

# Individual flux study via steady-state Poisson-Nernst-Planck systems: Effects from boundary conditions

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## Abstract

We provide a detailed study for ionic flow through ion channels for the case with *three* ion species, two positively charged having the same valence and one negatively charged, and with zero permanent charge. The work is based on the general geometric theory developed in [W. Liu, J. Differential Equations **246** (2009), 428-451] for a quasi-one-dimensional steady-state Poisson-Nernst-Planck (PNP) model. Our focus is on the effects of boundary conditions on the ionic flow. Beyond the existence of solutions of the model problem, we are able to obtain explicit approximations of individual fluxes and the I-V relations, from which effects of boundary conditions on ionic flows are examined in a great detail. Critical potentials are identified and their roles in characterizing these effects are studied. Compared to ionic mixtures with two ion species, a number of new features for mixtures of three ion species arise. Numerical simulations are performed, and numerical results are consistent with our analytical ones.

**Key words.** Ionic flow, individual flux, boundary effects.

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**Running head.** Individual flux from PNP models

## 1 Introduction

Ion channels are large cylindrical shaped proteins embedded in cell membranes with a hole down their middle axis that establish communication between the cells and its external environment. This way they can control a wide range of biological functions. The study of ion channel properties consists of two related topics: structures of ion channels and ionic flow properties. Here, our aim is to shed light on the steady-state

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ionic flows with three ions participating, such as potassium, sodium, and the chloride ion.

This is an example of a general process called Electrodifffusion, the diffusion of electric charge, which plays a central role in a wide range of important technological devices and physical phenomena [13, 14, 16, 38, 52, 53, 63]: semiconductors controls the migration and diffusion of quasi-particles of charge in transistors and integrated circuits [61, 67, 71], properties of electrolytic solutions and thin films [5, 10, 14, 15, 18, 25], all of biology occurs in solutions of ions and charged organic molecules in water [1, 17, 33, 70]. It is the goal of technology (and much of physical science and biological processes) to control these electrodifffusive systems to produce useful behavior. Our main concern in this work is to analyze the effect on ionic individual flows through membrane channels due to changes in boundary conditions.

A basic continuum model for electrodifffusion is the Poisson-Nernst-Planck (PNP) system. This is a reduced model that treats the medium (aqueous within which ions are migrating) as a dielectric continuum. The channel is assumed to be narrow so that it can be effectively viewed as a one-dimensional line segment  $[0, l]$  where  $l$ , typically in the range of 10 – 20 nanometers, is the length of the channel whose endpoints are the baths that the channel links. A quasi-one-dimensional *steady-state* PNP model for ion flows of  $n$  ion species through a single channel is (see [49, 55])

$$\begin{aligned} \frac{1}{A(X)} \frac{d}{dX} \left( \varepsilon_r(X) \varepsilon_0 A(X) \frac{d\Phi}{dX} \right) &= -e \left( \sum_{j=1}^n z_j C_j(X) + Q(X) \right), \\ \frac{d\mathcal{J}_i}{dX} &= 0, \quad -\mathcal{J}_i = \frac{1}{k_B T} \mathcal{D}_i(X) A(X) C_i(X) \frac{d\mu_i}{dX}, \quad i = 1, 2, \dots, n, \end{aligned} \quad (1.1)$$

where  $e$  is the elementary charge,  $k_B$  is the Boltzmann constant,  $T$  is the absolute temperature;  $\Phi$  is the electric potential,  $Q(X)$  is the permanent charge of the channel,  $\varepsilon_r(X)$  is the relative dielectric coefficient,  $\varepsilon_0$  is the vacuum permittivity;  $A(X)$  is the area of cross-section of the channel over the point  $X \in [0, l]$ . For the  $i$ th ion species,  $C_i$  is the concentration (number of  $i$ th ions per unit volume),  $z_i$  is the valence (number of charges per particle) that is positive for cations and negative for anions,  $\mu_i$  is the electrochemical potential,  $\mathcal{J}_i$  is the flux density, and  $\mathcal{D}_i(X)$  is the diffusion coefficient.

For system (1.1), we impose the following boundary conditions (see, [22] for justification), for  $k = 1, 2, \dots, n$ ,

$$\Phi(0) = \mathcal{V}, \quad C_i(0) = \mathcal{L}_i > 0; \quad \Phi(l) = 0, \quad C_i(l) = \mathcal{R}_i > 0. \quad (1.2)$$

The electrochemical potential  $\mu_k$  is the sum of the ideal component

$$\mu_k^{id}(X) = z_k e \Phi(X) + k_B T \ln \frac{C_k(X)}{C_0} \quad (1.3)$$

with some characteristic number density  $C_0$ , and the excess component  $\mu_k^{ex}(X)$ .

**Remark 1.1.** *The Nernst-Planck equation in (1.1) for the flux  $\mathcal{J}_k$  gives (first observed in [23])*

$$\mathcal{J}_k \int_0^l \frac{k_B T}{D_k(X) A(X) C_k(X)} dx = \mu_k(0) - \mu_k(l).$$

Due to the positivity of the integrand, one sees that  $\mathcal{J}_k$  has the same sign as  $\mu_k(0) - \mu_k(l)$ . In particular, for the classical PNP system, one has

$$\mu_k(0) - \mu_k(l) = z_k e (\Phi(0) - \Phi(1)) + k_B T \ln \frac{C_k(0)}{C_k(1)},$$

which is determined by the boundary conditions. This observation will be checked in Section 4 (see Remark 4.4).

The PNP system can be derived as a reduced model from molecular dynamics ([65]), from Boltzmann equations ([4]), and from variational principles ([34, 35, 36]). More sophisticated models have also been developed. Coupling PNP and Navier-Stokes equations for aqueous motions has also been proposed (see, e.g. [9, 19, 20, 26, 31, 68]). Reviews of various models for ion transport and comparisons among the models can be found in [11, 37, 62, 73]. While these sophisticated 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, the PNP system is an appropriate model for analysis and numerical simulations of ionic flows.

The simplest PNP system is the *classical* Poisson-Nernst-Planck (cPNP) system that includes the ideal component  $\mu_k^{id}(X)$  in (1.3) only. The ideal component  $\mu_k^{id}$  contains contributions by considering ion particles as point charges and ignoring the ion-to-ion interaction. For a wide range of purposes, the classical PNP models have been studied numerically and analytically to a great extent (see, e.g., [2, 4, 6, 7, 22, 23, 40, 45, 46, 47, 49, 51, 57, 64, 66, 72, 74]). The excess component  $\mu_k^{ex}(X)$  accounts for ion sizes, which is crucial 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, 12, 58, 59, 60]).

In this work, due to the complexity and challenges in analyzing the excess chemical potential  $\mu_k^{ex}$ , we will first study the cPNP model with *three* ion species, two positively charged and one negatively charged. Of particular interest are the qualitative properties of the ionic flows. More precisely, we will study effects of boundary conditions on individual fluxes based on system (1.1)-(1.2). We would like to point out that due to the miss of steric effect, important phenomena such as charge inversion and layering may not be detected by this simple model.

The framework for the analysis is a *geometric singular perturbation theory* ([22, 47]). In Section 2, we set up our problem with further assumptions. In particular, we assume that the two positively charged ion species have the same valence (as for sodium and potassium). In Section 3, following the same outline as in [46, 47, 49, 51], the existence and uniqueness of solutions of the singularly perturbed system are established. Explicit solutions of the *limiting slow system* (see Lemma 3.4) are obtained, from which an approximation to the individual flux is extracted. This information is extremely important for one to understand the control of the ionic flows. Our main results are in Section 4. Under electroneutrality boundary conditions, the qualitative properties of individual fluxes are studied in detail. Critical potentials or voltages are identified and their roles in characterizing the effects on the individual

fluxes from the boundary conditions are discussed. For fixed boundary concentrations, the monotonicity of the individual fluxes with respect to the boundary potential  $\bar{V}$  is examined (see Lemma 4.6). In particular, we compared the contributions from the two positively charged ion species to the current in terms of a quantity  $\mathcal{J}_{1,2}(\bar{V}; 0) = \mathcal{J}_1(\bar{V}; 0) - \mathcal{J}_2(\bar{V}; 0)$ . It turns out that under some further restrictions on the boundary concentrations and diffusion coefficients, the ion channel will prefer one positively charged ion species over the other determined by the boundary potential (see Theorems 4.8 and 4.9). The paper ends with concluding remarks in Section 5.

