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Finite Ion Size Effects on Ionic Flows via Poisson–Nernst–Planck Systems: Higher Order Contributions

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Abstract
Ions are crowded in ion channels, and finite ion sizes play essential roles in the study of ionic flows through membrane channels. Some significant properties of ion channels, such as selectivity, rely on ion sizes critically. Following the work done in (SIAM J Appl Dyn Syst 12:1613–1648, 2013), we focus on the higher order (in the diameter of the cation), mainly the second order, contributions from finite ion sizes to ionic flows in terms of both the total flow rate of charges and the individual fluxes. This is particularly essential because the first-order terms approach zero when the left boundary concentration is close to the right one for the same ion species. The interplays between the first-order terms and the second-order terms are characterized. Furthermore, several critical potentials are identified, which play critical roles in examining the dynamics of ionic flows. Some can be experimentally estimated. The analysis could provide deep insights into the future studies of ionic flows through membrane channels.

Keywords Ion channel · PNP · Local hard-sphere potential · I–V relation · Critical potentials · Finite ion sizes

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

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1 Introduction

The study of electrodiffusion is an extremely rich area for multidisciplinary research with diverse applications from computer science, through engineering to biology. Mathematical analysis plays unique and important roles in better understanding the mechanics of phenomena arising from life science and discovering new features, assuming that a more or less explicit solution of the associated mathematical model can be obtained. In this work, we analyze the qualitative properties of ionic flows through ion channels via a quasi-one-dimensional steady-state Poisson–Nernst–Planck (PNP) type system.

PNP system is a basic macroscopic model for electrodiffusion of charges through ion channels ([11,15–18,24,25,28,35,36,59,60,64,65], etc.). Under various reasonable conditions, the PNP system can be derived as a reduced model from molecular dynamics ([69]), from Boltzmann equations ([3]), and from variational principles ([31,32,34]).

The simplest PNP system is the classical Poisson-Nernst-Planck system, which treats ions as *point-charges*, and neglects ion-to-ion interaction. It has been simulated and analyzed to a great extent (see, e.g., [1,4,5,8–14,20,22,24,25,27,29,30,36–41,45,50–52,56–58,61,66–68,70–73,75–82]). However, since ions are crowded ([15]) and finite ion sizes perform fundamental roles in the study of ionic flows.

A lot of structural properties of ion channels, such as *selectivity*, rely on ion sizes critically. For example, Na^+ (sodium) and K^+ (potassium), having the *same* valence (number of charges per particle), are mainly distinguished by their ionic sizes. To examine ion size effects on ionic flows, one must consider ion-specific components of the electrochemical potential in the PNP models. A local hard-sphere potentials (derived in [48]) of the excess electrochemical potential is included in this work to account for ion size effects in the physiology of ion flows.

The PNP type models with ion sizes have been investigated computationally and analytically for ion channels and have shown great success ([2,6,7,19,23,25,26,31–34,42,44,48,54, 55,74,83], etc.). The existence and uniqueness of minimizers and saddle points of the free-energy equilibrium formulation with ionic interaction have been mathematically analyzed too (see, for example, [21,46,47]).

In [48], the authors provided an analytical treatment of a quasi-one-dimensional PNP system with two oppositely charged ion species and a local hard-sphere potential of the excess component in addition to the ideal component. They treated the model as a singularly perturbed system and rigorously established the existence and uniqueness results of the boundary value problem for small ion sizes. Furthermore, treating ion sizes as small parameters, they derived an approximation of the I–V relation of the form

$$\mathcal{I}(V) := z_1\mathcal{J}_1(V) + z_2\mathcal{J}_2(V) = \mathcal{I}_0(V) + d\mathcal{I}_1(V) + o(d),$$

where d is the diameter of the cation, z_k is the valence and $\mathcal{J}_k$ is the individual flux. Of particular interest is the leading term $\mathcal{I}_1(V)$ that contains finite ion size effects, from which many interesting results were established and deep insights into dynamics of ionic flows were provided. Following the work done in [48], the authors of [7] studied the finite ion size effects on the individual fluxes $\mathcal{J}_k$ and the interplays between the total flow rate of charges (that is, the I–V relations) and the individual fluxes characterized by some critical potentials.

In [48], the authors observed that the first-order term $\mathcal{I}_1(V)$ (similarly for the individual fluxes $\mathcal{J}_k(V),\ k = 1, 2$) approaches zero as the left boundary concentration is close enough to the right one for the same ion species (that is, either $L_1 \to R_1$ or $L_2 \to R_2$ for two ion species case, which is equivalent under electroneutrality conditions $z_1L_1 = -z_2L_2 := L$ and $z_1R_1 = -z_2R_2 := R$). In this work, we study the second-order terms in d, more precisely, $\mathcal{I}_2(V)$ and $\mathcal{J}_{k2}(V)$, which will be the leading terms that contain finite ion size effects as

$L \to R$ under electroneutrality conditions; the interaction with the first-order terms (the effect from the combination); and the characterization of ion size effects close to $L = R$.

The rest of this paper is organized as follows. In Sect. 2, we describe the one-dimensional PNP model for ion flows, a local model for hard-sphere potentials, and the setup of the boundary value problem of the singularly perturbed PNP system. In Sect. 3, under regular perturbation analysis, we focus on the asymptotic dynamics of the limiting PNP systems up to the second order in the diameter d of the cation. Section 4 deals with the discussion on finite ion size effects, which consists of three parts. In Sect. 4.1, a number of critical potentials are identified and their roles in studying finite ion size effects on ionic flows are characterized in details. In Sect. 4.2, we discuss the ion size effects from the combination of first-order and second-order terms. In Sect. 4.3, our interest lies in the case studies of ion size effects near $L = R$. Some remarks are provided in Sect. 5.

2 Problem Setup

2.1 A One-Dimensional PNP Type System

Considering that the ion channels have narrow cross-sections relative to their lengths, 3-D PNP type models can be effectively viewed as one-dimensional models that are normalized over the interval [0, 1], where the interior and the exterior of the channel are joined. A natural one-dimensional (time-evolution) PNP type model for ionic flows of n ion species is (see [53,58])

$$\begin{aligned} &\frac{1}{h(x)}\frac{\partial}{\partial x}\left(\varepsilon_r(x)\varepsilon_0 h(x)\frac{\partial \Phi}{\partial x}\right) = -e\left(\sum_{j=1}^{n} z_j c_j + Q(x)\right),\\ &\frac{\partial c_i}{\partial t} + \frac{\partial \mathcal{J}_i}{\partial x} = 0, \quad -\mathcal{J}_i = \frac{1}{k_B T} D_i(x) h(x) c_i \frac{\partial \mu_i}{\partial x}, \quad i = 1, 2, \dots, n, \end{aligned} \tag{2.1}$$

where e is the elementary charge, k_B is the Boltzmann constant, T is the absolute temperature; Φ is the electric potential, $Q(x)$ is the permanent charge of the channel, $\varepsilon_r(x)$ is the relative dielectric coefficient, ε_0 is the vacuum permittivity; $h(x)$ is the area of the cross-section of the channel over the point $x \in [0, 1]$; for the ith ion species, c_i is the concentration, z_i is the valence, μ_i is the electrochemical potential, $\mathcal{J}_i$ is the flux density, and $D_i(x)$ is the diffusion coefficient.

The boundary conditions are, for $i = 1, 2, \dots, n$,

$$\Phi(t, 0) = V, \;\; c_i(t, 0) = L_i > 0; \quad \Phi(t, 1) = 0, \;\; c_i(t, 1) = R_i > 0. \tag{2.2}$$

For ion channels, an important characteristic is the so-called *I–V relation* (current–voltage relation). For a solution of the *steady-state* boundary value problem of (2.1) and (2.2), the *rate of flow of charge through a cross-section* or *current* $\mathcal{I}$ is

$$\mathcal{I} = \sum_{j=1}^{n} z_j \mathcal{J}_j. \tag{2.3}$$

2.2 Excess Potential and a Local Hard Sphere Model

The electrochemical potential $\mu_i(x)$ for the ith ion species consists of the ideal component $\mu_i^{id}(x)$, the excess component $\mu_i^{ex}(x)$ and the concentration-independent component $\mu_i^0(x)$ (e.g. a hard-well potential):

$$\mu_i(x) = \mu_i^0(x) + \mu_i^{id}(x) + \mu_i^{ex}(x)$$

where

$$\mu_i^{id}(x) = z_i e\Phi(x) + k_B T \ln \frac{c_i(x)}{c_0} \tag{2.4}$$

with some characteristic number density c_0. The classical PNP system only uses the ideal component $\mu_i^{id}(x)$. This component reflects the collision between ion particles and the water molecules. It has been accepted that the classical PNP system is a reasonable model in, for example, the dilute case under which the ion particles can be treated as point particles and the ion-to-ion interaction can be more or less ignored. The excess chemical potential $\mu_i^{ex}(x)$ accounts for the finite size effect of charges (see, e.g., [62,63]).

In this work, we take the following local hard-sphere model for $\mu_i^{ex}(x)$

$$\frac{1}{k_B T}\mu_i^{LHS}(x) = -\ln\Big(1 - \sum_{j=1}^{n} d_j c_j(x)\Big) + \frac{d_i \sum_{j=1}^{n} c_j(x)}{1 - \sum_{j=1}^{n} d_j c_j(x)}, \tag{2.5}$$

where d_j is the diameter of the jth ion species. Note that the factor d_i in the second term of (2.5) makes the model ion-specific.

2.3 The Steady-State Boundary Value Problem and Assumptions

The main goal of this paper is to examine the qualitative effect of ion sizes via the steady-state boundary value problem of (2.1) and (2.2) with the local hard-sphere (LHS) model (2.5) for the excess potential. We will discuss the steady-state boundary value problem in Sect. 3. In Section 4, we will obtain approximations for (2.3) to study ion size effects on the I–V relation.

For definiteness, we will take the following settings:

(A1). We consider two ion species ($n = 2$) with $z_1 > 0$ and $z_2 < 0$.
(A2). The permanent charge is set to be zero: $Q(x) = 0$.
(A3). For the electrochemical potential μ_i, in addition to the ideal component μ_i^{id}, we also include the local hard-sphere potential μ_i^{LHS} in (2.5).
(A4). The relative dielectric coefficient and the diffusion coefficient are constants, that is, $\varepsilon_r(x) = \varepsilon_r$ and $D_i(x) = D_i$.

