

## EFFECTS OF (SMALL) PERMANENT CHARGE AND CHANNEL GEOMETRY ON IONIC FLOWS VIA CLASSICAL POISSON–NERNST–PLANCK MODELS\*

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**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

**AMS subject classifications.** 34A26, 34B16, 34D15, 37D10, 92C35

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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 with the outside world to perform group tasks. They are large proteins embedded in cell membranes that have “holes” open to the inside and outside of cells. Once channels open, ions (charged particles) flow from the outside to inside of cells and vice versa. The ionic flow produces electrical signals that

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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 *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 PNP-type systems, which are reduced models that treat the medium (aqueous within which ions are migrating) as a dielectric continuum:

$$\nabla \cdot (\varepsilon_r(X)\varepsilon_0\nabla\Phi) = -e \left( \sum_{s=1}^n z_s c_s + Q(X) \right),$$

$$\nabla \cdot \mathcal{J}_k = 0, \quad -\mathcal{J}_k = \frac{1}{k_B T} D_k(X) c_k \nabla \mu_k, \quad k = 1, 2, \dots, n,$$

where  $X \in \Omega$  with  $\Omega$  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,  $\varepsilon_0$  is the vacuum permittivity,  $e$  is the elementary charge,  $k_B$  is the Boltzmann constant,  $T$  is the absolute temperature;  $\Phi$  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),  $\mu_k$  is the electrochemical potential depending on  $\Phi$  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 was 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 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

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

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  $k = 1, 2, \dots, n$ ,

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

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

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

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  $\mu_k$ . It consists of the ideal component  $\mu_k^{id}(x)$  given by

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

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 agreement 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 effort 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 inversion, 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

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

Thus, the *sign* of  $\mathcal{J}_k$  is determined by the boundary conditions—*independently* 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

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

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 of which 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,

$$(1.7) \quad \mathcal{J}_k(Q_0) = \mathcal{J}_{k0} + \mathcal{J}_{k1} Q_0 + O(Q_0^2) \quad \text{and} \quad \mathcal{I}(Q_0) = \mathcal{I}_0 + \mathcal{I}_1 Q_0 + O(Q_0^2),$$

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 concluding 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]:

- (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  $\mu_k$ , we only include the ideal component  $\mu_k^{id}$  as in (1.4).
- (A4) We assume that  $\varepsilon_r(x) = \varepsilon_r$  and  $D_k(x) = D_k$  are constants.

In what follows, we will assume (A1)–(A4). With the rescaling

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

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

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

with the boundary conditions

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

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 an overdot and introduce  $u = \varepsilon \dot{\phi}$  and  $\tau = x$ . System (2.1) becomes, for  $k = 1, 2$ ,

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

System (2.3) is a singularly perturbed dynamical system with phase space  $\mathcal{R}^7$  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  $k = 1, 2$ ,

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

where prime denotes the derivative with respect to the variable  $\xi$ .

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

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

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 for 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 following.

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  $\phi$ ,  $c_1$ , and  $c_2$  at  $x = a$  and  $x = b$ :

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

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)  $\Gamma_l^0$  at  $x = 0$ ,  $\Gamma_l^a$  at  $x = a$ , and one regular layer (slow orbit)  $\Lambda_l$  over  $(0, a)$  with  $(\phi, c_1, c_2, \tau)$  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  $(\phi^a, c_1^a, c_2^a)$ , 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  $\Gamma_m^a$  at  $x = a$ ,  $\Gamma_m^b$  at  $x = b$ , and one regular layer  $\Lambda_m$  over  $(a, b)$  with  $(\phi, c_1, c_2, \tau)$  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  $(\phi^a, c_1^a, c_2^a)$  and  $(\phi^b, c_1^b, c_2^b)$ , 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  $\Gamma_r^b$  at  $x = b$ ,  $\Gamma_r^1$  at  $x = 1$ , and one regular layer  $\Lambda_r$  over  $(b, 1)$  with  $(\phi, c_1, c_2, \tau)$  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  $(\phi^b, c_1^b, c_2^b)$ , 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:

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

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  $\alpha$  and  $\beta$  in [14] are related to  $z_1$  and  $z_2$  in this paper as  $\alpha = z_1$  and  $\beta = -z_2$ ):

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

where  $y > 0$  is also unknown, and

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

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

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

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

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



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*

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

**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  $\phi_1^a$ ,  $c_{k1}^a$ , 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  $Q_0$ ,

