A simple time-dependent model of kidney

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1 Model equations

In this model, we consider the medulla of the kidney as a multiphasic continuum consisting of luminal compartments of nephrons and a single combined interstitium-vessel compartment, which we will refer to as simply the interstitium. We assume that there is no variation across the medullary tissue of the same depth so that the model can be represented in a one-dimensional spatial domain $(0, L)$, where $x = 0$ is the most superficial part of the outer medulla. Further, we suppose that the population of nephrons is homogeneous, so that we have three distinct luminal compartments: the descending tubules, the ascending tubules, and the collecting tubules.

For each compartment, the occupied volume is given by the volume density (per unit depth) α_k, as a function of space and time, where we use k to identify the compartment; $k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}$ are for the interstitium, the descending, ascending, and collecting tubules respectively. By assuming the total volume of the medulla is constant, we have

$$\sum_k \alpha_k = \alpha_* \tag{1}$$

where $\alpha_* : (0, L) \to \mathbb{R}_+$ is the total volume density of the medulla.

The dynamics of α_k are given by

$$\frac{\partial \alpha_k}{\partial t} + \frac{\partial}{\partial x}(\alpha_k u_k) = -\gamma_k w_k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{2}$$

$$\frac{\partial \alpha_0}{\partial t} + \frac{\partial}{\partial x}(\alpha_0 u_0) = \sum_{k=\mathrm{D},\mathrm{A},\mathrm{C}} \gamma_k w_k. \tag{3}$$

Here, u_k is the water flow velocity, w_k is the transmural flux of the water reabsorbed into the interstitium, and γ_k describes the area of the luminal wall per unit depth. For each compartment k, the flow velocity u_k depends on the hydrostatic pressure p_k, and is described by the Poiseuille equation:

$$\frac{\rho_k u_k}{\alpha_k} = -\frac{\partial p_k}{\partial x}, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{4}$$

with ρ_k is a constant so that ρ_k/α_k represents the hydraulic resistivity which depends on the volume density α_k. The transmural fluxes w_k on the right-hand side of (2) depend on the difference of both the hydrostatic pressures p_k and the osmotic pressures π_k between the luminal and the interstitial compartments. That is,

$$w_k := \zeta_{\mathrm{w}}^k \left(\psi_k - \psi_0\right), \quad \psi_k := p_k - \pi_k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C} \tag{5}$$

where ζ_{w}^k are the water permeability of the tubules, and ψ_k are called the 'water potential'.

We describe the hydrostatic pressure p_k by considering a mechanical property of the nephrons. We assume that this can be captured by the compliance ν_k, $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$, of the tubular walls, and we have

$$\nu_k(p_k - p_0) = \frac{\alpha_k}{\bar{\alpha}_k} - 1, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{6}$$

where $\bar{\alpha}_k$ are the resting volume density for which $p_k = p_0$. Note that the interstitial hydrostatic pressure is determined by the volume conservation given by (1).

The osmotic pressure π_k, on the other hand, depends on the total concentration of the solutes. In this model, for each compartment k, we will only consider two unknown concentrations of solute species: the salt concentration c_{s}^k, and the urea concentration c_{u}^k. The rest of the solute species will be treated as a fixed immobile solute, and we denote the total amount (per unit depth) by a_k. We define the osmotic pressure by

$$\pi_k := RT \left(2c_{\mathrm{s}}^k + c_{\mathrm{u}}^k + \frac{a_k}{\alpha_k}\right), \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}. \tag{7}$$

Now, similarly to the dynamics of the volume density, we have equations for the salt and urea concentrations:

$$\frac{\partial}{\partial t}\left(\alpha_k c_i^k\right) = -\frac{\partial}{\partial x} f_i^k - \gamma_k g_i^k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{8}$$

$$\frac{\partial}{\partial t}\left(\alpha_0 c_i^0\right) = -\frac{\partial}{\partial x} f_i^0 + \sum_{k=\mathrm{D},\mathrm{A},\mathrm{C}} \gamma_k g_i^k, \tag{9}$$

where $i = \mathrm{s}, \mathrm{u}$. The axial flow and transmural flux of the solute i are denoted by f_i^k and g_i^k respectively. The axial flow has two components: diffusion and advection. We write f_i^k as

$$f_i^k := -\alpha_k D_i^k \frac{\partial c_i^k}{\partial x} + \alpha_k u_k c_i^k, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{10}$$

where D_i^k are the diffusion coefficients. For the transmural fluxes g_i^k, we have

$$g_i^k := j_i^k + h_i^k, \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C} \tag{11}$$

where j_i^k is the passive transport of the solutes, and h_i^k is the active transport. We assume that the passive transports take the form:

$$j_i^k = \zeta_i^k \left(\mu_i^k - \mu_i^0\right), \quad k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \tag{12}$$

where ζ_i^k are the permeability of the solute i through the tubules, and μ_i^k is the chemical potential of the solute i in the compartment k:

$$\mu_i^k := RT \ln c_i^k, \quad k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}. \tag{13}$$

Note that, since we are considering only salt and urea, we essentially eliminate the need to address the electrical potential, i.e., the electroneutrality condition requires that the movement of Na^+ ions must be accompanied by that of Cl^- ions, so we can think of salt as having no charge. The active transport h_i^k represent the transport which requires external energy. In this case, we are interested the molecular pump of salt from the ascending tubules into the interstitium. So, h_s^A is a non-negative function and $h_i^k \equiv 0$ for $k = \mathrm{D}, \mathrm{C}$ or $i = \mathrm{u}$.

