

Non-localness of excess potentials and boundary value problems of Poisson-Nernst-Planck systems for ionic flow: a case study

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Abstract

Poisson-Nernst-Planck (PNP) type systems are basic primitive models for ionic flow through ion channels. Important properties of ion channels, such as current-voltage relations, permeation and selectivity, can be extracted from solutions of boundary value problems (BVP) of PNP type models. Many issues of BVP of PNP type systems with *local excess potentials* (including particularly classical PNP systems that treat ions as point-charges) are extensively examined analytically and numerically. On the other hand, for PNP type systems with *nonlocal excess potentials*, even the issue of well-posedness of BVP is poorly understood. In fact, the formulation of correct boundary conditions seems to be overlooked, even though complications of ionic behavior near the boundaries (locations of applied electrodes) have been long experienced in experiments and simulations. PNP type systems with nonlocal excess potentials can be viewed as functional differential systems and, for many approximation models of non-local excess potentials, as differential equations with both delays and advances. Thus PNP type systems with nonlocal excess potentials have infinite degree of freedoms and BVP with the traditional “two-point-boundary-conditions” would be severely under determined. The mathematical theory for PNP with nonlocal excess potential would be significantly different from that for PNP with local excess potentials. Taking into considerations of experimental designs of ionic flow through ion channels and in a relatively simple setting, we present a form of natural “boundary conditions” so that the corresponding BVP of PNP type systems with nonlocal excess potentials are generally well-posed. This work, at an early stage toward a better understanding of related issues, provides some insights on interpretations of experimental designs of imposing boundary conditions and for correct formulations of numerical simulations, and hopefully, will stimulate further mathematical analysis on this important issue.

Key Words. Ionic flows; nonlocal excess potentials; boundary value problems

Running Head. BVP of PNP with non-local excess potentials

1 Introduction

In this introduction, we discuss the basic issue treated in this work: Correct formulations of boundary conditions for boundary value problems (BVP) of Poisson-Nernst-

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Planck (PNP) type models with *nonlocal* excess potentials. We will first briefly describe the background, in layman’s terms, of ionic flow through ion channels and experimental designs and measurements of the so-called I-V relations, the primitive models of PNP type systems and the boundary conditions relevant to the experimental designs. A major difference between PNP type models with nonlocal excess potentials and those with local excess potentials will be addressed. We then provide, in a relatively simpler setting, a formulation of natural boundary conditions for PNP with nonlocal excess potentials.

1.1 Ion channels, ionic flow, and experiments

The process of diffusion and migration of charged particles plays a critical role in understanding of natures and in inventions of modern electric devices ([5, 11, 16, 17, 22, 24, 25, 55, 56, 63]). For examples, chemical sciences deal with charged molecules in water ([10, 11, 21, 31]), all of biology occurs in plasmas of ions and charged organic molecules in water ([3, 18, 39, 68]), and semiconductor technology controls the migration and diffusion of quasi-particles of charge in transistors and integrated circuits ([61, 67, 70]). It is clear that electrodiffusion is of great importance.

In this work, we focus on a specific electrodiffusion problem of ionic flows through ion channels. Ion channels are “nano-pores” of large proteins embedded on cell membranes with one end opens to the intracellular region and the other to the extracellular region. They provide major pathways for ions to flow between inside and outside (two macroscopic reservoirs) of cells that produces electric signals to control most of biological functions. In laboratory designs of experiments on ion channel properties, two large baths (reservoirs) are separated by the ion channel and are filled with ionic solutions with ion species dissolved in water (solvent). Transmembrane electric potential (voltage) is applied, together with the concentration gradient, to create ionic flows through the ion channel. Electrical properties of ionic flows can be measured and ion channel properties can be analyzed from the experimental measurements. For example, once the ionic movement approaches a steady-state, the corresponding current I can be recorded. The experiment is run for a range of voltage values V which results in an I-V relation: *The dependence of the current I on the applied voltage V* for fixed ionic concentrations in the baths. One can extract a great deal of information on ion channel properties such as permeation, selectivity, etc., from I-V relations.

Macroscopic boundary conditions imposed in reservoirs often introduce boundary layers of concentration and charge, which may not meet the expectation of experimental design perfectly. Those complications are not well-understood and cause problems for the measurements of I-V relations, to say the least. To remedy this difficulty, in practice, one implements the four-electrode (or, four-terminal) technique. Two electrodes (outer electrodes) are positioned in the baths and away from the channel to control “boundary conditions”, and the other two electrodes (inner electrodes) near the interfaces of the channel and the baths are used to measure quantities from the ionic flow through the ion channel. This four-electrode technique seems to resolve the problem, for practical purpose, of boundary conditions well. A couple of questions remain: *What causes the complications near the outer electrodes? What is the meaning of boundary conditions near the outer electrodes?* These are important questions

for a true understanding of the experimental designs and measurements. We will give a closer look of these questions in concrete terms of PNP type models for ionic flows in the next part and more discussions will be given in Section 2.

1.2 PNP type models and the issue of boundary conditions

PNP type systems are the basic primitive models for ionic flows. There are different levels of sophistications in PNP models. The classical PNP, using only ideal electrochemical potentials, is at low resolution which treats ions as point-charges. This is reasonable only for near infinite dilute ionic mixtures. The classical Debye-Hückel theory for electrolyte solutions is based on the equilibrium theory – Poisson-Boltzmann approximations – of the classical PNP models. The classical PNP models for ionic flows have been analyzed to a great extent ([1, 4, 7, 8, 9, 19, 20, 27, 28, 40, 42, 44, 47, 49, 50, 54, 57, 58, 64, 65, 71]).

For living organisms, ion sizes do play crucial roles. For example, potassium (K^+) and sodium (Na^+) have significantly different roles and the main distinction between them is their different ion sizes. To capture ion size effects in PNP models, one needs to include the excess (beyond the ideal) components of the electrochemical potentials. There are two types of models for excess components, *local* and *nonlocal*. Here local models refer to those models of which excess components at a point depend on the ionic concentrations *at the given point only*, and nonlocal models are those so that excess components at a point depend on the ionic concentrations *in a neighborhood of the given point*.

