Electrohydrodynamic activity of biological cells

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Fluid pumping and the generation of electric current by living tissues are required during morphogenetic processes and for maintainance of homeostasis. How these flows emerge from active and passive ion transport in cells has been well established. However, the interplay between flow and current generation is not well understood. Here, we study the electro-hydraulic coupling that arises from cell ion pumping. We develop a one-dimensional continuum model of fluid and ion transport across active cell membranes. Solving the Nernst-Planck and Poisson equations in the limit of weak charge imbalance allows us to derive approximate analytical solutions of the model. These approximations, consistent with the numerical results in physiologically relevant regime of parameters, allow us to describe electro-hydraulic activity of cells and tissues in terms of experimentally accessible parameters.

I. INTRODUCTION

The morphogenesis and homeostasis of tissues and organs involves the collective organisation of a large number of cells. In general cells respond to chemical, mechanical, hydraulic, electrical and osmotic cues. On large scales tissues are active polar materials that generate active stresses, but also fluid flows and electric currents [1-6]. This is particularly true for epithelial tissues, which have apical-basal polarity. These behaviours can be studied in coarse-grained continuum approaches, which reveal interesting tissue properties such as fluid pumping, current generation, and electro-hydraulic coupling as well as flexo-electricity [6, 7]. In order to understand how these large scale properties of tissues result from cellular properties, it is useful to develop simple models on the scale of cells that capture the physics of current and flow generation.

Ion channels and pumps have been extensively studied both experimentally and theoretically [8-10]. A large body of work has been done on the generation of electric fields and electric currents in the context of action potentials and their propagation [1-9]. The activity of ion pumps generate osmotic differences which give rise to water flows across membranes [11, 12]. Early work studied the interplay between flow and electric current generation; for example a comprehensive model of active epithelial transport was developed and applied to the transport in the Necturus gallbladder using numerical methods [13]. The hydraulics of water pumping has recently raised interest in the context of the dynamics of kidney and liver but without an explicit treatment of electric currents and fields [14, 15]. In addition, the coupling of ion pumping and water flows was studied to discuss flow driven locomotion of cells through narrow channels [12]. However, an analytical approach to the coupling of hydraulic and electric processes in cells is still lacking.

Here, we investigate the interplay of the electric fields and currents with fluid flows that are generated by ion pumping across membranes. We take into account the contributions of fluid flow to electric fields and ion currents in the Nernst-Planck equation and obtain a full non-linear solution close to electro-neutrality. The relative importance of fluid flow and ion diffusion is characterised by a Peclet number. We present a simplified one-dimensional setting that allows us to find exact non-linear solutions of the Nernst-Planck and Poisson equations in the limit of weak charge imbalance. We use this approach to first discuss a single membrane with active pumps and passive channels, both considering a closed system as well as a periodic system with a finite fluid flow and electric currents. We relate properties of ion channels and pumps to flow velocities and electric currents and we discuss the values of these quantities obtained under physiological conditions. We show that for physiological parameter ranges, the limit of small Peclet number provides analytic expressions for transport properties which are in excellent agreement with numerical solutions of the non-linear problem. We extend this approach to a system of two membranes which can be used as a model for a cell or an epithelium. Eventually we show how tissue flexo-electricity can emerge from ion pumping across membranes at the cell scale.
II. ION DENSITIES AND ELECTRIC POTENTIALS IN A FLOWING ELECTROLYTE SOLUTION

We first discuss the effects of fluid flow in a neutral ion solution. In thermodynamic equilibrium, the distances over which charges in an electrolyte interact are limited by the Debye length $\lambda_D$, due to screening by charges of opposite sign. On scales beyond the Debye length the electrolyte is essentially neutral. We consider for simplicity a one-dimensional geometry. Out of equilibrium, flows of fluid and electric currents affect ion distributions. The current density $J^\pm$ of positive and negative ions can be expressed in terms of the ion concentrations $\rho^\pm$ by the Nernst-Planck equation

$$J^\pm = \mp K^\pm q \partial_x \phi \rho^\pm - K^\pm k_B T \partial_x \rho^\pm + \rho^\pm v ,$$  

(1)

where $K^\pm$ are ion mobilities, $+q$ ($-q$) is the charge of positive (negative) ions, $x$ is the distance to the membrane, $\phi$ is the electric potential and $v$ is the fluid velocity. The electric current density is $I = q(J^+ - J^-)$. In steady state, current densities are divergence free, $\partial_x J^\pm = 0$.

The electric potential satisfies the Poisson equation $\epsilon \partial^2 \phi/\partial x^2 = -q(\rho^+ - \rho^-)$, which together with the Nernst-Planck equation (1) and charge conservation provides a one-dimensional description of the flowing electrolyte solution. For potential differences small compared to $k_B T/q$, the equations can be linearised to a good approximation, and at thermodynamic equilibrium fields and charge densities vary over the Debye length $\lambda_D$. The solvent flow introduces an additional length scale $\lambda$ over which the ion densities vary, while maintaining charge balance. At large length scales the electric potential differences can exceed $k_B T/q$ in the presence of flows and nonlinearities become important (see Appendix A).

To discuss the effects of nonlinearities in the presence of flows we consider the case where charge imbalances are small, $|\rho^+ - \rho^-| \ll \rho$, where $\rho = (\rho^+ + \rho^-)/2$. In this case the electric potential can be approximated by imposing the condition $\rho^+ = \rho^-$ in Eq. (1) while the small charge imbalance can be calculated from the electric potential using the Poisson equation. Using this approximation we find (see Appendix A)

$$\rho(x) = \frac{1}{v} \left( \frac{J^+}{K^+} + \frac{J^-}{K^-} \right) + Ce^{x/\lambda}$$  

(2)

$$\frac{q(\phi(x) - \phi(0))}{k_B T} = -\left( \frac{K^-}{K^+} + \frac{J^-}{K^-} \right) \frac{1}{\lambda} \ln \left( \frac{\rho(x)}{\rho(0)} \right)$$  

(3)

where, the length scale $\lambda = 2k_B T K^- K^+/(v(K^+ + K^-))$ and $C$ is an integration constant which in a finite system of length $L$ reads

$$C = \frac{L/\lambda}{\exp(L/\lambda) - 1} \left( \rho_0 - \frac{1}{v} \frac{J^+}{K^+} + \frac{J^-}{K^-} \right) ,$$  

(4)

where $\rho_0 = L^{-1} \int_0^L dx \rho(x)$ is the average ion concentration and $Pe = L/\lambda$ is a Peclét number characterising the importance of drift relative to diffusion. Note that the concentration difference across the system can be written as

$$\rho(L) - \rho(0) = Pe \left( \rho_0 - \frac{1}{v} \frac{J^+}{K^+} + \frac{J^-}{K^-} \right)$$  

(5)

and the charge imbalance is given by

$$\rho^+ - \rho^- = \frac{1}{4\pi \lambda_B} \frac{J^+}{K^+} - \frac{J^-}{K^-} \left( \frac{\partial^2 \rho(x)}{\partial x^2} - \frac{(\partial_x \rho)^2}{\rho^2} \right) ,$$  

(6)

where $\lambda_B = q^2/(\epsilon k_B T)$ is the Bjerrum length.