Now, we need to specify the boundary conditions. For the interstitial compartment, we assume no-flux boundary at $x = L$, i.e.,

$$u_0(t, L) = 0, \tag{14}$$

$$f_i^0(t, L) = 0, \quad i = \mathrm{s}, \mathrm{u}. \tag{15}$$

On the other hand, we allow interstitial water flow and advective solute flow at $x = 0$ in the negative direction. More precisely,

$$p_0(t, 0) = P_\mathrm{v}, \tag{16}$$

$$c_i^0(t, 0) = c_i^\mathrm{v}(t), \quad i = \mathrm{s}, \mathrm{u}, \tag{17}$$

where P_v is the pressure inside larger vessels which are coupled to the interstitial compartment.

For the luminal compartments, we have solute and water input from the proximal tubules in the descending compartment at $x = 0$. Formally, we write

$$(\alpha_\mathrm{D} u_\mathrm{D})(t, 0) = F_\mathrm{PCT}(t), \tag{18}$$

$$c_i^\mathrm{D}(t, 0) = c_i^\mathrm{PCT}(t), \quad i = \mathrm{s}, \mathrm{u}, \tag{19}$$

where F_PCT is a non-negative function of time, which can be given or depend on other model unknowns such as the pressure of the descending tubule or the salt concentration in the ascending tubule. We also have the concentration at the beginning of the descending tubule c_i^PCT given. Furthermore, we have couplings between the descending and ascending tubules at $x = L$ and between the ascending and collecting tubules at $x = 0$, i.e., we have

$$(\alpha_\mathrm{D} u_\mathrm{D} + \alpha_\mathrm{A} u_\mathrm{A})(t, L) = 0, \tag{20}$$

$$\left(f_i^\mathrm{D} + f_i^\mathrm{A}\right)(t, L) = 0, \tag{21}$$

$$p_\mathrm{D}(t, L) = p_\mathrm{A}(t, L), \tag{22}$$

$$c_i^\mathrm{D}(t, L) = c_i^\mathrm{A}(t, L). \tag{23}$$

To avoid modeling the distal convoluted tubules (DCT) and the connecting tubules (CNT), which join the distal end of the ascending tubules and the collecting tubules, we assume that the amount of urea at both ends stay the same while the salt content is reabsorbed by DCT and CNT by a factor of $1-q$ where $0 < q \leq 1$. Formally, we write

$$\left(f_{\mathrm{u}}^{\mathrm{A}} + f_{\mathrm{u}}^{\mathrm{C}}\right)(t,0) = 0, \tag{24}$$

$$\left(q f_{\mathrm{s}}^{\mathrm{A}} + f_{\mathrm{s}}^{\mathrm{C}}\right)(t,0) = 0. \tag{25}$$

Further, we assume that

$$p_{\mathrm{A}}(t,0) = p_{\mathrm{C}}(t,0), \tag{26}$$

$$f_i^{\mathrm{A}}(t,L) = (\alpha_{\mathrm{A}} u_{\mathrm{A}} c_i^{\mathrm{A}})(t,L), \quad i = \mathrm{s}, \mathrm{u}, \tag{27}$$

$$(2c_{\mathrm{s}}^{\mathrm{C}} + c_{\mathrm{u}}^{\mathrm{C}})(t,0) = c_{\mathrm{cortex}}(t), \tag{28}$$

i.e., the pressure drop across and the diffusive flux into the DCT and the CNT are negligible, and the water is reabsorbed so that the osmolarity of the fluid at the initial CNT is iso-osmotic, given by c_{cortex}.

Finally, since the volume density of the collecting tubule is the model unknown, we need to specify the solute and water flow at $x = L$ similarly to those in the interstitium:

$$p_{\mathrm{C}}(t,L) = P_{\mathrm{p}}(t), \tag{29}$$

$$f_i^{\mathrm{C}}(t,L) = (\alpha_{\mathrm{C}} u_{\mathrm{C}} c_i^{\mathrm{C}})(t,L), \quad i = \mathrm{s}, \mathrm{u}, \tag{30}$$

where P_{p} is the papillary pressure.

2 Non-dimensionalization

We now consider the rescaling of space and time:

$$x = L\hat{x}, \quad t = \tau\hat{t}, \tag{31}$$

where τ is an advection timescale given by

$$\tau := \frac{L^2}{\bar{\alpha} p_* / \rho_*} = \frac{\rho_* L^2}{\bar{\alpha} c_* RT}. \tag{32}$$

Here, $p_* = c_* RT$ is a typical magnitude of hydrostatic pressures with c_* being that of solute concentrations; $\bar{\alpha} = \frac{1}{L}\int_0^L \alpha_*(x)\,dx$ is the average volume density; ρ_* is a typical magnitude of hydraulic resistivity. With this, we rescale the model unknowns as follows:

$$\alpha_k = \bar{\alpha}\hat{\alpha}, \quad c_i^k = c_* \hat{c}_i^k, \quad p_k = p_* \hat{p}_k = c_* RT \hat{p}_k, \tag{33}$$

for $k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}$. The dimensionless unknowns with $\hat{\cdot}$ notation here are functions in the rescaled space and time $(\hat{t}, \hat{x})$.