Many issues of BVPs of PNP systems with *local* excess potentials (including particularly classical PNP systems) are extensively examined analytically and numerically ([2, 14, 33, 34, 35, 36, 41, 43, 45, 46, 48, 52, 53, 66]). However, for PNP systems with *nonlocal* excess potentials, even the issue of well-posedness of BVPs is poorly understood. In fact, the formulation of correct boundary conditions seems to be overlooked, even though complications of ionic flow near the boundaries have been long experienced in experiments as mentioned above. PNP systems with nonlocal excess potentials can be viewed as functional differential systems and, for many approximation models of the nonlocal excess potentials, as differential equations with both delays and advances. To bring the issue up in a simple way, we consider an initial value problem for a delay-differential equation

$$u'(x) = f(u(x-r)), \quad u \in \mathbb{R}^n \quad (1.1)$$

with a constant *delay* $r > 0$. The initial value problem for this delay-differential equation requires the knowledge of

$$u(x) = u_0(x) \quad \text{for } x \in [-r, 0], \quad (1.2)$$

more than the single value $u(0)$ as for ordinary differential equations. This is simply because that delay-differential equations are of *infinite degree of freedoms* and the phase space of (1.1) should be an infinite dimensional function space, for example, $C^0([-r, 0])$ (see, for example, [37, 38]). Thus, to determine one solution, an infinite number of conditions has to be prescribed, as that in (1.2) for system (1.1). Therefore, for PNP systems with *nonlocal* excess potentials, BVP with the traditional

“two-point-boundary-conditions” would be severely under determined. Initial value problems for functional differential equations such as (1.1) are well-understood. However, it is not the case for boundary value problems of functional differential equations. A correct formulation of boundary conditions for functional differential equations is still a serious concern, in general. In this work, taking into considerations of experimental designs of ionic flow through ion channels and in a relatively simple setting, we present a form of natural “boundary conditions” so that the corresponding BVP of PNP systems with nonlocal excess potentials is generally well-posed. Our formulation of natural “boundary conditions” will be provided in Section 2 after the description of the PNP models. This work, at an early stage toward a better understanding of the issues, provides some insights on interpretations of experimental designs of imposing boundary conditions and, hopefully, stimulates further mathematical analysis on this important issue.

The rest of the paper is organized as follows. In Section 2, we recall the three-dimensional PNP model and its quasi-one-dimensional version. The excess electrochemical potential will be carefully discussed and the boundary conditions will be introduced. In Section 3, we state our main result and describe a strategy for the proof, and provide a preparation for the proof. The main result is established in Section 4. We end the paper with a brief discussion in Section 5.

2 BVPs of PNP systems

2.1 Three-dimensional and quasi-one-dimensional PNP systems

We start with a brief description of a three-dimensional Poisson-Nernst-Planck type model for ionic flows. As an approximation, we consider an ion channel Ω_0 with two baths $\mathcal{U}_-$ and $\mathcal{U}_+$ attached to its ends (see Figure 1):

$$\begin{aligned}\mathcal{U}_- &= \{\mathbf{r} = (X, Y, Z) : b_- < X < b_0, Y^2 + Z^2 < g^2(X)\}, \\ \Omega_0 &= \{\mathbf{r} = (X, Y, Z) : b_0 \leq X \leq b_1, Y^2 + Z^2 < g^2(X)\}, \\ \mathcal{U}_+ &= \{\mathbf{r} = (X, Y, Z) : b_1 < X < b_+, Y^2 + Z^2 < g^2(X)\},\end{aligned}\tag{2.1}$$

where g is a smooth function, $b_- < b_0 < b_1 < b_+$.

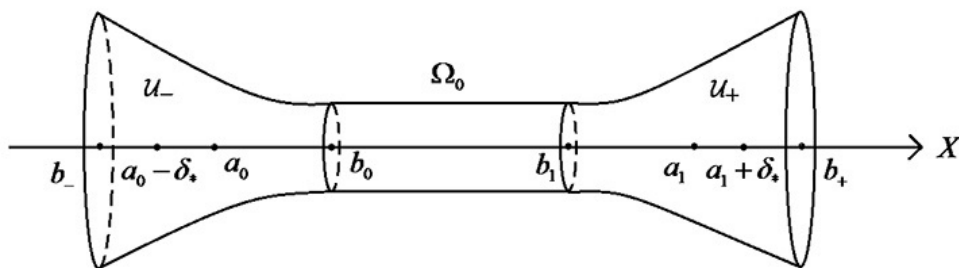


Figure 1: Representation of channel Ω_0 and baths $\mathcal{U}_\pm$.

The primitive (steady-state) Poisson-Nernst-Planck type systems for ion flow through the channel is (see, for example, [34, 36])

$$\begin{aligned} -\nabla \cdot (\varepsilon_r(\mathbf{r})\varepsilon_0\nabla\Phi) &= e\left(\sum_{j=1}^n z_j C_j + \mathcal{Q}(\mathbf{r})\right), \\ \nabla \cdot \mathcal{J}_k &= 0, \quad -\mathcal{J}_k = \frac{1}{k_B T} \mathcal{D}_k(\mathbf{r}) C_k \nabla \mu_k, \quad k = 1, 2, \dots, n \end{aligned} \quad (2.2)$$

where e is the elementary charge, k_B is the Boltzmann constant, T is the absolute temperature; Φ is the electric potential, $\mathcal{Q}(\mathbf{r})$ is the permanent charge of the channel ($\mathcal{Q}(\mathbf{r}) = 0$ for $\mathbf{r} \notin \Omega_0$), $\varepsilon_r(\mathbf{r})$ is the relative dielectric coefficient, ε_0 is the vacuum permittivity, n is the number of distinct types of ion species; for the k th ion species, C_k is the concentration (number density), z_k is the valence (number of charges per particle), μ_k is the electrochemical potential, $\mathcal{J}_k$ is the flux density, and $\mathcal{D}_k(\mathbf{r})$ is the diffusion coefficient.

On the basis that a typical ion channel is narrow and ionic flow along its longitudinal direction dominates the channel properties, a *quasi-one-dimensional* PNP model is proposed in ([57]):

$$\begin{aligned} -\frac{1}{g^2(X)} \frac{d}{dX} \left(g^2(X) \varepsilon_r(X) \varepsilon_0 \frac{d}{dX} \Phi \right) &= e \left(\sum_{j=1}^n z_j C_j + \mathcal{Q}(X) \right), \\ \frac{d}{dX} \mathcal{J}_k &= 0, \quad -\mathcal{J}_k = \frac{1}{k_B T} \pi g^2(X) \mathcal{D}_k(X) C_k \frac{d}{dX} \mu_k, \quad k = 1, 2, \dots, n. \end{aligned} \quad (2.3)$$

Note that $\pi g^2(X)$ is the area of the cross-section of the channel over X . The ion channel Ω_0 is represented by the interval $[b_0, b_1]$ and the two baths $\mathcal{U}_-$ and $\mathcal{U}_+$ are represented by the intervals (b_-, b_0) and (b_1, b_+) , respectively.

In special cases, this reduction has been mathematically justified to a certain extent in [51].

