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# Electroneutral models for dynamic Poisson-Nernst-Planck systems

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The Poisson-Nernst-Planck (PNP) system is a standard model for describing ion transport. In many applications, e.g., ions in biological tissues, the presence of thin boundary layers poses both modeling and computational challenges. In this paper, we derive simplified electroneutral (EN) models where the thin boundary layers are replaced by effective boundary conditions. There are two major advantages of EN models. First, it is much cheaper to solve them numerically. Second, EN models are easier to deal with compared to the original PNP system; therefore, it would also be easier to derive macroscopic models for cellular structures using EN models. Even though the approach used here is applicable to higher-dimensional cases, this paper mainly focuses on the one-dimensional system, including the general multi-ion case. Using systematic asymptotic analysis, we derive a variety of effective boundary conditions directly applicable to the EN system for the bulk region. This EN system can be solved directly and efficiently without computing the solution in the boundary layer. The derivation is based on matched asymptotics, and the key idea is to bring back higher-order contributions into the effective boundary conditions. For Dirichlet boundary conditions, the higher-order terms can be neglected and the classical results (continuity of electrochemical potential) are recovered. For flux boundary conditions, higher-order terms account for the accumulation of ions in boundary layer and neglecting them leads to physically incorrect solutions. To validate the EN model, numerical computations are carried out for several examples. Our results show that solving the EN model is much more efficient than the original PNP system. Implemented with the Hodgkin-Huxley model, the computational time for solving the EN model is significantly reduced without sacrificing the accuracy of the solution due to the fact that it allows for relatively large mesh and time-step sizes.

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## I. INTRODUCTION

The Poisson-Nernst-Planck (PNP) system describes the transport of ions under the influence of both an ionic concentration gradient and an electric field. It is a system coupling diffusion and electrostatics, and the nonlinearity comes from the drift effect of electric field on ions. Such a system and its variants have found extensive and successful applications in biological systems, in particular in the description of ion transport through cells and ion channels [1,2]. It has also been applied to many industrial fields, such as the semiconductor devices [3] and the detection of poisonous lead by ion-selective electrode [4].

One intriguing feature of this system is the presence of boundary layer (BL) near the boundary of concerned domain, often called Debye layer in literature. A large number of works have been devoted to the BL analysis of PNP systems. For example, singular perturbation analysis of PNP system has been carried out for narrow ion channels with certain geometric structure [5,6]. Geometric singular perturbation approach has been developed to investigate the existence and uniqueness of solutions in stationary PNP system [7,8] as well as the effects of permanent charge and ion size [9,10]. Recently, Wang *et al.* [11] have tackled the steady-state PNP system with arbitrary number of ion species and arbitrary valences and have successfully reduced the asymptotic solutions to a single scalar transcendental equation.

In general, the solution of the PNP system consists of two parts, a BL solution in a small neighborhood of boundary and a bulk solution in the interior region of the domain. In the one-dimensional (1D) case, the leading order solution in the BL can be constructed either explicitly or in an integral form. Based on the BL analysis, effective continuity conditions have been proposed to link the bulk solution and BL solution, e.g., in the form of the continuity of electrochemical potential [12]. These effective conditions have been applied to the study of steady states of 1D systems, showing the existence of multiple steady states with piecewise constant fixed charge [13]. One objective of our paper is to derive effective conditions for other boundary conditions. These conditions eliminate the BL, and the resulting electroneutral (EN) model has a big advantage over the original PNP system for deriving macroscopic models [14] for ion transport in regions with complicated structures. For example, some macroscopic continuum equations are derived for water circulation in lens [15,16], by taking into

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account the fluxes through membranes with an ad hoc model for the BL effect, where the fluxes calculated there might not be accurate.

The key idea to derive effective boundary conditions is to bring back the higher-order contributions. In the case of Dirichlet boundary conditions, we will derive a higher-order effective boundary condition with the continuity of electrochemical potential in Reference [12]. The higher-order effect of the new effective condition will be verified by numerical examples. In the case of flux boundary conditions, the solution is not unique by using leading order condition, and from a physical point of view, the higher-order contribution accounts for accumulation of ions in BL, which is essential in biophysical processes and cannot be ignored. The effectiveness of these conditions will be demonstrated in a concrete example of action potential for neuronal axon, where by further simplification the higher-order terms reduce to an equivalent capacitor often adopted in cable models.

The other objective of this paper is related to numerical computation of PNP systems. In addition to the BL analysis, many (conservative) numerical schemes have been developed for PNP systems, such as finite element method [17], finite difference scheme [18], and finite volume method [19,20], in one- and higher-dimensional spaces [21,22]. Due to the presence of BL, computation of the PNP system needs to be sufficiently accurate to capture the behavior of solution in BL. Since the solutions change rapidly in BL, more mesh points are needed in BL than in the bulk region to attain certain accuracy, requiring advanced techniques such as adaptive refined mesh and moving mesh [23,24]. In general, computational cost is higher and development of numerical method is more demanding, especially when there are many BLs in a region with complicated structure. Having effective conditions to eliminate the BL significantly reduces the computational time as well as the effort for developing sophisticated numerical methods, since under such a framework, the solutions in the bulk region can be obtained directly.

The rest of the paper is structured as follows. In Sec. II, we first present the formulation for the two-ion species case and related EN models, with Dirichlet or flux boundary conditions for ion concentration and Dirichlet or Robin boundary conditions for electric potential. A more general multi-ion species model is presented afterwards. In Sec. III, these effective boundary conditions are validated by one steady state and two dynamic examples. In Sec. IV, we combine the PNP system with the Hodgkin-Huxley model and derive an EN model for neuronal axon, capturing the phenomenon of action potential efficiently. Finally, conclusions and discussion of future directions are given in Sec. V.

## II. THE ELECTRO-NEUTRAL THEORIES

In this section, we present the EN systems with various effective boundary conditions. To introduce the main ideas, we first present the simplest PNP system, for ±1 ion species, where the solutions and effective boundary conditions are explicit. It is followed by the general multi-ion species case.

We consider the 1D dynamic PNP system for two ions with valences ±1 (e.g., NaCl) in the region $0 < x < L$,

$$\begin{aligned} -\epsilon_0\epsilon_r\partial_{xx}\psi &= e_0N_A(p-n),\\ \partial_t p = -\partial_x J_p,\quad J_p &= -D\left(\partial_x p + \frac{e_0}{k_BT}p\partial_x\psi\right),\\ \partial_t n = -\partial_x J_n,\quad J_n &= -D\left(\partial_x n - \frac{e_0}{k_BT}n\partial_x\psi\right),\end{aligned}\tag{1}$$

where the first equation is the electrostatic Poisson equation for electric potential $\psi(x,t)$, and the second and third equations are the transport equations for two ion concentrations $p(x,t)$ (cation) and $n(x,t)$ (anion), respectively. The quantities $J_p$ and $J_n$ are the associated two fluxes of positive and negative ions, respectively, and $D$ is the diffusion constant. The fluxes consist of two parts, the linear part due to ionic concentration gradient and the nonlinear part from the drift effect of electric field. Other parameters are vacuum permittivity $\epsilon_0$, relative permittivity $\epsilon_r$, elementary charge $e_0$, Avogadro constant $N_A$, Boltzmann constant $k_B$, and absolute temperature $T$. Here we have assumed that the diffusion constants for the two ionic species are the same for simplicity. Generalization to the multi-ion case with different diffusion constants will be addressed later.

In the following, we will consider the dimensionless and normalized version of the above PNP system; see Sec. IV for details of nondimensionalization process. We still adopt the same notations, and the PNP system for dimensionless quantities $p,n,\psi$ in the normalized interval $0 < x < 1$ is given by

$$\begin{aligned} -\epsilon^2\partial_{xx}\psi &= p-n,\\ \partial_t p &= -\partial_x(J_p) = \partial_x(\partial_x p + p\partial_x\psi),\\ \partial_t n &= -\partial_x(J_n) = \partial_x(\partial_x n - n\partial_x\psi),\end{aligned}\tag{2}$$

where $\epsilon \ll 1$ is a dimensionless small parameter and defined by

$$\epsilon = \sqrt{\frac{\epsilon_0\epsilon_r k_BT}{e^2N_A\tilde{c}L^2}},\tag{3}$$

where $\tilde{c}$ is some typical ion concentration. Physically, $\epsilon$ is the ratio of Debye length (order of boundary layer width) to the typical length $L$ of the system. We will consider various types of boundary conditions in the following subsections. For example, as in Sec. II B, we can adopt Dirichlet condition for $\psi$ and two flux conditions at $x = 0$,

$$\psi(0,t) = \psi_0(t),\ J_p(0,t) = J_{p,0}(t),\ J_n(0,t) = J_{n,0}(t).\tag{4}$$

We will also replace flux conditions by Dirichlet conditions of concentration (in Sec. II C) and Dirichlet condition of $\psi$ by Robin-type condition (in Sec. II D). The treatment will be similar at $x = 1$. To complete the system, we also need the initial conditions $p(x,0),n(x,0)$ for two ions. But the initial effect is not considered in this work, and we mainly limit ourselves to the large time behavior of solutions (when BL is already present) or the case near equilibrium state.

We focus on the case when local electroneutrality (LEN) condition in bulk region is satisfied, and there is no extra $O(1)$ unbalanced charge present in the system or interval, or more precisely there is only $O(\epsilon)$ unbalanced charge, here called near global electroneutrality (NGEN) condition. We will illustrate later what kinds of boundary conditions fall in this case. These conditions can be justified in many biological applications, for example, in the neuronal axon [25]. Thus, in the bulk region, we assume all the functions concerned and their derivatives are $O(1)$, i.e.,

$$\begin{aligned}&\psi,\partial_x\psi,\partial_{xx}\psi \sim O(1), p,\partial_t p,\partial_x p,\ldots \sim O(1),\\ &n,\partial_t n,\partial_x n,\ldots \sim O(1).\end{aligned} \tag{5}$$

Then, we obtain approximately the electroneutral condition $p \approx n$ from the first equations in Eq. (2) and more precisely we write

$$\begin{aligned}p(x,t;\epsilon) &= c(x,t;\epsilon) + O(\epsilon^2),\\ n(x,t;\epsilon) &= c(x,t;\epsilon) + O(\epsilon^2),\\ \psi(x,t;\epsilon) &= \phi(x,t;\epsilon) + O(\epsilon^2),\end{aligned} \tag{6}$$

where $c$ and $\phi$ may depend on $\epsilon$ due to boundary conditions; in other words, $c$ and $\phi$ can contain $O(\epsilon)$ terms if boundary conditions have such terms. Substituting into the second and third equation in Eq. (2) gives the EN equations,

$$\begin{aligned}\partial_t c &= \partial_x(\partial_x c + c\partial_x\phi) + O(\epsilon^2),\\ \partial_t c &= \partial_x(\partial_x c - c\partial_x\phi) + O(\epsilon^2).\end{aligned} \tag{7}$$

By addition and subtraction, we can also write them as

$$\partial_t c = \partial_{xx} c + O(\epsilon^2), \quad \partial_x(c\,\partial_x\phi) = 0 + O(\epsilon^2). \tag{8}$$

To complete this system, two effective boundary conditions are needed instead of the original three. Based on the behavior of BL solutions, we aim to derive effective conditions that connect real boundary values of $p,n,\psi$ (or boundary fluxes) and limit boundary values of bulk solution $c,\phi$ (or bulk fluxes). Finally, we get a EN system for $c,\phi$ in the bulk region, which can be solved directly. In the following, we will always take $x=0$, for example, and briefly state the results for $x=1$.

### A. The leading order solution in BL

From some steady-state analysis, e.g., with finite fluxes or Dirichlet conditions in Ref. [12] and for Poisson-Boltzmann type equations in Ref. [26] in the absence of extra $O(1)$ unbalanced charge, there is boundary layer with thickness $O(\epsilon)$. Also, some numerical evidence shows that, for finite fluxes, as long as the NGEN condition is satisfied, the system has BLs near $x=0$ and $x=1$ with all $p,n,\psi$ being $O(1)$. In this subsection, we present the leading order solutions for the PNP system. Although the solutions are well-known in literature, we give a brief derivation to be self-contained with more clear expressions for the remainder terms.

