A simple time-dependent kidney model

Chanoknun Sintavanuruk

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Outline

Model equations

Non-dimensionalization

Simulation

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Compartments

Multiphasic medulla on the domain $(0, L)$ (superficial $\rightarrow$ deep).

1. Combined interstitium-vascular compartment
2. Descending tubule
3. Ascending tubule
4. Collecting tubule

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$$\sum_k \alpha_k = \alpha_* \tag{1.1}$$

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$$\frac{\partial \alpha_k}{\partial t} + \frac{\partial}{\partial x}(\alpha_k u_k) = -\gamma_k w_k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{1.2}$$

$$\frac{\partial \alpha_0}{\partial t} + \frac{\partial}{\partial x}(\alpha_0 u_0) = \sum_{k=\mathrm{D,A,C}} \gamma_k w_k. \tag{1.3}$$

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Water flow and transport

Poiseuille's equation:

$$\frac{\rho_k u_k}{\alpha_k} = -\frac{\partial p_k}{\partial x}, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{1.4}$$

Water transport:

$$w_k := \zeta_{\mathrm{w}}^k \left(\psi_k - \psi_0\right), \quad \psi_k := p_k - \pi_k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C} \tag{1.5}$$

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Osmotic pressure:

$$\pi_k := \sum_{i=\mathrm{s},\mathrm{u}} c_i^k + \frac{a_k}{\alpha_k}, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}. \tag{1.6}$$

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Pressure-compliance relationship

$$\nu_k(p_k - p_0) = \frac{\alpha_k}{\bar{\alpha}_k} - 1, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{1.7}$$

p_0 is determined by the constaint total volume density (1.1).

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Solute dynamics

Only salt and urea

$$
\frac{\partial}{\partial t}\left(\alpha_k c_i^k\right) = -\frac{\partial}{\partial x} f_i^k - \gamma_k g_i^k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{1.8}
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Axial solute flow:

$$f_i^k := -\alpha_k D_i^k \frac{\partial c_i^k}{\partial x} + \alpha_k u_k c_i^k, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{1.10}$$

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solute transport

$$g_i^k := j_i^k + h_i^k, \tag{1.11}$$

$$j_i^k = \zeta_i^k \left(\mu_i^k - \mu_i^0\right), \quad , \tag{1.12}$$

$$\mu_i^k := RT \ln c_i^k, \tag{1.13}$$

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Boundary condition: interstitium

No flux at the bottom:

$$u_0(t, L) = 0, \tag{1.14}$$

$$f_i^0(t, L) = 0, \quad i = \mathrm{s}, \mathrm{u}. \tag{1.15}$$

~~Advective~~ flow at the top:

$$\xcancel{\begin{aligned}(\alpha_0 u_0)(t, 0) &= \min\left\{0, \frac{P_\mathrm{v} - p_0(t,0)}{R_\mathrm{v}}\right\}, \\ f_i^0(t, 0) &= (\alpha_0 u_0 c_i^0)(t, 0), \quad i = \mathrm{s}, \mathrm{u}.\end{aligned}}$$

$$p_0(t, 0) = P_\mathrm{v}(t), \tag{1.16}$$

$$c_i^0(t, 0) = c_i^\mathrm{v}(t). \tag{1.17}$$

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$$p_0(t, 0) = P_\mathrm{v}(t), \tag{1.16}$$

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Boundary condition: input from PCT

$$(\alpha_{\mathrm{D}} u_{\mathrm{D}})(t,0) = \overset{\text{end PCT flow}}{\cancel{\mathrm{GFR}(t)}}, \tag{1.18}$$

$$\cancel{f_i^{\mathrm{D}}(t,0) = (\alpha_{\mathrm{D}} u_{\mathrm{D}} c_i^{\mathrm{D}})(t,0), \qquad i = \mathrm{s}, \mathrm{u}}$$

$$\cancel{c_i^{\mathrm{D}}(t,0) = c_i^{\mathrm{filtrate}}(t)}$$

$$c_i^{\mathrm{D}}(t,0) = c_i^{\mathrm{end\ PCT}}(t) \tag{1.19}$$

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$$c_i^{\mathrm{D}}(t,0) = c_i^{\mathrm{end\ PCT}}(t) \tag{1.19}$$