We have the model equations in the dimensionless form:

$$\frac{\partial \hat{\alpha}_k}{\partial \hat{t}} + \frac{\partial}{\partial \hat{x}} \left(\hat{\alpha}_k \hat{u}_k \right) = -\hat{w}_k, \tag{34}$$

$$\frac{\partial \hat{\alpha}_0}{\partial \hat{t}} + \frac{\partial}{\partial \hat{x}} \left(\hat{\alpha}_0 \hat{u}_0 \right) = \sum_k \hat{w}_k, \tag{35}$$

$$\hat{\nu}_k \left(\hat{p}_k - \hat{p}_0 \right) = \frac{\hat{\alpha}_k}{\hat{\bar{\alpha}}_k} - 1, \tag{36}$$

$$\hat{\alpha}_0 + \sum_k \hat{\alpha}_k = \hat{\alpha}_*, \tag{37}$$

$$\frac{\partial}{\partial \hat{t}} \left(\hat{\alpha}_k \hat{c}_i^k \right) = -\frac{\partial}{\partial \hat{x}} \hat{f}_i^k - \hat{g}_i^k, \tag{38}$$

$$\frac{\partial}{\partial \hat{t}} \left(\hat{\alpha}_0 \hat{c}_i^0 \right) = -\frac{\partial}{\partial \hat{x}} \hat{f}_i^0 + \sum_k \hat{g}_i^k, \tag{39}$$

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

$$\hat{u}_\cdot := -\frac{\hat{\alpha}_\cdot}{\hat{\rho}_\cdot} \frac{\partial \hat{p}_\cdot}{\partial \hat{x}} = \frac{\tau}{L} u_\cdot, \tag{40}$$

$$\hat{f}_i^\cdot := -\hat{\alpha}_\cdot \hat{D}_i^\cdot \frac{\partial \hat{c}_i^\cdot}{\partial \hat{x}} + \hat{\alpha}_\cdot \hat{u}_\cdot \hat{c}_i^\cdot = \tau \bar{\alpha} c_* f_i^\cdot, \tag{41}$$

$$\hat{w}_k := \hat{\zeta}_{\mathrm{w}}^k \left(\hat{\psi}_k - \hat{\psi}_0 \right) = \frac{\tau \gamma_k}{\bar{\alpha}} w_k, \quad \hat{\psi}_\cdot := \hat{p}_\cdot - \hat{\pi}_\cdot, \quad \hat{\pi}_\cdot := \frac{\hat{a}_\cdot}{\hat{\alpha}_\cdot} + \sum_i \hat{c}_i^\cdot, \tag{42}$$

$$\hat{g}_i^k := \hat{j}_i^k + \hat{h}_i^k = \frac{\tau \gamma_k}{\bar{\alpha} c_*} g_i^k, \quad \hat{j}_i^k := \hat{\zeta}_i^k (\hat{\mu}_i^k - \hat{\mu}_i^0), \quad \hat{\mu}_i^\cdot := \ln \hat{c}_i^\cdot \tag{43}$$

for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$ and $i = \mathrm{s}, \mathrm{u}$. The label $\cdot$ here is for $0, \mathrm{D}, \mathrm{A}, \mathrm{C}$. Note that we have $\hat{h}_i^k = (\gamma_k \tau / \bar{\alpha} c_*) h_i^k$ for the dimensionless active transport $\hat{h}_i^k$. In this dimensionless formulation, we have identified parameters:

$$\hat{\rho}_\cdot = \frac{\rho_\cdot}{\rho_*}, \quad \hat{\nu}_k = p_* \nu_k, \quad \hat{\bar{\alpha}}_\cdot = \frac{\bar{\alpha}_\cdot}{\bar{\alpha}}, \quad \hat{\alpha}_* = \frac{\alpha_*}{\bar{\alpha}} \tag{44}$$

$$\hat{a}_\cdot = \frac{a_\cdot}{\bar{\alpha} c_*}, \quad \hat{D}_i^\cdot = \frac{\tau}{L^2} D_i^\cdot, \quad \hat{\zeta}_{\mathrm{w}}^k = \frac{\gamma_k p_* \tau}{\bar{\alpha}} \zeta_{\mathrm{w}}^k, \quad \hat{\zeta}_i^k = \frac{\gamma_k p_* \tau}{\bar{\alpha} c_*^2} \zeta_i^k, \tag{45}$$

for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$, where the subscript $*$ denotes the typical magnitudes of the parameters described in the previous section. The mechanical parameters, which are the hydraulic resistivity $\hat{\rho}_\cdot$, the tubular compliance $\hat{\nu}_\cdot$, the resting volume density $\hat{\bar{\alpha}}_\cdot$, immobile solutes $\hat{a}_\cdot$, and the diffusion coefficients $\hat{D}_\cdot$ persist through the non-dimensionalization. The transport parameters, however, are now reduced to only $\hat{\zeta}_{\mathrm{w}}^k$ and $\hat{\zeta}_i^k$ which combine the geometric parameters γ_k with the solute and water permeability.

The boundary conditions are of the same form as previously described, but with $\hat{\cdot}$ notations, where we have

$$F_{\mathrm{PCT}} = \frac{\bar{\alpha} L}{\tau} \hat{F}_{\mathrm{PCT}}, \quad P_\cdot = p_* \hat{P}_\cdot, \quad c_i^\cdot = c_* \hat{c}_i^*, \quad c_{\mathrm{cortex}} = c_* \hat{c}_{\mathrm{cortex}}, \tag{46}$$

where the subscript $\cdot$ represents v and p.

3 Numerical method

We now give an implicit scheme to numerically solve the dimensionless system (35) - (43) described in the previous section with $\hat{D}_i^k = 0$ for $k \neq 0$. To simplify the notation, we will omit the $\hat{}$ notation in these equations.

Let $N \in \mathbb{N}$ be the number of uniformly spaced grids in $(0,1)$, and $\delta x = 1/N$ be the spatial grid size. Similarly, we denote δt as the size of time steps. We will use the notation $\alpha_{kl}^n, c_{il}^{kn}, p_{kl}^n$ for the discretization of α_k, c_i^k and p_k at the l-th spatial grid and time $t = n\delta t$. These correspond to the values in between the spatial grid point, e.g., α_{kl}^n corresponds to $\alpha_k(n\delta t, l - \delta x/2)$.