In the sequel, we will assume (A1)–(A4). Under the assumptions (A1)–(A4), the steady-state system of (2.1) is

$$\begin{aligned} &\frac{1}{h(x)}\frac{d}{dx}\left(\varepsilon_r(x)\varepsilon_0 h(x)\frac{d\Phi}{dx}\right) = -e\left(z_1 c_1 + z_2 c_2\right), \\ &\frac{d\mathcal{J}_i}{dx} = 0, \quad -\mathcal{J}_i = \frac{1}{k_B T} D_i(x) h(x) c_i \frac{d\mu_i}{dx}, \quad i = 1, 2. \end{aligned} \tag{2.6}$$

Upon introducing the following dimensionless re-scaling

$$\phi = \frac{e}{k_B T}\Phi, \quad \bar{V} = \frac{e}{k_B T}V, \quad \varepsilon^2 = \frac{\varepsilon_r \varepsilon_0 k_B T}{e^2}, \quad J_i = \frac{\mathcal{J}_i}{D_i},$$

the boundary value problem (2.6) and (2.2) becomes

$$\begin{aligned}
&\frac{\varepsilon^2}{h(x)}\frac{d}{dx}\left(h(x)\frac{d}{dx}\phi\right) = -z_1c_1 - z_2c_2, \quad \frac{dJ_1}{dx} = \frac{dJ_2}{dx} = 0,\\
&h(x)\frac{dc_1}{dx} + z_1h(x)c_1\frac{d\phi}{dx} + \frac{h(x)c_1}{k_BT}\frac{d}{dx}\mu_1^{LHS}(x) = -J_1,\\
&h(x)\frac{dc_2}{dx} + z_2h(x)c_2\frac{d\phi}{dx} + \frac{h(x)c_2}{k_BT}\frac{d}{dx}\mu_2^{LHS}(x) = -J_2,
\end{aligned} \tag{2.7}$$

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

$$\phi(0) = \bar{V}, \ c_i(0) = L_i > 0; \quad \phi(1) = 0, \ c_i(1) = R_i > 0. \tag{2.8}$$

Substituting (2.5) into system (2.7), and after careful calculation, we obtain

$$\begin{aligned}
&\frac{\varepsilon^2}{h(x)}\frac{d}{dx}\left(h(x)\frac{d}{dx}\phi\right) = -z_1c_1 - z_2c_2, \quad \frac{dJ_1}{dx} = \frac{dJ_2}{dx} = 0,\\
&\frac{dc_1}{dx} = - f_1(c_1, c_2; d_1, d_2)\frac{d\phi}{dx} - \frac{1}{h(x)}g_1(c_1, c_2, J_1, J_2; d_1, d_2),\\
&\frac{dc_2}{dx} = f_2(c_1, c_2; d_1, d_2)\frac{d\phi}{dx} - \frac{1}{h(x)}g_2(c_1, c_2, J_1, J_2; d_1, d_2)
\end{aligned} \tag{2.9}$$

where $f_k = f_k(c_1, c_2; d_1, d_2)$ and $g_k = g_k(c_1, c_2, J_1, j_2; d_1, d_2)$ for $k = 1, 2$ are

$$\begin{aligned}
f_1 =& z_1c_1 - (d_1 + d_2 - d_1^2c_1 - d_2^2c_2)(z_1c_1 + z_2c_2)c_1 - z_1(d_1 - d_2)c_1^2,\\
f_2 =& - z_2c_2 + (d_1 + d_2 - d_1^2c_1 - d_2^2c_2)(z_1c_1 + z_2c_2)c_2 + z_2(d_2 - d_1)c_2^2,\\
g_1 =& \left((1 - d_1c_1)^2 + d_2^2c_1c_2\right) J_1 - c_1(d_1 + d_2 - d_1^2c_1 - d_2^2c_2)J_2,\\
g_2 =& \left((1 - d_2c_2)^2 + d_1^2c_1c_2\right) J_2 - c_2(d_1 + d_2 - d_1^2c_1 - d_2^2c_2)J_1.
\end{aligned} \tag{2.10}$$

Recall the boundary conditions are

$$\phi(0) = \bar{V}, \ c_i(0) = L_i > 0; \ \phi(1) = 0, \ c_i(1) = R_i > 0. \tag{2.11}$$

Denote the derivative with respect to x by overdot and introduce $u = \varepsilon\dot{\phi}$ and $\tau = x$. System (2.9) becomes

$$\begin{aligned}
&\varepsilon\dot{\phi} = u, \ \varepsilon\dot{u} = -z_1c_1 - z_2c_2 - \varepsilon\frac{h_\tau(\tau)}{h(\tau)}u,\\
&\varepsilon\dot{c}_1 = - f_1(c_1, c_2; d_1, d_2)u - \frac{\varepsilon}{h(\tau)}g_1(c_1, c_2, J_1, J_2; d_1, d_2),\\
&\varepsilon\dot{c}_2 = f_2(c_1, c_2; d_1, d_2)u - \frac{\varepsilon}{h(\tau)}g_2(c_1, c_2, J_1, J_2; d_1, d_2)\\
&\dot{J}_1 = \dot{J}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{2.12}$$

System (2.12) will be treated as a singularly perturbed system with ε as the singular parameter. Its phase space is $\mathbb{R}^7$ with state variables $(\phi, u, c_1, c_2, J_1, J_2, \tau)$.

For $\varepsilon > 0$, the rescaling $x = \varepsilon\xi$ of the independent variable x gives rise to

$$\begin{aligned}
&\phi' = u, \;\; u' = -z_1c_1 - z_2c_2 - \varepsilon\frac{h_\tau(\tau)}{h(\tau)}u,\\
&c_1' = - f_1(c_1, c_2; d_1, d_2)u - \frac{\varepsilon}{h(\tau)}g_1(c_1, c_2, J_1, J_2; d_1, d_2),\\
&c_2' = f_2(c_1, c_2; d_1, d_2)u - \frac{\varepsilon}{h(\tau)}g_2(c_1, c_2, J_1, J_2; d_1, d_2),\\
&J_1' = J_2' = 0, \quad \tau' = \varepsilon,
\end{aligned} \tag{2.13}$$

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

$$\begin{aligned}
B_L &= \{(\bar{V}, u, L_1, L_2, J_1, J_2, 0) \in \mathbb{R}^7 : \text{arbitrary } u, J_1, J_2\},\\
B_R &= \{(0, u, R_1, R_2, J_1, J_2, 1) \in \mathbb{R}^7 : \text{arbitrary } u, J_1, J_2\},
\end{aligned} \tag{2.14}$$

where $\bar{V}$, L_1, L_2, R_1 and R_2 are given in (2.11). Then the original boundary value problem is equivalent to a connecting problem: finding a solution of (2.12) or (2.13) from B_L to B_R (see, for example, [43]).

3 Asymptotic Dynamics of the Limiting PNP Systems

Our main focus in this section is to derive and study the second order system in d for both the limiting fast PNP system and the limiting slow PNP system. Some previous results from [48] will be briefly recalled, which will be used later in our discussion.

3.1 Limiting Fast Dynamics and Boundary Layers for the Second Order

By setting $\varepsilon = 0$ in (2.13), we get the *limiting fast system*

$$\begin{aligned}
&\phi' = u, \;\; u' = -z_1c_1 - z_2c_2,\\
&c_1' = - f_1(c_1, c_2; d_1, d_2)u, \quad c_2' = f_2(c_1, c_2; d_1, d_2)u,\\
&J_1' = J_2' = 0, \quad \tau' = 0.
\end{aligned} \tag{3.1}$$

Recall that d_1 and d_2 are the diameters of the two ion species. For small $d_1 > 0$ and $d_2 > 0$, we treat (3.1) as a regular perturbation of that with $d_1 = d_2 = 0$. While d_1 and d_2 are small, their ratio is of order $O(1)$. We thus set

$$d_1 = d \;\text{ and }\; d_2 = \lambda d \tag{3.2}$$

and look for solutions $\Gamma(\xi; d) = \big(\phi(\xi; d), u(\xi; d), c_1(\xi; d), c_2(\xi; d), J_1(d), J_2(d), \tau\big)$ of system (3.1) of the form

$$\begin{aligned}
\phi(\xi; d) &= \phi_0(\xi) + \phi_1(\xi)d + \phi_2(\xi)d^2 + o(d^2),\\
u(\xi; d) &= u_0(\xi) + u_1(\xi)d + u_2(\xi)d^2 + o(d^2),\\
c_k(\xi; d) &= c_{k0}(\xi) + c_{k1}(\xi)d + c_{k2}(\xi)d^2 + o(d^2),\\
J_k(d) &= J_{k0} + J_{k1}d + J_{k2}d^2 + o(d^2).
\end{aligned} \tag{3.3}$$

Substituting (3.3) into system (3.1), we obtain

(i) zeroth order limiting fast system in d

$$\begin{aligned} &\phi_0' = u_0, \;\; u_0' = -z_1c_{10} - z_2c_{20}, \quad c_{10}' = -z_1c_{10}u_0, \quad c_{20}' = -z_2c_{20}u_0, \\ &J_{10}' = J_{20}' = 0, \quad \tau' = 0, \end{aligned} \tag{3.4}$$

(ii) first order limiting fast system in d,

$$\begin{aligned} \phi_1' &= u_1, \;\; u_1' = -z_1c_{11} - z_2c_{21}, \\ c_{11}' &= -z_1u_0c_{11} - z_1c_{10}u_1 + u_0\left((\lambda+1)z_2c_{10}c_{20} + 2z_1c_{10}^2\right), \\ c_{21}' &= -z_2u_0c_{21} - z_2c_{20}u_1 + u_0\left((\lambda+1)z_1c_{10}c_{20} + 2\lambda z_2c_{20}^2\right), \\ J_{11}' &= J_{21}' = 0, \quad \tau' = 0, \end{aligned} \tag{3.5}$$

(iii) second order limiting fast system in d

$$\begin{aligned} \phi_2' &= u_2, \qquad u_2' = -z_1c_{12} - z_2c_{22}, \\ c_{12}' &= -z_1c_{10}u_2 - z_1c_{11}u_1 + \big(2z_1c_{10} + (1+\lambda)z_2c_{20}\big)c_{10}u_1 - z_1c_{12}u_0 \\ &\quad + \big(2z_1c_{10} + (1+\lambda)z_2c_{20}\big)c_{11}u_0 + \big(2z_1c_{11} + (1+\lambda)z_2c_{21}\big)c_{10}u_0 \\ &\quad - (c_{10} + \lambda^2c_{20})(z_1c_{10} + z_2c_{20})c_{10}u_0, \\ c_{22}' &= -z_2c_{20}u_2 - z_2c_{21}u_1 + \big(2\lambda z_2c_{20} + (1+\lambda)z_1c_{10}\big)c_{20}u_1 - z_2c_{22}u_0 \\ &\quad + \big(2\lambda z_2c_{20} + (1+\lambda)z_1c_{10}\big)c_{21}u_0 + \big(2\lambda z_2c_{21} + (1+\lambda)z_1c_{11}\big)c_{20}u_0 \\ &\quad - (c_{10} + \lambda^2c_{20})(z_1c_{10} + z_2c_{20})c_{20}u_0, \\ J_{12}' &= J_{22}' = 0, \qquad \tau' = 0, \end{aligned} \tag{3.6}$$

The zeroth order system and the first order system have been studied in [48], and we will not repeat them here. Instead, some results that will be used in our discussion will be briefly recalled in Proposition 3.2. To get started, we have the following result for our second order system (3.6), which is crucial to characterize the boundary layers and landing points.