Boudnary condition: couplings

$$(\alpha_{\mathrm{D}} u_{\mathrm{D}} + \alpha_{\mathrm{A}} u_{\mathrm{A}})(t, L) = 0, \tag{1.20}$$

$$\left(f_i^{\mathrm{D}} + f_i^{\mathrm{A}}\right)(t, L) = 0, \tag{1.21}$$

$$p_{\mathrm{D}}(t, L) = p_{\mathrm{A}}(t, L), \tag{1.22}$$

$$c_i^{\mathrm{D}}(t, L) = c_i^{\mathrm{A}}(t, L) \tag{1.23}$$

$$(\alpha_{\mathrm{A}} u_{\mathrm{A}} + \alpha_{\mathrm{C}} u_{\mathrm{C}})(t, 0) = \cancel{0}\ r_{\mathrm{w}}(t), \tag{1.24}$$

$$\left(f_i^{\mathrm{A}} + f_i^{\mathrm{C}}\right)(t, 0) = \cancel{0}\ r_i(t), \tag{1.25}$$

$$\cancel{p_{\mathrm{A}}(t, 0)} = \cancel{p_{\mathrm{C}}(t, 0)}\ \frac{\partial c_i^{\mathrm{C}}}{\partial x}(t, 0) = 0 \quad \text{or} \tag{1.26}$$

$$\cancel{c_i^{\mathrm{A}}(t, 0)} = \cancel{c_i^{\mathrm{C}}(t, 0)} \quad c_i^{\mathrm{C}}(t, 0) = c_i^{\text{end DCT}}(t)?.$$

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Boudnary condition: couplings

$(\alpha_{\mathrm{D}} u_{\mathrm{D}} + \alpha_{\mathrm{A}} u_{\mathrm{A}})(t, L) = 0,$ (1.20)
$\left(f_i^{\mathrm{D}} + f_i^{\mathrm{A}}\right)(t, L) = 0,$ (1.21)
$p_{\mathrm{D}}(t, L) = p_{\mathrm{A}}(t, L),$ (1.22)
$c_i^{\mathrm{D}}(t, L) = c_i^{\mathrm{A}}(t, L)$ (1.23)
$(\alpha_{\mathrm{A}} u_{\mathrm{A}} + \alpha_{\mathrm{C}} u_{\mathrm{C}})(t, 0) = \cancel{0}\ r_{\mathrm{w}}(t),$ (1.24)
$\left(f_i^{\mathrm{A}} + f_i^{\mathrm{C}}\right)(t, 0) = \cancel{0}\ r_i(t),$ (1.25)
$\cancel{p_{\mathrm{A}}(t, 0)} = \cancel{p_{\mathrm{C}}(t, 0)}\ \frac{\partial c_i^{\mathrm{C}}}{\partial x}(t, 0) = 0 \quad \text{or}$ (1.26)
$\cancel{c_i^{\mathrm{A}}(t, 0)} = \cancel{c_i^{\mathrm{C}}(t, 0)} \quad c_i^{\mathrm{C}}(t, 0) = c_i^{\text{end DCT}}(t)?.$

Boundary condition: papillary outflow

$$\cancel{(\alpha_{\mathrm{C}} u_{\mathrm{C}})(t, L) = \max\left\{0, \frac{p_{\mathrm{C}}(t, L) - P_{\mathrm{p}}}{R_{\mathrm{p}}}\right\},}$$
$$\cancel{f_i^{\mathrm{C}}(t, L) = (\alpha_{\mathrm{C}} u_{\mathrm{C}} c_i^{\mathrm{C}})(t, L), \qquad i = \mathrm{s}, \mathrm{u}.}$$

$$(\alpha_{\mathrm{C}} u_{\mathrm{C}})(t, L) = (\alpha_{\mathrm{D}} u_{\mathrm{D}})(t, 0) - r_w(t) + (\alpha_0 u_0)(t, 0), \tag{1.27}$$
$$\frac{\partial c_i^{\mathrm{C}}}{\partial x}(t, L) = 0. \tag{1.28}$$

Problem: can $\alpha_{\mathrm{C}} u_{\mathrm{C}}(t, L) < 0$?

