

Supplementary Material

A thermodynamically consistent approach to modelling epithelial solute and water transport in the proximal convoluted tubule

Leyla Noroozbabae*, Jarrah M. Dowrick, Pablo J. Blanco, David P. Nickerson

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*Corresponding author: MERLN Institute for Technology-Inspired Regenerative Medicine, Maastricht University, Maastricht, The Netherlands; leyla.noroozbabae@maastrichtuniversity.nl.

In this supplementary material, we include further details on the BG-PCT model membrane fluxes and present information on the full simulation experiments used to produce the results presented in the main manuscript.

Transporter fluxes: Coupled solute fluxes

Coupled solute fluxes in this model fall into three categories: *simple co-transporters*, *simple exchangers*, and *complex exchangers*. These transporters are described using linear non-equilibrium thermodynamics, where solute permeation rates are proportional to the electrochemical driving force of the aggregate species, with a single permeation coefficient.

Simple co-transporters

Examples include the peritubular K^+/Cl^- co-transporter and the luminal Na^+ /Glucose co-transporter, where the fluxes of the two species across the co-transporter follow a 1:1 stoichiometry. The fluxes through these transporters are defined as:

$$\begin{bmatrix} J_{IS}^{K^+} \\ J_{IS}^{Cl^-} \end{bmatrix} = L_{(K^+, Cl^-)} \begin{bmatrix} 1 & 1 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} \bar{\mu}_{IS}^{K^+} \\ \bar{\mu}_{IS}^{Cl^-} \end{bmatrix}, \quad (S1)$$

$$\begin{bmatrix} J_{MI}^{Na^+} \\ J_{MI}^{Gluc} \end{bmatrix} = L_{(Na^+, Gluc)} \begin{bmatrix} 1 & 1 \\ 1 & 1 \end{bmatrix} \begin{bmatrix} \bar{\mu}_{MI}^{Na^+} \\ \bar{\mu}_{MI}^{Gluc} \end{bmatrix}. \quad (S2)$$

Simple exchangers

An example is the Cl^-/HCO_3^- exchanger, defined as:

$$\begin{bmatrix} J_{MI}^{Cl^-} \\ J_{MI}^{HCO_3^-} \end{bmatrix} = L_{(Cl^-, HCO_3^-)} \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix} \begin{bmatrix} \bar{\mu}_{MI}^{Cl^-} \\ \bar{\mu}_{MI}^{HCO_3^-} \end{bmatrix}. \quad (S3)$$

Complex exchangers

Examples include the peritubular Na^+/HCO_3^- and $Na^+/2HCO_3^-/Cl^-$ exchangers, represented as:

$$\begin{bmatrix} J_{IS}^{\text{Na}^+} \\ J_{IS}^{\text{HCO}_3^-} \end{bmatrix} = L_{(\text{Na}^+, \text{HCO}_3^-)} \begin{bmatrix} 1 & 3 \\ 3 & 9 \end{bmatrix} \begin{bmatrix} \bar{\mu}_{IS}^{\text{Na}^+} \\ \bar{\mu}_{IS}^{\text{HCO}_3^-} \end{bmatrix}. \quad (\text{S4})$$

Transporter fluxes: Active solute fluxes

The model includes one ATPase: the peritubular Na^+/K^+ -ATPase, which exchanges three cytosolic Na^+ ions for two peritubular K^+ ions. The fluxes due to Na^+/K^+ -ATPase activity are:

$$J_{\alpha\beta}^{\text{NaK}} = L_{(\text{NaK})} \left(D_{\alpha\beta}^{\text{ATP}} - 3 \Delta \bar{\mu}_{\alpha\beta}^{\text{Na}^+} + 2 \Delta \bar{\mu}_{\alpha\beta}^{\text{K}^+} \right), \quad (\text{S5})$$

$$J_{\alpha\beta}^{\text{NaK-Na}^+} = 3 J_{\alpha\beta}^{\text{NaK}}, \quad (\text{S6})$$

$$J_{\alpha\beta}^{\text{NaK-K}^+} = -2 J_{\alpha\beta}^{\text{NaK}}. \quad (\text{S7})$$

Simulation parameters

A collection of tables detailing the initial conditions, boundary conditions, and parameter values used in all simulations.

Table S1: Global constants used in the bond graph model of the proximal convoluted tubule (BG-PCT).