III. ION PUMPS AND MEMBRANE PERMEABILITY

Fluid flows and electric currents can be generated by membranes which contain active pumps. In order to develop a simple model for the pumping activity we consider a membrane separating two fluid filled compartments, denoted $A$ and $B$. The membrane contains active pumps and passive channels for positive and negative ions. We describe the ion flux across the membrane by

$$J^\pm = J^\pm_0 + \nu^\pm (\mu^\pm_A - \mu^\pm_B)$$  

(7)

where $J^0_0$ is the flux due to pump activity and the coefficients $\nu^\pm$ describe the permeability through passive ion channels. A non-zero $J^0_0$ corresponds to an asymmetric membrane in which pumps are oriented, which defines membrane polarity. For $J^0_0 > 0$ pumps on average transport ions from $A$ to $B$. In general, $J^0_0$ as well as the coefficients $\nu^\pm$ depend on concentrations of ions and other factors such as mechanical stress. This simplified expression is a good description under physiological conditions. It can be obtained from a more detailed models [10], as shown in Appendix B.

The chemical potentials governing membrane transport can be written as

$$\mu^\pm = \mu^\pm_0 + k_B T \ln \rho^\pm \pm q \phi ,$$  

(8)

where $\mu^\pm_0$ are reference chemical potentials.

Fluid permeates through the membrane at a velocity $v$ which depends on the hydrostatic pressure difference $P_B - P_A$ and the osmotic pressure difference $\Pi_B - \Pi_A$ across the membrane

$$v = \xi (P_A - P_B - \Pi_A + \Pi_B)$$  

(9)

where $\xi$ is a permeation coefficient. The osmotic pressure is given by

$$\Pi = k_B T (\rho^+ + \rho^- + \rho_R) = k_B T (2\rho + \rho_R)$$  

(10)

where $\rho_R$ is the number density of other solutes which do not cross the membrane barrier.
IV. POLAR MEMBRANE WITH ION PUMPS AND CHANNELS

A. Membrane in a sealed channel

We first review the simple case of a closed system of length \( L \) filled with solvent containing equal densities \( \rho_0 \) of two oppositely charged ion species. Initially, ions are homogeneously distributed such that \( \rho(x) = \rho_0 \). A membrane containing active pumps divides the system in two equal volumes labeled \( A \) and \( B \), as illustrated in Fig. 1(a). Because the system is closed and the fluid is incompressible no fluid flow occurs, \( v = 0 \). Due to the activity of the pumps, ions flow across the membrane until a steady state is reached in which active and passive fluxes are balanced. In this steady state both volumes have different ion concentrations \( \rho_A \), \( \rho_B \), \( \rho_{R,A} \) and \( \rho_{R,B} \) and there exists a pressure and an electric potential difference:

\[
\rho_A = \rho_0 \left[ 1 - \tanh \left( \frac{J_0}{4v^+k_B T} \right) \right]
\]

\[
\rho_B = \rho_0 \left[ 1 + \tanh \left( \frac{J_0}{4v^+k_B T} \right) \right]
\]

\[
P_B - P_A = 4\rho_0 k_B T \tanh \left( \frac{J_0}{4v^+k_B T} \right) - k_B T \left( \rho_{R,B} - \rho_{R,A} \right)
\]

\[
\phi_B - \phi_A = \frac{J_0}{2v^+q}
\]

where, for simplicity, we consider positive ion pumps \( J^+_0 = J_0 \), \( J^-_0 = 0 \) and the pump permeability and the channel permeability are taken to be constant parameters.

We estimate typical parameter values to capture orders of magnitudes relevant in physiological conditions. Typical concentration of \( \rho_0 = 5 \cdot 10^{22} \text{m}^{-3} \), corresponds to about 75mM. Using the trans-membrane potential \( |\phi_B - \phi_A| \approx 75mV \) we estimate \( J_0/\nu^+ \approx 2.4 \cdot 10^{-20} \text{N.m} \). For these parameters \( \rho_B / \rho_A \approx 10 \). The order of magnitude of \( 4\rho_0 k_B T \) is \( 8 \cdot 10^9 Pa \). Because biological membranes cannot sustain large pressures Eq. 13 sets the estimated value of the required concentration difference of solutes on the two sides \( \rho_{R,A} - \rho_{R,B} \approx 4\rho_0 \).

B. Membrane in a periodic channel

We now consider an active membrane driving flow through a channel which forms a loop, as illustrated in Fig. 1(b). Such a situation could be realised in a microfluidic experiment. The pumping of ion couples to fluid flow and the active membrane acts as a battery and a water pump. In the one-dimensional description we use periodic boundary conditions and the conditions for the current and the flow given by Eqs. 4 and 9 at the membrane. To simplify the discussion we consider equal mobility of positive and negative ions \( K = K^+ = K^- \).

For a channel filled with a gel through which a fluid permeates, the pressure changes linearly along the channel. Therefore, the pressure jump across the membrane is \( P_B = P_A + vL\eta/a^2 \), where \( \eta \) is the fluid viscosity, \( a \) is the bulk permeation length, and \( v \) is the flow velocity. Using Eq. 9 the velocity can then be expressed as \( v = \xi(\Pi_B - \Pi_A) \), where we introduce an effective permeation coefficient \( \xi = \xi/(1 + \xi L/\alpha^2) \).

We first derive a relation between the solvent flow and ion current densities \( J^\pm \). From Eq. 5 and Eq. 9 we obtain

\[
v = \frac{J^+ + J^-}{2\rho_0(1 + \theta)} ,
\]

where

\[
\theta = \frac{K}{2\xi L\rho_0} .
\]

This allows us to express ion densities at the membrane as

\[
\rho_A = \rho(L) = \rho_0 \left( 1 + \theta - \theta e^{Pe} \right) ,
\]

\[
\rho_B = \rho(0) = \rho_0 \left( 1 + \theta - \theta e^{Pe} \right) .
\]

The membrane spontaneously generates a fluid flow with velocity \( v = \nu_0 \theta Pe \), which is proportional to the Peclet number. The velocity scale \( \nu_0 = 2L\rho_0 k_B T \) corresponds to the osmotic fluid flux through a membrane at concentration difference \( \rho_0 \). For our choice of parameters \( \nu_0 = 4 - 40 \mu \text{m/s} \). Furthermore, the fluid velocity depends on the channel length via a characteristic length-scale \( \theta L \). Here, we have used \( K \approx 3 \cdot 10^{11} \text{m}^2 \text{J}^{-1} \text{s}^{-1} \), and range \( \xi \approx 10^{-13} - 10^{-11} \text{mPa}^{-1} \text{s}^{-1} \), following reported values [17-19].

In the limit of weak flow, corresponding to a small Peclet number we can find explicit solutions of the problem. For ion densities at the membrane we find

\[
\rho_A \approx \rho_0 \left( 1 - \frac{1}{2} \frac{v}{\nu_m} \right) ,
\]

\[
\rho_B \approx \rho_0 \left( 1 + \frac{1}{2} \frac{v}{\nu_m} \right) .
\]

To determine the fluid velocity in the weak flow limit, we consider small values of \( \theta Pe \), corresponding to small relative ion density variations \( \ln(\rho_A / \rho_B) \approx \ln(1 - v/\nu_m) \approx -v/\nu_m \). For simplicity, we consider the case \( \nu = \nu^+ = \nu^- \). Using Eq. 15, we then obtain

\[
v \approx \frac{J_0}{2\rho_0 + \frac{v}{\nu_m} + \frac{K}{\xi L}}.
\]

Two reference concentrations \( (\nu/2\xi)^{1/2} \approx 45 \text{mM} \), and \( K/(\xi L) \approx 500 \text{mM} \), where we have used \( \xi \approx 10^{-11} \text{mPa}^{-1} \text{s}^{-1} \), and \( L \approx 100 \text{\mu m} \). For values of \( \rho_0 \) between these reference values we can estimate the order of
magnitude of the flow velocity as \( v \approx J_0 \xi L/K \approx 0.3 - 30 \mu m/s \), where we have used \( J_0 \approx 10^{17} - 10^{19} m^{-2} s^{-1} \), corresponding to an ion pump rate of \( 10^3 s^{-1} \) and area density of pumps of \( 10^2 - 10^4 \mu m^{-2} \).