We define difference quotient operators:

$$\mathcal{D}_x^+ y_l^n := \frac{y_{l+1}^n - y_l^n}{\delta x}, \quad \mathcal{D}_x^- y_l^n := \frac{y_l^n - y_{l-1}^n}{\delta x}, \quad \mathcal{D}_t y_l^n = \frac{y_l^n - y_l^{n-1}}{\delta t}, \tag{47}$$

and an average operator:

$$\mathcal{A} y_l^n := \frac{y_{l+1}^n + y_l^n}{2}, \tag{48}$$

where $\{y_l^n\}$ is any discretized variables with $l, n \in \mathbb{N} \cup \{0\}$.

Starting with known values of $\alpha_{kl}^{n-1}, c_{il}^{k,n-1}, p_{kl}^{n-1}$, $l = 1, \ldots, N$, the first step is to update the unknowns for the next time step n. We have the system of equations for $\alpha_{kl}^n, c_{il}^{kn}, p_{kl}^n$, $l = 1, \ldots, N$, to be solved using an iterative method:

$$\mathcal{D}_t \alpha_{kl}^n + \mathcal{D}_x^- v_{kl}^n = \begin{cases} -w_{kl}^n, & k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \\ \sum_{\kappa \neq 0} w_{\kappa l}^n, & k = 0, \end{cases} \tag{49}$$

$$\mathcal{D}_t (\alpha_{kl}^n c_{il}^{kn}) + \mathcal{D}_x^- f_{il}^{kn} = \begin{cases} -g_{kn}^{il}, & k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \\ \sum_{\kappa \neq 0} g_{il}^{\kappa n}, & k = 0. \end{cases} \tag{50}$$

$$p_{kl}^n = \begin{cases} p_{0l}^n + \frac{1}{\nu_k} \left(\frac{\alpha_{kl}^n}{\bar{\alpha}_{kl}} - 1 \right), & k = \mathrm{D}, \mathrm{A}, \mathrm{C}, \\ \frac{\alpha_{0l}^n - \alpha_* + \sum_{\kappa \neq 0} \bar{\alpha}_\kappa (\nu_\kappa p_\kappa + 1)}{\sum_{\kappa \neq 0} \bar{\alpha}_\kappa \nu_\kappa}, & k = 0. \end{cases} \tag{51}$$

where the transmural flux terms w_{kl}^n and g_{il}^{kn} are the discritization of w_k and g_i^k on the same grid as the unknowns:

$$w_{kl}^n := \zeta_{\mathrm{w}}^k \left(\psi_{kl}^n - \psi_{0l}^n \right), \quad \psi_{\cdot l}^n := p_{\cdot l}^n - \pi_{\cdot l}^n, \quad \pi_{\cdot l}^n := \sum_i c_{il}^{\cdot n}, \tag{52}$$

$$g_{il}^{kn} := j_{il}^{kn} + h_{il}^{kn}, \quad j_{il}^{kn} := \zeta_i^k \left(\mu_{il}^{kn} - \mu_{il}^{0n} \right), \quad \mu_{il}^{\cdot n} := \ln c_{il}^{\cdot}. \tag{53}$$

Here, the axial flows of water v_{kl}^n and solutes f_{il}^{kn} are assigned for $l = 0, \ldots, N$. These should be thought as the flow at the *grid points*, e.g., f_{il}^{kn} corresponds to $f_i^k(n\delta t, l\delta x)$. For $l = 1, \ldots, N-1$, we have

$$v_{kl}^n = -\frac{1}{\rho_{kl}} (\mathcal{A} \alpha_{kl}^n)^2 \mathcal{D}_x^+ p_{kl}^n, \tag{54}$$

$$f_{il}^{kn} = v_{kl}^n \mathcal{A} c_{il}^{kn}. \tag{55}$$

Further, we have the boundary conditions ($l = 0, N$):

$$v_{00}^n = \frac{(\alpha_{01}^n)^2}{\rho_{00}} \left(\frac{P_{\mathrm{v}}(n\delta t) - p_{01}^n}{\delta x/2} \right),$$

$$f_{00}^n = v_{00}^n c_i^{\mathrm{v}}(n\delta t) + \alpha_{01}^n D_{i0}^0 \left(\frac{c_i^{\mathrm{v}}(n\delta t) - c_{i0}^{0n}}{\delta x/2} \right), \tag{56}$$

$$v_{0N}^n = 0, \qquad f_{0N}^n = 0, \tag{57}$$

$$v_{\mathrm{D}0}^n = F_{\mathrm{PCT}}(n\delta t), \qquad f_{i0}^{\mathrm{D}n} = v_{\mathrm{D}0}^n c_i^{\mathrm{PCT}}(n\delta t), \tag{58}$$

$$v_{\mathrm{C}N}^n = \frac{(\alpha_{\mathrm{C}N}^n)^2}{\rho_{\mathrm{C}N}} \left(\frac{p_{\mathrm{C}N}^n - P_{\mathrm{p}}(n\delta t)}{\delta x/2} \right), \qquad f_{iN}^{\mathrm{C}n} = v_{\mathrm{C}N}^n c_{iN}^{\mathrm{C}n}. \tag{59}$$

