Modeling the voltage distribution in a non-locally but globally electroneutral confined electrolyte medium: applications for nanophysiology

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Abstract

The distribution of voltage in sub-micron cellular domains remains poorly understood. In neurons, the voltage results from the difference in ionic concentrations which are continuously maintained by pumps and exchangers. However, it not clear how electroneutrality could be maintained by an excess of fast moving positive ions that should be counter balanced by slow diffusing negatively charged proteins. Using the theory of electro-diffusion, we study here the voltage distribution in a generic domain, which consists of two concentric disks (resp. ball) in two (resp. three) dimensions, where a negative charge is fixed in the inner domain. When global but not local electro-neutrality is maintained, we solve the Poisson–Nernst–Planck equation both analytically and numerically in dimension 1 (flat) and 2 (cylindrical) and found that the voltage changes considerably on a spatial scale which is much larger than the Debye screening length, which assumes electro-neutrality. The present result suggests that long-range voltage drop changes are expected in neuronal microcompartments, probably relevant to explain the activation of far away voltage-gated channels located on the surface membrane.

Mathematics Subject Classification 35Q92 · 35J05 · 35J25 · 92-10 · 92C05

1 Introduction

How voltage and ionic concentrations are distributed and regulated in excitable cells such as neurons, astrocytes, etc. remains a challenging question, despite decades
of experimental and theoretical efforts (Hille 2001; Eisenberg and Johnson 1970; Bezanilla 2008; Koch and Segev 1989; Yuste 2010; Holcman and Yuste 2015; Sylantyev et al. 2013). In particular, the voltage in microdomains such as initial segments, dendrites, dendritic spines, remain difficult to study experimentally due to their small size. In neurons or astrocytes, the ionic concentrations are constantly regulated in order to maintain physiological gradients. For example, to maintain a high concentration of potassium ions inside a neuron (120 mM inside) compared to 4 mM outside, pumps and energy dependent exchangers are working continuously leading to local ion redistribution. The situation is the opposite for sodium. The distribution of exchangers is not necessarily uniform and they can form clusters (Liebmann et al. 2018): thus the incoming ions inside a neurons are not uniformly distributed, that could lead to local gradients of concentration (Hille 2001). This situation could also be worse at synapses where the exchanger Na,K-ATPase has a restricted mobility and reduced diffusion. In recent years, the voltage distribution and the ionic currents have been measured using nanopipettes (Novak et al. 2013; Jayant et al. 2019, 2017) and voltage dyes (Cartailler et al. 2018). Neuronal microdomains are characterized by an excess of positive ions (sodium and potassium), not compensated by chloride. However the missing negative charges should be carried by heavy proteins and molecules inside cytoplasm, characterized by smaller diffusion coefficients compared to the main ions. Yet, the overall cytoplasmic medium is expected to be electroneutral, although measurements should be performed (Cartailler et al. 2018; Holcman and Yuste 2015) in cellular domains such as dendritic spines, pre-synaptic terminal or glial protrusions.

The classical framework to study electric properties of cytoplasm which are electrolytes is the electro-diffusion theory (Hille 2001; Gillespie et al. 2002; Schuss et al. 2001) which consists of modeling the motion of diffusing ions in water, where the electrostatic force is due to the charge concentration differences between positive and negative species.

In the classical Debye theory (Hille 2001; Savtchenko et al. 2017), the voltage of a charge immersed is estimating in a neutral electrolyte. This theory predicts a screening of an excess charge, due to the exponential decay of the electric field. The theory is based on two main assumptions 1) the field induced by the excess charge is small compared to thermal fluctuations and 2) a strict electroneutrality condition imposed at infinity, where the concentration of positive and the negative charges are equal far away of the immersion of the test volume. The Debye characteristic length is

$$\lambda_D = \left( \frac{\varepsilon \varepsilon_0 k_B T}{z^2 e^2 N_A c_0} \right)^{\frac{1}{2}},$$

for the electron charge $e$, The temperature $T$, the Boltzmann constant $k_B$, the valence $z$, the vacuum permittivity $\varepsilon_0$ and $\varepsilon$ the relative permittivity of the ions, the avogadro number $N_A$ and the concentration of ions $c_0$.

In the extreme case of non-electroneutral medium, theoretical analysis and numerical simulations revealed a long-range log-decay of the electric field (Berg and Findlay 2011; Berg and Ladipo 2009; Cartailler et al. 2017a, b) and a modulation of the voltage distribution due to the presence of an oscillating membrane curvature (an example is the mitochondria inner membrane) (Cartailler et al. 2017c) or the presence of very high curvature at a cusp geometry (Cartailler et al. 2017b; Cartailler and Holcman 2019).
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In this manuscript, we compute the voltage and charge distribution when the condition of global but not local electro-neutrality is maintained. We consider a ball containing positive and negative charges, however a fraction of negative charges is fixed in the inner ball (Fig. 1). The external boundary does not allow charges to escape. The manuscript is organized as follows: in Sect. 1, we present general PNP model. We summarize our main results in Table 1. In Sect. 2, we treat the case of one dimension. We solve the PNP equation using elliptic integrals and obtain the decay of the voltage near the boundary. In Sect. 3, we study the solutions in dimensions two and three. We determine the voltage and charge distribution when we vary the static negative charges.

2 Model of global but not local electroneutrality

To model global but not local electro-neutrality, we use an elementary geometry of a domain $\Omega$ consisting in two concentric disks in dimension two and balls in dimension three. We impose a negative charge inside (Fig. 1).

2.1 The Poisson–Nernst–Planck equations in the domain $\Omega$

The coarse-grain Poisson–Nernst–Planck equations model electro-diffusion (Hille 2001; Singer and Norbury 2009; Schuss et al. 2001) in a electrolyte. In the domain $\Omega = D(0, R)$ (Fig. 1), which consist of a disk of radius $R$, the total charge is the sum of mobile positive $n^+$ and negative $n^-$ charges plus a fixed number negative charges $N^{static} = N$ located in an impenetrable (unaccessible) subregion $\Omega_0 = D(0, R_0) \subset \Omega$ (red circle in Fig. 1), representing a disk of radius $R_0$. 

![Fig. 1 Schematic representation of the geometry $\Omega = D(0, R)$ made of two concentric disks: the external one of radius $R$ and the small one $\Omega_0 = D(0, R_0)$ with radius $R_0$ containing the fixed charged $Q^- = -Nze$, modeling impenetrable proteins (red circle). Between the red boundary and the blue one, negative charges (total charge $q^- = -n^-ze$, that could represent chloride ions) is mixed in water with positive ions $q^+ = n^+ze$, representing potassium and sodium. The global electro-neutrality imposes $Q^- + q^- + q^+ = 0$ (equivalently $N + n^- = n^+$) (color figure online).](image-url)
rying immobile negatively charged proteins. We assume global electroneutrality:

\[ N + n^- = n^+. \]  

(1)

For a ionic valence \( z \), the total number of particles is

\[
\int_{\Omega - \Omega_0} \rho_p(\tilde{x}, t) d\tilde{x} = n^+, \quad \int_{\Omega - \Omega_0} \rho_n(\tilde{x}, t) d\tilde{x} = n^-
\]

(2)

and thus the total charge is

\[ q_{\pm} = \pm z e N, \quad Q^- + q^- + q^+ = 0 \]

where \( e \) is the electron charge. The particle density \( \rho_p(\tilde{x}, t) \) is the solution of the Nernst-Planck equation

\[
D \left[ \Delta \rho_p(\tilde{x}, t) + \frac{ze}{kT} \nabla \cdot (\rho_p(\tilde{x}, t) \nabla \Phi(\tilde{x}, t)) \right] = \frac{\partial \rho_p(\tilde{x}, t)}{\partial t} \quad \text{for } \tilde{x} \in \Omega - \Omega_0
\]

\[
D \left[ \Delta \rho_n(\tilde{x}, t) - \frac{ze}{kT} \nabla \cdot (\rho_n(\tilde{x}, t) \nabla \Phi(\tilde{x}, t)) \right] = \frac{\partial \rho_n(\tilde{x}, t)}{\partial t} \quad \text{for } \tilde{x} \in \Omega - \Omega_0
\]

\[
D \left[ \frac{\partial \rho(\tilde{x}, t)}{\partial n} + \frac{ze}{kT} \rho(\tilde{x}, t) \frac{\partial \Phi(\tilde{x}, t)}{\partial n} \right] = 0 \quad \text{for } \tilde{x} \in \partial \Omega - \partial \Omega_0
\]

(3)

\[
\rho(\tilde{x}, 0) = \rho_0(\tilde{x}) \quad \text{for } \tilde{x} \in \tilde{\Omega},
\]

(4)

where \( kT \) represents the thermal energy. The electric potential \( \Phi(\tilde{x}, t) \) in \( \tilde{\Omega} \) satisfies the Poisson equation

\[
\Delta \Phi(\tilde{x}, t) = - \frac{ze(\rho_p(\tilde{x}, t) - \rho_n(\tilde{x}, t))}{\varepsilon_r \varepsilon_0} \quad \text{for } \tilde{x} \in \tilde{\Omega}
\]

(5)

\[
\frac{\partial \Phi(\tilde{x}, t)}{\partial n} = - \tilde{\sigma}(\tilde{x}, t) \quad \text{for } \tilde{x} \in \partial \Omega - \partial \Omega_0,
\]

(6)

where \( \varepsilon_r \varepsilon_0 \) is the permittivity of the medium and \( \tilde{\sigma}(\tilde{x}, t) \) is the surface charge density on the boundary \( \partial \Omega \).

