POISSON-NERNST-PLANCK SYSTEMS FOR ION FLOW WITH DENSITY FUNCTIONAL THEORY FOR HARD-SPHERE POTENTIAL: I-V RELATIONS AND CRITICAL POTENTIALS. PART I: ANALYSIS

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Abstract. In this work, we analyze a one-dimensional steady-state Poisson-Nernst-Planck type model for ionic flow through a membrane channel including ionic interactions modeled from the Density Functional Theory in a simple setting: Two oppositely charged ion species are involved with electroneutrality boundary conditions and with zero permanent charge, and only the hard sphere component of the excess (beyond the ideal) electrochemical potential is included. The model can be viewed as a singularly perturbed integro-differential system with a parameter resulting from a dimensionless scaling of the problem as the singular parameter. Our analysis is a combination of geometric singular perturbation theory and functional analysis. The existence of a solution of the model problem for small ion sizes is established and, treating the sizes as small parameters, we also derive an approximation of the I-V (current-voltage) relation. For this relatively simple situation, it is found that the ion size effect on the I-V relation can go either way – enhance or reduce the current. More precisely, there is a critical potential value V_c so that, if $V > V_c$, then the ion size enhances the current; if $V < V_c$, it reduces the current. There is another critical potential value V^c so that, if $V > V^c$, the current is increasing with respect to $\lambda = r_2/r_1$ where r_1 and r_2 are, respectively, the radii of the positively and negatively charged ions; if $V < V^c$, the current is decreasing in λ. To our knowledge, the existence of these two critical values for the potential was not previously identified.

Key words. Ion flow, PNP-DFT, hard-sphere, I-V relation, critical potentials

AMS subject classifications. 34B16, 35Q92, 35R09, 92C35

1. Introduction.

Cells are basic units for all living organisms. While cell membrane protects individual cell identity, (atomic scale) ion channels – pores embedded on cell membranes – that link the inside and the outside of cells provide a major role for cells to communicate with each other. Once channel opens, ions are driven by the boundary concentration of charges and electrical potential through the channel and create macroscopic flows of charges that carry electrical signals. This electrodiffusion process of ion species plays a central role for physiological properties of biological units ([11, 13, 14, 17, 19, 20, 21, 22, 23, 24, 33, 34, 35, 39, 44, 45, 60, 62, 63, 71, 72, 73], etc.).

At the molecular scale, ion flows can be modeled by the Langevin-Poisson system that is arguably the most accurate description of the physical problem (see, for example, [2, 9, 10, 15, 35, 45, 58, 61, 71, 72, 78, 83]); for continuum versions, the Maxwell-Boltzmann equations serve as the fundamental models (see, for example, [4, 44, 45, 71, 83]). On the other hand, it is a great challenge to examine their dynamics analytically and even computationally. The Poisson-Nernst-Plack (PNP) type systems are simplified models but can capture key features of the biological system. The simplest PNP type model is the *classical* Poisson-Nernst-Planck (cPNP) system (see [4, 57] for a derivation and a justification from Boltzmann-Poisson system and [78] for a derivation from Langevin-Poisson equations). The cPNP system has been simulated to a great extent ([11, 12, 14, 16, 18, 33, 34, 35, 38, 40, 41, 45, 46, 47, 51, 59, 76]), and has been analyzed treating it as a singularly perturbed system with a parameter resulting from a dimensionless scaling of the problem as the singular parameter ([1, 5, 6, 27, 31, 52, 53, 56, 64, 74, 75, 79, 80, 81, 82]). In particular, the singular boundary value problem for one-dimensional steady-state cPNP systems was well studied to understand I-V relations, multiplicity of solutions and many other important properties of channels. In this classical model, a "dilute" assumption is made so that, for the electrochemical potential, only the ideal component is included, and hence, ions are treated as *point-charges* as such, say, Na^+ (sodium) and K^+ (potassium) are unfortunately indistinguishable since they differ mainly by

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their different sizes. [1]

However, many important biological functions, both quantitative and qualitative ones, of ion channels do rely on finite size of ions; this is why Na^+ and K^+ are so different and there are Na^+-channels and K^+-channels. Therefore, the excess (beyond the ideal) electrochemical potential for ion-to-ion interaction can be significant. One of most successful models for the excess electrochemical potential comes from the celebrated Density Functional Theory (DFT) ([28, 29], etc.): the excess electrochemical potential can be well approximated as functional of ion concentrations. The PNP system combined with DFT (PNP-DFT) has been investigated computationally for ion channels and has shown great success ([32, 35, 37, 50], etc.). Article [3] provides a critical and detailed account of some recent works on nonlinear electrokinetic phenomena including particularly ion-to-ion interactions. The recent activity of applying energy variational analysis *EnVarA* to modeling and numerics of PNP type systems for ion channel problems brings the study to an exciting level ([25, 26, 42, 43]). But there are essentially no analytic results on PNP-DFT to the best of our knowledge.

In this paper, we start an analysis of one-dimensional version of PNP-DFT systems in a simple setting; more precisely, we consider the case where two oppositely charged ions (those that make up salts Na^+Cl^-, K^+Cl^- or $Ca^{++}Cl_2^-$) are involved with electroneutrality boundary conditions, the permanent charge can be ignored and only the hard sphere component of the excess electrochemical potential is included beyond the ideal potential. The model can be viewed as a singularly perturbed system with *nonlocal* terms and our analysis is a combination of geometric singular perturbation theory and functional analysis. The former requires an extension of the geometric singular perturbation theory for cPNP systems developed in ([27, 52, 53]); the latter contains a new ingredient designed particularly for handling the nonlocal hard-sphere potential.

We rigorously establish the existence of solutions of the PNP-DFT model for small ion sizes and, treating the sizes as small parameters, we also derive an approximation of the I-V relation. The upshot of the approximation result, for this simple situation, is that the ion size effect on the I-V relation can go either way – enhance or reduce the current. More precisely, there is a critical potential V_c (Lemma 6.4) so that, if $V > V_c$, then the ion size enhances the current; if $V < V_c$, it reduces the current (Theorem 6.5). There is another critical potential V^c (Lemma 6.4) so that, if $V > V^c$, the current is increasing in $\lambda = r_2/r_1$ where r_1 and r_2 are, respectively, the radii of the positively and negatively charged ions; if $V < V^c$, the current is decreasing in λ (Theorem 6.6). The value V^c is probably more important since its relevance to when small ions are preferred and when large ions are preferred. We emphasis that the understanding of the role of V^c on preference between small and large ions is at the very early stage and a better understanding requires more extensive investigations and, definitely at stages, careful tests against experimental data.

It is the relative simplicity of the setting we take in this paper that allows us to obtain more or less explicit information on the solutions and, in turn, to realize the existence of these two important critical potential values V_c and V^c that necessarily depend on ion sizes. Of course, given the complexity and richness of ion channel structures, we stress that it is *not expected* that the formulas for the values of V_c and V^c obtained in this paper represents a general quantitative feature. However, we do believe these two critical potentials are qualitatively relevant for general realistic systems and being aware of the potential existence of these critical values can be significant for experimental, computational, and analytical study of ion channel functions. In a companion paper [55], we designed an algorithm for numerical detection of these critical voltages *without using any analytical formulas for I-V relations*. We also demonstrated the usage of this algorithm in [55] in two ways: (i) for the model problem in this paper, we numerically computed I-V relations and, applying the algorithm, we then computed the critical voltage values V_c and V^c, and found they agree well with the analytical values V_c and V^c in Lemma 6.4; (ii) for a PNP-DFT model with a nonzero permanent charge

[1] Strictly speaking, the cPNP system does not completely ignore ion sizes in the sense that it involves diffusion coefficients of each individual ions species that do depend on ion sizes.

Q that we don't have analytical formulas for the I-V relations and hence for the critical voltages, we applied the algorithm and found the critical voltages V_c and V^c.

We will examine more general cases particularly with the inclusion of the excess electrostatic potential, with the presence of permanent charges and multiple ion species in the future. It is our hope that a solid mathematical foundation for the study of the complicated and multi-scaled PNP type models will provide deep insights to the real biological systems.

The rest of the paper is organized as follows. In §2, we describe the one-dimensional version PNP-DFT model for ion flows, Rosenfeld's model for the hard-sphere component of the electrochemical potential, the setup of our problem, and the strategy of our analysis. In §3, we examine an auxiliary system with an extension of the geometric singular perturbation theory previously developed for cPNP systems. In §4, as a part of our analysis, we study a mapping associated to the hard-sphere potential. In §5, based on the results in §3 and §4, we formulate the original problem as a fixed point problem and establish the existence of its solutions. §6 is devoted to a derivation of an approximation of the I-V relation and, based on this approximation, two critical voltage values are identified and their important properties on ion size effects are discussed. A conclusion is given in §7. The paper ends with an Appendix where the Fréchet differentiability of a mapping defined in §3 is established.

2. Problem setup and the strategy of analysis.

2.1. A one-dimensional steady state PNP-DFT model. We start with a brief description of a three-dimensional Poisson-Nernst-Planck type model for ion flows. As an approximation, we consider an ion channel Ω, whose longitudinal length has been normalized to one,

$$\Omega = \{X = (x, y, z) : 0 < x < 1,\ y^2 + z^2 < g^2(x)\},$$

where g is a smooth function. The boundary $\partial\Omega$ of Ω consists of three portions:

$$\mathcal{L} = \{X \in \Omega : x = 0\},\ \mathcal{R} = \{X \in \Omega : x = 1\},$$
$$\mathcal{M} = \{X \in \Omega : y^2 + z^2 = g^2(x)\}.$$

Here, $\mathcal{L}$ and $\mathcal{R}$ are viewed as the two ends (inside and outside of the cell) and $\mathcal{M}$ the wall of the channel.

The basic electrodiffusion model of (steady-state) Poisson-Nernst-Planck type systems for ion flow through the channel is (see, for example, [35, 37])

$$\begin{aligned} -\nabla\cdot(\varepsilon_r(X)\varepsilon_0\nabla\phi) =& e\Big(\sum_{j=1}^{n} z_j c_j + Q(X)\Big), \\ -J_i = \frac{1}{kT} D_i(X) c_i \nabla\mu_i, &\quad \nabla\cdot J_i = 0, \quad i = 1, 2, \cdots, n \end{aligned} \tag{2.1}$$

where e is the elementary charge, k the Boltzmann constant, T the absolute temperature; ϕ is the electric potential, $Q(X)$ the permanent charge of the channel, $\varepsilon_r(X)$ the relative permittivity, ε_0 the vacuum permittivity, n the number of distinct types of ion species; for the ith ion species, c_i is the concentration (number density), z_i the valence (number of charges per particle), μ_i the electrochemical potential, J_i the flux density, and $D_i(X)$ the diffusion coefficient.

Depending on specific biological settings of ion channel problems, one may impose different boundary conditions. We will consider the situation that the concentration of charges and electrical potentials on $\mathcal{L}\cup\mathcal{R}$ are constants. An argument is that the inside and the outside of cells are macroscopic regions in which the concentration of charges and electrical potentials remain nearly constants. The wall of the channel will be assumed to be perfectly insulated. We thus assume the following boundary conditions

$$\phi|_{\mathcal{L}} = V,\ c_i|_{\mathcal{L}} = L_i, \quad \phi|_{\mathcal{R}} = 0,\ c_i|_{\mathcal{R}} = R_i, \quad \frac{\partial\phi}{\partial\mathbf{n}}|_{\mathcal{M}} = \frac{\partial c_i}{\partial\mathbf{n}}|_{\mathcal{M}} = 0, \tag{2.2}$$

where V, $L_i > 0$ and $R_i > 0$ are constants, and $\mathbf{n}$ is a unit normal vector to $\mathcal{M}$.