We can also estimate for ion current densities and potentials considering the same limit of small \( \theta Pe \). We first note that using Eq. 3 the membrane potential difference \( \Delta \phi_{AB} \equiv \phi_B - \phi_A \) can be expressed as

\[
\Delta \phi_{AB} = k_B T J^+ - J^- \left( \frac{\rho_B}{\rho_A} + \ln \left( \frac{\rho_B}{\rho_A} \right) \right).
\]  

(22)

Using Eqs. 15, 17, 18 for velocity and densities we can determine from Eqs. 7 currents

\[
J^+ \approx \frac{1}{2} \frac{1 + \theta (1 + \psi) + (1 + \theta)(1 + \psi)}{(1 + \psi)(1 + \theta(1 + \psi))} J_0,
\]

(23)

\[
J^- \approx \frac{1}{2} \frac{\psi}{(1 + \psi)(1 + \theta(1 + \psi))} J_0,
\]

(24)

where \( \psi = \nu L/(K \rho_0) \). The electric current density follows as

\[
I = q \left( J^+ - J^- \right) \approx q \frac{J_0}{1 + \psi}.
\]

(25)

Finally, the membrane potential difference has the form

\[
\Delta \phi_{AB} \approx \frac{J_0}{2\nu \psi} \frac{\psi}{1 + \psi}.
\]

(26)

We test the accuracy of these approximations by comparing them to numerical solutions of the full non-linear problem in the weak charge imbalance limit. Fig. 1c) shows numerically obtained ion density profiles along the channel, which exhibit approximately a linear profile consistent with Eqs. 19 and 20. Fig. 1d) shows velocity, currents and membrane potential difference as a function of the system size. It compares numerical solutions (symbols) to the analytical approximations (solid lines), showing excellent agreement. Thus, the approximations in the small \( \theta Pe \) regime apply in parameter regimes consistent with physiological conditions.

V. TWO ACTIVE MEMBRANES AS A SIMPLE MODEL FOR CELLULAR PUMPING

A. Model of cellular pumping

Using the formalism developed above we discuss pumping across a cell by introducing two active membranes separated by the thickness \( L_c \). The space between the membranes corresponds to the inside of the cell of volume \( V_c \), which confines \( N_R \) resident molecules. This could correspond for example to a cell in contact with different fluid compartments denoted \( A \) and \( D \), see Fig. 2a),b). The resident molecules in the cell contribute to the cell osmotic pressure \( \Pi_c = 2k_B T \rho + k_B T N_R / V_c \). Profile of resident molecules due to flow can be taken into account as an effective contribution to the \( \xi_2 \), see Appendix A.4 and therefore we do not account for it explicitly. Cell membranes exhibit an electric double layer of positive and negative charges confined within the Debye length near the membrane. In our approximation, relevant on large scales, this double layer could be taken into account as a membrane capacitance if surface charges were to be discussed.

We first consider a symmetric cell without apical-basal polarity, see Fig. 2a). The example shown in this figure corresponds to a symmetric cell in a circular microfluidic channel. We outline how ion concentration, membrane potential and pressure difference across cell membrane appear in this case. We then consider a polarised cell which generates fluid flows and electric currents, see Fig. 2b).

B. Symmetric cell

In the symmetric cell we consider, ions are pumped outwards with pump strengths of magnitude \( J_0 \), see Fig.
Due to symmetry $\phi_A = \phi_B$ and $\phi_B = \phi_C$ and membrane potentials difference at the two membranes are the same $\Delta \phi_{AB} = \Delta \phi_{DC}$ with

$$\Delta \phi_{AB} = \frac{-J_0}{2\nu q} . \quad (27)$$

This potential difference sets the ion concentration $\rho^c$ inside the cell relative to the outside concentration $\rho^w$ as

$$\rho^c = \rho^w e^{\frac{-J_0}{2\nu q}}, \quad (28)$$

where we define the average ion concentrations inside and outside of the cell as $\rho_0^c$ and $\rho_0^w$, respectively. They satisfy $\rho_0^c L^c + \rho_0^w (L - L^c) = \rho_0 L$, where $\rho_0$ is imposed. The pressure difference across the cell membrane $\Delta P \equiv P_B - P_A$ arises from the difference in osmotic pressures

$$\Delta P = k_B T \left[ \frac{N_R}{V_c} + 2\rho^w \left( e^{\frac{-J_0}{2\nu q}} - 1 \right) \right] . \quad (29)$$

Mechanical equilibrium requires balance of pressures which is achieved by adjusting the cell size to

$$L_c \approx \frac{N_R}{2\rho_0 A_c \left( 1 - e^{-J_0/(2\nu kBT)} \right)} , \quad (30)$$

where $A_c$ is the area of the channel cross-section.

C. Asymmetric cell in a periodic channel

We now consider a polarised cell in a periodic channel of length $L$ with overall amount of ions $L\rho_0$. Inspired by the apical-basal cell polarity the outwards pumping strengths are slightly biased by an amount $\delta J$, see Fig. 2 b). Note that Eqs. 31 and 32 for density profiles and electric potential still apply, separately inside and outside of the cell. The membrane fluxes are described by six equations that can be solved for unknowns $J^+, J^-, v, L^c, \rho_0^c$ and $\phi_B - \phi_A$, see SI for details, from which electric potentials $\phi_{A,B,C,D}$ and ion densities $\rho_{A,B,C,D}$ follow. Spatial profiles of ion densities obtained numerically using this approach are shown in Fig. 2 c). Currents, flow velocities and electric potentials as a function of system length $L$ are shown in Fig. 2 d).

In order to obtain explicit expressions for these quantities we consider the limit of weak bias $\delta J \ll J_0$ where the Peclet number is small $Pe \ll 1$. This allows us to approximate the density profiles to lowest order in $Pe$ as

$$\rho^c(x) = \rho_0^c e^{\frac{-J_0}{2\nu q}} \approx 1 + Pe \frac{L^c}{L} \left( 1 - \frac{\rho_0}{\rho_0^c} (1 + \theta_2) \right) \left( \frac{x}{L^c} - \frac{1}{2} \right) , \quad (31)$$

$$\rho^w(x) = \rho_0^w \approx 1 + Pe \frac{L - L^c}{L} \left( 1 - \frac{\rho_0}{\rho_0^w} (1 + \theta_2) \right) \left( \frac{x}{L^c} - \frac{1}{2} \right) , \quad (32)$$

where we have defined $\theta_2 = K/(\rho_0 L \xi_2)$, with $2/\xi_2 = 2/\xi + (L - L^c)\eta^w/(a^w)^2 + L^c\eta^c/(a^c)^2$. Here, $a^c$ and $a^w$ are the permeation lengths in the channel and surrounding medium. Even inside a cell, where we estimate $a^c \approx 5 nm$, the contribution from permeation in the cell cytoplasm $L^c\eta^c/(a^c)^2 \approx 4 \cdot 10^{-5} mPa^{-1} s^{-1}$ is typically smaller than that of the cell membrane $2\xi / \xi^2 \approx 2 \cdot 10^{11} mPa^{-1} s^{-1}$ to the effective overall permeation coefficient $\xi_2$.

