Reversal permanent charge and reversal potential: case studies via classical Poisson–Nernst–Planck models

2015 Nonlinearity 28 103

(http://iopscience.iop.org/0951-7715/28/1/103)

IOP Publishing | London Mathematical Society Nonlinearity

Nonlinearity **28** (2015) 103–127 doi:10.1088/0951-7715/28/1/103

Reversal permanent charge and reversal potential: case studies via classical Poisson–Nernst–Planck models

Bob Eisenberg[1], **Weishi Liu**[2] **and Hongguo Xu**[2]

[1] Department of Molecular Biophysics and Physiology, Rush Medical Center, Chicago, IL 60612, USA
[2] Department of Mathematics, University of Kansas, Lawrence, KS 66045, USA

E-mail: beisenbe@rush.edu, wliu@math.ku.edu and xu@math.ku.edu

Received 10 May 2014, revised 16 September 2014
Accepted for publication 6 November 2014
Published 8 December 2014

Recommended by T J Kaper

Abstract

In this work, we are interested in effects of a simple profile of permanent charges on ionic flows. We determine when a permanent charge produces current reversal. We adopt the classical Poisson–Nernst–Planck (PNP) models of ionic flows for this study. The starting point of our analysis is the recently developed geometric singular perturbation approach for PNP models. Under the setting in the paper for case studies, we are able to identify a single governing equation for the existence and the value of the permanent charge for a current reversal. A number of interesting features are established. The related topic on reversal potential can be viewed as a dual problem and is briefly examined in this work too.

Keywords: electrodiffusion, reversal permanent charge, reversal potential

(Some figures may appear in colour only in the online journal)
Mathematics Subject Classification: 34B16, 76Z05, 78A35, 92C35

1. Introduction

Electrodiffusion—migration of charges—exhibits incredibly rich phenomena. Indeed, our digital technology is a direct result of the rich but easily controlled behaviours of electrodiffusion. Recently, it has become clear that ion channels are described by physics fundamentally similar to that of semiconductor devices (see, e.g., [13–15]). Ion channels are proteins with a hole in their middle that control a wide range of biological functions. Indeed, almost all biological functions are controlled one way or another by ion channels, just as almost all digital functions are controlled by the channels of field effect transistors.

The study of electrodiffusion is thus an extremely rich area for multidisciplinary research with diverse applications from computer science, through engineering to biology in which mathematics may lend an important hand by generalizing and understanding the principles that allow control of electrodiffusion. For semiconductors and ion channels, permanent charges add an additional component—probably the most important one—to the rich behaviour. A single permanent distribution of charge (i.e., doping) creates several different devices, with robust reduced descriptions, when different electrical potentials are placed on its boundaries, e.g., amplifiers, limiters, multipliers, logarithmic convertors, exponentiators and so on. Permanent charges come into the picture in semiconductors and ion channels in different ways: for semiconductors, one would like to (at least theoretically) design a permanent charge (doping profile) for the semiconductor to achieve a desired performance; for ion channels, one would like to detect (see, e.g., [8–10]) the distribution of permanent charges—a structural property of ion channels—and to analyse its roles in ion channel functions (permeation, selectivity, stability, etc). Synthetic ion channels are now being created ([44], etc) in which the distributions of permanent charge can be created and tested and exploited for technological use.

In this work, we will focus on some basic questions about how permanent charges affect ionic flows; more precisely, we will study when and how a permanent charge produces current reversal using the classical Poisson–Nernst–Planck (PNP) model for ionic flows. It is important to remember that our model is a reduced model with effective parameters that depend on atomic scale details in many ways. In fact, for ion channels, a permanent charge reflects the structure of the channel protein, and its distribution of amino acid side chains, with acidic side chains contributing permanent negative charge and basic side chains contributing permanent positive charge, according to their ionization states, regulated by local pH. Thus, what we call permanent charge density can depend on the location of many atoms, the shape of the protein, etc. Reduced models are needed to compute current–voltage relations of channels in a variety of ionic conditions. As far as we know, all atom simulations cannot deal with the range of concentrations important for biological function, e.g., calcium ions at 10^{-8}M.

1.1. PNP models for ionic flows

There are many models, from low resolution to high, for ionic flows in various settings (see, e.g., [2–4, 11, 12, 16, 18, 21–24, 28–30, 35–37, 40, 41, 43, 45, 46, 51–54]). Among them, primitive PNP models have been extensively examined analytically and numerically.

In this work, we take a one-dimensional PNP model. A one-dimensional dimensionless steady-state PNP system for n types of ion species through ion channels is, for $k = 1, 2, \cdots, n$,

$$\begin{aligned} &\frac{\varepsilon^2}{h(x)}\frac{\mathrm{d}}{\mathrm{d}x}\left(h(x)\frac{\mathrm{d}}{\mathrm{d}x}\phi\right) = -\sum_{s=1}^{n}\alpha_s c_s - Q(x),\\ &\frac{\mathrm{d}J_k}{\mathrm{d}x} = 0, \quad -J_k = \qquad h(x)D_k c_k\frac{\mathrm{d}}{\mathrm{d}x}\mu_k \end{aligned} \tag{1.1}$$

with the boundary conditions

$$\phi(0) = \mathcal{V}_0,\ c_k(0) = l_k \geqslant 0; \quad \phi(1) = 0,\ c_k(1) = r_k \geqslant 0. \tag{1.2}$$

Here $\varepsilon^2 \ll 1$ is a dimensionless parameter, $h(x)$ represents the cross-section area of the ion channel over x, ϕ is the electric potential, $Q(x)$ is the permanent charge, and, for the kth ion species, c_k is its concentration (number density), α_k is its valence (number of charges per particle), D_k is the diffusion coefficient, μ_k is the electrochemical potential, J_k is its scaled ion flux density, l_k and r_k are its concentrations at the boundaries (left and right baths). For boundary conditions, one often imposes the electroneutrality conditions on the concentrations

$$\sum_{s=1}^{n} \alpha_s l_s = \sum_{s=1}^{n} \alpha_s r_s = 0. \tag{1.3}$$

The electrochemical potential $\mu_k(x)$ for the kth ion species consists of the ideal component $\mu_k^{id}(x)$ and the excess component $\mu_k^{ex}(x)$:

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

where the ideal component is

$$\mu_k^{id}(x) = \alpha_k \phi(x) + \ln \frac{c_k(x)}{c_0} \tag{1.4}$$

with some characteristic number density c_0. Since the only relevant quantity from the chemical potential $\ln \frac{c_k(x)}{c_0}$ is its gradient, without loss of generality, we will set $c_0 = 1$ in the sequel. The classical PNP model only deals with the ideal component $\mu_k^{id}(x)$, which reflects the collision between ion particles and water molecules and ignores the size of ions. The excess electrochemical potential $\mu_k^{ex}(x)$ accounts for the finite size effect of ions. This component is essential for dealing with properties of bulk ionic solutions containing divalents like calcium ions, or mixtures, and is in fact needed whenever concentrations exceed say 50mM, as they almost always do in technological and biological situations. This component is extremely important for many critical properties of ion channels, for example, ideal sodium and potassium solutions are indistinguishable, but life depends on the ability of channels to distinguish between these ions. We refer the readers to, for example, [5–7, 47, 49, 50] for concrete models. In applications, both local models for $\mu_k^{ex}(x)$ (a function of the values $\{c_j(x)\}$ at x) and nonlocal models for $\mu_k^{ex}(x)$ (a functional of the functions $\{c_j\}$) are employed for a variety of purposes.

1.2. An elementary property and a basic question

We will briefly discuss a particular aspect of ionic flows from the model which leads to our question in terms of specific quantities in the model.

Dividing $h(x)D_k c_k$ through the Nernst–Planck equation for the ion flux J_k in (1.1) and integrating from $x = 0$ to $x = 1$, one has

$$J_k \int_0^1 \frac{1}{h(x)D_k c_k(x)}\,\mathrm{d}x = \mu_k(0) - \mu_k(1). \tag{1.5}$$

Since $h(x)$ and $c_k(x)$ are positive, the sign of J_k is the same as that of $\mu_k(0) - \mu_k(1)$. For any local model of μ_k^{ex}, the latter is completely determined by the boundary values of electric potential $\mathcal{V}_0$ and of concentrations l_k's and r_k's; in particular, it is *independent* of a permanent charge. In the language of biologists and chemists, the sign of J_k is determined by the driving force (the gradient of electrochemical potential) and not the structure (permanent charge Q) of the channel protein.

For the classical PNP model where $\mu_k(x) = \mu_k^{id}(x) = \alpha_k\phi(x) + \ln c_k(x)$, one has the explicit formula for $\mu_k(0) - \mu_k(1)$:

$$J_k \int_0^1 \frac{1}{h(x)D_k c_k(x)}\,\mathrm{d}x = \mu_k(0) - \mu_k(1) = \alpha_k\mathcal{V}_0 + \ln \frac{l_k}{r_k}. \tag{1.6}$$

On the other hand, the actual *amount* of each J_k does depend on Q since the profile of concentration $c_k(x)$ does. An important quantity involving the amount of each J_k is the current

$\mathcal{I}$. For given $\mathcal{V}_0$, $Q(x)$, l_k's and r_k's, if $(\phi(x;\varepsilon), c_k(x;\varepsilon), J_k(\varepsilon))$ is a solution of the boundary value problem (1.1) and (1.2), then the current $\mathcal{I}$ is

$$\mathcal{I} = \mathcal{I}(\varepsilon) = \sum_{s=1}^{n} \alpha_s J_s(\varepsilon). \tag{1.7}$$

The electrical current is the important variable for a number of reasons. (1) It is what is almost always measured. (2) Almost all our technology involves electrical currents and potentials. Little involves ion fluxes. (3) Maxwell's equations can be viewed as the ultimate statement of conservation of charge, a generalization of Kirchhoff's current law that says current is always exactly conserved no matter how different the carrier of the current (electrons in a cathode ray tube, the displacement current in a vacuum, holes and 'electrons' in a semiconductor, ions in an electrolyte solution).

It is important to realize that the components of the current can be positive or negative because of the sign of α_k's of the charges. Thus the current has much more complexity than the individual ion fluxes. We are thus interested in how the sign of the current depends on the permanent charge via classical PNP models.

For classical PNP models with the electroneutrality assumption (1.3) and that $D_k = 1$, it is known (e.g., [4, 48] for $n = 2$ and [42] for general n) that, if $Q = 0$, then $\mathcal{V}_0$ and $\mathcal{I}$ have the same sign (independent of the boundary concentrations l_k's and r_k's). Furthermore, as an immediate consequence of (1.6), one has the simple property below.

Proposition 1.1. *If the quantities $\alpha_k(\alpha_k\mathcal{V}_0 + \ln l_k - \ln r_k)$, for $k = 1, 2, \ldots, n$, are all nonnegative (nonpositive), then the quantities $\alpha_k J_k$'s are all nonnegative (nonpositive), and hence, the current $\mathcal{I}$ is nonnegative (nonpositive) too, independent of a permanent charge Q; that is, under the above condition on $\mathcal{V}_0$, l_k's and r_k's, no permanent charge Q can reverse the sign of the current $\mathcal{I}$.*

In general, the sign of the current $\mathcal{I}$ could be reversed. This fact has been used to identify the type (i.e., selectivity) of ion channels in biological experiments since 1949 ([26, 27]). A natural question is then:

Question: *Under what conditions on $\mathcal{V}_0$, l_k's and r_k's, can current $\mathcal{I}$ be reversed for appropriate choices of permanent charges Q ?*

We raise this question from the mathematical analysis point of view, which captures the general physical and biological importance of the issue. The profile of Q in general governs many of the properties of ion channels and semiconductor devices.

A related well-known topic is the reversal potential: *for given Q, l_k's and r_k's, what is the so-called reversal potential $\mathcal{V}_0$ so that $\mathcal{I} = 0$?* Identification of reversal potentials is a central subject in experiments on channels; indeed, identification of reversal potentials is often a prerequisite for further identification of a channel or transporter.

1.3. Setup of our case study

To this end, we specify the case we will study in this paper. We will examine the question by working on the simplest model, *the classical PNP* (cPNP) model (1.1) with ideal electrochemical potential $\mu_k = \alpha_k\phi + \ln c_k$, and the boundary condition (1.2). We will focus on the case with equal diffusion coefficients (see remark 1.1 below) and with a simplest profile of a permanent charge Q. More precisely, we will assume

(A1) $D_k = 1$ for $k = 1, 2, \ldots, n$, and $h(x) = 1$;
(A2) Electroneutrality boundary conditions (1.3);

(A3) A piecewise constant permanent charge Q with one nonzero region; that is, for a partition $x_0 = 0 < x_1 < x_2 < x_3 = 1$ of $[0, 1]$,

$$Q(x) = \begin{cases} 0, & x \in (x_0, x_1) \cup (x_2, x_3) \\ Q_2, & x \in (x_1, x_2) \end{cases} \tag{1.8}$$

where Q_2 is a constant.