In the BL near $x=0$, we assume

$$\begin{aligned}&\psi,n,p \sim O(1), \quad \partial_t p,\partial_t n \sim O(1), \quad J_n,J_p \sim O(1),\\ &\partial_x\psi,\partial_x p,\partial_x n \sim O(1/\epsilon), \quad \partial_{xx}\psi \sim O(1/\epsilon^2),\end{aligned} \tag{9}$$

and thus we set

$$\Phi(X) = \psi(x), \quad N(X) = n(x), \quad P(X) = p(x), \quad X = \frac{x}{\epsilon}, \tag{10}$$

where the argument $t$ is omitted in above functions. The equations in BL are

$$\begin{aligned}-\partial_{XX}\Phi &= P - N,\\ \partial_X(\partial_X P + P\partial_X\Phi) &= \epsilon^2\partial_t P = O(\epsilon^2),\\ \partial_X(\partial_X N - N\partial_X\Phi) &= \epsilon^2\partial_t N = O(\epsilon^2).\end{aligned} \tag{11}$$

Integrating the second and third equations once, we get

$$\begin{aligned}\partial_X P + P\partial_X\Phi &= -\epsilon J_{p,0} + O(\epsilon^2),\\ \partial_X N - N\partial_X\Phi &= -\epsilon J_{n,0} + O(\epsilon^2),\end{aligned} \tag{12}$$

where $J_{p,0},J_{n,0}$ are the finite fluxes at $x=0$. We denote $c_0,\phi_0$ as the limit values of bulk solutions $c(x),\phi(x)$ at $x=0$, and they should match $P(\infty),\Phi(\infty)$ to leading order, implying

$$\begin{aligned}P(X) &= c_0 e^{\phi_0-\Phi(X)} + O(\epsilon),\\ N(X) &= c_0 e^{\Phi(X)-\phi_0} + O(\epsilon).\end{aligned} \tag{13}$$

Substituting into the first equation of Eq. (11), we get the Poisson-Boltzmann equation as leading order equation for $\Phi$,

$$-\partial_{XX}\Phi = c_0[e^{\phi_0-\Phi(X)} - e^{\Phi(X)-\phi_0}] + O(\epsilon). \tag{14}$$

This can be integrated out by using $\partial_X\Phi(\infty) \to 0$ and $\Phi(0) = \psi_0(t)$ (as a given function). Finally, we obtain

$$\Phi(X) = \phi_0 + 2\ln\frac{1 - e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)}{1 + e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)} + O(\epsilon). \tag{15}$$

Then the solutions for $P(X,t),N(X,t)$ become

$$\begin{aligned}P(X) &= c_0\left[\frac{1 + e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)}{1 - e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)}\right]^2 + O(\epsilon),\\ N(X) &= c_0\left[\frac{1 - e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)}{1 + e^{-\sqrt{2c_0}X}\tanh\left(\frac{\phi_0-\psi_0}{4}\right)}\right]^2 + O(\epsilon).\end{aligned} \tag{16}$$

Note that in general $c_0,\phi_0,\psi_0$ are functions of $t$. The composite solutions are given by

$$\begin{aligned}p(x) &= P(X) + c(x) - c_0 + O(\epsilon),\\ n(x) &= N(X) + c(x) - c_0 + O(\epsilon),\\ \psi(x) &= \Phi(X) + \phi(x) - \phi_0 + O(\epsilon),\end{aligned} \tag{17}$$

which are uniformly valid for some finite interval $[0,\delta]$, say $\delta = 1/2$, with remainder $O(\epsilon)$. One can also add the contribution of BL solution near $x=1$ (with transform $X = (1-x)/\epsilon$ and quantities $c_0,\phi_0,\psi_0$ being replaced by $c_1,\phi_1,\psi_1$) to make the composite solution valid for the whole interval $[0,1]$. Since in the bulk we have $p(x) = c(x) + O(\epsilon^2)$ by Eq. (6), it is reasonable to expect $p = c(x) + o(\epsilon)$ in some intermediate region $x \sim O(\epsilon^\alpha)$ with $0 < \alpha < 1$, particularly we may choose $\alpha = 1/2$.

### B. Flux boundary condition

In this subsection, we consider the case with the flux boundary conditions for two concentrations and Dirichlet condition for electric potential. More precisely, at $x = 0$, we have

$$\psi(0,t) = \psi_0(t), \quad J_p(0,t) = J_{p,0}(t), \quad J_n(0,t) = J_{n,0}(t), \tag{18}$$

where $\psi_0, J_{p,0}, J_{n,0}$ are given. The objective is to propose two effective boundary conditions for $c,\phi$ at $x = 0$ based on these three functions.

To this end, we define for the EN system two fluxes,

$$J_c^{\pm}(x,t) = -(\partial_x c \pm c\, \partial_x \phi), \tag{19}$$

and the limit values at $x = 0$ are denoted by $J_{c,0}^{\pm}(t)$, respectively. Based on assumption Eqs. (5) and (6) in the bulk region, the two fluxes are almost the same as the two fluxes of original PNP system,

$$J_c^{+}(\delta,t) = J_p(\delta,t) + O(\epsilon^2), \quad J_c^{-}(\delta,t) = J_n(\delta,t) + O(\epsilon^2), \tag{20}$$

where $\delta$ is some generic point in bulk region, say $\delta = 1/2$. Next, we intend to find the connection between $J_{c,0}^{+}$ and $J_{p,0}$, or similarly between $J_{c,0}^{-}$ and $J_{n,0}$ at boundary. For this purpose, by integration of transport Eqs. $(2)_2$ and $(7)_1$, we immediately get

$$\begin{aligned} J_p(\delta,t) &= J_{p,0}(t) - \partial_t \int_0^{\delta} p(x,t)dx, \\ J_c^{+}(\delta,t) &= J_{c,0}^{+}(t) - \partial_t \int_0^{\delta} c(x,t)dx. \end{aligned} \tag{21}$$

Combining these two and utilizing the composite solution Eq. (17), we obtain

$$\begin{aligned} J_{c,0}^{+} &= J_{p,0} - \partial_t \int_0^{\delta} (p-c)dx + O(\epsilon^2) \\ &= J_{p,0} - \partial_t \left[ \int_0^{\sqrt{\epsilon}} (p-c)dx + \int_{\sqrt{\epsilon}}^{\delta} (p-c)dx \right] + O(\epsilon^2) \\ &= J_{p,0} - \partial_t \int_0^{\sqrt{\epsilon}} [P(x/\epsilon) - c_0]dx + o(\epsilon) \\ &= J_{p,0} - \epsilon\, \partial_t \int_0^{\infty} [P(X) - c_0]dX + o(\epsilon) \\ &= J_{p,0} - \epsilon \partial_t \left[ \sqrt{2c_0}(e^{(\phi_0-\psi_0)/2} - 1) \right] + o(\epsilon), \end{aligned} \tag{22}$$

where we have used the assumption that $p = c + o(\epsilon)$ for $x \geqslant \sqrt{\epsilon}$, and by setting upper limit of integral as $\infty$ only exponentially small terms are neglected. In the above, $\phi_0, c_0, \psi_0$ may depend on $t$. Similarly for the other flux, we obtain the relation

$$J_{c,0}^{-} = J_{n,0} - \epsilon \partial_t [\sqrt{2c_0}(e^{(\psi_0-\phi_0)/2} - 1)] + o(\epsilon). \tag{23}$$

Physically, the quantity $\psi_0 - \phi_0$ in above formulas is often referred to as the $\zeta$ potential [27]. To see clearly the two conditions, we carry out a linearization regarding small $\psi_0 - \phi_0$. In this case, they reduce to

$$\begin{aligned} J_{c,0}^{+} - J_{p,0} &\approx \epsilon \partial_t [\sqrt{c_0/2}(\psi_0 - \phi_0)], \\ J_{c,0}^{-} - J_{n,0} &\approx -\epsilon \partial_t [\sqrt{c_0/2}(\psi_0 - \phi_0)]. \end{aligned} \tag{24}$$

Thus, by comparing these conditions, the total flux is the same while electric current differs at order $\epsilon$, i.e.,

$$\begin{aligned} (J_{c,0}^{+} + J_{c,0}^{-}) &\approx (J_{p,0} + J_{n,0}), \\ (J_{c,0}^{+} - J_{c,0}^{-}) - (J_{p,0} - J_{n,0}) &\approx 2\epsilon \partial_t [\sqrt{c_0/2}(\psi_0 - \phi_0)]. \end{aligned} \tag{25}$$

Physically, this means some cations/anions accumulate in the BL, and the second formula is similar to that of a capacitor. The treatment for the other end $x = 1$ is similar, and we summarize the results below.

*Proposition 1. Suppose the LEN and NGEN conditions are satisfied, and let* $\psi_0(t)$, $J_{p,0}(t)$, $J_{n,0}(t)$ *be the given electric potential and ion fluxes at* $x = 0$ *as in Eq. (18) and let* $\psi_1(t)$, $J_{p,1}(t)$, $J_{n,1}(t)$ *be given at* $x = 1$ *for original system Eq. (2), then we have the effective boundary conditions for the EN system Eq. (8)*

$$\begin{aligned} J_{c,0}^{+} &= J_{p,0} - \epsilon \partial_t \left( \sqrt{2c_0}(e^{(\phi_0-\psi_0)/2} - 1) \right) + o(\epsilon), \\ J_{c,0}^{-} &= J_{n,0} - \epsilon \partial_t \left( \sqrt{2c_0}(e^{(\psi_0-\phi_0)/2} - 1) \right) + o(\epsilon), \\ J_{c,1}^{+} &= J_{p,1} + \epsilon \partial_t \left( \sqrt{2c_1}(e^{(\phi_1-\psi_1)/2} - 1) \right) + o(\epsilon), \\ J_{c,1}^{-} &= J_{n,1} + \epsilon \partial_t \left( \sqrt{2c_1}(e^{(\psi_1-\phi_1)/2} - 1) \right) + o(\epsilon), \end{aligned} \tag{26}$$

*where* $J_c^{\pm}$ *are defined by Eq. (19) and subscripts 0 and 1 denote quantities at* $x = 0$ *and* $x = 1$, *respectively.*

*Remark 1.* Keeping the $O(\epsilon)$ terms in Eq. (26) is necessary for two reasons. First, in bulk Eqs. (7) we have assumed an $O(\epsilon^2)$ remainder, so it is reasonable and consistent to bring back the $O(\epsilon)$ terms on boundary conditions. Second, neglecting the $O(\epsilon)$ terms is physically incorrect for EN system as the solution would not be unique (e.g., $\phi$ can differ by a constant).

*Remark 2.* In this case, the fluxes $J_{p,0}, J_{n,0}$ can be either $O(1)$ or $O(\epsilon)$, as long as the NGEN is satisfied. This means when fluxes are $O(1)$, we should require the fluxes are almost balanced $J_{p,1} - J_{p,0} = J_{n,1} - J_{n,0} + O(\epsilon)$ or its integral over time satisfies

$$\int_0^t (J_{p,1} - J_{p,0})dt = \int_0^t (J_{n,1} - J_{n,0})dt + O(\epsilon). \tag{27}$$

Otherwise, the solution in BL will not be $O(1)$ anymore. For a steady state (Poisson-Boltzmann-type equation in Ref. [26]) with extra $O(1)$ unbalanced charge, the solution $\psi$ in BL is shown to have a span of $O[\log(1/\epsilon)]$.

### C. Dirichlet boundary condition revisited

In this subsection, we will consider the case with Dirichlet boundary conditions for two ion concentrations. We again use $x = 0$ as an example and have

$$\psi(0,t) = \psi_0(t), \quad p(0,t) = p_0(t), \quad n(0,t) = n_0(t). \tag{28}$$

The leading order effective boundary conditions for this case are well-known. With the same assumptions as previous subsection, we arrive at the same BL system, and easily get

$$\partial_X P + P\partial_X \Phi = O(\epsilon), \quad \partial_X N - N\partial_X \Phi = O(\epsilon). \tag{29}$$

By integration and using the matching condition, we obtain

$$\begin{aligned} \ln c_0 + \phi_0 &= \ln p_0 + \psi_0 + O(\epsilon), \\ \ln c_0 - \phi_0 &= \ln n_0 - \psi_0 + O(\epsilon). \end{aligned} \tag{30}$$

These connection conditions are referred to as *continuity of electrochemical potential*, widely adopted in literature [12]. And equivalently, the explicit effective boundary conditions for EN system are

$$c_0 = \sqrt{p_0 n_0}, \quad \phi_0 = \psi_0 + \tfrac{1}{2}\ln(p_0/n_0). \tag{31}$$

As in the bulk region, we keep the $O(\epsilon)$ terms. A natural question is how to bring back such $O(\epsilon)$ effect in the effective boundary conditions for the reduced EN system. One may want to seek a general expansion to $O(\epsilon)$ in the BL and assume

$$\begin{aligned} &\Phi = \Phi_0 + \epsilon\Phi_1 + \dots, \quad P = P_0 + \epsilon P_1 + \dots, \\ &N = N_0 + \epsilon N_1 + \dots \end{aligned} \tag{32}$$

The leading order solutions $\Phi_0, P_0, N_0$ can be immediately written down, which are the same as those in Eqs. (15) and (16) with replacement given by Eq. (31). However, getting the explicit expression for $\Phi_1, P_1, N_1$ seems difficult. Therefore, instead we try to avoid such a process and find the higher-order contributions directly based on leading-order solution.