The average ion density inside the cell is given by

$$\rho_0^c \approx \rho_0^c e^{\frac{-J_0}{2\nu q}} \ . \quad (33)$$

with

$$\rho_0^w \approx \frac{\rho_0}{1 - \frac{L^c}{L} \left( 1 - e^{\frac{-J_0}{2\nu q}} \right)} . \quad (34)$$

The force balanced cell size is determined by the average pump strength $J_0$

$$L_c = \frac{L}{1 - e^{\frac{-J_0}{2\nu q}}} \left( \frac{N_R}{N_I + N_R} \right) , \quad (35)$$

with $A_c$ the channel cross-sectional area and $N_I = 2\rho_0 A_c L$ total number of ions in the channel. Here, as for the symmetric cell, we neglect pressure difference across the membranes as compared to osmotic pressure differences.
Solvent flow velocity and electric current density can now be determined as

$$v \simeq \frac{\delta J/(2\rho_0)}{1 + \theta_2 + \frac{L^c}{2K\rho_0} \left(1 + \theta_2\right) \frac{\rho_0}{\rho_0} \left(\frac{L^c}{\rho_0} + \frac{L^c}{\rho_0} - 1\right)}$$

(36)

$$I \simeq \frac{q\delta J}{1 + \frac{\nu}{2K} \left(\frac{L^c}{\rho_0} + \frac{L^c}{\rho_0} - 1\right)}$$

(37)

The membrane potentials at the two membranes

$$\Delta \phi_{AB} = -\frac{J_0}{2q\nu} - J^+ - J^- - \delta J$$

(38)

$$\Delta \phi_{DC} = -\frac{J_0}{2q\nu} + J^+ - J^- + \delta J$$

(39)

exhibit small corrections to the value $-J_0/2q\nu$ found in the symmetric cell.

Finally, the electric potential change across the cell is

$$\Delta \phi_{DA} \simeq -\frac{L^c}{K} \frac{\rho_0}{\rho_0} (1 + \theta_2) \frac{\delta J}{1 + \frac{\nu}{2K} \left(\frac{L^c}{\rho_0} + \frac{L^c}{\rho_0} - 1\right) 2\rho_0 (1 + \theta_2).}$$

(40)

These approximate solutions are shown in Fig. 2(d) as solid line, which shows that they are in excellent agreement with numerical solutions of the non-linear equations.

VI. DISCUSSION

We have presented a one-dimensional model of electrohydraulic pumping of ions and water across membranes using the approximation of weak charge imbalance. At lengths large compared to the Debye length-scale this approximation is accurate with charge imbalances $|\rho^+ - \rho^-|/|\rho^+ + \rho^-| < 10^{-12}$ for parameter values in the physiological range that we use here. Using this weak charge imbalance limit we present a non-linear solution of the corresponding equations in the presence of advection and discuss the electrohydraulic activity of a single membrane and that of a pair of membranes, capturing hydroelectric activity of a cell or of an epithelium.

Our work is related to previous work concerning the migration of cells in channels in the presence of electric fields [12]. Here, we discuss endogenously generated electric fields rather than a response to an externally imposed field. In addition, we provide analytical expressions for ion densities, fluxes and currents, which we show hold to a very good approximation in the physiologically relevant range. The geometry discussed is fundamentally different from previous work on galvanotaxy where an external electric filed is oriented parallel to the membrane [21][22].

We have discussed a pair of membranes at a distance $L_c$ as a model for a cell in a microfluidic channel which generates an electric field and fluid flow. The same model can be interpreted as a model for an epithelium where fluid flow through the channel corresponds to the backflow of fluid through the cell-cell junctions of the epithelium where we do not account for lateral currents and flows, as shown in Fig. 3 where junctional backflow indicated by the dark blue arrows correspond to the channel flow. This flow leads to a pressure buildup across the epithelium. This pressure difference drives the backflow through the cell-cell junctions and a steady state is reached when the cell induced flow is balanced by the junction backflow. In this case the steady state pressure difference across the epithelium is $\Delta P \simeq \eta v d L_c/w^2 \simeq 2 \cdot 10^8 Pa$, where $d \simeq 10 \mu m$ is the linear cell dimension in the epithelial plane and $w \simeq 50nm$ is the width of cell-cell junctions, in agreement with recent experimental measurements of transepithelial pressure [4][24]. This pressure difference across the epithelium can be balanced for example by a gel substrate attached to the epithelium such as an extracellular matrix layer e.g. basement membrane, or by Laplace pressure across an epithelium that bends into a dome-like shape.

In many in-vivo cases, such as kidney [14], the epithelium maintains a steady state flow. Also, the water balance in fresh water fish is achieved by maintaining water influx through gills and outflux through the intestinal epithelium [24]. For parameters values in the physiological range, we estimate a fluid transport velocity across an epithelium on the order of $\simeq 1 - 10 nm/s$, where we use $\delta J/J_0 \simeq 0.1$, see Eq. 36.

In addition to the hydraulic properties, the epithelium is also an electric current generator, see Eq. 37. The effects of this current is analogous to those of the flow. The current first leads to a buildup of electric potential difference, corresponding to charging of a capacitor. This increasing potential difference drives a current through the cell-cell junctions. The steady state is reached when
the cell induced current is balanced by the leak current. Our model corresponds to an epithelium with high resistivity of lateral membranes where lateral electric currents are negligible. The observed trans-epithelial potentials are of the order of $\Delta \phi_{AD} \simeq 1 - 20 mV$. A naive estimate of the electric potential across the epithelium using Eq. 40 would lead to smaller values. This is because Eq. 40 considers a width of the channel equal to the width of the cell. Values in the $mV$ range can be understood as a consequence of reduced ion conductance across the cell-cell junctions by a geometric factor of about $w/d \simeq 0.05$. In our simplified model variable transport properties in the channel could be represented by changes of the effective ion mobility. Indeed, for reduced values of the ion mobility $K$ in our model, the pumping velocity is not significantly changed while the electric potential approaches $\delta J / (2q\nu)$. This allows us to estimate $\delta J / J_0 \simeq \Delta \phi_{AD} / \Delta \phi_{AB} \simeq 0.02 - 0.2$. The conductance across the cell-cell junction can be estimated based on the electric current per cell of the order of $q\delta J d^2 \simeq 10^{-9} A$, where we use $\delta J \simeq 0.1 J_0$. Then, using the reported transepithelial potential difference of $10 mV$ we obtain the resistance per junction on the order of $10^7 \Omega$. This can be compared to the resistance of a cell-cell junction $k_B T / (q^2 \rho_0 (1 + \theta) v_m w d) \simeq 10^7 \Omega$, which we estimate using linearised Eq. 3 and Eqs. 15, 19, and 20 to describe a narrow channel of width $w$. The relationship between hydraulic pumping and current generation by cells yields a prediction for the ratio of the electric current density and flow velocity $I / \nu \simeq 2q\rho_0 (1 + \theta (1 + \psi)) \simeq 6 \cdot 10^8 C/m^3$ which could be tested experimentally. It will be important to test the accuracy of the simple arguments presented here in a one-dimensional framework using a more realistic two or three-dimensional geometry.

Bending of an epithelium will create a relative difference in cell areas on the two sides of the epithelium $\delta A / A \simeq CL^e$, where $C$ is the epithelium curvature. If the ion pump density is kept constant this leads to an asymmetry in pumping strength is $\delta J_0 / J_0 = \delta A / A$. The transepithelial current due to epithelium bending can be written as $I = \Lambda_4 C$, where $\Lambda_4$ is the flexo-electric coefficient [6]. This current exists even for a symmetric cell layer if bending dynamics is slow compared to the turnover of ion pumps in the membrane. We can estimate it as $I \simeq q\delta J_0$ and find $I \simeq qL^e J_0 C$. Therefore, the flexo-electric coefficient is $\Lambda_4 \simeq qL^e J_0 \simeq 1.6 \cdot 10^{-5} A/m$, consistent with [6], where we used $L^e = 10^{-5} m$ and $J_0 = 10^{19} m^{-2} s^{-1}$.