For the coupling between the descending and ascending, we have

$$v_{kN}^n = \frac{(\alpha_{kN}^n)^2}{\rho_k} \left(\frac{p_{kN}^n - \bar{p}_{\mathrm{DA}}^n}{\delta x/2} \right), \tag{60}$$

$$f_{iN}^{kn} = v_{kN}^n \bar{c}_{i,\mathrm{DA}}^n, \tag{61}$$

for $k = \mathrm{D}, \mathrm{A}$, where

$$\bar{p}_{\mathrm{DA}}^n := \frac{\frac{(\alpha_{\mathrm{D}N}^n)^2}{\rho_{\mathrm{D}}} p_{\mathrm{D}N}^n + \frac{(\alpha_{\mathrm{A}N}^n)^2}{\rho_{\mathrm{A}}} p_{\mathrm{A}N}^n}{\frac{(\alpha_{\mathrm{D}N}^n)^2}{\rho_{\mathrm{D}}} + \frac{(\alpha_{\mathrm{A}N}^n)^2}{\rho_{\mathrm{A}}}}, \quad \bar{c}_{i,\mathrm{DA}}^n := \frac{\alpha_{\mathrm{D}N}^n D_{iN}^{\mathrm{D}} c_{iN}^{\mathrm{D}n} + \alpha_{\mathrm{A}N}^n D_{iN}^{\mathrm{A}} c_{iN}^{\mathrm{A}n}}{\alpha_{\mathrm{D}N}^n D_{iN}^{\mathrm{D}} + \alpha_{\mathrm{A}N}^n D_{iN}^{\mathrm{A}}}. \tag{62}$$

These are so that we have the coupling satisfies $v_{\mathrm{D}N}^n + v_{\mathrm{A}N}^n = 0$, and $f_{iN}^{\mathrm{D}n} + f_{iN}^{\mathrm{A}n} = 0$. Here, $\bar{p}_{\mathrm{DA}}^n$ and $\bar{c}_{i,\mathrm{DA}}^n$ correspond to the pressures and the concentrations at $x = 1$ of the descending and the ascending tubules. Similarly, we also have a condition for the coupling between the ascending and the descending tubules:

$$v_{k0}^n = \frac{(\alpha_{k0}^n)^2}{\rho_k} \left(\frac{\bar{p}_{\mathrm{AC}}^n - p_{k0}^n}{\delta x/2} \right), \quad k = \mathrm{A}, \mathrm{C}, \tag{63}$$

$$f_{i0}^{\mathrm{A}n} = v_{\mathrm{A}0}^n c_{i0}^{\mathrm{A}n}, \quad i = \mathrm{s}, \mathrm{u}, \tag{64}$$

$$f_{i0}^{\mathrm{C}n} = v_{\mathrm{C}0}^n c_{i0}^{\mathrm{C}n} + \alpha_{\mathrm{C}0}^n D_{i0}^{\mathrm{C}} \left(\frac{\bar{c}_{i,\mathrm{AC}}^n - c_{i0}^{\mathrm{C}n}}{\delta x/2} \right), \quad i = \mathrm{s}, \mathrm{u}, \tag{65}$$

$$\tag{66}$$

where $\bar{p}_{\mathrm{AC}}^n, \bar{c}_{i,\mathrm{AC}}^n$ satisfy the system of equations:

$$\left(\frac{q(\alpha_{\mathrm{A}0}^n)^2 c_{\mathrm{s}0}^{\mathrm{A}n}}{\rho_{\mathrm{A}}} + \frac{(\alpha_{\mathrm{C}0}^n)^2 c_{\mathrm{s}0}^{\mathrm{C}n}}{\rho_{\mathrm{C}}} \right) (\bar{p}_{\mathrm{AC}}^n - p_{\mathrm{A}0}^n) + \alpha_{\mathrm{C}0}^n D_{\mathrm{s}}^{\mathrm{C}} \left(\bar{c}_{\mathrm{s,AC}}^n - c_{\mathrm{s}0}^{\mathrm{C}n} \right) = 0, \tag{67}$$

$$\left(\frac{(\alpha_{\mathrm{A}0}^n)^2 c_{\mathrm{u}0}^{\mathrm{A}n}}{\rho_{\mathrm{A}}} + \frac{(\alpha_{\mathrm{C}0}^n)^2 c_{\mathrm{u}0}^{\mathrm{C}n}}{\rho_{\mathrm{C}}} \right) (\bar{p}_{\mathrm{AC}}^n - p_{\mathrm{A}0}^n) + \alpha_{\mathrm{C}0}^n D_{\mathrm{u}}^{\mathrm{C}} \left(\bar{c}_{\mathrm{u,AC}}^n - c_{\mathrm{u}0}^{\mathrm{C}n} \right) = 0, \tag{68}$$

$$2\bar{c}_{\mathrm{s,AC}}^n + \bar{c}_{\mathrm{u,AC}}^n - c_{\mathrm{cortex}}(n\delta t) = 0. \tag{69}$$

4 Simulation of the countercurrent mechanism

In this simulation, we will use a simple geometry of $\alpha_* \equiv 1$, with mechanical parameters $\bar{\alpha}_k = 1/4$ and $\nu_k = 0.01$ for $k = \mathrm{D}, \mathrm{A}, \mathrm{C}$. We suppose that $D_{\mathrm{s}}^k = D_{\mathrm{u}}^k = 1$, $\mathrm{Pe} = 20$, $\rho_k = 1$ for all k, and we assume that there is only immobile solute in the interstitium, where we have $a_0 = 1/2$ and $a_k = 0$ for luminal compartments. Furthermore, we set the resistance of the coupling with larger vessels and the renal papillae $R_{\mathrm{v}} = R_{\mathrm{p}} = 1$.