### 2.2 Steady-state solution

To study the effect of non-local electroneutrality, we study the solution of the steady-state Eq. 3 in the normalized domain \( \tilde{\Omega} \) (of radius 1). The Boltzmann distributions are given by

\[
\rho_p(\tilde{x}) = n^+ \frac{\exp \left\{ - \frac{ze \Phi(\tilde{x})}{kT} \right\}}{\int_{\tilde{\Omega} - \tilde{\Omega}_0} \exp \left\{ - \frac{ze \Phi(x)}{kT} \right\} dx}
\]

\[ \quad \text{(7)} \]
\[ \rho_n(\tilde{x}) = n - \frac{\exp \left\{ \frac{ze\Phi(\tilde{x})}{kT} \right\}}{\int_{\tilde{\Omega}_0} \exp \left\{ \frac{ze\Phi(x)}{kT} \right\} dx}, \quad (8) \]

hence (5) results in the nonlinear Poisson equation

\[
\Delta \Phi(\tilde{x}) = -\frac{zeN_p \exp \left\{ -\frac{ze\Phi(\tilde{x})}{kT} \right\}}{\varepsilon_r \varepsilon_0} \int_{\tilde{\Omega}_0} \exp \left\{ -\frac{ze\Phi(s)}{kT} \right\} ds + \frac{zeN_n \exp \left\{ \frac{ze\Phi(\tilde{x})}{kT} \right\}}{\varepsilon_r \varepsilon_0} \int_{\tilde{\Omega}_0} \exp \left\{ \frac{ze\Phi(s)}{kT} \right\} ds. \quad (9)
\]

In region \( \tilde{\Omega}_1 \), the Poisson equation is

\[ \Delta \Phi(\tilde{x}) = -\frac{zeN}{\varepsilon_r \varepsilon_0}, \quad (10) \]

and thus

\[ \int_{\Sigma_0} \frac{\partial \Phi(\tilde{x})}{\partial n} dS_x = -\frac{zeN}{\varepsilon_r \varepsilon_0}, \quad (11) \]

where \( \Sigma_0 \) is the boundary of \( \Omega_0 \). The global electro-neutrality (relation 1) leads to the compatibility condition imposed by Gauss flux integral

\[ \int_{\Sigma_0} \frac{\partial \Phi(\tilde{x})}{\partial n} dS_x - \int_{\Sigma} \frac{\partial \Phi(\tilde{x})}{\partial n} dS_x = n^+ - n^-. \quad (12) \]

Thus,

\[ \int_{\Sigma} \frac{\partial \Phi(\tilde{x})}{\partial n} dS_x = 0. \quad (13) \]

By symmetry, we impose that \( \frac{\partial \Phi}{\partial n} \) is constant on the two surfaces \( \Sigma \) and \( \Sigma_0 \) and thus we impose the conditions:

\[ \frac{\partial \Phi(\tilde{x})}{\partial n} = -\frac{zeN}{\varepsilon_r \varepsilon_0 |\Sigma_1|} \text{ for } \tilde{x} \in \Sigma_0. \quad (14) \]

\[ \frac{\partial \Phi(\tilde{x})}{\partial n} = 0 \text{ for } \tilde{x} \in \Sigma. \quad (15) \]
In spherical symmetry, the Poisson’s equation (9) reduces to

\[
\Phi''(r) + \frac{d - 1}{r} \Phi'(r) = \frac{ze}{\varepsilon\varepsilon_0 S_d} \left( n^- \exp \left( \frac{ze\Phi(r)}{k_B T} \right) \int_{R_0}^{R} \exp \left( \frac{ze\Phi(r)}{k_B T} \right) r^{d-1} dr - n^+ \exp \left( - \frac{ze\Phi(r)}{k_B T} \right) \int_{R_0}^{R} \exp \left( - \frac{ze\Phi(r)}{k_B T} \right) r^{d-1} dr \right).
\]

We normalize the radius by setting \( r = R x \) for \( a \leq x \leq 1 \) where \( a = \frac{R_0}{R} \). Here

\[
u = \frac{ze}{k_B T} \Phi, \quad \lambda_d = \frac{(ze)^2}{S_d R^{d-2} \varepsilon\varepsilon_0 k_B T}
\]

Here \( S_d \) is the surface area of the unit sphere in \( \mathbb{R}^d \) (that is \( 2\pi \) (dim 2) or \( 4\pi \) in dim 3). Eq. (16) becomes

\[
u''(x) + \frac{d - 1}{x} \nu'(x) = I_\lambda e^{\nu(x)} - J_\lambda e^{-\nu(x)},
\]

where we use the notations

\[
I_\lambda = \int_{a}^{1} \exp \left( \frac{ze\Phi(x)}{k_B T} \right) x^{d-1} dx, \quad J_\lambda = \int_{a}^{1} \exp \left( - \frac{ze\Phi(x)}{k_B T} \right) x^{d-1} dx
\]

We shall study the anionic \( I_\lambda \) and cationic \( J_\lambda \) strengths versus \( \lambda \) and the solution \( \nu \).

Our goal here is to determine \( \nu \) over the ball \( \tilde{\Omega} \). The condition \( \nu'(1) = 0 \) is satisfied due to the global electro-neutrality. We impose that the voltage is zero on \( \Sigma \), as it is defined to an additive constant. In summary the boundary conditions are

\[
u(1) = 0, \quad \nu'(1) = 0.
\]

Equation 18 and the boundary conditions in Eq. 20 together form a one dimensional boundary value problem with the following properties:

- the derivative \( \nu' \) is maximal at point \( a \) and decreases toward \( \nu'(1) = 0 \).
- \( \nu \) is minimal at \( x = a \) and increases toward \( \nu(1) = 0 \).
- \( \nu''(1) = I_\lambda - J_\lambda \leq 0 \) i.e. \( J_\lambda \geq I_\lambda \).

The strategy to find the solution is the following: since the parameters \( I_\lambda \) and \( J_\lambda \) depend on the solution \( \nu \), we will first search for an analytical solution for any value of the parameter \( \lambda \). We will then self-consistently compute the expression of \( I_\lambda \) and \( J_\lambda \). This steps imposes some restriction and we will show that solutions exist only for specific values of \((I_\lambda, J_\lambda)\).
Fig. 2  Normalized potential $u(r)$ in dimension 1 for $\tilde{\Omega} = [0, 1]$. a Schematic representation of the domain. b Allowed (red) and forbidden regions for the parameters $I_\lambda$ and $J_\lambda$. The squares, crosses and triangles respectively refer to the curves on panels c, d and e. c Solution $u(r)$ with constant cationic strength $J_\lambda$ and increasing anionic strength $I_\lambda$. By increasing $I_\lambda$, the amplitude of the solution decays. d No negative ions in the region $[0, a]$. The critical solution (dashed) develops a singularity in $r = a$. e Critical solutions with a singularity at $r = a$. The parameters $I_\lambda$ and $J_\lambda$ are on the boundary of the red domain satisfying relation $\sqrt{I_\lambda} + \sqrt{J_\lambda} = \sqrt{2}K(k)$ (color figure online)

3 Steady-state solution of PNP Eq. 18 in flat geometry (dimension 1)

In dimension 1, the normalized domain $\tilde{\Omega}$ is the interval $\tilde{\Omega} = [0, 1]$ (Fig. 2a). The fixed negative charges are located in $[0, a]$ while the mobile ions are in $a < x < 1$. The boundary value problem Eq. 18 reduces to

$$u''(x) = I_\lambda e^{u(x)} - J_\lambda e^{-u(x)} \quad \text{for } a < x < 1,$$
$$u(1) = 0, \quad u'(1) = 0.$$  \hspace{1cm} (21)

We show by direct integration in Appendices 7.1 and 7.2 that the general solution can be expressed in terms of the Jacobian elliptic functions (Abramowitz and Stegun 1972)

$$u(x) = -2 \ln \left( \frac{1}{2} \frac{\sqrt{T_a} + \sqrt{T_b}}{\sqrt{T_b}} \left( \text{dc} \left( \frac{\sqrt{T_a} + \sqrt{T_b}}{\sqrt{2}} (x - 1) \right) + \sqrt{1 - k^2} \text{nc} \left( \frac{\sqrt{T_a} + \sqrt{T_b}}{\sqrt{2}} (x - 1) \right) \right) \right),$$  \hspace{1cm} (22)
where $dc$ and $nc$ are the elliptic functions (Abramowitz and Stegun 1972) of modulus

$$k_\lambda = \frac{2\sqrt{I_\lambda J_\lambda}}{\sqrt{I_\lambda + J_\lambda}},$$