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

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 the 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 follow. The details will be omitted.  $\square$

Applying the same procedure as above to the last four identities in (2.7) and using the 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)} \\
&\quad \times \left( \phi_1^a - \frac{z_2(\phi^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} - \frac{c_{10}^a c_{21}^a - c_{20}^a c_{11}^a}{(z_1 - z_2)c_{10}^a c_{20}^a} \right) \\
&\quad - \frac{z_2(c_{11}^a + c_{21}^a)}{(z_2 - z_1)\alpha H(1)} \left( 1 + \frac{z_1(\phi^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)} \\
&\quad \times \left( \phi_1^b - \frac{z_2(\phi^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} - \frac{c_{10}^b c_{21}^b - c_{20}^b c_{11}^b}{(z_1 - z_2)c_{10}^b c_{20}^b} \right) \\
&\quad - \frac{z_2(c_{11}^b + c_{21}^b)}{(z_1 - z_2)(1 - \beta)H(1)} \left( 1 + \frac{z_1(\phi^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)} \\
&\quad \times \left( \phi_1^a - \frac{z_1(\phi^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} - \frac{c_{10}^a c_{21}^a - c_{20}^a c_{11}^a}{(z_1 - z_2)c_{10}^a c_{20}^a} \right) \\
&\quad - \frac{z_1(c_{11}^a + c_{21}^a)}{(z_1 - z_2)\alpha H(1)} \left( 1 + \frac{z_2(\phi^L - \phi_0^a)}{\ln c_2^L - \ln c_{20}^a} \right) \\
(3.4) \quad &= -\frac{z_2(c_{20}^b - c_2^R)}{(1 - \beta)H(1)(\ln c_2^R - \ln c_{20}^b)} \\
&\quad \times \left( \phi_1^b - \frac{z_1(\phi^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} - \frac{c_{10}^b c_{21}^b - c_{20}^b c_{11}^b}{(z_1 - z_2)c_{10}^b c_{20}^b} \right) \\
&\quad + \frac{z_1(c_{11}^b + c_{21}^b)}{(z_1 - z_2)(1 - \beta)H(1)} \left( 1 + \frac{z_2(\phi^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}$$

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*

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

where

$$\begin{aligned}
(3.5) \quad \lambda &= \frac{\phi_1^L - \phi_1^R}{\ln c_1^L - \ln c_1^R}, & A &= \frac{(c_1^L - c_1^R)(c_{10}^b - c_{10}^a)}{c_{10}^a c_{10}^b (\ln c_1^L - \ln c_1^R)}, \\
B &= \frac{\ln c_{10}^b - \ln c_{10}^a}{A} = \frac{(\ln c_1^L - \ln c_1^R)(\ln c_{10}^b - \ln c_{10}^a)}{(c_1^L - c_1^R)(c_{10}^b - c_{10}^a)} c_{10}^a c_{10}^b.
\end{aligned}$$

*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  $\phi_1^a, \phi_1^b, y_1$ , 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 with the first ion species. Of course, they can all be expressed in terms of zeroth order quantities associated with the second ion species; that is, on the right-hand sides of the formulas for  $\phi_1^a, \phi_1^b, y_1$ , 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

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

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

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

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

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

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

$$(4.4) \quad J_{10} = \frac{L - R}{z_1 H(1)(\ln L - \ln R)} \frac{\mu_1^\delta}{k_B T} = \frac{L_1 - R_1}{H(1)(\ln L_1 - \ln R_1)} \frac{\mu_1^\delta}{k_B T},$$

$$J_{20} = \frac{R - L}{z_2 H(1)(\ln L - \ln R)} \frac{\mu_2^\delta}{k_B T} = \frac{L_2 - R_2}{H(1)(\ln L_2 - \ln R_2)} \frac{\mu_2^\delta}{k_B T}.$$

Also, it follows from Proposition 3.5 that

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

$$J_{21} = \frac{A(z_1(1-B)V + \ln L - \ln R)}{(z_2 - z_1)H(1)(\ln L - \ln R)^2} \frac{\mu_2^\delta}{k_B T},$$

where, in terms of  $\alpha$  and  $\beta$  defined in (3.2),  $A$  and  $B$  defined in (3.5) become

$$(4.6) \quad A = A(L, R) = -\frac{(\beta - \alpha)(L - R)^2}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)},$$

$$B = B(L, R) = \frac{\ln((1 - \beta)L + \beta R) - \ln((1 - \alpha)L + \alpha R)}{A}.$$