## 2 Problem set-up

For simplicity, we make the following assumptions:

- (A1). We consider *three* ion species ( $n = 3$ ) with  $z_1 = z_2 := z > 0$  and  $z_3 < 0$ .
- (A2). We assume the permanent charge  $Q(X) = 0$  over the whole interval  $[0, 1]$ .
- (A3). For  $\mu_k$ , we only include the ideal component  $\mu_k^{id}$  as in (1.3).
- (A4). We assume the relative dielectric coefficient and the diffusion coefficient to be constants, that is,  $\varepsilon_r(X) = \varepsilon_r$  and  $D_i(X) = D_i$ .

In the sequel, we will assume (A1)–(A4). We first make a dimensionless rescaling following ([28]). Set  $C_0 = \max\{\mathcal{L}_i, \mathcal{R}_i : i = 1, 2\}$  and let

$$\begin{aligned} \varepsilon^2 &= \frac{\varepsilon_r \varepsilon_0 k_B T}{e^2 l^2 C_0}, \quad x = \frac{X}{l}, \quad h(x) = \frac{A(X)}{l^2}, \quad D_i = l C_0 \mathcal{D}_i; \\ \phi(x) &= \frac{e}{k_B T} \Phi(X), \quad c_i(x) = \frac{C_i(X)}{C_0}, \quad J_i = \frac{\mathcal{J}_i}{D_i}; \\ V &= \frac{e}{k_B T} \mathcal{V}, \quad L_i = \frac{\mathcal{L}_i}{C_0}; \quad R_i = \frac{\mathcal{R}_i}{C_0}. \end{aligned} \tag{2.4}$$

**Remark 2.1.** *The dimensionless parameter  $\varepsilon$  defined in (2.4) as*

$$\varepsilon = \frac{1}{l} \sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{e^2 C_0}}$$

*is directly related to the ratio  $\kappa_D/l$  where*

$$\kappa_D = \sqrt{\frac{\varepsilon_r \varepsilon_0 k_B T}{\sum_j (z_j e)^2 C_j}}$$

*is the Debye length; in particular,  $\varepsilon = \kappa_D/l$  when  $z_j^2 = 1$  and  $C_j = C_0$ . Typically, the parameter  $\varepsilon$  is small due to the fact that the two variables  $l$ , the length of the channel, and  $C_0$ , some characteristic number density could be very large (for many cases, the value of  $\varepsilon$  is of order  $O(10^{-3})$ ).*

The BVP (1.1)-(1.2) then becomes (noting that  $z_1 = z_2 = z$ )

$$\begin{aligned} \frac{\varepsilon^2}{h(x)} \frac{d}{dx} \left( h(x) \frac{d\phi}{dx} \right) &= -(zc_1 + zc_2 + z_3c_3), \\ \frac{dc_1}{dx} + zc_1 \frac{d\phi}{dx} &= -\frac{J_1}{h(x)}, \quad \frac{dc_2}{dx} + zc_2 \frac{d\phi}{dx} = -\frac{J_2}{h(x)}, \\ \frac{dc_3}{dx} + z_3c_3 \frac{d\phi}{dx} &= -\frac{J_3}{h(x)}, \quad \frac{dJ_k}{dx} = 0, \end{aligned} \quad (2.5)$$

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

$$\phi(0) = V, \quad c_i(0) = L_i > 0; \quad \phi(1) = 0, \quad c_i(1) = R_i > 0. \quad (2.6)$$

**Remark 2.2.** We will take  $h(x) = 1$  over the whole interval  $[0, 1]$  in our analysis. This is because for ion channels with zero permanent charge, it turns out that the variable  $h(x)$  contributes through an average, explicitly through the factor  $\frac{1}{\int_0^1 h^{-1}(x) dx}$  (for example, the individual flux will be  $\frac{D_k J_k}{\int_0^1 h^{-1}(x) dx}$ , see [48]), which does not affect our analysis of the qualitative properties of the ionic flows.

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

$$\mathcal{I} = \sum_{k=1}^n z_k \mathcal{J}_k = \sum_{k=1}^n z_k D_k J_k, \quad (2.7)$$

where  $z_k \mathcal{J}_k$  is the *individual flux of charge* of the  $k$ th ion species. For fixed boundary concentrations  $L_k$ 's and  $R_k$ 's,  $\mathcal{J}_k$ 's depend on  $V$  only and formula (2.7) provides a dependence of the current  $\mathcal{I}(V; \varepsilon)$  on the voltage  $V$ . Instead of studying the I-V relations, we will focus on the qualitative properties of the individual fluxes of charge.

With the assumption that  $\varepsilon$  is small, system (2.5) together with the boundary condition (2.6) will be treated as a singular boundary value problem.

### 3 Geometric singular perturbation theory for (2.5)–(2.6)

We first rewrite system (2.5) into a standard form for singularly perturbed systems and convert the boundary value problem (2.5)-(2.6) to a connecting problem.

Denote the derivative with respect to  $x$  by overdot and introduce  $u = \varepsilon \dot{\phi}$  and  $\tau = x$ . System (2.5) becomes

$$\begin{aligned} \varepsilon \dot{\phi} &= u, \quad \varepsilon \dot{u} = -zc_1 - zc_2 - z_3c_3, \quad \varepsilon \dot{c}_1 = -zc_1 u - \varepsilon J_1, \\ \varepsilon \dot{c}_2 &= -zc_2 u - \varepsilon J_2, \quad \varepsilon \dot{c}_3 = -z_3c_3 u - \varepsilon J_3, \quad \dot{J}_k = 0, \quad \dot{\tau} = 1. \end{aligned} \quad (3.1)$$

System (3.1), the so-called *slow system*, will be treated as a singularly perturbed system with  $\varepsilon$  as the singular parameter. Its phase space is  $\mathbb{R}^9$  with state variables  $(\phi, u, c_1, c_2, c_3, J_1, J_2, J_3, \tau)$ .

For  $\varepsilon > 0$ , the rescaling  $x = \varepsilon\xi$  of the independent variable gives rise to the so-called *fast system*

$$\begin{aligned} \phi' &= u, & u' &= -zc_1 - zc_2 - z_3c_3, & c_1' &= -zc_1u - \varepsilon J_1, \\ c_2' &= -zc_2u - \varepsilon J_2, & c_3' &= -z_3c_3u - \varepsilon J_3, & J_k' &= 0, & \tau' &= \varepsilon, \end{aligned} \quad (3.2)$$

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

For  $\varepsilon > 0$ , slow system (3.1) and fast system (3.2) have exactly the same phase portrait. But their limiting systems at  $\varepsilon = 0$  are different. The limiting system of (3.1) is called the *limiting slow system*, whose orbits are called *slow orbits* or regular layers. The limiting system of (3.2) is the *limiting fast system*, whose orbits are called *fast orbits* or singular (boundary and/or internal) layers. In this context, a *singular orbit* of system (3.1) or (3.2) is defined to be a continuous and piecewise smooth curve in  $\mathbb{R}^9$  that is a union of finitely many slow and fast orbits. Very often, limiting slow and fast systems provide complementary information on state variables. Therefore, the main task is to patch the limiting information together to form a solution for the entire  $\varepsilon > 0$  system.

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

$$\begin{aligned} B_L &= \{(V, u, L_1, L_2, L_3, J_1, J_2, J_3, 0) \in \mathbb{R}^9 : \text{arbitrary } u, J_1, J_2, J_3\}, \\ B_R &= \{(0, u, R_1, R_2, R_3, J_1, J_2, J_3, 1) \in \mathbb{R}^9 : \text{arbitrary } u, J_1, J_2, J_3\}. \end{aligned} \quad (3.3)$$

Then the original boundary value problem is equivalent to a connecting problem, namely, finding a solution of (3.1) or (3.2) from  $B_L$  to  $B_R$  (see, for example, [42]).

### 3.1 Geometric construction of singular orbits

We will first construct a singular orbit on  $[0, 1]$  that connects  $B_L$  to  $B_R$  ([22, 46, 47]). Such an orbit will generally consist of two boundary layers and a regular layer.

#### 3.1.1 Limiting fast dynamics and boundary layers

By setting  $\varepsilon = 0$  in (3.1), we obtain the so-called *slow manifold*

$$\mathcal{Z} = \{u = 0, z(c_1 + c_2) + z_3c_3 = 0\}. \quad (3.4)$$

By setting  $\varepsilon = 0$  in (3.2), we get the *limiting fast system*

$$\begin{aligned} \phi' &= u, & u' &= -zc_1 - zc_2 - z_3c_3, & c_1' &= -zc_1u, \\ c_2' &= -zc_2u, & c_3' &= -z_3c_3u, & J_k' &= 0, & \tau' &= 0. \end{aligned} \quad (3.5)$$

Note that the slow manifold  $\mathcal{Z}$  is the set of equilibria of (3.5). The following can be established directly ([47]).