2.2 Electrochemical potentials

For the k th ion species, the electrochemical potential

$$\mu_k = \mu_k^{id} + \mu_k^{ex}$$

where the ideal component μ_k^{id} associated to the point-charge part is given by

$$\mu_k^{id}(X) = z_k e \Phi(X) + k_B T \ln \frac{C_k(X)}{C_0} \quad (2.4)$$

with some characteristic concentration C_0 , and the excess component $\mu_k^{ex}(X)$ accounts for finite size effect of charges. The excess component μ_k^{ex} consists of two components: the hard-sphere component μ_k^{HS} and the electrostatic component μ_k^{ES} for screening effects, etc. of finite sizes of charges ([29, 30, 32, 59, 60, 69], etc.); that is,

$$\mu_k^{ex} = \mu_k^{HS} + \mu_k^{ES}.$$

Excess components A practical difficulty is that an exact form for the functional dependence of the excess component $\mu_k^{ex}(X)$ on $\{C_j\}$ is not available and is actually hard to expect. Approximation models for $\mu_k^{ex}(X)$ had been proposed and

tested for a long time. The first *local- or pointwise-dependent* approximation model $\mu_k^{HS}(X) = -k_B T \ln(1 - \sum v_j C_j(X))$ for the hard-sphere potential was proposed by Bikerman ([13]), where v_j is the volume of the j th ion species (for our one-dimensional version, $v_j = 2r_j$ where r_j is the radius of the ion). Bikerman's model is though not ion specific in the sense that $\mu_k^{HS}(X)$ is taken to be the same for all k 's. Refined local-dependent models for hard-sphere potentials $\mu_k^{HS}(X)$ include those of Carnahan-Starling and Boublik-Mansoori-Carnahan-Starling (see, e.g., [6, 12]) that are ion specific. Modeling for the excess electrostatic component μ_k^{ES} is less well developed. A major breakthrough was made by Rosenfeld ([59, 60]). He treated ions as charged spheres and introduced novel ideas for an approximation of $\mu_i^{ex}(X)$ based on the geometry of spheres. An outcome of Rosenfeld's theory is an approximation of $\mu_k^{ex}(X)$ depending *non-locally* on the concentrations $\{C_j\}$ over a neighborhood of X with size comparable to the characteristic diameter of the ionic mixture. Accuracy of Rosenfeld's model and its further refinements has been demonstrated by a number of applications ([35, 62, 69], etc.); in particular, applications to ion channel problems have been conducted numerically in [15, 33, 34, 36], etc. and they have shown a great improvement.

We will consider a general form of the excess components and impose conditions that are consistent with available approximation models. The excess component $\mu_k^{ex}(X)$ represents short range interactions and is typically approximated by functionals in $\{C_j\}$ as convolution integrals over a range of size $(r_j + r_k)$'s with r_j 's being the radius of the j th ion species. It has the general form

$$\mu_k^{ex}(X) = k_B T \sum_{j=1}^n \int_{X-r_{jk}}^{X+r_{jk}} C_{kj}^{(2)}(X-Y) C_j(Y) dY,$$

where $r_{jk} := r_j + r_k$ and $C_{kj}^{(2)}$'s are the so-called *second order direct correlation functions*. The direct correlation functions $C_{kj}^{(2)}$'s depend on $\{C_l\}$ and $\{r_l\}$. The explicit dependence is not completely understood and is still an active research topic.

In this work, to capture the essence of the nonlocal feature of excess potentials, we will take a simple form of excess potentials

$$\frac{1}{k_B T} \frac{d\mu_k^{ex}}{dX}(X) = r F_k(C_1(X \pm r_{1k}), C_2(X \pm r_{2k}), \dots, C_n(X \pm r_{nk})), \quad (2.5)$$

where $r = \max\{r_k : 1 \leq k \leq n\}$ and F_k is a smooth function in its argument

$$(C_1(X - r_{1k}), C_1(X + r_{1k}), C_2(X - r_{2k}), C_2(X + r_{2k}), \dots, C_n(X - r_{nk}), C_n(X + r_{nk})),$$

and, for easy of notation, the above argument of F_k in (2.5) is denoted by

$$(C_1(X \pm r_{1k}), C_2(X \pm r_{2k}), \dots, C_n(X \pm r_{nk})).$$

The appearance of the factor r in front of F_k in (2.5) is due to the fact that $\mu_k^{ex} \rightarrow 0$ as $r \rightarrow 0$.

2.3 Boundary conditions

Complications, such as boundary layers, caused by applied boundary conditions have been well-recognized in experiments on ion channel properties, which, to say the least, create some concerns in interpretation of experimental designs for measuring I-V relations. This motivated the *four-electrode (or, four-terminal) technique*: two electrodes (outer electrodes) are inserted in the left and right bathes away from the channel, respectively, to be viewed as providing boundary conditions and the other two (inner electrodes) near the left and right open ends of the channel – the interfaces of the channel and the bathes, where the measurements of the current and voltage are made that are used to construct the I-V curve. This four-electrode technique, bypassing the complications at the outer electrodes, seems to be successful at least for practical purposes. But it does not completely resolve the concern in terms of the BVP of PNP type models and should be viewed as a call for further investigation for the purpose of a true understanding.

In this work, we attempt to put an initial effort for such a task. It is hoped that the result in this paper would identify the key issue and provide an insight for an ultimate understanding of the problem.

As a rough approximation, one may view the experimental designs imposing boundary conditions at two points. Of course, this is oversimplified and too idealized. We propose that the experimental designs impose the concentrations in two appropriate intervals representing the outer electrodes regions in the baths, respectively, and the transmembrane potential difference is imposed between two points. More precisely, let

$$\delta_* = \max\{r_{jk} = r_j + r_k : 1 \leq j, k \leq n\}. \quad (2.6)$$

Since r_j 's are the radius of the j th ion species, they are much smaller than the length scales of the baths on both sides. Therefore,

$$\delta_* \ll \min\{b_+ - b_1, b_0 - b_-\}.$$

Choose $a_0 \in (b_-, b_0)$ and $a_1 \in (b_1, b_+)$ (see Fig. 1) so that

$$[a_0 - \delta_*, a_0] \subset (b_-, b_0) \quad \text{and} \quad [a_1, a_1 + \delta_*] \subset (b_1, b_+).$$

Here, a_0 is viewed as the center of the outer electrode region in the left bath $\mathcal{U}_-$ and a_1 is viewed as the center of the outer electrode region in the right bath $\mathcal{U}_+$.

We propose the following boundary conditions,

$$\begin{aligned} \Phi(a_0) &= \mathcal{V}, \quad C_k(X) = \mathcal{L}_k(X) > 0 \quad \text{for } X \in [a_0 - \delta_*, a_0], \\ \Phi(a_1) &= 0, \quad C_k(X) = \mathcal{R}_k(X) > 0 \quad \text{for } X \in [a_1, a_1 + \delta_*], \end{aligned} \quad (2.7)$$

where $\mathcal{V}$ is a given constant, $\mathcal{L}_k$'s and $\mathcal{R}_k$'s are given continuous functions on their respective intervals. We emphasize that the boundary conditions for the electric potential Φ are imposed at two points and the boundary conditions of the concentrations C_k 's are imposed over intervals.

We will assume the electroneutrality boundary conditions at $X = a_0$ and a_1 ,

$$\sum_{s=1}^n z_s \mathcal{L}_s(a_0) = \sum_{s=1}^n z_s \mathcal{R}_s(a_1) = 0. \quad (2.8)$$

This assumption is consistent with the experimental designs.

The main purpose of this paper is to show that BVP (2.3) and (2.7) is well-posed; that is, under further conditions, we show that BVP (2.3) and (2.7) has a unique solution. In general, the well-posedness of BVP is more complicated than that of initial value problems, in particular, BVP may have finite or even infinite (but discrete) many solutions.

In Section 5, among other issues, we comment on the specific choice of δ_* in (2.6) used in defining the boundary conditions (2.7).

2.4 Dimensionless of (2.3) and (2.7)

The following rescaling or its variations have been widely used for convenience of mathematical analysis.