(23)

with $0 < k \leq 1$. The parameters $I_\lambda$ and $J_\lambda$ satisfy the inequality (Appendix 7.1)

$$\sqrt{I_\lambda} + \sqrt{J_\lambda} \leq \frac{\sqrt{2}K(k)}{1-a},$$

(24)

where $K(k)$ is the complete elliptic integral of the first kind (Appendix 7.1). The possible region (red in Fig. 2b) is obtained by combining conditions 23 and 24. We plotted the solutions for various positive and negative charges (Fig. 2c–e). In the boundary of validity (Eq. 24), the solution $u$ develops a log-singularity at $x = a$ (Fig. 2d, e, dashed lines). This situation is similar to the case of a single charge in the entire ball (Cartailler et al. 2017a, b). It is interesting to observe the long-range voltage changes in this non-local electro-neutral medium, even in the limit of a small (size of the impenetrable region containing negative charges). To obtain a closed form of the solution, we compute $I_\lambda$ and $J_\lambda$ (relation 19) with respect to the parameters $\lambda_{d-}$, $\lambda_{d+}$ and $a$. A direct integration of the function $e^{u(x)}$ and $e^{-u(x)}$ over the interval $[a, 1]$ (In appendix 7.3) gives with

$$u_a = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}}(a - 1)$$

(25)

that

$$\lambda_{d-} = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{2\sqrt{2}} \left( f_{k_\lambda}(u_a) + \frac{\sqrt{J_\lambda} - \sqrt{I_\lambda}}{\sqrt{I_\lambda} + \sqrt{J_\lambda}} g(u_a) \right),$$

(26)

$$\lambda_{d+} = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{2\sqrt{2}} \left( f_{k_\lambda}(u_a) - \frac{\sqrt{J_\lambda} - \sqrt{I_\lambda}}{\sqrt{I_\lambda} + \sqrt{J_\lambda}} g(u_a) \right),$$

(27)

where we defined the two functions (Fig. 3)

$$f_k(x) = 2E(x) - (2 - k^2)x - 2\text{s}_n(x)\text{dc}(x),$$

(28)

$$g(x) = 2\text{s}_c(x), \text{ for } x \in ]K(k); K(k)].$$

(29)

Note that we can write (from relation 23)

$$1 - k_\lambda^2 = \left( \frac{\sqrt{J_\lambda} - \sqrt{I_\lambda}}{\sqrt{I_\lambda} + \sqrt{J_\lambda}} \right)^2.$$  

(30)

The parameter $k_\lambda$ represents the balance between the negative charges. Indeed,

- $k_\lambda \to 1$, $I_\lambda \approx J_\lambda$ and Eq. 31 implies $N \to 0$.
- $k_\lambda \to 0$, $J_\lambda \gg I_\lambda$. Using $I_\lambda$ in Eq. 19, we get $n^- \to 0$. 

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Finally, the global electro-neutrality condition leads to the relation

$$\lambda_d N = -\frac{\sqrt{J_\lambda} - \sqrt{I_\lambda}}{\sqrt{2}} g(u_a).$$

(31)

To conclude, for each positive and negative density \((n^+, n^-)\) satisfying electroneutrality 1, the system of Eqs. 26–27–30–31 can be resolved and there is a unique couple \((J_\lambda, I_\lambda)\) for which condition 24 is satisfied, and thus the solution \(u(x)\) is defined on the entire interval \([a, 1]\).

### 3.1 Explicit expressions for the difference of potential \(u(1) - u(a)\)

We study here the potential difference between the surfaces of the two balls.

$$u(1) - u(a) = 2 \ln \left( \frac{1}{2} \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{\sqrt{J_\lambda}} \left( dc(u_a) + \sqrt{1 - k_\lambda^2 nc(u_a)} \right) \right),$$

(32)

where

$$u_a = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}} (a - 1).$$

(33)

The potential difference \(u(1) - u(a)\) has a minimum when \(I_\lambda = J_\lambda\) and grows with the difference between \(I_\lambda\) and \(J_\lambda\). The limit value for this difference depends on the value of the sum \(\sqrt{I_\lambda} + \sqrt{J_\lambda}\) as shown by Eq. 24. We shall now study some limit cases for the potential difference \(u(1) - u(a)\).
3.1.1 When negative charges are only concentrated in the inner region \( n^- \rightarrow 0 \) 
\((n^+ = N)\)

In the case \( n^- = 0 \), we have \( I_{\lambda} = 0 \) (Eq. 19) and \( k_{\lambda} = 0 \). From Eq. 27, we obtain

\[
\lambda_{d} n^+ = \frac{\sqrt{J_{\lambda}}}{2\sqrt{2}} (f(u_a) - g(u_a)).
\]

(34)

When \( k = 0 \), the Jacobian elliptic functions simplifies to trigonometric functions

\[
f(u_a) = -2 \tan(u_a), \quad g(u_a) = 2 \tan(u_a),
\]

(35)

with \( u_a = \sqrt{\frac{J_{\lambda}}{2}}(a - 1) \), Eq. 34 becomes

\[
\lambda_{d} n^+ = \sqrt{2J_{\lambda}} \tan \left( \frac{\sqrt{2J_{\lambda}}}{2} (1 - a) \right).
\]

(36)

We recover the asymptotic result (Cartailler et al. 2017a) for positive ions in a ball. The solutions for \( n^+ \geq 0 \) leads to \( 0 \leq J_{\lambda} \leq \frac{\pi^2}{2(1-a)^2} \). The potential difference is

\[
u(1) - u(a) = -2 \ln \left( 2 \cos \left( \frac{J_{\lambda}}{2} (1 - a) \right) \right),
\]

(37)

where \( J_{\lambda} \) is the solution of Eq. 36 for a given \( n^+ \).

3.1.2 No charges in the inner region \( N = 0 \) and electroneutrality in the ring \( n^+ = n^- \)

In the case \( N = 0 \), Eq. 31 implies \( I_{\lambda} = J_{\lambda} \) and thus \( k_{\lambda} = 1 \). Equation 27 becomes

\[
\lambda_{d} n^+ = \frac{\sqrt{J_{\lambda}}}{2} f(u_a).
\]

(38)

When \( k_{\lambda} = 1 \), Jacobian elliptic functions simplify to hyperbolic functions, which gives \( E(u) = \tanh(u) \), \( \sn(u) = \tanh(u) \), \( \cn(u) = \dn(u) = \frac{1}{\cosh(u)} \), and \( f(u_a) = 2 \tanh(u_a) - u_a - 2 \tanh(u_a) = -u_a \). Equation 38 becomes

\[
J_{\lambda} = \frac{\lambda_{d} n^+}{1 - a},
\]

(39)

the Jacobian function \( \dc = 1 \), and thus \( u(r) = 0 \) for \( r \in [a, 1] \). The behavior of \( u \) for small \( N \) is shown in Fig. 4 with \( J_{\lambda} = 1.01 I_{\lambda} \). Expanding the Jacobian elliptic functions for \( k \) near 1, we obtain

\[
dc(u) = 1 + \frac{1}{2} (1 - k^2) \sinh^2(u) + o(1 - k^2),
\]

(40)
nc(u) = \cosh(u) + o(1 - k^2), \quad (41)

and thus

\[ u(1) - u(a) = 2 \ln \left( \frac{1}{2} \sqrt{I_\lambda} + \sqrt{J_\lambda} \left( 1 + \frac{1}{2} (1 - k^2) \sinh^2(u_a) \right) \right) \]

Since \( k \to 1 \), we finally obtain

\[ u(1) - u(a) \sim \frac{\sqrt{J_\lambda} - \sqrt{I_\lambda}}{\sqrt{J_\lambda}} \left( \frac{1}{2} \sqrt{I_\lambda} - \sqrt{J_\lambda} \sinh^2(u_a) + \cosh(u_a) - 1 \right). \quad (42) \]

### 3.1.3 For a small amount of positive and negative charges \( n^+, n^- \ll 1 \)

When the amount of positive and negative charges \( n^+, n^- \) is small, then we have that

\[ u_a = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}} (a - 1) \ll 1 \] (see equations Eq. 46). We can obtain from Appendix 7.2 (expression of \( f \) and \( g \) in Eq. 28) the expressions

\[ f(u_a) \sim (k^2 - 2) u_a = \frac{2}{\sqrt{2}} \frac{I_\lambda + J_\lambda}{\sqrt{I_\lambda} + \sqrt{J_\lambda}} (1 - a), \quad (43) \]
\[ g(u_a) \sim 2u_a = -\frac{2}{\sqrt{2}} \left( \sqrt{I_\lambda} + \sqrt{J_\lambda} \right) (1 - a), \quad (44) \]

so Eq. 27 gives
\[
\frac{\lambda_d n^-}{1 - a} = \frac{1}{2} (I_\lambda + J_\lambda - (J_\lambda - I_\lambda)), \quad \text{and}
\frac{\lambda_d n^+}{1 - a} = \frac{1}{2} (I_\lambda + J_\lambda + J_\lambda - I_\lambda).
\] (45)

For \( u_a \ll 1 \),
\[
\frac{\lambda_d n^-}{1 - a} = I_\lambda \quad \text{and} \quad \frac{\lambda_d n^+}{1 - a} = J_\lambda.
\] (46)