A natural one-dimensional version of the steady-state PNP type model is

$$\begin{aligned} &-\frac{1}{h(x)}\frac{d}{dx}\Big(\varepsilon_r(x)\varepsilon_0 h(x)\frac{d\phi}{dx}\Big) = e\Big(\sum_{j=1}^{n} z_j c_j(x) + Q\Big), \\ &-J_i = \frac{1}{kT} D_i(x) h(x) c_i(x) \frac{d\mu_i}{dx}, \quad \frac{dJ_i}{dx} = 0, \quad i = 1, 2, \cdots, n \end{aligned} \tag{2.3}$$

on $x \in (0, 1)$ with the boundary conditions

$$\phi(0) = V, \quad \phi(1) = 0, \quad c_i(0) = L_i, \quad c_i(1) = R_i \tag{2.4}$$

where $h(x) = \pi g^2(x)$ is the cross-section area of the channel over the longitudinal location x. This one-dimensional version PNP system was suggested in [59] and it differs from the traditional one-dimensional PNP system in that it contains the cross-section area function $h(x)$ that captures the main geometric property of a non-uniform channel. For example, for a conical-shaped ion channel, one can choose an appropriate function $h(x)$ to encode this geometry in the one-dimensional version PNP system. We point out that the inclusion of the function $h(x)$ in this one-dimensional version PNP system is not only physically meaningful but also mathematically justified. In fact, for special cases, it has been rigorously reduced from the three-dimensional PNP system (2.1) by letting, mathematically, the maximum of the radii of the cross-sections approach zero, and the reduction is mathematically justified to some extents in [54].

From a solution of (2.3) and (2.4), for fixed L_i and R_i and for varied V, one can extract the I-V (current-voltage) relation

$$I = \sum_{j=1}^{n} z_j e J_j. \tag{2.5}$$

A goal of this paper is to establish the existence of solutions for the boundary value problem (2.3) and (2.4) and to examine ion size effects on the I-V relations.

2.1.1. Density functional theory and one-dimensional hard-sphere potential. The electrochemical potential μ_i for the ith ion species consists of the ideal component $\mu_i^{id}(x)$, the excess component $\mu_i^{ex}(x)$ and the concentration-independent component $\mu_i^0(x)$ (e.g. a hard-well potential): $\mu_i(x) = \mu_i^0(x) + \mu_i^{id}(x) + \mu_i^{ex}(x)$ where

$$\mu_i^{id}(x) = z_i e\phi(x) + kT \ln \frac{c_i(x)}{c_0} \tag{2.6}$$

with some characteristic number density c_0 which will be normalized to one in the sequal. The cPNP system takes the ideal component $\mu_i^{id}(x)$ only. This component reflects the collision between ion particles and the water molecules. It has been accepted that the cPNP system is a reasonable model in, for example, the dilute case under which the ions can be treated as point charges and the ion-to-ion interaction can be ignored. As remarked in the footnote 1, D_i's involve the ionic radii through the Einstein relation so that the classical PNP does not completely ignore ion sizes.

The most intriguing component is the excess electrochemical potential $\mu_i^{ex}(x)$ to account for the finite size effect of charges. It consists of two components: the hard-sphere component μ_i^{HS} and the electrostatic component μ_i^{ES} for screening effects, etc. of finite sizes of charges ([3, 28, 29, 30, 68, 69, 84, 85], etc.); that is,

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

In this paper, as a first step, we will only include the hard-sphere component μ_i^{HS}.

The hard-sphere component $\mu_i^{HS}(x)$ is naturally defined as a functional of the *probability distributions*, $\{f_j(x,v)\}$, where $f_j(x,v)dxdv$ is the number of jth ions at the location in $(x, x+dx)$ with the velocity in $(v, v+dv)$. There are different proposals for the specifics of $\mu_i^{HS}(x)$. The most successful one comes from the Density Functional Theory (DFT). The celebrated Density Functional Theory ([28, 29], etc.) states that $\mu_i^{HS}(x)$ is actually a functional of the *concentrations*, $\{c_j(x)\}$, where the concentration c_j and the probability distribution are related by $c_j(x) = \int f_j(x,v)dv$.

A practical difficulty is that an exact formula for the functional dependence of $\mu_i^{HS}(x)$ on $\{c_j(x)\}$ cannot be expected. A major breakthrough was made by Rosenfeld ([68, 69]). He treated ions as charged spheres and introduced novel ideas for an approximation of $\mu_i^{HS}(x)$ based on the geometry of spheres. An outcome of Rosenfeld's theory is an explicit approximation of $\mu_i^{HS}(x)$ depending *non-locally* on the concentrations $\{c_j\}$. (See also the recent review article [70] on hard-sphere mixtures and the references therein.) Accuracy of Rosenfeld's model and its further refinements has been demonstrated by a number of applications ([36, 77, 84, 85], etc.); in particular, applications to ion channel problems have been conducted numerically in [10, 34, 35, 37], etc. and they have shown a great improvement.

Local- or *pointwise-dependent* models for hard sphere potentials $\mu_i^{HS}(x)$ had been proposed and tested for a long time; for example, $\mu_i^{HS}(x) = -\ln\left(1 - \sum v_j c_j(x)\right)$ by Bikerman ([8]), where v_j is the volume of the jth ion species (for our one-dimensional version, $v_j = 2r_j$ where r_j is the radius of the ion). Other refined local-dependent models include those of Carnahan-Starling and Boubik-Mansoori-Carnadan-Starling (see, e.g., [3, 7]).

As mentioned above, in this paper, we will only include the hard-sphere component μ_i^{HS}. We will use Rosenfeld's nonlocal models for μ_i^{HS} and assume the ion channel to be narrow so that it can be effectively treated as one-dimensional. In this case, for two ion species ($n = 2$), Rosefeld's one-dimensional model for μ_i^{HS} is exactly the same as that of Percus-Yevick ([30, 65, 66, 67, 68, 69]) and is given by

$$\mu_i^{HS} = kT\frac{\delta\Omega(\{c_j\})}{\delta c_i}, \tag{2.7}$$

where

$$\begin{aligned}
\Omega(\{c_j\}) =& -\int n_0(x;c_1,c_2)\ln(1-n_1(x;c_1,c_2))dx,\\
n_l(x;c_1,c_2) =& \sum_{j=1}^{2}\int c_j(x')\omega_l^j(x-x')dx', \quad (l=0,1),\\
\omega_0^j(x) =& \frac{\delta(x-r_j)+\delta(x+r_j)}{2}, \quad \omega_1^j(x) = \Theta(r_j-|x|),
\end{aligned} \tag{2.8}$$

where δ is the Dirac delta function, Θ the Heaviside function with $\Theta(x) = 0$ for $x < 0$ and $\Theta(x) = 1$ for $x \geq 0$, and r_j the radius of the jth ion species.

REMARK 2.1. *In [69], Rosenfeld discussed a reduction from his three-dimensional model of hard spheres potential to a one-dimensional version of hard spheres (hard rods) potential. He concluded that, the one-dimensional reduced version from the three-dimensional model recovers the one-dimensional model given in (2.7) and (2.8) but there is an extra divergent term. Rosefeld's three-dimensional model for hard-sphere potential has been modified to resolve this problem so that the new models produce exactly the one-dimensional model (2.7) and (2.8) through the reduction procedure ([84, 85]).*

2.1.2. Our problem and a strategy of analysis. The main goal is to examine the qualitative effect of ion sizes via the one-dimensional version PNP-DFT model (2.3) and (2.4). Here we collect the basic assumptions for the situation considered in this paper.

(A1). We consider two ion species ($n = 2$) with $z_1 > 0$ and $z_2 < 0$, and assume electroneutrality boundary conditions: $z_1L_1 + z_2L_2 = z_1R_1 + z_2R_2 = 0$.

(A2). The permanent charge is set to be zero: $Q(x) = 0$.
(A3). For the electrochemical potential μ_i, in addition to the ideal component μ_i^{id}, we only include the hard-sphere component μ_i^{HS} of the excess potential μ_i^{ex}.
(A4). The relative permittivity and the diffusion coefficients are constants, that is, $\varepsilon_r(x) = \varepsilon_r$ and $D_i(x) = D_i$.

After substituting (2.6) for $\mu_i^{id}(x)$ and making the dimensionless re-scaling,

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

we get the following one-dimensional version PNP-DFT system for two ion species with valences $\alpha = z_1 > 0$ and $-\beta = z_2 < 0$:

$$\begin{aligned}
&\frac{1}{h(x)}\frac{d}{dx}\Big(\varepsilon^2 h(x)\frac{d}{dx}\bar{\phi}\Big) = -(\alpha c_1 - \beta c_2), \quad \frac{d\bar{J}_i}{dx} = 0,\\
&h(x)\frac{dc_1}{dx} + \alpha h(x)c_1\frac{d\bar{\phi}}{dx} + \frac{h(x)c_1(x)}{kT}\frac{d}{dx}\mu_1^{HS}(x) = -\bar{J}_1,\\
&h(x)\frac{dc_2}{dx} - \beta h(x)c_2\frac{d\bar{\phi}}{dx} + \frac{h(x)c_2(x)}{kT}\frac{d}{dx}\mu_2^{HS}(x) = -\bar{J}_2,
\end{aligned} \tag{2.9}$$

with the boundary conditions

$$\bar{\phi}(0) = \bar{V}, \quad c_i(0) = L_i; \quad \bar{\phi}(1) = 0, \quad c_i(1) = R_i. \tag{2.10}$$

Due to the nonlocal dependence of μ_i^{HS} on $\{c_j\}$ in (2.7), system (2.9) is an integro-differential system. A description of the strategy of our analysis on the singularly perturbed boundary value problem (2.9) and (2.10) is in place.

First of all, using the model (2.7) for μ_i^{HS} of (c_1, c_2), we define a mapping

$$\mathcal{G} : \mathcal{C}^1([0,1], \mathbb{R}^2) \to \mathcal{C}^0([0,1], \mathbb{R}^2) \ \text{ by } \ \mathcal{G}(c_1, c_2)(x) = (G_1(x), G_2(x)),$$

where

$$G_i(x) = \frac{h(x)c_i(x)}{kT}\frac{d}{dx}\mu_i^{HS}(x), \quad i = 1, 2. \tag{2.11}$$

Now, for arbitrary but fixed continuous functions $G_i(x)$ for $x \in [0,1]$, we introduce an auxiliary boundary value problem

$$\begin{aligned}
&\frac{\varepsilon^2}{h(x)}\frac{d}{dx}\Big(h(x)\frac{d}{dx}\bar{\phi}\Big) = -(\alpha c_1 - \beta c_2), \quad \frac{d\bar{J}_i}{dx} = 0,\\
&h(x)\frac{dc_1}{dx} + \alpha h(x)c_1\frac{d\bar{\phi}}{dx} + G_1(x) = -\bar{J}_1,\\
&h(x)\frac{dc_2}{dx} - \beta h(x)c_2\frac{d\bar{\phi}}{dx} + G_2(x) = -\bar{J}_2,
\end{aligned} \tag{2.12}$$

with the boundary conditions

$$\bar{\phi}(0) = \bar{V}, \quad c_i(0) = L_i; \quad \bar{\phi}(1) = 0, \quad c_i(1) = R_i. \tag{2.13}$$

Our original boundary value problem (2.9) and (2.10) is thus equivalent to the auxiliary boundary value problem (2.12) and (2.13) subject to the constraints on G_i's given by (2.11).

To study the latter problem, we first extend the geometric singular perturbation analysis in ([27, 52, 53]) for the classical PNP problem to this auxiliary problem (2.12) and (2.13) for any fixed G_i's in §3. As a result, we will get a solution $\big(\bar{\phi}(x;\varepsilon), c_i(x;\varepsilon), J_i(\varepsilon)\big)$ in terms of $G_i(x)$. In this way, we obtain another mapping

$$\mathcal{F} : \mathcal{C}^0([0,1], \mathbb{R}^2) \to \mathcal{C}^1([0,1], \mathbb{R}^2) \ \text{ by } \ \mathcal{F}(G_1, G_2)(x) = (c_1(x;\varepsilon), c_2(x;\varepsilon)).$$

Finally, the original problem (2.9) and (2.10) is reduced to a fixed point problem

$$(G_1(x), G_2(x)) = (\mathcal{G} \circ \mathcal{F})(G_1, G_2)(x) \text{ for } (G_1, G_2) \in \mathcal{C}^0([0,1], \mathbb{R}^2).$$

We analyze relevant properties of the mapping $\mathcal{G}$ in §4 and those of the mapping $\mathcal{F}$ in the Appendix. The existence of a fixed point of $(\mathcal{G} \circ \mathcal{F})$ will be established in §5 by an application of the Implicit Function Theorem.