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  $A$  and  $B$  in (4.6), and for  $\mu_k^\delta$  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  $s > 0$ ,*

$$J_{k0}(V; sL, sR) = sJ_{k0}(V; L, R), \quad \mathcal{I}_0(V; sL, sR) = s\mathcal{I}_0(V; L, R),$$

$$J_{k1}(V; sL, sR) = J_{k1}(V; L, R), \quad \mathcal{I}_1(V; sL, sR) = \mathcal{I}_1(V; L, R).$$

*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 the 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  $\alpha$  and  $\beta$  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

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

One establishes easily the following.

LEMMA 4.4. *For  $t > 0$ ,  $0 < \gamma(t) < 1$ ,  $\gamma'(t) > 0$ ,*

$$\lim_{t \rightarrow 0} \gamma(t) = 0, \quad \lim_{t \rightarrow \infty} \gamma(t) = 1.$$

**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  $(\alpha, \beta)$  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).  $\square$

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 to 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 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*

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

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 a 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

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

Note that, from (4.4),  $J_{k0}$  is a scalar multiple of  $\mu_k^\delta$  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  $(\alpha, \beta)$  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

$$p_1(\alpha, \beta) = \frac{(\alpha - \beta)(L - R)^2(z_2 V + \ln L - \ln R)}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)} - z_2 V \ln \frac{(1 - \beta)L + \beta R}{(1 - \alpha)L + \alpha R},$$

$$p_2(\alpha, \beta) = \frac{(\alpha - \beta)(L - R)^2(z_1 V + \ln L - \ln R)}{((1 - \alpha)L + \alpha R)((1 - \beta)L + \beta R)(\ln L - \ln R)} - z_1 V \ln \frac{(1 - \beta)L + \beta R}{(1 - \alpha)L + \alpha R}.$$

**LEMMA 4.10.** *If  $\gamma_1^* = \gamma(L/R) - \frac{1}{z_2 V} \in (0, 1)$ , 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  $\gamma_2^* = \gamma(L/R) - \frac{1}{z_1 V} \in (0, 1)$ , 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  $p_1(\alpha, \alpha) = 0$ .

$$\begin{aligned}\partial_\alpha p_1(\alpha, \beta) &= \frac{(L-R)^2(z_2 V + \ln L - \ln R)}{((1-\alpha)L + \alpha R)^2(\ln L - \ln R)} + z_2 V \frac{R-L}{(1-\alpha)L + \alpha R}, \\ \partial_\beta p_1(\alpha, \beta) &= -\frac{(L-R)^2(z_2 V + \ln L - \ln R)}{((1-\beta)L + \beta R)^2(\ln L - \ln R)} - z_2 V \frac{R-L}{(1-\beta)L + \beta R}.\end{aligned}$$

Therefore, any critical point  $(\alpha, \beta)$  satisfies  $\alpha = \beta$  where  $p_1$  vanishes. Hence, the maximum of  $|p_1(\alpha, \beta)|$  on  $\Omega$  is attained on the boundary

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

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

$$\begin{aligned}p_1(0, \beta) &= -\frac{\beta(L-R)^2(z_2 V + \ln L - \ln R)}{L((1-\beta)L + \beta R)(\ln L - \ln R)} - z_2 V \ln \frac{(1-\beta)L + \beta R}{L}, \\ \partial_\beta p_1(0, \beta) &= -\frac{(L-R)^2(z_2 V + \ln L - \ln R)}{((1-\beta)L + \beta R)^2(\ln L - \ln R)} - z_2 V \frac{R-L}{(1-\beta)L + \beta R}.\end{aligned}$$

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

$$\beta = \gamma_1^* = \frac{L}{L-R} - \frac{1}{\ln L - \ln R} - \frac{1}{z_2 V}.$$

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

$$-\gamma(t) < -\frac{1}{z_2 V} < 1 - \gamma(t) \quad \text{or} \quad \gamma(t) - 1 < \frac{1}{z_2 V} < \gamma(t),$$

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

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

$$\begin{aligned}p_1(\alpha, 1) &= \frac{(\alpha-1)(L-R)^2(z_2 V + \ln L - \ln R)}{R((1-\alpha)L + \alpha R)(\ln L - \ln R)} - z_2 V \ln \frac{R}{(1-\alpha)L + \alpha R}, \\ \partial_\alpha p_1(\alpha, 1) &= \frac{(L-R)^2(z_2 V + \ln L - \ln R)}{((1-\alpha)L + \alpha R)^2(\ln L - \ln R)} + z_2 V \frac{R-L}{(1-\alpha)L + \alpha R}.\end{aligned}$$