To compute potential difference, we expand the Jacobian elliptic functions \( dc \) and \( nc \) for \( u \ll 1 \):
\[
dc(u) = 1 + (1 - k^2) \frac{u^2}{2} + o(u^2), \quad nc(u) = 1 + \frac{u^2}{2} + o(u^2),
\] (47)

which gives
\[
dc(u_a) + \sqrt{1 - k^2} nc(u_a) = 1 + \sqrt{1 - k^2} + \frac{1}{2} \left(1 - k^2 + \sqrt{1 - k^2}\right) u^2 + o(u^2)
\approx \frac{2\sqrt{J_\lambda}}{\sqrt{I_\lambda} + \sqrt{J_\lambda}} + \frac{1}{2} \sqrt{J_\lambda} \left(\sqrt{J_\lambda} - \sqrt{I_\lambda}\right) (1 - a)^2
\] (48)

and thus
\[
u(1) - u(a) \sim 2 \ln \left(1 + \frac{1}{4} (J_\lambda - I_\lambda) (1 - a)^2\right) \sim \frac{1}{2} \lambda_d N (1 - a).
\] (49)

3.1.4 When the static charge is very large \( N \to \infty \)

A very large static charge \( N \gg 1 \) leads to \( u_a \to -K(k) \), we can expand \( u_a + K(k) \) using the functions \( f \) and \( g \) with relation Eq. 28 leading to
\[
f(u_a) = -2 E(K(k)) + \left(2 - k^2\right) K(k) + \frac{2}{u_a + K(k)}, \quad (50)
g(u_a) = -\frac{2}{\sqrt{1 - k^2} (u_a + K(k))}.
\] (51)

From Eq. 27, we get
\[
\frac{\lambda_d n^-}{1 - a} = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{2\sqrt{2}} \left(-2 E(K(k)) + \left(2 - k^2\right) K(k)\right),
\] (52)
\[
\frac{\lambda_d n^+}{1 - a} = \frac{\sqrt{I_\lambda} + \sqrt{J_\lambda}}{2\sqrt{2}} \left(-2 E(K(k)) + \left(2 - k^2\right) K(k) + \frac{4}{u_a + K(k)}\right).
\] (53)
thus \( n^+ \rightarrow \infty \). Using

\[
\lambda_d (n^+ - n^-) = \lambda_d N = \frac{\sqrt{J_\lambda} + \sqrt{J_\lambda}}{2\sqrt{2}} \frac{4}{u_a + K(k)},
\]

we obtain that \( N \rightarrow \infty \). Note that for \( k = 0 \), \( E(K(0)) = K(0) = \frac{\pi}{2} \) so \( n^- = 0 \). However, when \( k \rightarrow 1 \), \( K(k) \rightarrow \infty \), then \( n^- \rightarrow \infty \). The singularity is located at \( r = a - \varepsilon \) with \( \varepsilon \ll 1 \). Since \( u_a = \frac{\sqrt{J_\lambda + \sqrt{J_\lambda}}}{\sqrt{2}} (a - 1) \), we have

\[
u_a - \varepsilon = \frac{\sqrt{J_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}} (a - \varepsilon - 1) = -K(k)
\]

and

\[
u_a = -K(k) + \frac{\sqrt{J_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}} \varepsilon.
\]

Expanding the Jacobian elliptic functions nc and dc near \(-K(k):\)

\[
dc(u) \sim \frac{1}{u + K(k)}, \quad nc(u) \sim \frac{1}{\sqrt{1 - k^2 (u + K(k))}},
\]

using Eqs. 32 and 56, we obtain

\[
u(1) - \nu(a) = 2 \ln \left( \frac{\sqrt{2}}{\sqrt{J_\lambda, \varepsilon}} \right).
\]

From the expression of \( u_a + K(k) \) in Eq. 56 and the formula for \( \lambda_d N \) in Eq. 54, we get \( \lambda_d N = \frac{2}{\varepsilon} \) and finally

\[
u(1) - \nu(a) = 2 \ln \left( \frac{\lambda_d N}{\sqrt{2J_\lambda}} \right).
\]

When \( n^- = 0 \), similar to Sect. 3.1.1, we get

\[
\lambda_d n^+ = \sqrt{2J_\lambda} \tan \left( \frac{\sqrt{2J_\lambda}}{2} (1 - a) \right)
\]

and since \( n^+ \rightarrow \infty, \sqrt{2J_\lambda} \rightarrow \frac{\pi}{1-a} \), we finally get

\[
u(1) - \nu(a) \sim 2 \ln \left( \frac{(1-a)\lambda_d N}{\pi} \right).
\]
If \( n^- \to \infty \), from Eq. 52 \( K(k) \to \infty \), which means that \( k \to 1 \) and thus \( Jsus - Isus \to 0 \). We can make the approximation

\[
\sqrt{Isus} + \sqrt{Jsus} \approx 2\sqrt{Jsus}
\]  

(62)

and write

\[
\lambda_d n^- = \frac{\sqrt{Isus} + \sqrt{Jsus}}{2\sqrt{2}} \left( -2E(K(k)) + \left( 2 - k^2 \right) K(k) \right)
\]

\[
\sim \frac{\sqrt{Isus} + \sqrt{Jsus}}{2\sqrt{2}} K(k) \sim Jsus(1 - a)
\]

Then using the expression of the potential difference in Eq. 59, we obtain

\[
u(1) - u(a) \sim 2 \ln \left( \sqrt{\lambda_d (1 - a)} \frac{N}{\sqrt{n^-}} \right).
\]  

(63)

In particular, when \( n^- = N \), we get

\[
u(1) - u(a) \sim \ln \left( \lambda_d N (1 - a) \right).
\]  

(64)

We have also plotted the function normalized potential \( u(r) \) in Fig. 4-Right.

### 3.2 Summary of the potential difference \( \Phi(R) - \Phi(R_0) \) at the boundary of the bulk domain where charges can move

We summarize in the Table 1 below the differences of potential \( u(1) - u(a) \) for the explicit solution in dimension 1, depending on the different condition on the mobile positive \( n^+ \) and negative \( n^- \) charges satisfying the global electro-neutrality conditions \( N + n^- = n^+ \).

Finally, in Fig. 5 we show the distribution of positive (red) and negative (blue) charge density computed in dimension 1 inside \([a, 1]\), associated to \( u(a) - u(1) = 7.207 \) and \( \lambda_d N = 0.0887 \). Note that the difference of charge persists deep inside the domain.

### 4 Steady-solution in two dimensions

In this section, we resolve the PNP equation 18 in two dimensions (Fig. 6a), which reduces to

\[
u''(r) + \frac{1}{r} u'(r) = I_s e^{u(r)} - J_s e^{-u(r)},
\]  

(65)

with the boundary conditions

\[
u(1) = u'(1) = 0.
\]  

(66)
Table 1  Electrodiffusion relations for the potential difference $\Phi(R) - \Phi(R_0)$ between two ball surfaces (bulk), where immobile negative charges are contained in the inner ball of radius $R_0$ contained in the entire ball of radius $R$

| Conditions | Difference of potential $\Phi(R) - \Phi(R_0)$ |
|------------|-----------------------------------------------|
| $n^- \rightarrow 0 (n^+ = N)$ | $-2\frac{k_B T}{ze} \ln \left( 2 \cos \left( \sqrt{\frac{J_\lambda}{2}} (1 - a) \right) \right)$ |
| $N = 0 (n^+ \sim n^-)$ | $\frac{k_B T}{ze} \sqrt{J_\lambda} = \sqrt{J_\lambda} \left( \frac{1}{2} \sqrt{J_\lambda} + \sqrt{\frac{J_\lambda}{2}} \sin^2(u_a) + \cosh(u_a) - 1 \right)$ |
| $I_\lambda = I_{\lambda_{-1-a}}$ | $\lambda_{-a} n^+ = 2 \frac{k_B T}{ze} \ln \left( 1 + \frac{1}{4} (J_\lambda - I_\lambda) (1 - a)^2 \right) \sim \frac{1}{2} \lambda_d N (1 - a)$ |
| $J_\lambda = \lambda_{-1-a} n^+$ | $\frac{2 k_B T}{ze} \ln \left( \frac{\sqrt{\lambda_d (1 - a)} N}{\sqrt{n}} \right)$ |

Here $a = \frac{R_0}{R}$

Fig. 5  Distribution of positive and negative charges for $I_\lambda = 15$ and $J_\lambda = 16$ and $a = 0.25$ associated to $n^+ \lambda_d = 9.308$ and $n^- \lambda_d = 15.58$

We first solve this equation when there are no moving negative ions (Fig. 6b, c) and then use a regular perturbation to find the general solution.