For a bounded function $g(X)$ defined on an interval U , we will denote

$$\|g\| = \sup\{|g(X)| : X \in U\}.$$

For example, for the functions $\mathcal{L}_k$ and $\mathcal{R}_k$ in (2.7) defined on different intervals,

$$\|\mathcal{L}_k\| = \sup\{|\mathcal{L}_k(X)| : X \in [a_0 - \delta_*, a_0]\} \quad \text{and} \quad \|\mathcal{R}_k\| = \sup\{|\mathcal{R}_k(X)| : X \in [a_1, a_1 + \delta_*]\}.$$

Set

$$C_0 = \max_{1 \leq k \leq n} \{\|\mathcal{Q}\|, \|\mathcal{L}_k\|, \|\mathcal{R}_k\|\}, \quad \mathcal{D}_0 = \sup_{1 \leq k \leq n} \{\|\mathcal{D}_k\|\}, \quad \bar{\varepsilon}_r = \|\varepsilon_r\|. \quad (2.9)$$

We make the re-scaling

$$\begin{aligned} \varepsilon^2 &= \frac{\bar{\varepsilon}_r \varepsilon_0 k_B T}{e^2 (a_1 - a_0)^2 C_0}, \quad x = \frac{X - a_0}{a_1 - a_0}, \quad h(x) = \frac{\pi g^2(X)}{(a_1 - a_0)^2}, \quad \delta_0 = \frac{\delta_*}{a_1 - a_0}, \\ \hat{\varepsilon}_r(x) &= \frac{\varepsilon_r(X)}{\bar{\varepsilon}_r}, \quad D_k(x) = \frac{\mathcal{D}_k(X)}{\mathcal{D}_0}, \quad Q(x) = \frac{\mathcal{Q}(X)}{C_0}, \\ \phi(x) &= \frac{e}{k_B T} \Phi(X), \quad c_k(x) = \frac{C_k(X)}{C_0}, \quad J_k = \frac{\mathcal{J}_k}{(a_1 - a_0) C_0 \mathcal{D}_0}. \end{aligned} \quad (2.10)$$

Note that the intervals $[a_0, a_1]$, $[a_0 - \delta_*, a_0]$, and $[a_1, a_1 + \delta_*]$ in the X -variable correspond to intervals $[0, 1]$, $[-\delta_0, 0]$, and $[1, 1 + \delta_0]$ in the x -variable, respectively.

The dimensionless parameter $\varepsilon = \lambda_D / (a_1 - a_0)$ is an important physical parameter, where

$$\lambda_D = \sqrt{\frac{\bar{\varepsilon}_r \varepsilon_0 k_B T}{e^2 C_0}}$$

is the so-called Debye length that describes screening of electric potential effects on charges. Our main result is valid for small ε . For ion channel problems, the parameter ε is small mostly because of the length scale $(a_1 - a_0)$ and the characteristic concentration C_0 of the ionic mixture. For example, if $C_0 = 1(\text{M})$, $a_1 - a_0 = 25(\text{nm})$, $\bar{\varepsilon}_r = 80$, then ε is of order $10^{-2} \sim 10^{-3}$. We comment that, in other electrochemical systems, the value of ε may not be small.

In terms of the new variables, the BVP (2.3) and (2.7) becomes

$$\begin{aligned} \frac{\varepsilon^2}{h(x)} \frac{d}{dx} \left(\hat{\varepsilon}_r(x) h(x) \frac{d\phi}{dx} \right) &= - \sum_{s=1}^n z_s c_s - Q(x), \quad \frac{dJ_k}{dx} = 0, \\ D_k(x) h(x) \frac{dc_k}{dx} + z_k D_k(x) h(x) c_k \frac{d\phi}{dx} + \frac{1}{k_B T} D_k(x) h(x) c_k \frac{d}{dx} \mu_k^{ex} &= -J_k, \end{aligned} \quad (2.11)$$

with boundary conditions

$$\begin{aligned} \phi(0) &= V_0, \quad c_k(x) = L_k(x) \quad \text{for } x \in [-\delta_0, 0] \\ \phi(1) &= 0, \quad c_k(x) = R_k(x) \quad \text{for } x \in [1, 1 + \delta_0], \end{aligned} \quad (2.12)$$

where, from (2.7),

$$V_0 = \frac{e}{k_B T} \mathcal{V}, \quad L_k(x) = \frac{\mathcal{L}_k(a_0 + (a_1 - a_0)x)}{C_0}, \quad R_k(x) = \frac{\mathcal{R}_k(a_0 + (a_1 - a_0)x)}{C_0}.$$

Recall $r = \max\{r_k : 1 \leq k \leq n\}$. Set

$$\nu = r(a_1 - a_0)C_0 \quad \text{and} \quad \lambda_{jk} = \frac{r_{jk}}{a_1 - a_0}. \quad (2.13)$$

It follows from (2.5) that

$$\begin{aligned} \frac{1}{k_B T} \frac{d}{dx} \mu_k^{ex}(x) &= r(a_1 - a_0) F_k \left(C_0 c_1(x \pm \lambda_{1k}), C_0 c_2(x \pm \lambda_{2k}), \dots, C_0 c_n(x \pm \lambda_{nk}) \right) \\ &\approx r(a_1 - a_0) C_0 f_k \left(c_1(x \pm \lambda_{1k}), c_2(x \pm \lambda_{2k}), \dots, c_n(x \pm \lambda_{nk}) \right) \\ &= \nu f_k \left(c_1(x \pm \lambda_{1k}), c_2(x \pm \lambda_{2k}), \dots, c_n(x \pm \lambda_{nk}) \right), \end{aligned}$$

where, in the second step, we use the reason that F_k 's are often approximated by linear mappings.

Note that ν and λ_{jk} 's are dimensionless parameters, and $\lambda_{jk} \leq \delta_0$ since $r_{jk} \leq \delta_*$. Thus, we will take the following general form for a model of the excess component

$$\frac{1}{k_B T} \frac{d}{dx} \mu_k^{ex}(x) = \nu f_k(c_1(x \pm \lambda_{1k}), c_2(x \pm \lambda_{2k}), \dots, c_n(x \pm \lambda_{nk})). \quad (2.14)$$

3 BVP (2.11) and (2.12) for $n = 2$ and $Q = 0$

We will examine the well-posedness of BVP (2.11) and (2.12) for the simple cases where

$$n = 2, \quad z_1 > 0 > z_2, \quad Q(x) = 0, \quad D_k(x) = 1, \quad \hat{\varepsilon}_r(x) = 1. \quad (3.1)$$

Note that, we could combine $D_k(x)$ and $\hat{\varepsilon}_r(x)$ with $h(x)$. Thus, the assumption that $D_k(x) = 1$ and $\hat{\varepsilon}_r(x) = 1$ is not critical. But the assumption that $Q(x) = 0$ is not easy to remove for the concrete results in this paper and we will get back to this issue in the future.

3.1 A Strategy for the well-posedness of BVP

We describe our strategy for the well-posedness of BVP (2.11) and (2.12).