**Lemma 3.1.** *For system (3.5), the slow manifold  $\mathcal{Z}$  is normally hyperbolic.*

We denote the stable (resp. unstable) manifold of  $\mathcal{Z}$  by  $W^s(\mathcal{Z})$  (resp.  $W^u(\mathcal{Z})$ ). Let  $M_L$  be the collection of orbits from  $B_L$  in forward time under the flow of system (3.5) and  $M_R$  be the collection of orbits from  $B_R$  in backward time under the flow of system (3.5). Then, for a singular orbit connecting  $B_L$  to  $B_R$ , the boundary layer

at  $x = 0$  must lie in  $N_L = M_L \cap W^s(\mathcal{Z})$  and the boundary layer at  $x = 1$  must lie in  $N_R = M_R \cap W^u(\mathcal{Z})$ . In this subsection, we will determine the boundary layers  $N_L$  and  $N_R$ , and their landing points  $\omega(N_L)$  and  $\alpha(N_R)$  on the slow manifold  $\mathcal{Z}$ . The regular layer, determined by the limiting slow system in §3.1.2, will lie in  $\mathcal{Z}$  and connect the landing points  $\omega(N_L)$  at  $x = 0$  and  $\alpha(N_R)$  at  $x = 1$ .

The next two results are Propositions 3.1 and 3.2 in [47] for the special case considered in this paper.

**Proposition 3.2.** *The following functions are the first integrals of system (3.5),*

$$H_1 = \ln c_1 + z\phi, \quad H_2 = \ln c_2 + z\phi, \quad H_3 = \ln c_3 + z_3\phi, \quad H_4 = \frac{u^2}{2} - c_1 - c_2 - c_3,$$

$$H_5 = J_1, \quad H_6 = J_2, \quad H_7 = J_3, \quad H_8 = \tau.$$

**Proposition 3.3.** (i) *The stable manifold  $W^s(\mathcal{Z})$  intersects  $B_L$  transversally at points*

$$(V, u^l, L_1, L_2, L_3, J_1, J_2, J_3, 0),$$

*and the  $\omega$ -limit set of  $N_L = M_L \cap W^s(\mathcal{Z})$  is*

$$\omega(N_L) = \{(\phi^L, 0, c_1^L, c_2^L, c_3^L, J_1, J_2, J_3, 0)\},$$

*where  $J_i$  for  $i = 1, 2, 3$  are arbitrary, and*

$$\phi^L = V - \frac{1}{z - z_3} \ln \frac{z(L_1 + L_2)}{-z_3 L_3}, \quad c_1^L = L_1 \left( \frac{z(L_1 + L_2)}{-z_3 L_3} \right)^{\frac{-z}{z - z_3}},$$

$$c_2^L = L_2 \left( \frac{z(L_1 + L_2)}{-z_3 L_3} \right)^{\frac{-z}{z - z_3}}, \quad c_3^L = L_3 \left( \frac{z(L_1 + L_2)}{-z_3 L_3} \right)^{\frac{-z_3}{z - z_3}},$$

$$u^l = \text{sgn}(\phi^L - V) \sqrt{2(L_1 + L_2)(1 - e^{z(V - \phi^L)}) + 2L_3(1 - e^{z_3(V - \phi^L)})}.$$

(ii) *The unstable manifold  $W^u(\mathcal{Z})$  intersects  $B_R$  transversally at points*

$$(0, u^r, R_1, R_2, R_3, J_1, J_2, J_3, 1),$$

*and the  $\alpha$ -limit set of  $N_R = M_R \cap W^u(\mathcal{Z})$  is*

$$\alpha(N_R) = \{(\phi^R, 0, c_1^R, c_2^R, c_3^R, J_1, J_2, J_3, 1)\},$$

*where  $J_i$  for  $i = 1, 2, 3$  are arbitrary, and*

$$\phi^R = \frac{1}{z - z_3} \ln \frac{z(R_1 + R_2)}{-z_3 R_3}, \quad c_1^R = R_1 \left( \frac{z(R_1 + R_2)}{-z_3 R_3} \right)^{\frac{-z}{z - z_3}},$$

$$c_2^R = R_2 \left( \frac{z(R_1 + R_2)}{-z_3 R_3} \right)^{\frac{-z}{z - z_3}}, \quad c_3^R = R_3 \left( \frac{z(R_1 + R_2)}{-z_3 R_3} \right)^{\frac{-z_3}{z - z_3}},$$

$$u^r = \text{sgn}(-\phi^R) \sqrt{2(R_1 + R_2)(1 - e^{-z\phi^R}) + 2R_3(1 - e^{-z_3\phi^R})}.$$

For later use, let  $\Gamma^0$  denote the boundary layer at  $x = 0$  and let  $\Gamma^1$  denote the boundary layer at  $x = 1$  for system (3.5).

### 3.1.2 Limiting slow dynamics and regular layers

Next we construct the regular layer on  $\mathcal{Z}$  that connects  $\omega(N_L)$  and  $\alpha(N_R)$ . Note that, for  $\varepsilon = 0$ , system (3.1) loses most information. To remedy this degeneracy, we follow the idea in [22, 46, 47] and make a rescaling  $u = \varepsilon p$  and  $-z_3 c_3 = z(c_1 + c_2) + \varepsilon q$  in system (3.1). In term of the new variables, system (3.1) becomes

$$\begin{aligned} \dot{\phi} &= p, & \varepsilon \dot{p} &= q, & \varepsilon \dot{q} &= (z(z - z_3)(c_1 + c_2) - \varepsilon z_3 q) p + z(J_1 + J_2) + z_3 J_3, \\ \dot{c}_1 &= -z c_1 p - J_1, & \dot{c}_2 &= -z c_2 p - J_2, & \dot{J}_k &= 0, & \dot{\tau} &= 1. \end{aligned} \quad (3.6)$$

It is again a singular perturbation problem and its limiting slow system is

$$\begin{aligned} \dot{\phi} &= p, & q &= 0, & p &= -\frac{z(J_1 + J_2) + z_3 J_3}{z(z - z_3)(c_1 + c_2)}, \\ \dot{c}_1 &= -z c_1 p - J_1, & \dot{c}_2 &= -z c_2 p - J_2, & \dot{J}_k &= 0, & \dot{\tau} &= 1. \end{aligned} \quad (3.7)$$

For system (3.7), the slow manifold is

$$\mathcal{S} = \left\{ q = 0, p = -\frac{z(J_1 + J_2) + z_3 J_3}{z(z - z_3)(c_1 + c_2)} \right\}.$$

Therefore, the limiting slow system on  $\mathcal{S}$  is

$$\begin{aligned} \dot{\phi} &= -\frac{z(J_1 + J_2) + z_3 J_3}{z(z - z_3)(c_1 + c_2)}, & \dot{c}_1 &= \frac{(z(J_1 + J_2) + z_3 J_3)c_1}{(z - z_3)(c_1 + c_2)} - J_1, \\ \dot{c}_2 &= \frac{(z(J_1 + J_2) + z_3 J_3)c_2}{(z - z_3)(c_1 + c_2)} - J_2, & \dot{J}_k &= 0, & \dot{\tau} &= 1. \end{aligned} \quad (3.8)$$

**Lemma 3.4.** *There is a unique solution  $(\phi(x), c_1(x), c_2(x), J_1, J_2, J_3, \tau(x))$  of (3.8) such that*

$$(\phi(0), c_1(0), c_2(0), \tau(0)) = (\phi^L, c_1^L, c_2^L, 0) \quad \text{and} \quad (\phi(1), c_1(1), c_2(1), \tau(1)) = (\phi^R, c_1^R, c_2^R, 1),$$

where  $\phi^L, \phi^R, c_1^L, c_1^R, c_2^L$  and  $c_2^R$  are given in Proposition 3.3. It is given by

$$\begin{aligned} \phi(x) &= \phi^L - \frac{z(J_1 + J_2) + z_3 J_3}{z z_3 (J_1 + J_2 + J_3)} \ln \left( 1 + \frac{z_3 (J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right), \\ c_1(x) &= \frac{c_1^L J_2 - c_2^L J_1}{J_1 + J_2} \left( 1 + \frac{z_3 (J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right)^{\frac{z(J_1 + J_2) + z_3 J_3}{z_3 (J_1 + J_2 + J_3)}} \\ &\quad + \frac{(c_1^L + c_2^L) J_1}{J_1 + J_2} \left( 1 + \frac{z_3 (J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right), \\ c_2(x) &= -\frac{c_1^L J_2 - c_2^L J_1}{J_1 + J_2} \left( 1 + \frac{z_3 (J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right)^{\frac{z(J_1 + J_2) + z_3 J_3}{z_3 (J_1 + J_2 + J_3)}} \\ &\quad + \frac{(c_1^L + c_2^L) J_2}{J_1 + J_2} \left( 1 + \frac{z_3 (J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right), \\ \tau(x) &= x, \end{aligned} \quad (3.9)$$

where  $J_1$ ,  $J_2$  and  $J_3$  are uniquely determined as

$$\begin{aligned} J_1 &= \frac{c_1^L + c_2^L - c_1^R - c_2^R}{\ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)} \frac{\ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)e^{z(\phi^R - \phi^L)}}{c_1^L + c_2^L - (c_1^R + c_2^R)e^{z(\phi^R - \phi^L)}} (c_1^L - c_1^R e^{z(\phi^R - \phi^L)}), \\ J_2 &= \frac{c_1^L + c_2^L - c_1^R - c_2^R}{\ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)} \frac{\ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)e^{z(\phi^R - \phi^L)}}{c_1^L + c_2^L - (c_1^R + c_2^R)e^{z(\phi^R - \phi^L)}} (c_2^L - c_2^R e^{z(\phi^R - \phi^L)}), \\ J_3 &= -\frac{z}{z_3} \frac{c_1^L + c_2^L - c_1^R - c_2^R}{\ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)} \left( \ln(c_1^L + c_2^L) - \ln(c_1^R + c_2^R)e^{z_3(\phi^R - \phi^L)} \right). \end{aligned}$$