4.1 No negative ions : $I_\lambda = 0$

In the new variables

$$r = e^{-t} \tilde{u}(t) = u(r) + 2t.$$  \hspace{1cm} (67)
Equation 65 is transformed into

\[ \ddot{\tilde{u}}(t) = -J_\lambda e^{-\tilde{u}(t)}, \]  

with boundary conditions \( \tilde{u}(0) = 0, \quad \dot{\tilde{u}}(0) = 2. \) A first integration gives

\[ \frac{1}{2} \dot{\tilde{u}}^2 = J_\lambda e^{-\tilde{u}(t)} + 2 - J_\lambda. \]  

There are three cases: \( J_\lambda < 2, \quad J_\lambda = 2 \) and \( J_\lambda > 2 \) we show in appendix 7.4 the following explicit solutions

\[
J_\lambda < 2 : \quad u_0(r) = 2 \ln \left( \frac{1}{2} \left( 1 + \frac{1}{p} \right) r^{1-p} - \frac{1}{2} \left( \frac{1}{p} - 1 \right) r^{1+p} \right), \quad p = \sqrt{1 - \frac{J_\lambda}{2}}.
\]

\[
J_\lambda = 2 : \quad u_0(r) = 2 \ln(r(1 - \ln(r))),
\]

\[
J_\lambda > 2 : \quad u_0(r) = 2 \ln \left( r \left( \frac{1}{p} \sin(-p \ln(r)) + \cos(-p \ln(r)) \right) \right), \quad p = \sqrt{\frac{J_\lambda}{2} - 1}.
\]

4.1.1 Regular perturbation solution for \( I_N / NAK = \varepsilon \ll 1 \)

We expand the solution \( u_\varepsilon = u_0 + \varepsilon u_1 + o(\varepsilon) \), where \( u_\varepsilon \) is the solution of

\[
\ddot{u}_\varepsilon(r) + \frac{1}{r} \dot{u}_\varepsilon(r) = \varepsilon e^{u_\varepsilon(r)} - J_\lambda e^{-u_\varepsilon(r)}
\]

\[
u_\varepsilon(1) = u_\varepsilon'(1) = 0,
\]

where \( u_0 \) is given in 70 and \( u_1 \) satisfies (see appendix 7.5):

\[
\ddot{u}_1(r) + \frac{1}{r} \dot{u}_1(r) = e^{u_0(r)} + J_\lambda e^{-u_0(r)} u_1(r),
\]

with the initial conditions \( u_1(1) = u_1'(1) = 0. \) We now discuss the solution in the three cases \( J_\lambda < 2, J_\lambda = 2 \) and \( J_\lambda > 2. \) For \( J_\lambda = 2, \) the solution of Eq. 72 is

\[ u_1(r) = \left( A + \lambda(r) \right) \left( 1 - \ln(r) \right)^2 + \frac{B + \mu(r)}{1 - \ln(r)}, \]

where \( A = \frac{5}{48}, \quad B = -\frac{103}{384} \lambda(r) = \frac{r^4}{12} \left( -\frac{5}{8} + \ln(r) \right), \quad \) and \( \mu(r) = \frac{r^4}{384} \left( 32 \ln(r)^4 - 160 \ln(r)^3 + 312 \ln(r)^2 - 284 \ln(r) + 103 \right). \) In the cases \( J_\lambda < 2 \) and \( J_\lambda > 2, \) we use numerical simulations to estimate the perturbation \( u_1 \) and plotted in Fig. 6 the normalized voltage obtained numerically and using expansion 71. We found a very good agreement between the numerical and the approximation solutions for \( J_\lambda \leq 2 \) in the entire domain (Fig. 6d, e). However, for \( J_\lambda \leq 2, \) the approximation diverged from the numerical solution near the boundary of the inner domain \( (r = 0.25), \) Fig. 6f). Finally, we show in Fig. 7a the distribution of positive and negative charges. We further
compare the Debye length for 150 mM leading to $\lambda_D = 30 \text{nm}$ (see next paragraph) with various voltage decay computed for various values of positive and negative charge contributions (Fig. 7b): in all cases, the voltage decay (computed from Eq. 18) is slower than the Debye solution.

5 Numerical evaluation of the voltage distribution in three dimensions

In this paragraph, we briefly mention the numerical results in three dimensions. The domain consists of two concentric balls of radius $R$ (outer) and $R_0$ (inner). Static negative charges are located $B(R_0)$, while moving charges are in the annulus $B(R) - B(R_0)$. We use for the modeling electro-diffusion the PNP equations at steady-state, formulated by Eq. 18. In spherical symmetry the equation reduces to Eq. 16, which can be re-written in normalized coordinates $r = Rx$ for $a \leq x \leq 1$ where $a = \frac{R_0}{R} = 0.25$ and $u = \frac{ze}{k_B T} \Phi$:

$$u''(x) + \frac{2}{x} u'(x) = I_\lambda e^{u(x)} - J_\lambda e^{-u(x)}. \quad (74)$$
In the absence of an analytical expression, to determine the distribution of ion density in the bulk, we solved numerically Eq. 74 with boundary conditions 20. The results show a slightly difference with the equivalent simulations in dimension 2 (Fig. 7).

We also plotted the normalized difference of potential \(u_{1}(1) - u(0.25)\) with respect to the static positive charges \(I_\lambda\) for various values of the normalized negative charges \(J_\lambda = 0.2; 3; 4; 5\). Note that the normalization factor to the potential is \(k_B T / e = 25.8 \text{ mV}\). The results show both linear and nonlinear regimes (Fig. 8).

Finally, we compare the decay of the voltage computed from PNP (Eq. 74) with the classical Debye length near the inner boundary, where the static charge is \(N\). The Debye length is computed here in the approximation of an infinite domain, which is valid here because the boundary layer is very small compared to the rest of the bulk \(B(R) - B(R_0)\). Using that the solution of PNP (Eq. 74) satisfies the Neumann’s boundary condition 14:

\[
\frac{\partial \Phi(x)}{\partial n} = -\frac{eN}{\varepsilon\varepsilon_0} \Sigma_1 \text{ for } \Sigma_1 \in \Sigma_0,
\]

we obtain the expression for

\[\text{Debye}\]

---

Fig. 7  
(a) Distribution of positive and negative charges for \(I_\lambda = 2.5\) and \(J_\lambda = 3\) and \(a = 0.25\) in dimension 2 and 3. Positive (resp. negative) charges in dimension 3 (red, resp. blue) and dimension 2 (orange resp. cyan).

(b) Comparison of Debye length for 150 mM leading to \(\lambda_D = 30\text{ nm}\) versus voltage decay computed for various \((i,j) = (18, .35), (4, 7), (3, 3), (15, 16)\) [black, yellow, red, blue] showing that in all case, the voltage decay is slower than the Debye solution (color figure online).

Fig. 8  
Normalized potential difference versus the charge \(I_\lambda\) for various negative charge \(J_\lambda = 0.2\) orange; 4 cyan; 3 grey, 5 cyan (color figure online).
### Table 2 Parameters

| Parameter | Description | Value |
|-----------|-------------|-------|
| \( z \)  | Valence of ion | \( z = 1 \) (for sodium) |
| \( \Omega \) | Spine head | \( \Omega \) (volume \(|\Omega| = 1 \mu m^3\)) |
| \( a \)  | size of the negative charge region | (typical) \( a = 0.25 \mu m \) |
| \( R \)  | radius of spine head | (typical) \( R = 1 \mu m \) |
| \( T \)  | Temperature | \( T = 300 K \) |
| \( E \)  | Energy | \( kT = 2.58 \times 10^{-2} eV \) |
| \( e \)  | Electron charge | \( e = 1.6 \times 10^{-19} C \) |
| \( \varepsilon \) | Dielectric constant | \( \varepsilon = 80 \) |
| \( \varepsilon_0 \) | Dielectric constant | \( \varepsilon = 8.85 \times 10^{-12} F/m \) |

the voltage

\[
\Phi(r) = \frac{zeN}{\varepsilon_r\varepsilon_0\lambda_D \mid \Sigma_1 \mid} \exp(-\lambda_D(r - a)).
\]  

(75)

In addition, the Debye length can be computed when the total number of positive and negative charge is \( n^+ + n^- \), from the relation

\[
\lambda_D^2 = \left( \frac{\varepsilon\varepsilon_0 k_B T}{z^2 e^2 N A c_0} \right). \tag{76}
\]

For \( c_0 = 150 \text{ mM} \), we obtain (Table 2) \( \lambda_D = 30 \text{ nm} \) and the voltage decay (computed from Eq. 18) is always slower than the Debye solution. This result confirms a longer penetration of the voltage inside the bulk.