In §6, we will investigate the I-V relation, particularly, the qualitative effect of ion sizes on the I-V relation based on the analysis on $\mathcal{F}$ and $\mathcal{G}$.

REMARK 2.2. *From (2.7) and (2.8), the definition of $\mu_i^{HS}(x)$ for $x \in [0,1]$ requires (c_1, c_2) to be defined for $x \in [-\rho, 1+\rho]$ where $\rho = \max\{r_1 + r_2, 2r_1, 2r_2\}$. Hence, the domain of the mapping $\mathcal{G}$ should be $\mathcal{C}^1([-\rho, 1+\rho], \mathbb{R}^2)$. To form the composition $\mathcal{G} \circ \mathcal{F}$, the range of $\mathcal{F}$ should also be $\mathcal{C}^1([-\rho, 1+\rho], \mathbb{R}^2)$. This technical issue will be handled in the actual constructions of $\mathcal{F}$ and $\mathcal{G}$ in later sections.*

3. Geometry singular perturbation theory for problem (2.12)–(2.13). In this section, we extend the geometric singular perturbation theory for cPNP models developed in [27, 52, 53] to the auxiliary boundary value problem (2.12)–(2.13). The general framework is essentially the same and the main difference involves the terms G_i's in system (2.12). We will follow the procedure in [27] and refer the readers to the reference for details.

The first step is to rewrite the system (2.12) into a standard form for singularly perturbed systems and reformulate the boundary value problem to a connecting problem. We thus denote the derivative with respect to x by overdot and introduce $u = \varepsilon\dot{\bar{\phi}}$ and $\tau = x$. System (2.12) becomes an autonomous system of first order ordinary differential equations

$$\begin{aligned}
\varepsilon\dot{\bar{\phi}} =& u, \quad \varepsilon\dot{u} = \beta c_2 - \alpha c_1 - \varepsilon\frac{h'(\tau)}{h(\tau)}u,\\
\varepsilon\dot{c}_1 =& -\alpha c_1 u - \varepsilon h^{-1}(\tau)(G_1(\tau) + \bar{J}_1),\\
\varepsilon\dot{c}_2 =& \beta c_2 u - \varepsilon h^{-1}(\tau)(G_2(\tau) + \bar{J}_2),\\
\dot{\bar{J}}_1 =& \dot{\bar{J}}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{3.1}$$

The phase space for system (3.1) is $\mathbb{R}^7$ with state variables $(\bar{\phi}, u, c_1, c_2, \bar{J}_1, \bar{J}_2, \tau)$. System (3.1) is the so-called *slow system* of this singularly perturbed problem. In terms of the fast variable $\xi = x/\varepsilon$, one obtains the so-called *fast system*

$$\begin{aligned}
\bar{\phi}' =& u, \quad u' = \beta c_2 - \alpha c_1 - \varepsilon\frac{h'(\tau)}{h(\tau)}u,\\
c_1' =& -\alpha c_1 u - \varepsilon h^{-1}(\tau)(G_1(\tau) + \bar{J}_1),\\
c_2' =& \beta c_2 u - \varepsilon h^{-1}(\tau)(G_2(\tau) + \bar{J}_2),\\
\bar{J}_1' =& \bar{J}_2' = 0, \quad \tau' = \varepsilon,
\end{aligned} \tag{3.2}$$

where prime denotes the derivative with respect to the independent variable ξ.

While systems (3.1) and (3.2) have exactly the same phase portrait for $\varepsilon > 0$, their limiting systems at $\varepsilon = 0$ often provide complementary information on state variables: the limiting fast system (3.2) at $\varepsilon = 0$ captures *singular layer* behavior of the solution and the limiting slow system (3.1) at $\varepsilon = 0$ describes *regular layer* behavior. An orbit of the limiting fast system (3.2) at $\varepsilon = 0$ is called a *fast orbit* and an orbit of the limiting slow system (3.1) at $\varepsilon = 0$ is called a *slow orbit*. *A singular orbit* is thus a continuous and piecewise smooth curve in $\mathbb{R}^7$ that is a union of finitely many slow orbits and fast orbits. The main task of singularly perturbed problems is to lift a singular orbit to a solution for $\varepsilon > 0$ systems.

Now let B_L and B_R be the subsets of the phase space $\mathbb{R}^7$ defined by

$$\begin{aligned}
B_L =& \left\{(\bar{V}, u, L_1, L_2, \bar{J}_1, \bar{J}_2, 0) \in \mathbb{R}^7 : \text{arbitrary } u, \bar{J}_1, \bar{J}_2\right\},\\
B_R =& \left\{(0, u, R_1, R_2, \bar{J}_1, \bar{J}_2, 1) \in \mathbb{R}^7 : \text{arbitrary } u, \bar{J}_1, \bar{J}_2\right\}.
\end{aligned} \tag{3.3}$$

It is clear that the boundary value problem (2.12)–(2.13) is equivalent to a connecting problem, namely, finding a solution of (3.1) or (3.2) from B_L to B_R. The advantage of introducing the variable $\tau = x$ is that the existence of a solution for the connecting problem depends only on the phase portrait of (3.1) (the same as that of (3.2)); in particular, one can apply any rescaling of the independent variables.

In what follows, we will first construct a singular orbit and then apply the geometric singular perturbation theory to show that there is a unique solution of the connecting problem near the singular orbit for small $\varepsilon > 0$.

3.1. Construction of singular orbits. The construction of a singular orbit follows closely the line in [27, 52, 53]. Typically, such an orbit consists of singular boundary layers and regular layers.

3.1.1. Limiting fast dynamics and boundary layers. By setting $\varepsilon = 0$ in (3.1), we obtain the so-called *slow manifold* $\mathcal{Z} = \{u = 0, \alpha c_1 = \beta c_2\}$. Meanwhile, by setting $\varepsilon = 0$ in (3.2), we get the *limiting fast system*

$$\begin{aligned} \bar{\phi}' =& u, \quad u' = \beta c_2 - \alpha c_1, \\ c_1' =& -\alpha c_1 u, \quad c_2' = \beta c_2 u, \\ \bar{J}_1' =& \bar{J}_2' = 0, \quad \tau' = 0. \end{aligned} \tag{3.4}$$

REMARK 3.1. *Since $G_i(x)$ should have a layer whenever $c_j(x)$'s have, it seems not correct that the terms $G_i(x)$'s do not appear in the layer system (3.4). The reason is the following. Although the term $G_i(x)$ is related to $\{c_j(x)\}$ through $d\mu_i^{HS}/dx$, it can be seen from the formulas in Lemma 4.2 that $d\mu_i^{HS}/dx$ can be expressed in terms of $c_j(x)$'s (*not the gradients of $c_j(x)$'s*); in particular, from (2.11), $G_i(x)$ is expected to be of order $O(1)$ in ε (it is the* gradient *of $G_i(x)$ that would be of order $O(1/\varepsilon)$ at layer locations of c_j's). Hence the terms $G_i(x)$'s disappear in system (3.4) due to the factor ε for the terms $\varepsilon G_i(x)$'s in system (3.2).*

The situation would be different if one uses local- *or* pointwise-dependent *models for $\mu_i^{HS}(x)$ such as those mentioned in Section 2.1.1. In all these cases, if c_j's have layers at a point x, then $G_i(x)$* itself*, which involves dc_j/dx's, would be of order $O(1/\varepsilon)$ in ε, and hence, the term $\varepsilon G_i(x)$ would survive in layer system (3.4). We mention that our approach can be modified to handle this situation. The observation is that, for those local-dependent models, although G_i's become of order $O(1/\varepsilon)$ in ε, there are factors of like r_j's in the term εG_i, and hence, the term survived in system (3.4) would be of order $O(r_j)$'s. We can then treat system (3.4) as a* regular perturbation *to the problem with $r_j = 0$. Without going into details, we claim that our results could be proved in a much simpler way. We would be interesting in looking at local-dependent models and compare the results to those of the non-local model.*

The limiting fast system (3.4) has been completely analyzed in [27, 52, 53]. Here we briefly recall the results in [27].

The slow manifold $\mathcal{Z}$ consists of equilibria of (3.4). A simple computation shows that the linearized matrix of (3.4) at each point of $(\bar{\phi}, 0, c_1, c_2, \bar{J}_1, \bar{J}_2, \tau) \in \mathcal{Z}$ has five zero eigenvalues whose generalized eigenspace is the tangent space of the five-dimensional slow manifold $\mathcal{Z}$, and the other two eigenvalues are $\pm\sqrt{\alpha^2 c_1 + \beta^2 c_2} \neq 0$ whose eigenvectors are not tangent to $\mathcal{Z}$. Thus $\mathcal{Z}$ is normally hyperbolic. We denote the stable and unstable manifolds of $\mathcal{Z}$ by $W^s(\mathcal{Z})$ and $W^u(\mathcal{Z})$, respectively.

Let M_L be the collection of orbits from B_L in forward time under the flow of system (3.4) and M_R be the collection of orbits from B_R in backward time under the flow of system (3.4). Then, for a singular orbit connecting B_L to B_R, the boundary layer at $x = 0$ must lie in $N_L = M_L \cap W^s(\mathcal{Z})$ and the boundary layer at $x = 1$ must lie in $N_R = M_R \cap W^u(\mathcal{Z})$. The following two propositions are established in [27, 52].

PROPOSITION 3.1. *System (3.4) has a complete set of first integrals as follows:*

$$H_1 = e^{\alpha\bar{\phi}} c_1,\ H_2 = e^{-\beta\bar{\phi}} c_2,\ H_3 = c_1 + c_2 - \frac{1}{2}u^2,\ H_4 = \bar{J}_1,\ H_5 = \bar{J}_2,\ H_6 = \tau.$$

With the help of the integrals, one can characterize the boundary layer behavior.

PROPOSITION 3.2. (i) *The stable manifold $W^s(\mathcal{Z})$ intersects B_L transversally at points with*

$$u_0 =[\mathrm{sgn}(\alpha L_1 - \beta L_2)]\sqrt{2\Big(L_1 + L_2 - \frac{\alpha+\beta}{\alpha\beta}(\alpha L_1)^{\frac{\beta}{\alpha+\beta}}(\beta L_2)^{\frac{\alpha}{\alpha+\beta}}\Big)},$$

and arbitrary $\bar{J}_i$'s, where sgn *denotes the sign function.*

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

$$u_1 =[\mathrm{sgn}(\beta R_2 - \alpha R_1)]\sqrt{2\Big(R_1 + R_2 - \frac{\alpha+\beta}{\alpha\beta}(\alpha R_1)^{\frac{\beta}{\alpha+\beta}}(\beta R_2)^{\frac{\alpha}{\alpha+\beta}}\Big)},$$

and arbitrary $\bar{J}_i$'s.