Remark 1.1. In general, it is limiting to assume that all diffusion coefficients are equal. It is known experimentally that many phenomena (e.g., diffusion potentials) disappear altogether when diffusion coefficients of anion and cation are equal (in a two species solution). In other words this is a degenerate case and whatever phenomena presented here serve as motivation to study the additional important phenomena of non-degenerate cases. □

For the current reversal effect caused by a permanent charge Q in (A3), we look for the value(s) Q^* for Q_2 so that the corresponding current $\mathcal{I}$ is zero. Suppose Q^* exists. Then, generically, the current $\mathcal{I}$ will change sign as Q_2 crosses Q^*. Motivated by the terminology of reversal potential, we give the following definition.

Definition 1.2. *If, for $Q_2 = Q^*$, the current $\mathcal{I} = 0$, then we call the permanent charge Q in (A3) a reversal permanent charge; or, we simply call Q^* a reversal permanent charge.*

To answer the questions about reversal permanent charges and reversal potentials, one has to examine the dependences of the current $\mathcal{I}$ on the boundary potential $\mathcal{V}_0$ and the permanent charge Q. In terms of the cPNP model, we need to analyse the BVP (1.1) and (1.2). We will treat system (1.1) as a singularly perturbed system with ε as the singular parameter. Also, we will focus on information from the zeroth order approximation of solutions of the BVP (1.1) and (1.2), which dominates the quantitative and qualitative properties of the problem interested in this work.

2. Geometric singular perturbations for the BVP (1.1) and (1.2)

In [39], a geometric singular perturbation framework, combining with special structures of PNP systems, has been developed for studying the BVP (1.1) and (1.2). This general dynamical system framework and the subsequent analysis have demonstrated the great power of analysing PNP type problems with potential boundary and internal layers (see [17, 38, 39, 42] for study on cPNP models, [37] for PNP with a local excess hard-sphere components, and [30, 40] for PNP with nonlocal excess hard-sphere components).

For convenience, we will give a brief account of the relevant results in [39] (with slightly different notations) and refer the readers to the paper for details. We remind the readers that we will work on cPNP with ideal electrochemical potential $\mu_k = \alpha_k \phi + \ln c_k$.

2.1. Converting the BVP to a connecting orbit problem

We rewrite system (1.1) into a standard form of singularly perturbed systems and convert the BVP to a *connecting orbit problem*.

Denote the derivative with respect to x by overdot and introduce $u = \varepsilon\dot{\phi}$ and $w = x$. System (1.1) becomes, for $k = 1, 2, \ldots, n$,

$$\begin{aligned} &\varepsilon\dot{\phi} = u, \quad \varepsilon\dot{u} = -\sum_{s=1}^{n} \alpha_s c_s - Q(w), \\ &\varepsilon\dot{c}_k = -\alpha_k c_k u - \varepsilon J_k, \quad \dot{J}_k = 0, \quad \dot{w} = 1. \end{aligned} \tag{2.1}$$

System (2.1) will be treated as a dynamical system with the phase space $\mathbb{R}^{2n+3}$ and the independent variable x is viewed as time for the dynamical system. The boundary condition (1.2) becomes, for $k = 1, 2, \ldots, n$,

$$\phi(0) = \mathcal{V}_0,\ c_k(0) = l_k,\ w(0) = 0; \quad \phi(1) = 0,\ c_k(1) = r_k,\ w(1) = 1.$$

Let B_L and B_R be the subsets of the phase space $\mathbb{R}^{2n+3}$ defined by

$$\begin{aligned} B_L &= \{(\phi, u, C, J, w) : \phi = \mathcal{V}_0,\ C = L,\ w = 0\}, \\ B_R &= \{(\phi, u, C, J, w) : \phi = 0,\ C = R,\ w = 1\}, \end{aligned} \tag{2.2}$$

where $C = (c_1, c_2, \ldots, c_n)^T$, $J = (J_1, J_2, \ldots, J_n)^T$, $L = (l_1, l_2, \ldots, l_n)^T$, $R = (r_1, r_2, \ldots, r_n)^T$. Note that $\dim B_L = \dim B_R = n + 1$.

Then, the BVP (1.1) and (1.2) is equivalent to the following *connecting orbit problem*: finding an orbit of (2.1) from B_L to B_R.

We now explain the idea for a construction of a connecting orbit. Let M_L^ε be the collection of all forward orbits of (2.1) starting from B_L and M_R^ε be the collection of all backward orbits starting from B_R. For $\varepsilon > 0$ small, due to w-equation in (2.1), the vector field of (2.1) is not tangent to B_L and B_R. It implies that both M_L^ε and M_R^ε are smooth invariant manifolds of (2.1) and $\dim M_L^\varepsilon = \dim M_R^\varepsilon = \dim B_L + 1 = \dim B_R + 1 = n + 2$. Generically, one expects that M_L^ε and M_R^ε intersect transversally. If this is the case, then $\dim(M_L^\varepsilon \cap M_R^\varepsilon) = \dim M_L^\varepsilon + \dim M_R^\varepsilon - \dim \mathbb{R}^{2n+3} = 1$, and hence, the intersection $M_L^\varepsilon \cap M_R^\varepsilon$ would consist of a discrete set of orbits of (2.1). To find a connecting orbit from B_L to B_R, it amounts to show that M_L^ε and M_R^ε intersect. The geometric procedure for the latter involves two steps:

(i) to construct a *singular orbit*: a union of fast and slow orbits of different limiting systems of (2.1), where fast orbits represent boundary/internal layers and slow orbits connect boundary/internal layers;

(ii) to examine the evolutions of M_L^ε and M_R^ε along the singular orbit and apply the exchange lemma (see, e.g., [31, 32]) to show a nonempty intersection.

For this work, we will be interested in only singular orbits of the problem and will recall the procedure of constructing singular orbits from [39].

Due to the jumps of $Q(x)$ at x_j's, we preassign (unknown) values of ϕ and c_k's at x_j as

$$\phi(x_j) = \phi^{[j]}, \quad c_k(x_j) = c_k^{[j]}, \tag{2.3}$$

and, for each jump point x_j of $Q(x)$, introduce the set,

$$B_j = \{(\phi, u, C, J, w) :\ \phi = \phi^{[j]}, C = C^{[j]}, w = x_j\}. \tag{2.4}$$

We then construct singular orbits over each interval $[x_{j-1}, x_j]$ for the connecting problem between B_{j-1} and B_j. At the end, we match those singular orbits at each x_j to obtain one singular orbit over the whole interval [0, 1].

2.2. Construction of singular orbits connecting B_{j-1} and B_j.

A typical singular connecting orbit between B_{j-1} and B_j will consist of two fast orbits (singular layers) $\Gamma^{[j-1,+]}$ at x_{j-1} and $\Gamma^{[j,-]}$ at x_j, and one slow orbit (regular layer) Λ_j over $[x_{j-1}, x_j]$ (see figure 1).

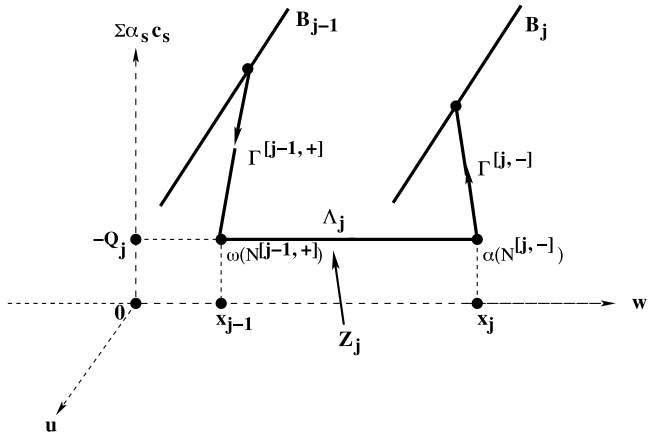

Figure 1. A singular orbit over $[x_{j-1}, x_j]$ projected to the space of variables u, $\sum \alpha_s c_s$ and w: $\Gamma^{[j-1,+]}$ is a singular layer at $x = x_{j-1}$ from B_{j-1} to $\mathcal{Z}_j$ and $\Gamma^{[j,-]}$ from $\mathcal{Z}_j$ to B_j, and Λ_j connects 'landing' points of $\Gamma^{[j-1,+]}$ in $\omega(N^{[j-1,+]})$ and 'departing' points of $\Gamma^{[j,-]}$ in $\alpha(N^{[j,-]})$ on $\mathcal{Z}_j$.

2.2.1. Fast dynamics for singular layers at x_{j-1} and x_j By setting $\varepsilon = 0$ in system (2.1), we get the *slow manifold*

$$\mathcal{Z}_j = \Big\{u = 0,\ \sum_{s=1}^{n} \alpha_s c_s + Q_j = 0\Big\}.$$

Note that $\mathcal{Z}_j$ is of co-dimension two, i.e., $\dim \mathcal{Z}_j = 2n + 1$. In terms of the independent variable $\xi = x/\varepsilon$, we obtain *the fast system* of (2.1), for $k = 1, 2, \ldots, n$,

$$\phi' = u,\ u' = -\sum_{s=1}^{n} \alpha_s c_s - Q_j,\ c_k' = -\alpha_k c_k u - \varepsilon J_k,\ J' = 0,\ w' = \varepsilon, \tag{2.5}$$

where prime denotes the derivative with respect to ξ. The limiting fast system is, for $k = 1, 2, \ldots, n$,

$$\phi' = u,\ u' = -\sum_{s=1}^{n} \alpha_s c_s - Q_j,\ c_k' = -\alpha_k c_k u,\ J' = 0,\ w' = 0. \tag{2.6}$$

The slow manifold $\mathcal{Z}_j$ is precisely the set of equilibria of (2.6). Recall that $\dim \mathcal{Z}_j = 2n+1$. For the linearization of (2.6) at each point on $\mathcal{Z}_j$, there are $(2n+1)$ zero eigenvalues associated to the tangent space of $\mathcal{Z}_j$ and the other two eigenvalues are $\pm\sqrt{\sum_{s=1}^{n} \alpha_s^2 c_s}$. Thus, $\mathcal{Z}_j$ is normally hyperbolic (see [19,25]). We will denote the stable and unstable manifolds of $\mathcal{Z}_j$ by $W^s(\mathcal{Z}_j)$ and $W^u(\mathcal{Z}_j)$, respectively.

Let $M^{[j-1,+]}$ be the collection of all forward orbits from B_{j-1} under the flow of (2.6) and let $M^{[j,-]}$ be the collection of all backward orbits from B_j. Then the set of forward orbits from B_{j-1} to $\mathcal{Z}_j$ is $N^{[j-1,+]} = M^{[j-1,+]} \cap W^s(\mathcal{Z}_j)$, and the set of backward orbits from B_j to $\mathcal{Z}_j$ is $N^{[j,-]} = M^{[j,-]} \cap W^u(\mathcal{Z}_j)$. Therefore, the singular layer $\Gamma^{[j-1,+]}$ at x_{j-1} satisfies $\Gamma^{[j-1,+]} \subset N^{[j-1,+]}$ and the singular layer $\Gamma^{[j,-]}$ at x_j satisfies $\Gamma^{[j,-]} \subset N^{[j,-]}$.

All those important geometric objects in the previous paragraph are *explicitly* characterized in [39]. For general *nonlinear* singular perturbation problems, this is of course unexpected. It is only possible for the problem at hand due to the *special structures* of cPNP stated next. We suspect that this special property of cPNP (and relate systems) is related to their importance in semiconductor technology and biology.

Proposition 2.1. *The following functions are first integrals of system (2.6),*

$$G_k = \ln c_k + \alpha_k \phi \ \ for \ \ k = 1, 2, \ldots, n \ \ and \ \ G_{n+1} = \frac{u^2}{2} - \sum_{s=1}^{n} c_s + Q_j \phi.$$

Proof. This is proposition 3.1 in [39] and can also be verified directly. □

In [39], intermediate variables $\phi^{[j-1,+]}$ and $\phi^{[j,-]}$ are introduced for characterizing the singular layers.

Lemma 2.2. *There is a unique* $\phi = \phi^{[j-1,+]}$ *satisfying*

$$\sum_{s=1}^{n} \alpha_s c_s^{[j-1]} e^{\alpha_s(\phi^{[j-1]}-\phi)} + Q_j = 0; \tag{2.7}$$

and a unique $\phi = \phi^{[j,-]}$ *satisfying*

$$\sum_{s=1}^{n} \alpha_s c_s^{[j]} \mathrm{e}^{\alpha_s(\phi^{[j]}-\phi)} + Q_j = 0. \tag{2.8}$$

One can then characterize all layers $\Gamma^{[j-1,+]}$ from B_{j-1} to $\mathcal{Z}_j$ and $\Gamma^{[j,-]}$ from $\mathcal{Z}_j$ to B_j, which is the content of proposition 3.3 in [39] recast below.