Now, we take $P(X)$ as an illustration, where the argument $t$ is omitted here and in the following. The second equation in the BL system implies

$$\partial_X P + P\partial_X \Phi = -\epsilon J_{p,0} + O(\epsilon^2 X), \tag{33}$$

where $J_{p,0}$ is some unknown flux constant. Dividing both sides by $P$, we get

$$\begin{aligned} \partial_X(\ln P + \Phi) &= -\epsilon J_{p,0}/P + O(\epsilon^2 X) \\ &= -\epsilon J_{p,0}/P_0 + O(\epsilon^2 X). \end{aligned} \tag{34}$$

From the previous subsection, we know that $J_{p,0} = J_{c,0}^{+} + O(\epsilon)$. Therefore, we obtain

$$\begin{aligned} &\ln[P(X)] + \Phi(X) \\ &\quad = \ln p_0 + \psi_0 - \epsilon J_{c,0}^{+}\int_0^X 1/P_0(z)dz + O(\epsilon^2 X). \end{aligned} \tag{35}$$

By matching Ref. [28], let $X = \epsilon^{\alpha-1}s$ or $x = \epsilon^{\alpha}s$ with $1/2 < \alpha < 1$, we can expect that

$$\begin{aligned} P(\epsilon^{\alpha-1}s) &= c(\epsilon^{\alpha}s) + o(\epsilon), \\ \Phi(\epsilon^{\alpha-1}s) &= \phi(\epsilon^{\alpha}s) + o(\epsilon). \end{aligned} \tag{36}$$

Substituting $X = \epsilon^{\alpha-1}s$ into previous relation Eq. (35), we get from the left-hand side

$$\begin{aligned} &\ln[P(X)] + \Phi(X) \\ &\quad = \ln(c_0) + \phi_0 + \left(\frac{\partial_x c(0)}{c_0} + \partial_x\phi(0)\right)\epsilon^{\alpha}s + o(\epsilon), \end{aligned} \tag{37}$$

and from the integral on the right-hand side we get

$$\epsilon\int_0^X \frac{1}{P_0(z)}dz = \frac{\epsilon^{\alpha}s}{c_0} + \frac{\sqrt{2}\epsilon}{c_0^{3/2}}\left(e^{\frac{\psi_0-\phi_0}{2}} - 1\right) + o(\epsilon). \tag{38}$$

Since $J_{c,0}^{+} = -[\partial_x c(0) + c_0\partial_x\phi(0)]$ by definition Eq. (19), the $\epsilon^{\alpha}s$ terms automatically cancel each other (which partially verifies the correctness of matching), and we are left with

$$\ln c_0 + \phi_0 + \frac{\sqrt{2}J_{c,0}^{+}\epsilon}{c_0^{3/2}}[e^{(\psi_0-\phi_0)/2} - 1] = \ln p_0 + \psi_0 + o(\epsilon). \tag{39}$$

Compared with previous leading-order condition Eq. (30), there is an $O(\epsilon)$ correction term in the above formula, so it can be considered as a generalization of continuity of electrochemical potential. Treatments for the other condition and two conditions at $x = 1$ are similar, and we summarize the results as follows.

*Proposition 2. Suppose the LEN and NGEN conditions are satisfied, and let $\psi_0(t)$, $p_0(t)$, $n_0(t)$ be the given electric potential and ion concentrations at $x = 0$ as in Eq. (28) and let $\psi_1(t)$, $p_1(t)$, $n_1(t)$ be given at $x = 1$ for original system Eq. (2), then we have the effective boundary conditions for the EN system Eq. (8):*

$$\begin{aligned} &\ln c_0 + \phi_0 + \frac{\sqrt{2}J_{c,0}^{+}\epsilon}{c_0^{3/2}}[e^{(\psi_0-\phi_0)/2} - 1] = \ln p_0 + \psi_0 + o(\epsilon), \\ &\ln c_0 - \phi_0 + \frac{\sqrt{2}J_{c,0}^{-}\epsilon}{c_0^{3/2}}[e^{(\phi_0-\psi_0)/2} - 1] = \ln n_0 - \psi_0 + o(\epsilon), \\ &\ln c_1 + \phi_1 - \frac{\sqrt{2}J_{c,1}^{+}\epsilon}{c_1^{3/2}}[e^{(\psi_1-\phi_1)/2} - 1] = \ln p_1 + \psi_1 + o(\epsilon), \\ &\ln c_1 - \phi_1 - \frac{\sqrt{2}J_{c,1}^{-}\epsilon}{c_1^{3/2}}[e^{(\phi_1-\psi_1)/2} - 1] = \ln n_1 - \psi_1 + o(\epsilon), \end{aligned} \tag{40}$$

*where $J_c^{\pm}$ are defined by Eq. (19) and subscripts 0 and 1 denote quantities at $x = 0$ and $x = 1$, respectively.*

*Remark 3.* We can alternatively derive asymptotically equivalent expressions,

$$\begin{aligned} c_0 &= \sqrt{p_0 n_0} + \frac{\epsilon}{\sqrt{2}}\big\{\big(n_0^{-1/4} - p_0^{-1/4}\big)^2\partial_x c(0,t) \\ &\quad + (\sqrt{n_0} - \sqrt{p_0})\partial_x\phi(0,t)\big\}, \\ \phi_0 &= \psi_0 + \frac{1}{2}\ln(p_0/n_0) + \frac{\epsilon}{\sqrt{2}}\left\{\frac{\sqrt{n_0} - \sqrt{p_0}}{n_0 p_0}\partial_x c(0,t)\right. \\ &\quad \left. + \big(n_0^{-1/4} - p_0^{-1/4}\big)^2\partial_x\phi(0,t)\right\}, \\ c_1 &= \sqrt{p_1 n_1} - \frac{\epsilon}{\sqrt{2}}\big\{\big(n_1^{-1/4} - p_1^{-1/4}\big)^2\partial_x c(1,t) \\ &\quad + (\sqrt{n_1} - \sqrt{p_1})\partial_x\phi(1,t)\big\}, \end{aligned}$$

$$\begin{aligned}\phi_1 = \psi_1 + \frac{1}{2}\ln(p_1/n_1) - \frac{\epsilon}{\sqrt{2}}\Bigg\{&\frac{\sqrt{n_1}-\sqrt{p_1}}{n_1 p_1}\partial_x c(1,t)\\ &+ \big(n_1^{-1/4} - p_1^{-1/4}\big)^2\partial_x\phi(1,t)\Bigg\},\end{aligned} \qquad (41)$$

which are Robin-type boundary conditions. Compared with Eq. (31), there are $O(\epsilon)$ corrections in above conditions. For a special case, say $n_0 = p_0 + O(\epsilon)$ at $x = 0$, the correction terms will be of higher order, then continuity of electrochemical potential Eq. (31) holds with remainder $o(\epsilon)$.

*Remark 4.* In some cases, $p(0,t) = p_0(t)$ is not explicitly given but is related to flux $J_{p,0}$, so proper modification is needed. For example, in biological applications, there is certain relation between flux and ion concentration across cell membrane or ion channel, such as Hodgkin-Huxley model [25] or GHK flux model [29]. And, in electrolyte there is the Chang-Jaffle boundary condition [30,31] or modified Chang-Jaffle condition [4]. Suppose the boundary condition is in the form $J_{p,0} = f(p_0)$, where $f$ is some given function, then we need to supplement the two conditions at $x = 0$ with

$$f(p_0) = J^+_{c,0} + \epsilon\partial_t[\sqrt{2c_0}(e^{(\phi_0-\psi_0)/2} - 1)]. \qquad (42)$$

If mixed conditions are given (e.g., one Dirichlet and one flux), then we need to combine the two relevant boundary conditions from the two propositions, e.g., if $p_0$ and $J_{n,0}$ are given, we should use Eqs. $(40)_1$ and $(26)_2$.

### D. Robin-type boundary condition for $\psi$

In this subsection, we consider the case when Dirichlet condition of electric potential $\psi$ is replaced by Robin-type boundary condition. The Robin-type condition is often used to model the property of membrane or the stern layer near boundary. The previous effective conditions need to be modified since the quantity $\psi_0$ in those formulas is unknown.

#### 1. Dirichlet conditions for two ion concentrations

Suppose we have the boundary conditions at $x = 0$,

$$\begin{aligned}\eta\partial_x\psi(0,t) &= \psi(0,t) - g_0(t),\\ p(0,t) = p_0(t),&\quad n(0,t) = n_0(t),\end{aligned} \qquad (43)$$

where $\eta$ is a parameter that is assumed to be $\eta \leqslant O(\epsilon)$, and $g_0$ is some given function.

With previous assumptions, we still have Eqs. (13) and (14). Integrating once and using $\partial_X\Phi(\infty) = 0$, we obtain

$$(\partial_X\Phi)^2 = 2c_0[e^{\phi_0-\Phi(X)} + e^{\Phi(X)-\phi_0} - 2] + O(\epsilon), \qquad (44)$$

or equivalently

$$\partial_X\Phi = \sqrt{2c_0}\big[e^{\frac{\phi_0-\Phi(X)}{2}} - e^{\frac{\Phi(X)-\phi_0}{2}}\big] + O(\epsilon). \qquad (45)$$

Using the identity $\partial_X\Phi = \epsilon\partial_x\psi$, the above condition at $x = 0$ becomes

$$\begin{aligned}\epsilon\partial_x\psi(0,t) &= \sqrt{2c_0}\big(e^{\frac{\phi_0-\psi_0}{2}} - e^{\frac{\psi_0-\phi_0}{2}}\big) + O(\epsilon)\\ &= \sqrt{2p_0} - \sqrt{2n_0} + O(\epsilon).\end{aligned} \qquad (46)$$

Combining with the Robin-type condition Eq. $(43)_1$ leads to

$$\psi_0 \equiv \psi(0,t) = \frac{\eta}{\epsilon}(\sqrt{2p_0} - \sqrt{2n_0}) + g_0 + O(\eta). \qquad (47)$$

We conclude that we have the same effective conditions as before

$$\begin{aligned}\ln c_0 + \phi_0 + \frac{\sqrt{2}J^+_{c,0}\epsilon}{c_0^{3/2}}&[e^{(\psi_0-\phi_0)/2} - 1]\\ &= \ln p_0 + \psi_0 + o(\epsilon) + O(\eta),\\ \ln c_0 - \phi_0 + \frac{\sqrt{2}J^-_{c,0}\epsilon}{c_0^{3/2}}&[e^{(\phi_0-\psi_0)/2} - 1]\\ &= \ln n_0 - \psi_0 + o(\epsilon) + O(\eta),\end{aligned} \qquad (48)$$

except that $\psi_0$ is given by Eq. (47) in this case.

Note that if $\eta = O(\epsilon)$, we can omit the $O(\epsilon)$ terms in above conditions since they are not exact. If $\eta = o(\epsilon)$, the condition will become close to that in the Dirichlet case for $\psi$. In particular, for $\eta = o(\epsilon^2)$, the $\eta/\epsilon$ term can be neglected in Eq. (47), which essentially reduces to the Dirichlet case $\psi(0,t) = g_0$ [see Eq. (43)]. If $\eta/\epsilon$ tends to infinity (not considered here), the previous BL assumptions might not be true unless $n_0 \approx p_0$, and this is left for future study.

The treatment for $x = 1$ is similar and we summarize the results below.

*Proposition 3. Suppose for original system Eq. (2), the assumptions and conditions are the same as Proposition 2 except that the conditions for* $\psi_0(t),\psi_1(t)$ *are replaced by*

$$\begin{aligned}\eta\partial_x\psi(0,t) &= \psi(0,t) - g_0(t),\\ \eta\partial_x\psi(1,t) &= g_1(t) - \psi(1,t),\end{aligned} \qquad (49)$$

*where* $\eta \leqslant O(\epsilon)$, *then we have the same effective boundary conditions for the EN system Eq. (8) as Proposition 2 except that* $\psi_0(t),\psi_1(t)$ *in Eq. (40) are calculated by*

$$\psi_i \equiv \psi(i,t) = \frac{\eta}{\epsilon}(\sqrt{2p_i} - \sqrt{2n_i}) + g_i + O(\eta), \qquad (50)$$

where $i = 0,1$.

#### 2. Flux conditions

For this case, the boundary conditions at $x = 0$ are of the form

$$\begin{aligned}\eta\partial_x\psi(0,t) &= \psi(0,t) - g_0(t),\\ J_p(0,t) = J_{p,0}(t),&\quad J_n(0,t) = J_{n,0}(t),\end{aligned} \qquad (51)$$

where $\eta \leqslant O(\epsilon)$. The manipulation follows similar lines as before, and we summarize the results below.