Boundary condition: papillary outflow

$(\alpha_{\mathrm{C}} u_{\mathrm{C}})(t, L) = (\alpha_{\mathrm{D}} u_{\mathrm{D}})(t, 0) - r_w(t) + (\alpha_0 u_0)(t, 0),$ (1.27)
$\frac{\partial c_i^{\mathrm{C}}}{\partial x}(t, L) = 0.$ (1.28)

Problem: can $\alpha_{\mathrm{C}} u_{\mathrm{C}}(t, L) < 0$?

Non-dimensionalization

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Rescaling

$$x = L\hat{x}, \quad t = \frac{L^2}{D_*}\hat{t}, \tag{2.1}$$

Unknowns:

$$\alpha_k = \bar{\alpha}\hat{\alpha}, \quad c_i^k = c_* \hat{c}_i^k, \quad p_k = p_* \hat{p}_k, \tag{2.2}$$

Dimensionless model

$$\frac{\partial \hat{\alpha}_k}{\partial \hat{t}} + \mathrm{Pe}\frac{\partial}{\partial \hat{x}}\left(\hat{\alpha}_k \hat{u}_k\right) = -\hat{w}_k, \tag{2.3}$$

$$\frac{\partial \hat{\alpha}_0}{\partial \hat{t}} + \mathrm{Pe}\frac{\partial}{\partial \hat{x}}\left(\hat{\alpha}_0 \hat{u}_0\right) = \sum_k \hat{w}_k, \tag{2.4}$$

$$\hat{\nu}_k\left(\hat{p}_k - \hat{p}_0\right) = \frac{\hat{\alpha}_k}{\bar{\hat{\alpha}}_k} - 1, \tag{2.5}$$

$$\hat{\alpha}_0 + \sum_k \hat{\alpha}_k = \hat{\alpha}_*, \tag{2.6}$$

$$\frac{\partial}{\partial \hat{t}}\left(\hat{\alpha}_k \hat{c}_i^k\right) = -\frac{\partial}{\partial \hat{x}}\hat{f}_i^k - \hat{g}_i^k, \tag{2.7}$$

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Dimensionless flows and transports

$$\hat{u}_{\cdot} := -\frac{\hat{\alpha}_{\cdot}}{\hat{\rho}_{\cdot}}\frac{\partial \hat{p}_{\cdot}}{\partial \hat{x}}, \tag{2.9}$$

$$\hat{f}_i := -\hat{\alpha}_{\cdot}\hat{D}_{\cdot}\frac{\partial \hat{c}_i^{\cdot}}{\partial \hat{x}} + \mathrm{Pe}(\hat{\alpha}_{\cdot}\hat{u}_{\cdot}\hat{c}_i^{\cdot}), \tag{2.10}$$

$$\hat{w}_k := \hat{\zeta}_{\mathrm{w}}^k\left(\hat{\psi}_k - \hat{\psi}_0\right), \quad \hat{\psi}_{\cdot} := \hat{p}_{\cdot} - \hat{\pi}_{\cdot}, \quad \hat{\pi}_{\cdot} := \frac{\hat{a}_{\cdot}}{\hat{\alpha}_{\cdot}} + \sum_i \hat{c}_i^{\cdot}, \tag{2.11}$$

$$\hat{g}_i^k := \hat{j}_i^k + \hat{h}_i^k, \quad \hat{j}_i^k := \hat{\zeta}_i^k(\hat{\mu}_i^k - \hat{\mu}_i^0), \quad \hat{\mu}_i^{\cdot} := \ln \hat{c}_i^{\cdot} \tag{2.12}$$

for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$ and $i = \mathrm{s}, \mathrm{u}$.

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for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$ and $i = \mathrm{s}, \mathrm{u}$.