Proposition 2.3. *(i) Let* $\Gamma^{[j-1,+]} \subset N^{[j-1,+]}$ *be a singular layer at* $x = x_{j-1}$*. Suppose* $\Gamma^{[j-1,+]}$ *is the orbit of the solution* $z(\xi) = (\phi(\xi), u(\xi), C(\xi), J, x_{j-1})$ *with* $z(0) \in B_{j-1}$ *and* $\lim_{\xi\to+\infty} z(\xi) = z(+\infty) \in \mathcal{Z}_j$*. Then,* $\phi(\xi)$ *is determined by the Hamiltonian system*

$$\phi'' + \sum_{s=1}^{n} \alpha_s c_s^{[j-1]} e^{-\alpha_s(\phi-\phi^{[j-1]})} + Q_j = 0$$

together with the conditions $\phi(0) = \phi^{[j-1]}$ *and* $\phi(+\infty) = \phi^{[j-1,+]}$ *where* $\phi^{[j-1,+]}$ *is as in lemma 2.2;* $u(\xi) = \phi'(\xi)$ *with* $u(0) = u_+^{[j-1]}$ *and* $u(+\infty) = 0$*, where*

$$u_+^{[j-1]} = \delta_+^{[j-1]} \sqrt{\sum_{s=1}^{n} 2c_s^{[j-1]}(1 - e^{\alpha_s(\phi^{[j-1]}-\phi^{[j-1,+]})}) - 2Q_j(\phi^{[j-1]} - \phi^{[j-1,+]})} \tag{2.9}$$

where $\delta_+^{[j-1]} = sgn(\phi^{[j-1,+]} - \phi^{[j-1]})$ *is the sign function; and*

$$c_k(\xi) = c_k^{[j-1]} \mathrm{e}^{-\alpha_k(\phi(\xi)-\phi^{[j-1]})}$$

with $c_k(0) = c_k^{[j-1]}$ *and*

$$c_k^{[j-1,+]} := c_k(+\infty) = c_k^{[j-1]} \mathrm{e}^{-\alpha_k(\phi^{[j-1,+]}-\phi^{[j-1]})}. \tag{2.10}$$

Let $\Gamma^{[j,-]} \subset N^{[j,-]}$ *be a singular layer at* $x = x_j$*. Suppose* $\Gamma^{[j,-]}$ *is the orbit of the solution* $z(\xi) = (\phi(\xi), u(\xi), C(\xi), J, x_j)$ *with* $z(0) \in B_j$ *and* $\lim_{\xi\to-\infty} z(\xi) = z(-\infty) \in \mathcal{Z}_j$*. Then,* $\phi(\xi)$ *is determined by the Hamiltonian system*

$$\phi'' + \sum_{s=1}^{n} \alpha_s c_s^{[j]} \mathrm{e}^{-\alpha_s(\phi-\phi^{[j]})} + Q_j = 0$$

together with the conditions $\phi(0) = \phi^{[j]}$ *and* $\phi(-\infty) = \phi^{[j,-]}$ *where* $\phi^{[j,-]}$ *is as in lemma 2.2;* $u(\xi) = \phi'(\xi)$ *with* $u(0) = u_-^{[j]}$ *and* $u(-\infty) = 0$*, where*

$$u_-^{[j]} = \delta_-^{[j]} \sqrt{\sum_{s=1}^{n} 2c_s^{[j]}(1 - e^{\alpha_s(\phi^{[j]}-\phi^{[j,-]})}) - 2Q_j(\phi^{[j]} - \phi^{[j,-]})}, \tag{2.11}$$

where $\delta_-^{[j]} = \mathrm{sgn}(\phi^{[j]} - \phi^{[j,-]})$*;* $c_k(\xi) = c_k^{[j]} e^{-\alpha_k(\phi(\xi)-\phi^{[j]})}$ *with* $c_k(0) = c_k^{[j]}$ *and*

$$c_k^{[j,-]} := c_k(-\infty) = c_k^{[j]} e^{-\alpha_k(\phi^{[j,-]}-\phi^{[j]})}. \tag{2.12}$$

(ii) The intersections $M^{[j-1,+]} \cap W^s(\mathcal{Z}_j)$ *and* $M^{[j,-]} \cap W^u(\mathcal{Z}_j)$ *are transversal.*

(iii) The ω*-limit set of* $N^{[j-1,+]}$ *and the* α*-limit set of* $N^{[j,-]}$ *are*

$$\omega\left(N^{[j-1,+]}\right) = \left\{\left(\phi^{[j-1,+]}, 0, C^{[j-1,+]}, J, x_{j-1}\right) : \text{ all } J\right\} \subset \mathcal{Z}_j,$$
$$\alpha\left(N^{[j,-]}\right) = \left\{\left(\phi^{[j,-]}, 0, C^{[j,-]}, J, x_j\right) : \text{ all } J\right\} \subset \mathcal{Z}_j.$$

We end this part with a discussion of interfacial behaviour of electric potential at jump points of permanent charges.

Proposition 2.4. *If* $Q_j < Q_{j+1}$ *(resp.* $Q_j > Q_{j+1}$*), then*

$$\phi^{[j,-]} < \phi^{[j]} < \phi^{[j,+]} \ (resp.\ \phi^{[j,-]} > \phi^{[j]} > \phi^{[j,+]}).$$

Proof. We show the result for the case where $Q_j < Q_{j+1}$. Set

$$f(t) = \sum_{s=1}^{n} \alpha_s c_s^{[j]} e^{\alpha_s t}.$$

It follows from (2.7) and (2.8) that

$$f(\phi^{[j]} - \phi^{[j,-]}) = -Q_j > f(\phi^{[j]} - \phi^{[j,+]}) = -Q_{j+1}.$$

Since $f'(t) > 0$, $\phi^{[j]} - \phi^{[j,-]} > \phi^{[j]} - \phi^{[j,+]}$, and hence, $\phi^{[j,-]} < \phi^{[j,+]}$. □

The remark below will be useful for readers to have a better understanding of the possibility of the results obtained in the paper and difficulties involved in obtaining the results.

Remark 2.1. Proposition 2.4 indicates that a jump-up of permanent charge $Q_{j+1} > Q_j$ at the junction causes a jump-up of the potential $\phi^{[j,+]} > \phi^{[j,-]}$ and a jump-down of permanent charge $Q_{j+1} < Q_j$ causes a jump-down of the potential $\phi^{[j,+]} < \phi^{[j,-]}$.

The amount of jump-up or jump-down of the potential is NOT determined by that of Q alone but involves other system parameters. For example, if $Q_{j-1} = Q_{j+1} < Q_j$, that is, the amount of jump-up of Q at x_{j-1} equals the amount of jump-down at x_j, the jump-up $\phi^{[j-1,+]} - \phi^{[j-1,-]} > 0$ at x_{j-1} and the jump-down $\phi^{[j,+]} - \phi^{[j,-]} < 0$ at x_j do not cancel each other in general; that is, $|\phi^{[j-1,+]} - \phi^{[j-1,-]}| \neq |\phi^{[j,+]} - \phi^{[j,-]}|$.

The above property is extremely important since it allows even simple permanent charge distributions to have a great impact on ionic flows (see results in sections 3 and 4). We believe that it is this property that allows doping distributions in semiconductor devices to control their behaviour. One can anticipate similar controls in biological channels, although they have not yet been definitively identified. □

2.2.2. Slow dynamics for regular layers over (x_{j-1}, x_j). We will now construct slow orbits Λ_j on the slow manifold

$$\mathcal{Z}_j = \left\{u = 0,\ \sum_{s=1} \alpha_s c_s + Q_j = 0\right\}.$$

From proposition 2.3, possible landing points of $\Gamma^{[j-1,+]}$ onto $\mathcal{Z}_j$ are $\omega(N^{[j-1,+]})$ and possible departing points of $\Gamma^{[j,-]}$ from $\mathcal{Z}_j$ are $\alpha(N^{[j,-]})$. If Λ_j connects $\omega(N^{[j-1,+]})$ to $\alpha(N^{[j,-]})$, then the union $\Gamma^{[j-1,+]} \cup \Lambda_j \cup \Gamma^{[j,-]}$ is a singular orbit connecting B_{j-1} to B_j.

Note that system (2.1) is degenerate at $\varepsilon = 0$ in the sense that all dynamical information on $(\phi, c_1, \cdots, c_n)$ would be lost when setting $\varepsilon = 0$. In [39], the dependent variables are rescaled as

$$u = \varepsilon p, \quad \alpha_n c_n = -\sum_{s=1}^{n-1} \alpha_s c_s - Q_j - \varepsilon q. \tag{2.13}$$

Replacing (u, c_n) with (p, q), system (2.1) becomes, for $k = 1, 2, \ldots, n-1$,

$$\begin{aligned}
\dot\phi &= p, \quad \varepsilon \dot p = q,\\
\varepsilon \dot q &= \Big(\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j - \varepsilon \alpha_n q\Big) p + \mathcal{I},\\
\dot c_k &= -\alpha_k p c_k - J_k, \quad \dot J = 0, \quad \dot w = 1,
\end{aligned} \tag{2.14}$$

where $\mathcal{I} = \sum_{s=1}^n \alpha_s J_s$ is the current. We remark that this is the reason that $D_k = 1$ assumption (A1) simplifies the analysis of the problem greatly. Without assumption (A1), the term $\mathcal{I}$ in (2.14) would be $\sum_{s=1}^n D_s^{-1} \alpha_s J_s$ and the analysis in section 3 would be much more complicated.

The limiting slow system of (2.14) is, for $k = 1, 2, \ldots, n-1$,

$$\begin{aligned}
\dot\phi &= p, \quad q = \Big(\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j\Big) p + \mathcal{I} = 0,\\
\dot c_k &= -\alpha_k p c_k - J_k, \quad \dot J = 0, \quad \dot w = 1.
\end{aligned} \tag{2.15}$$

For this system, the slow manifold is

$$\mathcal{S}_j = \left\{ p = -\frac{\mathcal{I}}{\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j},\ q = 0 \right\}.$$

Therefore, on $\mathcal{S}_j$ system (2.15) reads, for $k = 1, 2, \ldots, n-1$,

$$\begin{aligned}
\dot\phi &= -\frac{\mathcal{I}}{\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j},\\
\dot c_k &= \frac{\mathcal{I}}{\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j} \alpha_k c_k - J_k,\\
\dot J &= 0, \quad \dot w = 1.
\end{aligned} \tag{2.16}$$

Another *special structure* of the cPNP comes in to play a crucial role for analysing the limiting slow dynamics.

On $\mathcal{S}_j$ where $q = \sum_{s=1}^n \alpha_s c_s + Q_j = 0$, it follows from (2.13) that

$$\sum_{s=1}^{n-1} (\alpha_s - \alpha_n)\alpha_s c_s - \alpha_n Q_j = \sum_{s=1}^{n} \alpha_s^2 c_s.$$

Note that c_k's are the concentrations of ion species. Therefore, we will be interested in solutions with $c_k > 0$ for $k = 1, 2, \cdots, n$, and hence, $\sum_{s=1}^n \alpha_s^2 c_s > 0$. If we multiply $\sum_{s=1}^n \alpha_s^2 c_s > 0$

on the right hand side of system (2.16), the phase portrait remains the same. In doing so, the system becomes, in term of the new independent variable, say τ, for $k = 1, 2, \ldots, n-1$,

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}\tau}\phi &= -\mathcal{I}, \quad \frac{\mathrm{d}}{\mathrm{d}\tau}c_k = \mathcal{I}\alpha_k c_k - J_k\sum_{s=1}^{n}\alpha_s^2 c_s, \\ \frac{\mathrm{d}}{\mathrm{d}\tau}J &= 0, \quad \frac{\mathrm{d}}{\mathrm{d}\tau}w = \sum_{s=1}^{n}\alpha_s^2 c_s. \end{aligned} \tag{2.17}$$

The further treatment below was motivated by that in [42] for cPNP with $Q = 0$. The observation is that, since $\sum_{s=1}^{n}\alpha_s c_s + Q_j = 0$ on $\mathcal{S}_j$, one has

$$\alpha_n\frac{\mathrm{d}}{\mathrm{d}\tau}c_n = \mathcal{I}\alpha_n^2 c_n - \alpha_n J_n\sum_{s=1}^{n}\alpha_s^2 c_s.$$

Therefore, system (2.17) on $\mathcal{S}_j$ is equivalent to, for $k = 1, 2, \ldots, n$,

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}\tau}\phi &= -\mathcal{I}, \quad \sum_{s=1}^{n}\alpha_s c_s + Q_j = 0, \\ \frac{\mathrm{d}}{\mathrm{d}\tau}C &= D(J)C, \quad \frac{\mathrm{d}}{\mathrm{d}\tau}J = 0, \quad \frac{\mathrm{d}}{\mathrm{d}\tau}w = b^T C, \end{aligned} \tag{2.18}$$

where $D(J) = \mathcal{I}\Gamma - Jb^T$ with

$$\Gamma = \mathrm{diag}\{\alpha_1, \alpha_2, \cdots, \alpha_n\} \quad \text{and} \quad b^T = \left(\alpha_1^2, \alpha_2^2, \cdots, \alpha_n^2\right).$$

We comment that $\sum_{s=1}^{n}\alpha_s c_s$ is a first integral of the system for C in (2.18). The condition $\sum_{s=1}^{n}\alpha_s c_s + Q_j = 0$ reflects that (2.18) is restricted to $\mathcal{S}_j$ which is invariant under (2.18).