Lemma 3.1 *The second order system (3.6) has a complete set of first integrals as follows:*

$$\begin{aligned} G_1 &= \frac{c_{12}}{c_{10}} - \frac{c_{11}^2}{2c_{10}^2} + z_1\phi_2 + (c_{11} + \lambda c_{21}) + u_0u_1 + \frac{1}{2}(c_{10} + \lambda c_{20})^2, \\ G_2 &= \frac{c_{22}}{c_{20}} - \frac{c_{21}^2}{2c_{20}^2} + z_2\phi_2 + (c_{11} + \lambda c_{21}) + \lambda u_0u_1 + \frac{1}{2}(c_{10} + \lambda c_{20})^2, \\ G_3 &= c_{12} + c_{22} - u_0u_2 - \frac{1}{2}u_1^2 + (c_{10} + c_{20})(c_{11} + \lambda c_{21}) \\ &\quad + (c_{11} + c_{21})(c_{10} + \lambda c_{20}) + (c_{10} + c_{20})(c_{10} + \lambda c_{20})^2, \\ G_4 &= J_{12}, \qquad G_5 = J_{22}, \qquad G_6 = \tau. \end{aligned} \tag{3.7}$$

Following the results for the zeroth and first order systems from [48], together with Lemma 3.1, one has

Proposition 3.2 *Assume that $d \geq 0$ is small. One has*

(i) The stable manifold $W^s(\mathcal{Z})$ intersects B_L transversally at points $\big(V, u_0^l + u_1^l d + u_2^l d^2 + o(d^2), L_k, J_k(d), 0\big)$ for $k = 1, 2$, and the ω−limit set of $N^L = M^L \cap W^s(\mathcal{Z})$ is

$$\omega(N^L) = \Big\{\big(\phi_0^L + \phi_1^L d + \phi_2^L d^2 + o(d^2), 0, c_{k0}^L + c_{k1}^L d + c_{k2}^L d^2 + o(d^2), J_k(d), 0\big)\Big\},$$

where $J_k(d) = J_{k0} + J_{k1}d + J_{k2}d^2 + o(d^2)$, $k = 1, 2$, *can be arbitrary, the zeroth order and first order results recalled from* [48]

$$\phi_0^L = V - \frac{1}{z_1 - z_2} \ln \frac{-z_2 L_2}{z_1 L_1}, \quad z_1 c_{10}^L = -z_2 c_{20}^L = \big(z_1 L_1\big)^{\frac{-z_2}{z_1 - z_2}} \big(-z_2 L_2\big)^{\frac{z_1}{z_1 - z_2}},$$

$$u_0^l = sgn(z_1 l_1 + z_2 l_2)\sqrt{2\Big(L_1 + L_2 + \frac{z_1 - z_2}{z_1 z_2}\big(z_1 L_1\big)^{\frac{-z_2}{z_1 - z_2}}\big(-z_2 L_2\big)^{\frac{z_1}{z_1 - z_2}}\Big)},$$

$$\phi_1^L = \frac{1 - \lambda}{z_1 - z_2}\big(L_1 + L_2 - c_{10}^L - c_{20}^L\big),$$

$$z_1 c_{11}^L = -z_2 c_{21}^L = z_1 c_{10}^L \Big(L_1 + \lambda l_2 + \frac{\lambda z_1 - z_2}{z_1 - z_2}(L_1 + L_2) + \frac{2(\lambda z_1 - z_2)}{z_2} c_{10}^L\Big),$$

$$u_1^l = \frac{1}{u_0^l}\Big((L_1 + L_2)(L_1 + \lambda L_2) - (c_{10}^L + c_{20}^L)(c_{10}^L + \lambda c_{20}^L) - c_{11}^L - c_{21}^L\Big).$$

and the result for the second order limiting fast system

$$\phi_2^L = \frac{1 - \lambda}{z_1 - z_2}(L_1 + L_2)(L_1 + \lambda L_2) + \frac{1 - \lambda}{z_2}\Big(c_{11}^L - \frac{\lambda z_1 - z_2}{z_2}(c_{10}^L)^2\Big),$$

$$z_1 c_{12}^L = -z_2 c_{22}^L = z_1 c_{10}^L \Bigg(\frac{1}{2}\omega^2(L_1, L_2) + \frac{4(\lambda z_1 - z_2)}{z_2} c_{10}^L \omega(L_1, L_2)$$

$$+ \big(L_1 + \lambda L_2\big)\omega(L_1, L_2) + \frac{9(\lambda z_1 - z_2)^2}{2 z_2^2}\big(c_{10}^L\big)^2 - \frac{1}{2}\big(L_1 + \lambda L_2\big)^2\Bigg),$$

$$u_2^l = \frac{(L_1 + L_2)(L_1 + \lambda L_2)^2 - \frac{1}{2}(u_1^l)^2 - c_{12}^L - c_{22}^L - (c_{10}^L + c_{20}^L)(c_{11}^L + \lambda c_{21}^L)}{u_0^l}$$

$$- \frac{(c_{11}^L + c_{21}^L)(c_{10}^L + \lambda c_{20}^L) + (c_{10}^L + c_{20}^L)(c_{10}^L + \lambda c_{20}^L)^2}{u_0^l},$$

where

$$w(\alpha, \beta) = \alpha + \lambda\beta + \frac{\lambda z_1 - z_2}{z_1 - z_2}(\alpha + \beta). \tag{3.8}$$

(ii) *The unstable manifold* $W^u(\mathcal{Z})$ *intersects* B_R *transversally at points* $\big(0, u_0^r + u_1^r d + u_2^r d^2 + o(d^2), R_1, R_2, J_1(d), J_2(d), 1\big)$, *and the* $\alpha-$*limit set of* $N^r = M^r \cap W^u(\mathcal{Z})$ *is*

$$\alpha\big(N^R\big) = \Big\{\big(\phi_0^R + \phi_1^R d + \phi_2^r d^2 + o(d^2), 0, c_{k0}^R + c_{k1}^R d + c_{k2}^R d^2 + o(d^2), J_k(d), 1\big)\Big\},$$

where $J_k(d) = J_{k0} + J_{k1}d + J_{k2}d^2 + o(d^2)$, $k = 1, 2$, *can be arbitrary, and the zeroth order and first order results recalled from* [48]

$$\phi_0^R = -\frac{1}{z_1 - z_2} \ln \frac{-z_2 r_2}{z_1 r_1}, \quad z_1 c_{10}^R = -z_2 c_{20}^R = \big(z_1 R_1\big)^{\frac{-z_2}{z_1 - z_2}} \big(-z_2 R_2\big)^{\frac{z_1}{z_1 - z_2}}$$

$$u_0^r = sgn(z_1 R_1 + z_2 R_2)\sqrt{2\Big(R_1 + R_2 + \frac{z_1 - z_2}{z_1 z_2}\big(z_1 R_1\big)^{\frac{-z_2}{z_1 - z_2}}\big(-z_2 R_2\big)^{\frac{z_1}{z_1 - z_2}}\Big)}$$

$$\phi_1^R = \frac{1 - \lambda}{z_1 - z_2}\big(R_1 + R_2 - c_{10}^R - c_{20}^R\big),$$

$$
\begin{aligned}
z_1 c_{11}^R &= -z_2 c_{21}^R = z_1 c_{10}^R \Big(R_1 + \lambda R_2 + \frac{\lambda z_1 - z_2}{z_1 - z_2}(R_1 + R_2) + \frac{2(\lambda z_1 - z_2)}{z_2} c_{10}^R \Big), \\
u_1^r &= \frac{(R_1 + R_2)(R_1 + \lambda R_2) - (c_{10}^R + c_{20}^R)(c_{10}^R + \lambda c_{20}^R) - c_{11}^R - c_{21}^R}{u_0^r},
\end{aligned}
$$

and the result for the second order limiting fast system

$$
\begin{aligned}
\phi_2^R &= \frac{1-\lambda}{z_1 - z_2}(R_1 + R_2)(R_1 + \lambda R_2) + \frac{1-\lambda}{z_2}\Big(c_{11}^R - \frac{\lambda z_1 - z_2}{z_2}(c_{10}^R)^2 \Big), \\
z_1 c_{12}^R &= -z_2 c_{22}^R = z_1 c_{10}^R \Bigg(\frac{1}{2}\omega^2(R_1, R_2) + \frac{4(\lambda z_1 - z_2)}{z_2} c_{10}^R \omega(R_1, R_2) \\
&\quad + \big(R_1 + \lambda R_2\big)\omega(R_1, R_2) + \frac{9(\lambda z_1 - z_2)^2}{2z_2^2}\big(c_{10}^R\big)^2 - \frac{1}{2}\big(R_1 + \lambda R_2\big)^2 \Bigg), \\
u_2^r &= \frac{(R_1 + R_2)(R_1 + \lambda R_2)^2 - \frac{1}{2}(u_1^r)^2 - c_{12}^R - c_{22}^R - (c_{10}^R + c_{20}^R)(c_{11}^R + \lambda c_{21}^R)}{u_0^r} \\
&\quad - \frac{(c_{11}^R + c_{21}^R)(c_{10}^R + \lambda c_{20}^R) + (c_{10}^R + c_{20}^R)(c_{10}^R + \lambda c_{20}^R)^2}{u_0^r}.
\end{aligned}
$$

Recall that we are interested in the solutions $\Gamma^0(\xi; d) \subset N_L = M_L \cap W^s(\mathcal{Z})$ with $\Gamma^0(0; d) \in B_L$ and $\Gamma^1(\xi; d) \subset N_R = M_R \cap W^u(\mathcal{Z})$ with $\Gamma^1(0; d) \in B_R$.

3.2 Limiting Slow Dynamics and Regular Layer for the Second Order

Next we construct the regular layer on $\mathcal{Z}$ that connects $\omega(N_L)$ and $\alpha(N_R)$. After suitable treatment (see [48] for details), the limiting slow system reads

$$
\begin{aligned}
\dot{\phi} &= -\frac{z_1 g_1\big(c_1, -\frac{z_1}{z_2}c_1, J_1, J_2; d, \lambda d\big) + z_2 g_2\big(c_1, -\frac{z_1}{z_2}c_1, J_1, J_2; d, \lambda d\big)}{z_1(z_1 - z_2)h(\tau)c_1}, \\
\dot{c}_1 &= -f_1\big(c_1, -\frac{z_1}{z_2}c_1; d, \lambda d\big)p - \frac{1}{h(\tau)} g_1\big(c_1, -\frac{z_1}{z_2}c_1, J_1, J_2; d, \lambda d\big), \\
\dot{J}_1 &= \dot{J}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{3.9}
$$

As for the layer problem, we look for solutions of (3.9) of the form

$$
\begin{aligned}
\phi(x) &= \phi_0(x) + \phi_1(x)d + +\phi_2(x)d^2 + o(d^2), \\
c_1(x) &= c_{10}(x) + c_{11}(x)d + c_{12}(x)d^2 + o(d^2), \\
J_k &= J_{k0} + J_{k1}d + J_{k2}d^2 + o(d^2)
\end{aligned} \tag{3.10}
$$

to connect $\omega(N_L)$ and $\alpha(N_R)$ given in Proposition 3.2; in particular, for $j = 0, 1, 2$, $\big(\phi_j(0), c_{1j}(0)\big) = \big(\phi_j^L, c_{1j}^L\big)$ and $\big(\phi_j(1), c_{1j}(1)\big) = \big(\phi_j^R, c_{1j}^R\big)$. To get started, we introduce the following notations for simplicity.

$$
T_k^m = J_{1k} + J_{2k}, \quad T_k^c = z_1 J_{1k} + z_2 J_{2k}, \quad \Lambda_k = J_{1k} + \lambda J_{2k}, \quad k = 0, 1, 2. \tag{3.11}
$$

From system (3.9) and the definitions of f_j's and g_j's in (2.10), we have

(i) the zeroth order limiting slow system in d

$$\begin{aligned}\dot{\phi}_0 =& -\frac{T_0^c}{z_1(z_1-z_2)h(\tau)c_{10}}, \quad \dot{c}_{10} = \frac{z_2 T_0^m}{(z_1-z_2)h(\tau)},\\ \dot{J}_{10} =& \dot{J}_{20} = 0, \quad \dot{\tau} = 1,\end{aligned} \tag{3.12}$$