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

$$p_1(0, \gamma_1^*) = -(1 - w_L + \ln w_L) z_2 V, \quad p_1(\gamma_1^*, 1) = (1 - w_R + \ln w_R) z_2 V,$$

where

$$w_L = \frac{(L-R)(z_2 V + \ln L - \ln R)}{z_2 V(\ln L - \ln R)L} \quad \text{and} \quad w_R = \frac{(L-R)(z_2 V + \ln L - \ln R)}{z_2 V(\ln L - \ln R)R}.$$

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 the following.

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 many 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

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

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

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

and  $A$  and  $B$  are defined in (4.6).

THEOREM 4.13. *For  $Q_0 = 0$ , the zeroth order in  $\varepsilon$  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  $\lambda$  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 sign 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  $\alpha$ ,  $\beta$ ,  $L$ , 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 the abovementioned 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 on 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.

## REFERENCES

- [1] N. ABAID, R. S. EISENBERG, AND W. LIU, *Asymptotic expansions of I-V relations via a Poisson–Nernst–Planck system*, SIAM J. Appl. Dynam. Systems, 7 (2008), pp. 1507–1526.
- [2] M. Z. BAZANT, M. S. KILIC, B. D. STOREY, AND A. AJDARI, *Towards an understanding of induced-charge electrokinetics at large applied voltages in concentrated solutions*, Adv. Colloid Interface Sci., 152 (2009), pp. 48–88.
- [3] M. Z. BAZANT, B. D. STOREY, AND A. A. KORNYCHEV, *Double layer in ionic liquids: Over-screening versus crowding*, Phys. Rev. Lett., 106 (2011), 046102.
- [4] V. BARCILON, *Ion flow through narrow membrane channels: Part I*, SIAM J. Appl. Math., 52 (1992), pp. 1391–1404.
- [5] V. BARCILON, D.-P. CHEN, AND R. S. EISENBERG, *Ion flow through narrow membrane channels: Part II*, SIAM J. Appl. Math., 52 (1992), pp. 1405–1425.
- [6] V. BARCILON, D.-P. CHEN, R. S. EISENBERG, AND J. W. JEROME, *Qualitative properties of steady-state Poisson–Nernst–Planck systems: Perturbation and simulation study*, SIAM J. Appl. Math., 57 (1997), pp. 631–648.
- [7] P. M. BIESHEUVEL, *Two-fluid model for the simultaneous flow of colloids and fluids in porous media*, J. Colloid Interface Sci., 355 (2011), pp. 389–395.
- [8] L. BLUM, *Mean spherical model for asymmetric electrolytes*, Mol. Phys., 30 (1975), pp. 1529–1535.
- [9] L. BLUM AND J. S. HØYE, *Mean spherical model for asymmetric electrolytes. 2. Thermodynamic properties and the pair correlation function*, J. Phys. Chem., 81 (1977), pp. 1311–1316.
- [10] D. CHEN, R. EISENBERG, J. JEROME, AND C. SHU, *Hydrodynamic model of temperature change in open ionic channels*, Biophys. J., 69 (1995), pp. 2304–2322.
- [11] B. EISENBERG, *Ion Channels as Devices*, J. Comput. Electron., 2 (2003), pp. 245–249.
- [12] B. EISENBERG, *Proteins, channels, and crowded ions*, Biophys. Chem., 100 (2003), pp. 507–517.
- [13] B. EISENBERG, Y. HYON, AND C. LIU, *Energy variational analysis of ions in water and channels: Field theory for primitive models of complex ionic fluids*, J. Chem. Phys., 133 (2010), 104104.
- [14] B. EISENBERG AND W. LIU, *Poisson–Nernst–Planck systems for ion channels with permanent charges*, SIAM J. Math. Anal., 38 (2007), pp. 1932–1966.