The solution of (2.18) with the initial condition $(\phi^{[j-1,+]}, C^{[j-1,+]}, J, x_{j-1}) \in \omega(N^{[j-1,+]})$ is

$$\begin{aligned} \phi(\tau) &= \phi^{[j-1,+]} - \mathcal{I}\tau, \quad C(\tau) = \mathrm{e}^{D(J)\tau}C^{[j-1,+]}, \\ w(\tau) &= x_{j-1} + \int_0^\tau b^T C(z)\,\mathrm{d}z. \end{aligned} \tag{2.19}$$

Recall that we are looking for regular orbit Λ_j from $\omega(N^{[j-1,+]})$ to $\alpha(N^{[j,-]})$. Assume $w(\tau_j) = x_j$ for some τ_j. Necessarily, $\phi(\tau_j) = \phi^{[j,-]}$ and $C(\tau_j) = C^{[j,-]}$. Evaluate (2.19) at $\tau = \tau_j$ to get

$$\begin{aligned} \phi^{[j,-]} &= \phi^{[j-1,+]} - \mathcal{I}\tau_j, \quad C^{[j,-]} = \mathrm{e}^{D(J)\tau_j}C^{[j-1,+]}, \\ x_j &= x_{j-1} + \int_0^{\tau_j} b^T C(z)\,\mathrm{d}z. \end{aligned} \tag{2.20}$$

Note that $\tau_j > 0$ from the last identity above and that $b^T C(z) \geqslant 0$.

System (2.20) is the condition for the existence of singular orbits connecting B_{j-1} to B_j. In [42], it is shown that, for given $(\phi^{[j-1,+]}, C^{[j-1,+]})$ and $(\phi^{[j,-]}, C^{[j,-]})$, there is a unique solution of (2.19) satisfying (2.20) and $c_k(x) > 0$ for all $x \in (x_{j-1}, x_j)$. We denote the unique J by

$$J^T = \left(J_1^{[j]}, J_2^{[j]}, \ldots, J_n^{[j]}\right). \tag{2.21}$$

The following result is a direct consequence of (2.20) and that $\tau_j > 0$.

Corollary 2.5. *For each j, the drop $\phi^{[j-1,+]} - \phi^{[j,-]}$ of electric potential along the regular orbit Λ_j from x_{j-1} to x_j has the same sign as that of the current $\mathcal{I}$; in particular, $\mathcal{I} = 0$ if and only if $\phi^{[j-1,+]} = \phi^{[j,-]}$ for each j.*

2.3. Matchings at x_j's for singular orbits over $[0, 1]$

Once a singular orbit $\Gamma^{[j-1,+]} \cup \Lambda_j \cup \Gamma^{[j,-]}$ connecting B_{j-1} to B_j over each subinterval $[x_{j-1}, x_j]$ is constructed, those singular orbits will be matched to form one singular orbit to connect B_L to B_R over the whole interval $[0, 1]$. The matching conditions are

$$u_-^{[j]} = u_+^{[j]} \text{ for each } j \text{ and, for each } k,\ J_k^{[j]} \text{ is the same for all } j. \tag{2.22}$$

It turns out the number of matching conditions is exactly the number of pre-assigned unknowns in (2.3). As the result, the matching conditions provide an *algebraic system* that governs the existence and multiplicity of solutions for the BVP (see [39]).

3. Results on current reversal for the case study

We now apply the analysis in previous section to our case study for Q in (A3). Recall that we are searching conditions on the potential $\mathcal{V}_0$ and the permanent charge Q for current reversal moment $\mathcal{I} = \sum_{s=1}^n \alpha_s J_s = 0$.

3.1. Slow and fast dynamics with $\mathcal{I} = 0$

Concerning the slow dynamics, the following results follow directly from (2.16) with $\mathcal{I} = 0$.

Lemma 3.1. *The slow dynamics over $(0, x_1)$ with $\sum_{s=1}^n \alpha_s c_s(x) = -Q_1 = 0$ is given by $\phi(x) = \mathcal{V}_0$ and $c_k(x) = l_k - J_k x$ for $k = 1, 2, \ldots, n$; in particular, $\phi^{[1,-]} = \phi^{[0,+]} = \mathcal{V}_0$ and $c_k^{[1,-]} = l_k - J_k x_1$.*

Lemma 3.2. *The slow dynamics over (x_1, x_2) with $\sum_{s=1}^n \alpha_s c_s(x) + Q_2 = 0$ is given by $\phi(x) = \mathcal{V}^*$ for some unknown $\mathcal{V}^*$ and $c_k(x) = c_k^{[1,+]} - J_k(x - x_1)$ for $k = 1, 2, \ldots, n$; in particular, $\phi^{[2,-]} = \phi^{[1,+]} = \mathcal{V}^*$ and $c_k^{[2,-]} = c_k^{[1,+]} - J_k(x_2 - x_1)$.*

Lemma 3.3. *The slow dynamics over $(x_2, 1)$ with $\sum_{s=1}^n \alpha_s c_s^{[2,+]} = -Q_3 = 0$ is given by $\phi(x) = 0$ and $c_k(x) = r_k + J_k(1 - x)$ for $k = 1, 2, \ldots, n$; in particular, $\phi^{[2,+]} = \phi^{[3,-]} = 0$ and $c_k^{[2,+]} = r_k + J_k(1 - x_2)$.*

We now collect results for the fast dynamics from section 2.2.1 under $\mathcal{I} = 0$.

Lemma 3.4. *The fast layer dynamics over x_1 provides, for $k = 1, 2, \ldots, n$,*

(i) relative to $(0, x_1)$ where $Q(x) = Q_1 = 0$ and $\phi^{[1,-]} = \mathcal{V}_0$:

$$\sum_{s=1}^n \alpha_s c_s^{[1]} \mathrm{e}^{\alpha_s(\phi^{[1]} - \mathcal{V}_0)} = 0, \quad c_k^{[1,-]} = c_k^{[1]} \mathrm{e}^{\alpha_k(\phi^{[1]} - \mathcal{V}_0)};$$

(ii) relative to (x_1, x_2) where $Q(x) = Q_2$ and $\phi^{[1,+]} = \mathcal{V}^*$:

$$\sum_{s=1}^n \alpha_s c_s^{[1]} e^{\alpha_s(\phi^{[1]} - \mathcal{V}^*)} + Q_2 = 0, \quad c_k^{[1,+]} = c_k^{[1]} e^{\alpha_k(\phi^{[1]} - \mathcal{V}^*)};$$

(iii) the matching $u_-^{[1]} = u_+^{[1]}$: $\sum_{s=1}^n c_s^{[1,-]} = \sum_{s=1}^n c_s^{[1,+]} + Q_2(\phi^{[1]} - \mathcal{V}^*)$.

Lemma 3.5. *The fast layer dynamics over x_2 provides, for $k = 1, 2, \ldots, n$,*

(i) relative to (x_1, x_2) where $Q(x) = Q_2$ and $\phi^{[2,-]} = \mathcal{V}^*$:

$$\sum_{s=1}^n \alpha_s c_s^{[2]} \mathrm{e}^{\alpha_s(\phi^{[2]} - \mathcal{V}^*)} + Q_2 = 0, \quad c_k^{[2,-]} = c_k^{[2]} \mathrm{e}^{\alpha_k(\phi^{[2]} - \mathcal{V}^*)};$$

(ii) relative to $(x_2, 1)$ *where* $Q(x) = Q_3 = 0$ *and* $\phi^{[2,+]} = 0$*:*

$$\sum_{s=1}^{n} \alpha_s c_s^{[2]} \mathrm{e}^{\alpha_s \phi^{[2]}} = 0, \quad c_k^{[2,+]} = c_k^{[2]} \mathrm{e}^{\alpha_s \phi^{[2]}};$$

(ii) the matching $u_-^{[2]} = u_+^{[2]}$*:* $\sum_{s=1}^{n} c_s^{[2,-]} + Q_2(\phi^{[2]} - \mathcal{V}^*) = \sum_{s=1}^{n} c_s^{[2,+]}$.

Following from the above lemmas, we immediately have, for $k = 1, 2, \ldots, n$,

$$\begin{aligned}
&\phi^{[1,-]} = \phi^{[0,+]} = \mathcal{V}_0, \quad \phi^{[2,-]} = \phi^{[1,+]} = \mathcal{V}^*, \quad \phi^{[2,+]} = \phi^{[3,-]} = 0,\\
&c_k^{[1,-]} = c_k^{[1]} \mathrm{e}^{\alpha_k(\phi^{[1]} - \mathcal{V}_0)}, \quad c_k^{[1,+]} = c_k^{[1]} \mathrm{e}^{\alpha_k(\phi^{[1]} - \mathcal{V}^*)},\\
&c_k^{[2,-]} = c_k^{[2]} \mathrm{e}^{\alpha_k(\phi^{[2]} - \mathcal{V}^*)}, \quad c_k^{[2,+]} = c_k^{[2]} \mathrm{e}^{\alpha_k \phi^{[2]}}.
\end{aligned}$$

The remaining relations are

$$\begin{aligned}
&c_k^{[1]} \mathrm{e}^{\alpha_k(\phi^{[1]} - \mathcal{V}_0)} = l_k - J_k x_1; \quad c_k^{[2]} \mathrm{e}^{\alpha_k \phi^{[2]}} = r_k + J_k(1 - x_2);\\
&c_k^{[2]} \mathrm{e}^{\alpha_k(\phi^{[2]} - \mathcal{V}^*)} = c_k^{[1]} \mathrm{e}^{\alpha_k(\phi^{[1]} - \mathcal{V}^*)} - J_k(x_2 - x_1);\\
&\sum_{s=1}^{n} \alpha_s c_s^{[1]} \mathrm{e}^{\alpha_s(\phi^{[1]} - \mathcal{V}^*)} + Q_2 = 0,\\
&\sum_{s=1}^{n} c_s^{[1]} \mathrm{e}^{\alpha_s(\phi^{[1]} - \mathcal{V}_0)} = \sum_{s=1}^{n} c_s^{[1]} \mathrm{e}^{\alpha_s(\phi^{[1]} - \mathcal{V}^*)} + Q_2(\phi^{[1]} - \mathcal{V}^*),\\
&\sum_{s=1}^{n} c_s^{[2]} \mathrm{e}^{\alpha_s(\phi^{[2]} - \mathcal{V}^*)} + Q_2(\phi^{[2]} - \mathcal{V}^*) = \sum_{s=1}^{n} c_s^{[2]} \mathrm{e}^{\alpha_s \phi^{[2]}}.
\end{aligned} \tag{3.1}$$

Together with $\mathcal{I} = 0$, we will determine $(\phi^{[1]}, \mathcal{V}^*, \phi^{[2]}, c_k^{[1]}, c_k^{[2]}, J_k, Q_2)$.

3.2. A general result for reversal permanent charges Q^*.

For fixed $\mathcal{V}_0$, l_k's and r_k's, we consider the equation

$$g(V, \mathcal{V}_0) := \sum_{s=1}^{n} \frac{\alpha_s (l_s \mathrm{e}^{\alpha_s \mathcal{V}_0} - r_s)}{1 - x_2 + x_1 \mathrm{e}^{\alpha_s \mathcal{V}_0} + (x_2 - x_1)\mathrm{e}^{\alpha_s V}} = 0. \tag{3.2}$$

Our main result for reversal permanent charges is

Theorem 3.6. *Assume (A1)–(A3). Then* $\mathcal{I} = 0$ *if and only if* $\mathcal{V}^*$ *is a real root of (3.2). To any real root* $V = \mathcal{V}^*$ *of (3.2), there corresponds to a reversal permanent charge* $Q_2 = Q^*$ *given by*

$$Q^* = -\sum_{s=1}^{n} \alpha_s \mathrm{e}^{\alpha_s(\mathcal{V}_0 - \mathcal{V}^*)} \frac{(1 - x_2 + (x_2 - x_1)\mathrm{e}^{\alpha_s \mathcal{V}^*}) l_s + x_1 r_s}{1 - x_2 + x_1 \mathrm{e}^{\alpha_s \mathcal{V}_0} + (x_2 - x_1)\mathrm{e}^{\alpha_s \mathcal{V}^*}}, \tag{3.3}$$

and the corresponding ion fluxes J_k*'s are given by, for* $k = 1, 2, \ldots, n$*,*

$$J_k = \frac{l_k \mathrm{e}^{\alpha_k \mathcal{V}_0} - r_k}{1 - x_2 + x_1 \mathrm{e}^{\alpha_k \mathcal{V}_0} + (x_2 - x_1)\mathrm{e}^{\alpha_k \mathcal{V}^*}}. \tag{3.4}$$

Proof. From the first three equations in (3.1), one has, for $k = 1, 2, \ldots, n$,

$$\left(1 - x_2 + x_1 \mathrm{e}^{\alpha_k \mathcal{V}_0} + (x_2 - x_1)\mathrm{e}^{\alpha_k \mathcal{V}^*}\right) J_k = l_k \mathrm{e}^{\alpha_k \mathcal{V}_0} - r_k.$$

The formula (3.4) for J_k then follows directly. In turn, the equation (3.2) for $\mathcal{V}^*$ follows from $\mathcal{I} = \sum \alpha_s J_s = 0$ and (3.4).