(ii) *The potential boundary layer Γ^0 at $x = 0$ are determined up to $(\bar{J}_1, \bar{J}_2)$ as follows: $\bar{\phi}(\xi)$ satisfies the Hamiltonian system*

$$\bar{\phi}'' + \alpha L_1 e^{\alpha(\bar{V}-\bar{\phi})} - \beta L_2 e^{-\beta(\bar{V}-\bar{\phi})} = 0,$$

together with $\bar{\phi}(0) = \bar{V}$ and $\bar{\phi}(\xi) \to \bar{\phi}^L = \bar{V} - \frac{1}{\alpha+\beta}\ln\frac{\beta L_2}{\alpha L_1}$ as $\xi \to \infty$; and

$$u(\xi) = \bar{\phi}'(\xi), \quad c_1(\xi) = L_1 e^{\alpha(\bar{V}-\bar{\phi}(\xi))}, \quad c_2(\xi) = L_2 e^{-\beta(\bar{V}-\bar{\phi}(\xi))},$$

with $u(0) = u_0$ and, as $\xi \to \infty$,

$$u(\xi) \to 0, \quad c_1(\xi) \to c_1^L = \frac{1}{\alpha}(\alpha L_1)^{\frac{\beta}{\alpha+\beta}}(\beta L_2)^{\frac{\alpha}{\alpha+\beta}}, \quad c_2(\xi) \to c_2^L = \frac{1}{\beta}(\alpha L_1)^{\frac{\beta}{\alpha+\beta}}(\beta L_2)^{\frac{\alpha}{\alpha+\beta}}.$$

Similarly, the potential boundary layer Γ^1 at $x = 1$ are determined in the following way: $\bar{\phi}(\xi)$ satisfies the Hamiltonian system

$$\bar{\phi}'' + \alpha R_1 e^{-\alpha\bar{\phi}} - \beta R_2 e^{\beta\bar{\phi}} = 0,$$

together with $\bar{\phi}(0) = 0$ and $\bar{\phi}(\xi) \to \bar{\phi}^R = -\frac{1}{\alpha+\beta}\ln\frac{\beta R_2}{\alpha R_1}$ as $\xi \to -\infty$; and

$$u(\xi) = \bar{\phi}'(\xi), \quad c_1(\xi) = R_1 e^{-\alpha\bar{\phi}(\xi)}, \quad c_2(\xi) = R_2 e^{\beta\bar{\phi}(\xi)},$$

with $u(0) = u_1$ and, as $\xi \to -\infty$,

$$u(\xi) \to 0, \quad c_1(\xi) \to c_1^R = \frac{1}{\alpha}(\alpha R_1)^{\frac{\beta}{\alpha+\beta}}(\beta R_2)^{\frac{\alpha}{\alpha+\beta}}, \quad c_2(\xi) \to c_2^R = \frac{1}{\beta}(\alpha R_1)^{\frac{\beta}{\alpha+\beta}}(\beta R_2)^{\frac{\alpha}{\alpha+\beta}}.$$

(iii) *The ω-limit set of $N_L = M_L \cap W^s(\mathcal{Z})$ and the α-limit set of $N_R = M_R \cap W^u(\mathcal{Z})$ are*

$$\omega(N_L) = \left\{(\bar{\phi}^L, 0, c_1^L, c_2^L, \bar{J}_1, \bar{J}_2, 0) : \text{ all } \bar{J}_1, \bar{J}_2\right\},$$
$$\alpha(N_R) = \left\{(\bar{\phi}^R, 0, c_1^R, c_2^R, \bar{J}_1, \bar{J}_2, 1) : \text{ all } \bar{J}_1, \bar{J}_2\right\},$$

where $\bar{\phi}^L, \bar{\phi}^R, c_j^L, c_j^R$ are given explicitly in parts (i) and (ii).

COROLLARY 3.3. *Under the electro-neutrality conditions at both ends of the channel, that is, $\alpha L_1 = \beta L_2$ and $\alpha R_1 = \beta R_2$, we have $\bar{\phi}^L = \bar{V}, c_1^L = L_1, c_2^L = L_2$ and $\bar{\phi}^R = 0, c_1^R = R_1, c_2^R = R_2$, and hence, there is no boundary layers.*

3.1.2. Limiting slow dynamics and regular layer. Next we construct the regular layer on $\mathcal{Z}$ that connects $\omega(N_L)$ and $\alpha(N_R)$. Note that, for $\varepsilon = 0$, system (3.1) losses most information. To remedy this degeneracy, we follow the idea in [27, 52, 53] and make a rescaling $u = \varepsilon p$ and $\beta c_2 - \alpha c_1 = \varepsilon q$ in system (3.1). In terms of the new variables, system (3.1) becomes

$$\begin{aligned}
\dot{\bar{\phi}} =& p, \quad \varepsilon \dot{p} = q - \varepsilon \frac{h'(\tau)}{h(\tau)} p, \\
\varepsilon \dot{q} =& (\alpha(\alpha+\beta)c_1 + \varepsilon\beta q)p - h^{-1}(\tau)\big(\beta(G_2(\tau)+\bar{J}_2) - \alpha(G_1(\tau)+\bar{J}_1)\big), \\
\dot{c}_1 =& -\alpha c_1 p - h^{-1}(\tau)(G_1(\tau)+\bar{J}_1), \\
\dot{\bar{J}}_1 =& \dot{\bar{J}}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{3.5}$$

It is again a singular perturbation problem. Its limiting slow system for $\varepsilon = 0$ is

$$\begin{aligned}
\dot{\bar{\phi}} =& p, \quad 0 = q, \\
0 =& \alpha(\alpha+\beta)c_1 p - h^{-1}(\tau)\big(\beta(G_2(\tau)+\bar{J}_2) - \alpha(G_1(\tau)+\bar{J}_1)\big), \\
\dot{c}_1 =& -\alpha c_1 p - h^{-1}(\tau)(G_1(\tau)+\bar{J}_1), \\
\dot{\bar{J}}_1 =& \dot{\bar{J}}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{3.6}$$

For this system, the slow manifold is

$$\mathcal{S} = \left\{ p = \frac{\beta(G_2(\tau)+\bar{J}_2) - \alpha(G_1(\tau)+\bar{J}_1)}{\alpha(\alpha+\beta)h(\tau)c_1},\ q = 0 \right\}.$$

The limiting slow dynamics on $\mathcal{S}$ is

$$\begin{aligned}
&\dot{\bar{\phi}} = \frac{\beta(G_2(\tau)+\bar{J}_2) - \alpha(G_1(\tau)+\bar{J}_1)}{\alpha(\alpha+\beta)h(\tau)c_1}, \quad \dot{c}_1 = -\frac{\beta(G_1(\tau)+G_2(\tau)+\bar{J}_1+\bar{J}_2)}{(\alpha+\beta)h(\tau)}, \\
&\dot{\bar{J}}_1 = \dot{\bar{J}}_2 = 0, \quad \dot{\tau} = 1.
\end{aligned} \tag{3.7}$$

We are looking for regular layer orbits that connect $\omega(N_L)$ at $\tau = x = 0$ with $\alpha(N_R)$ at $\tau = x = 1$. Note that the point $(\bar{\phi}^L, 0, c_1^L, c_2^L, \bar{J}_1, \bar{J}_2, 0) \in \omega(N_L)$ corresponds to the point $(\bar{\phi}^L, c_1^L, \bar{J}_1, \bar{J}_2, 0)$ for system (3.7). The solution of (3.7) with the initial condition $(\bar{\phi}^L, c_1^L, \bar{J}_1, \bar{J}_2, 0)$ is

$$\begin{aligned}
&\tau(x) = x, \quad c_1(x) = c_1^L - \frac{\beta}{\alpha+\beta}\int_0^x \frac{G_1(s)+G_2(s)}{h(s)}ds - \frac{\beta(\bar{J}_1+\bar{J}_2)}{\alpha+\beta}\int_0^x \frac{1}{h(s)}ds, \\
&\bar{\phi}(x) = \bar{\phi}^L + \frac{1}{\alpha(\alpha+\beta)}\int_0^x \frac{\beta G_2(s) - \alpha G_1(s)}{h(s)c_1(s)}ds + \frac{\beta\bar{J}_2 - \alpha\bar{J}_1}{\alpha(\alpha+\beta)}\int_0^x \frac{1}{h(s)c_1(s)}ds.
\end{aligned} \tag{3.8}$$

For the solution to land on $\alpha(N_R)$ at $\tau = x = 1$, we have

$$\begin{aligned}
&c_1^R = c_1^L - \frac{\beta}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds - \frac{\beta(\bar{J}_1+\bar{J}_2)}{\alpha+\beta}\int_0^1 \frac{1}{h(s)}ds, \\
&\bar{\phi}^R = \bar{\phi}^L + \frac{1}{\alpha(\alpha+\beta)}\int_0^1 \frac{\beta G_2(s) - \alpha G_1(s)}{h(s)c_1(s)}ds + \frac{\beta\bar{J}_2 - \alpha\bar{J}_1}{\alpha(\alpha+\beta)}\int_0^1 \frac{1}{h(s)c_1(s)}ds.
\end{aligned} \tag{3.9}$$

It follows from (3.8), (3.9) and the relations $\alpha c_1^L = \beta c_2^L$ and $\alpha c_1^R = \beta c_2^R$ that

$$
\begin{aligned}
\bar{J}_1 &= \Big(\int_0^1 \frac{1}{h(s)}ds\Big)^{-1}\Big(c_1^L - c_1^R - \frac{\beta}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds\Big)\\
&\quad -\alpha\Big(\int_0^1 \frac{1}{h(s)c_1(s)}ds\Big)^{-1}\Big(\bar{\phi}^R - \bar{\phi}^L - \frac{1}{\alpha(\alpha+\beta)}\int_0^1 \frac{\beta G_2(s)-\alpha G_1(s)}{h(s)c_1(s)}ds\Big),\\
\bar{J}_2 &= \Big(\int_0^1 \frac{1}{h(s)}ds\Big)^{-1}\Big(c_2^L - c_2^R - \frac{\alpha}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds\Big)\\
&\quad +\alpha\Big(\int_0^1 \frac{1}{h(s)c_1(s)}ds\Big)^{-1}\Big(\bar{\phi}^R - \bar{\phi}^L - \frac{1}{\alpha(\alpha+\beta)}\int_0^1 \frac{\beta G_2(s)-\alpha G_1(s)}{h(s)c_1(s)}ds\Big),
\end{aligned}
\tag{3.10}
$$

where

$$
\begin{aligned}
c_1(x) &= c_1^L - \frac{\beta}{\alpha+\beta}\int_0^x \frac{G_1(s)+G_2(s)}{h(s)}ds\\
&\quad -\Big(\int_0^1 \frac{1}{h(s)}ds\Big)^{-1}\int_0^x \frac{1}{h(s)}ds\Big(c_1^L - c_1^R - \frac{\beta}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds\Big)
\end{aligned}
$$

can be obtained from (3.8) and (3.9). Thus, we have

PROPOSITION 3.4. *The regular layer Λ is given by*

$$
\begin{aligned}
\bar{\phi}(x) &= \bar{\phi}^L + \frac{1}{\alpha(\alpha+\beta)}\int_0^x \frac{\beta G_2(s)-\alpha G_1(s)}{h(s)c_1(s)}ds + \frac{\beta\bar{J}_2-\alpha\bar{J}_1}{\alpha(\alpha+\beta)}\int_0^x \frac{1}{h(s)c_1(s)}ds,\\
c_1(x) &= c_1^L - \frac{\beta}{\alpha+\beta}\int_0^x \frac{G_1(s)+G_2(s)}{h(s)}ds\\
&\quad -\Big(\int_0^1 \frac{1}{h(s)}ds\Big)^{-1}\int_0^x \frac{1}{h(s)}ds\Big(c_1^L - c_1^R - \frac{\beta}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds\Big),\\
u(x) &= 0, \quad \alpha c_1(x) = \beta c_2(x), \quad \tau(x) = x,
\end{aligned}
$$

where $\bar{J}_1$ and $\bar{J}_2$ are given by (3.10).