*Proposition 4. Suppose for original system Eq. (2), the assumptions and conditions are the same as Proposition 1 except that the conditions for* $\psi_0(t),\psi_1(t)$ *are replaced by*

$$\begin{aligned}\eta\partial_x\psi(0,t) &= \psi(0,t) - g_0(t),\\ \eta\partial_x\psi(1,t) &= g_1(t) - \psi(1,t),\end{aligned} \qquad (52)$$

*where* $\eta \leqslant O(\epsilon)$, *then we have the same effective boundary conditions for the EN system Eq. (8) as Proposition 1 except that* $\psi_0(t),\psi_1(t)$ *in Eq. (40) are determined by the nonlinear algebraic equation*

$$\psi_i - g_i = \frac{\eta}{\epsilon}\sqrt{2c_i}\big(e^{\frac{\phi_i-\psi_i}{2}} - e^{\frac{\psi_i-\phi_i}{2}}\big) + O(\eta), \qquad (53)$$

where $i = 0,1$.

*Remark 5.* For the steady case, the above algebraic equation is the same as Eq. (1.23) in Ref. [26], with substitution $g_0=\phi_0(1)$, $\phi_0=0$, $\psi_0=\phi^*$, $c_0=\alpha/2$. With $\eta=o(\epsilon)$, the effective boundary conditions reduce to those for Dirichlet case, with $\psi(0,t)=g_0$.

*Remark 6.* The case $O(\epsilon)<\eta\leqslant O(1)$ is not considered above, since the boundary layer structure would be different. For the NGEN case considered here, it is expected that there is still a BL with thickness $O(\epsilon)$, and the above relation Eq. (53) implies that $\psi_i-\phi_i=o(1)$ in the BL. We postulate that in the BL near $x=0$,

$$\begin{aligned}&\psi-\phi_0, p-c_0, n-c_0=O(\epsilon/\eta),\\ &\partial_x\psi,\partial_x p,\partial_x n=O(1/\eta),\quad \partial_{xx}\psi=O(1/(\eta\epsilon)),\ldots,\end{aligned}\tag{54}$$

and it is proper to adopt the scaling $x=X/\epsilon$ and the transform $\Phi(X)=\psi-\phi_0, P(X)=p-c_0, N(X)=n-c_0$ instead. This seems true for Poisson-Boltzmann-type equations in Ref. [26] with their electroneutral case, where boundary layer with $O(\epsilon)$ thickness gradually disappears when $\eta/\epsilon$ becomes larger. Then, the above condition Eqs. (53) and (26) are still valid to leading order with new remainder $O(\epsilon)$, which will be verified by numerical examples in later sections.

### E. The general multi-ion species case

In this subsection we consider the general case with $n$ species of ions. The concentrations of ions are denoted by $p_i$ with valences $z_i$ $(i=1,..,n)$, where the valences are not necessarily different. The original PNP system for $p_i$ $(i=1,..,n)$ and $\psi$ is given by

$$\begin{aligned}-\epsilon^2\partial_{xx}\psi&=\sum_{k=1}^{n}z_kp_k,\\ \partial_tp_i&=-\partial_x\left(J_{p_i}\right)=D_i\partial_x(\partial_xp_i+z_ip_i\partial_x\psi),\end{aligned}\tag{55}$$

where $i=1,..,n$, and $D_i$ are some dimensionless diffusion constants. The reduced EN system for bulk region is

$$\partial_tc_i=-\partial_x\left(J_{c_i}\right)=D_i\partial_x(\partial_xc_i+z_ic_i\partial_x\phi),\tag{56}$$

where $i=1,..,n$. By the LEN condition $\sum z_kc_k=0$, the last concentration $c_n$ can be expressed by previous ones. Finally, the EN system for $n$ unknowns $c_1,..,c_{n-1},\phi$ can be written as

$$\begin{aligned}&\partial_tc_i=-\partial_x\left(J_{c_i}\right)=D_i\partial_x(\partial_xc_i+z_ic_i\partial_x\phi),\\ &\sum_{k=1}^{n}z_kD_k\partial_x(\partial_xc_k+z_kc_k\partial_x\phi)=0,\end{aligned}\tag{57}$$

where $i=1,..,n-1$ and whenever $c_n$ appears we should replace it by $c_n=-\frac{1}{z_n}\sum_{k=1}^{n-1}z_kc_k$.

First, at $x=0$, we consider the boundary conditions of the type

$$\psi(0,t)=\psi_0(t),\quad J_{p_i}(0,t)=J_{p_i,0}(t),\quad i=1,..,n.\tag{58}$$

*Theorem 1. Suppose the LEN and NGEN conditions are satisfied, and let $\psi_0(t),J_{p_i,0}(t)$ be the given electric potential and ion fluxes at $x=0$ as in Eq. (58) and let $\psi_1(t),J_{p_i,1}(t)$ be given at $x=1$ for original system Eq. (55), then for the EN system Eq. (57) we have the effective boundary conditions*

$$\begin{aligned}J_{c_i,0}&=J_{p_i,0}-\epsilon\partial_tF_i(c_{k0},\phi_0-\psi_0)+o(\epsilon),\\ J_{c_i,1}&=J_{p_i,1}+\epsilon\partial_tF_i(c_{k1},\phi_1-\psi_1)+o(\epsilon),\end{aligned}\tag{59}$$

*where $i=1,..,n$, $J_{c_i}=-D_i(\partial_xc_i+z_ic_i\partial_x\phi)$ are defined in Eq. (56), the argument $c_{k0}$ represents a vector $(c_{10},..,c_{(n-1)0})$, subscripts 0 and 1 denote quantities at $x=0$ and $x=1$, respectively, and*

$$F_i(c_{k0},\phi_0-\psi_0)=\pm\frac{c_{i0}}{\sqrt{2}}\int_1^{e^{\phi_0-\psi_0}}\frac{u^{z_i}-1}{\sqrt{\sum_{k=1}^{n}c_{k0}(u^{z_k}-1)}}\frac{du}{u}.\tag{60}$$

*Here, the $\pm$ are chosen for the cases $\psi_0\leqslant\phi_0$ and $\psi_0\geqslant\phi_0$ respectively, but $F_i$ is well-defined around $\phi_0=\psi_0$, and if $F_i$ can be integrated out, the expressions from the two cases are the same.*

*Proof.* The derivation follows similar lines as in Secs. II A and II B, and here we only give the key steps different from previous case. Near $x=0$, with the scalings

$$\Phi(X)=\psi(x),\quad P_i(X)=p_i(x),\quad X=\frac{x}{\epsilon},\tag{61}$$

where $i=1,..,n$, and by the BL analysis, we get

$$-\partial_{XX}\Phi=\sum_{i=1}^{n}z_iP_i(X)=\sum_{i=1}^{n}z_ic_{i0}e^{z_i[\phi_0-\Phi(X)]}.\tag{62}$$

Integrating once gives

$$\partial_X\Phi=\pm\sqrt{2\sum_{i=1}^{n}c_{i0}\{e^{z_i[\phi_0-\Phi(X)]}-1\}},\tag{63}$$

where $\pm$ are chosen for the cases $\psi_0\leqslant\phi_0$ and $\psi_0\geqslant\phi_0$ respectively. Here in the derivation of Eqs. (62) and (63) we have omitted the remainder $O(\epsilon)$. By utilizing the transport equations, we obtain

$$J_{c_i,0}=J_{p_i,0}-\epsilon\partial_tF_i(c_{k0},\phi_0-\psi_0)+o(\epsilon),\tag{64}$$

where $F_i$ depends on all ion concentrations $c_{k0}$ $(k=0,..,n-1$, $c_{n0}$ is replaced by previous ones) and is given by

$$\begin{aligned}F_i(c_{k0},\phi_0-\psi_0)&=\int_0^\infty[P_i(X)-c_{i0}]dX\\ &=\pm\frac{c_{i0}}{\sqrt{2}}\int_1^{e^{\phi_0-\psi_0}}\frac{u^{z_i}-1}{\sqrt{\sum_{k=1}^{n}c_{k0}(u^{z_k}-1)}}\frac{du}{u},\end{aligned}\tag{65}$$

where we have made change of variable $u=e^{\phi_0-\Phi(X)}$, and $\pm$ are chosen for the cases $\psi_0\leqslant\phi_0$ and $\psi_0\geqslant\phi_0$, respectively.

It can be easily seen that $F_i$ is well-defined around $\phi_0=\psi_0$, in particular, $F_i=0$ when $\phi_0=\psi_0$. Further, if $F_i$ can be integrated out, the expressions from the two cases are the same. This is readily verified from the fact that there is a factor $(u-1)^2$ inside square root in the denominator of the integrand, which cancels with the $\pm$ sign and the factor $u-1$ in the numerator (see Appendix A for details). ■

*Remark 7.* For some special cases, the explicit expressions for $F_i$ are available. For the previous case $z_1 = 1,\ z_2 = -1$, we recover the result

$$F_1(c_{10},\phi_0 - \psi_0) = \sqrt{2c_{10}}[e^{(\phi_0-\psi_0)/2} - 1],$$
$$F_2(c_{10},\phi_0 - \psi_0) = \sqrt{2c_{10}}[e^{(\psi_0-\phi_0)/2} - 1]. \tag{66}$$

For the case $z_1 = 2,\ z_2 = -1$, we get

$$F_1(c_{10},\phi_0 - \psi_0) = \sqrt{\frac{c_{10}}{2}}[e^{\frac{\phi_0-\psi_0}{2}}\sqrt{e^{(\phi_0-\psi_0)} + 2} - \sqrt{3}],$$
$$F_2(c_{10},\phi_0 - \psi_0) = \sqrt{2c_{10}}(\sqrt{1 + 2e^{(\psi_0-\phi_0)}} - \sqrt{3}). \tag{67}$$

For the three-ion case with $z_1 = 1,\ z_2 = 1,\ z_3 = -1$, we have

$$F_j(c_{10},c_{20},\phi_0 - \psi_0) = \sqrt{\frac{c_{j0}}{c_{10} + c_{20}}}\sqrt{2c_{j0}}\big(e^{\frac{\phi_0-\psi_0}{2}} - 1\big),$$
$$F_3(c_{10},c_{20},\phi_0 - \psi_0) = \sqrt{2(c_{10} + c_{20})}(e^{(\psi_0-\phi_0)/2} - 1), \tag{68}$$

where $j = 1,2$.

Next, at $x = 0$, we consider the boundary conditions of the type

$$\psi(0,t) = \psi_0(t), \quad p_i(0,t) = p_{i0}(t), \quad i = 1,..,n. \tag{69}$$

We summarize the results in the following theorem.

*Theorem 2. Suppose the LEN and NGEN conditions are satisfied, and let $\psi_0(t), p_{i0}(t)$ be the given electric potential and ion concentrations at $x = 0$ as in Eq. (69) and let $\psi_1(t), p_{i1}(t)$ be given at $x = 1$ for original system Eq. (55), then for the EN system Eq. (57) we have the effective boundary conditions*

$$\ln c_{i0} + z_i\phi_0 + \frac{\epsilon J_{c_i,0}}{D_i} f_i(c_{k0},\phi_0 - \psi_0)$$
$$= \ln p_{i0} + z_i\psi_0 + o(\epsilon),$$
$$\ln c_{i1} + z_i\phi_1 - \frac{\epsilon J_{c_i,1}}{D_i} f_i(c_{k1},\phi_1 - \psi_1)$$
$$= \ln p_{i1} + z_i\psi_1 + o(\epsilon), \tag{70}$$

*where $i = 1,..,n$, $J_{c_i}$ is defined in Eq. (56), the argument $c_{k0}$ represents a vector $(c_{10},..,c_{(n-1)0})$, subscripts 0 and 1 denote quantities at $x = 0$ and $x = 1$, respectively, and*

$$f_i(c_{k0},\phi_0 - \psi_0) = \pm\frac{1}{\sqrt{2}c_{i0}}\int_1^{e^{\phi_0-\psi_0}} \frac{u^{-z_i} - 1}{\sqrt{\sum_{k=1}^n c_{k0}(u^{z_k} - 1)}}\frac{du}{u}. \tag{71}$$

*Here, the $\pm$ are chosen for the cases $\psi_0 \leqslant \phi_0$ and $\psi_0 \geqslant \phi_0$, respectively, but $f_i$ is well-defined around $\phi_0 = \psi_0$, and if $f_i$ can be integrated out, the expressions from the two cases are the same.*

*Remark 8.* For the case $z_1 = 1, z_2 = -1$, we will recover the previous formulas in Proposition 2. For the case $z_1 = 2, z_2 = -1$, we get

$$f_1 = \frac{\sqrt{2 + e^{\phi_0-\psi_0}}(1 + 2e^{\phi_0-\psi_0})e^{\frac{3}{2}(\psi_0-\phi_0)} - 3\sqrt{3}}{3\sqrt{2}c_{10}^{3/2}},$$
$$f_2 = \frac{\text{arcsinh}(e^{(\phi_0-\psi_0)/2}/\sqrt{2}) - \text{arccsch}(\sqrt{2})}{\sqrt{2}c_{10}^{3/2}}. \tag{72}$$

For the case with $z_1 = 1,\ z_2 = 1,\ z_3 = -1$, we have

$$f_j(c_{10},c_{20},\phi_0 - \psi_0) = \frac{\sqrt{2}(e^{(\psi_0-\phi_0)/2} - 1)}{c_{j0}\sqrt{c_{10} + c_{20}}},$$
$$f_3(c_{10},c_{20},\phi_0 - \psi_0) = \frac{\sqrt{2}(e^{(\phi_0-\psi_0)/2} - 1)}{(c_{10} + c_{20})^{3/2}}, \tag{73}$$

where $j = 1,2$.