The first equation and the fourth equation in (3.1) give that

$$Q^* = -\sum_{s=1}^{n} \alpha_s (l_s - J_s x_1) e^{\alpha_s(\mathcal{V}_0 - \mathcal{V}^*)}. \tag{3.5}$$

Substitution of (3.4) into (3.5) yields the formula (3.3). □

Note that

$$g(-\infty, \mathcal{V}_0) = \lim_{V\to-\infty} g(V, \mathcal{V}_0) = \sum_{\alpha_s>0} \frac{\alpha_s(l_s e^{\alpha_s \mathcal{V}_0} - r_s)}{1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}},$$
$$g(+\infty, \mathcal{V}_0) = \lim_{V\to+\infty} g(V, \mathcal{V}_0) = \sum_{\alpha_s<0} \frac{\alpha_s(l_s e^{\alpha_s \mathcal{V}_0} - r_s)}{1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}}.$$

Concerning the equation (3.2), the following result is straightforward and is consistent with the simple property in proposition 1.1.

Lemma 3.7. *If $g(-\infty, \mathcal{V}_0)g(\infty, \mathcal{V}_0) < 0$, then $g(V, \mathcal{V}_0) = 0$ has at least one real root $V = \mathcal{V}^*$, and hence, there is a reversal permanent charge Q^*.*

In general, the existence of a real root of $g(V, \mathcal{V}_0) = 0$ can be formulated as an eigenvalue problem of a matrix or a matrix pencil (see section 3.4). But, a simple version of a sufficient and necessary condition for the existence is not yet available.

Corollary 3.8. *For any reversal permanent charge Q^* associated to a real root $\mathcal{V}^*$ of (3.2), the zeroth order approximation of the electric potential $\phi(x; \varepsilon)$ is given explicitly by*

$$\phi(x; 0) = \begin{cases} \mathcal{V}_0, & x \in (x_0, x_1) \\ \mathcal{V}^*, & x \in (x_1, x_2) \\ 0, & x \in (x_2, x_3), \end{cases}$$

and the zeroth order approximation of concentrations $c_k(x; \varepsilon)$ are

$$c_k(x; 0) = \begin{cases} l_k - J_k x, & x \in (x_0, x_1) \\ (l_k - J_k x_1) e^{\alpha_k(\mathcal{V}_0 - \mathcal{V}^*)} - J_k(x - x_1), & x \in (x_1, x_2) \\ r_k + J_k(1 - x), & x \in (x_2, x_3). \end{cases}$$

The values $\phi^{[1]}$ and $\phi^{[2]}$ are determined explicitly as

$$\begin{aligned} \phi^{[1]} &= \frac{1}{Q^*} \sum_{s=1}^{n} (l_s - J_s x_1) \left(1 - e^{\alpha_s(\mathcal{V}_0 - \mathcal{V}^*)}\right) + \mathcal{V}^*, \\ \phi^{[2]} &= \frac{1}{Q^*} \sum_{s=1}^{n} (r_s + J_s(1 - x_2)) \left(1 - e^{-\alpha_s \mathcal{V}^*}\right) + \mathcal{V}^*. \end{aligned} \tag{3.6}$$

The values for $c_k^{[1]}$ and $c_k^{[2]}$ are determined explicitly as

$$c_k^{[1]} = (l_k - J_k x_1) e^{-\alpha_k(\phi^{[1]} - \mathcal{V}_0)}, \quad c_k^{[2]} = (r_k + J_k(1 - x_2)) e^{-\alpha_k \phi^{[2]}}. \tag{3.7}$$

Proof. Substituting the first and third equations in (3.1) into the last two equations, one has

$$\sum_{s=1}^{n} (l_s - J_s x_1) = \sum_{s=1}^{n} (l_s - J_s x_1) e^{\alpha_s(\mathcal{V}_0 - \mathcal{V}^*)} + Q^*(\phi^{[1]} - \mathcal{V}^*),$$
$$\sum_{s=1}^{n} (r_s + J_s(1 - x_2)) e^{-\alpha_s \mathcal{V}^*} + Q^*(\phi^{[2]} - \mathcal{V}^*) = \sum_{s=1}^{n} (r_s + J_s(1 - x_2)).$$

The formulas (3.6) for $\phi^{[1]}$ and $\phi^{[2]}$ follow immediately. The first and third equations in (3.1) now give the formulas for $c_k^{[1]}$ and $c_k^{[2]}$. $\square$

We note that the jumps of $\phi(x;0)$ and $c_k(x;0)$ at each location x_1 and x_2 are realized by double layers: $\Gamma^{[1,-]}\cup\Gamma^{[1,+]}$ at x_1 and $\Gamma^{[2,-]}\cup\Gamma^{[2,+]}$ at x_2 (see, e.g., [17, 39]).

We do need $c_k^{[1]}\geqslant 0$ and $c_k^{[2]}\geqslant 0$. It turns out this is always true.

Lemma 3.9. *For $k=1,2,\dots,n$, we have $c_k^{[1]}\geqslant 0$ and $c_k^{[2]}\geqslant 0$, and hence, $c_k^{[1,\pm]}\geqslant 0$ and $c_k^{[2,\pm]}\geqslant 0$. Thus, any solution $\mathcal{V}^*$ of (3.2) provides a physical solution for a current reversal.*

Proof. It follows directly from (3.4) that, for any $1\leqslant k\leqslant n$,

$$l_k - J_k x_1 = \frac{((1-x_2)+(x_2-x_1)e^{\alpha_k\mathcal{V}^*})l_k + x_1 r_k}{1-x_2+x_1e^{\alpha_k\mathcal{V}_0}+(x_2-x_1)e^{\alpha_k\mathcal{V}^*}} > 0, \tag{3.8}$$

$$r_k + J_k(1-x_2) = \frac{l_k(1-x_2)e^{\alpha_k\mathcal{V}_0}+(x_1e^{\alpha_k\mathcal{V}_0}+(x_2-x_1)e^{\alpha_k\mathcal{V}^*})r_k}{1-x_2+x_1e^{\alpha_k\mathcal{V}_0}+(x_2-x_1)e^{\alpha_k\mathcal{V}^*}} > 0.$$

The claim then follows from (3.7). $\square$

3.3. A general result for reversal potential $\mathcal{V}_0$.

In view of the duality of reversal potential $\mathcal{V}_0$ and the reversal permanent charge Q^*, we now present a general result for reversal potential $\mathcal{V}_0$ with Q in (A3). We comment that there are differences between these two problems. There is a simple necessary condition for the existence of the reversal permanent charge Q^* as discussed above. On the other hand, as probably expected, reversal potentials should always exist. This is indeed established below for the special case of permanent charges Q in (A3).

Theorem 3.10. *For any given permanent charge Q in (A3), reversal potentials always exist, and the number of reversal potentials is odd.*

Proof. Due to (3.2) and (3.3), it amounts to prove that, for any Q_2, there is a (real) solution $(V,\mathcal{V}_0)$ of the system

$$g(V,\mathcal{V}_0)=0 \qquad \text{and} \qquad f(V,\mathcal{V}_0)+Q_2=0$$

where $g(V,\mathcal{V}_0)$ is defined in (3.2) and

$$f(V,\mathcal{V}_0)=\sum_{s=1}^n \alpha_s e^{\alpha_s(\mathcal{V}_0-V)}\frac{(1-x_2+(x_2-x_1)e^{\alpha_s V})l_s + x_1 r_s}{1-x_2+x_1e^{\alpha_s\mathcal{V}_0}+(x_2-x_1)e^{\alpha_s V}}.$$

This will be accomplished in three steps.

Claim 1. For any fixed V, there is a unique $\mathcal{V}_0$ so that $g(V,\mathcal{V}_0)=0$.

Indeed, for any fixed V, one has

$$\lim_{\mathcal{V}_0\to+\infty} g(V,\mathcal{V}_0)>0,\qquad \lim_{\mathcal{V}_0\to-\infty} g(V,\mathcal{V}_0)<0,\qquad \frac{d}{d\mathcal{V}_0}g(V,\mathcal{V}_0)>0.$$

Claim 1 then follows. Denote the solution of $g(V,\mathcal{V}_0)=0$ by $\mathcal{V}_0=h(V)$.

Claim 2. There are $m<M$, independent of V, so that $\mathcal{V}_0=h(V)\in[m,M]$.

Suppose, on the contrary, that the claim is wrong. Then, at least one of the following occurs

(i) $\exists V_n$ such that, as $n\to\infty$, $V_n\to+\infty$ and $\mathcal{V}_0=h(V_n)\to+\infty$;
(ii) $\exists V_n$ such that, as $n\to\infty$, $V_n\to-\infty$ and $\mathcal{V}_0=h(V_n)\to-\infty$;

(iii) $\exists V_n$ such that, as $n \to \infty$, $V_n \to +\infty$ and $\mathcal{V}_0 = h(V_n) \to -\infty$;
(iv) $\exists V_n$ such that, as $n \to \infty$, $V_n \to -\infty$ and $\mathcal{V}_0 = h(V_n) \to +\infty$.

Simple calculations, from the formula of $g(V, \mathcal{V}_0)$ in (3.2), give

$$\lim_{n\to\infty} g(V_n, h(V_n)) > 0 \text{ for case (i)}, \quad \lim_{n\to\infty} g(V_n, h(V_n)) < 0 \text{ for case (ii)},$$
$$\lim_{n\to\infty} g(V_n, h(V_n)) < 0 \text{ for case (iii)}, \quad \lim_{n\to\infty} g(V_n, h(V_n)) > 0 \text{ for case (iv)}.$$

Each case contradicts to that $g(V_n, h(V_n)) = 0$. Claim 2 is then established.

Based on claim 2, one can show easily that

$$\lim_{V\to+\infty} f(V, h(V)) = -\infty \text{ and } \lim_{V\to-\infty} f(V, h(V)) = +\infty. \tag{3.9}$$

Therefore, there is an odd number of roots $V = \mathcal{V}^*$ of $f(\mathcal{V}^*, h(\mathcal{V}^*)) + Q_2 = 0$. With $\mathcal{V}_0 = h(\mathcal{V}^*)$, one then has $g(\mathcal{V}^*, \mathcal{V}_0) = f(\mathcal{V}^*, \mathcal{V}_0) + Q_2 = 0$. □

3.4. An equivalent eigenvalue problem of equation (3.2)

In this part, we transform equation (3.2) to an eigenvalue problem. First of all, it can be checked directly that (3.2) is equivalent to

$$g(V, \mathcal{V}_0) = d + \sum_{s=1}^{n} \frac{w_s}{m_s + n_s e^{|\alpha_s| V}} = 0, \tag{3.10}$$

where

$$d = \sum_{\alpha_s<0} \frac{\alpha_s (l_s e^{\alpha_s \mathcal{V}_0} - r_s)}{1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}}, \quad w_s = \begin{cases} \alpha_s (l_s e^{\alpha_s \mathcal{V}_0} - r_s), & \alpha_s > 0, \\ \dfrac{-\alpha_s (l_s e^{\alpha_s \mathcal{V}_0} - r_s)(x_2 - x_1)}{1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}}, & \alpha_s < 0, \end{cases}$$

$$m_s = \begin{cases} 1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}, & \alpha_s > 0, \\ x_2 - x_1, & \alpha_s < 0, \end{cases} \quad n_s = \begin{cases} x_2 - x_1, & \alpha_s > 0, \\ 1 - x_2 + x_1 e^{\alpha_s \mathcal{V}_0}, & \alpha_s < 0. \end{cases}$$

Note that $m_s > 0$ and $n_s > 0$ for all s. We assume

$$\frac{m_i}{n_i} + e^{|\alpha_i| \mathcal{V}} \neq \frac{m_j}{n_j} + e^{|\alpha_j| V} \quad \text{for } i \neq j.$$

Otherwise, the corresponding two terms can be combined into a single term. Using the substitution $t = e^V$, one has

$$h(t) = g(V, \mathcal{V}_0) = d + \sum_{s=1}^{n} \frac{w_s}{m_s + n_s t^{|\alpha_s|}}.$$