Here, we have presented a theory of fluid flows and electric currents driven by the ion pumping activity across membranes. We estimated orders of magnitude, relevant to pumping by biological cells. Our theory could be tested in microfluidic experiments. On the tissue scale such currents and flows give rise to electrohydraulic behaviours that could play an important role in tissue morphogenesis and homeostasis [6, 25, 26]. More generally, understanding electrohydraulics and its role in biological processes provides exciting challenges for future work.
Appendix A: Electrostatics of a flowing electrolyte solution

1. Debye-Hückel approximation with flow

Here, we derive the ion density profiles in a flowing electrolyte by linearising the corresponding Nernst-Planck and Poisson equations presented in the main text. We consider a semi-infinite system bounded on one side by a membrane located at \( x = 0 \). Solvent flow is oriented perpendicular to the membrane in the direction of the \( x \)-axis and has magnitude \( v \). We consider the boundary condition at positive infinity \( \rho^\pm(x \to \infty) = \rho_0 \). In presence of a constant electric field \( E(x \to \infty) = E_0 \) at positive infinity the ion number currents are

\[
J^+ = K^+ q E_0 \rho_0 + v \rho_0 \quad \text{(A1)}
\]
\[
J^- = -K^- q E_0 \rho_0 + v \rho_0 \quad \text{(A2)}
\]

The corresponding steady state electric current is \( I = q^2 (K^+ + K^-) \rho_0 E_0 \).

We now linearise the Nernst-Planck and Poisson equations around the state at \( x \to \infty \)

\[
\pm \frac{q \rho_0 E_0}{k_B T} \left( \frac{\delta E}{E_0} + \frac{\delta \rho}{\rho_0} \right) = \partial_x \delta \rho^+ - u^+ \delta \rho^+ \quad , \quad \text{(A3)}
\]
\[
e \partial_x \delta E = q (\delta \rho^+ - \delta \rho^-) \quad , \quad \text{(A4)}
\]

where we have introduced \( \delta E = E - E_0 \), \( \delta \rho^+ = \rho^+ - \rho_0 \) and \( u^\pm = v/(K^+ k_B T) \). By taking a gradient of Eqs. A3 together with Eq. A4 we find

\[
\partial_x^2 \delta \rho^+ - w^+ \partial_x \delta \rho^+ - \frac{1}{2} k_D^2 \delta \rho^+ + \frac{1}{2} k_D^2 \delta \rho^- = 0 \quad , \quad \text{(A5)}
\]
\[
\partial_x^2 \delta \rho^- - w^- \partial_x \delta \rho^- - \frac{1}{2} k_D^2 \delta \rho^- + \frac{1}{2} k_D^2 \delta \rho^+ = 0 \quad , \quad \text{(A6)}
\]

where we have introduced \( w^\pm = u^\pm \pm (q E_0)/(k_B T) \) and the Debye wavevector \( k_D^2 = (2 \rho_0 q^2)/(\epsilon k_B T) \). Using an exponential ansatz \( \delta \rho^\pm \sim e^{kx} \) leads to the equation for the wavevector \( k \)

\[
k^3 - (w^+ + w^-) k^2 + (w^+ w^- - k_D^2) k + \frac{1}{2} (w^+ + w^-) k_D^2 = 0 \quad . \quad \text{(A7)}
\]

As expected, for \( w^+ = w^- = 0 \) the solutions of this equations are \( k_1^{(0)} = 0 \) and \( k_{2,3}^{(0)} = \mp k_D \). In the regime of small solvent velocity and electric field, where \( |w^\pm| \ll k_D \), we find solutions in the form \( k_i = k_i^{(0)} + \delta k_i \), assuming \( \delta k_i \ll k_D \)

\[
k_1 = \frac{u}{2} \quad , \quad \text{(A8)}
\]
\[
k_2 = -k_D + \frac{u}{4} \quad , \quad \text{(A9)}
\]
\[
k_3 = k_D + \frac{u}{4} \quad . \quad \text{(A10)}
\]

Here, \( u = u^+ + u^- \). For \( u < 0 \), corresponding to \( v < 0 \) i.e. solvent flow towards the membrane, the ion number densities are

\[
\delta \rho^+ = A e^{-(k_D^{-1})x} + B e^{2x} \quad , \quad \text{and} \quad \text{w^+} \quad \text{(A11)}
\]
\[
\delta \rho^- = -A \left[ 1 - \frac{w^+ + w^-}{k_D} \right] e^{-(k_D^{-1})x} + B e^{2x} \quad . \quad \text{(A11)}
\]

where Eqs. A3 require \( A^+ = A^- \) and \( B^+ = B^- \). The latter equality demonstrates that the ion density distribution associated with the velocity dependent length-scale \( 2/u \) is neutral, which corresponds to the weak charge imbalance limit we consider in the main text.

2. Ion density and electric potential profiles

We now apply the weak charge imbalance approximation \( |\rho^+ - \rho^-| \ll (\rho^+ + \rho^-) \) to the problem of a single active periodic membrane presented in the main text. We write the Nernst-Planck equations as

\[
J^\pm = k_B T K^\pm \left( \mp \frac{q}{k_B T} \rho \partial_x \phi - \partial_x \rho \right) + v \rho \quad . \quad \text{(A12)}
\]

Eliminating \( \phi \) further yields

\[
\partial_x \rho = \frac{\rho}{\lambda} - \frac{J^+/K^+ + J^-/K^-}{2k_B T} \quad , \quad \text{(A13)}
\]

where \( \lambda = 2k_B T K^+ K^-/(v(K^+ + K^-)) \). Solution of this equation

\[
\rho(x) = \frac{1}{v} \frac{J^+/K^+ + J^-/K^-}{1/K^+ + 1/K^-} + C e^{x} \quad , \quad \text{(A14)}
\]

where \( C \) is an integration constant. Now, we use this result and the difference of the two equations to obtain

\[
\partial_x \phi = \frac{1}{2q} \left[ \frac{1}{v} \left( \frac{1}{K^+} - \frac{1}{K^-} \right) - \frac{J^+/K^+ + J^-/K^-}{\rho(x)} \right] \quad , \quad \text{(A15)}
\]

which is straightforward to integrate and we find
3. Two membranes in a channel

Here we outline the main equations required to solve the system of two active membranes in a periodic channel discussed in the main text. Six equations describing the two active membranes read

\[
\begin{align*}
J^+ &= -J_0 + \delta J + \nu \left( k_B T \ln \left( \frac{\rho_A}{\rho_B} \right) - q (\phi_B - \phi_A) \right) \quad (A17) \\
J^- &= \nu \left( k_B T \ln \left( \frac{\rho_A}{\rho_B} \right) + q (\phi_B - \phi_A) \right) \quad (A18) \\
v &= \bar{\xi} \left( P_A - P_B - 2k_B T \left( \rho_A - \rho_B - \frac{N_R}{2V_\xi} \right) \right) \quad (A19) \\
J^+ &= J_0 + \delta J + \nu \left( k_B T \ln \left( \frac{\rho_C}{\rho_D} \right) - q (\phi_D - \phi_C) \right) \quad (A20) \\
J^- &= \nu \left( k_B T \ln \left( \frac{\rho_C}{\rho_D} \right) + q (\phi_D - \phi_C) \right) \quad (A21) \\
v &= \bar{\xi} \left( P_C - P_D - 2k_B T \left( \rho_C + \frac{N_R}{2V_\xi} - \rho_D \right) \right) \quad (A22)
\end{align*}
\]

Now, we sum the two water flux equations to obtain

\[
\frac{2v}{\bar{\xi}} = P_A - P_D + P_C - P_B - 2k_B T (\rho_A - \rho_B + \rho_C - \rho_D) \quad (A23)
\]

where pressure differences inside and outside of the cell are \( P_A - P_D = -vL^w \eta^w/(a^w)^2 \) and \( P_C - P_B = -vL^w \eta^f/(a^f)^2 \). We expect any pressure difference across the membranes to be negligible as compared to osmotic pressure differences. Therefore, we find

\[
v = -\frac{k_B T}{\bar{\xi}} (\rho_A - \rho_B + \rho_C - \rho_D) \quad , \quad (A24)
\]

where \( 2/\bar{\xi}_2 = 2/\bar{\xi} + L^w \eta^w/(a^w)^2 + L^f \eta^f/(a^f)^2 \). Now, adding up all ion flux equations and applying Eq. (A23) we find

\[
J^+ + J^- = 2v_0 (1 + \theta_2) \quad , \quad (A25)
\]

where \( \theta_2 = K/(\bar{\xi} L \rho_0) \). Note that we do not explicitly account for the osmotic contributions of the resident molecules since they can be included in the term \( \bar{\xi}_2 \), as explained in Appendix A4 below.