## III. NUMERICAL EXAMPLES

### A. A steady-state problem

As a first example to verify the preceding effective conditions, we take the steady-state problem from Rubinstein [12, pp. 133–134], since this problem can be solved analytically with effective conditions. Consider the stationary ionic transport in a unity thick unstirred layer adjacent to an ideally cation-permselective interface, and the PNP system with $\pm 1$ ions for $x \in [0,1]$ is

$$-\epsilon^2\psi'' = p - n, \quad p' + p\psi' = -j, \quad n' - n\psi' = 0, \tag{74}$$

together with boundary conditions

$$p(0) = n(0) = 1, \quad \psi(0) = 0,$$
$$p(1) = 1, \quad J_n(1) = 0, \quad \psi(1) = -V, \tag{75}$$

where prime denotes the derivative with respect to $x$, and $j$ is the constant flux to be determined with given potential $V$. Physically, the $j$-$V$ relation is the current-voltage relation in this example. Since it is electroneutral at $x = 0$, there is only a boundary layer near $x = 1$.

One can easily write down the EN system for $c(x)$ and $\phi(x)$ in bulk region, and the solutions are given by

$$c(x) = 1 - \frac{j}{2}x, \quad \phi(x) = \ln\left(1 - \frac{j}{2}x\right). \tag{76}$$

By using the usual continuity of electrochemcial potential as in Ref. [12], we get

$$j = 2(1 - e^{-V/2}). \tag{77}$$

By the effective condition Eq. (40) at $x = 1$, we get

$$2\ln\left(1 - \frac{j}{2}\right) - 4j\epsilon\left(\frac{\sqrt{2}e^{-\frac{V}{2}}}{(2 - j)^2} - \frac{1}{(2 - j)^{3/2}}\right) = -V, \tag{78}$$

where there is an $O(\epsilon)$ correction term.

In the numerical verification, we use Eq. (2) with boundary conditions Eq. (75) and the following initial conditions at $t = 0$:

$$p(x,0) = 1, \quad n(x,0) = 1. \tag{79}$$

TABLE I. Comparison of flux $j$ with fixed $V = 1$ and different $\epsilon$, where "Rubinstein" and "Present" are from Eqs. (77) and (78), respectively; "PNP" is obtained by solving the original PNP system.

| $\epsilon$ | 0.1 | 0.05 | 0.01 |
|---|---|---|---|
| Rubinstein | 0.7869 | 0.7869 | 0.7869 |
| Present | 0.8191 | 0.8029 | 0.7901 |
| PNP | 0.8192 | 0.8029 | 0.7901 |

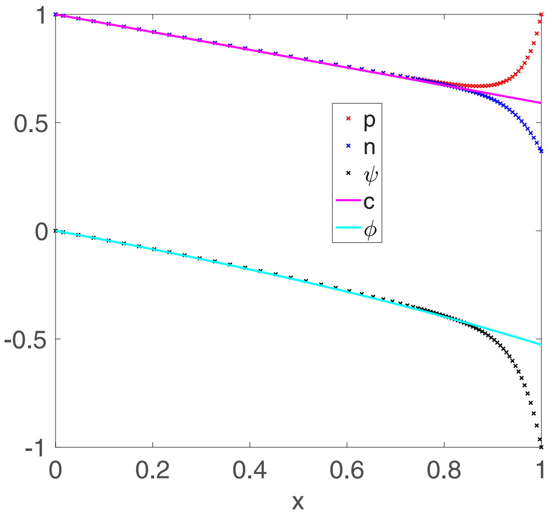


FIG. 1. Comparison between analytic bulk solution with numerical solution at $t = 20$, with $\epsilon = 0.05$.

The solution tends to the steady state solution of Eqs. (74) and (75), and the flux $j$ near the steady state can be found. Finite-volume method with a refined mesh near $x = 1$ is adopted in the numerical simulation. With $V = 1$ and $\epsilon = 0.1, 0.05, 0.01$, we give the results of flux $j$ using Rubinstein's condition Eq. (77) and the new condition Eq. (78) in Table I. It can be seen that the new effective condition produces better results and the $O(\epsilon)$ term is correct. Figure 1 shows the comparison between bulk solution Eq. (76) and the numerical solution at $t = 20$ with $\epsilon = 0.05$. In order to show the error of solution with respect to small parameter $\epsilon$, Table II compares the maximum errors of concentration $c$ by Eq. (76), in the bulk region [0,0.5] with different $\epsilon$. It shows that the result obtained using the effective condition Eq. (78) enjoys a higher-order accuracy than that obtained with Rubinstein's condition Eq. (77).

Next, we replace Dirichlet boundary condition for $\psi(1)$ by a Robin-type condition $\eta\partial_x\psi(1) = -1 - \psi(1)$ and keep others the same as before. The effective condition Eqs. (40) and (50) imply that

$$2\log\left(1-\frac{j}{2}\right)-\frac{4j\epsilon(\sqrt{2}e^{\psi_1/2}-\sqrt{2-j})}{(j-2)^2}=\psi_1,$$

$$\psi_1=-1+\sqrt{2}\frac{\eta}{\epsilon}-2W(e^{(\sqrt{2}\eta-\epsilon)/(2\epsilon)}\eta/(\sqrt{2}\epsilon)), \qquad (80)$$

where $W$ is the Lambert-W function. For $\epsilon = 0.01$ and different $\eta$, we compare in Table III the results of flux $j$ using Eq. (80) and the original PNP with initial condition Eq. (79).

TABLE II. Comparison of maximum errors of concentration $c$ in the bulk region [0,0.5] with different $\epsilon$, where $p$ and $n$ are from PNP system and $c$ is from Eq. (76) with associated flux $j$ in Table I.

| $\epsilon$ | 0.1 | 0.05 | 0.01 |
|---|---|---|---|
| Rubinstein $\lvert c-p\rvert$ | $5.6\times10^{-3}$ | $3.7\times10^{-3}$ | $7.9\times10^{-4}$ |
| Present $\lvert c-p\rvert$ | $2.4\times10^{-3}$ | $3.7\times10^{-4}$ | $7.3\times10^{-6}$ |
| PNP $\lvert p-n\rvert$ | $4.2\times10^{-3}$ | $6.5\times10^{-4}$ | $2.4\times10^{-5}$ |

TABLE III. Comparison of flux $j$ using the present Eq. (80) and the original PNP system.

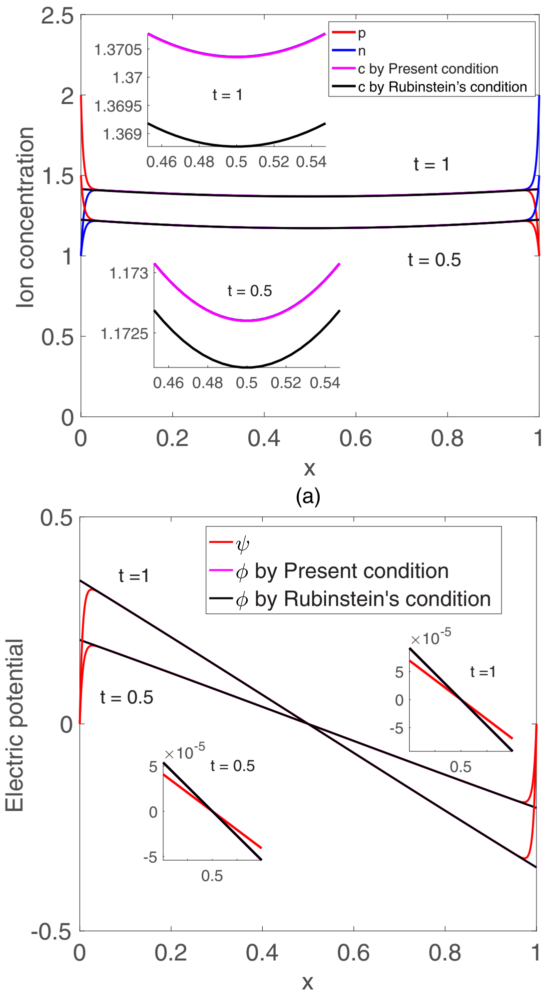
| $\eta$ | $10^{-2}$ | $10^{-3}$ | $10^{-4}$ |
|---|---|---|---|
| Present | 0.5358 | 0.7570 | 0.7867 |
| PNP | 0.5406 | 0.7590 | 0.7871 |

For the Robin-type condition, in general the results are correct at the leading order, and the error is roughly $O(\eta)$.

### B. Two dynamic examples

In this subsection, we investigate two time-dependent examples to verify the EN models. In these examples, the previous assumptions on the BL structure are satisfied, so we can solve the EN system in bulk region directly and efficiently with effective boundary conditions.

As the first example, we examine the PNP system Eq. (2) with Dirichlet boundary conditions for $p,n,\psi$ like Eq. (28).



(a)

(b)

FIG. 2. Comparison between numerical results of original PNP system with Dirichlet conditions and those of the EN model using Rubinstein's condition Eq. (83) and present condition Eq. (41): (a) for ion concentrations, (b) for electric potential.

TABLE IV. Maximum error in concentration $c(x,t)$ and potential $\phi(x,t)$ in some bulk region $x \in [0.25,0.75]$ and $t = 0.5,1$, using Rubinstein's condition Eq. (83) and the present condition Eq. (41).

| | $c$ at $t = 0.5$ | $c$ at $t = 1$ | $\phi$ at $t = 0.5$ | $\phi$ at $t = 1$ |
|---|---|---|---|---|
| Rubinstein | $4.5 \times 10^{-4}$ | $1.7 \times 10^{-3}$ | $9.5 \times 10^{-5}$ | $6.2 \times 10^{-5}$ |
| Present | $4.9 \times 10^{-6}$ | $8.4 \times 10^{-6}$ | $1.1 \times 10^{-5}$ | $2.3 \times 10^{-5}$ |
| $\lvert p - n \rvert$ | $3.6 \times 10^{-6}$ | $4.6 \times 10^{-6}$ | – | – |

More precisely the boundary conditions at $x = 0$ and 1 are given by

$$\begin{aligned} p(0,t) &= 1 + t, \quad n(0,t) = 1, \quad \psi(0,t) = 0, \\ p(1,t) &= 1, \quad n(1,t) = 1 + t, \quad \psi(1,t) = 0, \end{aligned} \tag{81}$$

and the initial conditions at $t = 0$ are

$$n(x,0) = p(x,0) = 1, \quad 0 < x < 1. \tag{82}$$

In this case, the BL develops gradually over time, and we will demonstrate it with $\epsilon = 0.01$. Finite-Volume method with refined mesh in the BL is adopted to solve the original PNP system Eq. (2). The EN system Eq. (8) for $c(x,t)$ and $\phi(x,t)$ is solved with a fixed uniform mesh with the aid of effective boundary conditions. For the original PNP system, we use a fixed non-uniform mesh in computation, with mesh size $\Delta x = 8.0 \times 10^{-4}$ in the BL, which gradually increases to $\Delta x = 3.0 \times 10^{-3}$ in the bulk region. For the EN model, we use a uniform mesh size $\Delta x = 5.0 \times 10^{-3}$ over the entire domain. And we try two implementations with the following effective boundary conditions, (i) the leading order Dirichlet conditions (called Rubinstein's condition here)

$$c_0 = c_1 = \sqrt{1 + t}, \quad \phi_0 = -\phi_1 = \tfrac{1}{2} \ln(1 + t), \tag{83}$$

and (ii) the Robin-type conditions in Eq. (41) with $O(\epsilon)$ correction term. All the above effective boundaries are explicit and linear and thus can be easily applied.