Note $|\alpha_1|, |\alpha_2|, \ldots, |\alpha_n|$ are positive integers. For each fixed s, define

$$P_s = \begin{bmatrix} 0 & \ldots & 0 & -\dfrac{m_s}{n_s} \\ 1 & \ddots & \ddots & \vdots \\ & \ddots & \ddots & \vdots \\ & & 1 & 0 \end{bmatrix}_{|\alpha_s| \times |\alpha_s|}, \quad e_1 = \begin{bmatrix} 1 \\ 0 \\ \vdots \\ 0 \end{bmatrix}, \quad e_{|\alpha_s|} = \begin{bmatrix} 0 \\ \vdots \\ 0 \\ 1 \end{bmatrix}.$$

Then, for $t > 0$,

$$\det(tI - P_s) = t^{|\alpha_s|} + \frac{m_s}{n_s},$$

and the $(|\alpha_s|, 1)$-entry of $(tI - P_s)^{-1}$ is $(\det(tI - P_s))^{-1}$. Hence

$$\frac{w_s}{n_s} \mathrm{e}^T_{|\alpha_s|}(tI - P_s)^{-1} e_1 = \frac{w_s}{m_s + n_s t^{|\alpha_s|}}.$$

Define

$$u = \begin{bmatrix} \frac{w_1}{n_1} e_{|\alpha_1|} \\ \vdots \\ \frac{w_n}{n_n} e_{|\alpha_n|} \end{bmatrix}, \quad v = \begin{bmatrix} e_1 \\ \vdots \\ e_1 \end{bmatrix}, \quad P = \mathrm{diag}(P_1, \ldots, P_n).$$

Then $h(t) = d + u^T(tI - P)^{-1} v$. For the pencil

$$t \begin{bmatrix} I & 0 \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} P & v \\ u^T & d \end{bmatrix} = \begin{bmatrix} tI - P & -v \\ -u^T & -d \end{bmatrix}, \tag{3.11}$$

one has

$$\begin{bmatrix} I & 0 \\ u^T(tI - P)^{-1} & 1 \end{bmatrix} \begin{bmatrix} tI - P & -v \\ -u^T & -d \end{bmatrix} = \begin{bmatrix} tI - P & -v \\ 0 & -h(t) \end{bmatrix}.$$

Since $tI - P$ is invertible for $t > 0$, one has $h(t) = 0$ if and only if

$$\det \left(t \begin{bmatrix} I & 0 \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} P & v \\ u^T & d \end{bmatrix} \right) = 0,$$

or equivalently, t is a positive zero of $h(t)$ if and only if t is a positive eigenvalue of the pencil (3.11). If $d \neq 0$, then

$$\begin{bmatrix} I & -\frac{1}{d} v \\ 0 & 1 \end{bmatrix} \left(t \begin{bmatrix} I & 0 \\ 0 & 0 \end{bmatrix} - \begin{bmatrix} P & v \\ u^T & d \end{bmatrix} \right) = \begin{bmatrix} tI - (P - vu^T/d) & 0 \\ -u^T & -d \end{bmatrix}.$$

The eigenvalues of the pencil are just those of the matrix $P - d^{-1} vu^T$. Although P, u, v have simple forms, it is still hard to detect whether the matrix has a positive eigenvalue analytically. On the other hand, the eigenvalue formulation provides a numerical tool for testing the existence of $\mathcal{V}^*$ when the values of the other parameters are given.

The above process is called a *minimal realization*, which is a fundamental tool in systems and control theory [20,33,34]. Here it serves as a tool that transforms the problem about zeros of a rational matrix function to the eigenvalue problem of a matrix or matrix pencil.

4. Further specifics and more features

In this section, we will illustrate applications of equation (3.2) for more specific cases, provide a number of interesting features for reversal permanent charges, and include a discussion on the results from physical considerations.

4.1. $n = 2$ with $\alpha_1 > 0 > \alpha_2$.

This might be Na^+Cl^-, K^+Cl^-, or $Ca^{++}Cl_2^-$. For this case, we are able to give a precise condition for the existence of a reversal permanent charge and will discuss an interesting feature.

4.1.1. A complete result on reversal permanent charges

Proposition 4.1. *There exists a reversal permanent charge Q^* if and only if*

$$(l_1 e^{\alpha_1 \mathcal{V}_0} - r_1)(l_2 e^{\alpha_2 \mathcal{V}_0} - r_2) > 0. \tag{4.1}$$

In this case, the reversal permanent charge Q^* is unique.

The values of Q^* and $\mathcal{V}^*$ have the same sign that is determined as follows.

(i) If $l_2 e^{\alpha_2 \mathcal{V}_0} - r_2 > 0$ and $\mathcal{V}_0 > 0$, then $\mathcal{V}^* > \mathcal{V}_0 > 0$ and $Q^* > 0$;
(ii) If $l_1 e^{\alpha_1 \mathcal{V}_0} - r_1 > 0$ and $\mathcal{V}_0 < 0$, then $\mathcal{V}^* < \mathcal{V}_0 < 0$ and $Q^* < 0$;
(iii) If $l_1 e^{\alpha_1 \mathcal{V}_0} - r_1 < 0$ and $\mathcal{V}_0 > 0$, then $\mathcal{V}^* < 0 < \mathcal{V}_0$ and $Q^* < 0$;
(iv) If $l_2 e^{\alpha_2 \mathcal{V}_0} - r_2 < 0$ and $\mathcal{V}_0 < 0$, then $\mathcal{V}^* > 0 > \mathcal{V}_0$ and $Q^* > 0$.

In particular, $\mathcal{V}^*$ lies outside of the interval between 0 and $\mathcal{V}_0$ but could be on either side, and Q^* always has the same sign as that of $\mathcal{V}^*$.

Proof. Using the electroneutrality conditions $\alpha_1 l_1 + \alpha_2 l_2 = \alpha_1 r_1 + \alpha_2 r_2 = 0$, equation (3.2) becomes $\chi(V) = \delta(r_1/l_1)$ where

$$\chi(V) = \frac{1 - x_2 + x_1 e^{\alpha_2 \mathcal{V}_0} + (x_2 - x_1) e^{\alpha_2 V}}{1 - x_2 + x_1 e^{\alpha_1 \mathcal{V}_0} + (x_2 - x_1) e^{\alpha_1 V}} \quad \text{and} \quad \delta(\rho) = \frac{e^{\alpha_2 \mathcal{V}_0} - \rho}{e^{\alpha_1 \mathcal{V}_0} - \rho}. \tag{4.2}$$

The left hand side is positive. Thus, a necessary condition for the existence of a real root of (3.2) is $(l_1 e^{\alpha_1 \mathcal{V}_0} - r_1)(l_1 e^{\alpha_2 \mathcal{V}_0} - r_1) > 0$, or equivalently,

$$(l_1 e^{\alpha_1 \mathcal{V}_0} - r_1)(l_2 e^{\alpha_2 \mathcal{V}_0} - r_2) > 0. \tag{4.3}$$

The function $\chi(V)$ is decreasing in V with the range $(0, \infty)$. Therefore, the necessary condition (4.3) implies that (3.2) has a unique solution, which leads to a reversal permanent charge Q^*.

For the statement on the signs of Q^* and $\mathcal{V}^*$, we demonstrate the proof for (i). Under the conditions in (i), it can be verified directly that

$$\chi(\mathcal{V}_0) = \frac{1 - x_2 + x_1 e^{\alpha_2 \mathcal{V}_0} + (x_2 - x_1) e^{\alpha_2 \mathcal{V}_0}}{1 - x_2 + x_1 e^{\alpha_1 \mathcal{V}_0} + (x_2 - x_1) e^{\alpha_1 \mathcal{V}_0}} > \frac{l_1 e^{\alpha_2 \mathcal{V}_0} - r_1}{l_1 e^{\alpha_1 \mathcal{V}_0} - r_1} = \delta(r_1/l_1).$$

Since $\chi(V)$ is decreasing in V, we have $\mathcal{V}^* > \mathcal{V}_0$. Now, from (3.5),

$$Q^* = \alpha_1 (l_1 - J_1 x_1)\Big(e^{\alpha_2(\mathcal{V}_0 - \mathcal{V}^*)} - e^{\alpha_1(\mathcal{V}_0 - \mathcal{V}^*)}\Big).$$

The right-hand-side is positive due to $l_1 - J_1 x_1 > 0$ from (3.8), $\alpha_1 > 0 > \alpha_2$ and $\mathcal{V}^* > \mathcal{V}_0$. One concludes that $Q^* > 0$. □

We comment that case (i) and case (iv) are equivalent—one can be obtained from the other by flipping the channel. Similarly, case (ii) and case (iii) are equivalent.

Example 4.2. We provide a simple numerical study to illustrate our result. Consider $\alpha_1 = 2$, $\alpha_2 = -1$, $\mathcal{V}_0 = 0.1$, $l_1 = 1$, $l_2 = 2$, $r_1 = r$, $r_2 = 2r$, $x_1 = 1/4$ and $x_2 = 3/8$. Recall, from (4.2), $V = \mathcal{V}^*$ solves $\chi(V) = \delta(r)$ where

$$\chi(V) = \frac{5 + 2e^{-1/10} + e^{-V}}{5 + 2e^{1/5} + e^{2V}} \text{ and } \delta(r) = \frac{e^{-1/10} - r}{e^{1/5} - r}.$$

Figure 2 shows the graph of $\chi(V)$ and the lines of $\delta(r)$ with $r = 0, 0.5, 2, \infty$. For $r = 0.5$ and 2, the corresponding values are given in table 1.

Note when r increases from 0 to $e^{-\mathcal{V}_0}$, $\delta(r)$ decreases from $e^{-3\mathcal{V}_0}$ to 0; and when r increases from $e^{2\mathcal{V}_0}$ to ∞, $\delta(r)$ decreases from ∞ to 1. For $r \geqslant 0$, $\delta(r)$ can not take any value in the interval $(\delta(0),\ 1)$.

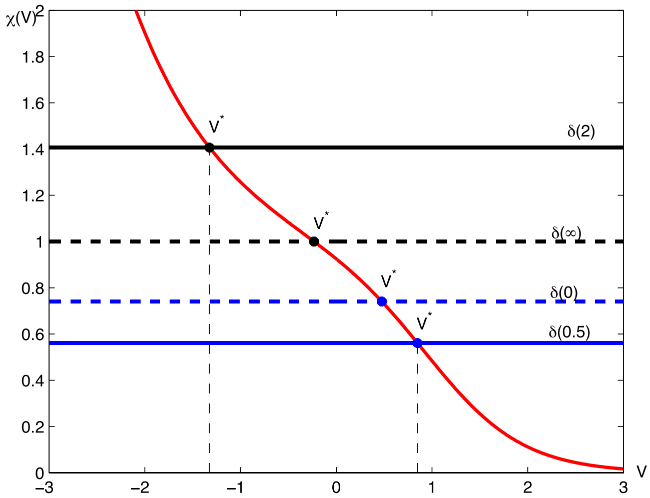

Figure 2. Values of $\mathcal{V}^*$ with different r in example 4.2.

Table 1. Data in the first row correspond to case (i) in proposition 4.1 and second row to case (iii).

$r_1 = r$	$\mathcal{V}^*$	Q^*	J_1	J_2
0.5	0.8482	3.356	0.4475	0.895
2	−1.324	−41.09	−0.829	−1.658

4.1.2. An interesting property of individual ion fluxes. In attempting to understand how the reversal permanent charge Q^* affects individual ion fluxes J_1 and J_2, *an interesting feature was discovered that may not be totally intuitive*. Take the case (i) in proposition 4.1 with $\alpha_1 = 1$ and $\alpha_2 = -1$ for example. To make the discussion easy to follow, we use $J_k(Q_2)$ to denote the dependence of J_k on the value Q_2 for the permanent charge Q in (A3). In this case, $l_1 = l_2$ and $r_1 = r_2$. If $r_2 < e^{-\mathcal{V}_0} l_2$ (and hence $r_1 < e^{\mathcal{V}_0} l_1$ as well), then $J_1(Q_2) > 0$ and $J_2(Q_2) > 0$ from (1.6). If $Q = 0$, then $\mathcal{I}$ and $\mathcal{V}_0$ have the same sign; that is, $\mathcal{I} = J_1(0) - J_2(0) > 0$ since $\mathcal{V}_0 > 0$. As Q_2 increases from 0 to $Q^* > 0$, one might suspect that the ion flux $J_1(Q_2)$ of the positively charged ions should tend to *reduce* while the ion flux $J_2(Q_2)$ should *increase*, and the value $Q^* > 0$ would be the right amount of positive charges to produce zero current. This is NOT true in general. In fact, we have the following result.