### 6 Discussion and concluding remarks

We have studied in this article the distribution of the voltage field in a global but non-local electroneutral electrolyte. We found that the voltage does not decay quickly, but quite slowly inside the bulk region due to the local charge imbalance. We could completely resolve the electrodiffusion equations in dimension one (flat geometry) and partially in dimension 2 (cylindrical) using a regular perturbation around the solution with positive ions only and a negative charge in a disk. The solution in dimension three could only be estimated numerically. In all three dimensions, the potential difference between the inner and outer surfaces of the electrolyte should depend on the log of the charges, as we have shown in dimensions 1 and 2 (see Table 1). It will be interesting to extend the present analysis to the case of non-concentric disk and in particular to examine the situation where the inner and outer boundaries could be very close. We also expect that curved membrane will create voltage drops, as shown in Cartailler et al. (2017c) the case of global non-electroneutrality.
In many biological nanodomains, such as inside dendritic spines, the concentration of mobile chloride ions is not counterbalanced by the mobile positive ions (potassium, sodium and free calcium ions essentially). For a total of 150 mM positive, the mobile ions are divided into $\sim 18$ mM Na$^+$, $\sim 135$ mM K$^+$ and $\sim 0.0001$ mM Ca$^{2+}$ and $\sim 7$ mM Cl$^-$ ions and it is expected that most negative charges are located in membranes and consist of almost immobile macromolecules. These differences in ion mobility might result in important junction potentials (that is, local depletions in specific ion species), especially during transient synaptic activation, following an important influx of positive charges through AMPA-type glutamate receptors. In the present model, if we consider $n_+ = 150$ mM $n_- = 7$ mM and $N = 143$ in a ball of radius $R = 1$ $\mu$m and an inner domain of $R_0 = 100$ nm, then using the dimension 1 approximation for $N \approx 10^8$, $n_+ \approx 9 \times 10^7 \gg 1$ and $n_- \approx 44 \times 10^5$, we have from Eq. 63 that

$$u(1) - u(a) \sim 2 \ln \left( \frac{\lambda_d (1 - a)}{\sqrt{n_-}} \right) = 0.167$$

where $\lambda_d = 6.97 \times 10^{-10}$, $a = 0.25$ and the parameters are given in Table 2. Thus the voltage difference is $\Delta V = 4.33$ mV in a region of length 750 nm. This high voltage difference could affect locally voltage sensitive channels, a prediction that should be experimentally checked using nanopipette measurements.

Finally, this study pushes to test the spatial limit of the electro-neutrality hypothesis in neuronal cell. When a large amount of negatively charged proteins are distributed in a confined microdomain, it would be interesting to investigate the consequences on the regulation of positive ionic distribution entering through channels. In particular, we expect from the present study that injecting a current in a cell when electroneutrality is not satisfied at a scale of 10–100 nm, will lead to long penetrating voltage drop inside the bulk.

After sodium positive ions enter a dendritic spine, other positive potassium ions could be expelled quickly, a process that would not happen if positive and negative charges would enter at the same time. A transient entry of positive ions in a non-electroneutrality medium could thus generate an electric field much further away compared to an electroneutrality medium, possibly responsible for the fast propagation of opening and closing of channels along dendrites and axons, a mechanism that could also challenge the classical Hodgkin–Huxley paradigm.

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7 Appendices

7.1 Direct integration

We solve Eq. 21 by a direct integration after multiplying by $u'(x)$ equation

$$u''(x) = I_\lambda e^{u(x)} - J_\lambda e^{-u(x)} \quad \text{for } a < x < 1,$$

(78)

we get

$$\frac{1}{2}u'^2(x) = I_\lambda e^{u(x)} + J_\lambda e^{-u(x)},$$

(79)

where we used the boundary conditions

$$u(1) = 0, \quad u'(1) = 0.$$

(80)

We now set $u(x) = v(x) + D$ with $D = \frac{1}{2} \ln \left( \frac{J_\lambda}{I_\lambda} \right) \geq 0$ and get

$$v'^2(x) = A(\cosh(v(x)) + c),$$

(81)

where

$$A = 4\sqrt{I_\lambda J_\lambda}, \quad c = -\frac{I_\lambda + J_\lambda}{2\sqrt{I_\lambda J_\lambda}}.$$  

(82)

In order to integrate Eq. 81, we compute the integral

$$I(v) = \int^v \frac{du}{\sqrt{\cosh(u) + c}} = \int^v \frac{du}{\sqrt{2 \cosh^2 \left( \frac{u}{2} \right) - 1 + c}}.$$  

(83)

Changing the variable $x = \frac{1}{\cosh \left( \frac{u}{2} \right)}$, we transform integral 83 into

$$I(v) = -2 \int \frac{dx}{\sqrt{1 - x^2} \left( 2 - (1 - c)x^2 \right)}.$$  

(84)

We define

$$k = \frac{2}{1 - c} = \frac{2\sqrt{I_\lambda J_\lambda}}{I_\lambda + \sqrt{J_\lambda}}, \quad 0 < k \leq 1$$

(85)
and set $x = kt$ to obtain the incomplete elliptic integral of the first kind of amplitude $1/k\cosh\left(\frac{\alpha}{2}\right)$ and modulus $k$ (Eq. 85 leads to $0 < k \leq 1$):

$$I(v) = -\sqrt{2}k \int \frac{1}{k \cosh\left(\frac{v}{2}\right)} \frac{dt}{\sqrt{(1-k^2t^2)(1-t^2)}} = K\left(\frac{1}{k \cosh\left(\frac{v}{2}\right)}, k\right). \quad (86)$$

Thus from Eq. 81, we get

$$K\left(\frac{1}{k \cosh\left(\frac{u(1)}{2}\right)}, k\right) = \alpha - \sqrt{A/x}, \quad (87)$$

where $\alpha$ is a constant. Since $u(1) = 0$, $v(1) = -D$ thus $\cosh\left(\frac{v(1)}{2}\right) = \frac{1}{k}$ and $\alpha = K(1, k) + \sqrt{A_1/k}$. Using the Jacobian elliptic functions of modulus $k$, we obtain the explicit expression for $v$ with respect to $x$ using the identity $K(., k) = sn^{-1}(.)$. Finally,

$$\frac{1}{k \cosh\left(\frac{v(x)}{2}\right)} = sn\left(K(1, k) + \sqrt{A 1 - x/k}\right) = cd\left(\sqrt{A x - 1} / k\right), \quad (88)$$

and $v(x) \leq 0$ for $a \leq x \leq 1$,

$$v(x) = -2 \text{arcosh} \left[\frac{1}{k} \text{dc} \left(\sqrt{A x - 1} / k\right)\right]. \quad (89)$$

In the following part, we will write $K(k) = K(1, k)$ the complete elliptic integral of the first kind. The normalize potential is

$$u(x) = -2 \ln \left(\frac{1}{2} \frac{(J_\alpha^+ + J_\alpha^-) \left(\text{dc} \left(\frac{(J_\alpha^+ + J_\alpha^-)(x-1)}{\sqrt{2}}\right) + \sqrt{1-k^2} \text{nc} \left(\frac{(J_\alpha^+ + J_\alpha^-)(x-1)}{\sqrt{2}}\right)\right)}{(J_\alpha^+ + J_\alpha^-)}\right). \quad (90)$$

### 7.2 Classical relations between elliptic functions

The incomplete elliptic integral of the first kind of modulus $k$ and argument $x$ is defined by

$$K(x, k) = \int_0^\Phi \frac{d\theta}{\sqrt{(1-k^2 \sin^2(\theta))(1-t^2)(1-k^2 t^2)}} = \int_0^x \frac{dt}{\sqrt{(1-t^2)(1-k^2 t^2)}}. \quad (91)$$
where $x = \sin \Phi$. For $x = 1$, we obtain the complete elliptic integral of modulus $k$:

$$K(k) = \int_0^1 \frac{dt}{(1-t^2)(1-k^2t^2)} \quad (92)$$

The elliptic sine $\text{sn}$ of modulus $k$ and the elliptic cosine $\text{cn}$ of modulus $k$ are defined by

$$\text{sn}(K(x, k), k) = \sin \Phi = x, \quad \text{cn}(K(x, k), k) = \cos \Phi. \quad (93)$$

We shall omit the $k$ argument so that $\text{sn}(u, k) = \text{sn}(u)$. The delta amplitude is defined by

$$dn(u) = \sqrt{1-k^2\text{sn}(u)}. \quad (94)$$

The other nine Jacobian elliptic functions are obtained as ratios of the three first ones, following the formula

$$pq(u) = \frac{pn(u)}{qn(u)}, \quad (95)$$

where $p$ and $q$ are any of the letter $n, s, c, d$, and $nn(u) = 1$. For example,

$$sc(u) = \frac{\text{sn}(u)}{\text{cn}(u)} \quad \text{and} \quad nc(u) = \frac{1}{\text{cn}(u)}. \quad (96)$$

Squares of the functions are obtained from the two relations:

$$\text{sn}^2(u) + \text{cn}^2(u) = 1, \quad (97)$$

$$(1-k^2)\text{sn}^2(u) + \text{cn}^2(u) = dn^2(u). \quad (98)$$

### 7.3 Relations between parameters $I_\lambda$ and $J_\lambda$

We provide here expressions between $I_\lambda$ and $J_\lambda$: since $\text{arcosh}(x) = \ln \left( x + \sqrt{x^2-1} \right)$ for $x \geq 1$, we have

$$e^{-v(x)} = \left( \frac{1}{k} \text{dc} \left( \sqrt{\frac{A}{2} \frac{x-1}{k}} \right) + \sqrt{\frac{1}{k^2} \text{dc}^2 \left( \sqrt{\frac{A}{2} \frac{x-1}{k}} \right) - 1} \right)^2. \quad (99)$$