*Proof.* Adding the second equation to the third one in (3.8), one has

$$\dot{c}_1 + \dot{c}_2 = \frac{z_3}{z - z_3} (J_1 + J_2 + J_3),$$

which gives

$$c_1(x) + c_2(x) = c_1^L + c_2^L + \frac{z_3}{z - z_3} (J_1 + J_2 + J_3)x. \quad (3.10)$$

Substitute (3.10) into the second equation in (3.8) to get

$$\dot{c}_1 = \frac{z(J_1 + J_2) + z_3 J_3}{(z - z_3)(c_1^L + c_2^L) + z_3(J_1 + J_2 + J_3)x} c_1 - J_1.$$

By the variation of constants formula, we obtain

$$\begin{aligned} c_1(x) &= \frac{c_1^L J_2 - c_2^L J_1}{J_1 + J_2} \left( 1 + \frac{z_3(J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right)^{\frac{z(J_1 + J_2) + z_3 J_3}{z_3(J_1 + J_2 + J_3)}} \\ &\quad + \frac{(c_1^L + c_2^L) J_1}{J_1 + J_2} \left( 1 + \frac{z_3(J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right). \end{aligned}$$

Similarly,

$$\begin{aligned} c_2(x) &= -\frac{c_1^L J_2 - c_2^L J_1}{J_1 + J_2} \left( 1 + \frac{z_3(J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right)^{\frac{z(J_1 + J_2) + z_3 J_3}{z_3(J_1 + J_2 + J_3)}} \\ &\quad + \frac{(c_1^L + c_2^L) J_2}{J_1 + J_2} \left( 1 + \frac{z_3(J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right). \end{aligned}$$

Now substitute (3.10) into the first equation in (3.8) to get

$$\dot{\phi} = -\frac{z(J_1 + J_2) + z_3 J_3}{z(z - z_3)(c_1^L + c_2^L) + \frac{z_3}{z - z_3} (J_1 + J_2 + J_3)x}.$$

The solution is

$$\phi(x) = \phi^L - \frac{z(J_1 + J_2) + z_3 J_3}{z z_3 (J_1 + J_2 + J_3)} \ln \left( 1 + \frac{z_3(J_1 + J_2 + J_3)}{(z - z_3)(c_1^L + c_2^L)} x \right).$$

Evaluating  $c_1(x)$ ,  $c_2(x)$  and  $\phi(x)$  at  $x = 1$  yield the formulas for  $J_1$ ,  $J_2$  and  $J_3$ .  $\square$

The slow orbit

$$\Lambda(x) = (\phi(x), c_1(x), c_2(x), J_1, J_2, J_3, \tau(x)) \quad (3.11)$$

given in Lemma 3.4 connects  $\omega(N_L)$  and  $\alpha(N_R)$ . Let  $\bar{M}_L$  (resp.,  $\bar{M}_R$ ) be the forward (resp., backward) image of  $\omega(N_L)$  (resp.,  $\alpha(N_R)$ ) under the slow flow (3.8). One has the following result whose proof can be established by a similar argument as those in [41, 47, 48, 51].

**Proposition 3.5.** *On the seven-dimensional slow manifold  $\mathcal{S}$ ,  $\bar{M}_L$  and  $\bar{M}_R$  intersect transversally along the unique orbit  $\Lambda(x)$  given in (3.11).*

To end this section, we would like to point out that the capability of constructing an explicit solution to the limiting slow system, from which the approximated individual flux can be extracted explicitly in terms of boundary conditions and other physical parameters, is crucial for us to further examine the qualitative properties of ionic flows (see Section 4 for details). This is due to the assumption that the two positively charged ion species have the same valences. Previous results from Prof. Liu ([22, 23, 41, 46, 47, 48, 49, 51]) cannot be directly applied to our case for concrete results in this paper, while our analysis does include his under some assumptions on boundary concentration conditions.

### 3.2 Existence of solutions near the singular orbit

We have constructed a unique singular orbit on  $[0,1]$  that connects  $B_L$  to  $B_R$ . It consists of two boundary layer orbits  $\Gamma^0 \cup \Gamma^1$  and a regular layer  $\Lambda$  with  $\Gamma^0$  from the point

$$(V, u^l, L_1, L_2, L_3, J_1, J_2, J_3, 0) \in B_L$$

to the point

$$(\phi^L, 0, c_1^L, c_2^L, c_3^L, J_1, J_2, J_3, 0) \in \omega(N_L) \subset \mathcal{Z},$$

and  $\Gamma^1$  from the point

$$(\phi^R, 0, c_1^R, c_2^R, c_3^R, J_1, J_2, J_3, 1) \in \alpha(N_R) \subset \mathcal{Z}$$

to the point

$$(0, u^r, R_1, R_2, R_3, J_1, J_2, J_3, 1) \in B_R,$$

and finally  $\Lambda \subset \mathcal{Z}$  connecting the two landing points

$$(\phi^L, 0, c_1^L, c_2^L, c_3^L, J_1, J_2, J_3, 0) \in \omega(N_L) \quad \text{and} \quad (\phi^R, 0, c_1^R, c_2^R, c_3^R, J_1, J_2, J_3, 1) \in \alpha(N_R)$$

of the two boundary layers.

We now establish the existence of a solution to (2.5)-(2.6) near the singular orbit constructed above which is a union of two boundary layers and one regular layer  $\Gamma^0 \cup \Lambda \cup \Gamma^1$ . The proof follows the same line as that in [22, 41, 46, 47, 48] and the main tool used is the Exchange Lemma (see, for example [42, 43, 44, 69]) of geometric singular perturbation theory.

**Theorem 3.6.** *Let  $\Gamma^0 \cup \Lambda \cup \Gamma^1$  be the singular orbit of the connecting problem for (3.1) associated with  $B_L$  and  $B_R$  in (3.3). Then, for  $\varepsilon > 0$  small, the boundary value problem (2.5)-(2.6) has a unique smooth solution near the singular orbit.*

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

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

For  $\varepsilon > 0$ , let  $M_L(\varepsilon, \delta)$  be the forward trace of  $B_L(\delta)$  under the flow of system (3.1) or equivalently of system (3.2) and let  $M_R(\varepsilon)$  be the backward trace of  $B_R$ . To prove the existence and uniqueness statement, it suffices to show that  $M_L(\varepsilon, \delta)$  intersects  $M_R(\varepsilon)$  transversally in a neighborhood of the singular orbit  $\Gamma^0 \cup \Lambda \cup \Gamma^1$ . The latter will be established by an application of the Exchange Lemma.

Notice that  $\dim B_L(\delta) = 4$ . It is clear that the vector field of the fast system (3.2) is not tangent to  $B_L(\delta)$  for  $\varepsilon \geq 0$ , and hence,  $\dim M_L(\varepsilon, \delta) = 5$ . We next apply the Exchange Lemma to track  $M_L(\varepsilon, \delta)$  in the vicinity of  $\Gamma^0 \cup \Lambda \cup \Gamma^1$ . First of all, the transversality of the intersection  $B_L(\delta) \cap W^s(\mathcal{Z})$  along  $\Gamma^0$  in Proposition 3.3 implies the transversality of the intersection  $M_L(0, \delta) \cap W^s(\mathcal{Z})$ . Secondly, we have also established that  $\dim \omega(N_L) = \dim N_L - 1 = 3$  in Proposition 3.3 and that the limiting slow flow is not tangent to  $\omega(N_L)$  in Section 3.1.2. Under these conditions, the Exchange Lemma ([42, 43, 44, 69]) states that there exist  $\rho > 0$  and  $\varepsilon_1 > 0$  so that, if  $0 < \varepsilon \leq \varepsilon_1$ , then  $M_L(\varepsilon, \delta)$  will first follow  $\Gamma^0$  toward  $\omega(N_L) \subset \mathcal{Z}$ , then follow the trace of  $\omega(N_L)$  in the vicinity of  $\Lambda$  toward  $\{\tau = 1\}$ , leave the vicinity of  $\mathcal{Z}$ , and, upon exiting, a portion of  $M_L(\varepsilon, \delta)$  is  $C^1$   $O(\varepsilon)$ -close to  $W^u(\omega(N_L) \times (1 - \rho, 1 + \rho))$  in the vicinity of  $\Gamma^1$ . Note that  $\dim W^u(\omega(N_L) \times (1 - \rho, 1 + \rho)) = \dim M_L(\varepsilon, \delta) = 5$ .