Now we have constructed a unique singular orbit on $[0,1]$ that connects B_L to B_R. It consists of two boundary layer orbits Γ^0 from the point $(\bar{V}, u_0, L_1, L_2, \bar{J}_1, \bar{J}_2, 0) \in B_L$ to the point $(\bar{\phi}^L, 0, c_1^L, c_2^L, \bar{J}_1, \bar{J}_2, 0) \in \omega(N_L) \subset \mathcal{Z}$ and Γ^1 from point $(\bar{\phi}^R, 0, c_1^R, c_2^R, \bar{J}_1, \bar{J}_2, 1) \in \alpha(N_R) \subset \mathcal{Z}$ to the point $(0, u_1, R_1, R_2, \bar{J}_1, \bar{J}_2, 1) \in B_R$, and a regular layer Λ on $\mathcal{Z}$ that connects the two foot points $(\bar{\phi}^L, 0, c_1^L, c_2^L, \bar{J}_1, \bar{J}_2, 0) \in \omega(N_L)$ and $(\bar{\phi}^R, 0, c_1^R, c_2^R, \bar{J}_1, \bar{J}_2, 1) \in \alpha(N_R)$ of the two boundary layers. In particular, when $\alpha L_1 = \beta L_2$ and $\alpha R_1 = \beta R_2$ (electro-neutrality conditions at both ends of the channel), $\bar{\phi}^L = \bar{V}$, $c_1^L = L_1$, $c_2^L = L_2$, $\bar{\phi}^R = 0$, $c_1^R = R_1$, $c_2^R = R_2$. In this case, the singular orbit consists of only the regular layer Λ that connects B_L to B_R.

3.2. Existence of solutions of (2.12)–(2.13) near the singular orbit. We now establish the existence of a solution of (2.12)–(2.13) near the singular orbit constructed above; in fact, we will prove a general result without assuming the electro-neutrality so the singular orbit is a union of two boundary layers and one regular layer $\Gamma^0 \cup \Lambda \cup \Gamma^1$. The proof follows the same line as that in [27, 53] and the main tool used is the Exchange Lemma (see, for example, [48, 49, 86]) of geometric singular perturbation theory.

We note that the singular orbit $\Gamma^0 \cup \Lambda \cup \Gamma^1$ are obtained from the limiting fast system (3.4) and the limiting slow system (3.6) for $\varepsilon = 0$. In particular, the formulas (3.10) provide the zeroth order (in ε) approximations for $\bar{J}_1$ and $\bar{J}_2$. In the following, we will denote these zeroth order approximations by $\bar{J}_{10}$ and $\bar{J}_{20}$, respectively.

THEOREM 3.5. *Let $\Gamma^0 \cup \Lambda \cup \Gamma^1$ be the singular orbit of the connecting problem (3.1) associated to B_L and B_R in (3.3). Then, for $\varepsilon > 0$ small, the auxiliary boundary value*

problem (2.12)–(2.13) has a unique smooth solution near the singular orbit. Furthermore, the solution is Fréchet differentiable with respect to $G_i(x)$.

Proof. For $\varepsilon > 0$ small, choose $\delta > 0$ small. Let

$$B_L(\delta) = \left\{(\bar{V}, u, L_1, L_2, \bar{J}_1, \bar{J}_2, 0) : |u - u_0| < \delta, |\bar{J}_i - \bar{J}_{i0}| < \delta\right\}.$$

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

To establish the transversal intersection of $M_L(\varepsilon)$ and $M_R(\varepsilon)$ near the singular orbit, we apply the Exchange Lemma successively along $\Gamma^0 \cup \Lambda \cup \Gamma^1$. Note that $\dim B_L(\delta) = 3$. Since the fast flow is not tangent to $B_L(\delta)$, one has $\dim M_L(\varepsilon) = 4$. The transversality of the intersection $B_L \cap W^s(\mathcal{Z})$ along Γ^0 implies the transversality of the intersection $M_L(0) \cap W^s(\mathcal{Z}_l)$. The Exchange Lemma implies that $M_L(\varepsilon)$ will first follow Γ^0 toward $N_L \subset \mathcal{Z}$, then follow the trace of N_L in the vicinity of Λ toward $\{x = 1\}$, leave the vicinity of $\mathcal{Z}$, and upon exit $M_L(\varepsilon)$ is C^1 $O(\varepsilon)$-close to $W^u(N_R \times (1-\delta, 1))$ in the vicinity of Γ^1. Since $W^u(N_R \times (1-\delta, 1))$ intersects $M_R(\varepsilon)$ transversally along Γ^1, we have that $M_L(\varepsilon)$ intersects $M_R(\varepsilon)$ transversally.

For the uniqueness, we note that the transversality of the intersection $M_L(\varepsilon) \cap M_R(\varepsilon)$ implies that $\dim(M_L(\varepsilon) \cap M_R(\varepsilon)) = \dim M_L(\varepsilon) + \dim M_R(\varepsilon) - 7 = 1$. Thus, $M_L(\varepsilon) \cap M_R(\varepsilon)$ consists of precisely one solution near the singular orbit.

A proof of the Fréchet differentiability of the solutions with respect to $G_i(x)$ is provided in Appendix. □

COROLLARY 3.6. *Under the electro-neutrality conditions $\alpha L_1 = \beta L_2$ and $\alpha R_1 = \beta R_2$, the $(c_1(x;\varepsilon), c_2(x;\varepsilon))$-component of the solution of the auxiliary boundary value problem (2.12)–(2.13) has the form $c_i(x;\varepsilon) = c_{i0}(x) + \varepsilon c_{iR}(x)$, $i = 1, 2$, where $c_{i0}(x)$ denotes the zeroth order approximation of $c_i(x;\varepsilon)$ in ε, and $c_{iR}(x)$ denotes the remainder. Also, denoting $L = \alpha L_1 = \beta L_2$ and $R = \alpha R_1 = \beta R_2$,*

$$\begin{aligned}\alpha c_{10}(x) = \beta c_{20}(x) = L - \frac{\alpha\beta}{\alpha+\beta}\int_0^x \frac{G_1(s)+G_2(s)}{h(s)}ds \\ -\Big(\int_0^1 \frac{1}{h(s)}ds\Big)^{-1}\int_0^x \frac{1}{h(s)}ds\Big(L - R - \frac{\alpha\beta}{\alpha+\beta}\int_0^1 \frac{G_1(s)+G_2(s)}{h(s)}ds\Big).\end{aligned}$$

Proof. It follows from Corollary 3.3 that, under the electro-neutrality conditions $\alpha L_1 = \beta L_2 = L$ and $\alpha R_1 = \beta R_2 = R$, there are no boundary layers Γ^0 and Γ^1. The form of $(c_1(x;\varepsilon), c_2(x;\varepsilon))$ then follows. Note that, under the electro-neutrality conditions, $\bar{\phi}^L = \bar{V}$, $c_1^L = L_1$, $c_2^L = L_2$, $\bar{\phi}^R = 0$, $c_1^R = R_1$, $c_2^R = R_2$. We then have the formulas for $c_{10}(x)$ and $c_{20}(x)$ from Proposition 3.4. □

4. The mapping from the hard-sphere potential μ_i^{HS}. In this section, we derive a convenient form for μ_i^{HS}. As remarked in §2 (Remark 2.2), in order to define $\mu_i^{HS}(x)$ for $x \in [0,1]$, we need an extension of $(c_1, c_2) \in \mathcal{C}^1([0,1], \mathbb{R}^2)$ to $\mathcal{C}^1([-\rho, 1+\rho], \mathbb{R}^2)$ where $\rho = \max\{r_1 + r_2, 2r_1, 2r_2\}$.

It turns out, up to $O(\rho)$, $\mu_i^{HS}(x)$ is independent of a particular extension. Since we will focus on the results up to $O(\rho)$ in this work, we can take any extension $(\hat{c}_1, \hat{c}_2) \in \mathcal{C}^1([-\rho, 1+\rho], \mathbb{R}^2)$ of $(c_1, c_2) \in \mathcal{C}^1([0,1], \mathbb{R}^2)$. In particular, for any small number $0 < \nu < \rho$, we can fix an extension that requires $(\hat{c}_1(x), \hat{c}_2(x)) = (L_1, L_2)$ for $x \in [-\rho, -\nu]$ and $(\hat{c}_1(x), \hat{c}_2(x)) = (R_1, R_2)$ for $x \in [1+\nu, 1+\rho]$, which is consistent with the physical consideration that the concentrations in the macroscopic reservoirs are nearly constants.

In the sequel, we will abuse the notation to denote an extension $(\hat{c}_1, \hat{c}_2)$ by (c_1, c_2).

LEMMA 4.1. *For the model μ_i^{HS} in (2.7) and (2.8) associated to $(c_1(x), c_2(x))$, we have, for $x \in [0,1]$,*

$$\mu_i^{HS}(x) = -\frac{kT}{2}\ln\Big(\Big(1-\sum_j\int_{x-r_i-r_j}^{x-r_i+r_j} c_j(x')dx'\Big)\Big(1-\sum_j\int_{x+r_i-r_j}^{x+r_i+r_j} c_j(x')dx'\Big)\Big) + \frac{kT}{2}\int_{x-r_i}^{x+r_i}\frac{\sum_j(c_j(x'-r_j)+c_j(x'+r_j))}{1-\sum_j\int_{x'-r_j}^{x'+r_j}c_j(x'')dx''}dx'.$$

Proof. We will only derive the formula for $\mu_1^{HS}(x)$. As mentioned above, we abuse the notion (c_1, c_2) in the lemma and in the sequel for its extension $(\hat{c}_1, \hat{c}_2)$. It follows from (2.7) and (2.8) that

$$\begin{aligned}\Omega(c_1+k,c_2)-\Omega(c_1,c_2) &= -\int n_0(x;c_1+k,c_2)\ln(1-n_1(x;c_1+k,c_2))dx \\ &\quad +\int n_0(x;c_1,c_2)\ln(1-n_1(x;c_1,c_2))dx \\ &= -\int\Big(\int k(x')\omega_0^1(x-x')dx'\Big)\ln(1-n_1(x;c_1,c_2))dx \\ &\quad +\int\frac{n_0(x;c_1,c_2)}{1-n_1(x;c_1,c_2)}\int k(x')\omega_1^1(x-x')dx'dx+o(\|k\|).\end{aligned}$$

Note that

$$\begin{aligned}\int k(x')\omega_0^1(x-x')dx' &= \int k(x')\frac{\delta(x-x'-r_1)+\delta(x-x'+r_1)}{2}dx \\ &= \frac{k(x-r_1)+k(x+r_1)}{2},\end{aligned}$$

and

$$\int k(x')\omega_1^1(x-x')dx' = \int k(x')\Theta(r_1-|x-x'|)dx' = \int_{x-r_1}^{x+r_1}k(x')dx'.$$

Therefore, for any $a(x)$ and $b(x)$,

$$\begin{aligned}\int a(x)\Big(\int k(x')\omega_0^1(x-x')dx'\Big)dx &= \int a(x)\frac{k(x-r_1)+k(x+r_1)}{2}dx \\ &= \int\frac{a(x-r_1)+a(x+r_1)}{2}k(x)dx,\end{aligned}$$

and

$$\int b(x)\int k(x')\omega_1^1(x-x')dx'dx = \int b(x)\int_{x-r_1}^{x+r_1}k(x')dx'dx = \int\int_{x-r_1}^{x+r_1}b(x')dx'k(x)dx.$$

Hence,

$$\begin{aligned}\Omega(c_1+k,c_2)-\Omega(c_1,c_2) &= -\frac{1}{2}\int\ln\Big((1-n_1(x-r_1))(1-n_1(x+r_1))\Big)k(x)dx \\ &\quad +\int\int_{x-r_1}^{x+r_1}\frac{n_0(x')}{1-n_1(x')}dx'k(x)dx+o(\|k\|);\end{aligned}$$

that is,

$$\frac{\delta\Omega(\{c_j\})}{\delta c_1} = -\frac{1}{2}\ln\left((1-n_1(x-r_1))(1-n_1(x+r_1))\right)+\int_{x-r_1}^{x+r_1}\frac{n_0(x')}{1-n_1(x')}dx'.$$

Note that

$$\begin{aligned} n_0(x) &= \sum_{j=1}^{2} \int c_j(x')\omega_0^j(x-x')dx' \\ &= \frac{1}{2}\sum_{j=1}^{2} \int c_j(x')(\delta(x-x'-r_j)+\delta(x-x'+r_j))dx' \\ &= \frac{1}{2}\sum_{j=1}^{2}(c_j(x-r_j)+c_j(x+r_j)), \end{aligned}$$

and

$$\begin{aligned} n_1(x) &= \sum_{j=1}^{2} \int c_j(x')\omega_1^j(x-x')dx' \\ &= \sum_{j=1}^{2} \int c_j(x')\Theta(r_j-|x-x'|)dx' = \sum_{j=1}^{2} \int_{x-r_j}^{x+r_j} c_j(x')dx'. \end{aligned}$$

The formula for μ_1^{HS} claimed in the lemma follows immediately. □

Set $r_1 = r$ and $r_2 = \lambda r$, and denote

$$\begin{aligned} K_1(x) &= \int_x^{x+2r} c_1(s)ds + \int_{x-(\lambda-1)r}^{x+(\lambda+1)r} c_2(s)ds, \\ K_2(x) &= \int_{x-2r}^{x} c_1(s)ds + \int_{x-(\lambda+1)r}^{x+(\lambda-1)r} c_2(s)ds, \\ K_3(x) &= \int_{x+(\lambda-1)r}^{x+(\lambda+1)r} c_1(s)ds + \int_{x}^{x+2\lambda r} c_2(s)ds, \\ K_4(x) &= \int_{x-(\lambda+1)r}^{x-(\lambda-1)r} c_1(s)ds + \int_{x-2\lambda r}^{x} c_2(s)ds. \end{aligned} \tag{4.1}$$

It is obvious that $K_1(x) = K_2(x+2r) = K_3(x-(\lambda-1)r) = K_4(x+(\lambda+1)r)$.