Proposition 4.3. *Consider $n = 2$ with $\alpha_1 = 1$ and $\alpha_2 = -1$ (so $l_1 = l_2 = l$ and $r_1 = r_2 = r$ due to electroneutrality boundary conditions). Assume $r < \mathrm{e}^{-\mathcal{V}_0} l$ and $\mathcal{V}_0 > 0$ (so that $J_1(0) > J_2(0) > 0$). For some choices of parameters, one may have $J_1(0) > J_2(0) > J_1(Q^*) = J_2(Q^*)$.*

Proof. It is known (see, e.g. [1, 38]) that, for $Q_2 = 0$,

$$J_1(0) = (l - r)\Big(1 + \frac{\mathcal{V}_0}{\ln l - \ln r}\Big) \text{ and } J_2(0) = (l - r)\Big(1 - \frac{\mathcal{V}_0}{\ln l - \ln r}\Big).$$

Therefore, $J_2(0) > J_1(Q^*) = J_2(Q^*)$ if and only if

$$(x_2 - x_1)\mathrm{e}^{\mathcal{V}^*} > \frac{l\mathrm{e}^{\mathcal{V}_0} - r}{l - r} \frac{\ln l - \ln r}{\ln l - \ln r - \mathcal{V}_0} - 1 + x_2 - x_1 \mathrm{e}^{\mathcal{V}_0}. \tag{4.4}$$

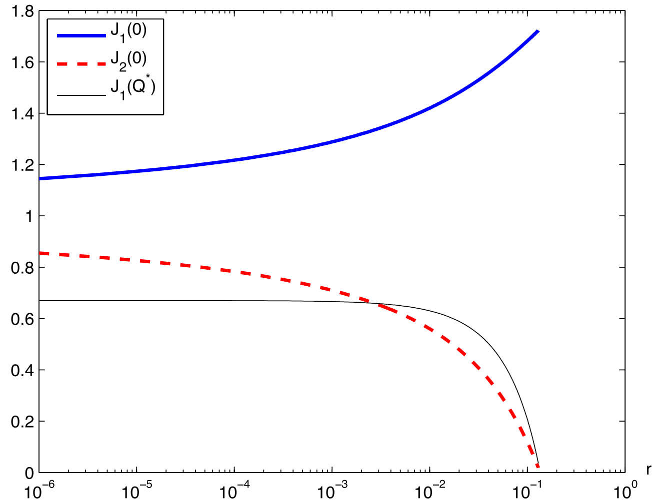

Figure 3. Graphs of $J_1(0)$, $J_2(0)$ and $J_1(Q^*) = J_2(Q^*)$ as functions of r. The top curve is the graph of $J_1(0)$, the dashed curve is that of $J_2(0)$, and the thin curve is that of $J_1(Q^*) = J_2(Q^*)$.

It follows from (3.2) that $\mathcal{V}^*$ satisfies

$$e^{\mathcal{V}^*} = \frac{B + \sqrt{B^2 + 4(x_2 - x_1)^2(l\mathrm{e}^{-\mathcal{V}_0} - r)(l\mathrm{e}^{\mathcal{V}_0} - r)}}{2(x_2 - x_1)(l\mathrm{e}^{-\mathcal{V}_0} - r)},$$

where $B = ((1 - x_2)l + x_1 r)(\mathrm{e}^{\mathcal{V}_0} - \mathrm{e}^{-\mathcal{V}_0})$.

For fixed $\mathcal{V}_0$, as $l/r \to \infty$, one has

$$e^{\mathcal{V}^*} \to \frac{(1 - x_2)(\mathrm{e}^{2\mathcal{V}_0} - 1) + \sqrt{(1 - x_2)^2(\mathrm{e}^{2\mathcal{V}_0} - 1)^2 + 4(x_2 - x_1)^2\mathrm{e}^{2\mathcal{V}_0}}}{2(x_2 - x_1)}.$$

As $l/r \to \infty$, the right-hand-side of (4.4) approaches $(1 - x_1)e^{\mathcal{V}_0} - 1 + x_2$.

Therefore, for any fixed x_1 and x_2 with $0 < x_1 < x_2 < 1$, the inequality (4.4) holds if $\mathcal{V}_0$ is large enough and l/r is large enough. □

Example 4.4. In this example we consider

$$\alpha_1 = 1 = -\alpha_2; \quad \mathcal{V}_0 = 2, \; l_1 = l_2 = 1, \; r_1 = r_2 = r; \quad x_1 = 1/4, \; x_2 = 7/8$$

and vary r in $[10^{-6}, 0.1296]$ ($0.1296 < \mathrm{e}^{-2}$). The graphs of $J_1(0)$, $J_2(0)$, and $J_1(Q^*) = J_2(Q^*)$, which are considered as functions of r, are plotted in figure 3. For $r < 0.0027$, one has $J_2(0) > J_1(Q^*) = J_2(Q^*)$.

4.2. $n = 3$ with $\alpha_1 = 1$, $\alpha_2 = 2$ and $\alpha_3 = -1$

This case might be for a mixture of $Ca^{++}Cl_2^-$ and Na^+Cl^-.

In this case, $l_1 + 2l_2 - l_3 = 0$ and $r_1 + 2r_2 - r_3 = 0$. We will show it is possible that, for fixed $\mathcal{V}_0$, $g(V, \mathcal{V}_0)$ has two real zeros, each leading to a reversal permanent charge—*a new feature that does not occur for ion solutions with only two distinct valences*.

Proposition 4.5. *For appropriate choices of $\mathcal{V}_0$, l_k's and r_k's, $g(V, \mathcal{V}_0) = 0$ has at least two real roots.*

Proof. The statement will be established by showing that, it is possible to have $g(-\infty, \mathcal{V}_0) > 0$, $g(+\infty, \mathcal{V}_0) > 0$ and $g(V_1, \mathcal{V}_0) < 0$ for some V_1.

We first rewrite $g(V, \mathcal{V}_0)$ as

$$g(V, \mathcal{V}_0) = \frac{N - (x_2 - x_1)\left(2(r_2 - l_2 e^{2\mathcal{V}_0}) - (l_1 e^{\mathcal{V}_0} - r_1)e^{V}\right)e^{V}}{(1 - x_2 + x_1 e^{\mathcal{V}_0} + (x_2 - x_1)e^{V})(1 - x_2 + x_1 e^{2\mathcal{V}_0} + (x_2 - x_1)e^{2V})} + \frac{r_1 + 2r_2 - (l_1 + 2l_2)e^{-\mathcal{V}_0}}{1 - x_2 + x_1 e^{-\mathcal{V}_0} + (x_2 - x_1)e^{-V}},$$

where

$$N = (l_1 e^{\mathcal{V}_0} - r_1)(1 - x_2 + x_1 e^{2\mathcal{V}_0}) + 2(l_2 e^{2\mathcal{V}_0} - r_2)(1 - x_2 + x_1 e^{\mathcal{V}_0}).$$

It is clear that $g(-\infty, \mathcal{V}_0)$ has the same sign as that of N.

We now fix $\mathcal{V}_0 > 0$ and choose (l_1, r_1) so that $0 < l_1 e^{-\mathcal{V}_0} < r_1 < l_1 e^{\mathcal{V}_0}$. We will also fix l_2. Next, we choose V_1 to be determined later on so that

$$N = (x_2 - x_1)(l_1 e^{\mathcal{V}_0} - r_1)e^{2V_1} > 0;$$

in particular, $g(-\infty, \mathcal{V}_0) > 0$. In view of the definition of N, we have

$$r_2 = l_2 e^{2\mathcal{V}_0} + \frac{l_1 e^{\mathcal{V}_0} - r_1}{2}\,\frac{1 - x_2 + x_1 e^{2\mathcal{V}_0} - (x_2 - x_1)e^{2V_1}}{1 - x_2 + x_1 e^{\mathcal{V}_0}}. \tag{4.5}$$

It is clear that there is a number M such that, if $V_1 < M$, then

$$1 - x_2 + x_1 e^{2\mathcal{V}_0} - (x_2 - x_1)e^{2V_1} > 0,$$

and hence, $r_2 - l_2 e^{2\mathcal{V}_0} > 0$, and

$$r_3 - l_3 e^{-\mathcal{V}_0} = r_1 + 2r_2 - (l_1 + 2l_2)e^{-\mathcal{V}_0} > 2r_2 - 2l_2 e^{2\mathcal{V}_0} > 0. \tag{4.6}$$

In particular,

$$g(+\infty, \mathcal{V}_0) = -\frac{l_3 e^{-\mathcal{V}_0} - r_3}{1 - x_2 + x_1 e^{-\mathcal{V}_0}} > 0.$$

Note that

$$g(V_1, \mathcal{V}_0) = \frac{-(x_2 - x_1)\left(2(r_2 - l_2 e^{2\mathcal{V}_0}) - 2(l_1 e^{\mathcal{V}_0} - r_1)e^{V_1}\right)e^{V_1}}{(1 - x_2 + x_1 e^{\mathcal{V}_0} + (x_2 - x_1)e^{V_1})(1 - x_2 + x_1 e^{2\mathcal{V}_0} + (x_2 - x_1)e^{2V_1})} + \frac{r_1 + 2r_2 - (l_1 + 2l_2)e^{-\mathcal{V}_0}}{1 - x_2 + x_1 e^{-\mathcal{V}_0} + (x_2 - x_1)e^{-V_1}}.$$

It follows from (4.5) and (4.6) that, as $V_1 \to -\infty$,

$$r_2 \to l_2 e^{2\mathcal{V}_0} + \frac{l_1 e^{\mathcal{V}_0} - r_1}{2}\,\frac{1 - x_2 + x_1 e^{2\mathcal{V}_0}}{1 - x_2 + x_1 e^{\mathcal{V}_0}},$$

$$r_3 \to r_1 + 2l_2 e^{2\mathcal{V}_0} + (l_1 e^{\mathcal{V}_0} - r_1)\frac{1 - x_2 + x_1 e^{2\mathcal{V}_0}}{1 - x_2 + x_1 e^{\mathcal{V}_0}}.$$

A direct calculation also gives, as $V_1 \to -\infty$,

$$e^{-V_1} g(V_1, \mathcal{V}_0) \to -\frac{(x_2 - x_1)(l_1 e^{\mathcal{V}_0} - r_1)}{(1 - x_2 + x_1 e^{\mathcal{V}_0})^2}\left(1 - \frac{(1 - x_2 + x_1 e^{\mathcal{V}_0})(1 - x_2 + x_1 e^{2\mathcal{V}_0})}{(x_2 - x_1)^2}\right) + \frac{1}{x_2 - x_1}\left(r_1 - l_1 e^{-\mathcal{V}_0} + 2l_2(e^{2\mathcal{V}_0} - e^{-\mathcal{V}_0})\right).$$

It is easy to see that, as $(x_1, x_2) \to (0, 1)$, the first term on the right-hand-side approaches $-\infty$ and the second term approaches a finite number. Thus one can choose x_1 and x_2 so that the right-hand-side is strictly less than zero. By continuity, if V_1 is small enough, then $g(V_1, \mathcal{V}_0) < 0$. $\square$

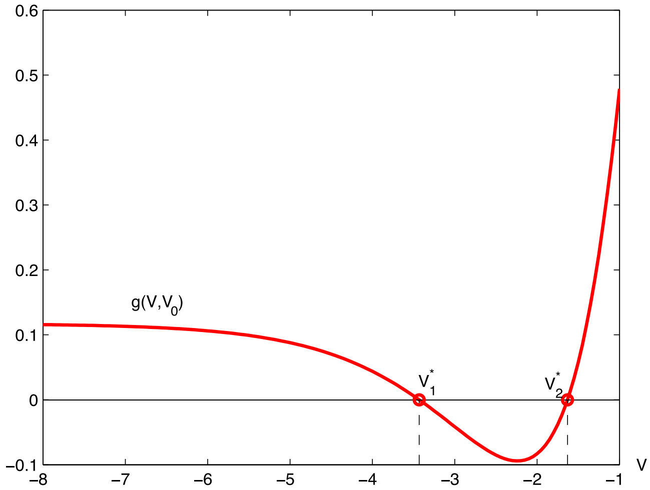

Figure 4. Graph of $g(V, \mathcal{V}_0)$ in example 4.6.

Table 2. First row correspond to $\mathcal{V}_1^*$ and second row to $\mathcal{V}_2^*$ in example 4.6.

$\mathcal{V}^*$	Q^*	J_1	J_2	J_3
−3.4328	−3509.028	1.9038	−0.99783	−0.091840
−1.6314	−99.138	1.2574	−0.89723	−0.53702

Example 4.6. We illustrate the result in proposition 4.5 for a concrete set of boundary conditions and locations for a permanent charge. We choose

$$\mathcal{V}_0 = 1/4, \quad (l_1, l_2, l_3) = (1, 1, 3), \quad (r_1, r_2, r_3) = (0.8,\ 1.91385,\ 4.62770),$$

$x_1 = 0.1$ and $x_2 = 0.9$. Note that electroneutrality conditions are satisfied.

Figure 4 shows the graph of $g(V, \mathcal{V}_0)$ on interval $[-8, -1]$. The function $g(V, \mathcal{V}_0)$ is decreasing on $(-\infty, V_{\rm min})$ and is increasing on $(V_{\rm min}, \infty)$, and has one minimum at a point $V_{\rm min} \in (-3, -2)$. So $g(V, \mathcal{V}_0) = 0$ has exactly two roots, which are $\mathcal{V}_1^* \approx -3.4328$ and $\mathcal{V}_2^* \approx -1.6314$.

