V > V^0$ and $\mathcal{I}_1 < 0$ for $V < V^0$.
- If $z_1^2 D_1 - z_2^2 D_2 > 0$, then $\mathcal{I}_1 > 0$ for $V < V^0$ and $\mathcal{I}_1 < 0$ for $V > V^0$.

If $B \neq 1$, then $P = 0$, where P is defined in (4.11), is a quadratic equation in λ whose discriminant is $\Delta = z_1^2 z_2^2 (D_1 - D_2)^2 (1 - B - r_-)(1 - B - r_+)$, where $r_- < r_+ \leq 0$ are given by

$$r_- = \frac{(z_1 \sqrt{D_1} - z_2 \sqrt{D_2})^2}{z_1 z_2 (\sqrt{D_1} - \sqrt{D_2})^2} \quad \text{and} \quad r_+ = \frac{(z_1 \sqrt{D_1} + z_2 \sqrt{D_2})^2}{z_1 z_2 (\sqrt{D_1} + \sqrt{D_2})^2}.$$

Note that, if $D_1 = D_2$, then

$$r_- = -\infty \quad \text{and} \quad r_+ = \frac{(z_1 + z_2)^2}{4z_1 z_2}.$$

Theorem 4.15. *For the factor $\mathcal{I}_1$ in (4.10), one has the following results.*

- (i) *If $1 - B \in (r_-, r_+)$, then $P(V; L, R) > 0$, and hence, $\mathcal{I}_1 > 0$ for $L < R$ and $\mathcal{I}_1 < 0$ for $L > R$.*
- (ii) *If $1 - B = r_{\pm}$, then there is one potential $V_q^0 = V_q^0(L, R)$ such that*
 - (ii1) *if $V = V_q^0$, then $P(V_q^0; L, R) = 0$, and hence, $\mathcal{I}_1 = 0$;*
 - (ii2) *if $V \neq V_q^0$, then $P(V; L, R) > 0$, and hence, $\mathcal{I}_1 > 0$ for $L < R$ and $\mathcal{I}_1 < 0$ for $L > R$.*
- (iii) *If $1 - B \notin [r_-, r_+]$, then there are two potentials $V_q^{\pm} = V_q^{\pm}(L, R)$ such that*
 - (iii1) *if $V = V_q^{\pm}$, then $P(V_q^{\pm}; L, R) = 0$, and hence, $\mathcal{I}_1 = 0$;*
 - (iii2) *if $V \in (V_q^-, V_q^+)$ and $1 - B < 0$, then $P(V; L, R) < 0$, and hence, $\mathcal{I}_1 > 0$ for $L > R$ and $\mathcal{I}_1 < 0$ for $L < R$; if $V \in (V_q^-, V_q^+)$ and $1 - B > 0$, then $P(V; L, R) > 0$, and hence, $\mathcal{I}_1 > 0$ for $L < R$ and $\mathcal{I}_1 < 0$ for $L > R$;*
 - (iii3) *if $V \notin [V_q^-, V_q^+]$ and $1 - B > 0$, then $P(V; L, R) < 0$, and hence, $\mathcal{I}_1 > 0$ for $L > R$ and $\mathcal{I}_1 < 0$ for $L < R$; if $V \notin [V_q^-, V_q^+]$ and $1 - B < 0$, then $P(V; L, R) > 0$, and hence, $\mathcal{I}_1 > 0$ for $L < R$ and $\mathcal{I}_1 < 0$ for $L > R$.*

Proof. The statements follow from the sign of P determined by the conditions in each case and that A has the opposite signs as that of $L - R$ in Lemma 4.5. $\square$

Remark 4.16. *In Theorem 4.15, conditions in terms of $1 - B$ can be made in terms of α , β , L and R incorporating with Lemma 4.6.*

Proposition 4.17. *The critical potentials $V_{rev}(L, R)$, $V_q^0(L, R)$ and $V_q^{\pm}(L, R)$ scale invariantly in (L, R) .*

Proof. The scaling invariance of $V_{rev}(L, R)$ follows from the formula for $V_{rev}(L, R)$. Since B is scaling invariant and other quantities in the coefficients of P are independent of L and R , the scaling invariance of the other critical potentials, as roots of $P(V; L, R) = 0$, follows directly. $\square$

5 Concluding Remarks

In this work, we analyzed effects of a simple permanent charge profile with a small nonzero portion and channel geometry on individual fluxes and on I-V relations for ionic flows with two ion species via a quasi-one-dimensional classical PNP model.

Without permanent charges, the flux of one ion species is independent of the other based on the classical PNP models for dilute mixtures (as is well-known); for PNP with hard-sphere potentials, the flux of one ion species does depend on the other in the first order of characteristic ionic radius (see, e.g. [27, 34, 38]) due to ion-to-ion interactions. In this case, for both classical PNP and PNP with hard-sphere potentials studied in above mentioned papers, only the average quantity $H(1)$ of the channel geometry affects the fluxes.

With the presence of a permanent charge, as expected, the classical PNP model also shows the dependence of the flux of one ion species on the other ion species. Most importantly, effects of permanent charges on ionic flows could be very complicated, depending the interplays between boundary conditions and the channel geometry. Our analysis leads to an interesting conclusion that, to optimize the effects of a permanent charge, the neck of the channel to which the permanent charge is confined should be *short* and *narrow*.

For large $|Q_0|$ or a more general form of a piecewise constant permanent charge $Q(x)$, although a governing system for singular orbits is available ([14, 36]), it is very challenging to obtain reasonably explicit expressions for the fluxes. It would be extremely important for a comprehensive analysis of permanent charge effect if this difficulty can be overcome in some way.

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