(ii) the first order limiting slow system in d

$$\begin{aligned}\dot{\phi}_1 =& \frac{T_0^c c_{11}}{z_1(z_1-z_2)h(\tau)c_{10}^2} + \frac{z_1(1-\lambda)T_0^m c_{10} - T_1^c}{z_1(z_1-z_2)h(\tau)c_{10}},\\ \dot{c}_{11} =& \frac{2(\lambda z_1 - z_2)T_0^m c_{10} + z_2 T_1^m}{(z_1-z_2)h(\tau)}, \quad \dot{J}_{11} = \dot{J}_{21} = 0, \quad \dot{\tau} = 1.\end{aligned} \tag{3.13}$$

(iii) the second order limiting slow system in d

$$\begin{aligned}\dot{\phi}_2 =& -\frac{T_2^c}{z_1(z_1-z_2)h(\tau)c_{10}} + \frac{T_1^c c_{11}}{z_1(z_1-z_2)h(\tau)c_{10}^2} - \frac{(\lambda-1)T_1^m}{(z_1-z_2)h(\tau)}\\ &- \frac{T_0^c(c_{11}^2 - c_{10}c_{12})}{z_1(z_1-z_2)h(\tau)c_{10}^3},\\ \dot{c}_{12} =& \frac{z_2 T_2^m}{(z_1-z_2)h(\tau)} + \frac{2\big(\lambda z_1 - z_2\big)T_1^m}{(z_1-z_2)h(\tau)}c_{10} + \frac{2\big(\lambda z_1 - z_2\big)T_0^m}{(z_1-z_2)h(\tau)}c_{11}\\ &+ \frac{(\lambda z_1 - z_2)^2 T_0^m}{z_2(z_1-z_2)h(\tau)}c_{10}^2,\\ \dot{J}_{12} =& \dot{J}_{22} = 0, \qquad \dot{\tau} = 1,\end{aligned} \tag{3.14}$$

For convenience, we denote

$$H(x) = \int_0^x h^{-1}(s)ds. \tag{3.15}$$

Systems (3.12) and (3.13) have been analyzed in [48] under the condition that there is no permanent charge in the channel, and explicit solutions were obtained, from which the zeroth and first-order (in d) individual fluxes were derived. This is crucial for our study in this work, and we state it as follows:

Lemma 3.3 *For the zeroth order and the first order individual fluxes (in d), one has*

$$\begin{aligned}J_{10} =& \frac{c_{10}^L - c_{10}^R}{H(1)}\left(1 + \frac{z_1\left(\phi_0^L - \phi_0^R\right)}{\ln c_{10}^L - \ln c_{10}^R}\right), \quad J_{20} = -\frac{z_1(c_{10}^L - c_{10}^R)}{z_2 H(1)}\left(1 + \frac{z_2\left(\phi_0^L - \phi_0^R\right)}{\ln c_{10}^L - \ln c_{10}^R}\right),\\ J_{11} =& \frac{M}{z_1 H(1)} + \frac{N}{H(1)}, \quad J_{21} = -\frac{M}{z_2 H(1)} - \frac{N}{H(1)},\end{aligned}$$

where

$$
\begin{aligned}
M =& z_1 c_{10}^L w(L_1, L_2) - z_1 c_{10}^R w(R_1, R_2) + \frac{z_1(\lambda z_1 - z_2)}{z_2}\Big((c_{10}^L)^2 - (c_{10}^R)^2\Big),\\
N =& \frac{z_1(c_{10}^L - c_{10}^R)}{\ln c_{10}^L - \ln c_{10}^R}(\phi_1^L - \phi_1^R) - \frac{(1-\lambda)z_1}{z_2}\frac{(c_{10}^L - c_{10}^R)^2}{\ln c_{10}^L - \ln c_{10}^R} + \frac{\phi_0^L - \phi_0^R}{\ln c_{10}^L - \ln c_{10}^R}M\\
&- \frac{z_1(c_{10}^L - c_{10}^R)(w(L_1, L_2) - w(R_1, R_2))}{(\ln c_{10}^L - \ln c_{10}^R)^2}(\phi_0^L - \phi_0^R),\\
P(x) =& \frac{\lambda z_1 - z_2}{z_2}\frac{(c_{10}^L - c_{10}^R)H(x)}{(\ln c_{10}^L - \ln c_{10}^R)H(1)}\\
&+ \frac{c_{10}^L - c_{10}(x)}{\ln c_{10}^L - \ln c_{10}^R}\left(\frac{w(L_1, L_2)}{c_{10}(x)} + \frac{\lambda z_1 - z_2}{z_2}\frac{c_{10}^L}{c_{10}(x)}\right)\\
&- \frac{H(x)}{z_1(\ln c_{10}^L - \ln c_{10}^R)c_{10}(x)H(1)}M + \frac{\ln c_{10}^L - \ln c_{10}(x)}{z_1(\ln c_{10}^L - \ln c_{10}^R)(c_{10}^L - c_{10}^R)}M,
\end{aligned}
\tag{3.16}
$$

where ω is defined in (3.8).

For the second order system (3.14), one has

Lemma 3.4 *There is a unique solution $(\phi_2(x), c_{12}(x), J_{12}, J_{22}, \tau(x))$ of* (3.14) *such that $(\phi_2(0), c_{12}(0), \tau(0)) = (\phi_2^L, c_{12}^L, 0)$ and $(\phi_2(1), c_{12}(1), \tau(1)) = (\phi_2^R, c_{12}^R, 1)$, where ϕ_2^L, ϕ_2^R, c_{12}^L, and c_{12}^R are given in Proposition* 3.2*. It is given by*

$$
\begin{aligned}
\phi_2(x) =& \phi_2^L + \left(\frac{2(\lambda z_1 - z_2)T_1^c}{z_1 z_2(z_1 - z_2)} - \frac{(\lambda - 1)T_1^m}{z_1 - z_2}\right)H(x)\\
&+ \frac{T_0^m(T_0^c T_2^m - T_2^c T_0^m) + T_1^m(T_1^c T_0^m - T_0^c T_1^m)}{z_1 z_2 (T_0^m)^3}\big(\ln c_{10}(x) - \ln c_{10}^L\big)\\
&+ \frac{T_0^c T_1^m - T_1^c T_0^m}{z_1 z_2 (T_0^m)^2}\left(\frac{c_{11}(x)}{c_{10}(x)} - \frac{c_{11}^L}{c_{10}^L}\right) + \frac{T_0^c}{2 z_1 z_2 T_0^m}\left(\frac{c_{11}^2(x)}{c_{10}^2(x)} - \frac{(c_{11}^L)^2}{(c_{10}^L)^2}\right)\\
&- \frac{T_0^c}{z_1 z_2 T_0^m}\left(\frac{c_{12}(x)}{c_{10}(x)} - \frac{c_{12}^L}{c_{10}^L} - \frac{(\lambda z_1 - z_2)^2}{2 z_2^2}\big(c_{10}^2(x) - (c_{10}^L)^2\big)\right),\\
c_{12}(x) =& c_{12}^L + \frac{z_2 T_2^m}{z_1 - z_2}H(x) + \frac{2(\lambda z_1 - z_2)}{z_2}\big(c_{11}(x)c_{10}(x) - c_{11}^L c_{10}^L\big)\\
&- \frac{(\lambda z_1 - z_2)^2}{z_2^2}\big(c_{10}^3(x) - (c_{10}^L)^3\big).
\end{aligned}
\tag{3.17}
$$

In particular, one has

$$
\begin{aligned}
J_{12} =& \frac{z_1 z_2 T_0^m}{(z_1 - z_2)(\ln c_{10}^R - \ln c_{10}^L)}\Bigg\{\phi_2^L - \phi_2^R + \left(\frac{2(\lambda z_1 - z_2)T_1^c}{z_1 z_2(z_1 - z_2)} - \frac{(\lambda - 1)T_1^m}{z_1 - z_2}\right)H(1)\\
&+ \frac{T_0^c T_1^m - T_1^c T_0^m}{z_1 z_2 (T_0^m)^2}\left(\frac{c_{11}^R}{c_{10}^R} - \frac{c_{11}^L}{c_{10}^L}\right) + \frac{T_0^c}{2 z_1 z_2 T_0^m}\left(\frac{(c_{11}^R)^2}{(c_{10}^R)^2} - \frac{(c_{11}^L)^2}{(c_{10}^L)^2}\right) + \frac{J_{10}}{T_0^m}T_2^m\\
&- \frac{T_0^c}{z_1 z_2 T_0^m}\left(\frac{c_{12}^R}{c_{10}^R} - \frac{c_{12}^L}{c_{10}^L} - \frac{(\lambda z_1 - z_2)^2\big((c_{10}^R)^2 - (c_{10}^L)^2\big)}{2 z_2^2}\right)\Bigg\} - \frac{T_1^m(T_0^c T_1^m - T_1^c T_0^m)}{(z_1 - z_2)(T_0^m)^2},\\
J_{22} =& -\frac{z_1 z_2 T_0^m}{(z_1 - z_2)(\ln c_{10}^R - \ln c_{10}^L)}\Bigg\{\phi_2^L - \phi_2^R + \left(\frac{2(\lambda z_1 - z_2)T_1^c}{z_1 z_2(z_1 - z_2)} - \frac{(\lambda - 1)T_1^m}{z_1 - z_2}\right)H(1)
\end{aligned}
$$

$$+\frac{T_0^cT_1^m-T_1^cT_0^m}{z_1z_2(T_0^m)^2}\left(\frac{c_{11}^R}{c_{10}^R}-\frac{c_{11}^L}{c_{10}^L}\right)+\frac{T_0^c}{2z_1z_2T_0^m}\left(\frac{(c_{11}^R)^2}{(c_{10}^R)^2}-\frac{(c_{11}^L)^2}{(c_{10}^L)^2}\right)+\frac{J_{20}}{T_0^m}T_2^m$$
$$-\frac{T_0^c}{z_1z_2T_0^m}\left(\frac{c_{12}^R}{c_{10}^R}-\frac{c_{12}^L}{c_{10}^L}-\frac{(\lambda z_1-z_2)^2\big((c_{10}^R)^2-(c_{10}^L)^2\big)}{2z_2^2}\right)\Bigg\}+\frac{T_1^m(T_0^cT_1^m-T_1^cT_0^m)}{(z_1-z_2)(T_0^m)^2},$$

where

$$T_2^m=\frac{z_1-z_2}{z_2H(1)}\left(c_{12}^R-c_{12}^L-\frac{2(\lambda z_1-z_2)}{z_2}(c_{11}^Rc_{10}^R-c_{11}^Lc_{10}^L)+\frac{(\lambda z_1-z_2)^2}{z_2^2}\big((c_{10}^R)^3-(c_{10}^L)^3\big)\right),$$
$$T_2^c=\frac{T_0^c}{T_0^m}T_2^m+\frac{z_1z_2T_0^m}{\ln c_{10}^R-\ln c_{10}^L}\Bigg\{\phi_2^L-\phi_2^R+\left(\frac{2(\lambda z_1-z_2)T_1^c}{z_1z_2(z_1-z_2)}-\frac{(\lambda-1)T_1^m}{z_1-z_2}\right)H(1)$$
$$+\frac{T_0^cT_1^m-T_1^cT_0^m}{z_1z_2(T_0^m)^2}\left(\frac{c_{11}^R}{c_{10}^R}-\frac{c_{11}^L}{c_{10}^L}\right)+\frac{T_0^c}{2z_1z_2T_0^m}\left(\frac{(c_{11}^R)^2}{(c_{10}^R)^2}-\frac{(c_{11}^L)^2}{(c_{10}^L)^2}\right)$$
$$-\frac{T_0^c}{z_1z_2T_0^m}\left(\frac{c_{12}^R}{c_{10}^R}-\frac{c_{12}^L}{c_{10}^L}-\frac{(\lambda z_1-z_2)^2\big((c_{10}^R)^2-(c_{10}^L)^2\big)}{2z_2^2}\right)\Bigg\}-\frac{T_1^m(T_0^cT_1^m-T_1^cT_0^m)}{(T_0^m)^2}.$$