Lemma 4.2. *For the model μ_i^{HS} in (2.7) and (2.8) associated to $(c_1(x), c_2(x)) \in \mathcal{C}^1([0,1],\mathbb{R}^2)$, we have, for $x \in [0,1]$,*

$$\begin{aligned} G_1(x) &= \frac{h(x)c_1(x)}{kT}\frac{d}{dx}\mu_1^{HS}(x) \\ &= h(x)c_1(x)\Big(\frac{c_1(x+2r)+c_2(x+(\lambda+1)r)}{1-K_1(x)} - \frac{c_1(x-2r)+c_2(x-(\lambda+1)r)}{1-K_2(x)}\Big), \\ G_2(x) &= \frac{h(x)c_2(x)}{kT}\frac{d}{dx}\mu_2^{HS}(x) \\ &= h(x)c_2(x)\Big(\frac{c_1(x+(\lambda+1)r)+c_2(x+2\lambda r)}{1-K_3(x)} - \frac{c_1(x-(\lambda+1)r)+c_2(x-2\lambda r)}{1-K_4(x)}\Big). \end{aligned}$$

The mapping $(G_1, G_2) = \mathcal{G}(c_1, c_2) : \mathcal{C}^1([0,1],\mathbb{R}^2) \to \mathcal{C}^0([0,1],\mathbb{R}^2)$ defined above is Fréchet

differentiable, and its Fréchet derivative is as follows:

$$
\begin{aligned}
&(D\mathcal{G}_1)[d_1,d_2](x)\\
&\quad= h(x)\Big(\frac{c_1(x+2r)+c_2(x+(\lambda+1)r)}{1-K_1(x)}-\frac{c_1(x-2r)+c_2(x-(\lambda+1)r)}{1-K_2(x)}\Big)d_1(x)\\
&\qquad+h(x)c_1(x)\Big(\frac{d_1(x+2r)}{1-K_1(x)}-\frac{d_1(x-2r)}{1-K_2(x)}\Big)\\
&\qquad+\frac{h(x)c_1(x)(c_1(x+2r)+c_2(x+(\lambda+1)r))}{(1-K_1(x))^2}\int_x^{x+2r}d_1(s)ds\\
&\qquad-\frac{h(x)c_1(x)(c_1(x-2r)+c_2(x-(\lambda+1)r))}{(1-K_2(x))^2}\int_{x-2r}^{x}d_1(s)ds\\
&\qquad+h(x)c_1(x)\Big(\frac{d_2(x+(\lambda+1)r)}{1-K_1(x)}-\frac{d_2(x-(\lambda+1)r)}{1-K_2(x)}\Big)\\
&\qquad+\frac{h(x)c_1(x)(c_1(x+2r)+c_2(x+(\lambda+1)r))}{(1-K_1(x))^2}\int_{x-(\lambda-1)r}^{x+(\lambda+1)r}d_2(s)ds\\
&\qquad-\frac{h(x)c_1(x)(c_1(x-2r)+c_2(x-(\lambda+1)r))}{(1-K_2(x))^2}\int_{x-(\lambda+1)r}^{x+(\lambda-1)r}d_2(s)ds,
\end{aligned}
$$

$$
\begin{aligned}
&(D\mathcal{G}_2)[d_1,d_2](x)\\
&\quad= h(x)c_2(x)\Big(\frac{d_1(x+(\lambda+1)r)}{1-K_3(x)}-\frac{d_1(x-(\lambda+1)r)}{1-K_4(x)}\Big)\\
&\qquad+\frac{h(x)c_2(x)(c_1(x+(\lambda+1)r)+c_2(x+2\lambda r)}{(1-K_3(x))^2}\int_{x+(\lambda-1)r}^{x+(\lambda+1)r}d_1(s)ds\\
&\qquad-\frac{h(x)c_2(x)(c_1(x-(\lambda+1)r)+c_2(x-2\lambda r))}{(1-K_4(x))^2}\int_{x-(\lambda+1)r}^{x+(\lambda-1)r}d_1(s)ds\\
&\qquad+h(x)\Big(\frac{c_1(x+(\lambda+1)r)+c_2(x+2\lambda r)}{1-K_3(x)}-\frac{c_1(x-(\lambda+1)r)+c_2(x-2\lambda r)}{1-K_4(x)}\Big)d_2(x)\\
&\qquad+\frac{h(x)c_2(x)(c_1(x+(\lambda+1)r)+c_2(x+2\lambda r))}{(1-K_3(x))^2}\int_x^{x+2\lambda r}d_2(s)ds\\
&\qquad-\frac{h(x)c_2(x)(c_1(x-(\lambda+1)r)+c_2(x-2\lambda r))}{(1-K_4(x))^2}\int_{x-2\lambda r}^{x}d_2(s)ds\\
&\qquad+h(x)c_2(x)\Big(\frac{d_2(x+2\lambda r)}{1-K_3(x)}-\frac{d_2(x-2\lambda r)}{1-K_4(x)}\Big),
\end{aligned}
$$

where $K_i(x)$ $(i=1,\cdots,4)$ are given in (4.1). Moreover, $\|D\mathcal{G}\|=O(r)$ as $r\to 0$.

Proof. The formula for $\mathcal{G}$ as well as its Fréchet derivative follow directly from a computation using the expression μ_i^{HS} in Lemma 4.1. □

5. A fixed point problem and its solution. We are ready to give a precise setup of a fixed point problem whose solution is the solution of (2.9)–(2.10).

For any $(G_1,G_2)\in\mathcal{C}^0([0,1],\mathbb{R}^2)$, let $(\bar\phi,c_1,c_2)$ be the solution of the auxiliary problem (2.12)–(2.13). Define $\mathcal{F}:\mathcal{C}^0([0,1],\mathbb{R}^2)\to\mathcal{C}^1([-\rho,1+\rho],\mathbb{R}^2)$ via

$$(c_1,c_2)=\mathcal{F}(G_1,G_2). \tag{5.1}$$

Recall that (c_1,c_2) in (5.1) is actually its extension $(\hat c_1,\hat c_2)$ to $x\in[-\rho,1+\rho]$.

The mapping $\mathcal{G}:\mathcal{C}^1([-\rho,1+\rho],\mathbb{R}^2)\to\mathcal{C}^0([0,1],\mathbb{R}^2)$ is defined in Lemma 4.2

$$(G_1,G_2)=\mathcal{G}(c_1,c_2). \tag{5.2}$$

Let $\mathcal{J} = \mathcal{G} \circ \mathcal{F} : \mathcal{C}^0([0,1], \mathbb{R}^2) \to \mathcal{C}^0([0,1], \mathbb{R}^2)$. The fixed point problem is then

$$(G_1, G_2) = \mathcal{J}(G_1, G_2), \quad (G_1, G_2) \in \mathcal{C}^0([0,1], \mathbb{R}^2). \tag{5.3}$$

THEOREM 5.1. *Under the electro-neutrality conditions $\alpha L_1 = \beta L_2$ and $\alpha R_1 = \beta R_2$, if the parameter ε, the radii r_1 and r_2 are small enough, then the boundary value problem (2.9) and (2.10) has a unique solution.*

Proof. It suffices to show, under the condition in the theorem, that the fixed point problem (5.3) has a unique solution. The latter is equivalent to

$$\mathcal{H}(G_1, G_2)(x) := (G_1(x), G_2(x)) - \mathcal{J}(G_1, G_2)(x) = 0. \tag{5.4}$$

Note that $\mathcal{J}(G_1, G_2) = \big(\mathcal{G} \circ \mathcal{F}\big)(G_1, G_2)$ depends on r and ε implicitly. The Fréchet derivative $D\mathcal{G}$ of $\mathcal{G}$ is of order $O(r)$ as $r \to 0$ and that $D\mathcal{F}$ of $\mathcal{F}$ is uniformly bounded in ε for small $\varepsilon > 0$ (Theorem 3.5 and Lemma 4.2). We thus conclude, for $\varepsilon > 0$ small and as $r \to 0$, the Fréchet derivative $D\mathcal{H}$ of $\mathcal{H}$ is of order $O(r)$ close to the identity. The Implicit Function Theorem implies that, for $\varepsilon > 0$ small and $r > 0$ small, the equation (5.4) has a unique solution (G_1, G_2). □

6. Ion size effect on I-V relations. The analysis in the previous sections not only establishes the existence of a unique solution for boundary value problem (2.9) and (2.10) but also provides quantitative information on the solution that allows us to extract a useful approximation to the I-V relation for small r. A number of nontrivial consequences can be drawn from the approximated I-V relation.

We will drive an approximation of the I-V relation (2.5) in r for the case where $n = 2$ and $h(x) = 1$ under the electro-neutrality conditions $\alpha L_1 = \beta L_2 = L$ and $\alpha R_1 = \beta R_2 = R$. For $\varepsilon > 0$ small, let

$$I(V; \varepsilon, r) = I_0(V; \varepsilon) + I_1(V; \varepsilon) r + o(r). \tag{6.1}$$

We will be interested in $I_0(V; \varepsilon)$ and $I_1(V; \varepsilon)$ in the expansion (6.1).