It remains to show that  $W^u(\omega(N_L) \times (1 - \rho, 1 + \rho))$  intersects  $M_R(\varepsilon)$  transversally since  $M_L(\varepsilon, \delta)$  is  $C^1$   $O(\varepsilon)$ -close to  $W^u(\omega(N_L) \times (1 - \rho, 1 + \rho))$ . Recall that, for  $\varepsilon = 0$ ,  $M_R$  intersects  $W^u(\mathcal{Z})$  transversally along  $N_R$  (Proposition 3.3); in particular, at  $\gamma_1 := \alpha(\Gamma^1) \in \alpha(N_R) \subset \mathcal{Z}$ , we have

$$T_{\gamma_1} M_R = T_{\gamma_1} \alpha(N_R) \oplus T_{\gamma_1} W^u(\gamma_1) \oplus \text{span}\{V_s\},$$

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

$$T_{\gamma_1} W^u(\omega(N_L) \times (1 - \rho, 1 + \rho)) = T_{\gamma_1}(\omega(N_L) \cdot 1) \oplus \text{span}\{V_\tau\} \oplus T_{\gamma_1} W^u(\gamma_1),$$

where the vector  $V_\tau$  is the tangent vector to the  $\tau$ -axis as a result of the interval factor  $(1 - \rho, 1 + \rho)$ . From Proposition 3.5,  $\omega(N_L) \cdot 1$  and  $\alpha(N_R)$  are transversal on  $\mathcal{Z} \cap \{\tau = 1\}$ . Therefore, at  $\gamma_1$ , the tangent spaces  $T_{\gamma_1} M_R$  and  $T_{\gamma_1} W^u(\omega(N_L) \times (1 - \rho, 1 + \rho))$  contain seven linearly independent vectors:  $V_s$ ,  $V_\tau$ ,  $T_{\gamma_1} W^u(\gamma_1)$  and the other four from  $T_{\gamma_1}(\omega(N_L) \cdot 1)$  and  $T_{\gamma_1} \alpha(N_R)$ ; that is,  $M_R$  and  $W^u(\omega(N_L) \times (1 - \rho, 1 + \rho))$  intersect transversally. We thus conclude that, there exists  $0 < \varepsilon_0 \leq \varepsilon_1$  such that, if  $0 < \varepsilon \leq \varepsilon_0$ , then  $M_L(\varepsilon, \delta)$  intersects  $M_R(\varepsilon)$  transversally.

For uniqueness, note that the transversality of the intersection  $M_L(\varepsilon, \delta) \cap M_R(\varepsilon)$  implies  $\dim(M_L(\varepsilon, \delta) \cap M_R(\varepsilon)) = \dim M_L(\varepsilon, \delta) + \dim M_R(\varepsilon) - 9 = 1$ . Thus, there exists  $\delta_0 > 0$  such that, if  $0 < \delta \leq \delta_0$ , the intersection  $M_L(\varepsilon, \delta) \cap M_R(\varepsilon)$  consists of precisely one solution near the singular orbit  $\Gamma^0 \cup \Lambda \cup \Gamma^1$ .  $\square$

## 4 Individual fluxes under electroneutrality conditions

In this section, we examine qualitative properties of solutions of the steady-state classical PNP systems under electroneutrality boundary conditions

$$z(L_1 + L_2) + z_3 L_3 = 0 \quad \text{and} \quad z(R_1 + R_2) + z_3 R_3 = 0. \quad (4.1)$$

We mainly focus on the analysis of each individual flux  $\mathcal{J}_i(V; \varepsilon)$  (more precisely, it is the individual flux of matter, but since  $z_1 = z_2 = z > 0$ , it has the same qualitative properties as the individual flux of charge  $z_i \mathcal{J}_i(V; \varepsilon)$ ). Of particular interest is the zeroth order approximations in  $\varepsilon$ , namely,  $\mathcal{J}_i(V; 0)$ , which can be extracted explicitly from the solutions of the *limiting slow system* established in Lemma 3.4. Numerical simulations are performed for the boundary value problem (2.5)-(2.6) for small  $\varepsilon > 0$  to compare with the zeroth order (in  $\varepsilon$ ) individual flux.

**Remark 4.1.**  $\mathcal{J}_i(V; \varepsilon)$  also depends on other parameters, such as, the boundary concentrations  $L'_i$ s and  $R'_i$ s, the valences  $z_i$ , the diffusion coefficients  $D_i$ , and so on.

As a corollary of Proposition 3.3 and Lemma 3.4, one has

**Proposition 4.2.** *Assume electroneutrality conditions (4.1). Then,*

$$\phi^L = V, \quad c_1^L = L_1, \quad c_2^L = L_2, \quad c_3^L = L_3; \quad \phi^R = 0, \quad c_1^R = R_1, \quad c_2^R = R_2, \quad c_3^R = R_3.$$

Furthermore, from (2.4), the zeroth order (in  $\varepsilon$ ) approximations of the fluxes are

$$\begin{aligned} \mathcal{J}_1(V; 0) &= D_1 J_1(V; 0) = D_1 f_0(L_3, R_3) f_1(L_3, R_3, V) (L_1 - R_1 e^{-zV}), \\ \mathcal{J}_2(V; 0) &= D_2 J_2(V; 0) = D_2 f_0(L_3, R_3) f_1(L_3, R_3, V) (L_2 - R_2 e^{-zV}), \\ \mathcal{J}_3(V; 0) &= D_3 J_3(V; 0) = -\frac{z}{z_3} D_3 f_0(L_3, R_3) f_2(L_3, R_3, V) (L_3 - R_3 e^{-z_3 V}), \end{aligned} \quad (4.2)$$

where

$$\begin{aligned} f_0(L_3, R_3) &= \frac{L_3 - R_3}{\ln L_3 - \ln R_3}, \quad f_1(L_3, R_3, V) = \frac{\ln L_3 - \ln R_3 + zV}{L_3 - R_3 e^{-zV}}, \\ f_2(L_3, R_3, V) &= \frac{\ln L_3 - \ln R_3 + z_3 V}{L_3 - R_3 e^{-z_3 V}}. \end{aligned} \quad (4.3)$$

For the functions  $f_0(L_3, R_3)$ ,  $f_1(L_3, R_3, V)$  and  $f_2(L_3, R_3, V)$  defined in (4.3), one has the elementary observation:

**Lemma 4.3.** (i) *If  $L_3 \neq R_3$ , then  $f_0(L_3, R_3) > 0$ , and  $\lim_{L_3 \rightarrow R_3} f_0(L_3, R_3) = R_3$ .*

(ii) *If  $L_3 \neq \frac{R_3}{e^{zV}}$ , then  $f_1(L_3, R_3, \bar{V}) > 0$ , and  $\lim_{L_3 \rightarrow R_3 e^{-zV}} f_1(L_3, R_3, V) = \frac{e^{zV}}{R_3}$ .*

(iii) *If  $L_3 \neq \frac{R_3}{e^{z_3 V}}$ , then  $f_2(L_3, R_3, V) > 0$ , and  $\lim_{L_3 \rightarrow R_3 e^{-z_3 V}} f_2(L_3, R_3, V) = \frac{e^{z_3 V}}{R_3}$ .*

**Remark 4.4.** *Recall from Remark 1.1 that  $\mathcal{J}_k$  and  $\mu_k(0) - \mu_k(1)$  have the same sign. Under the re-scaling (2.4) and electroneutrality conditions (4.1), one has*

$$\mu_k(0) - \mu_k(1) = z_k e (\phi(0) - \phi(1)) + k_B T \ln \frac{c_k(0)}{c_k(1)} = k_B T \left( z_k V + \ln \frac{L_k}{R_k} \right).$$

Therefore,  $\mu_k(0) - \mu_k(1) > 0$  (resp.  $\mu_k(0) - \mu_k(1) < 0$ ) if  $z_k V > z_k V_{k^*}$  (resp.  $z_k V < z_k V_{k^*}$ ), where (recalling that  $z_1 = z_2 = z$ )

$$V_{1^*} = \frac{\ln R_1 - \ln L_1}{z}, \quad V_{2^*} = \frac{\ln R_2 - \ln L_2}{z} \quad \text{and} \quad V_{3^*} = \frac{\ln R_3 - \ln L_3}{z_3}.$$

It also follows from formulas (4.2) that  $\mathcal{J}_k > 0$  (resp.  $\mathcal{J}_k < 0$ ) if  $z_k V > z_k V_{k^*}$  (resp.  $z_k V < z_k V_{k^*}$ ),  $k = 1, 2, 3$ . Thus, formulas (4.2) are consistent with the observation in Remark 1.1.