Proof Taking the integral from 0 to x for the first two equations in (3.14), respectively, together with $c_{12}(0)=c_{12}^L$ and $\phi_2(0)=\phi_2^L$, one has

$$\begin{aligned}\phi_2(x)&=\phi_2^L-\frac{T_2^c}{z_1(z_1-z_2)}\int_0^x\frac{1}{h(s)c_{10}(s)}ds+\frac{T_1^c}{z_1(z_1-z_2)}\int_0^x\frac{c_{11}(s)}{h(s)c_{10}^2(s)}ds\\&\quad-\frac{T_0^c}{z_1(z_1-z_2)}\left(\int_0^x\frac{c_{11}^2(s)}{h(s)c_{10}^3(s)}ds-\int_0^x\frac{c_{12}(s)}{h(s)c_{10}^2(s)}ds\right)\\&\quad-\frac{(\lambda-1)T_1^m}{(z_1-z_2)}H(x),\\c_{12}(x)&=c_{12}^L+\frac{z_2T_2^m}{(z_1-z_2)}H(x)+\frac{2\big(\lambda z_1-z_2\big)T_1^m}{(z_1-z_2)}\int_0^x\frac{c_{10}(s)}{h(s)}ds\\&\quad+\frac{2\big(\lambda z_1-z_2\big)T_0^m}{(z_1-z_2)}\int_0^x\frac{c_{11}(s)}{h(s)}ds+\frac{(\lambda z_1-z_2)^2T_0^m}{z_2(z_1-z_2)}\int_0^x\frac{c_{10}^2(s)}{h(s)}ds,\end{aligned}\tag{3.18}$$

where

$$\int_0^x\frac{1}{h(s)c_{10}(s)}ds=\frac{z_1-z_2}{z_2T_0^m}\int_0^x\frac{\dot c_{10}}{c_{10}(s)}ds=\frac{z_1-z_2}{z_2T_0^m}\big(\ln c_{10}(x)-\ln c_{10}^L\big),$$
$$\int_0^x\frac{c_{11}(s)}{h(s)c_{10}^2(s)}ds=\frac{z_1-z_2}{z_2T_0^m}\int_0^x\frac{c_{11}(s)\dot c_{10}(s)}{c_{10}^2(s)}ds$$
$$=-\frac{z_1-z_2}{z_2T_0^m}\left(\frac{c_{11}(x)}{c_{10}(x)}-\frac{c_{11}^L}{c_{10}^L}-\frac{2(z_1\lambda-z_2)T_0^m}{z_1-z_2}H(x)-\frac{T_1^m}{T_0^m}\big(\ln c_{10}(x)-\ln c_{10}^L\big)\right),$$
$$\int_0^x\frac{c_{11}^2(s)}{h(s)c_{10}^3(s)}ds=\frac{z_1-z_2}{z_2T_0^m}\int_0^x\frac{c_{11}^2(s)\dot c_{10}(s)}{c_{10}^3(s)}ds$$
$$=-\frac{z_1-z_2}{2}z_2T_0^m\left(\frac{c_{11}^2(x)}{c_{10}^2(x)}-\frac{(c_{11}^L)^2}{(c_{10}^L)^2}-\frac{2z_2T_1^m}{z_1-z_2}\int_0^x\frac{c_{11}(s)}{c_{10}^2(s)h(s)}ds\right.$$
$$\left.-\frac{4(z_1\lambda-z_2)T_0^m}{z_1-z_2}\int_0^x\frac{c_{11}(s)}{c_{10}(s)h(s)}ds\right),$$

$$\begin{aligned}\int_0^x \frac{c_{12}(s)}{c_{10}^2(s)h(s)}ds &= -\frac{z_1-z_2}{z_2T_0^m}\Big[\frac{c_{12}(x)}{c_{10}(x)} - \frac{c_{12}^L}{c_{10}^L} - \frac{z_2T_2^m}{z_1-z_2}\int_0^x \frac{1}{c_{10}(s)h(s)}ds \\ &\quad - \frac{2(z_1\lambda - z_2)T_1^m}{z_1-z_2}H(x) - \frac{2(z_1\lambda-z_2)T_0^m}{z_1-z_2}\int_0^x \frac{c_{11}(s)}{c_{10}(s)h(s)}ds \\ &\quad - \frac{(z_1\lambda-z_2)^2T_0^m}{z_2(z_1-z_2)}\int_0^x \frac{c_{10}(s)}{h(s)}ds\Big], \\ \int_0^x \frac{c_{11}(s)}{h(s)}ds &= \frac{z_1-z_2}{z_2T_0^m}\int_0^x c_{11}(s)dc_{10}(s) \\ &= \frac{z_1-z_2}{z_2T_0^m}\Big(c_{11}(x)c_{10}(x) - c_{11}^Lc_{10}^L - \frac{2(z_1\lambda-z_2)T_0^m}{z_1-z_2}\int_0^x \frac{c_{10}^2(s)}{h(s)}ds \\ &\quad - \frac{z_2T_1^m}{z_1-z_2}\int_0^x \frac{c_{10}(s)}{h(s)}ds\Big), \\ \int_0^x \frac{c_{10}(s)}{h(s)}ds &= \frac{z_1-z_2}{z_2T_0^m}\int_0^x c_{10}(s)\dot{c}_{10}(s)ds = \frac{z_1-z_2}{2z_2T_0^m}\big(c_{10}^2(x)-(c_{10}^L)^2\big), \\ \int_0^x \frac{c_{10}^2(s)}{h(s)}ds &= \frac{z_1-z_2}{z_2T_0^m}\int_0^x c_{10}^2(s)\dot{c}_{10}(s)ds = \frac{z_1-z_2}{3z_2T_0^m}\big(c_{10}^3(x)-(c_{10}^L)^3\big),\end{aligned}$$

where

$$\begin{aligned}\int_0^x \frac{c_{11}(s)}{c_{10}(s)h(s)}ds =& \frac{z_1-z_2}{z_2T_0^m}\Big[c_{11}(x)\ln c_{10}(x) - c_{11}^L\ln c_{10}^L \\ &- \frac{z_1\lambda-z_2}{z_2}\Big(c_{10}^2(x)\ln c_{10}(x) - (c_{10}^L)^2\ln c_{10}^L - \frac{c_{10}^2(x)-(c_{10}^L)^2}{2}\Big) \\ &- \frac{T_1^m}{T_0^m}\Big(c_{10}(x)\ln c_{10}(x) - c_{10}^L\ln c_{10}^L - c_{10}(x) + c_{10}^L\Big)\Big].\end{aligned}$$

Substituting these integrals into (3.18) and regrouping some terms, one obtain (3.17). Evaluating the ϕ_2 and c_{12} equations in (3.17) at $x = 1$, together with $\phi_2(1) = \phi_2^R$ and $c_{12}(1) = c_{12}^R$, one can uniquely solve the two resulting algebraic equations in J_{12} and J_{22}, and obtain the expressions for them. This completes the proof. □

4 Finite Ion Size Effects on Ionic Flows

In this section, we examine the finite ion size effect on the I–V relations $\mathcal{I} = z_1D_1J_1+z_2D_2J_2$ and the individual fluxes $\mathcal{J}_k = D_kJ_k,\ k = 1, 2$ based on the explicit approximations obtained from the solutions to the limiting PNP systems. Of particular interest is the ion size effects from the higher order terms, more precisely, the second order terms $\mathcal{I}_2 = z_1D_1J_{12}+z_2D_2J_{22}$ and $\mathcal{J}_{k2} = D_kJ_{k2}$; the interplay with the first order terms (the effect from the combination); and the characterization of ion size effects close to $L = R$.

For our following discussions, we assume the electroneutrality boundary conditions

$$z_1L_1 = -z_2L_2 = L, \quad z_1R_1 = -z_2R_2 = R. \tag{4.1}$$

Corollary 4.1 *Under electroneutrality boundary conditions* (4.1)*, one has*

$$\phi_0^L = \bar{V},\ z_1c_{10}^L = -z_2c_{20}^L = L;\ \phi_0^R = 0,\ z_1c_{10}^R = -z_2c_{20}^R = R,$$
$$\phi_1^L = c_{11}^L = c_{21}^L = \phi_1^R = c_{11}^R = c_{21}^R = 0 \text{ and } \phi_2^L = c_{12}^L = c_{22}^L = \phi_2^R = c_{12}^R = c_{22}^R = 0.$$

In particular, up to $O(d^2)$, there is no boundary layer at $x = 0$ and $x = 1$.

Note that $\bar{V} = \frac{e}{k_B T} V$. From Lemmas 3.3 and 3.4, and Corollary 4.1, we have

Corollary 4.2 *Assume $L \neq R$. Under electroneutrality conditions (4.1), one has*

$$
\begin{aligned}
J_{10} &= \frac{L-R}{z_1 H(1)}\left(1 + \frac{z_1 \frac{e}{k_B T} V}{\ln L - \ln R}\right), \quad J_{20} = -\frac{L-R}{z_2 H(1)}\left(1 + \frac{z_2 \frac{e}{k_B T} V}{\ln L - \ln R}\right);\\
J_{11} &= \frac{2(\lambda z_1 - z_2)}{z_1 z_2 H(1)} f_0(L,R) f_1(L,R) \frac{e}{k_B T} V + \frac{(\lambda - 1)(L-R)}{z_1 z_2 H(1)} f_2(\lambda; L, R),\\
J_{21} &= -\frac{2(\lambda z_1 - z_2)}{z_1 z_2 H(1)} f_0(L,R) f_1(L,R) \frac{e}{k_B T} V - \frac{(\lambda - 1)(L-R)}{z_1 z_2 H(1)} f_3(\lambda; L, R),\\
J_{12} &= -\frac{(\lambda z_1 - z_2)^2 f_0(L,R)}{z_1^2 z_2^2 H(1)} f_4(L,R) \frac{e}{k_B T} V + \frac{(\lambda z_1 - z_2)(L-R)}{z_1^3 z_2^2 H(1)} f_5(\lambda; L, R),\\
J_{22} &= \frac{(\lambda z_1 - z_2)^2 f_0(L,R)}{z_1^2 z_2^2 H(1)} f_4(L,R) \frac{e}{k_B T} V - \frac{(\lambda z_1 - z_2)(L-R)}{z_1^2 z_2^3 H(1)} f_6(\lambda; L, R),
\end{aligned}
$$

where

$$
\begin{aligned}
f_0(L,R) &= \frac{L-R}{\ln L - \ln R}, \quad f_1(L,R) = f_0(L,R) - \frac{L+R}{2},\\
f_2(\lambda; L, R) &= f_0(L,R) - \frac{z_1\lambda - z_2}{z_1(\lambda - 1)}(L+R),\\
f_3(\lambda; L, R) &= f_0(L,R) - \frac{z_1\lambda - z_2}{z_2(\lambda - 1)}(L+R),\\
f_4(L,R) &= 4 f_1^2(L,R) + \frac{L+R}{2} f_0(L,R) + LR,\\
f_5(\lambda; L, R) &= (\lambda z_1 - z_2)(L^2 + LR + R^2) - 2z_1(\lambda - 1) f_0^2(L,R),\\
f_6(\lambda; L, R) &= (\lambda z_1 - z_2)(L^2 + LR + R^2) - 2z_2(\lambda - 1) f_0^2(L,R).
\end{aligned}
$$