THEOREM 6.1. *Under the electro-neutrality conditions $\alpha L_1 = \beta L_2 = L$ and $\alpha R_1 = \beta R_2 = R$, we have*

$$\begin{aligned}
I_0(V;0) &= e(D_1 - D_2)(L - R) + \frac{e^2(\alpha D_1 + \beta D_2)(L - R)}{kT(\ln L - \ln R)} V, \\
I_1(V;0) &= \frac{2e(D_1 - D_2)(\alpha\lambda + \beta)(L^2 - R^2)}{\alpha\beta} - \frac{2e(\alpha D_1 + \beta D_2)(\lambda - 1)(L - R)^2}{\alpha\beta(\ln L - \ln R)} \\
&\quad + \frac{2e^2(\alpha D_1 + \beta D_2)(\alpha\lambda + \beta)[(L^2 - R^2)(\ln L - \ln R) - 2(L - R)^2]V}{\alpha\beta kT(\ln L - \ln R)^2}.
\end{aligned}$$

Proof. Note that, for $\varepsilon = 0$, $I(V; 0, r) = \alpha e J_{10} - \beta e J_{20} = \alpha e D_1 \bar{J}_{10} - \beta e D_2 \bar{J}_{20}$ (see (2.5)) where $\bar{J}_{10}$ and $\bar{J}_{20}$ are the zeroth order (in ε) approximation of $\bar{J}_1$ and $\bar{J}_2$ given in (3.10). Using the electro-neutrality conditions $\alpha L_1 = \beta L_2 = L$ and $\alpha R_1 = \beta R_2 = R$, and its

consequences $\bar\phi^L=\bar V=\frac{e}{kT}V,\ c_i^L=L_i,\ \bar\phi^R=0,\ c_i^R=R_i$, we have

$$\begin{aligned}
I(V;0,r)&=\alpha eD_1\bar J_{10}-\beta eD_2\bar J_{20}\\
&=\alpha eD_1\Big(L_1-R_1-\int_0^1\frac{\beta(G_{10}(s)+G_{20}(s))}{\alpha+\beta}ds\Big)\\
&\quad-\frac{\alpha^2eD_1}{\int_0^1\frac{1}{c_{10}(s)}ds}\Big(-\bar V-\int_0^1\frac{\beta G_{20}(s)-\alpha G_{10}(s)}{\alpha(\alpha+\beta)c_{10}(s)}ds\Big)\\
&\quad-\beta eD_2\left(L_2-R_2-\int_0^1\frac{\alpha(G_{10}(s)+G_{20}(s))}{\alpha+\beta}ds\right)\\
&\quad-\frac{\alpha\beta eD_2}{\int_0^1\frac{1}{c_{10}(s)}ds}\Big(-\bar V-\int_0^1\frac{\beta G_{20}(s)-\alpha G_{10}(s)}{\alpha(\alpha+\beta)c_{10}(s)}ds\Big)\\
&=e(D_1-D_2)\Big(L-R-\int_0^1\frac{\alpha\beta(G_{10}(s)+G_{20}(s))}{\alpha+\beta}ds\Big)\\
&\quad+\frac{\alpha e^2(\alpha D_1+\beta D_2)}{kT\int_0^1\frac{1}{c_{10}(s)}ds}V+\frac{\alpha eD_1+\beta eD_2}{\int_0^1\frac{1}{c_{10}(s)}ds}\int_0^1\frac{\beta G_{20}(s)-\alpha G_{10}(s)}{(\alpha+\beta)c_{10}(s)}ds,
\end{aligned}\tag{6.2}$$

where the subscript $i0$ refers to the zeroth order approximation quantities of system (2.9)–(2.10) in ε; in particular, from Corollary 3.6 and Lemma 4.2,

$$\begin{aligned}
G_{10}(x)&=c_{10}(x)\frac{c_{10}(x+2r)+c_{20}(x+(\lambda+1)r)}{1-\int_x^{x+2r}c_{10}(s)ds-\int_{x-(\lambda-1)r}^{x+(\lambda+1)r}c_{20}(s)ds}\\
&\quad-c_{10}(x)\frac{c_{10}(x-2r)+c_{20}(x-(\lambda+1)r)}{1-\int_{x-2r}^{x}c_{10}(s)ds-\int_{x-(\lambda+1)r}^{x+(\lambda-1)r}c_{20}(s)ds},\\
G_{20}(x)&=c_{20}(x)\frac{c_{10}(x+(\lambda+1)r)+c_{20}(x+2\lambda r)}{1-\int_{x+(\lambda-1)r}^{x+(\lambda+1)r}c_{10}(s)ds-\int_{x}^{x+2\lambda r}c_{20}(s)ds}\\
&\quad-c_{20}(x)\frac{c_{10}(x-(\lambda+1)r)+c_{20}(x-2\lambda r)}{1-\int_{x-(\lambda+1)r}^{x-(\lambda-1)r}c_{10}(s)ds-\int_{x-2\lambda r}^{x}c_{20}(s)ds},
\end{aligned}\tag{6.3}$$

and

$$\begin{aligned}
\alpha c_{10}(x)=\beta c_{20}(x)&=L-\frac{\alpha\beta}{\alpha+\beta}\int_0^x(G_{10}(s)+G_{20}(s))ds\\
&\quad-\Big(L-R-\frac{\alpha\beta}{\alpha+\beta}\int_0^1(G_{10}(s)+G_{20}(s))ds\Big)x.
\end{aligned}\tag{6.4}$$

To simplify the expressions of $(G_{10}(x),G_{20}(x))$ and $(c_{10}(x),c_{20}(x))$, we first write

$$\alpha c_{10}(x)=\beta c_{20}(x)=A_0(x)+A_1(x)r+o(r)\tag{6.5}$$

for some functions $A_0(x)$ and $A_1(x)$ to be determined later on. Then we expand G_{10} and G_{20} in r from (6.3) to get

$$\begin{aligned}
G_{10}(x)&=2c_{10}(x)\left(2c_{10}'(x)+(\lambda+1)c_{20}'(x)\right)r+o(r)\\
&=\frac{2(\alpha(\lambda+1)+2\beta)}{\alpha^2\beta}A_0(x)A_0'(x)r+o(r),\\
G_{20}(x)&=2c_{20}(x)\left((\lambda+1)c_{10}'(x)+2\lambda c_{20}'(x)\right)r+o(r)\\
&=\frac{2(2\alpha\lambda+\beta(\lambda+1))}{\alpha\beta^2}A_0(x)A_0'(x)r+o(r).
\end{aligned}\tag{6.6}$$

Substitute (6.6) into (6.4) and use (6.5) to get

$$A_0(x) = L - (L-R)x, \quad A_1(x) = \frac{2(\alpha\lambda+\beta)(L-R)^2}{\alpha\beta}x(1-x).$$

Thus,

$$\begin{aligned}
\alpha c_{10}(x) = \beta c_{20}(x) &= L - (L-R)x + \frac{2(\alpha\lambda+\beta)(L-R)^2}{\alpha\beta}x(1-x)r + o(r),\\
G_{10}(x) &= -\frac{2(\alpha(\lambda+1)+2\beta)(L-R)}{\alpha^2\beta}[L-(L-R)x]r + o(r),\\
G_{20}(x) &= -\frac{2(2\alpha\lambda+\beta(\lambda+1))(L-R)}{\alpha\beta^2}[L-(L-R)x]r + o(r).
\end{aligned} \tag{6.7}$$

It follows from (6.7) that

$$\begin{aligned}
\int_0^1 \frac{1}{c_{10}(x)}dx &= \int_0^1 \frac{\alpha}{L-(L-R)x + \frac{2(\alpha\lambda+\beta)(L-R)^2}{\alpha\beta}x(1-x)r + o(r)}dx\\
&= \frac{\alpha(\ln L - \ln R)}{L-R} + \frac{2(\alpha\lambda+\beta)}{\beta}\Big(2-(L+R)\frac{\ln L-\ln R}{L-R}\Big)r + o(r),
\end{aligned}$$

and hence,

$$\begin{aligned}
\frac{1}{\int_0^1 \frac{1}{c_{10}(x)}dx} &= \frac{1}{\frac{\alpha(\ln L-\ln R)}{L-R} + \frac{2(\alpha\lambda+\beta)}{\beta}\left(2-(L+R)\frac{\ln L-\ln R}{L-R}\right)r + o(r)}\\
&= \frac{L-R}{\alpha(\ln L-\ln R)} - \frac{2(\alpha\lambda+\beta)\big(2(L-R)^2-(L^2-R^2)(\ln L-\ln R)\big)}{\alpha^2\beta(\ln L-\ln R)^2}r + o(r).
\end{aligned} \tag{6.8}$$

Also, from (6.7), we have

$$\int_0^1 (G_{10}(s)+G_{20}(s))ds = -\frac{2(\alpha+\beta)(\alpha\lambda+\beta)(L^2-R^2)}{\alpha^2\beta^2kT}r + o(r), \tag{6.9}$$

and

$$\begin{aligned}
\int_0^1 \frac{\beta G_{20}(s)-\alpha G_{10}(s)}{c_{10}(s)}ds &= \Big(2\alpha(\lambda-1)\int_0^1 (c'_{10}(x)+c'_{20}(x))dx\Big)r + o(r)\\
&= -\frac{2(\alpha+\beta)(\lambda-1)(L-R)}{\beta}r + o(r).
\end{aligned} \tag{6.10}$$

Finally, by (6.2), (6.8), (6.9) and (6.10), we have

$$\begin{aligned}
I(V;0,r) = e(D_1-D_2)(L-R) &+ \frac{e^2(\alpha D_1+\beta D_2)(L-R)}{kT(\ln L-\ln R)}V\\
&+\frac{2e(D_1-D_2)(\alpha\lambda+\beta)(L^2-R^2)}{\alpha\beta}r\\
&+\frac{2e^2(\alpha D_1+\beta D_2)(\alpha\lambda+\beta)[(L^2-R^2)(\ln L-\ln R)-2(L-R)^2]V}{\alpha\beta kT(\ln L-\ln R)^2}r\\
&-\frac{2e(\alpha D_1+\beta D_2)(\lambda-1)(L-R)^2}{\alpha\beta(\ln L-\ln R)}r + o(r).
\end{aligned}$$

The claimed formulas for $I_0(V;0)$ and $I_1(V;0)$ follow directly. □

With the formulas in Theorem 6.1, we now make some crucial observations. Set

$$f_0(L,R) = \frac{L-R}{\ln L - \ln R}, \quad f_1(L,R) = \frac{(L^2-R^2)(\ln L - \ln R) - 2(L-R)^2}{(\ln L - \ln R)^2}.$$

Then,

$$\begin{aligned}
I_0(V;0) &= e(D_1-D_2)(L-R) + \frac{e^2(\alpha D_1+\beta D_2)}{kT} f_0(L,R)V,\\
I_1(V;0) &= \frac{2e(L-R)}{\alpha\beta}[(D_1-D_2)(\alpha\lambda+\beta)(L+R) - (\alpha D_1+\beta D_2)(\lambda-1)f_0(L,R)]\\
&\quad + \frac{2e^2(\alpha D_1+\beta D_2)(\alpha\lambda+\beta)}{\alpha\beta kT} f_1(L,R)V,\\
\frac{d}{d\lambda} I_1(V;0) &= \frac{2e(L-R)}{\alpha\beta}(\alpha(D_1-D_2)(L+R) - (\alpha D_1+\beta D_2)f_0(L,R))\\
&\quad + \frac{2e^2(\alpha D_1+\beta D_2)}{\beta kT} f_1(L,R)V.
\end{aligned}$$

LEMMA 6.2. *If $L \neq R$, then $f_0(L,R) > 0$ and $f_1(L,R) > 0$. As $|L-R| \to 0$, say $L \to R$ with R being fixed,*

$$f_0(L,R) \to R \quad \text{and} \quad \frac{f_1(L,R)}{(L-R)^2} \to \frac{1}{6}.$$

DEFINITION 6.3. *Let V_c be the value so that $I_1(V_c;0) = 0$ and let V^c be the value so that $\frac{d}{d\lambda} I_1(V^c;0) = 0$.*

The next lemma follows directly from the above explicit formulas.

LEMMA 6.4. *If $L \neq R$, then*

$$\begin{aligned}
V_c &= \frac{kT}{e}\frac{(\lambda-1)(L-R)(\ln L - \ln R)}{(\alpha\lambda+\beta)((L+R)(\ln L - \ln R) - 2(L-R))}\\
&\quad - \frac{kT}{e}\frac{(D_1-D_2)(L+R)(\ln L - \ln R)^2}{(\alpha D_1+\beta D_2)((L+R)(\ln L - \ln R) - 2(L-R))},\\
V^c &= \frac{kT}{e}\frac{(L-R)(\ln L - \ln R)}{\alpha((L+R)(\ln L - \ln R) - 2(L-R))}\\
&\quad - \frac{kT}{e}\frac{(D_1-D_2)(L+R)(\ln L - \ln R)^2}{(\alpha D_1+\beta D_2)((L+R)(\ln L - \ln R) - 2(L-R))}.
\end{aligned}$$

The significance of the two critical values V_c and V^c is apparent from their definitions. The value V_c is the potential that balances ion size effect and the value V^c is the potential related to the relative size effect. We now state the properties explicitly in two theorems whose proofs follow directly from the definitions of V_c and V^c and the fact that $f_1(L,R) > 0$ for $L \neq R$ in Lemma 6.2.