- [15] B. EISENBERG, W. LIU, AND H. XU, *Reversal permanent charge and reversal potential: Case studies via classical Poisson-Nernst-Planck models*, *Nonlinearity*, 28 (2015), pp. 103–128.
- [16] A. ERN, R. JOUBAUD, AND T. LELIÉVRE, *Mathematical study of non-ideal electrostatic correlations in equilibrium electrolytes*, *Nonlinearity*, 25 (2012), pp. 1635–1652.
- [17] J. C. FAIR AND J. F. OSTERLE, *Reverse electrodialysis in charged capillary membranes*, *J. Chem. Phys.*, 54 (1971), pp. 3307–3316.
- [18] D. GILLESPIE AND R. S. EISENBERG, *Physical descriptions of experimental selectivity measurements in ion channels*, *Eur. Biophys. J.*, 31 (2002), pp. 454–466.
- [19] D. GILLESPIE, W. NONNER, AND R. S. EISENBERG, *Coupling Poisson-Nernst-Planck and density functional theory to calculate ion flux*, *J. Phys. Condens. Matter*, 14 (2002), pp. 12129–12145.
- [20] D. GILLESPIE, W. NONNER, AND R. S. EISENBERG, *Crowded charge in biological ion channels*, *Nanotech.*, 3 (2003), pp. 435–438.
- [21] D. GILLESPIE, L. XU, Y. WANG, AND G. MEISSNER, *(De)constructing the Ryanodine receptor: Modeling ion permeation and selectivity of the Calcium release channel*, *J. Phys. Chem. B*, 109 (2005), pp. 15598–15610.
- [22] R. J. GROSS AND J. F. OSTERLE, *Membrane transport characteristics of ultra fine capillary*, *J. Chem. Phys.*, 49 (1968), pp. 228–234.
- [23] Y. HYON, B. EISENBERG, AND C. LIU, *A mathematical model for the hard sphere repulsion in ionic solutions*, *Commun. Math. Sci.*, 9 (2010), pp. 459–475.
- [24] Y. HYON, J. FONSECA, B. EISENBERG, AND C. LIU, *Energy variational approach to study charge inversion (layering) near charged walls*, *Discrete Contin. Dynam. Systems Ser. B*, 17 (2012), pp. 2725–2743.
- [25] Y. HYON, C. LIU, AND B. EISENBERG, *PNP equations with steric effects: A model of ion flow through channels*, *J. Phys. Chem. B*, 116 (2012), pp. 11422–11441.
- [26] W. IM AND B. ROUX, *Ion permeation and selectivity of OmpF porin: A theoretical study based on molecular dynamics, Brownian dynamics, and continuum electrodiffusion theory*, *J. Mol. Biol.*, 322 (2002), pp. 851–869.
- [27] S. JI AND W. LIU, *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. Dynam. Differential Equations*, 24 (2012), pp. 955–983.
- [28] C. JONES, *Geometric singular perturbation theory*, in *Dynamical Systems (Montecatini Terme, Italy, 1994)*, Lecture Notes in Math. 1609, Springer, Berlin, 1995, pp. 44–118.
- [29] C. JONES AND N. KOPELL, *Tracking invariant manifolds with differential forms in singularly perturbed systems*, *J. Differential Equations*, 108 (1994), pp. 64–88.
- [30] M. S. KILIC, M. Z. BAZANT, AND A. AJDARI, *Steric effects in the dynamics of electrolytes at large applied voltages: I. Double-layer charging*, *Phys. Rev. E* (3), 75 (2007), 021502.
- [31] M. S. KILIC, M. Z. BAZANT, AND A. AJDARI, *Steric effects in the dynamics of electrolytes at large applied voltages. II. Modified Poisson-Nernst-Planck equations*, *Phys. Rev. E* (3), 75 (2007), 021503.
- [32] C.-C. LEE, H. LEE, Y. HYON, T.-C. LIN, AND C. LIU, *New Poisson-Boltzmann type equations: One-dimensional solutions*, *Nonlinearity*, 24 (2011), pp. 431–458.
- [33] B. LI, *Continuum electrostatics for ionic solutions with non-uniform ionic sizes*, *Nonlinearity*, 22 (2009), pp. 811–833.
- [34] G. LIN, W. LIU, Y. YI, AND M. ZHANG, *Poisson-Nernst-Planck systems for ion flow with a local hard-sphere potential for ion size effects*, *SIAM J. Appl. Dynam. Systems*, 12 (2013), pp. 1613–1648.
- [35] W. LIU, *Geometric singular perturbation approach to steady-state Poisson-Nernst-Planck systems*, *SIAM J. Appl. Math.*, 65 (2005), pp. 754–766.
- [36] W. LIU, *One-dimensional steady-state Poisson-Nernst-Planck systems for ion channels with multiple ion species*, *J. Differential Equations*, 246 (2009), pp. 428–451.
- [37] W. LIU AND B. WANG, *Poisson-Nernst-Planck systems for narrow tubular-like membrane channels*, *J. Dynam. Differential Equations*, 22 (2010), pp. 413–437.
- [38] W. LIU, X. TU, AND M. ZHANG, *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. Dynam. Differential Equations*, 24 (2012), pp. 985–1004.
- [39] W. LIU AND H. XU, *A complete analysis of a classical Poisson-Nernst-Planck model for ionic flow*, *J. Differential Equations*, 258 (2015), pp. 1192–1228.
- [40] A. MALASICS, D. GILLESPIE, W. NONNER, D. HENDERSON, B. EISENBERG, AND D. BODA, *Protein structure and ionic selectivity in calcium channels: Selectivity filter size, not shape, matters*, *Biochim. Biophys. Acta*, 1788 (2009), pp. 2471–2480.
- [41] W. NONNER AND R. S. EISENBERG, *Ion permeation and glutamate residues linked by Poisson-Nernst-Planck theory in L-type Calcium channels*, *Biophys. J.*, 75 (1998), pp. 1287–1305.