Parameters

$$\mathrm{Pe} = \frac{\bar{\alpha} p_* / \rho_*}{D_*}, \quad \hat{\rho}_{\cdot} = \frac{\rho_{\cdot}}{\rho_*}, \quad \hat{\nu}_k = p_* \nu_k, \quad \hat{\bar{\alpha}}_{\cdot} = \frac{\bar{\alpha}_{\cdot}}{\bar{\alpha}}, \quad \hat{\alpha}_* = \frac{\alpha_*}{\bar{\alpha}} \tag{2.13}$$

$$\hat{a}_{\cdot} = \frac{a_{\cdot}}{\bar{\alpha} c_*}, \quad \hat{D}_{\cdot} = \frac{D_{\cdot}}{D_*}, \quad \hat{\zeta}_{\mathrm{w}}^k = \frac{\gamma_k c_* L^2}{\bar{\alpha} D_*} \zeta_{\mathrm{w}}^k, \quad \hat{\zeta}_i^k = \frac{\gamma_k R T L^2}{\bar{\alpha} c_* D_*} \zeta_i^k, \tag{2.14}$$

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Simulation

Simulation

Specification

- $\alpha_* \equiv 1$, $\bar{\alpha}_k = 1/4$, and $\nu_k = 0.01$ for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$.
- Suppose that $D_{\mathrm{s}}^k = D_{\mathrm{u}}^k = 1$, $\mathrm{Pe} = 20$, $\rho_k = 1$ for all k
- Only immobile solute in the interstitium, i.e., $a_0 = 1/2$ and $a_k = 0$.
- $R_{\mathrm{v}} = R_{\mathrm{p}} = 1$ and $P_{\mathrm{v}} = P_{\mathrm{p}} = 1$

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- $R_{\mathrm{v}} = R_{\mathrm{p}} = 1$ and $P_{\mathrm{v}} = P_{\mathrm{p}} = 1$

Solute transports

Passive transport of salt only in the descending and the ascending tubules: $\zeta_{\mathrm{s}}^{\mathrm{D}} = \zeta_{\mathrm{s}}^{\mathrm{A}} = 1$ and $\zeta_{\mathrm{s}}^{\mathrm{C}} = 0$.

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Active transport:

$$h_s^A = \begin{cases} h_* c_s^A, & \text{in} \quad (0, \tfrac{1}{2}), \\ 0 & \text{in} \quad [\tfrac{1}{2}, 1), \end{cases} \tag{3.1}$$

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Active transport:

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Urea permeable in the inner medulla: $\zeta_{\mathrm{u}}^{k} = 10$ for all k and $x \in (\frac{1}{2}, 1)$ and $\zeta_{\mathrm{u}}^{k} = 0$ elsewhere.

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High water permeability in the descending tubule, $\zeta_{\mathrm{w}}^{\mathrm{D}} = 100$, while the ascending tubule is completely insulated: $\zeta_{\mathrm{w}}^{\mathrm{A}} = 0$.

Solute transports

Passive transport of salt only in the descending and the ascending tubules: $\zeta_{\mathrm{s}}^{\mathrm{D}} = \zeta_{\mathrm{s}}^{\mathrm{A}} = 1$ and $\zeta_{\mathrm{s}}^{\mathrm{C}} = 0$.

Active transport:

$$h_{\mathrm{s}}^{\mathrm{A}} = \begin{cases} h_* c_{\mathrm{s}}^{\mathrm{A}}, & \text{in} \quad (0, \frac{1}{2}), \\ 0 & \text{in} \quad [\frac{1}{2}, 1), \end{cases} \tag{3.1}$$

Urea permeable in the inner medulla: $\zeta_{\mathrm{u}}^{k} = 10$ for all k and $x \in (\frac{1}{2}, 1)$ and $\zeta_{\mathrm{u}}^{k} = 0$ elsewhere.