Recall the functions $L_k(x)$ and $R_k(x)$ from (2.12). Let

$$X_0 = \left\{ C = (c_1, c_2) \in \mathcal{C}^0([0, 1], \mathbb{R}^2) : c_k(0) = L_k(0), c_k(1) = R_k(1) \right\}$$

equipped with the usual norm $\|C\| = \max \{|c_1(x)| + |c_2(x)| : x \in [0, 1]\}$, and let

$$X_{\delta_0} = \left\{ C \in \mathcal{C}^0([-\delta_0, 1 + \delta_0], \mathbb{R}^2) : c_k(x)|_{[-\delta_0, 0]} = L_k(x), c_k(x)|_{[1, 1 + \delta_0]} = R_k(x) \right\}$$

equipped with the norm $\|C\| = \max \{|c_1(x)| + |c_2(x)| : x \in [-\delta_0, 1 + \delta_0]\}$.

The model (2.14) for μ_k^{ex} then allows us to define a mapping

$$\mathcal{G} : X_{\delta_0} \rightarrow \mathcal{C}^0([0, 1], \mathbb{R}^2) \quad \text{by} \quad \mathcal{G}(C)(x) = \hat{G}(x) = (\hat{G}_1(x), \hat{G}_2(x)), \quad (3.2)$$

where, for $k = 1, 2$,

$$\hat{G}_k(x) = \nu h(x) c_k(x) f_k(c_1(x - \lambda_{1k}), c_1(x + \lambda_{1k}), c_2(x - \lambda_{2k}), c_2(x + \lambda_{2k})). \quad (3.3)$$

Note that, with the given $L_k(x)$ and $R_k(x)$ in (2.12), one can uniquely extend any function $C \in X_0$ to a function $\hat{C} \in X_{\delta_0}$. This gives a one-to-one and onto correspondence between X_0 and X_{δ_0} . We denote the correspondence by

$$\mathcal{E} : X_0 \rightarrow X_{\delta_0} \quad \text{by} \quad \mathcal{E}(C) = \hat{C}. \quad (3.4)$$

Also, for $\rho > 0$ to be determined later on, let

$$Y_\rho = \left\{ G = (G_1, G_2) \in \mathcal{C}^0([0, 1], \mathbb{R}^2) : \|G\| \leq \rho \right\}.$$

We now introduce an auxiliary boundary value problem as did in [45]. For any $(G_1, G_2) \in Y_\rho$, consider the auxiliary boundary value problem (auxi-BVP)

$$\begin{aligned} \frac{\varepsilon^2}{h(x)} \frac{d}{dx} \left(h(x) \frac{d}{dx} \phi \right) &= -z_1 c_1 - z_2 c_2, \\ \frac{dJ_k}{dx} &= 0, \quad h(x) \frac{dc_k}{dx} + z_k h(x) c_k \frac{d\phi}{dx} + G_k(x) = -J_k, \quad k = 1, 2 \end{aligned} \quad (3.5)$$

with the boundary conditions

$$\phi(0) = V_0, c_k(0) = L_k(0); \quad \phi(1) = 0, c_k(1) = R_k(1). \quad (3.6)$$

For each given $G \in Y_\rho$, auxi-BVP (3.5) and (3.6) is a usual two-point-boundary value problem. It is shown in [45] that, for $\varepsilon > 0$ small, auxi-BVP (3.5) and (3.6) has a unique solution $(\phi, c_1, c_2, J_1, J_2)$. Based on this conclusion, we define a mapping

$$\Psi_\varepsilon : Y_\rho \rightarrow X_0 \quad \text{by} \quad \Psi_\varepsilon(G_1, G_2) = (c_1, c_2). \quad (3.7)$$

The composition $\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon$ gives a mapping from $Y_\rho \rightarrow \mathcal{C}^0([0, 1], \mathbb{R}^2)$.

Finally, BVP (2.11) and (2.12) is reduced to a fixed point problem of the mapping

$$\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon : Y_\rho \rightarrow Y_\rho;$$

that is, to establish the well-posedness of BVP (2.11) and (2.12), it suffices to show that, for some choices of $\rho > 0$, the mapping $\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon$ maps Y_ρ into itself and has a fixed point.

We now state our main result whose proof will be given in Section 4 after a preparation of several estimates.

For the boundary concentrations $L_k(x)$ and $R_k(x)$ in (2.12), denote

$$M_L = \max_{x \in [-\delta_0, 0]} \{L_k(x) : k = 1, 2\} \text{ and } M_R = \max_{x \in [1, 1+\delta_0]} \{R_k(x) : k = 1, 2\},$$

and set

$$M = \max\{M_L, M_R\} \text{ and } H(x) = \int_0^x h^{-1}(s) ds. \quad (3.8)$$

Recall that $r = \max\{r_1, r_2\}$ and $C_0 = M$ from (2.9) and $Q = 0$. Denote $f = (f_1, f_2)$ where f_1 and f_2 are the functions in (2.14). Note that f is a mapping from $\mathbb{R}^4$ to $\mathbb{R}^2$. We denote its derivative by Df and the norm of Df by $\|Df\|$.

Theorem 3.1. *Assume (3.1) and that excess potentials μ_k^{ex} 's are given in (2.14). If*

$$\nu = r(a_1 - a_0)C_0 < \frac{1}{\|h\|H(1)(3\|f\| + M\|Df\|)}, \quad (3.9)$$

then, for $\varepsilon > 0$ small, BVP (2.11) and (2.12) has a unique solution. More precisely, if

$$\frac{\nu M \|h\| \|f\|}{1 - 2\nu \|h\| \|f\| H(1)} \leq \rho < \frac{1}{2\nu \|h\| \|Df\| H^2(1)} - \frac{\|f\|}{2\|Df\| H(1)} - \frac{M}{2H(1)}, \quad (3.10)$$

then, for $\varepsilon > 0$ small, $\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon : Y_\rho \rightarrow Y_\rho$ and it is a contraction.

It is easy to check that, under the condition (3.9) on ν , the quantity on the far right-hand side in (3.10) is strictly greater than the quantity on the far left-hand side, which guarantees the existence of ρ . The condition (3.9) also implies

$$\nu < \frac{1}{\|h\|H(1)} \min \left\{ \frac{1}{2\|f\|}, \frac{1}{\|f\| + M\|Df\|} \right\}, \quad (3.11)$$

which will be used in Section 4.

Remark 3.2. *Roughly speaking, the condition (3.9) will be satisfied when C_0 is not so large; that is, when the ionic mixture is not extremely crowded. But, for extremely crowded ionic mixtures where C_0 is very large, the condition (3.9) may not be satisfied. Since the condition is only a sufficient condition for our result, we cannot draw the conclusion that there does not exist a solution when C_0 is large. It would be interesting to know what happens to the existence of solutions when (3.9) fails. This is important since it might relate to the question whether or not PNP type continuum models are valid for extremely crowded ionic mixtures.*

3.2 Properties of $\mathcal{G}$, $\mathcal{E}$ and Ψ_ε

We will examine the mappings $\mathcal{G}$, $\mathcal{E}$ and Ψ_ε for the necessary properties; in particular, we will estimate the Fréchet derivatives of these mappings.