Using the modulus $k$ of the Jacobian elliptic function $dc$, we have $dc^2(u) - k^2 = (1-k^2)nc^2(u)$ and then

$$e^{-v(x)} = \left( \frac{1}{k} \text{dc} \left( \sqrt{\frac{A}{2} \frac{x-1}{k}} \right) + \frac{\sqrt{1-k^2}}{k} \text{nc} \left( \sqrt{\frac{A}{2} \frac{x-1}{k}} \right) \right)^2. \quad (100)$$
We expand this expression and use the following integrals

\[
\int u \text{dc}^2(x) dx = -E(u) + u + \text{sn}(u) \text{dc}(u),
\]

\[
\int u \text{nc}(x) \text{dc}(x) dx = \text{sc}(u),
\]

\[
(1 - k^2) \int u \text{nc}^2(x) dx = -E(u) + \left(1 - k^2\right) u + \text{sn}(u) \text{dc}(u), \quad (101)
\]

where \( E \) is the incomplete elliptic integral of the second kind of modulus \( k \),

\[
E(u) = \int_0^{\text{sn}(u)} \sqrt{\frac{1 - k^2 x^2}{1 - x^2}} dx. \quad (102)
\]

This leads to

\[
\int_a^1 e^{-v(x)} dx = \frac{1}{k} \sqrt{\frac{2}{A}} \left(2E(u_a) - 2 \text{sn}(u_a) \text{dc}(u_a)\right)
\]

\[
- \left(2 - k^2\right) u_a - 2\sqrt{1 - k^2} \text{sc}(u_a),
\]

with \( u_a = \sqrt{\frac{A}{2}} \frac{a - 1}{k} = \frac{\sqrt{T_\lambda} + \sqrt{J_\lambda}}{\sqrt{2}} (a - 1). \quad (103)
\]

Then we compute the second integral

\[
\int_a^1 e^{v(x)} dx = \int_a^1 \frac{dx}{\left(\frac{1}{k} \text{dc} \left(\sqrt{\frac{A}{2}} \frac{x - 1}{k}\right) + \sqrt{1 - k^2} \text{nc} \left(\sqrt{\frac{A}{2}} \frac{x - 1}{k}\right)\right)^2}
\]

\[
= k^3 \sqrt{\frac{2}{A}} \int_{u_a}^0 \frac{du}{\left(\text{dc}(u) + \sqrt{1 - k^2} \text{nc}(u)\right)^2}
\]

\[
= k^3 \sqrt{\frac{2}{A}} \int_{u_a}^0 \frac{\left(\text{dc}(u) - \sqrt{1 - k^2} \text{nc}(u)\right)^2}{\left(\text{dc}^2(u) - (1 - k^2) \text{nc}^2(u)\right)^2} du. \quad (104)
\]

Since \( \text{dc}^2(u) - (1 - k^2) \text{nc}^2(u) = k^2 \), we finally obtain

\[
\int_a^1 e^{v(x)} dx = \frac{1}{k} \sqrt{\frac{2}{A}} \int_{u_a}^0 \left(\text{dc}(u) - \sqrt{1 - k^2} \text{nc}(u)\right)^2 du, \quad (105)
\]
which is very similar to the previous integral Eq. 99. We thus compute Eq. 106 similarly, leading to

\[
\int_{a}^{1} e^{v(x)} \, dx = \frac{1}{k} \sqrt{\frac{2}{A}} \left( 2E(u_a) - 2 \text{sn}(u_a) \, dc(u_a) - \left( 2 - k^2 \right) u_a \\
+ 2\sqrt{1 - k^2} \text{sc}(u_a) \right). \tag{106}
\]

We define for \( u \in ] - K(k); K(k)[ \)

\[
f(u) = 2E(u) - (2 - k^2)u - 2 \text{sn}(u) \, dc(u),
\]

\[
g(u) = 2 \text{sc}(u), \tag{107}
\]

so we can now write Eqs. 106 and 103

\[
\int_{a}^{1} e^{v(x)} \, dx = \frac{1}{k} \sqrt{\frac{2}{A}} \left( f(u_a) + \sqrt{1 - k^2} g(u_a) \right),
\]

\[
\int_{a}^{1} e^{-v(x)} \, dx = \frac{1}{k} \sqrt{\frac{2}{A}} \left( f(u_a) - \sqrt{1 - k^2} g(u_a) \right). \tag{108}
\]

Because \( u = v + D \) we have

\[
\int_{a}^{1} e^{v} = e^{-D} \int_{a}^{1} e^{u} = \sqrt{\frac{I_{\lambda}}{J_{\lambda}}} \frac{\lambda_d n^{-}}{I_{\lambda}} = \frac{\lambda_d n^{-}}{\sqrt{I_{\lambda} J_{\lambda}}}, \tag{109}
\]

\[
\int_{a}^{1} e^{-v} = e^{D} \int_{a}^{1} e^{-u} = \sqrt{\frac{J_{\lambda}}{I_{\lambda}}} \frac{\lambda_d n^{+}}{J_{\lambda}} = \frac{\lambda_d n^{+}}{\sqrt{I_{\lambda} J_{\lambda}}}, \tag{110}
\]

and from Eqs. 82 and 85 we obtain

\[
\frac{1}{k} \sqrt{\frac{2}{A}} = \frac{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}}{2\sqrt{2I_{\lambda} J_{\lambda}}}, \quad \sqrt{1 - k^2} = \frac{\sqrt{I_{\lambda}} - \sqrt{J_{\lambda}}}{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}},
\]

which finally gives the system

\[
\lambda_d n^{-} = \frac{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}}{2\sqrt{2}} \left( f(u_a) + \frac{\sqrt{J_{\lambda}} - \sqrt{I_{\lambda}}}{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}} g(u_a) \right), \tag{111a}
\]

\[
\lambda_d n^{+} = \frac{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}}{2\sqrt{2}} \left( f(u_a) - \frac{\sqrt{J_{\lambda}} - \sqrt{I_{\lambda}}}{\sqrt{I_{\lambda}} + \sqrt{J_{\lambda}}} g(u_a) \right). \tag{111b}
\]

We can also notice that

\[
\lambda_d N = -\frac{\sqrt{J_{\lambda}} - \sqrt{I_{\lambda}}}{\sqrt{2}} g(u_a). \tag{112}
\]
7.4 Computing the leading order term $u_0$ in dimension 2

The first term $u_0$ is the solution of

$$u_0''(r) + \frac{1}{r} u_0'(r) = -J_\lambda e^{-u_0(r)},$$

$$u_0(1) = u'_0(1) = 0,$$ (113)

which we obtained by setting $\delta = 0$ in Eq. 65. Using the change of variables $r = e^{-t} \tilde{u}(t) = u(r) + 2t$, Eq. 65 reduces to $\tilde{u}''(t) = -J_\lambda e^{-\tilde{u}(t)}$, with boundary conditions $\tilde{u}(0) = 0, \quad \tilde{u}'(0) = 2$. We resolve here

$$\frac{1}{2} \tilde{u}'^2 = J_\lambda e^{-\tilde{u}(t)} + 2 - J_\lambda,$$ (114)

in the three cases $J_\lambda < 2$, $J_\lambda = 2$ and $J_\lambda > 2$.

Case $J_\lambda < 2$

We integrate

$$I(\tilde{u}) = \int \frac{dx}{\sqrt{J_\lambda e^{-x} + 2 - J_\lambda}} = \frac{2}{\sqrt{2 - J_\lambda}} \int \frac{\sqrt{\frac{2 - J_\lambda}{J_\lambda}} \exp(\frac{\tilde{u}}{2})}{\sqrt{1 + v^2}} dv.$$ (115)

leading to $\sqrt{2 - J_\lambda} \text{arsinh} \left( \sqrt{\frac{2 - J_\lambda}{J_\lambda}} \exp\left(\frac{\tilde{u}}{2}\right) \right) = t + C$, where $C = \sqrt{\frac{2 - J_\lambda}{2}} \text{arsinh}\left( \sqrt{\frac{2 - J_\lambda}{J_\lambda}} \right)$. This leads to the simplified relation

$$u(r) = 2 \ln \left( \frac{1}{2} \left( 1 + \frac{1}{p} \right) r^{1-p} - \frac{1}{2} \left( \frac{1}{p} - 1 \right) r^{1+p} \right),$$ (116)

where $p = \sqrt{\frac{2 - J_\lambda}{2}}$. To evaluate how $J_\lambda$ depends on $\lambda, d_n^+$, we compute the integral in Eq. 19:

$$\int_1^1 e^{-u(r)} r dr = \int_1^1 \frac{r dr}{\left( \frac{1}{2} \left( 1 + \frac{1}{p} \right) r^{1-p} - \frac{1}{2} \left( \frac{1}{p} - 1 \right) r^{1+p} \right)^2} = 4p^2 \int_1^1 \frac{r^{2p-1} dr}{(p + 1 - (1 - p)r^{2p})^2} = \frac{1 - a^{2p}}{(1 + a^{2p}) p + 1 - a^{2p}}$$

and $\lambda, d_n^+ = \frac{J_\lambda (1 - a^{2p})}{(1 + a^{2p}) p + 1 - a^{2p}}$. In the limit $p \to 0$, expanding $a^{2p}$ leads to

$$\lambda, d_n^+ \to \frac{2 \ln(a)}{\ln(a) - 1} \quad \text{when} \quad J_\lambda \to 2.$$ (117)
Case $J_\lambda = 2$

When $J_\lambda = 2$, Eq. 69 becomes $\frac{1}{2} \tilde{u}'^2 = 2e^{-\tilde{u}}$, thus $e^{\frac{3}{2} \tilde{u}'} = 2$, gives the solution $\tilde{u}(t) = 2 \ln(1 + t)$. Since $u(r) = \tilde{u}(-\ln(r)) + 2 \ln(r)$, we obtain the solution

$$u(r) = 2 \ln(r(1 - \ln(r))).$$ (118)

We evaluate $\lambda_d n^+$ by computing the integral in Eq. 19:

$$\int_a^1 e^{-u(r)} r \, dr = \int_a^1 \frac{dr}{r(1 - \ln(r))^2} = \frac{\ln(a)}{(\ln(a) - 1)},$$ (119)

and get $\lambda_d n^+ = \frac{2 \ln(a)}{\ln(a) - 1}$.