**Proposition 4.5.** *Assume electroneutrality conditions (4.1). Fixing  $V$  and treating the zeroth order (in  $\varepsilon$ ) approximations  $\mathcal{J}_k$ 's as functions of boundary concentrations  $L_i$  and  $R_i$ , then  $\mathcal{J}_k$  is homogeneous of degree one, that is, for any  $\alpha > 0$ ,*

$$\mathcal{J}_k(\alpha L_1, \alpha L_2, \alpha L_3; \alpha R_1, \alpha R_2, \alpha R_3) = \alpha \mathcal{J}_k(L_1, L_2, L_3; R_1, R_2, R_3).$$

*Proof.* It follows from (4.3) that, for any  $\alpha > 0$ ,

$$f_0(\alpha L_3, \alpha R_3) = \alpha f_0(L_3, R_3), \quad f_1(\alpha L_3, \alpha R_3; V) = \frac{1}{\alpha} f_1(L_3, R_3; V),$$

and  $f_2(\alpha L_3, \alpha R_3; V) = \frac{1}{\alpha} f_2(L_3, R_3; V)$ . The claim then follows from (4.2).  $\square$

We emphasize that the above results only hold for the zeroth order (in  $\varepsilon$ ) approximations  $\mathcal{J}_k$ 's of fluxes. In general, these do not hold for  $\varepsilon \neq 0$ , which can be seen from, for example, system (2.5).

We comment, from Proposition 4.2, that, under electroneutrality conditions (4.1) and for fixed boundary concentrations, both  $\mathcal{J}_1(V; 0)$  and  $\mathcal{J}_2(V; 0)$  are nonlinear functions of potential  $V$  while  $\mathcal{J}_3(V; 0)$  is affine in potential  $V$ . We have the following monotonicity result.

**Proposition 4.6.** *Assume electroneutrality conditions (4.1). One has*

- (i)  $\mathcal{J}_1(V; 0)$  increases in the potential  $V$ ;
- (ii)  $\mathcal{J}_2(V; 0)$  increases in the potential  $V$ ;
- (iii)  $\mathcal{J}_3(V; 0)$  decreases in the potential  $V$ .

*Proof.* From Proposition 4.2, a direct calculation gives

$$\frac{d\mathcal{J}_1}{dV}(V; 0) = \frac{zD_1R_1R_3e^{-zV}}{(L_3 - R_3e^{-zV})^2} f_0(L_3, R_3) g_0(zV; L_3/R_3, L_1/R_1),$$

where, with  $x = zV$ ,  $a = L_3/R_3 > 0$  and  $b = L_1/R_1 > 0$ ,

$$g_0(x; a, b) = (a - b)(\ln a + x) + (b - e^{-x})(a - e^{-x})e^x.$$

Since  $g_0'(x) = (a - e^{-x})(b + e^{-x})e^x$ ,  $g_0(x; a, b)$  has only one critical point  $x^* = -\ln a$ . It follows from  $g_0(x^*; a, b) = 0$  and  $\lim_{x \rightarrow \infty} g_0(x; a, b) = \infty$  that  $g_0(x; a, b) > 0$  for  $x \neq x^*$ . Statement (i) is then established. Statement (ii) can be established in the same way.

The third statement follows from  $\frac{d\mathcal{J}_3}{dV}(V; 0) = -zD_3f_0(L_3, R_3) < 0$  for all  $V$ .  $\square$

We next study the contribution from the two positively charged ion species to the total flux. For convenience, we define  $\mathcal{J}_{1,2}(V; 0)$  as

$$\begin{aligned}\mathcal{J}_{1,2}(V; 0) &= \mathcal{J}_1(V; 0) - \mathcal{J}_2(V; 0) \\ &= f_0(L_3, R_3) f_1(L_3, R_3; V) (D_1 L_1 - D_2 L_2 - (D_1 R_1 - D_2 R_2) e^{-zV}).\end{aligned}\quad (4.4)$$

It follows directly from (4.4) that

**Proposition 4.7.** *Under electroneutrality conditions (4.1), one has*

- (i) *if  $D_1 R_1 - D_2 R_2 = 0$ , then  $\mathcal{J}_{1,2}(V; 0)$  and  $D_1 L_1 - D_2 L_2$  have the same sign;*
- (ii) *if  $D_1 R_1 - D_2 R_2 > 0$  and  $D_1 L_1 - D_2 L_2 \leq 0$ , then  $\mathcal{J}_{1,2}(V; 0) < 0$  for all  $V$ ;*
- (iii) *if  $D_1 R_1 - D_2 R_2 < 0$  and  $D_1 L_1 - D_2 L_2 \geq 0$ , then  $\mathcal{J}_{1,2}(V; 0) > 0$  for all  $V$ ;*
- (iv) *if  $(D_1 R_1 - D_2 R_2)(D_1 L_1 - D_2 L_2) > 0$ , then  $\mathcal{J}_{1,2}(V; 0)$  has the same sign as that of  $(D_1 R_1 - D_2 R_2)(V - V_d)$  where*

$$V_d = \frac{1}{z} \ln \frac{D_1 R_1 - D_2 R_2}{D_1 L_1 - D_2 L_2}. \quad (4.5)$$

*Proof.* Note that from Lemma 4.3,  $f_0(L_3, R_3) > 0$  and  $f_1(L_3, R_3, V) > 0$  for all  $V$ . The result follows directly.  $\square$

We next study the monotonicity of  $\mathcal{J}_{1,2}(V; 0)$  with respect to the potential  $V$  for fixed boundary concentrations.

**Theorem 4.8.** *Assume electroneutrality conditions (4.1) and  $\frac{D_1}{D_2} > \frac{R_2}{R_1}$ .*

- (i) *For  $\frac{D_1}{D_2} > \frac{L_2}{L_1}$ , one has  $\mathcal{J}_{1,2}(V; 0)$  is increasing in potential  $V$ . And  $\mathcal{J}_{1,2}(V; 0) = 0$  has a unique zero  $V_d$  defined in (4.5);*
- (ii) *For  $\frac{D_1}{D_2} < \frac{L_2}{L_1}$ , one has  $\mathcal{J}_{1,2}(V; 0)$  increases in the potential  $V$  if  $V < V_1^b$  and decreases in  $V$  if  $V > V_1^b$ , where  $V_1^b$  is uniquely defined by  $\frac{d\mathcal{J}_{1,2}}{dV}(V_1^b; 0) = 0$ .*

*Proof.* With  $x = zV$ , from (4.4), a careful calculation gives

$$\frac{d\mathcal{J}_{1,2}(x; 0)}{dx} = \alpha(x) \mathcal{J}_{1,2}(x; 0) + \beta(x), \quad (4.6)$$

where

$$\alpha(x) = \frac{k_0(x)}{(L_3 - R_3 e^{-x})^2 f_1(L_3, R_3; x)}, \quad \beta(x) = \frac{(D_1 R_1 - D_2 R_2) f_0(L_3, R_3) f_1(L_3, R_3; x)}{e^x},$$

where

$$k_0(x) = L_3 - R_3 e^{-x} - R_3 e^{-x} (\ln L_3 - \ln(R_3 e^{-x})).$$

Notice that,  $x^* = \ln \frac{R_3}{L_3}$  is the unique critical point of  $k_0(x)$ . It then follows from  $k_0(x^*) = 0$  and  $k_0'(x) > 0$  if  $x > x^*$  and  $k_0'(x) < 0$  if  $x < x^*$  that  $k_0(x)$  attains its absolute minimum at  $x = x^*$ , and  $k_0(x) \geq 0$  for all  $x$ . From Lemma 4.3,  $f_1(L_3, R_3; x) > 0$ . Therefore,  $\alpha(x) > 0$  for  $x \neq x^*$ , and  $\alpha(x) \rightarrow \frac{1}{2}$  as  $x \rightarrow x^*$ .