Note that, for $(c_1, c_2) \in X_0$, the tangent space $T_{(c_1, c_2)}X_0$ of X_0 at (c_1, c_2) is

$$T_{(c_1, c_2)}X_0 = \left\{ (d_1, d_2) \in \mathcal{C}^0([0, 1], \mathbb{R}^2) : d_k(0) = d_k(1) = 0, k = 1, 2 \right\},$$

for $(c_1, c_2) \in X_{\delta_0}$, the tangent space $T_{(c_1, c_2)}X_{\delta_0}$ of X_{δ_0} at (c_1, c_2) is

$$T_{(c_1, c_2)}X_{\delta_0} = \left\{ (d_1, d_2) \in \mathcal{C}^0([-\delta_0, 1 + \delta_0], \mathbb{R}^2) : d_k(x) = 0 \text{ for } x \notin (0, 1), k = 1, 2 \right\},$$

and, for $(G_1, G_2) \in Y_\rho$, the tangent space $T_{(G_1, G_2)}Y_\rho$ of Y_ρ at (G_1, G_2) is

$$T_{(G_1, G_2)}Y_\rho = \left\{ g = (g_1, g_2) \in \mathcal{C}^0([0, 1], \mathbb{R}^2) \right\} = \mathcal{C}^0([0, 1], \mathbb{R}^2).$$

3.2.1 Properties of Ψ_ε

We will give a detailed examination of the properties of $\Psi = \Psi_0$ and these of Ψ_ε can be treated as perturbations for small ε . For the properties of Ψ given below, we will borrow some results from [45].

For any given $(G_1, G_2) \in Y_\rho$, if $(\phi(x; \varepsilon), c_1(x; \varepsilon), c_2(x; \varepsilon), J_1(\varepsilon), J_2(\varepsilon), \tau(x))$ is the solution of auxi-BVP (3.5) and (3.6), then

$$\Psi_\varepsilon(G_1, G_2)(x) = (c_1(x; \varepsilon), c_2(x; \varepsilon)) = (c_{10}(x), c_{20}(x)) + O(\varepsilon),$$

and hence, $\Psi(G_1, G_2)(x) = (c_{10}(x), c_{20}(x))$. Recall $H(x) = \int_0^x h^{-1}(s)ds$ from (3.8).

The following result is established in [45].

Proposition 3.3. *For $\varepsilon > 0$ small and for any $(G_1, G_2) \in Y_\rho$, the corresponding auxi-BVP (3.5) and (3.6) has a unique solution $(\phi(x; \varepsilon), c_1(x; \varepsilon), c_2(x; \varepsilon), J_1(\varepsilon), J_2(\varepsilon))$. Furthermore, for the zeroth order (in ε) terms $c_{k0}(x) = c_k(x; 0)$, $k = 1, 2$, one has*

$$\begin{aligned} c_{10}(x) &= L_1(0) + \frac{z_2}{z_1 - z_2} \int_0^x \frac{G_1(s) + G_2(s)}{h(s)} ds \\ &\quad - \frac{H(x)}{H(1)} \left(L_1(0) - R_1(1) + \frac{z_2}{z_1 - z_2} \int_0^1 \frac{G_1(s) + G_2(s)}{h(s)} ds \right), \\ c_{20}(x) &= L_2(0) - \frac{z_1}{z_1 - z_2} \int_0^x \frac{G_1(s) + G_2(s)}{h(s)} ds \\ &\quad - \frac{H(x)}{H(1)} \left(L_2(0) - R_2(1) - \frac{z_1}{z_1 - z_2} \int_0^1 \frac{G_1(s) + G_2(s)}{h(s)} ds \right). \end{aligned} \tag{3.12}$$

The above result allows us to obtain the following estimates.

Corollary 3.4. *For $\varepsilon > 0$ small and for any $(G_1, G_2) \in Y_\rho$, let the unique solution of the corresponding auxi-BVP (3.5) and (3.6) be $(\phi(x; \varepsilon), c_1(x; \varepsilon), c_2(x; \varepsilon), J_1(\varepsilon), J_2(\varepsilon))$. Recall that $(c_{10}(x), c_{20}(x)) = \Psi(G_1, G_2)(x) \in X_0$. Then, for $k = 1, 2$,*

$$\|c_{k0}\| \leq \max \{L_k(0), R_k(1)\} + H(1)\rho. \tag{3.13}$$

The mapping $\Psi = (\Psi_1, \Psi_2)$ is Fréchet differentiable and its Fréchet derivative

$$D\Psi(G_1, G_2) : T_{(G_1, G_2)}Y_\rho \rightarrow T_{(c_1, c_2)}X_0$$

at $(G_1, G_2) \in Y_\rho$ is independent of (G_1, G_2) and is given by, for $g = (g_1, g_2)$,

$$\begin{aligned} (D\Psi_1[g])(x) &= \frac{z_2}{z_1 - z_2} \left(\int_0^x \frac{g_1(s) + g_2(s)}{h(s)} ds - \frac{H(x)}{H(1)} \int_0^1 \frac{g_1(s) + g_2(s)}{h(s)} ds \right), \\ (D\Psi_2[g])(x) &= \frac{z_1}{z_2 - z_1} \left(\int_0^x \frac{g_1(s) + g_2(s)}{h(s)} ds + \frac{H(x)}{H(1)} \int_0^1 \frac{g_1(s) + g_2(s)}{h(s)} ds \right), \end{aligned} \quad (3.14)$$

and has the estimate

$$\|D\Psi\| \leq H(1). \quad (3.15)$$

Proof. The estimate (3.13) follows directly from (3.12). Furthermore, calculating directly from (3.12), we obtain

$$\begin{aligned} &\Psi_1(G_1 + g_1, G_2 + g_2)(x) - \Psi_1(G_1, G_2)(x) \\ &= \frac{z_2}{z_1 - z_2} \int_0^x \frac{g_1(s) + g_2(s)}{h(s)} ds - \frac{z_2}{z_1 - z_2} \frac{H(x)}{H(1)} \int_0^1 \frac{g_1(s) + g_2(s)}{h(s)} ds, \end{aligned}$$

from which one has the first formula in (3.14). The second formula in (3.14) can be obtained similarly. Hence,

$$\|D\Psi_1\| \leq \frac{|z_2|}{|z_1 - z_2|} H(1) \quad \text{and} \quad \|D\Psi_2\| \leq \frac{|z_1|}{|z_1 - z_2|} H(1),$$

from which (3.15) follows since $z_1 > 0 > z_2$. $\square$

3.2.2 Properties of $\mathcal{E}$

The properties of $\mathcal{E}$ can be easily obtained.

Lemma 3.5. *The mapping $\mathcal{E}$ is Fréchet differentiable and its Fréchet derivative $D\mathcal{E}(c_1, c_2) : T_{(c_1, c_2)}X_0 \rightarrow T_{(\hat{c}_1, \hat{c}_2)}X_{\delta_0}$ at (c_1, c_2) is independent of (c_1, c_2) and is given by, for $x \in [-\delta_0, 1 + \delta_0]$,*

$$D\mathcal{E}[d_1, d_2](x) = \left(\hat{d}_1(x), \hat{d}_2(x) \right),$$

where $\hat{d}_k(x) = d_k(x)$ for $x \in [0, 1]$ and $\hat{d}_k(x) = 0$ for $x \in [-\delta_0, 0] \cup [1, 1 + \delta_0]$; in particular, $\|D\mathcal{E}\| = 1$.