We now rewrite the original six membrane equations as remaining five independent equations

\[
\begin{align*}
J^+ + J^- &= \delta J + \nu k_B T \ln \left( \frac{\rho_A \rho_D}{\rho_B \rho_C} \right) \quad (A26) \\
\rho_A + \rho_D &= \rho_B + \rho_C + \frac{N_R}{V_\xi} \quad (A27) \\
\rho_B \rho_C &= \rho_A \rho_D e^{-\frac{2v_0}{k_B T}} \quad (A28) \\
J^+ - J^- &= \delta J + q \nu (\phi_C - \phi_B + \phi_A - \phi_D) \quad (A29) \\
J_0 &= -q \nu (\phi_C + \phi_B - \phi_A - \phi_D) \quad (A30)
\end{align*}
\]

Now, recalling that

\[
\begin{align*}
q (\phi_C - \phi_B) &= \frac{J^+ - J^-}{k_B T} = \left( \ln \left( \frac{\rho_C}{\rho_B} \right) - Pe^\lambda \right) \\
q (\phi_A - \phi_D) &= \frac{J^+ - J^-}{k_B T} = \left( \ln \left( \frac{\rho_A}{\rho_D} \right) - Pe^\lambda \right)
\end{align*}
\]

we find an simple expression for ion number currents difference as a function of solvent velocity

\[
J^+ - J^- = \frac{\nu k_B T \bar{\xi}}{v_0} (1 + \theta_2) v \delta J \quad , \quad (A33)
\]

To obtain analytical solution of these equations we now proceed by considering the limit \( \delta J \ll J_0 \) and \( Pe \ll 1 \) in which we expand ion density profiles to the lowest order and obtain Eqs. 31 and 32 in the main text.

4. Contribution of neutral ion species to osmotic pressure differences

Current of neutral molecules \( J_R \) in a fluid flowing at velocity \( v \) follows

\[
J_R = -k_B T K_R \partial_x \rho_R + v \rho_R \quad , \quad (A34)
\]

where \( \rho_R \) and \( K_R \) are density and mobility of the molecules, respectively. Therefore, their spatial profile is of the form

\[
\rho_R(x) = \frac{J_R}{v} + C_R e^{\frac{x}{\lambda_R}} \quad , \quad (A35)
\]

where \( C_R \) is an integration constant and \( \lambda_R = k_B T K_R/v \). For resident molecules in a cell which cannot leave the cell \( J_R = 0 \) and the ratio of \( \rho_R \) at the two sides of a cell of
length $L^c$ is exp (Pe$_R$), where Pe$_R$ = $L_c/\lambda_R$ is the Peclet number of resident molecules.

Contribution from resident molecules to osmotic pressure differences discussed below Eq. A23 would be represented by a term in Eq. A24 that is linear in fluid velocity

$$k_B T (\rho_R(0) - \rho_R(L^c)) = -k_B T N_R L^c \frac{\xi}{\lambda_R V} = - \frac{v L^c N_R}{K_R V} .$$

(A36)

Therefore, this effect can be absorbed in the effective value of $\xi_2$ as

$$\frac{2}{\xi_2} = \frac{2}{\xi} + \frac{L^w \eta^w}{(\alpha^w)^2} + \frac{L^c \eta^c + N_R L^c}{K_R V} .$$

(A37)

Using $\rho_R \simeq 10^{26}m^{-3}$ (150mM), $L^c \simeq 10^{-5}m$ and mobility of the ion species (which might be too high for large molecules) $K_R \simeq 3 \cdot 10^{11}m^2J^{-1}s^{-1}$ we find $N_R L^c/(K_R V) \simeq 3 \cdot 10^3mPa^{-1}s^{-1}$, which is well below the lowest estimated value of $2/\xi = 2 \cdot 10^{11}$ we use in the main text.

5. Contribution of electroosmotic effects to cellular pumping

Here we take into account electroosmotic effects and we solve the system of equations describing the two active membranes in a periodic channel to estimate their contribution to the overall flow. Six equations that describe the ion and water fluxes across the two membranes read

$$J^+ = -J_0 + \delta J + \nu \left[ k_B T \ln \frac{\rho_A}{\rho_B} - q (\phi_B - \phi_A) \right]$$

(A38)

$$J^- = \nu \left[ k_B T \ln \frac{\rho_A}{\rho_B} + q (\phi_B - \phi_A) \right]$$

(A39)

$$v = \frac{L^w \eta^w}{(\alpha^w)^2} + L^c \eta^c + N_R L^c$$

(A40)

$$v = \frac{L^c \eta^c}{\rho_B} - q (\phi_B - \phi_D)$$

(A41)

$$J^+ = J_0 + \delta J + \nu \left[ k_B T \ln \frac{\rho_C}{\rho_D} - q (\phi_D - \phi_C) \right]$$

(A42)

$$J^- = \nu \left[ k_B T \ln \frac{\rho_C}{\rho_D} + q (\phi_D - \phi_C) \right]$$

(A43)

Bulk solvent flow with electroosmosis are given by

$$v = -(P_C - P_B) \frac{\eta^c L^c}{\eta^c L^c} - \gamma \frac{\phi_C - \phi_B}{L^c} ,$$

(A44)

$$v = -(P_A - P_D) \frac{\eta^w L^w}{\eta^w L^w} ,$$

(A45)

Electric potential differences are given by

$$\frac{q}{k_B T} (\phi_C - \phi_B) = \frac{J^+ + J^-}{J^+ + J^-} \left[ \ln \frac{\rho_C}{\rho_B} - \text{Pe}^c \right]$$

(A46)

$$\frac{q}{k_B T} (\phi_A - \phi_D) = \frac{J^+ + J^-}{J^+ + J^-} \left[ \ln \frac{\rho_A}{\rho_D} - \text{Pe}^w \right]$$

(A47)

Ion density differences are given by

$$\rho_C - \rho_B = \text{Pe}^c \left( \rho_0^c - \frac{J^+ + J^-}{2v} \right)$$

(A48)

$$\rho_A - \rho_D = \text{Pe}^w \left( \rho_0^w - \frac{J^+ + J^-}{2v} \right)$$

(A49)

Sum of ion currents can be written in two ways, first using Eqs. A38, A39, A41 and A42

$$J^+ + J^- = \frac{1}{\alpha_1} \left[ \nu L^c + \delta J \right]$$

(A50)

where

$$\alpha_1 = 1 + \psi^c + \psi^w$$

(A51)

$$\psi_{c,w} = \frac{\nu L^c \eta^c}{2K \rho_0^c}$$

(A52)

and second using Eqs. A40, A43, A48 and A49

$$J^+ + J^- = 2\rho_0 v (1 + \theta_2) + \frac{K N_R}{L^c} \gamma (\phi_C - \phi_B)$$