We first consider the case where  $\frac{d\mathcal{J}_{1,2}}{dx}(x; 0) = 0$ , which is equivalent to

$$\mathcal{J}_{1,2}(x; 0) = -\frac{\beta(x)}{\alpha(x)} = cg(x), \quad (4.7)$$

where  $c = c(D_1, D_2; R_1, R_2; L_3, R_3)$  and  $g(x) = g(x; L_3, R_3)$  are

$$c = (D_1 R_1 - D_2 R_2) f_0(L_3, R_3) \quad \text{and} \quad g(x) = -\frac{\left(x - \ln \frac{R_3}{L_3}\right)^2}{e^x k_0(x)}.$$

Note that from Lemma 4.3,  $f_0(L_3, R_3) > 0$ . One then has  $c > 0$  since  $\frac{D_1}{D_2} > \frac{R_2}{R_1}$ .

For convenience, we let  $y = \ln \frac{R_3}{L_3}$  ( $= x^*$ ) and set  $w = x - y$  in the following. Then,  $g(x)$  can be rewritten as  $g(w) = \frac{1}{R_3 e^y} \tilde{g}(w)$ , where

$$\tilde{g}(w) = -\frac{w^2}{e^w - w - 1}.$$

Notice that  $\tilde{g}(w) \rightarrow -2$  as  $w \rightarrow 0$ ,  $\tilde{g}(w) \rightarrow 0$  as  $w \rightarrow \infty$ , and  $\tilde{g}'(w) = \frac{w\bar{g}(w)}{(e^w - w - 1)^2}$ , where

$$\bar{g}(w) = (w - 2)e^w + w + 2.$$

A direct calculation shows that  $w\bar{g}(w) \geq 0$  for all  $w$ , and hence, one has  $\tilde{g}'(w) > 0$  for all  $w$ . Thus,  $g(w) < 0$  for all  $w$ , which is equivalent to  $g(x) < 0$  for all  $x$ . It follows that  $cg(x) < 0$  and  $cg'(x) > 0$ .

The following discussion automatically requires that  $\frac{R_2}{R_1} < \frac{L_2}{L_1}$  (The result related to the case  $\frac{R_2}{R_1} > \frac{L_2}{L_1}$  is stated in Theorem 4.9). It includes two cases.

**Case I:**  $\mathcal{J}_{1,2}(x; 0) = 0$  has a unique zero  $x_d = zV_d$  if  $\frac{D_1}{D_2} > \frac{L_2}{L_1}$  (see Proposition 4.7).

Note that  $\alpha(x) > 0$  and  $\mathcal{J}_{1,2}(x; 0) > 0$  for  $x > x_d$ . Note also that  $\beta(x) > 0$  if  $\frac{D_1}{D_2} > \frac{R_2}{R_1}$ . Since  $\frac{d\mathcal{J}_{1,2}}{dx}(x_d) > 0$ ,  $cg(x) < 0$ , and  $cg'(x) > 0$  for all  $x$ , then  $\frac{d\mathcal{J}_{1,2}}{dx} > 0$ . Together with the fact that  $\mathcal{J}_{1,2}(x; 0) \rightarrow -\infty$  as  $x \rightarrow -\infty$ , one can easily conclude that  $\mathcal{J}_{1,2}(x; 0)$  also increases in  $x$  if  $x < x_d$ . This leads to our first statement.

**Case II:**  $\mathcal{J}_{1,2}(x; 0) < 0$  for all  $x$  if  $\frac{R_2}{R_1} < \frac{D_1}{D_2} < \frac{L_2}{L_1}$  (see Proposition 4.7). A similar argument establishes the proof of the second statement. This is left to the reader.  $\square$

Similarly, one has

**Theorem 4.9.** Assume electroneutrality conditions (4.1) and  $\frac{D_1}{D_2} < \frac{R_2}{R_1}$ .

- (i) For  $\frac{D_1}{D_2} < \frac{L_2}{L_1}$ , one has  $\mathcal{J}_{1,2}(V; 0)$  is decreasing in potential  $V$ . And  $\mathcal{J}_{1,2}(V; 0) = 0$  has a unique zero  $\bar{V}_d$  defined as in Lemma 4.5;
- (ii) For  $\frac{D_1}{D_2} > \frac{L_2}{L_1}$ , one has  $\mathcal{J}_{1,2}(V; 0)$  decreases in the potential  $V$  if  $V < V_2^b$  and increases in  $V$  if  $V > V_2^b$ , where  $V_2^b$  is uniquely defined by  $\frac{d\mathcal{J}_{1,2}(V_2^b; 0)}{dV} = 0$ .

**Remark 4.10.** *The significance of Theorems 4.8 and 4.9 is that as the potential  $V$  changes (either increases or decrease under different conditions in terms of  $(D_1, D_2)$ ,  $(L_1, L_2)$  and  $(R_1, R_2)$ ), the ion channel will eventually prefer one positively charged ion species over the other. More precisely, the individual flux of one positively charged ion species becomes stronger and stronger as the potential changes. For example, in Theorem 4.8, the individual flux  $\mathcal{J}_1$  becomes stronger as the potential increases if  $\frac{D_1}{D_2} > \frac{L_2}{L_1}$ . In other words, the ionic flows through membrane channels can be controlled by the boundary potential while the boundary concentrations and diffusion coefficients satisfy certain conditions.*

It follows from Proposition 4.7 that

**Proposition 4.11.** *Assume electroneutrality conditions (4.1).*

- (i) For  $\frac{D_1}{D_2} = \frac{L_2}{L_1}$ , one has
  - (i1) if  $\frac{D_1}{D_2} < \frac{R_2}{R_1}$ , then  $\mathcal{J}_{1,2}(V; 0)$  decreases in the potential  $V$ .
  - (i2) if  $\frac{D_1}{D_2} > \frac{R_2}{R_1}$ , then  $\mathcal{J}_{1,2}(V; 0)$  increases in the potential  $V$ .
- (ii) For  $\frac{D_1}{D_2} = \frac{R_2}{R_1}$ , one has
  - (ii1) if  $\frac{D_1}{D_2} < \frac{L_2}{L_1}$ , then  $\mathcal{J}_{1,2}(V; 0)$  decreases in the potential  $V$ .
  - (ii2) if  $\frac{D_1}{D_2} > \frac{L_2}{L_1}$ , then  $\mathcal{J}_{1,2}(V; 0)$  increases in the potential  $V$ .

Although our interest in this work is not the I-V relations defined in (2.7), we would like to point out one new observation compared to PNP systems with *two* ion species. Again, this indicates the more complicated properties of the ionic flows when more ion species are involved.

**Theorem 4.12.** *Under electroneutrality conditions (4.1), for fixed boundary concentrations, the zeroth order (in  $\varepsilon$ ) approximation  $\mathcal{I}(V; 0)$  of current is increasing in the potential  $V$  and there is a unique potential (reversal potential)  $V_{rev}$ , such that  $\mathcal{I}(V_{rev}; 0) = 0$ .*

*Proof.* The increasing property of  $\mathcal{I}(V; 0)$  in  $V$  is a direct consequence of Proposition 4.6 since  $z > 0$  and  $z_3 < 0$ . Concerning the reversal potential, we note that, from (2.7) and Proposition 4.2,

$$\begin{aligned} \mathcal{I}(V; 0) &= z_1 \mathcal{J}_1(V; 0) + z_2 \mathcal{J}_2(V; 0) + z_3 \mathcal{J}_3(V; 0) \\ &= z f_0(L_3, R_3) \left[ f_1(L_3, R_3; V) (D_1 L_1 + D_2 L_2 - (D_1 R_1 + D_2 R_2) e^{-zV}) \right. \\ &\quad \left. - D_3 (\ln L_3 - \ln R_3 + z_3 V) \right]. \end{aligned} \quad (4.8)$$

It is easy to check that  $\lim_{V \rightarrow \infty} \mathcal{I}(V; 0) = \infty$  and  $\lim_{V \rightarrow -\infty} \mathcal{I}(V; 0) = -\infty$ . The existence and uniqueness of a reversal potential  $V_{rev}$  then follow from the monotonicity of  $\mathcal{I}(V; 0)$ .  $\square$

Clearly, for fixed boundary concentrations,  $\mathcal{I}(V;0)$  is a *nonlinear* function of potential  $V$  in the mixture of three ion species. This is different from mixtures of two ion species for which  $\mathcal{I}(V;0)$  is a *linear* function of potential  $V$  (see, e.g., [2, 39, 48, 50, 74]). In fact, to obtain the I-V relation for two ion species, one positively charged with valence  $z$  and one negatively charged with valence  $z_3$ , one can simply set the individual flux  $\mathcal{J}_2(V;0)$  to be zero in (4.8). Note that now the electroneutrality condition (4.1) becomes  $zL_1 + z_3L_3 = 0$  and  $zR_1 + z_3R_3 = 0$ , which gives

$$L_1 = -\frac{z_3}{z}L_3 \quad \text{and} \quad R_1 = -\frac{z_3}{z}R_3.$$

Substituting this into (4.8), together with  $\mathcal{J}_2(V;0) = 0$ , one has

$$\mathcal{I}(V;0) = -f_0(L_3, R_3)(z_3D_1 + zD_3)(\ln L_3 - \ln R_3 + zV), \quad (4.9)$$

which is indeed a *linear* function in the potential  $V$ .