Case $J_\lambda > 2$

Following 115, a direct integration leads to

$$I(\tilde{u}) = \int \tilde{u} \frac{dx}{\sqrt{J_\lambda e^{-x} - (J_\lambda - 2)}} = \frac{2}{\sqrt{J_\lambda - 2}} \int \sqrt{\frac{2}{J_\lambda - 2}} \exp\left(\frac{\tilde{u}}{2}\right) \frac{dv}{\sqrt{1 - v^2}}.$$ (120)

Thus, $\sqrt{\frac{2}{J_\lambda - 2}} \arcsin\left(\sqrt{\frac{J_\lambda - 2}{J_\lambda}} \exp\left(\frac{\tilde{u}}{2}\right)\right) = t + C$, where $C = \sqrt{\frac{2}{J_\lambda - 2}} \arcsin\left(\sqrt{\frac{J_\lambda - 2}{J_\lambda}}\right)$, leading to

$$u(r) = 2 \ln\left(r \left(\frac{1}{p} \sin(-p \ln(r)) + \cos(-p \ln(r))\right)\right),$$ (121)

where $p = \sqrt{\frac{J_\lambda - 2}{2}}$. We can now evaluate the relation with $\lambda_d n^+$ in $J_\lambda$, we compute the integral in Eq. 19:

$$\int_a^1 e^{-u(r)} r \, dr = \int_a^1 \frac{dr}{r\left(\frac{1}{p} \sin(-p \ln(r)) + \cos(-p \ln(r))\right)^2} = \frac{1}{1 - p \cot(p \ln(a))},$$ (122)

and $\lambda_d n^+ = \frac{J_\lambda}{1 - p \cot(p \ln(a))}$. Since $J_\lambda \to 2, p \to 0$ and we obtain $\lambda_d n^+ \to \frac{2 \ln(a)}{\ln(a) - 1}$ when $J_\lambda \to 2$. In addition,

$$\lambda_d n^+ \to \infty \quad \text{when} \quad J_\lambda \to J_{lim}(a),$$ (123)
where \( J_{lim}(a) \) is the first positive solution of the equation

\[
\sqrt{\frac{J - 2}{2}} \cot \left( \sqrt{\frac{J - 2}{2}} \ln(a) \right) = 1. \tag{124}
\]

### 7.5 Computing the first term \( u_1 \) of the regular perturbation

The second term \( u_1 \) of the regular perturbation is the solution of

\[
u''(r) + \frac{1}{r} u'(r) = e^{u_0(r)} + J_\lambda e^{-u_0(r)} u_1(r), \tag{125}\]

with boundary conditions

\[
u(1) = u'(1) = 0. \tag{126}\]

We distinguish three cases \( J_\lambda < 2, J_\lambda = 2 \) and \( J_\lambda > 2 \). For \( J_\lambda < 2 \), the homogeneous equation is

\[
u''(r) + \frac{1}{r} u'(r) - \frac{8 p^2 (1 - p^2)}{r^2 ((p + 1)r^p - (1 - p)p)^2} u(r) = 0, \tag{127}\]

where \( p = \sqrt{1 - \frac{J_\lambda}{2}} \). We use the change of variable \( x = r^p \) and \( u(r) = v(x) \), to transform the equation into

\[
v''(x) + \frac{1}{r} v'(x) - \frac{8 q}{(q - x^2)^2} v(r) = 0, \tag{128}\]

\[
v(1) = v'(1) = 0, \tag{129}\]

where \( q = \frac{1 + p}{1 - p} \). The two independent solutions are

\[
y_1(x) = \frac{x^2 + q}{x^2 - q}, \tag{130}\]

\[
y_2(x) = y_1(x) \ln(x) - 1, \tag{131}\]

thus the solutions to Eq. 127 are

\[
Y_1(r) = \frac{r^{2p} + q}{r^{2p} - q}, \tag{132}\]

\[
Y_2(r) = p Y_1(r) \ln(r) - 1. \tag{133}\]

Finally, the general solution of Eq. 125 with initial conditions 126 is

\[
u_1(r) = (\lambda(r) + A) Y_1(r) + (\mu(r) + B) Y_2(r), \tag{134}\]
where

\[
\mu(r) = \frac{(1 - p)^2}{4p^3(4 + 2p)} r^{4+2p} - \frac{(1 + p)^2}{4p^3(4 - 2p)} r^{4-2p},
\]

\[
\lambda(r) = -p \mu(r) \ln(r) - \frac{1 - p^2}{8p^3} r^4 + \frac{(1 - p)^2(4 + 3p)}{4p^3(4 + 2p)^2} r^{4+2p}
\]

\[
+ \frac{(1 + p)^2(4 - 3p)}{4p^3(4 - 2p)^2} r^{4-2p},
\]

\[
A = -\frac{1}{8} \frac{p^4 - 23p^2 + 40}{p(p^2 - 4)^2}, \quad B = -\frac{1}{4} \frac{p^2 + 5}{p^2(p^2 - 4)}. \quad (135)
\]

When \( J_\lambda = 2 \), Eq. 72 becomes

\[
u''(r) + \frac{1}{r} u'(r) - \frac{2}{r^2(1 - \ln(r))^2} u_1(r) = r^2 (1 - \ln(r))^2. \quad (136)
\]

The solution is

\[
u_1(r) = (A + \lambda(r)) (1 - \ln(r))^2 + \frac{B + \mu(r)}{1 - \ln(r)}, \quad \text{where}
\]

\[
A = \frac{5}{48}, \quad B = -\frac{103}{384},
\]

\[
\lambda(r) = \frac{r^4}{12} \left( -\frac{5}{4} + \ln(r) \right),
\]

\[
\mu(r) = \frac{r^4}{384} \left( 32 \ln(r)^4 - 160 \ln(r)^3 + 312 \ln(r)^2 - 284 \ln(r) + 103 \right).
\]

Finally, when \( J_\lambda > 2 \), the homogeneous Eq. 72 is

\[
u''(r) + \frac{1}{r} u'(r) - \frac{2(1 + p^2)}{r^2 \cos^2(p \ln(r)) \left( 1 - \frac{1}{p} \tan(p \ln(r)) \right)^2} u_1(r) = 0, \quad (137)
\]

where \( p = \sqrt{\frac{J_\lambda}{2}} - 1 \). We use the change of variable \( x = \tan(p \ln(r)) \) and \( v(x) = u(r) \) to get

\[
u''(x) + \frac{2x}{1 + x^2} v'(x) - \frac{2(1 + p^2)}{(p - x)^2(1 + x^2)} v(x) = 0. \quad (138)
\]

The independent solutions are

\[
y_1(x) = \frac{1 + px}{x - p},
\]

\[
y_2(x) = y_1(x) \arctan(x) - 1.
\]
Therefore the solutions to the homogenous Eq. 137 are

\[
Y_1(r) = \frac{1 + p \tan(p \ln(r))}{\tan(p \ln(r)) - p}, \quad (139)
\]

\[
Y_2(r) = pY_1(r) \ln(r) - 1. \quad (140)
\]

Finally, the solution of Eq. 72 with initial conditions 126 is

\[
u_1(r) = (\lambda(r) + A)Y_1(r) + (\mu(r) + B)Y_2(r), \quad (141)
\]

where

\[
\mu(r) = \frac{r^4}{p^3(16 + 4p^2)} \left( \left(5p - p^3\right) \cos(2p \ln(r)) - (2 - 4p^2) \sin(2p \ln(r)) \right),
\]

\[
\lambda(r) = -p\mu(r) \ln(r) - \frac{(1 + p^2)r^4}{8p^3} - \frac{7p^4 + 8p^2 - 8}{4p^3(p^2 + 4)^2} r^4 \cos(2p \ln(r))
\]

\[
-\frac{3p^4 - 15p^2 - 36}{8p^2(p^2 + 4)^2} r^4 \sin(2p \ln(r)),
\]

\[
A = \frac{1}{8} \frac{p^4 + 23p^2 + 40}{p^2 + 4},
\]

\[
B = \frac{1}{4} \frac{p^2 - 5}{p^2 + 4}.
\]

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