Table 2 provides corresponding values of the reversal permanent charges Q^* and the ion fluxes. Since $\mathcal{V}_1^* < 0 < \mathcal{V}_0$ and $\mathcal{V}_2^* < 0 < \mathcal{V}_0$, proposition 2.4 implies that the reversal permanent charge should be negative. Also, the signs of J_k's are determined by the boundary conditions and are consistent with (1.6).

4.3. Physical discussion

Note that, for both cases (i) and (ii) in proposition 4.1, the individual ion fluxes J_1 and J_2 are positive due to (3.4) and (4.1). But the reversal permanent charges for these two cases have opposite signs. This indicates a complex dependence of the ion current on the boundary conditions and permanent charges. The result in proposition 4.3 suggests another complexity. The existence of possible multiple reversal permanent charges could be thought of a certain version of instability of biological functions.

All these results are presented for the simple setting in this section and already provide strong evidence for a very rich and complex phenomena of electrodiffusion. Of course, extensive further studies should reveal more important phenomena.

The complexity presented in these results reflect the physical essence of the problem. The ion flux of each ion contains diffusion and migration terms and these can have opposite signs depending on the size and sign of the gradients of electrical and chemical potential (e.g., concentration). It is precisely the various combinations of these gradients that make possible the rich behaviour of semiconductor devices and (presumably) channels and transporters. Engineers adjust parameters so that particular terms dominate in particular parts of a transistor (e.g., the junctions between source and gate or gate and drain in field effect transistors) and thus can combine to produce particular characteristics of semiconductor devices. Evolution may use similar tactics, but that has not yet been established.

5. Conclusion

In this paper, we provide a mathematical analysis of qualitative properties of cPNP models of ion channels. The specific questions about reversal potentials and reversal permanent charges studied in this paper are among the central issues of biological functions. Based on the cPNP model with the equal diffusion coefficients assumption and for a simple profile of permanent charges, we are able to reduce the problem significantly to a single equation (3.2) that involves only physical parameters of the biological problem. As an illustration, a number of interesting properties are resulted from analyses of this governing equation. The success of our case study relies heavily on a recent advance of a *general* geometric singular perturbation framework and, most importantly, some *special* structures of the cPNP models—the integrals in proposition 2.1 for the nonlinear limiting fast system (2.6) and the rescaling that converts the nonlinear limiting slow system (2.16) to a linear system (2.17) or (2.18). (Strictly speaking, the linear system (2.18) presents a nonlinear problem due to the dependence of the coefficient matrix D on the unknown ion fluxes J. See [42] for a rather complete analysis of system (2.18).) It is our belief that these special structures of the cPNP model reflect some intrinsic properties of ionic flows of large number of ions through ion channels. A better understanding of these macroscopic structures deserves further extensive study.

The study in this paper as well as those analytical studies appeared in recent literatures suggest that mathematical analysis can directly address central issues of biological functions, assuming of course that the underlying model of the ion channel is good enough. Extending, refining, and testing the model are thus of great importance. The analysis also suggests that qualitative properties of semiconductor systems could be analysed in a similar way, if this analysis is extended to include more complex geometries of doping, that represent combinations of the junctions that define field effect and bipolar transistors.

Acknowledgments

WL is partially supported by University of Kansas GRF 2301763-099. HX is partially supported by *Deutsche Forschungsgemeinschaft*, through the DFG Research Center MATHEON *Mathematics for Key Technologies* in Berlin, and by *Alexander von Humboldt Foundation*.

References

[1] Abaid N, Eisenberg R S and Liu W 2008 Asymptotic expansions of I–V relations via a Poisson–Nernst–Planck system *SIAM J. Appl. Dyn. Syst.* **7** 1507–26

[2] Barcilon V 1992 Ion flow through narrow membrane channels: I *SIAM J. Appl. Math.* **52** 1391–404

[3] Barcilon V, Chen D-P and Eisenberg R S 1992 Ion flow through narrow membrane channels: II *SIAM J. Appl. Math.* **52** 1405–25

[4] Barcilon V, Chen D-P, Eisenberg R S and Jerome J W 1997 Qualitative properties of steady-state Poisson–Nernst–Planck systems: perturbation and simulation study *SIAM J. Appl. Math.* **57** 631–48

[5] Besteman K, Zevenbergen M A G and Lemay S G 2005 Charge inversion by multivalent ions: dependence on dielectric constant and surface-charge density *Phys. Rev.* E **72** 061501

[6] Blum L 1975 Mean spherical model for asymmetric electrolytes *Mol. Phys.* **30** 1529–35

[7] Blum L and Høye J S 1977 Mean spherical model for asymmetric electrolytes: part 2. Thermodynamic properties and the pair correlation function *J. Phys. Chem.* **81** 1311–16

[8] Burger M, Engl H W, Markowich P A and Pietra P 2001 Identification of doping profiles in semiconductor devices *Inverse Problems* **17** 1765–95

[9] Burger M, Engl H W, Leitao A and Markowich P A 2004 On inverse problems for semiconductor equations *Milan J. Math.* **72** 273–313

[10] Burger M, Eisenberg R S and Engl H W 2007 Inverse problems related to ion channel selectivity *SIAM J. Appl. Math.* **67** 960–89

[11] Chen D P and Eisenberg R S 1993 Charges, currents and potentials in ionic channels of one conformation *Biophys. J.* **64** 1405–21

[12] Chung S and Kuyucak S 2001 Predicting channel function from channel structure using Brownian dynamics simulations *Clin. Exp. Pharmacol. Physiol.* **28** 89–94

[13] Eisenberg B 2003 Ion channels as devices *J. Comput. Electron.* **2** 245–9

[14] Eisenberg R S 1990 Channels as enzymes *J. Memb. Biol.* **115** 1–12

[15] Eisenberg B 2012 Ions in fluctuating channels: transistors alive *Fluctuation Noise Lett.* **11** 76–96

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

[17] Eisenberg B and Liu W 2007 Poisson–Nernst–Planck systems for ion channels with permanent charges *SIAM J. Math. Anal.* **38** 1932–66

[18] Ern A, Joubaud R and Lelièvre T 2012 Mathematical study of non-ideal electrostatic correlations in equilibrium electrolytes *Nonlinearity* **25** 1635–52

[19] Fenichel N 1979 Geometric singular perturbation theory for ordinary differential equations *J. Diff. Eqns* **31** 53–98

[20] Gilbert E G 1963 Controllability and observability in multi-variable control systems *J. SIAM Control Ser.* A **1** 128–51

[21] Gillespie D, Nonner W and Eisenberg R S 2002 Coupling Poisson–Nernst–Planck and density functional theory to calculate ion flux *J. Phys.: Condens. Matter* **14** 12129–45

[22] Gillespie D, Nonner W and Eisenberg R S 2003 Density functional theory of charged and hard-sphere fluids *Phys. Rev.* E **68** 0313503

[23] Hyon Y, Eisenberg B and Liu C 2011 A mathematical model for the hard sphere repulsion in ionic solutions *Commun. Math. Sci.* **9** 459–75

[24] Hyon Y, Fonseca J, Eisenberg B and Liu C 2012 Energy variational approach to study charge inversion (layering) near charged walls *Discrete Contin. Dyn. Syst.* B **17** 2725–43

[25] Hirsch M, Pugh C and Shub M 1977 *Invariant Manifolds* (*Lecture Notes in Mathematics* vol 583) (New York: Springer)

[26] Hodgkin A L, Huxley A and Katz B 1949 Ionic Currents underlying activity in the giant axon of the squid *Arch. Sci. Physiol.* **3** 129–50

[27] Hodgkin A L and Katz B 1949 The effect of sodium ions on the electrical activity of the giant axon of the squid *J. Physiol.* **108** 37–77

[28] Hollerbach U, Chen D-P and Eisenberg R S 2001 Two- and three-dimensional Poisson–Nernst–planck simulations of current flow through Gramicidin-A *J. Comput. Science* **16** 373–409

[29] Im W and Roux B 2002 Ion permeation and selectivity of OmpF porin: a theoretical study based on molecular dynamics, Brownian dynamics and continuum electrodiffusion theory *J. Mol. Biol.* **322** 851–69

[30] Ji S and Liu W 2012 Poisson–Nernst–Planck systems for ion flow with density functional theory for hard-sphere potential: I-V relations and critical potentials: part 1. Analysis *J. Dyn. Diff. Eqns* **24** 955–83

[31] Jones C 1995 Geometric singular perturbation theory *Dynamical systems (Montecatini Terme, 1994)* (*Lecture Notes in Mathematics* vol 1609) (Berlin: Springer) pp 44–118

[32] Jones C and Kopell N 1994 Tracking invariant manifolds with differential forms in singularly perturbed systems *J. Diff. Eqns* **108** 64–88

[33] Kailath T 1980 *Linear Systems* (Englewood Cliffs, NJ: Prentice-Hall)

[34] Kalman R E 1963 Mathematical description of linear dynamical systems *J. SIAM Control Ser.* A **1** 152–92

[35] Li B 2009 Minimizations of electrostatic free energy and the Poisson–Boltzmann equation for molecular solvation with implicit solvent *SIAM J. Math. Anal.* **40** 2536–66

[36] Li B 2009 Continuum electrostatics for ionic solutions with non-uniform ionic sizes *Nonlinearity* **22** 811–33
[37] Lin G, Liu W, Yi Y and Zhang M 2013 Poisson–Nernst–Planck systems for ion flow with a local hard-sphere potential for ion size effects *SIAM J. Appl. Dyn. Syst.* **12** 1613–48
[38] Liu W 2005 Geometric singular perturbation approach to steady-state Poisson–Nernst–Planck systems *SIAM J. Appl. Math.* **65** 754–66
[39] Liu W 2009 One-dimensional steady-state Poisson–Nernst–Planck systems for ion channels with multiple ion species *J. Diff. Eqns* **246** 428–51
[40] Liu W, Tu X and Zhang M 2012 Poisson–Nernst–Planck systems for ion flow with density functional theory for hard-sphere potential: I–V relations and critical potentials: part 2. Numerics *J. Dyn. Diff. Eqns* **24** 985–1004
[41] Liu W and Wang B 2010 Poisson–Nernst–Planck systems for narrow tubular-like membrane channels *J. Dyn. Diff. Eqns* **22** 413–37
[42] Liu W and Xu H 2014 A complete analysis of a classical Poisson–Nernst–Planck model for ionic flow *J. Diff. Eqns* (doi:10.1016/j.jde.2014.10.015)
[43] Luchinsky D G, Tindjong R, Kaufman I, McClintock P V E and Eisenberg R S 2009 Self-consistent analytic solution for the current and the access resistance in open ion channels *Phys. Rev.* E **80** 021925
[44] Miedema H, Vrouenraets M, Wierenga J, Meijberg W, Robillard G and Eisenberg B 2007 A biological porin engineered into a molecular and nanofluidic diode *Nano Lett.* **7** 2886–91
[45] Nadler B, Schuss Z, Singer A and Eisenberg B 2003 Diffusion through protein channels: from molecular description to continuum equations *Nanotechnology* **3** 439–42
[46] Nonner W and Eisenberg R S 1998 Ion permeation and glutamate residues linked by Poisson–Nernst–Planck theory in L-type Calcium channels *Biophys. J.* **75** 1287–305
[47] Nonner W, Catacuzzeno L and Eisenberg B 2000 Binding and selectivity in L-type Calcium channels: a mean spherical approximation *Biophys. J.* **79** 1976–92
[48] Park J-K and Jerome J W 1997 Qualitative properties of steady-state Poisson–Nernst–Planck systems: mathematical study *SIAM J. Appl. Math.* **57** 609–30
[49] Rosenfeld Y 1989 Free-energy model for the inhomogeneous hard-sphere fluid mixture and density-functional theory of freezing *Phys. Rev. Lett.* **63** 980–3
[50] Rosenfeld Y 1993 Free energy model for the inhomogeneous fluid mixtures: Yukawa-charged hard spheres, general interactions and plasmas *J. Chem. Phys.* **98** 8126–48
[51] Schuss Z, Nadler B and Eisenberg R S 2001 Derivation of Poisson and Nernst–Planck equations in a bath and channel from a molecular model *Phys. Rev.* E **64** 1–14
[52] Wei G, Zheng Q, Chen Z and Xia K 2012 Variational multiscale models for charge transport *SIAM Rev.* **54** 699–754
[53] Zhang M Asymptotic expansion and numerical simulations of I–V relation via steady-state Poisson–Nernst–Planck systems *Rocky Mountain J. Math.* in press
[54] Zhou S, Wang Z and Li B 2011 Mean-field description of ionic size effects with nonuniform ionic sizes: a numerical approach *Phys. Rev.* E **84** 021901