In particular,

$$
\begin{aligned}
I_0(V;0) &= z_1 D_1 J_{10}(V;0) + z_2 D_2 J_{20}(V;0)\\
&= \frac{(z_1 D_1 - z_2 D_2) f_0(L,R)}{H(1)} \frac{e}{k_B T} V + \frac{(D_1 - D_2)(L-R)}{H(1)},\\
I_1(V;\lambda,0) &= z_1 D_1 J_{11}(V;\lambda,0) + z_2 D_2 J_{21}(V;\lambda,0)\\
&= 2\frac{(\lambda z_1 - z_2)(z_1 D_1 - z_2 D_2)}{z_1 z_2 H(1)} f_0(L,R) f_1(L,R) \frac{e}{k_B T} V\\
&\quad + \frac{(\lambda - 1)(z_1 D_1 - z_2 D_2)(L-R)}{z_1 z_2 H(1)} f_7(\lambda; L, R),\\
I_2(V;\lambda,0) &= z_1 D_1 J_{12}(V;\lambda,0) + z_2 D_2 J_{22}(V;\lambda,0)\\
&= -\frac{(z_1 D_1 - z_2 D_2)(\lambda z_1 - z_2)^2}{z_1^2 z_2^2 H(1)} f_0(L,R) f_4(L,R) \frac{e}{k_B T} V\\
&\quad - \frac{2(\lambda - 1)(z_1\lambda - z_2)(z_1 D_1 - z_2 D_2)(L-R)}{z_1^2 z_2^2 H(1)} f_8(\lambda; L, R),
\end{aligned}
\tag{4.2}
$$

where

$$f_7(\lambda; L, R) = f_0(L, R) + \frac{(z_1\lambda - z_2)(D_2 - D_1)}{(\lambda - 1)(z_1 D_1 - z_2 D_2)}(L + R),$$
$$f_8(\lambda; L, R) = f_0^2(L, R) + \frac{(z_1\lambda - z_2)(D_2 - D_1)}{2(\lambda - 1)(z_1 D_1 - z_2 D_2)}(L^2 + LR + R^2).$$

4.1 Critical Potentials and Their Role Descriptions

In this section, our main concern is identifying the critical potentials and the roles they play in the study of finite ion size effects on ionic flows.

Definition 4.3 We define nine potentials $V_0,\ V_{10},\ V_{20}, V_c^F,\ V_c^S,\ V_{1c}^F, V_{1c}^S,\ V_{2c}^F$, and V_{2c}^S by

$$I_0(V_0; 0) = 0,\ I_1(V_c^F; \lambda, 0) = 0,\ I_2(V_c^S; \lambda, 0) = 0,\ J_{10}(V_{10}; 0) = 0,\ J_{11}(V_{1c}^F; \lambda, 0) = 0,$$
$$J_{12}(V_{1c}^S; \lambda, 0) = 0,\ J_{20}(V_{20}; 0) = 0,\ J_{21}(V_{2c}^F; \lambda, 0) = 0,\ J_{22}(V_{2c}^S; \lambda, 0) = 0.$$

Remark 4.4 The critical potentials $V_0,\ V_c^F,\ V_{1c}^F$ and V_{2c}^F have been defined in [7,48] without the notation F. For consistence, we include them in Definition 4.3. F in all notations stands for "first" while S stands for "second". $V_0,\ V_{10}$ and V_{20}, in general, are referred to as the reversal potentials of the total flux $I(V)$, the individual flux $J_1(V)$ and the individual flux $J_2(V)$, respectively.

Lemma 4.5 *Suppose $L \neq R$. Then,*

$$V_0 = \frac{k_B T}{e}\frac{(D_2 - D_1)(L - R)}{(z_1 D_1 - z_2 D_2) f_0(L, R)},\quad V_{10} = -\frac{k_B T}{z_1 e}\ln\frac{L}{R},\quad V_{20} = -\frac{k_B T}{z_2 e}\ln\frac{L}{R},$$
$$V_c^F = -\frac{k_B T}{e}\frac{(\lambda - 1)(L - R) f_7(\lambda; L, R)}{2(z_1\lambda - z_2) f_0(L, R) f_1(L, R)},\quad V_{1c}^F = -\frac{k_B T}{e}\frac{(\lambda - 1)(L - R) f_2(\lambda; L, R)}{2(z_1\lambda - z_2) f_0(L, R) f_1(L, R)},$$
$$V_{2c}^F = -\frac{k_B T}{e}\frac{(\lambda - 1)(L - R) f_3(\lambda; L, R)}{2(z_1\lambda - z_2) f_0(L, R) f_1(L, R)},\quad V_c^S = -\frac{k_B T}{e}\frac{2(\lambda - 1)(L - R) f_8(\lambda; L, R)}{(z_1\lambda - z_2) f_0(L, R) f_4(L, R)},$$
$$V_{1c}^S = \frac{k_B T}{e}\frac{(L - R) f_5(\lambda; L, R)}{z_1(z_1\lambda - z_2) f_0(L, R) f_4(L, R)},\quad V_{2c}^S = \frac{k_B T}{e}\frac{(L - R) f_6(\lambda; L, R)}{z_2(z_1\lambda - z_2) f_0(L, R) f_4(L, R)}.$$

In particular, one has

$$V_0 = \frac{z_1 D_1 V_{10} - z_2 D_2 V_{20}}{z_1 D_1 - z_2 D_2},\quad V_c^F = \frac{z_1 D_1 V_{1c}^F - z_2 D_2 V_{2c}^F}{z_1 D_1 - z_2 D_2},\quad V_c^S = \frac{z_1 D_1 V_{1c}^S - z_2 D_2 V_{2c}^S}{z_1 D_1 - z_2 D_2}.$$

Recall from [7] and [48] that, under electroneutrality conditions (4.1), one has

$$\partial_V I_1(V; \lambda, 0) > 0,\quad \partial_V J_{11}(V; \lambda, 0) > 0 \text{ and } \partial_V J_{21}(V; \lambda, 0) < 0.$$

However, for the second order terms in d, we have

Lemma 4.6 *Assume $L \neq R$. Under the electroneutrality conditions (4.1), one has*

$$\partial_V I_2(V; \lambda, 0) < 0,\quad \partial_V J_{12}(V; \lambda, 0) < 0 \textit{ and } \partial_V J_{22}(V; \lambda, 0) > 0.$$

Directly, the following statement can be established.

Proposition 4.7 *Assume $L \neq R$. Viewing $I_k,\ J_{1k}$ and J_{2k}, $k = 0, 1, 2$ as functions of V, one has* *(i) Both I_0 and I_1 are increasing in V, while I_2 is decreasing in V. Furthermore, $I_0 > 0$ (resp. $I_0 < 0$) if $V > V_0$ (resp. $V < V_0$); $I_1 > 0$ (resp. $I_1 < 0$) if $V > V_c^F$ (resp. $V < V_c^F$); and $I_2 > 0$ (resp. $I_2 < 0$) if $V < V_c^S$ (resp. $V > V_c^S$).*

(ii) Both J_{10} and J_{11} are increasing in V, while J_{12} is decreasing in V. Furthermore, $J_{10} > 0$ (resp. $J_{10} < 0$) if $V > V_{10}$ (resp. $V < V_{10}$); $J_{11} > 0$ (resp. $J_{11} < 0$) if $V > V_{1c}^F$ (resp. $V < V_{1c}^F$); and $J_{12} > 0$ (resp. $J_{12} < 0$) if $V < V_{1c}^S$ (resp. $V > V_{1c}^S$).

(iii) Both J_{20} and J_{21} are decreasing in V, while J_{22} is increasing in V. Furthermore, $J_{20} > 0$ (resp. $J_{20} < 0$) if $V < V_{20}$ (resp. $V > V_{20}$); $J_{21} > 0$ (resp. $J_{21} < 0$) if $V < V_{2c}^F$ (resp. $V > V_{2c}^F$); and $J_{22} > 0$ (resp. $J_{22} < 0$) if $V > V_{2c}^S$ (resp. $V < V_{2c}^S$).

The scaling laws for I_k, J_{k0}, J_{k1} and the critical potentials V_0, V_c^F, V_{kc}^F, V_F^c, and V_F^{kc} have been discussed in [7,48]. For I_2, J_{k2} and other critical potentials defined in Definition 4.3, one has

Proposition 4.8 *Viewing I_2, J_{k2}, V_{k0}, V_c^S and V_{kc}^S as functions of (L, R) for $k = 1, 2$, one has*

(i) I_2, J_{12} and J_{22} are homogeneous of degree three in (L, R), that is, for any $s > 0$, $I_2(V; sL, sR) = s^3 I_2(V; L, R)$, $J_{12}(V; sL, sR) = s^3 J_{12}(V; L, R)$ and $J_{22}(V; sL, sR) = s^3 J_{22}(V; L, R)$.

(ii) V_c^S and V_{kc}^S are homogeneous of degree zero in (L, R), that is, taking V_c^S for example, for any $s > 0$, $V_c^S(sL, sR) = V_c^S(L, R)$.

In terms of the parameters (D_1, D_2), (L, R) and λ, we can provide a partial order for the critical potentials identified in Definition 4.3, which provides deep insights into finite ion size effects on ionic flows.

Lemma 4.9 *Assume $L > R$, $D_2 > D_1$ and $\lambda > 1$. One has*

$$V_{1c}^F < V_{10} < V_{1c}^S, \quad V_{2c}^S < V_{20} < V_{2c}^F \ \text{and}\ V_c^S < V_0 < V_c^F.$$

From Lemmas 4.7 and 4.9, we have

Theorem 4.10 *Assume $L > R$, $D_2 > D_1$ and $\lambda > 1$. For the individual fluxes $J_k(V)$, $k = 1, 2$ and the total flux $I(V)$, with $|J_1(V)|$, $|J_2(V)|$ and $|I(V)|$ denoting the magnitude of $J_1(V)$, $J_2(V)$ and $I(V)$, respectively, one has*

(i) For the individual flux $J_1(V)$,

(i1) if $V < V_{1c}^F$, then, $J_{10}(V) < 0$, $J_{11}(V) < 0$ and $J_{12}(V) > 0$, that is, the ion size effect from $J_{11}(V)$ reduces $J_1(V)$ while the one from $J_{12}(V)$ enhances $J_1(V)$. Furthermore, $J_{11}(V)$ enhances $|J_1(V)|$ while $J_{12}(V)$ reduces $|J_1(V)|$;

(i2) if $V_{1c}^F < V < V_{10}$, then, $J_{10}(V) < 0$, $J_{11}(V) > 0$ and $J_{12}(V) > 0$, that is, the ion size effect from $J_{11}(V)$ and $J_{12}(V)$ both enhance $J_1(V)$. Furthermore, they both reduce $|J_1(V)|$;

(i3) if $V_{10} < V < V_{1c}^S$, then, $J_{10}(V) > 0$, $J_{11}(V) > 0$ and $J_{12}(V) > 0$, that is, the ion size effect from $J_{11}(V)$ and $J_{12}(V)$ both enhance the $J_1(V)$. Furthermore, they both enhance $|J_1(V)|$;

(i4) if $V > V_{1c}^S$, then, $J_{10}(V) > 0$, $J_{11}(V) > 0$ and $J_{12}(V) < 0$, that is, the ion size effect from $J_{11}(V)$ enhances $J_1(V)$ while the one from $J_{12}(V)$ reduces $J_1(V)$. Furthermore, $J_{11}(V)$ enhances $|J_1(V)|$ while $J_{12}(V)$ reduces $|J_1(V)|$.