Figure 2 shows the comparison between the numerical result of original PNP system and two direct numerical implementations for EN system. Figure 2(a) shows that the present higher-order effective conditions produce better results for ion concentration than the leading order Rubinstein's condition, and so does Fig. 2(b) for electric potential (note that red and pink curves coincide in the enlarged figure). By using the numerical results of $p(x,t)$ and $\psi(x,t)$ of the original system as a reference solution, Table IV gives the maximum errors of $c(x,t)$ and $\phi(x,t)$ in some bulk region [0.25,0.75]. The results indicate that the accuracy is acceptable with the effective boundary conditions. Table V compares the maximum errors of concentration $c(x,t)$ using both the new and Rubinstein's conditions for several values of $\epsilon$, in the bulk region $x \in [0.25,0.75]$ at $t = 0.5$. It shows that the new effective condition produces a more accurate solution for $\epsilon$. Furthermore, the EN system allows for relatively large mesh and time-step sizes, and as a result the computational time is greatly reduced. For instance, it takes roughly 1 h to compute the original PNP system up to $t = 1$, while it takes only 8 min for the EN system on a Mac laptop (Processor: 1.8 GHz Intel Core i5; Memory: 8 GB 1600 MHz DDR3)

TABLE V. Maximum errors of concentration $c(x,t)$ in some bulk region $x \in [0.25,0.75]$ at $t = 0.5$ for varying $\epsilon$, using Rubinstein's condition Eq. (83) and the present condition Eq. (41).

| $\epsilon$ | 0.1 | 0.05 | 0.01 |
|---|---|---|---|
| Rubinstein | $1.0 \times 10^{-2}$ | $2.5 \times 10^{-3}$ | $4.5 \times 10^{-4}$ |
| Present | $5.9 \times 10^{-3}$ | $2.2 \times 10^{-4}$ | $5.0 \times 10^{-6}$ |
| $\lvert p - n \rvert$ | $9.5 \times 10^{-3}$ | $2.7 \times 10^{-4}$ | $3.6 \times 10^{-6}$ |

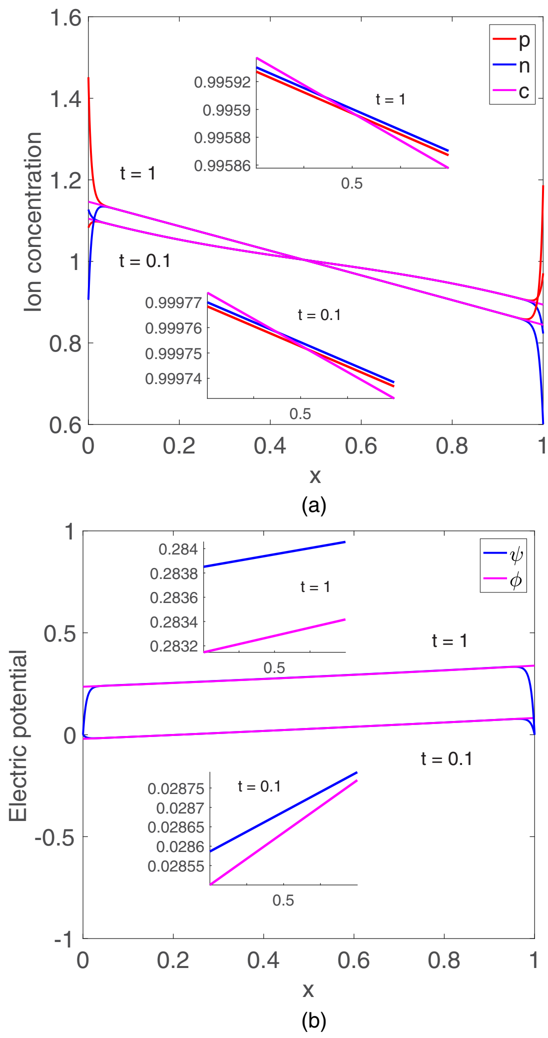


FIG. 3. Comparison between numerical results of original PNP system with flux conditions and those of the EN system with effective boundary conditions Eq. (26): (a) for ion concentrations, (b) for electric potential.

As a second example, we solve the PNP system Eq. (2) with the flux conditions

$$\begin{aligned} J_p(0,t) &= 0.2, \quad J_n(0,t) = 0.4, \quad \psi(0,t) = 0, \\ J_p(1,t) &= 0.2, \quad J_n(1,t) = 0.4(1 + 2\epsilon), \quad \psi(1,t) = 0. \end{aligned} \tag{84}$$

Here, the fluxes are $O(1)$ but the unbalanced flux is only $O(\epsilon)$, which is consistent with previous assumptions. The initial conditions are the same as in Eq. (82). The original PNP system for $p,n,\psi$ is solved using a finite volume method on a refined

TABLE VI. Maximum error in concentration $c(x,t)$ and potential $\phi(x,t)$ in some bulk region $x \in [0.25,0.75]$ and $t = 0.1$ and 1.

| | $c$ at $t = 0.1$ | $c$ at $t = 1$ | $\phi$ at $t = 0.1$ | $\phi$ at $t = 1$ |
|---|---|---|---|---|
| Present | $9.1 \times 10^{-7}$ | $3.6 \times 10^{-7}$ | $4.4 \times 10^{-5}$ | $6.7 \times 10^{-4}$ |
| $\lvert p - n \rvert$ | $2.3 \times 10^{-6}$ | $3.7 \times 10^{-6}$ | – | – |

mesh, while the EN system Eq. (8) for $c,\phi$ is computed on a uniform mesh and the linearized version of the effective boundary conditions Eqs. (26).

Figure 3 shows the comparison between the numerical results of $p,n,\psi$ from the original PNP system and those of $c,\phi$ from the EN model at $t = 0.1$ and 1. It can be seen that the two solutions agree very well with each other in the bulk region. By using the numerical results of $p(x,t)$ and $\psi(x,t)$ from original system as a reference solution, Table VI shows the maximum errors of $c(x,t)$ and $\phi(x,t)$ in a portion of the bulk region [0.25,0.75]. Similarly, it takes less computational time to solve the EN system with effective boundary conditions (6 min) compared to approximately 1 h to solve the original PNP system on a Mac laptop (Processor: 1.8 GHz Intel Core i5; Memory: 8 GB 1600 MHz DDR3)

## IV. AN ELECTRONEUTRAL MODEL FOR NEURONAL AXON

As a final example, we consider a region representing part of a neuronal axon with a membrane in between [32]. The interval is set to be $[0,L]$, where $L$ is typical cell length with the membrane placed in the middle $x = L/2$. The left part $[0,L/2)$ is the extracellular space and $(L/2,L]$ is the intracellular space. Only three basic types of ions $\mathrm{Na}^+,\mathrm{K}^+,\mathrm{Cl}^-$ are considered (fixed negative charge are incorporated into $\mathrm{Cl}^-$ ion as an approximation), and LEN condition in bulk region is valid in this biological application.

We first formulate the original system in dimensional form. Let $p_i$ $(i = 1,2,3)$ denote ion concentrations of $\mathrm{Na}^+,\mathrm{K}^+,\mathrm{Cl}^-$, with valences $z_1 = z_2 = 1, z_3 = -1$. The dimensional PNP system for $p_i$ and electric potential $\psi$ in left region $x \in (0,L/2)$ is

$$-\epsilon_0\epsilon_r^L \partial_{xx}\psi = e_0 N_A\left(\sum_{k=1}^{3} z_k p_k\right),$$
$$\partial_t p_i = -\partial_x(J_{p_i}) = D_i\partial_x\left(\partial_x p_i + \frac{e_0}{k_B T} z_i p_i \partial_x\psi\right), \tag{85}$$

where $i = 1,2,3$, $\epsilon_0$ is vacuum permittivity, $\epsilon_r^L$ is the relative permittivity of left region (extracellular space), $e_0$ is elementary charge, $N_A$ is Avogadro constant, $D_i$ is the diffusion constant, $k_B$ is Boltzmann constant, and $T$ is absolute temperature. The system for right half region is the same except a possibly different relative permittivity $\epsilon_r^R$. The boundary conditions at $x = 0,1$ are omitted here, and will be presented in dimensionless form.

The membrane at $x = L/2$ is described by Hodgkin-Huxley (HH) model [25], to simulate action potential for neuronal axon (one might use GHK flux model [29] for other purpuses). Thus, the dimensional relation for the current through membrane/ion channel, from intracellular region to extracellular region, is

$$I_i = G_{p_i}(V_m - E_i), \tag{86}$$

or in terms of flux at $x = L/2$,

$$-z_i e_0 N_A J_{p_i} = z_i e_0 N_A D_i\left(\partial_x p_i + \frac{e_0}{k_B T} z_i p_i \partial_x\psi\right)$$
$$= G_{p_i}\left(\psi_R - \psi_L - \frac{k_B T}{z_i e_0}\ln\frac{p_{iL}}{p_{iR}}\right), \tag{87}$$

where $G_{p_i}$ is the conductance for ion $p_i$, $V_m = \psi_R - \psi_L$ is the membrane potential, $E_i$ is the Nernst potential of ion $p_i$, subscripts $L$ and $R$ denote the left and right limits of quantities at membrane $x = L/2$.

Assuming that the membrane has thickness $h_m$ and relative permittivity $\epsilon_r^m$, and there are no ions in membrane. Thus, the electric potential is linear inside membrane. The other two jump conditions on the interface $x = L/2$ are

$$\epsilon_r^L \partial_x\psi\big|_{x=\frac{L}{2}-} = \epsilon_r^R \partial_x\psi\big|_{x=\frac{L}{2}+} = \epsilon_r^m \frac{\psi_R - \psi_L}{h_m}, \tag{88}$$

where $\frac{L}{2}\pm$ mean the left and right limits at $x = L/2$.

The conductances depend on membrane potential $V_m$. Following Ref. [32], we set $G_{p_3} \equiv G_{\mathrm{Cl}} = 0$ and

$$G_{p_1} \equiv G_{\mathrm{Na}} = \bar{G}_{\mathrm{Na}} m^3 h + G_{\mathrm{Na,leak}},$$
$$G_{p_2} \equiv G_{\mathrm{K}} = \bar{G}_{\mathrm{K}} n^4 + G_{\mathrm{K,leak}}, \tag{89}$$

where

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n,$$
$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m,$$
$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h. \tag{90}$$

The coefficients depend on $V_m$ and are given by

$$\alpha_n = \frac{1}{100}\frac{10-\bar{V}}{[e^{(10-\bar{V})/10}-1]}, \quad \beta_n = \frac{1}{8e^{\bar{V}/80}},$$
$$\alpha_m = \frac{1}{10}\frac{25-\bar{V}}{[e^{(25-\bar{V})/10}-1]}, \quad \beta_m = 4e^{-\bar{V}/18}, \tag{91}$$
$$\alpha_h = \frac{7}{100}e^{-\bar{V}/20}, \quad \beta_h = \frac{1}{e^{(30-\bar{V})/10}+1},$$

where $\bar{V} = V_m - V_r$ and $V_r$ is some fixed resting potential. In the above coefficients, the unit for $\bar{V}$ is millivolt. Theoretically, there is no singularity in above coefficients, but for computation when $\bar{V}$ is near 10 or 25, it is sensitive as denominator approaches 0. We can use the Taylor expansions in a small neighborhood, say $\delta = 0.01$,

$$\alpha_n(\bar{V}) = \frac{1}{10} + \frac{\bar{V}-10}{200} + \frac{(\bar{V}-10)^2}{12000}, \quad |\bar{V}-10| < \delta,$$
$$\alpha_m(\bar{V}) = 1 + \frac{\bar{V}-25}{20} + \frac{(\bar{V}-25)^2}{1200}, \quad |\bar{V}-25| < \delta, \tag{92}$$

and the error by choosing $\delta = 0.01$ is at least at the order of $10^{-12}$. With $\bar{V} = 0$, we obtain the steady-state solution

$$n_0 = \frac{4}{5e-1} \approx 0.3177, \quad m_0 = \frac{5}{8e^{5/2}-3} \approx 0.05293,$$
$$h_0 = \frac{7(1+e^3)}{107+7e^3} \approx 0.5961, \tag{93}$$

which are used as initial values of the time-dependent problem to simulate action potential.

### A. Nondimensionalization

In this subsection, we present the dimensionless PNP formulation combined with the HH model. We adopt the following scalings:

$$\tilde{\psi} = \frac{\psi}{k_B T/e_0}, \quad \tilde{p}_i = \frac{p_i}{p_0}, \quad \tilde{x} = \frac{x}{L}, \quad \tilde{h}_m = \frac{h_m}{L},$$
$$\tilde{D}_i = \frac{D_i}{D_0}, \quad \tilde{t} = \frac{t}{L^2/D_0}, \quad \tilde{G}_{p_i} = \frac{G_{p_i}}{G_0}, \tag{94}$$

where $p_0$ is the typical concentration of ions, $D_0$ is the typical diffusion constant, and typical conductance $G_0$ is defined by $G_0 = p_0 D_0 e^2 N_A/(k_B T L)$. All the parameter values and typical values are given in Appendix B. In the following, we will remove the tilde and still use the same notations but they represent dimensionless quantities.