Proof. The statement follows from the definition of $\mathcal{E}$. $\square$

3.2.3 Properties of $\mathcal{G}$

The formula (3.2) allows us to obtain the following properties of $\mathcal{G}$.

Lemma 3.6. *Let $(c_1, c_2) \in X_{\delta_0}$ and $(\hat{G}_1, \hat{G}_2) = \mathcal{G}(c_1, c_2) \in Y_\rho$. Then,*

$$\|\hat{G}_k\| \leq \nu \|h\| \|f_k\| \|c_k\|. \quad (3.16)$$

The mapping $\mathcal{G}$ is Fréchet differentiable and its Fréchet derivative

$$D\mathcal{G} = D\mathcal{G}(c_1, c_2) : T_{(c_1, c_2)}X_{\delta_0} \rightarrow T_{(G_1, G_2)}Y_\rho$$

at $(c_1, c_2) \in X_{\delta_0}$ is given by, for $k = 1, 2$,

$$\begin{aligned} D\mathcal{G}_k[\theta_1, \theta_2](x) &= \nu h(x) f_k \cdot \theta_k(x) \\ &\quad + \nu h(x) c_k(x) \partial_1 f_k \cdot \theta_1(x - \lambda_{1k}) + \nu h(x) c_k(x) \partial_2 f_k \cdot \theta_1(x + \lambda_{1k}) \\ &\quad + \nu h(x) c_k(x) \partial_3 f_k \cdot \theta_2(x - \lambda_{2k}) + \nu h(x) c_k(x) \partial_4 f_k \cdot \theta_2(x + \lambda_{2k}), \end{aligned} \quad (3.17)$$

where f_k and its partial derivatives $\partial_j f_k$ are evaluated at

$$(c_1(x - \lambda_{1k}), c_1(x + \lambda_{1k}), c_2(x - \lambda_{2k}), c_2(x + \lambda_{2k})).$$

Moreover,

$$\|D\mathcal{G}\| \leq \nu \|h\| \left((\|c_1\| + \|c_2\|) \|Df\| + \|f\| \right). \quad (3.18)$$

Proof. The estimate (3.16) follows from (3.3) directly.

To compute the Fréchet derivative of $\mathcal{G}_k$ from (3.3), we will use the short notation

$$(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21}))$$

for the argument

$$(c_1(x - \lambda_{11}), c_1(x + \lambda_{11}), c_2(x - \lambda_{21}), c_2(x + \lambda_{21}))$$

of f_1 and f_2 .

Now, let $(\theta_1, \theta_2) \in T_{(c_1, c_2)}X_{\delta_0}$. It follows from (3.3) that

$$\begin{aligned} &\mathcal{G}_1(c_1 + \theta_1, c_2 + \theta_2)(x) - \mathcal{G}_1(c_1, c_2)(x) \\ &= \nu h(x) (c_1(x) + \theta_1(x)) f_1((c_1 + \theta_1)(x \pm \lambda_{11}), (c_2 + \theta_2)(x \pm \lambda_{21})) \\ &\quad - \nu h(x) c_1(x) f_1(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})) \\ &= \nu h(x) c_1(x) f_1((c_1 + \theta_1)(x \pm \lambda_{11}), (c_2 + \theta_2)(x \pm \lambda_{21})) \\ &\quad - \nu h(x) c_1(x) f_1(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})) \\ &\quad + \nu h(x) \theta_1(x) f_1((c_1 + \theta_1)(x \pm \lambda_{11}), (c_2 + \theta_2)(x \pm \lambda_{21})). \end{aligned} \quad (3.19)$$

The difference of the first two terms in the last expression of (3.19) can be estimated as

$$\begin{aligned} &\nu h(x) c_1(x) \left(f_1((c_1 + \theta_1)(x \pm \lambda_{11}), (c_2 + \theta_2)(x \pm \lambda_{21})) - f_1(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})) \right) \\ &= \nu h(x) c_1(x) \partial_1 f_1 \cdot \theta_1(x - \lambda_{11}) + \nu h(x) c_1(x) \partial_2 f_1 \cdot \theta_1(x + \lambda_{11}) \\ &\quad + \nu h(x) c_1(x) \partial_3 f_1 \cdot \theta_2(x - \lambda_{21}) + \nu h(x) c_1(x) \partial_4 f_1 \cdot \theta_2(x + \lambda_{21}) + o(\|\theta\|), \end{aligned}$$

where f_1 and its partial derivatives $\partial_j f_1$ are evaluated at

$$(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})).$$

The last term in the last expression of (3.19) can be estimated as

$$\begin{aligned} & \nu h(x) \theta_1(x) f_1((c_1 + \theta_1)(x \pm \lambda_{11}), (c_2 + \theta_2)(x \pm \lambda_{21})) \\ &= \nu h(x) \theta_1(x) f_1(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})) + o(\|\theta\|). \end{aligned}$$

Therefore,

$$\begin{aligned} & \mathcal{G}_1(c_1 + \theta_1, c_2 + \theta_2)(x) - \mathcal{G}_1(c_1, c_2)(x) \\ &= \nu h(x) c_1(x) \partial_1 f_1 \cdot \theta_1(x - \lambda_{11}) + \nu h(x) c_1(x) \partial_2 f_1 \cdot \theta_1(x + \lambda_{11}) \\ & \quad + \nu h(x) c_1(x) \partial_3 f_1 \cdot \theta_2(x - \lambda_{21}) + \nu h(x) c_1(x) \partial_4 f_1 \cdot \theta_2(x + \lambda_{21}) \\ & \quad + \nu h(x) \theta_1(x) f_1(c_1(x \pm \lambda_{11}), c_2(x \pm \lambda_{21})) + o(\|\theta\|), \end{aligned}$$

which implies the formula for $D\mathcal{G}_1$ in (3.17).

Similarly, one obtains the formula for $D\mathcal{G}_2$ in (3.17). Therefore, $\mathcal{G}$ is Fréchet differentiable with its Fréchet derivative given in (3.17). The estimate (3.18) then follows directly from (3.17). $\square$

4 Proof of Theorem 3.1

First of all, we will show that, under the assumptions on ν and ρ in (3.9) and (3.10), $(\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon)$ maps $Y_\rho \rightarrow Y_\rho$. Indeed, for $(G_1, G_2) \in Y_\rho$, let $(c_1, c_2) = \Psi(G_1, G_2)$, $(\hat{c}_1, \hat{c}_2) = \mathcal{E}(c_1, c_2)$, and $(\hat{G}_1, \hat{G}_2) = \mathcal{G}(\hat{c}_1, \hat{c}_2)$. Then, it follows from (3.13) in Corollary 3.4 that,

$$\|c_k\| \leq \max\{L_k(0), R_k(1)\} + H(1)\rho,$$

and hence,

$$\|(\hat{c}_1, \hat{c}_2)\| \leq M + 2H(1)\rho, \tag{4.1}$$

where M is defined in (3.8).