(ii) For the individual flux $J_2(V)$,

(ii1) *if* $V < V_{2c}^S$, *then,* $J_{20}(V) > 0, J_{21}(V) > 0$ *and* $J_{22}(V) < 0$, *that is, the ion size effect from* $J_{21}(V)$ *enhances* $J_1(V)$ *while the one from* $J_{22}(V)$ *reduces* $J_1(V)$. *Furthermore,* $J_{11}(V)$ *enhances* $|J_1(V)|$ *while* $J_{12}(V)$ *reduces* $|J_1(V)|$;

(ii2) *if* $V_{2c}^S < V < V_{20}$, *then,* $J_{20}(V) > 0$, $J_{11}(V) > 0$ *and* $J_{12}(V) > 0$, *that is, the ion size effect from* $J_{11}(V)$ *and* $J_{12}(V)$ *both enhance* $J_1(V)$. *Furthermore, they both enhance* $|J_1(V)|$;

(ii3) *if* $V_{20}^F < V < V_{2c}^F$, *then,* $J_{20}(V) < 0$, $J_{21}(V) > 0$ *and* $J_{22}(V) > 0$, *that is, the ion size effect from* $J_{21}(V)$ *and* $J_{22}(V)$ *both enhance* $J_2(V)$. *Furthermore, they both reduce* $|J_2(V)|$;

(ii4) *if* $V > V_{2c}^F$, *then,* $J_{20}(V) < 0, J_{21}(V) < 0$ *and* $J_{22}(V) > 0$, *that is, the ion size effect from* $J_{11}(V)$ *reduces* $J_2(V)$ *while the one from* $J_{22}(V)$ *enhances* $J_2(V)$. *Furthermore,* $J_{21}(V)$ *enhances* $|J_2(V)|$ *while* $J_{22}(V)$ *reduces* $|J_2(V)|$.

(iii) *For the total flow rate of charge* $I(V)$,

(iii1) *if* $V < V_c^S$, *then,* $I_0(V) < 0,\ I_1(V) < 0$ *and* $I_2(V) > 0$, *that is, the ion size effect from* $I_1(V)$ *reduces* $I(V)$ *while the one from* $I_2(V)$ *enhances* $I(V)$. *Furthermore,* $I_1(V)$ *enhances* $|I(V)|$ *while* $I_2(V)$ *reduces* $|I(V)|$;

(iii2) *if* $V_c^S < V < V_0$, *then,* $I_0(V) < 0,\ I_1(V) < 0$ *and* $I_2(V) < 0$, *that is, the ion size effect from* $I_1(V)$ *and* $I_2(V)$ *both reduce* $I(V)$. *Furthermore, they both enhance* $|I(V)|$;

(iii3) *if* $V_0 < V < V_c^F$, *then,* $I_0(V) > 0,\ I_1(V) < 0$ *and* $I_2(V) < 0$, *that is, the ion size effect from* $I_1(V)$ *and* $I_2(V)$ *both reduce* $I(V)$. *Furthermore, they both reduce* $|I(V)|$;

(iii4) *if* $V > V_c^F$, *then,* $I_0(V) > 0,\ I_1(V) < 0$ *and* $I_2(V) < 0$, *that is, the ion size effect from* $I_1(V)$ *enhances* $I(V)$ *while* $I_2(V)$ *reduces* $I(V)$. *Furthermore,* $I_1(V)$ *enhances* $|I(V)|$ *while* $I_2(V)$ *reduces* $|I(V)|$.

Remark 4.11 Similar results can be established for the case with $L > R$, $D_2 < D_1$ and $0 < \lambda < 1$.

To end this section, we comment that for the system (2.6) with dimensions, one may consider the cation to be Na^+ and the anion to be Cl^-, and λ is the ratio of the diameter of Na^+ to Cl^-. Then, we may take (the diffusion constants are from [49])

$$D_{Na} = 1.334 \times 10^{-9} m^2/s,\ D_{Cl} = 2.032 \times 10^{-9} m^2/s,\ L = 0.2mol,\ R = 0.02mol,$$
$$k_B = 1.381 \times 10^{-23} JK^-,\ T = 273.16K,\ e = 1.602 \times 10^{-19} C,\ z_1 = -z_2 = 1 \text{ and}$$
$$\lambda = 1.885.$$

It follows directly that

$$V_{1c}^F = -1.6696 \times 10^{-1} JC^-,\ V_{10} = -5.4221 \times 10^{-2} JC^{-1},\ V_{1c}^S = 1.3239 \times 10^{-1} JC^{-1},$$

which satisfies the relation $V_{1c}^F < V_{10} < V_{1c}^S$ as started in Lemma 4.9. Similarly, one can check others. Also, this relation should hold for $\varepsilon > 0$ small.

4.2 Combining Effects from the First and the Second Order Terms

In Theorem 4.10, the critical potentials identified in Definition 4.3 split the potential region into different subregions, over which distinct dynamics of ionic flows are oberved, in particular, the ion size effects from different orders (in d) are characterized in details. However, the essential effects (combination effects from the first order term and the second order term) from finite ion size on ionic flows are not clear. To better understand the finite ion size effects on ionic flows, we introduce another three critical potentials V_c^b, V_{1c}^b and V_{2c}^b defined as follows:

Definition 4.12 We define three critical potentials V_c^b, V_{1c}^b and V_{2c}^b by

$$I_1(V_c^b;\lambda,0)+dI_2(V_c^b;\lambda,0)=0,\quad J_{11}(V_{1c}^b;\lambda,0)+dJ_{12}(V_{1c}^b;\lambda,0)=0,$$
$$J_{21}(V_{2c}^b;\lambda,0)+dJ_{22}(V_{2c}^b;\lambda,0)=0.$$

Lemma 4.13 *Assume $L\neq R$ and $\lambda>1$. For $d>0$ small, one has*

$$V_c^b=-\frac{k_BT}{e}\frac{(\lambda-1)(L-R)\Big(f_7(\lambda;L,R)-\frac{2(z_1\lambda-z_2)}{z_1z_2}f_8(\lambda;L,R)d\Big)}{2(z_1\lambda-z_2)f_0(L,R)\Big(f_1(L,R)-\frac{z_1\lambda-z_2}{2z_1z_2}f_4(L,R)d\Big)},$$
$$V_{1c}^b=-\frac{k_BT}{e}\frac{(\lambda-1)(L-R)\Big(f_2(\lambda;L,R)+\frac{z_1\lambda-z_2}{z_1^2z_2(\lambda-1)}f_5(\lambda;L,R)d\Big)}{2(z_1\lambda-z_2)f_0(L,R)\Big(f_1(L,R)-\frac{z_1\lambda-z_2}{2z_1z_2}f_4(L,R)d\Big)},$$
$$V_{2c}^b=-\frac{k_BT}{e}\frac{(\lambda-1)(L-R)\Big(f_3(\lambda;L,R)+\frac{z_1\lambda-z_2}{z_1z_2^2(\lambda-1)}f_6(\lambda;L,R)d\Big)}{2(z_1\lambda-z_2)f_0(L,R)\Big(f_1(L,R)-\frac{z_1\lambda-z_2}{2z_1z_2}f_4(L,R)d\Big)}.$$

In particular,

$$V_c^b=\frac{z_1D_1V_{1c}^b-z_2D_2V_{2c}^b}{z_1D_1-z_2D_2}.$$

Remark 4.14 In Lemma 4.13, the critical potentials V_c^b and V_{kc}^b, $k=1,2$ as functions of (L,R) don't share the scaling laws as other critical potentials defined in the Definition 4.3, which is not a surprise since it reflects the mixed finite ion size effects from both the first order and the second order corrections. On the other hand, the critical potentials identified in Definition 4.3 except the reversal potentials V_0, V_{10} and V_{20}, all depend on the parameter λ (recall that $\lambda=d/d_2$, where $d=d_1$ the diameter of the cation and d_2 the diameter of the anion), which provides information of relative ion size effects. However, the critical potentials identified in Definition 4.12 do depend on the diameter of the cation explicitly, and this further provides important information on the study of ion size effects on ionic flows. We would also like to point out that the critical potentials defined in (4.12) could be experimentally estimated. To be specific, one can take an experimental I–V relation as $I(V;\lambda,d)$ and numerically (or analytically) compute $I_0(V)$ for ideal case that allows one to get an estimate of V_c^b.

For convenience in our following discussion, we introduce three functions I^d, J_1^d and J_2^d of the potential V defined by

$$I^d(V)=I_1(V)+dI_2(V),\quad J_1^d(V)=J_{11}(V)+dJ_{12}(V),\quad J_2^d=J_{21}(V)+dJ_{22}(V).$$

Clearly, they contain ion size effects on ionic flows. The potentials defined in Definition 4.12 are the critical potentials that balance the ion size effects on the total flux $I(V)$, and the individual fluxes $J_1(V)$ and $J_2(V)$.