The dimensionless PNP system is given by

$$-\epsilon_L^2 \partial_{xx}\psi = \sum_{k=1}^{3} z_k p_k, \quad 0 < x < 1/2,$$
$$-\epsilon_R^2 \partial_{xx}\psi = \sum_{k=1}^{3} z_k p_k, \quad 1/2 < x < 1,$$
$$\partial_t p_i = -\partial_x(J_{p_i}) = D_i \partial_x(\partial_x p_i + z_i p_i \partial_x \psi),$$
$$i = 1,2,3 \quad 0 < x < 1, \tag{95}$$

together with the conditions on interface $x = 1/2$,

$$-z_i J_{p_i}\big|_{x=\frac{1}{2}} \equiv z_i D_i(\partial_x p_i + z_i p_i \partial_x \psi)|_{x=\frac{1}{2}}$$
$$= G_{p_i}\left(\psi_R - \psi_L - \frac{1}{z_i}\ln\frac{p_{iL}}{p_{iR}}\right), \tag{96}$$

and

$$\epsilon_L^2 \partial_x \psi\big|_{x=\frac{1}{2}-} = \epsilon_R^2 \partial_x \psi\big|_{x=\frac{1}{2}+} = \epsilon_m^2 \frac{\psi_R - \psi_L}{h_m}. \tag{97}$$

Here the dimensionless parameters $\epsilon_L, \epsilon_R, \epsilon_m$ are defined by

$$\epsilon_s \equiv \sqrt{\frac{\epsilon_0 \epsilon_r^s k_B T}{e^2 N_A p_0 L^2}}, \quad s = L,R,m. \tag{98}$$

The values of the dimensionless parameters are given in Appendix B.

We use typical bulk concentrations as the initial values (see Appendix B) at $t = 0$:

$$p_1(x,0) = 1, \quad p_2(x,0) = 0.04, \quad p_3(x,0) = 1.04,$$
$$\text{for} \quad 0 < x < 1/2,$$
$$p_1(x,0) = 0.12, \quad p_2(x,0) = 1.25, \quad p_3(x,0) = 1.37,$$
$$\text{for} \quad 1/2 < x < 1. \tag{99}$$

For the boundary conditions at $x = 0,1$, we adopt

$$\psi(0,t) = 0, \quad p_1(0,t) = 1,$$
$$p_2(0,t) = 0.04, \quad p_3(0,t) = 1.04, \tag{100}$$
$$\frac{\partial \psi}{\partial x}(1,t) = 0, \quad J_{p_i}(1,t) = 0, \quad i = 1,2,3,$$

where the first two lines give fixed concentrations and electric potential in extracellular region, and the third line are the symmetric conditions at the center of the neuronal axon.

This system is solved with Eq. (89) for conductances and the dynamics of $n,m,h$ given by Eq. (90). We will not scale the quantities in the coefficients Eq. (91), where the quantity $\bar{V}$ (in millivolts) is related to normalized membrane potential $V_m = \psi_R - \psi_L$ through

$$\bar{V} = \frac{k_B T}{e_0}(\psi_R - \psi_L) - V_r, \tag{101}$$

and $V_r$ is the resting potential in millivolts [see Eq. (109) below].

### B. The effective flux conditions for the electro-neutral model

The reduced EN model consists of the equations in Eq. (57) for $c_1, c_2, \phi$, with $n = 3$ and $z_1 = z_2 = 1, z_3 = -1$. Next, we need to propose approximate jump conditions at middle interface for bulk quantities $c_{iL}, \phi_L, c_{iR}, \phi_R$ $(i = 1,2)$, where subscripts $L,R$ indicate the left and right limits of quantities at interface $x = 1/2$. Based on previous analysis in Secs. II D and II E, we derive the following 14 conditions to close the system (normally six conditions are needed, but we have introduced eight auxiliary quantities $p_{iL}, p_{iR}, \psi_L, \phi_R$ with $i = 1,2,3$ at interface $x = 1/2$),

$$\frac{\epsilon_m^2}{h_m}(\psi_R - \psi_L) = \epsilon_R\sqrt{2c_{3R}}\left(e^{(\phi_R-\psi_R)/2} - e^{(\psi_R-\phi_R)/2}\right)$$
$$= -\epsilon_L\sqrt{2c_{3L}}\left(e^{(\phi_L-\psi_L)/2} - e^{(\psi_L-\phi_L)/2}\right), \tag{102}$$

where $c_{3R} = c_{1R} + c_{2R}, c_{3L} = c_{1L} + c_{2L}$ by the electroneutrality condition, and

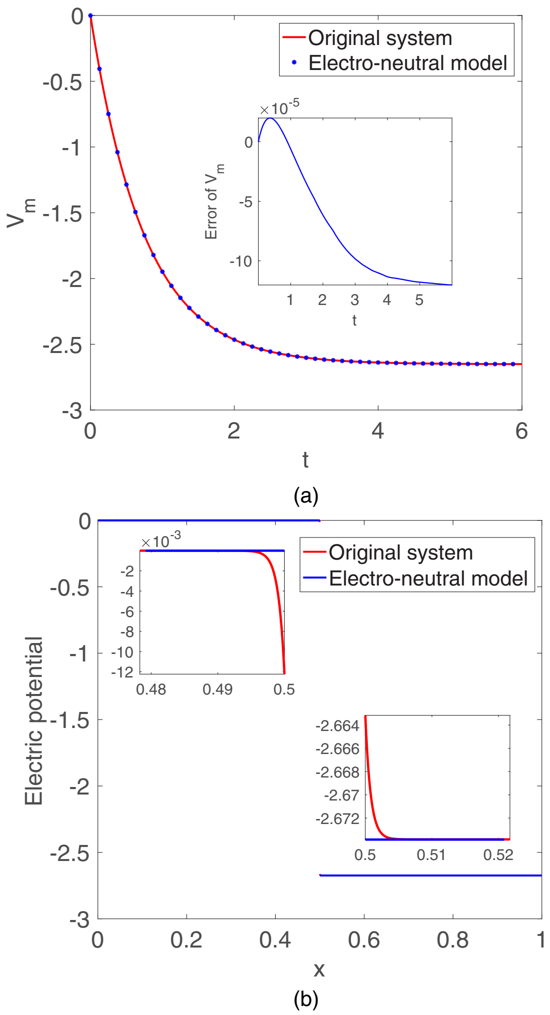
$$G_{p_i}\left(\psi_R - \psi_L - \frac{1}{z_i}\ln\frac{p_{iL}}{p_{iR}}\right) = -z_i\left(J_{c_i,R} + \epsilon_R \partial_t F_{iR}\right)$$
$$= -z_i\left(J_{c_i,L} - \epsilon_L \partial_t F_{iL}\right),$$
$$\ln c_{iR} + z_i\phi_R + \frac{\epsilon_R J_{c_i,R}}{D_i} f_{iR} = \ln p_{iR} + z_i \psi_R,$$
$$\ln c_{iL} + z_i\phi_L - \frac{\epsilon_L J_{c_i,L}}{D_i} f_{iL} = \ln p_{iL} + z_i \psi_L, \tag{103}$$

where $i = 1,2,3$, $J_{c_i}$ is given in Eq. (56), and we have defined

$$F_{is} = F_i(c_{1s}, c_{2s}, \phi_s - \psi_s),$$
$$f_{is} = f_i(c_{1s}, c_{2s}, \phi_s - \psi_s), \tag{104}$$

for $s = L,R$. Here $F_i$ and $f_i$ are given by Eqs. (68) and (73).

From definition Eq. (89) and the data in Appendix B, the conductances $G_{p_i}$ have at most the same order as the



(a)

(b)

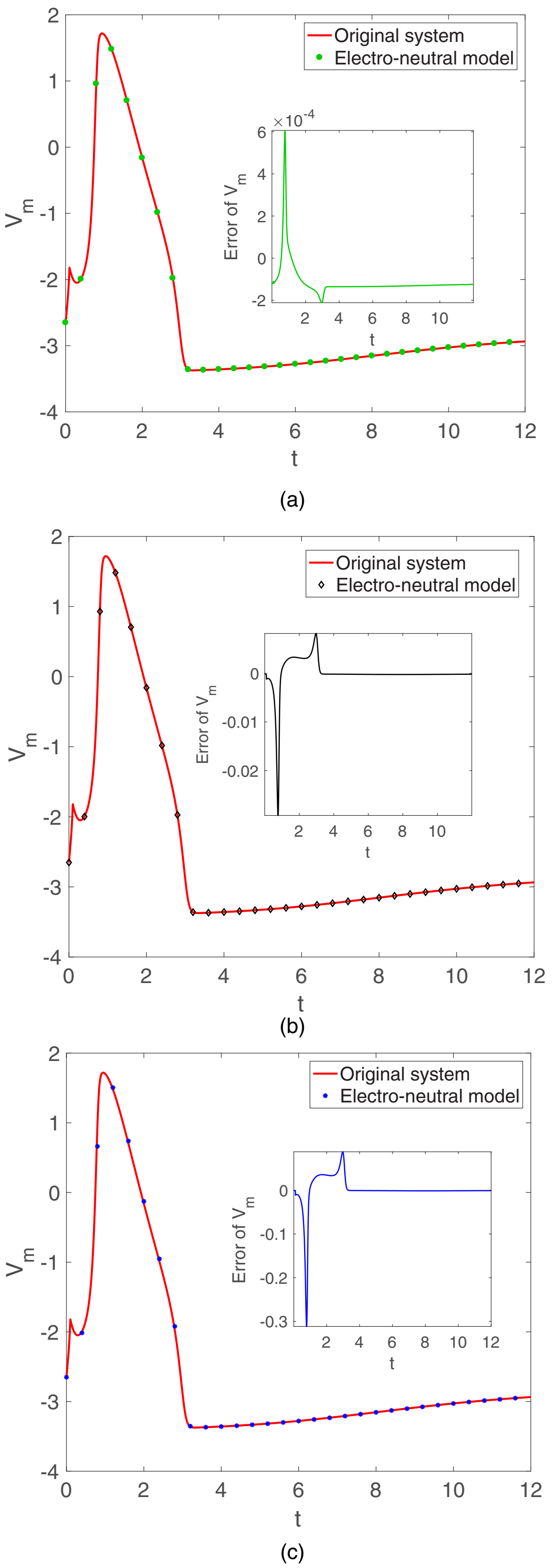
FIG. 4. Numerical results of original system and electroneutral (EN) model to generate the resting state in step 1: (a) the dynamics of membrane potential $V_m$; (b) distribution of electric potential at resting state.

dimensionless small parameter $\epsilon_R = \epsilon_L$. Now we simplify the conditions in Eq. (103) asymptotically and get

$$\begin{aligned} -z_i J_{c_i,R} &= G_{p_i}\left(\phi_R - \phi_L - \frac{1}{z_i}\ln\frac{c_{iL}}{c_{iR}}\right) + z_i\epsilon_R\partial_t F_{iR} \\ &\quad + \frac{G_{p_i}\epsilon_R}{D_i z_i}\left[J_{c_i,R} f_{iR} + \frac{\epsilon_R}{\epsilon_L} J_{c_i,L} f_{iR}\right], \\ &= G_{p_i}\left(\phi_R - \phi_L - \frac{1}{z_i}\ln\frac{c_{iL}}{c_{iR}}\right) \\ &\quad + z_i\epsilon_R\partial_t F_{iR} + O(\epsilon_R^2). \end{aligned} \tag{105}$$

We expect the flux is $O(\epsilon_R)$, so the higher-order term $O(\epsilon_R^2)$ can be ignored while the term $\epsilon_R\partial_t F_{iR}$ should be kept. Similarly, we obtain the condition for flux $J_{c_i,L}$ as

$$\begin{aligned} -z_i J_{c_i,L} &= G_{p_i}\left(\phi_R - \phi_L - \frac{1}{z_i}\ln\frac{c_{iL}}{c_{iR}}\right) \\ &\quad - z_i\epsilon_L\partial_t F_{iL} + O(\epsilon_L^2). \end{aligned} \tag{106}$$



(a)

(b)

(c)

FIG. 5. Numerical results of the original PNP system and EN model in the dynamics of action potential in step 2, with different time steps: (a) $\Delta t = 5 * 10^{-6}$; (b) $\Delta t = 5 * 10^{-5}$; (c) $\Delta t = 5 * 10^{-4}$.

These two conditions take the same form of the original HH model with boundary values replaced by the bulk quantities, with correction terms involving $F_{iR}$ and $F_{iL}$, which in general are not negligible.

TABLE VII. Comparison of computation time between original system and EN model and the maximum error for membrane potential $V_m$ in EN model.

| | Original system $\Delta t = \frac{5}{8} * 10^{-6}$ | EN model, $\Delta t = 5 * 10^{-6}$ | EN model, $\Delta t = 5 * 10^{-5}$ | EN model, $\Delta t = 5 * 10^{-4}$ |
|---|---|---|---|---|
| Error | – | $6 * 10^{-4}$ | 0.03 | 0.3 |
| Time | 8 h | 1.7 h | 10 min | 1 min |

To summarize, the final EN system consists of Eqs. (57) with conditions Eqs. (102), (105), and (106), and dynamics of conductances Eqs. (89)–(91).