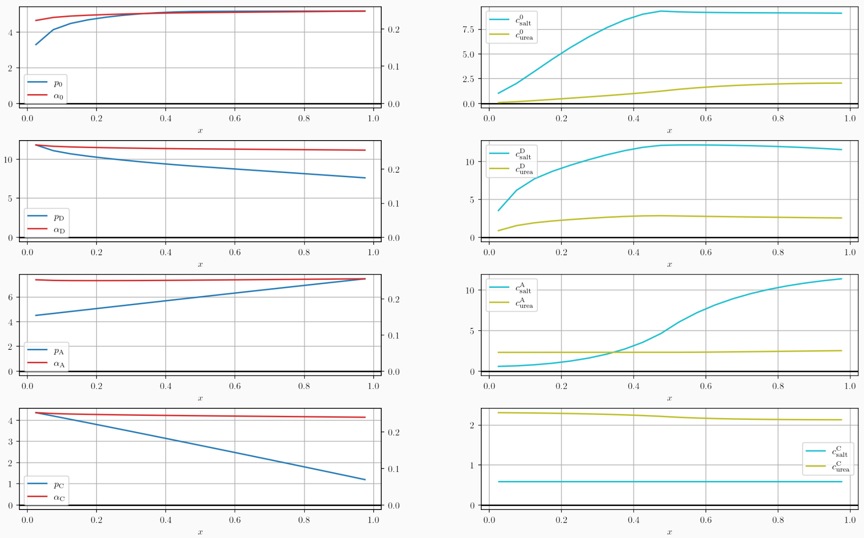
High water permeability in the descending tubule, $\zeta_{\mathrm{w}}^{\mathrm{D}} = 100$, while the ascending tubule is completely insulated: $\zeta_{\mathrm{w}}^{\mathrm{A}} = 0$.

ADH on/off

- ADH on: $\zeta_{\mathrm{w}}^{\mathrm{C}} = 0$
- ADH off: $\zeta_{\mathrm{w}}^{\mathrm{C}} = 50$

ADH on/off
- ADH on: $\zeta_{\mathrm{w}}^{\mathrm{C}} = 0$
- ADH off: $\zeta_{\mathrm{w}}^{\mathrm{C}} = 50$

ADH off



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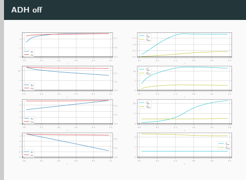
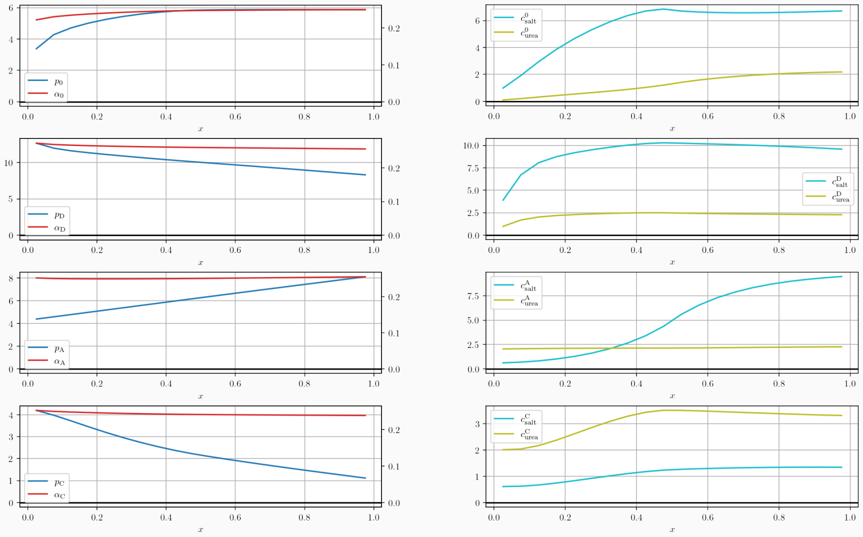


ADH on



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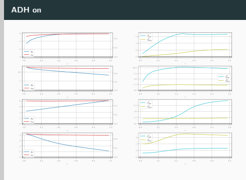
Simulation

ADH on



References i

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Simulation

References

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