(A53)

where

$$\theta_2 = \frac{K}{\xi_2 L \rho_0}$$

(A54)

Now, we can write density differences as:

$$\rho_C - \rho_B = \alpha_3 v + \beta_3 \delta J$$

(A55)

$$\rho_A - \rho_D = \alpha_4 v + \beta_4 \delta J$$

(A56)

where

$$\alpha_3 = \frac{\rho_0^c}{TK} \left( L^c - \frac{\psi^c L}{\alpha_1} \right)$$

(A57)

$$\beta_3 = - \frac{L^c}{2TK}$$

(A58)

$$\alpha_4 = \frac{\rho_0^w}{TK} \left( L^w - \frac{\psi^w L}{\alpha_1} \right)$$

(A59)

$$\beta_4 = - \frac{L^w}{2TK}$$

(A60)

Linearising the logarithms of densities in electric potential equations we find

$$J^+ - J^- = \delta J \frac{\alpha_3 v + \beta_3 \delta J}{\alpha_3 v + \beta_3 \delta J}$$

(A61)
where

\[ \alpha_5 = \frac{\nu L}{\alpha_1 K} \quad (A62) \]

\[ \beta_5 = \frac{1}{\alpha_1} \quad (A63) \]

\[ \overline{\alpha}_5 = \frac{\nu L}{K\alpha_1} (\alpha_1 - 1) - \nu T \left( \frac{\alpha_3}{\rho_0} + \frac{\alpha_4}{\rho_0} \right) = \frac{\nu L}{K} \quad (A64) \]

\[ \overline{\beta}_5 = \frac{1}{\alpha_1} - \nu T \left( \frac{\beta_3}{\rho_0} + \frac{\beta_4}{\rho_0} \right) = 1 \quad . \quad (A65) \]

We next note that this leads to a simpler expression

\[ J^+ - J^- = \frac{1}{\alpha_1} \delta J \quad . \quad (A66) \]

Finally, we can use Eq. A46 in Eq. A53 and eliminate ion current sum and difference using Eqs. A50, A61 as well as ion density difference using Eq. A55 to find

\[ v = \frac{1 + \frac{\eta L^r}{2\alpha_1 \rho_0 (1 + \theta_2)} - \frac{\eta L^l}{\delta J}}{2\alpha_1 \rho_0 (1 + \theta_2) - \frac{\eta L^l}{\delta J}} \quad . \quad (A67) \]

Here, the relative contribution from the electroosmosis can be estimated by evaluating \( \eta L^r / (2\alpha_1 \rho_0 L q) \approx 0.025 \), where we have used \( L = L_c \), \( a_c = 5nm \), \( \rho_0 = 5 \times 10^{25} m^{-3} \) and \( \gamma = 10^{-8} m^2/(V s) \). Therefore, we can neglect the contribution of electroosmosis in the calculation of the flow generated by pumping of ions across a membrane.

### Appendix B: Model for ion pumps

We introduce a simple model for ion transport across a membrane that contains active ion pumps. A single pump in this model consist of two membrane states \( A \) and \( B \). Ions can bind from the solution on one side of membrane to the state \( A \) and from the other side of the membrane to the state \( B \). Corresponding binding and unbinding rates \( k_{A,B}^{\text{On}} \) and \( k_{A,B}^{\text{Off}} \) satisfy detailed balance

\[ \frac{\rho_{A,B}^{k_{A,B}^{\text{On}}}}{k_{A,B}^{\text{Off}}} = e^{-\frac{\Delta E_{A,B} - \mu_{A,B}}{k_B T}} \quad , \quad (B1) \]

where \( \Delta E_{A,B} \) are energies of binding to the membrane and \( \mu_{A,B} \) is a chemical potential. We denote the transition rates between states \( A \) and \( B \) as \( r(A \rightarrow B) = r_{AB} \) and \( r(B \rightarrow A) = r_{BA} \). States \( A \) and \( B \) can contain either one or zero ions and therefore there are four possible states of the system \((a,b)\), \(a,b \in \{0,1\}\). Probabilities of finding the system in one of these states are determined by the transition rates

\[ \partial_t P_{0,0} = - (\rho_A k_{A}^{\text{On}} + \rho_B k_{B}^{\text{On}}) P_{0,0} + k_{A}^{\text{Off}} P_{1,0} + k_{B}^{\text{Off}} P_{0,1} \quad (B2) \]

\[ \partial_t P_{1,0} = \rho_A k_{A}^{\text{On}} P_{0,0} - (k_{A}^{\text{Off}} + r_{AB}) P_{1,0} + r_{BA} P_{0,1} + k_{B}^{\text{Off}} P_{1,1} \quad (B3) \]

\[ \partial_t P_{0,1} = \rho_B k_{B}^{\text{On}} P_{0,0} + r_{AB} P_{1,0} - (k_{B}^{\text{Off}} + r_{BA}) P_{0,1} + k_{A}^{\text{Off}} P_{1,1} \quad (B4) \]

\[ \partial_t P_{1,1} = \rho_B k_{B}^{\text{On}} P_{1,0} + \rho_A k_{A}^{\text{On}} P_{0,1} - (k_{A}^{\text{Off}} + k_{B}^{\text{Off}}) P_{1,1} \quad . \quad (B5) \]

This system of equations has 3 degrees of freedom because

\[ P_{0,0} + P_{1,0} + P_{0,1} + P_{1,1} = 1 \quad . \quad (B6) \]

The ion transport rate can be expressed as

\[ J_a = P_{1,0} r_{AB} - P_{0,1} r_{BA} \quad . \quad (B7) \]

In the steady state we find

\[ J_a = k_{A}^{\text{Off}} k_{A}^{\text{On}} r_{AB} - k_{B}^{\text{Off}} k_{B}^{\text{On}} r_{BA} \quad , \quad (B8) \]

For simplicity we consider \( k_{A}^{\text{Off}} = k_{B}^{\text{Off}} \) and \( k_{A}^{\text{On}} = k_{B}^{\text{On}} \)

\[ J_a = \frac{k_{A}^{\text{On}} \rho_{A} r_{AB} - \rho_{B} r_{BA}}{1 + (\rho_A + \rho_B) k_{A}^{\text{On}} \left[ 1 + r_{BA} + r_{AB} \right]} \quad . \quad (B9) \]

Now, we include the electric potential difference across the membrane in the model by specifying transition rates \( r_{AB} \) and \( r_{BA} \). When pumps in the membrane are not active and the membrane is in thermodynamic equilibrium,
the transition rates satisfy

\[ r_{eq}^{AB} = e^{-\frac{\varphi_A - \varphi_B}{k_B T}}, \]

(B10)

where \( \varphi_{AB} \) are electric potentials at the two sides of membrane.

To specify the absolute values of equilibrium rates we introduce a parameter \( r_0 \)

\[ r_{eq}^{AB} = r_0 e^{-\frac{\varphi_A - \varphi_B}{k_B T}}, \]

\[ r_{eq}^{BA} = r_0 e^{\frac{\varphi_B - \varphi_A}{k_B T}}. \]

(B11)

(B12)

Consumption of fuel by the ion pumps produces an additional contribution to the transition rates

\[ r_{AB} = r_0 e^{-\frac{\varphi_B - \varphi_A}{k_B T}} + r_0 e^{\frac{\varphi_B - \varphi_A}{k_B T}} + \frac{\Delta \mu_{ATP}}{r_B T}, \]

\[ r_{BA} = r_0 e^{-\frac{\varphi_B - \varphi_A}{k_B T}} + r_0 e^{\frac{\varphi_B - \varphi_A}{k_B T}} - \frac{\Delta \mu_{ATP}}{r_B T}. \]

(B13)

(B14)

Here, \( \Delta \mu_{ATP} \) is the energy released by consumption of an ATP molecule and \( r_\alpha \) sets the magnitude of active pumping rate.