THEOREM 6.5. *Suppose $L \neq R$. If $V > V_c$, then, for small $\varepsilon > 0$ and $r > 0$, the ion sizes enhance the current I; that is, $I(V;\varepsilon,r) > I(V;\varepsilon,0)$;*

If $V < V_c$, then, for small $\varepsilon > 0$ and $r > 0$, the ion sizes reduce the current I; that is, $I(V;\varepsilon,r) < I(V;\varepsilon,0)$.

THEOREM 6.6. *Suppose $L \neq R$. If $V > V^c$, then, for small $\varepsilon > 0$ and $r > 0$, the larger the negatively charged ion the larger the current I; that is, the current I is increasing in λ. If $V < V^c$, then, for small $\varepsilon > 0$ and $r > 0$, the smaller the negatively charged ion the larger the current I; that is, the current I is decreasing in λ.*

7. Conclusion and discussion. In this paper, we analyze a one-dimensional version of PNP type model for ion flows through a membrane channel. In this one-dimensional PNP type model, we add a hard sphere (hard rod) correction to the classical PNP model by including a one-dimensional hard sphere potential. The corresponding mathematical problem becomes a boundary value problem of an integro-differential system. We have established the existence of solutions to the boundary value problems and, most importantly, we have identified two critical potential values V_c and V^c in Lemma 6.4 that characterize some ion size effects on I-V relations (Theorems 6.5 and 6.6). The critical value V^c is probably more important due to its property in Theorem 6.6: it is related to a possible mechanism on when small ions are preferred and when large ions are preferred. As we emphasized in the introduction that the understanding of the roles of V_c and V^c in this paper is at the very early stage. There are a great deal of fundamental questions needed to be answered before one can take these values seriously. For example, we have tried hard to stress that the specific setting of our problem may not reflect precisely any realistic biological settings. The one-dimensional version for the true three-dimensional problem and missing the excess electrostatic potential could result in a serious limitation on the applicability of the critical values. However, we believe the *existence* of these critical potentials are generally valid, and the awareness of the potential existence of these critical voltages itself would be very useful for the community.

In a companion paper [55], among other things, we specifically devoted our effort to designing an algorithm (based on a rigorous mathematical analysis in Proposition 4.6 of [55]) for numerically detecting these critical voltages *without using any analytical formulas for I-V relations*. We have demonstrated the usage of this algorithm in [55] in two ways: (i) for the model problem in this paper, we numerically computed I-V relations and, applying the algorithm, we then computed the critical voltage values V_c and V^c, and found they agree well with the analytical values V_c and V^c in Lemma 6.4; (ii) for the PNP-DFT model with a nonzero permanent charge Q that we don't have analytical formulas for the I-V relations and for the critical voltages, we applied the algorithm and found the critical voltages.

We hope our work will stimulate more investigations regarding these critical potentials and, possibly, revealing other new characteristic parameters for ion size effects.

8. Appendix. Fréchet differentiability in ODEs. Consider the connecting problem (boundary value problem)

$$u' = F(x, u, G(x)), \quad x \in [0,1],\ u \in \mathbb{R}^n \tag{8.1}$$

$$u(0) \in B_0, \quad u(1) \in B_1 \tag{8.2}$$

where $G \in \mathcal{C}^0([0,1], \mathbb{R}^m)$, $F : [0,1] \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ are differentiable; B_0 and B_1 are submanifolds of $\mathbb{R}^n$ with $\dim B_0 = k$ and $\dim B_1 = n - k$.

Note that the augmented system

$$\begin{aligned} u' =& F(x, u, G(x)), \quad x' = 1 \end{aligned} \tag{8.3}$$

is an autonomous system with phase space $\mathbb{R}^{n+1}$. The boundary value problem is then equivalent to the connecting problem: finding an orbit of (8.3) that connects $B_0 \times \{0\}$ and $B_1 \times \{1\}$. Let M_0 and M_1 be the collections of orbits through $B_0 \times \{0\}$ and $B_1 \times \{1\}$. Let $\phi(x; v)$ be the solution of (8.1) with $\phi(0; v) = v$. Then, $\phi_* : \mathbb{R}^n \to \mathbb{R}^n$ given by $\phi_*(v) = \phi(1, v)$ is a diffeomorphism. The next lemma is simple.

LEMMA 8.1. *Suppose M_0 and M_1 intersect transversally along an orbit $(u(x), x)$ of (8.3) associated with $G \in \mathcal{C}^0([0,1], \mathbb{R}^m)$. Then B_0 and $\phi_*^{-1}(B_1)$ intersect transversally at $u(0)$. If $\Phi(x)$ is the principal fundamental matrix solution at $x = 0$ for*

$$U' = F_u(x, u(x), G(x))U,$$

then $D\phi_*^{-1}(u(1)) = \Phi^{-1}(1)$, and hence, $T_{u(0)}\phi_*^{-1}(B_1) = \Phi^{-1}(1)T_{u(1)}B_1$ and

$$T_{u(0)}B_0 \oplus \Phi^{-1}(1)T_{u(1)}B_1 = \mathbb{R}^n. \tag{8.4}$$

Let $P_0 : \mathbb{R}^n \to T_{u(0)}B_0$ be the projection associated to the decomposition in (8.4).

Let $u(x)$ be a solution of the boundary value problem (8.1) and (8.2) associated with $G \in \mathcal{C}^0([0,1],\mathbb{R}^m)$ that is resulted as a transversal intersection described in Lemma 8.1. Then, by continuity, there is a neighborhood $\mathcal{N}$ of zero in $\mathcal{C}^0([0,1],\mathbb{R}^m)$ such that, for $g \in \mathcal{N}$, the boundary value problem (8.1) and (8.2) with G replaced by $G+g$ has a unique solution $u_g(x)$ near $u(x)$.

PROPOSITION 8.2. *The mapping $S : \mathcal{N} \to \mathcal{C}^1([0,1],\mathbb{R}^n)$ defined by $S(g) = u_g(x)$ is Fréchet differentiable at $g = 0$; that is, there exists a bounded linear operator $L : \mathcal{C}^0([0,1],\mathbb{R}^m) \to \mathcal{C}^1([0,1],\mathbb{R}^n)$ such that, with $S(0) = u(x)$,*

$$\lim_{g\to 0} \frac{\|S(g) - S(0) - Lg\|_{\mathcal{C}^1}}{\|g\|_{\mathcal{C}^0}} = 0.$$

In fact, the Fréchet derivative $L = DS$ of the mapping S is given by

$$\begin{aligned}(Lg)(x) = \Phi(x)\int_0^x \Phi^{-1}(s)F_G(s,u(s),G(s))g(s)ds \\ -\Phi(x)P_0\int_0^1 \Phi^{-1}(s)F_G(s,u(s),G(s))g(s)ds.\end{aligned} \tag{8.5}$$

Proof. Without loss of generality, we assume that B_0 and B_1 are linear near $u(0)$ and $u(1)$, respectively, so that

$$P_0(u_g(0) - u(0)) = u_g(0) - u(0) \ \text{ and } \ P_0 : \Phi^{-1}(1)(u_g(1) - u(1)) = 0. \tag{8.6}$$

Note that

$$\begin{aligned}(u_g - u)' &= F(x,u_g,G(x)+g(x)) - F(x,u,G(x)) \\ &= F_u(x,u(x),G(x))(u_g - u) + F_G(x,u(x),G(x))g(x) + o(\|u_g - u\|_{\mathcal{C}^0} + \|g\|_{\mathcal{C}^0}).\end{aligned}$$

In the following, we will denote $F_G(x,u(x),G(x))$ by $F_G(x)$. Thus,

$$\begin{aligned}u_g(x) - u(x) = \Phi(x)(u_g(0) - u(0)) + \Phi(x)\int_0^x \Phi^{-1}(s)F_G(s)g(s)ds \\ +o(\|u_g - u\|_{\mathcal{C}^0} + \|g\|_{\mathcal{C}^0}),\end{aligned} \tag{8.7}$$

and hence, $\|u_g - u\|_{\mathcal{C}^0} \le K\left(|u_g(0) - u(0)| + \|g\|_{\mathcal{C}^0}\right)$. We now have

$$\Phi^{-1}(1)\left(u_g(1) - u(1)\right) = u_g(0) - u(0) + \int_0^1 \Phi^{-1}(s)F_G(s)g(s)ds + o(\|u_g - u\|_{\mathcal{C}^0} + \|g\|_{\mathcal{C}^0}).$$

Applying the projection P_0 to the above relation, it follows from (8.6) that

$$u_g(0) - u(0) = -P_0\int_0^1 \Phi^{-1}(s)F_G(s)g(s)ds + o(\|u_g - u\|_{\mathcal{C}^0} + \|g\|_{\mathcal{C}^0}). \tag{8.8}$$

Substitute into (8.7) to get

$$\begin{aligned}u_g(x) - u(x) = -\Phi(x)P_0\int_0^1 \Phi^{-1}(s)F_G(s)g(s)ds + \Phi(x)\int_0^x \Phi^{-1}(s)F_G(s)g(s)ds \\ +o(\|u_g - u\|_{\mathcal{C}^0} + \|g\|_{\mathcal{C}^0}),\end{aligned} \tag{8.9}$$

which implies that $\|u_g - u\|_{\mathcal{C}^0} \le K\|g\|_{\mathcal{C}^0}$. Substitute back into (8.9) to have

$$u_g(x) - u(x) + \Phi(x)P_0\int_0^1 \Phi^{-1}(s)F_G(s)g(s)ds - \Phi(x)\int_0^x \Phi^{-1}(s)F_G(s)g(s)ds = o(\|g\|_{\mathcal{C}^0}).$$

With Lg defined in (8.5), we then have,

$$\lim_{g\to 0}\frac{\|u_g-u-Lg\|_{\mathcal{C}^0}}{\|g\|_{\mathcal{C}^0}}=0. \tag{8.10}$$

Furthermore, we note, from (8.8) and (8.10), that

$$\lim_{g\to 0}\frac{\left|u_g(0)-u(0)+P_0\int_0^1\Phi^{-1}(s)F_G(s)g(s)ds\right|}{\|g\|_{\mathcal{C}^0}}=0.$$

To complete the proof, we need to show that

$$\|u_g'-u'-(Lg)'\|_{\mathcal{C}^0}=o\left(\|g\|_{\mathcal{C}^0}\right).$$

From the equation, we have

$$\begin{aligned}u_g'(x)-u'(x)&=F(x,u_g(x),G(x)+g(x))-F(x,u(x),G(x))\\&=F_u(x,u(x),G(x))(u_g(x)-u(x))+F_G(x,u(x),G(x))g(x)\\&\quad+o(u_g(x)-u(x))+o(g(x))\\&=F_u(x,u(x),G(x))(Lg)(x)+F_G(x,u(x),G(x))g(x)+o(g(x)).\end{aligned}$$

Therefore

$$u_g'(x)-u'(x)-(F_u(x,u(x),G(x))(Lg)(x)+F_G(x,u(x),G(x))g(x))=o(g(x)).$$

One checks directly that

$$(Lg)'(x)=F_u(x,u(x),G(x))(Lg)(x)+F_G(x,u(x),G(x))g(x).$$

We thus obtain

$$\lim_{g\to 0}\frac{\|u_g'-u'-(Lg)'\|_{\mathcal{C}^0}}{\|g\|_{\mathcal{C}^0}}=0.$$

This together with (8.10) establishes the result. □

Acknowledgments. The authors thank Robert Eisenberg for his interest in and for his comments on a draft of this work. SJ is grateful to the Math Department at KU for the hospitality during his half-year visit to the department when the main part of this work is completed. The work is partially supported by NSF Grant DMS-0807327. SJ is also partially supported by NSFC Grant 11171130, the Natural Science Foundation Grant 20101591 of Jilin Province, the Scientific Research Foundation for the Returned Overseas Chinese Scholars of State Education Ministry, the National Basic Research Program of China (973 Program) No. 2012CB821200, and the 985 Project of Jilin University.

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