- [42] J. H. PARK AND J. W. JEROME, *Qualitative properties of steady-state Poisson–Nernst–Planck systems: Mathematical study*, SIAM J. Appl. Math., 57 (1997), pp. 609–630.
- [43] Y. ROSENFELD, *Free-energy model for the inhomogeneous hard-sphere fluid mixture and density-functional theory of freezing*, Phys. Rev. Lett., 63 (1989), pp. 980–983.
- [44] Y. ROSENFELD, *Free energy model for the inhomogeneous fluid mixtures: Yukawa-charged hard spheres, general interactions, and plasmas*, J. Chem. Phys., 98 (1993), pp. 8126–8148.
- [45] R. ROTH, *Fundamental measure theory for hard-sphere mixtures: A review*, J. Phys. Condens. Matter, 22 (2010), 063102.
- [46] B. ROUX, T. W. ALLEN, S. BERNECHE, AND W. IM, *Theoretical and computational models of biological ion channels*, Quart. Rev. Biophys., 37 (2004), pp. 15–103.
- [47] V. SASIDHAR AND E. RUCKENSTEIN, *Electrolyte osmosis through capillaries*, J. Colloid Interface Sci., 82 (1981), pp. 439–457.
- [48] Z. SCHUSS, B. NADLER, AND R. S. EISENBERG, *Derivation of Poisson and Nernst–Planck equations in a bath and channel from a molecular model*, Phys. Rev. E (3), 64 (2001), pp. 1–14.
- [49] A. SINGER AND J. NORBURY, *A Poisson–Nernst–Planck model for biological ion channels—An asymptotic analysis in a three-dimensional narrow funnel*, SIAM J. Appl. Math., 70 (2009), pp. 949–968.
- [50] A. SINGER, D. GILLESPIE, J. NORBURY, AND R. S. EISENBERG, *Singular perturbation analysis of the steady-state Poisson–Nernst–Planck system: Applications to ion channels*, European J. Appl. Math., 19 (2008), pp. 541–560.
- [51] S.-K. TIN, N. KOPELL, AND C. K. R. T. JONES, *Invariant manifolds and singularly perturbed boundary value problems*, SIAM J. Numer. Anal., 31 (1994), pp. 1558–1576.
- [52] X.-S. WANG, D. HE, J. WYLIE, AND H. HUANG, *Singular perturbation solutions of steady-state Poisson–Nernst–Planck systems*, Phys. Rev. E (3), 89 (2014), 022722.
- [53] G. W. WEI, *Differential geometry based multiscale models*, Bull. Math. Biol., 72 (2010), pp. 1562–1622.
- [54] G.-W. WEI, Q. ZHENG, Z. CHEN, AND K. XIA, *Variational multiscale models for charge transport*, SIAM Rev., 54 (2012), pp. 699–754.
- [55] M. ZHANG, *Asymptotic expansions and numerical simulations of I-V relations via a steady-state Poisson–Nernst–Planck system*, Rocky Mountain J. Math., to appear.
- [56] S. ZHOU, Z. WANG, AND B. LI, *Mean-field description of ionic size effects with nonuniform ionic sizes: A numerical approach*, Phys. Rev. E (3), 84 (2011), 021901.