Constant	Definition	Value	Unit
R	Universal gas constant	8.314	$\text{J mol}^{-1} \text{K}^{-1}$
T	Temperature	273.15	K
F	Faraday's constant	96.5×10^3	C mol^{-1}
z^{Na^+}	Na^+ valency	+1	—
z^{K^+}	K^+ valency	+1	—
z^{Cl^-}	Cl^- valency	-1	—
$z^{\text{HCO}_3^-}$	HCO_3^- valency	-1	—
z^{Gluc}	Glucose valency	0	—

Table S2: Membrane property parameter values and initial conditions. ME = mucosal–epithelial, MI = mucosal–interstitial, IE = interstitial–epithelial, ES = epithelial–serosal, IS = interstitial–serosal.

Parameter	ME	MI	IE	ES	IS
<i>Membrane area</i> [$\text{cm}^2 / \text{cm}^2_{\text{epithelial}}$]					
$A_{\alpha\beta}$	0.001	36.0	36.0	2.0×10^{-2}	1.0
<i>Hydraulic permeability</i> $\times RT$ [$\text{cm s}^{-1} \text{Osmol}^{-1}$]					
$L_{\alpha\beta}^v$	4.0×10^0	2.0×10^{-4}	2.0×10^{-4}	6.0×10^0	2.0×10^{-4}
<i>Permeability coefficient</i> $\omega_{\alpha\beta}^s$ [cm s^{-1}]					
Na^+	2.6×10^{-2}	0	3.9×10^{-9}	5.0×10^{-2}	1.0
K^+	2.9×10^{-1}	2.5×10^{-7}	2.0×10^{-6}	7.0×10^{-2}	2.0×10^{-6}
Cl^-	1.0×10^0	0	0	6.0×10^{-2}	0
HCO_3^-	8.0×10^{-2}	1.0×10^{-8}	0	5.0×10^{-2}	0
Glucose	1.6×10^{-2}	0	7.5×10^{-6}	3.0×10^{-2}	7.5×10^{-6}
<i>Reflection coefficient</i> $\sigma_{\alpha\beta}^s$					
Na^+	0.75	1.0	1.0	0.0	1.0
K^+	0.60	1.0	1.0	0.0	1.0
Cl^-	0.30	1.0	1.0	0.0	1.0
HCO_3^-	0.90	1.0	1.0	0.0	1.0
Glucose	1.0	1.0	1.0	0.0	1.0
<i>Coupled transport pathways</i> [$\text{mol}^2 \text{J}^{-1} \text{s}^{-1} \text{cm}^{-2}$]					
$\text{K}^+ - \text{Cl}^-$	—	—	6.5×10^{-5}	—	5.0×10^{-7}
$\text{Na}^+ - 2\text{HCO}_3^- / \text{Cl}^-$	—	—	1.0×10^{-7}	—	5.0×10^{-7}
$\text{Na}^+ - 3\text{HCO}_3^-$	—	—	5.0×10^{-11}	—	5.0×10^{-10}
$\text{Na}^+ - \text{Glucose}$	—	5.0×10^{-11}	—	—	—
$\text{Cl}^- / \text{HCO}_3^-$	—	2.0×10^{-9}	—	—	—
<i>Active transport</i> [$\text{mol}^2 \text{J}^{-1} \text{s}^{-1} \text{cm}^{-2}$]					
$\text{Na}^+ / \text{K}^+ - \text{ATPase}$	—	—	6.0×10^{-11}	—	1.0×10^{-9}

Table S3: Compartment property parameter values and initial conditions. M = mucosal, E = epithelial, I = interstitial, S = serosal.

Parameter	M	E	I	S
<i>Concentration c_α^s [mol/L]</i>				
Na ⁺	0.14	0.14	0.02	0.14
K ⁺	4.9×10^{-3}	4.6×10^{-3}	0.10	4.9×10^{-3}
Cl ⁻	1.7×10^{-2}	0.11	1.6×10^{-2}	0.113
HCO ₃ ⁻	0.024	2.0×10^{-2}	1.5×10^{-3}	0.024
Glucose	0.005	7.7×10^{-3}	2.4×10^{-2}	0.005
<i>Electrical potential [mV]</i>				
ψ_α	Eq. 20	Variable	Variable	0.0
<i>Hydrostatic pressure [mmHg]</i>				
p_α^0	15.0	-0.1	15.0	9.0