For the transport parameters, we allow the passive transport of salt only in the descending and the ascending tubules, where we set $\zeta_{\mathrm{s}}^{\mathrm{D}} = \zeta_{\mathrm{s}}^{\mathrm{A}} = 1$ and $\zeta_{\mathrm{s}}^{\mathrm{C}} = 0$. Additionally, all the tubular segments are permeable to urea in the inner medulla, i.e., $\zeta_{\mathrm{u}}^k = 10$ for all k and $x \in (\frac{1}{2}, 1)$ and $\zeta_{\mathrm{u}}^k = 0$ elsewhere. Furthermore, for illustrating purpose, we consider a simple active transport of salt in the outer medulla of the form

$$h_{\mathrm{s}}^{\mathrm{A}} = \begin{cases} h_* c_{\mathrm{s}}^{\mathrm{A}}, & \text{in} \quad (0, \frac{1}{2}), \\ 0 & \text{in} \quad [\frac{1}{2}, 1), \end{cases} \tag{70}$$

where $h_* > 0$ is the pump strength, which we set to be $h_* = 50$. For the water transport, the descending tubule will be highly permeable to water with $\zeta_{\mathrm{w}}^{\mathrm{D}} = 100$ while the ascending tubule will be completely insulated with $\zeta_{\mathrm{w}}^{\mathrm{A}} = 0$. We will consider two cases for the collecting tubules: without ADH, in which we have $\zeta_{\mathrm{w}}^{\mathrm{C}} = 0$, and when there is some ADH so that $\zeta_{\mathrm{w}}^{\mathrm{C}} = 50$.

We initialize the simulation by setting the initial condition to be no axial solute and flow with

$$\alpha_k(0, x) = \frac{1}{4}, \quad c_{\mathrm{s}}^k(0, x) = 1, \quad c_{\mathrm{u}}^k(0, x) = \frac{1}{4}, \quad p_k(0, x) = P_{\mathrm{v}} = P_{\mathrm{p}} = 1 \tag{71}$$

for all $x \in (0, 1)$ and $k = 0, \mathrm{D}, \mathrm{A}, \mathrm{C}$. Then, the glomerular filtration rate gradually increases until it reaches 2.5:

$$\mathrm{GFR}(t) = \min\{2.5, t/8\}. \tag{72}$$

4.1 Results

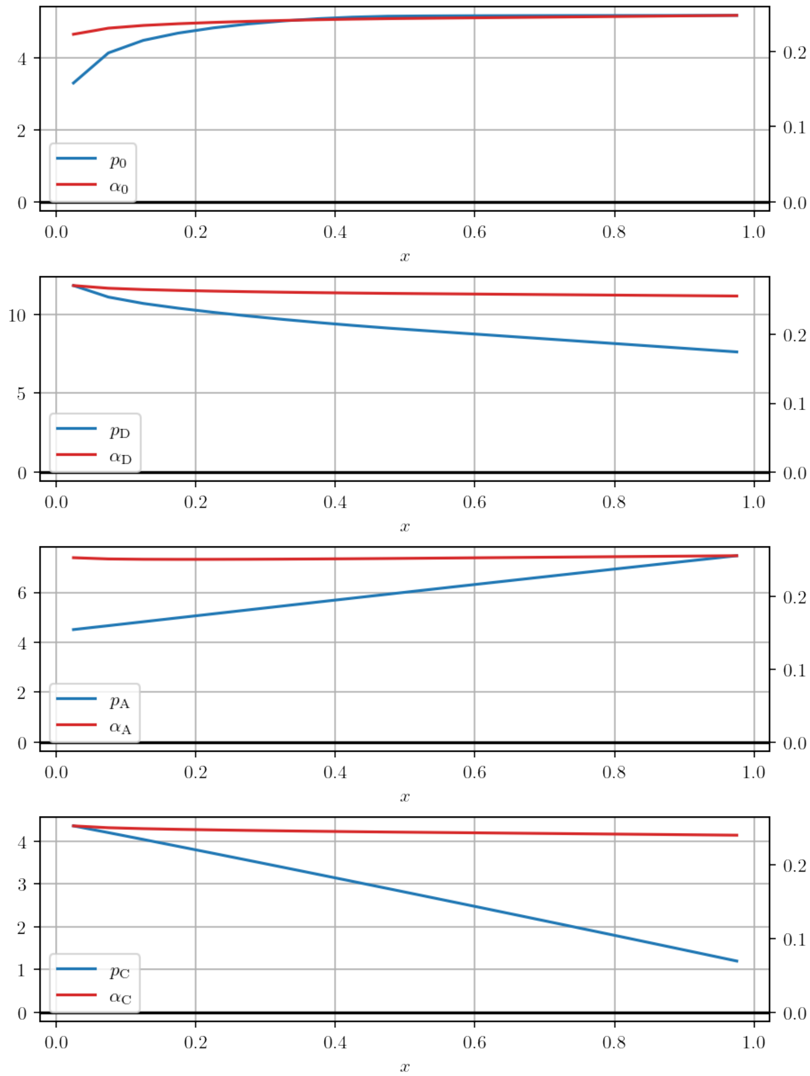

Figure 1: The pressures and volume densities without ADH

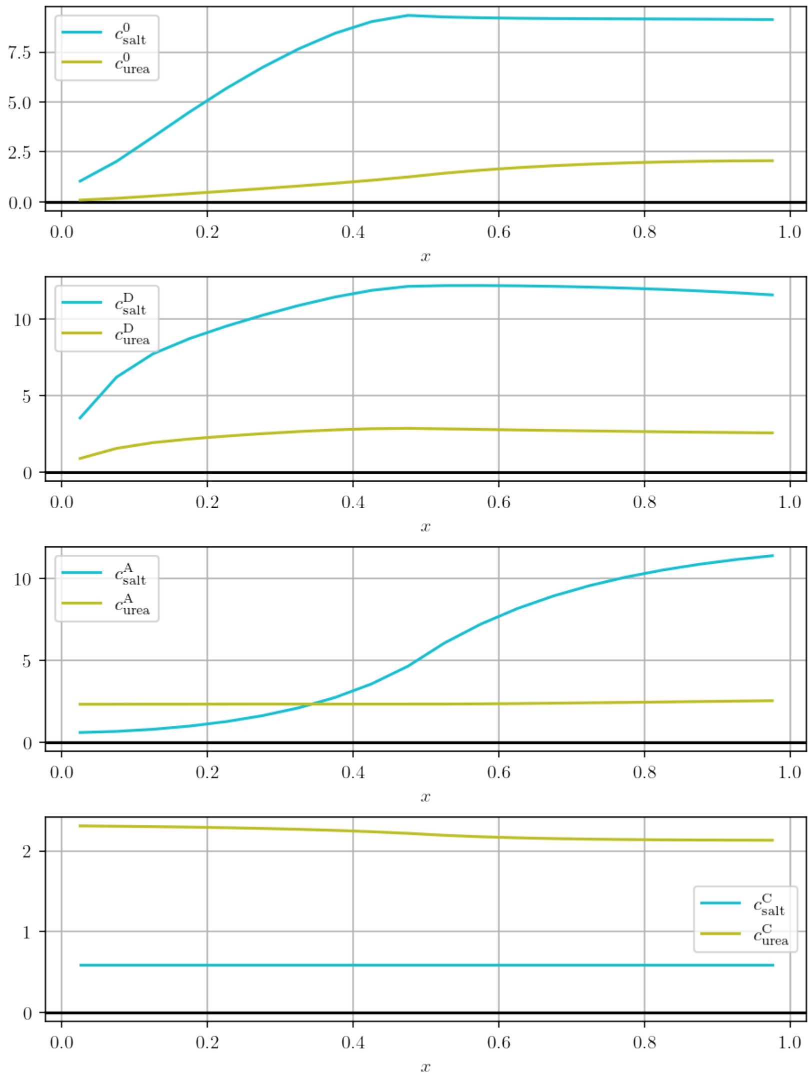

Figure 2: The concentration of salt and urea without ADH

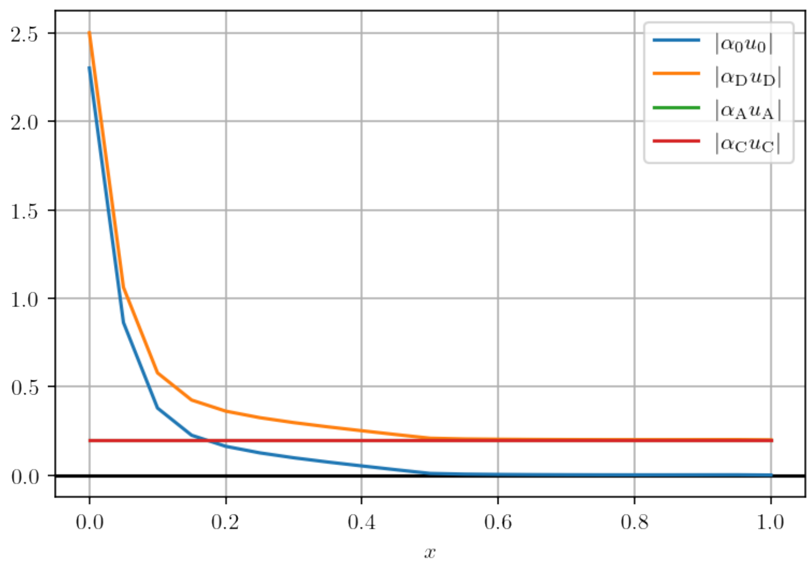