Theorem 4.15 *Assume $L>R$, $D_2>D_1$ and $\lambda>1$. For $d>0$ small, one has*

(i) *$I^d(V)$ is increasing (resp. decreasing) in the potential V if $x > x_1^*$ (resp. $1 < x < x_1^*$), where, with $x = L/R > 1$, x_1^* is the root of*

$$g_1(x) = \frac{x-1}{\ln x} - \frac{x+1}{2} - \frac{(z_1\lambda - z_2)dR}{2z_1z_2}\left[4\left(\frac{x-1}{\ln x} - \frac{x+1}{2}\right)^2 + \frac{x^2-1}{2\ln x} + x\right].$$

Hence,

- (i1) *For $1 < x < x_1^*$, $I^d(V) > 0$ (resp. $I^d(V) < 0$) if $V < V_c^b$ (resp. $V > V_c^b$); that is, the ion size effect eventually enhances the total flux $I(V)$ if $V < V_c^b$, while eventually reduces it if $V > V_c^b$.*
- (i2) *For $x > x_1^*$, $I^d(V) > 0$ (resp. $I^d(V) < 0$) if $V > V_c^b$ (resp. $V < V_c^b$); that is, the ion size effect eventually enhances the total flux $I(V)$ if $V > V_c^b$, while eventually reduces it if $V < V_c^b$.*

(ii) *$J_1^d(V)$ is increasing (resp. decreasing) in the potential V if $x > x_1^*$ (resp. $1 < x < x_1^*$). Hence,*

- (ii1) *For $1 < x < x_1^*$, $J_1^d(V) > 0$ (resp. $J_1^d(V) < 0$) if $V < V_{1c}^b$ (resp. $V > V_{1c}^b$); that is, the ion size effect eventually enhances the total flux $J_1(V)$ if $V < V_{1c}^b$, while eventually reduces it if $V > V_{1c}^b$.*
- (ii2) *For $x > x_1^*$, $J_1^d(V) > 0$ (resp. $J_1^d(V) < 0$) if $V > V_{1c}^b$ (resp. $V < V_{1c}^b$); that is, the ion size effect eventually enhances the total flux $J_1(V)$ if $V > V_{1c}^b$, while eventually reduces it if $V < V_{1c}^b$.*

(iii) *$J_2^d(V)$ is increasing (resp. decreasing) in the potential V if $1 < x < x_1^*$ (resp. $x > x_1^*$). Hence,*

- (iii1) *For $1 < x < x_1^*$, $J_2^d(V) > 0$ (resp. $J_2^d(V) < 0$) if $V > V_{2c}^b$ (resp. $V < V_{2c}^b$); that is, the ion size effect eventually enhances the total flux $J_2(V)$ if $V > V_{2c}^b$, while eventually reduces it if $V < V_{2c}^b$.*
- (iii2) *For $x > x_1^*$, $J_2^d(V) > 0$ (resp. $J_2^d(V) < 0$) if $V < V_{2c}^b$ (resp. $V > V_{2c}^b$); that is, the ion size effect eventually enhances the total flux $J_2(V)$ if $V < V_{2c}^b$, while eventually reduces it if $V > V_{2c}^b$.*

Lemma 4.16 *Assume $L > R$, $D_2 > D_1$ and $\lambda > 1$. For $d > 0$ small, one has $V_{2c}^b < V_c^b < V_{1c}^b$ if $1 < x < x_1^*$; $V_{1c}^b < V_c^b < V_{2c}^b$ if $x > x_1^*$, where x_1^* is identified in Theorem 4.15.*

Recall that $\mathcal{I} = z_1D_1J_1 + z_2D_2J_2$ with $z_1 > 0$, $z_2 < 0$ and $\mathcal{J}_k = D_kJ_k$. Together with the total order of the critical potentials V_c^b, V_{1c}^b and V_{2c}^b provided by Lemma 4.16, we have

Theorem 4.17 *Assume $L > R$, $D_2 > D_1$ and $\lambda > 1$. For $d > 0$ small, one has*

(i) *With $1 < x < x_1^*$,*

- (i1) *For $V < V_{2c}^b$, the ion size effect eventually reduces $J_2(V)$ while enhances $J_1(V)$, but enhances $I(V)$;*
- (i2) *For $V_{2c}^b < V < V_c^b$, the ion size effect eventually enhances both $J_1(V)$ and $J_2(V)$, but enhances $I(V)$;*
- (i3) *For $V_c^b < V < V_{1c}^b$, the ion size effect eventually enhances both $J_1(V)$ and $J_2(V)$, but reduces $I(V)$;*
- (i4) *For $V > V_{1c}^b$, the ion size effect eventually reduces $J_1(V)$ while enhances $J_2(V)$, and reduces $I(V)$.*

(ii) With $x > x_1^*$,

(ii1) For $V < V_{1c}^b$, the ion size effect eventually enhances $J_2(V)$ while reduces $J_1(V)$, but reduces $I(V)$;
(ii2) For $V_{1c}^b < V < V_c^b$, the ion size effect eventually enhances both $J_1(V)$ and $J_2(V)$, but reduces $I(V)$;
(ii3) For $V_c^b < V < V_{2c}^b$, the ion size effect eventually enhances both $J_1(V)$ and $J_2(V)$, and enhances $I(V)$;
(ii4) For $V > V_{2c}^b$, the ion size effect eventually reduces $J_2(V)$ while enhances $J_1(V)$, but enhances $I(V)$.

Remark 4.18 In Theorem 4.10, we focus on the ion size effect from the first order terms $I_1(V;\lambda)$, $J_{k1}(V;\lambda)$ and the second order terms $I_2(V;\lambda)$, $J_{k2}(V;\lambda)$ separately, more precisely, we considered whether the ion size effect from the first order terms or from the second order terms enhances/reduces the ionic flux, and did not characterize the essential ion size effect from the combination of the first order terms and the second order terms, which is studied in Theorem 4.15. In particular, in Theorem 4.17, both statement (i) and statement (ii) provide very interesting results. Take the statement (i) for example, for $V_{2c}^b < V < V_c^b$, the ion size effect enhances the individual fluxes $J_1(V)$ and $J_2(V)$, and hence, enhances $z_1J_1(V)$ and reduces $z_2J_2(V)$ since $z_1 > 0$ and $z_2 < 0$, but eventually enhances the total flow rate of charges $I(V) = z_1D_1J_1(V) + z_2J_2D_2(V)$ since $D_1 > 0$ and $D_2 > 0$. However, in the distinct potential subregion $V_c^b < V < V_{1c}^b$, the ion size effect enhances the individual fluxes $J_1(V)$ and $J_2(V)$ too, but reduces the total flow rate of charges $I(V)$. This observation further indicates the sensitive dependence of the ionic flow properties on the interplays among different system parameters. This process is not intuitive and mathematical analysis is necessary to help better understand the dynamics of ionic flows.

To end this section, we provide a partial order of the critical potentials V_0, V_{10}, V_{20}, V_c^F, V_{1c}^F, V_{2c}^F, V_c^S, V_{1c}^S, V_{2c}^S, V_c^b, V_{1c}^b and V_{c2}^b identified in Definitions 4.3 and 4.12, which further depends on more complicate nonlinear interplays among other system parameters, such as the diffusion coefficients (D_1, D_2), the ionic valences (z_1, z_2), the boundary concentrations (L, R) and the ion sizes (d, λ).

Lemma 4.19 *Assume $L > R$, $D_2 > D_1$ and $\lambda > 1$. For $d > 0$ small, with x_1^* identified in Theorem 4.15, one has*

(i) $V_{1c}^F < V_{10} < V_{1c}^S < V_{1c}^b$ if $\frac{f_0^2(L,R)}{L^2+LR+R^2} < \frac{z_1\lambda - z_2}{2z_1(\lambda-1)}$ and $1 < x < x_1^*$.
(ii) $V_{2c}^S < V_{20} < V_{2c}^F < V_{2c}^b$ if $x > x_1^*$.
(iii) $V_c^S < V_0 < V_c^F < V_c^b$ if $x > x_1^*$.
(iv) $V_{10} < V_0 < V_{20}$, $V_{1c}^F < V_c^F < V_{2c}^F$ and $V_{2c}^S < V_c^S < V_{1c}^S$.

Remark 4.20 With the partial orders of the critical potentials provided in Lemma 4.19, in particular the first three statements, one is allowed to further examine the finite ion size effects on the total flux $I(V;\lambda)$ and the individual fluxes $J_k(V;\lambda)$, $k = 1, 2$. The argument will be similar to those in Theorems 4.10 and 4.17, and we leave it to the reader.

4.3 Case Studies of Ion Size Effects Near $L = R$

Recall that one motivation of this work is due to the observation $I_1(V;\lambda,0) \to 0$, $J_{11}(V;\lambda,0) \to 0$ and $J_{21}(V;\lambda,0) \to 0$ as $L \to R$. In other words, as L approaches

R, the leading terms $I_1(V;\lambda,0)$, $J_{11}(V;\lambda,0)$ and $J_{21}(V;\lambda,0)$ cannot provide information for the effects from finite ion size, and higher order terms need to be considered. We now take a further look at this special case.

Lemma 4.21 *For fixed $R>0$, one has*

$$\begin{aligned}
&\lim_{L\to R} J_{10}(V;0) = -\lim_{L\to R} J_{20}(V;0) = \frac{e}{k_BT}\frac{R}{H(1)}V,\\
&\lim_{L\to R} J_{11}(V;\lambda,0) = \lim_{L\to R} J_{21}(V;\lambda,0) = 0,\\
&\lim_{L\to R} J_{12}(V;\lambda,0) = -\lim_{L\to R} J_{22}(V;\lambda,0) = -\frac{2(z_1\lambda - z_2)^2R^3}{z_1^2z_2^2H(1)}\frac{e}{k_BT}V.
\end{aligned}$$

From (4.2), we have

$$\begin{aligned}
&\lim_{L\to R} I_0(V;0) = \frac{(z_1D_1 - z_2D_2)R}{H(1)}\frac{e}{k_BT}V, \quad \lim_{L\to R} I_1(V;\lambda,0) = 0,\\
&\lim_{L\to R} I_2(V;\lambda,0) = -2\frac{(z_1D_1 - z_2D_2)(\lambda z_1 - z_2)^2R^3}{z_1^2z_2^2H(1)}\frac{e}{k_BT}V.
\end{aligned}$$

Directly, the following statement can be established.

Theorem 4.22 *As $L\to R$, one has*

(i) $V_0 = V_{10} = V_{20} = V_{1c}^S = V_{2c}^S = V_c^S = 0$*;*

(ii) $I_0(V)I_2(V;\lambda) < 0$ *and* $J_{k0}(V)J_{k2}(V;\lambda) < 0,\ k=1,2,$ *if* $V\neq 0$*; that is, the ion size effect always reduces the total flux* $I(V)$ *and the individual flux* $J_k,\ k=1,2$ *if* $V\neq 0$*; and hence the magnitudes* $|I(V)|$ *and* $|J_k(V)|$ *for* $k=1,2$.

We would like to comment that the first statement of Theorem 4.22 can be verified directly either from Lemma 4.21 or from the expressions obtained in Lemma 4.5 by taking the limit as $L\to R$.

Proposition 4.23 *As $L\to R$, one has*

$$\frac{J_{12}(V;\lambda)}{J_{10}(V)} = \frac{J_{22}(V;\lambda)}{J_{20}(V)} = \frac{I_2(V;\lambda)}{I_0(V)} = -\frac{2(z_1\lambda - z_2)^2R^2}{z_1^2z_2^2}.$$

Remark 4.24 Proposition 4.23 indicates that the finite ion size effects from the second order terms $J_{k2}(V;\lambda),\ k=1,2$ and $I_2(V;\lambda)$ will be significant as $L\to R$ for $Rd>1$.

5 Concluding Remarks

In this work, we further study the effects on ionic flows from finite ion sizes via the method of asymptotic expansions up to the second order due to the observation that the first-order terms approach zero, in other words, the finite ion size effects on ionic flows disappear, when the left and right boundary concentrations are close for the same ion species. On the other hand, considering higher order terms may help us perceive the properties of the expansion and generalize it for any size, not just the small sizes of ions. The interactions between the first-order and the second-order terms are also described to better understand the ionic flow properties. Moreover, critical potentials are identified to help us monitor the dynamics of ionic flows. For this simple setup, complicated nonlinear interplays among system parameters, particularly, the diffusion constants (D_1, D_2) and the boundary concentrations (L, R) are characterized, which are not intuitive, and provide insights into the internal dynamics of ionic flows through membrane channels. This could be very helpful for the future studies along this direction, not only mathematically or numerically, but experimentally since the internal dynamics of ion channels cannot be measured with present technology.

We would also like to point out that since ions are crowded, more general setups, such as more cations are included, for the PNP model should be studied. Of particular interest is the case with multiple cations that have the same valences but different ion sizes, like Na^+ and K^+. We believe mathematical studies will provide deep insights into the selectivity of ion channels over different cations.

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