To end this section, we perform numerical simulations for system (2.5)-(2.6) directly with small  $\varepsilon > 0$  to compare with our zeroth order approximations of the individual flux of charge  $z_k D_k J_k$  and the current  $\mathcal{I}$  defined by (2.7) under electroneutrality conditions (Figure 1).

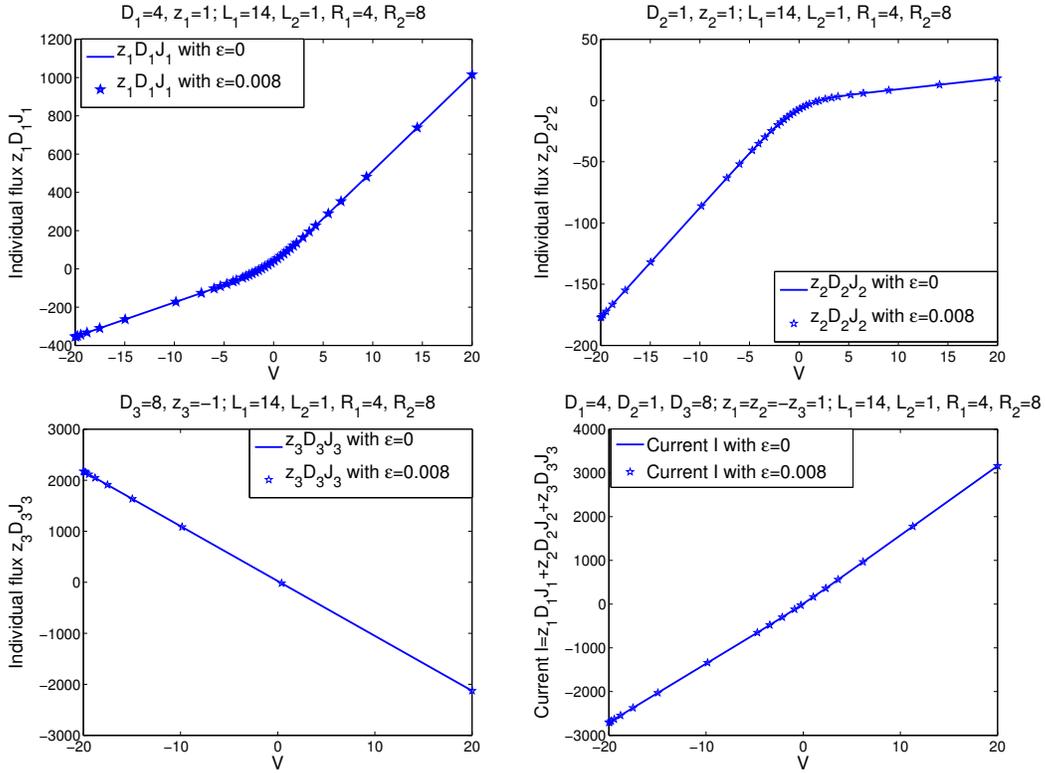


Figure 1: *Zeroth order approximation (solid curve); numerical simulations to (2.5)-(2.6) (curve with  $\star$ ).*

## 5 Concluding remarks

In this work, we studied a quasi-one-dimensional classical PNP model with *three* ion species, two positively charged with the same valence and one negatively charged, and zero permanent charge. Explicit zeroth order approximation solutions (the solutions of the *limiting slow system*) are obtained. This allows us to further analyze effects of boundary conditions on ionic flows in detail. In general, the existence of the zeroth order solutions is determined by a set of nonlinear algebraic equations (see [51] for more details).

Along our analysis, we find some new phenomena arising from the cPNP with three ion species, which are different from the case with two ion species (see [40, 48] for example). More precisely,

- (i) the fluxes (zeroth order terms in  $\varepsilon$ ) of the ion species depend on each other which indicates rich interactions among different charged ions, while for two ion species case, the fluxes are independent of each other (see [40] for example);
- (ii) for fixed boundary concentrations, the zeroth order individual flux of positively charged ion species and the current, as functions of the potential  $V$ , are *nonlinear*, while for two ion species, they are *linear* (see Lemma 4.2 and Proposition 4.12).

We also have the following observation.

**Lemma 5.1.** *For the classical PNP system with a mixture of  $n$  ion species, if the  $(n-1)$  positively charged ion species have the same valence, then explicit solutions to the limiting cPNP system with  $n \geq 4$  can be derived.*

*Proof.* For the derivation of the solutions to the *limiting fast system*, we refer the readers to [51]. We will consider the *limiting slow system* here. It is not difficult to obtain the following *limiting slow system* from (1.1) under the assumption imposed in Section 2 with  $z_1 = z_2 = \dots = z_{n-1} = z > 0$  and  $z_n < 0$

$$\begin{aligned}\dot{\phi} &= -\frac{zJ_1 + \dots + zJ_{n-1} + z_nJ_n}{(z - z_n)zc_1 + \dots + (z - z_n)zc_{n-1}}, \\ \dot{c}_k &= \frac{zJ_1 + \dots + zJ_{n-1} + z_nJ_n}{(z - z_n)zc_1 + \dots + (z - z_n)zc_{n-1}}zc_k - J_k, \quad \text{for } k = 1, \dots, n-1, \\ \dot{J}_1 &= \dots = \dot{J}_n = 0.\end{aligned}$$

Following the proof of Lemma 3.4, we obtain explicit solutions of the limiting slow system as follows for  $k = 1, \dots, n-1$

$$\begin{aligned}\phi(x) &= \phi^L - \frac{\mathcal{T}^c}{zz_n\mathcal{T}^m} \ln \left( 1 + \frac{z_n\mathcal{T}^m}{(z - z_n)(c_1^L + c_2^L + \dots + c_{n-1}^L)}x \right), \\ c_k(x) &= \left( 1 + \frac{z_n\mathcal{T}^m}{(z - z_n)(c_1^L + c_2^L + \dots + c_{n-1}^L)}x \right)^{\frac{\mathcal{T}^c}{z_n\mathcal{T}^m}} \left( c_k^L - \frac{J_k(c_1^L + \dots + c_{n-1}^L)}{J_1 + \dots + J_{n-1}} \right) \\ &\quad + \frac{J_k(c_1^L + \dots + c_{n-1}^L)}{J_1 + \dots + J_{n-1}} \left( 1 + \frac{z_n\mathcal{T}^m}{(z - z_n)(c_1^L + c_2^L + \dots + c_{n-1}^L)}x \right),\end{aligned}$$

where  $\mathcal{T}^m = J_1 + J_2 + \cdots + J_n$  and  $\mathcal{T}^c = z_1 J_1 + z_2 J_2 + \cdots + z_n J_n$ .

In particular,

$$J_k = \left( c_k^R - c_k^L e^{z(\phi^L - \phi^R)} \right) \mathcal{F}, \quad \text{for } k = 1, \dots, n-1,$$

$$J_n = \frac{z(c_1^R + \cdots + c_{n-1}^R - (c_1^L + \cdots + c_{n-1}^L))}{z_n} \\ \times \left( 1 - \frac{z_n(\phi^L - \phi^R)}{\ln(c_1^R + \cdots + c_{n-1}^R) - \ln(c_1^L + \cdots + c_{n-1}^L)} \right).$$

where  $\mathcal{F} = \mathcal{F}(c_1^L, \dots, c_{n-1}^L; c_1^R, \dots, c_{n-1}^R; \phi^L, \phi^R)$  is defined as

$$\mathcal{F} = \frac{(c_1^L + \cdots + c_{n-1}^L - (c_1^R + \cdots + c_{n-1}^R)) \left( 1 - \frac{z(\phi^L - \phi^R)}{\ln(c_1^R + \cdots + c_{n-1}^R) - \ln(c_1^L + \cdots + c_{n-1}^L)} \right)}{c_1^R + \cdots + c_{n-1}^R - (c_1^L + \cdots + c_{n-1}^L) e^{z(\phi^L - \phi^R)}}.$$

□

**Remark 5.2.** *Similar result can be obtained for the classical PNP system with a mixture of  $n$  ion species, where the  $(n-1)$  negatively charged ion species have the same valence.*

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