The description of ion pumping by Eq. 7 corresponding to a saturated regime, where the pumping rate is insensitive to \( \Delta \mu_{ATP} \). Such regime is obtained when transport is strongly biased, \( \rho_A r_{AB} \gg \rho_B r_{BA} \) and \( r_{AB} \gg r_{BA} \), and transport is limited by the ion unbinding rate, \( (\rho_A + \rho_B)k_{On}/k_{Off} \gg 1 \) together with \( (r_{AB} + r_{BA})/k_{Off} \gg 1 \). In this limit we find

\[ J_a \approx \frac{\rho_A}{\rho_A + \rho_B} k_{Off} \simeq \frac{1}{2} k_{Off}. \]

(B15)

We use this equation as an approximation for physiological conditions where \( \rho_A \approx \rho_B \) and \( r_{AB} \gg r_{BA} \). The latter follows from \( \varphi_B - \varphi_A \ll \Delta \mu_{ATP} \) using the physiological values. The ion pump strengths in Eq. 7 are therefore \( J_a^\pm = \sigma^\pm J_a^\pm \), where \( \sigma^\pm \) are ion pump area densities and \( J_a^\pm \) ion transport rates.

[1] Alan L Hodgkin and Andrew F Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. The Journal of physiology, 117(4):500, 1952.

[2] Marco Piccolino. Luigi galvani’s path to animal electricity. Comptes Rendus Biologies, 329(5-6):303–318, May 2006.

[3] Y. Zhang and A.L. Greer. Thickness of shear bands in metallic glasses. Appl. Phys. Lett., 89(7):071907, 2006.

[4] Ernest Latorre, Sohan Kale, Laura Casares, Manuel Gómez-González, Marina Uroz, Léo Valon, Rosshna V. Nair, Elena Garreta, Nuria Montserrat, Aránzazu del Campo, and et al. Active superelasticity in three-dimensional epithelia of controlled shape. Nature, 563(7730):203–208, Nov 2018.

[5] Alexis Pietak and Michael Levin. Bioelectrical control of positional information in development and regeneration: A review of conceptual and computational advances. Progress in Biophysics and Molecular Biology, 137:52–68, Sep 2018.

[6] Charlie Duchut, Niladri Sarkar, Jacques Prost, and Frank Jülicher. Fluid pumping and active flexoelectricity can promote lumen nucleation in cell assemblies. Proceedings of the National Academy of Sciences, 116(39):19264–19273, Sep 2019.

[7] Ben Greenebaum and Frank Baros. Bioengineering and biophysical aspects of electromagnetic fields. CRC press, 2018.

[8] Erwin Neher and Bert Sakmann. Single-channel currents recorded from membrane of denervated frog muscle fibres. Nature, 260(5554):799–802, Apr 1976.

[9] Philip Nelson. Biological physics. WH Freeman New York, 2004.

[10] William Bialek. Biophysics: searching for principles. Princeton University Press, 2012.

[11] Sriram Ramaswamy, John Toner, and Jacques Prost. Nonequilibrium fluctuations, traveling waves, and instabilities in active membranes. Physical Review Letters, 84(15):3494–3497, Apr 2000.

[12] Yizeng Li, Yoichiro Mori, and Sean X. Sun. Flow-driven cell migration under external electric fields. Physical Review Letters, 115(26), Dec 2015.

[13] A.M. Weinstein and J.L. Stephenson. Electrolyte transport across a simple epithelium. steady-state and transient analysis. Biophysical Journal, 27(2):165–186, Aug 1979.

[14] S. Marbach and L. Bocquet. Active osmotic exchanger for efficient nanofiltration inspired by the kidney. Physical Review X, 6(031008), 2016.

[15] Sabyasachi Dasgupta, Kapish Gupta, Yue Zhang, Virgile Viasnoff, and Jacques Prost. Physics of lumen growth. Proceedings of the National Academy of Sciences, 115(21):E4751–E4757, May 2018.

[16] Feiran Huang, David Rabson, and Wei Chen. Distribution of the na/k pumps’ turnover rates as a function of membrane potential, temperature, and ion concentration gradients and effect of fluctuations. The Journal of Physical Chemistry B, 113(23):8096–8102, Jun 2009.

[17] Jorge Fischbarg. Fluid transport across leaky epithelia: Central role of the tight junction and supporting role of aquaporins. Physiological Reviews, 90(4):1271–1290, Oct 2010.

[18] K. Olbrich, W. Rawicz, D. Needham, and E. Evans. Water permeability and mechanical strength of polynonsaturated lipid bilayers. Biophysical Journal, 79(1):321–327, Jul 2000.

[19] Alejandro Torres-Sánchez, Max Kerr Winter, and Guillame Salmon. Tissue hydraulics: Physics of lumen formation and interaction. Cells & Development, 168:203724, Dec 2021.

[20] M. Belgrave, G.P. Brittingham, S. Pfeffer, I.V. Surovtsev, S. Pinglay, K.J. Kennedy, M. Schaffer, J.I. Gutierrez, D. Sang, G. Poterewicz, J.K. Chung, J.M. Plitzko, J.T. Groves, C. Jacobs-Wagner, B.D. Engel, and L.J. Holt. mtorc1 controls phase separation and the biophysical properties of the cytoplasm by tuning crowding. Cell,
[21] Greg M. Allen, Alex Mogilner, and Julie A. Theriot. Electrophoresis of cellular membrane components creates the directional cue guiding keratocyte galvanotaxis. Current Biology, 23(7):560–568, Apr 2013.

[22] Thuan Beng Saw, Xumei Gao, Muchun Li, Jianan He, Anh Phuong Le, Supatra Marsh, Keng-hui Lin, Alexander Ludwig, Jacques Prost, and Chwee Teck Lim. Transepithelial potential difference governs epithelial homeostasis by electromechanics. Nature Physics, 18(9):1122–1128, Sep 2022.

[23] Mohammad Ikbal Choudhury, Yizeng Li, Panagiotis Mistriotis, Eryn E. Dixon, Jing Yang, Debonil Maity, Rebecca Walker, Morgen Benson, Leigha Martin, Fatima Koroma, Feng Qian, Konstantinos Konstantopoulos, Owen M. Woodward, and Sean X. Sun. Trans-epithelial fluid pumping performance of renal epithelial cells and mechanics of cystic expansion. bioRxiv, 2019.

[24] Steffen S Madsen, Morten B Engelund, and Christopher P Cutler. Water transport and functional dynamics of aquaporins in osmoregulatory organs of fishes. The Biological Bulletin, 229(1):70–92, 2015.

[25] Lin Cao, Colin D McCaig, Roderick H Scott, Siwei Zhao, Gillian Milne, Hans Clevers, Min Zhao, and Jin Pu. Polarizing intestinal epithelial cells electrically through ror2. Journal of Cell Science, page jcs.146357, Jan 2014.

[26] Jacob M. Daane, Jennifer Lanni, Ina Rothenberg, Guiscard Seebohm, Charles W. Higdon, Stephen L. Johnson, and Matthew P. Harris. Bioelectric-calcineurin signaling module regulates allometric growth and size of the zebrafish fin. Scientific Reports, 8(1):10391, Dec 2018.

[27] Daniel Riveline, Albrecht Ott, Frank Jülicher, Donald A Winkelmann, Olivier Cardoso, Jean-Jacques Lacapère, Soffia Magnúsdóttir, Jean-Louis Viovy, Laurence Gorret-Talini, and Jacques Prost. Acting on actin: the electric motility assay. page 6.