*Remark 9.* If we carry out a linearization of $\phi_L - \psi_L$ and $\phi_R - \psi_R$ in exponential functions [in $F_i, f_i$, and Eq. (102)], then we obtain

$$\begin{aligned} -\sum_{i=1}^{3} z_i J_{c_i,L} - \sum_{i=1}^{3} G_{p_i}\left(\phi_R - \phi_L - \frac{1}{z_i}\ln\frac{c_{iL}}{c_{iR}}\right) \\ = -\epsilon_L \sum_{i=1}^{3} z_i \partial_t F_{iL} \approx -\epsilon_L \partial_t[\sqrt{2c_{3L}}(\phi_L - \psi_L)] \\ \approx \frac{\epsilon_m^2}{h_m}\partial_t(\psi_R - \psi_L), \end{aligned} \tag{107}$$

where we have used linearized version of Eq. (102) in last approximation. Similarly, we have

$$\begin{aligned} -\sum_{i=1}^{3} z_i J_{c_i,R} - \sum_{i=1}^{3} G_{p_i}\left(\phi_R - \phi_L - \frac{1}{z_i}\ln\frac{c_{iL}}{c_{iR}}\right) \\ \approx \frac{\epsilon_m^2}{h_m}\partial_t(\psi_R - \psi_L). \end{aligned} \tag{108}$$

Physically, on the left-hand side, the first term is the total current from/to bulk region, where the minus sign means from intracellular space to extracellular space; and the second term is total current through membrane or ion channels, approximated by bulk quantities (they differ by higher-order term). On the right-hand side, the quantity $\epsilon_m^2/h_m$ is the normalized membrane capacitance [scaled by $e^2 N_A p_0 L/(k_B T)$]. Under such linearization, this equation reduces to the HH cable model. It is worth noting that a similar electroneutral model was proposed by Mori [33]. A quantity $\sigma_i$ introduced in Ref. [33], Eq. (35), plays the same role as $F_{iR}$ and $F_{iL}$ here.

### C. Numerical results

In this subsection, we present numerical results using both the original PNP system and the present EN model. The computation is divided into two steps: first, we generate a resting state; second, we simulate the phenomenon of action potential.

Step 1. To generate a resting state, we only use two leak conductance as in Ref. [32], by setting $\bar{G}_{\mathrm{Na}} = \bar{G}_{\mathrm{K}} = 0$ in Eq. (89). Flux of sodium ion is positive, i.e., from extracellular region to intracellular region, while flux of potassium ion is negative. After certain period, e.g., at $t = 6$, the net flux across membrane tends to 0, i.e., $J_{p_1} + J_{p_2}|_{x=1/2} = 0$, which is set as the resting solution. Figure 4(a) shows the variation of membrane potential $V_m = \psi_R - \psi_L$ for both the original model and the new EN model, and the two solutions agree very well with each other. Figure 4(b) shows the distributions of electric potential $\psi$ for the original system and $\phi$ for the EN model, at resting state $t = 6$. They agree very well in the bulk region. The resting potential is calculated as

$$\begin{aligned} V_m|_{t=6} &= \psi_R - \psi_L|_{t=6} \approx -2.65, \\ V_r &= \frac{k_B T}{e_0}(\psi_R - \psi_L)|_{t=6} \approx -63.8\,\mathrm{mV}. \end{aligned} \tag{109}$$

In the computation using the original model, nonuniform fixed mesh is adopted, with mesh size $\Delta x = 1.7 \times 10^{-4}$ in boundary layer region of width $5\epsilon$ on each side of membrane, gradually increasing to $\Delta x = 9.0 \times 10^{-3}$ in bulk region. For the EN model, we adopt a uniform mesh size $\Delta x = 8.3 \times 10^{-3}$. The total number of points for the original and EN models are 200 and 120, respectively. More importantly, much smaller time step size is required for solving the original system due to stability issues, whereas the EN model allows a relatively large time step size. Therefore, the EN model is more efficient in computation. To calculate the resting state by original system, it costs roughly 3.7 h, while it takes only 4 min by the EN model on a Thinkpad laptop (Processor: 2.6 GHz Intel Core i5-4210M; Memory: 8 GB)

Step 2. To evoke the action potential [32], we use both leak conductance and voltage-gated conductances, with initial values in Eq. (93) for $n,m,h$. To speed up the process, we modify $\bar{G}_{\mathrm{Na}}$ to allow more flux of $\mathrm{Na}^+$ into the intracellular region. In the simulation, we change $\bar{G}_{\mathrm{Na}}$ to $50\bar{G}_{\mathrm{Na}}$ for the period $0 < t < 0.1$. In the computation, we have adopted the same mesh as in step 1 and have used time-step size $\Delta t = \frac{5}{8} \times 10^{-6}$ for the original model and much larger time-step size for the EN model. Figure 5 shows the variation of membrane potential $V_m = \psi_R - \psi_L$ obtained using the original PNP system and the new EN model with different time step sizes, which reproduces the generation of an action potential. Table VII compares the computational time between the original system and EN model, and shows the maximum error for the entire duration of the action potential with different time steps (numerical results from original system is treated as exact value). This indicates that the EN model is more efficient with acceptable error. The saving in computational time is mainly due to the larger time step size and partially due to the smaller number of mesh points.

*Remark 10.* In this case, across the membrane, we have Robin-type boundary conditions for $\psi$ in Eq. (97) with an effective $\eta$ as in Sec. II D:

$$\eta = \frac{\epsilon_L^2 h_m}{\epsilon_m^2} \approx 0.2 \gg O(\epsilon). \tag{110}$$

As expected in Remark 6 (this three-ion case is similar to the two-ion case with $\pm 1$ valences), the variation of $\psi, p_i$ is roughly $O(\epsilon_L/\eta) \sim 10^{-2}$, which is consistent with numerical simulations like Fig. 4(b).

## V. CONCLUSIONS

In this work, we have investigated a 1D time-dependent PNP system with various boundary conditions, and have derived the corresponding EN system with effective boundary conditions. In the case of Dirichlet boundary conditions, the effective conditions can be considered as generalization of continuity of electrochemical potential. For flux conditions, we derived a physically correct effective conditions by bringing back an essential higher-order contribution. The effective conditions for the general multi-ion species case involves elliptic integrals, and these extra terms of elliptic integrals account for the accumulation of ions in the BL. We have validated our EN models with several examples and demonstrated the effectiveness of the EN system with the implementation of the well-known Hodgkin-Huxley model for generating action potential on a cell membrane.

As a next step, we will extend our approach to 2D, and illustrate the signal transmission in neuronal axon in a more realistic framework. For the 2D case under the LEN and NGEN assumptions in this paper, preliminary results show that the metric of the boundary will enter the effective boundary conditions whereas the curvature will not affect them. Besides accumulation of ions in the BL, the diffusion of ions along the domain boundary will be essential. We also plan to extend our approach to modified PNP system where size effect of the ions are included.

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## APPENDIX A: THE FUNCTIONS $F_i$, $f_i$ IN THEOREMS 1, 2

We show that the functions $F_i$, $f_i$ are well defined. We take $F_i$ for example, and recall that

$$F_i = \pm\frac{c_{i0}}{\sqrt{2}}\int_1^{e^{\phi_0-\psi_0}} \frac{u^{z_i}-1}{\sqrt{\sum_{k=1}^n c_{k0}(u^{z_k}-1)}}\frac{du}{u}. \tag{A1}$$

We analyze the integrand, and since all $z_k$ are integers, we can write the numerator as

$$u^{z_i}-1 = \frac{P(u)}{Q(u)}(u-1), \tag{A2}$$

where $u=1$ is a simple zero, and polynomials $P(u)$ and $Q(u)$ are well defined near $u=1$. We write the function inside square root as

$$H(u) = \sum_{k=1}^n c_{k0}(u^{z_k}-1), \tag{A3}$$

then, one easily finds (note $z_k \neq 0$)

$$H(1)=0,\ H'(u)=\sum_{k=1}^n c_{k0}z_k u^{z_k-1},\quad H'(1)=\sum_{k=1}^n c_{k0}z_k=0,$$
$$H''(1)=\sum_{k=1}^n c_{k0}z_k(z_k-1)=\sum_{k=1}^n c_{k0}z_k^2>0. \tag{A4}$$

Therefore, $u=1$ is a double zero of $H(u)$. Since all $z_k$ are integers, $H(u)$ is a rational function in $u$, and we can write

$$H(u) = \frac{P_1(u)}{Q_1(u)}(u-1)^2, \tag{A5}$$

where polynomials $P_1(u)$ and $Q_1(u)$ are well-defined and $P_1(u)/Q_1(u) > 0$ near $u=1$. Then the integrand together with $\pm$ is given by

$$\pm\frac{u^{z_i}-1}{u\sqrt{\sum_{k=1}^n c_{k0}(u^{z_k}-1)}} = \frac{\pm(u-1)}{\sqrt{(u-1)^2}}\frac{P(u)}{uQ(u)}\sqrt{\frac{Q_1(u)}{P_1(u)}} = \frac{P(u)}{uQ(u)}\sqrt{\frac{Q_1(u)}{P_1(u)}}, \tag{A6}$$

where $\pm$ are chosen for cases $u>1$ and $u<1$, and hence the first factor disappears. This implies that $F_i$ has the same form for both cases.

## APPENDIX B: THE DATA USED IN SEC. IV

The data are mainly from Refs. [25,32] and the book in Ref. [34]. The temperature in Ref. [25] is set to be 6.3°C, so we get $T = 279.45$ K. The other constants are

$$k_B = 1.38\times10^{-23}\,\mathrm{J/K},\quad N_A = 6.022\times10^{23}/\mathrm{mol},$$
$$e_0 = 1.602\times10^{-19}\,\mathrm{C},\quad \epsilon_0 = 8.854\times10^{-12}\,\mathrm{C/(V\cdot m)}. \tag{B1}$$

The typical bulk concentrations for $\mathrm{Na^+}$,$\mathrm{K^+}$,$\mathrm{Cl^-}$ are

| | $p_1$,$\mathrm{Na^+}$ | $p_2$,$\mathrm{K^+}$ | $p_3$,$\mathrm{Cl^-}$ |
|---|---|---|---|
| Extracellular | 100 mM | 4 mM | 104 mM |
| Intracellular | 12 mM | 125 mM | 137 mM |

which are used as initial conditions (scaled by $p_0$ below). Some typical values are (diffusivity of $\mathrm{Cl^-}$ is from Ref. [35])

$$\epsilon_r^L = \epsilon_r^R = 80,\quad \epsilon_r^m = 2,\quad h_m = 5\mathrm{nm},$$
$$p_0 = 100\,\mathrm{mM} = 100\,\mathrm{mol/m^3},\quad L = 1\mu\mathrm{m},$$
$$D_0 = 10^{-5}\,\mathrm{cm^2/s} = 10^{-9}\,\mathrm{m^2/s},$$
$$D_1 = 1.33D_0,\quad D_2 = 1.96D_0,\quad D_3 = 2.03D_0. \tag{B2}$$

The conductances are given by

$$\bar{G}_{\mathrm{Na}} = 120\,\mathrm{mS/cm^2} = 1200\,\mathrm{C/(V\times s\times m^2)},$$
$$\bar{G}_K = 360\,\mathrm{C/(V\times s\times m^2)},$$
$$\bar{G}_{\mathrm{Na,leak}} = 0.65\,\mathrm{C/(V\times s\times m^2)},$$
$$\bar{G}_{K,\mathrm{leak}} = 4.35\,\mathrm{C/(V\times s\times m^2)}. \tag{B3}$$

From the above data, we get

$$\frac{k_BT}{e_0} \approx 24\,\mathrm{mV},\quad \frac{L^2}{D_0} = 1\,\mathrm{ms},$$
$$G_0 = \frac{p_0D_0e^2N_A}{k_BTL} \approx 400\,758\,\mathrm{C/(V\times s\times m^2)}. \tag{B4}$$

For the dimensionless system we have

$$\begin{aligned}&\epsilon_L = \epsilon_R = 1.33\times 10^{-3},\quad \epsilon_m = 2.1\times 10^{-4},\quad h_m = 5\times 10^{-3},\quad D_1 = 1.33,\quad D_2 = 1.96,\quad D_3 = 2.03,\\ &\bar{G}_{\mathrm{Na}} = 3\times 10^{-3},\quad \bar{G}_{\mathrm{K}} = 9\times 10^{-4},\quad \bar{G}_{\mathrm{Na,leak}} = 1.6\times 10^{-6},\quad \bar{G}_{\mathrm{K,leak}} = 1\times 10^{-5}.\end{aligned} \tag{B5}$$

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