Figure 3: The water flow without ADH

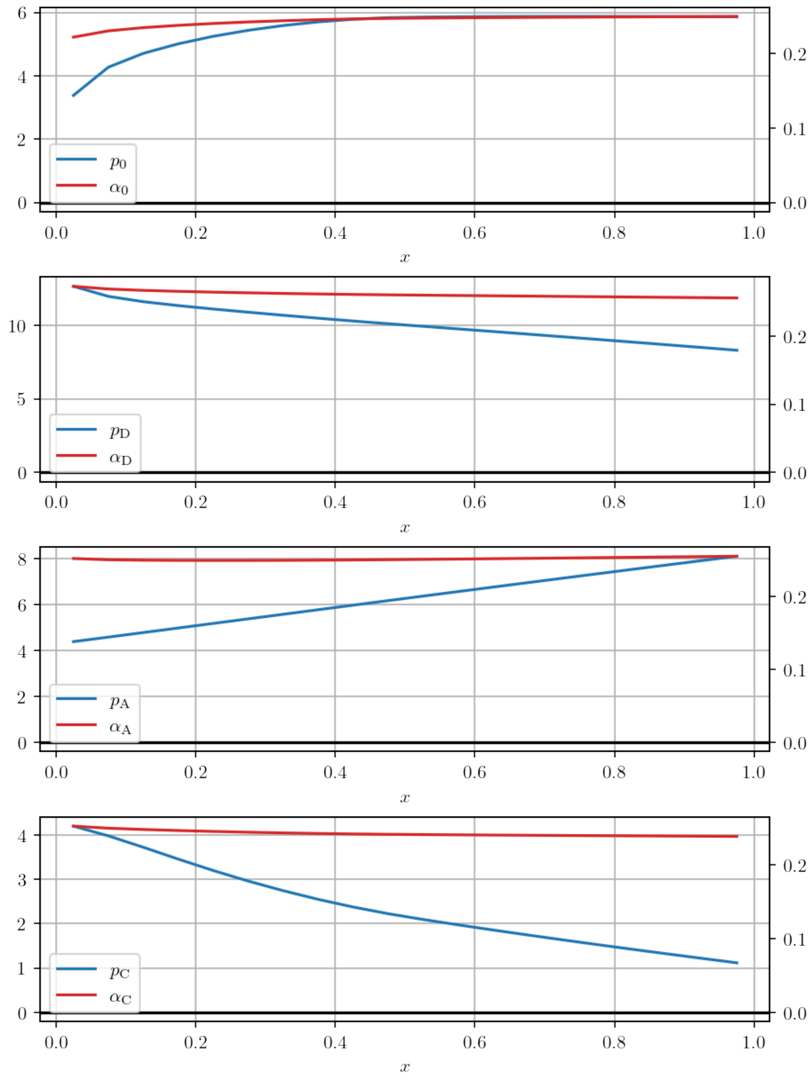

Figure 4: The pressures and volume densities with ADH

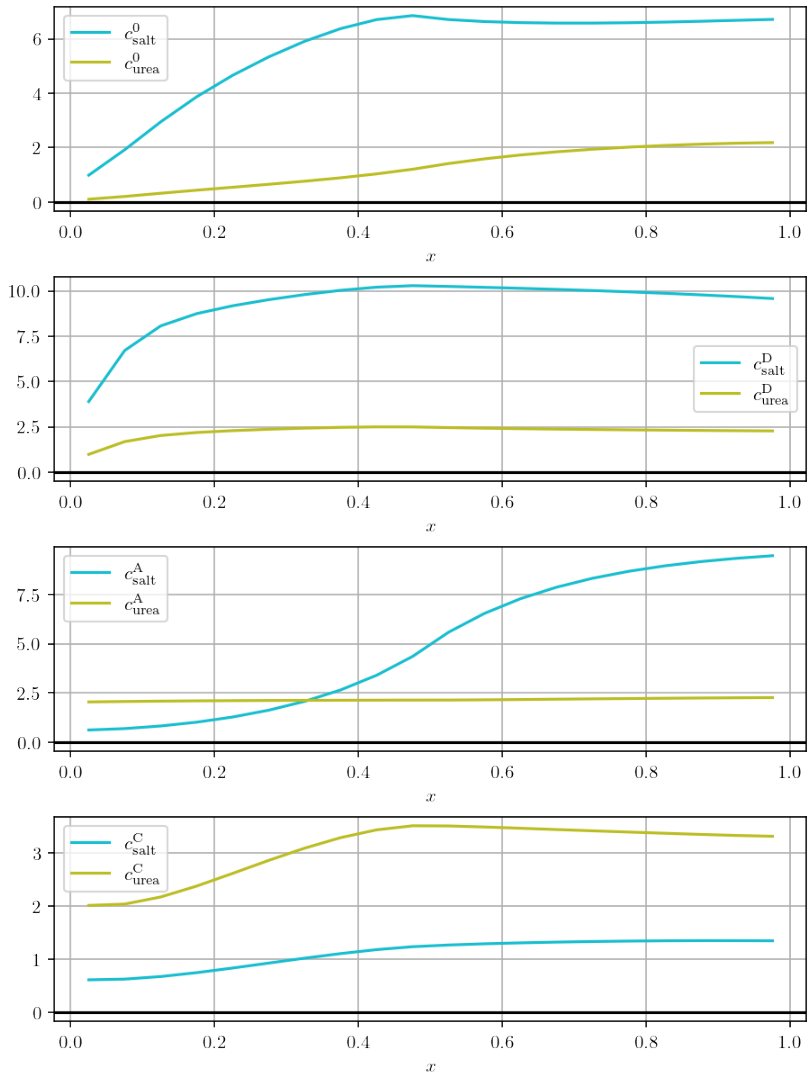

Figure 5: The concentration of salt and urea with ADH

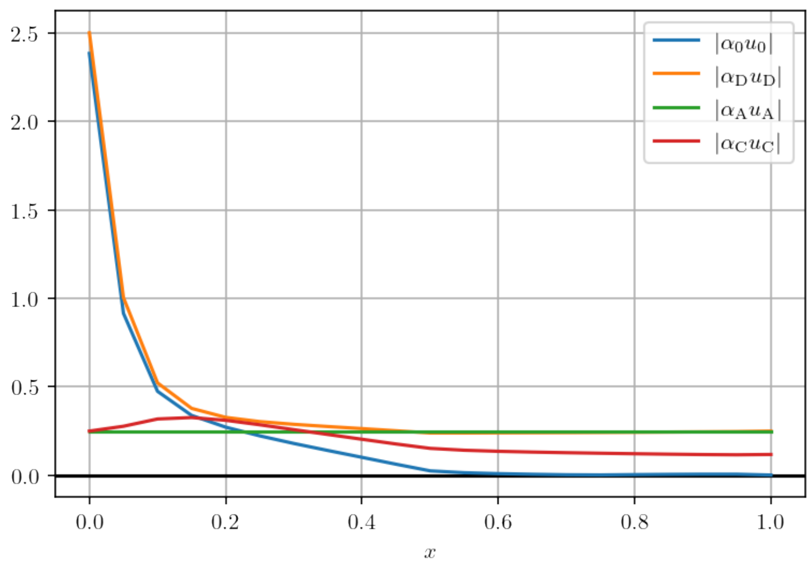

Figure 6: The water flow with ADH