The estimate (3.16) in Lemma 3.6 gives

$$\|\hat{G}\| \leq \nu \|h\| \|f\| \|\hat{c}\| \leq \nu \|h\| \|f\| (M + 2H(1)\rho).$$

It can be checked easily that $\nu \|h\| \|f\| (M + 2H(1)\rho) \leq \rho$ if and only if

$$\nu < \frac{1}{2\|h\|\|f\|H(1)} \quad \text{and} \quad \rho \geq \frac{\nu\|h\|\|f\|M}{1 - 2\nu\|h\|\|f\|H(1)}.$$

The above inequalities about ν and ρ are implied by conditions (3.9) and (3.10) in Theorem 3.1. Therefore, under the conditions (3.9) and (3.10), $\mathcal{G} \circ \mathcal{E} \circ \Psi$ maps $Y_\rho \rightarrow Y_\rho$, and hence, for $\varepsilon > 0$ small enough, $\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon$ maps $Y_\rho \rightarrow Y_\rho$ too.

It remains to show that $\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon$ is a contraction. Applying (3.15), (3.18) and $\|D\mathcal{E}\| = 1$, we obtain

$$\begin{aligned} \|D(\mathcal{G} \circ \mathcal{E} \circ \Psi)\| &\leq \|D\mathcal{G}\| \|D\mathcal{E}\| \|D\Psi\| \\ &\leq \nu \|h\| \left((\|\hat{c}_1\| + \|\hat{c}_2\|) \|Df\| + \|f\| \right) H(1) \\ &\leq \nu \|h\| \left((M + 2H(1)\rho) \|Df\| + \|f\| \right) H(1). \end{aligned}$$

It follows from conditions (3.9) and (3.10) in Theorem 3.1 that

$$\begin{aligned} \nu &< \frac{1}{\|h\| \|f\| H(1) + M \|h\| \|Df\| H(1)}, \\ \rho &< \frac{1}{2\nu \|h\| \|Df\| H^2(1)} - \frac{\|f\|}{2\|Df\| H(1)} - \frac{M}{2H(1)}, \end{aligned}$$

which then imply that $\|D(\mathcal{G} \circ \mathcal{E} \circ \Psi)\| < 1$. Hence, for $\varepsilon > 0$ small, $\|D(\mathcal{G} \circ \mathcal{E} \circ \Psi_\varepsilon)\| < 1$.

An application of the Contraction Mapping Theorem then completes the proof of Theorem 3.1.

5 Discussion

In this paper, we have examined the issue of well-posedness of BVP of PNP models with nonlocal excess potentials for ionic flow through ion channels. A set of natural boundary conditions is proposed under which we obtained the well-posedness of BVP. We will end the paper with several comments.

5.1 Choices of δ_* for boundary conditions (2.7)

We first discuss the choice of δ_* in (2.6) for the length of intervals over which the boundary concentrations are imposed. It turns out that the choice of δ_* is optimal.

For this purpose, we set

$$r_M := \max\{r_{jk} = r_j + r_k : 1 \leq j, k \leq n\}.$$

(a) As shown in Theorem 3.1, the boundary condition (2.7) with $\delta_* = r_M$ determines $\Phi(X)$, $C_k(X)$'s and J_k 's for $X \in [a_0, a_1]$ from the PNP system (2.3) with nonlocal excess potentials μ_k^{ex} in (2.5). In particular, this implies that one needs $\delta_* \geq r_M$ in order to determine a unique solution of the BVP.

(b) Suppose now one chooses $\delta_* > r_M$ so that $a_0 - \delta_* + r_M < a_0$. From (a), the conditions on $C_k(X)$ for $X \in [a_0 - r_M, a_0] \cup [a_1, a_1 + r_M]$ together with $\Phi(a_0) = \mathcal{V}$ and $\Phi(a_1) = 0$ already determine the solution $(\Phi(X; r_M), C_k(X; r_M), \mathcal{J}_k(r_M))$ for $X \in [a_0, a_1]$. (We include the variable r_M to indicate the quantities are determined by the values of $C_k(X)$ for $X \in [a_0 - r_M, a_0] \cup [a_1, a_1 + r_M]$.) One can then determine $\Phi(X)$ for $X \in [a_0 - \delta_*, a_0]$ from the Poisson equation in (2.3) from $(\Phi, d\Phi/dX)(a_0)$ and $C_k(X)$ for $X \in [a_0 - \delta_*, a_0]$. As a result, one can determine the excess potentials $\mu_k^{ex}(X)$'s for $X \in [a_0 - \delta_* + r_M, a_0]$, which is a nonempty subset of $[a_0 - \delta_*, a_0]$ since $a_0 - \delta_* + r_M < a_0$; for example, to determine $\mu_k^{ex}(X_0)$'s for $X_0 = a_0 - \delta_* + r_M$, one needs $C_j(X)$'s for $X \in [X_0 - r_M, X_0 + r_M] = [a_0 - \delta_*, a_0 - \delta_* + 2r_M]$. It then follows from the

Nernst-Planck equations in (2.3) that the fluxes $\mathcal{J}_k(\delta_*)$'s can be determined over the subinterval $[a_0 - \delta_* + r_M, a_0]$ that depend on the specific values of $C_k(X) = \mathcal{L}_k(X)$ for $X \in [a_0 - \delta_*, a_0 - \delta_* + r_M] \subset [a_0 - \delta_*, a_0]$; in particular, $\mathcal{J}_k(\delta_*) \neq \mathcal{J}_k(r_M)$ in general. This inconsistency shows that one cannot choose $\delta_* > r_M$, and hence, $\delta_* = \max\{r_{jk} = r_j + r_k : 1 \leq j, k \leq n\}$ as in (2.6) is optimal.

5.2 Implications to experimental designs

In this paper, we attempt to investigate PNP models with non-local excess potentials. As a starting point, we take a simple setting to bring out the relevant boundary quantities for the ionic flows, whether maintained by the experimental designs or measured from actual experiments. We show that, when the non-localness of the excess potential is relevant, the I-V relation does depend on the boundary concentrations in an neighborhood of the electrode points, more than those just at the electrode points. This would imply that, if one thought only the boundary concentrations at the electrode points are relevant, then one would have different I-V relations for fixed boundary concentrations at the electrode points but different boundary concentrations nearby either maintained by the experimental design or measured from experiments. It is not clear whether the differences could be significant. On the other hand, if one views the boundary conditions are imposed over the whole baths, then the boundary value problem would be over determined from the analysis of PNP type models.

We stress that, for practical purposes and from mathematical analysis viewpoints, there are many directions to be improved from this study: the permanent charge could be included in quasi-one-dimensional PNP type models, three-dimensional PNP type models could be better for more features of non-localness and more accurate interaction between the permanent charges and channel geometry, and the free ions inside the channel, the primitive PNP type models could be coupled with the Navier-Stokes equation for the flow of medium (water), etc.

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