Analysis of a simplified model of the urine concentration mechanism

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Abstract

We study a non linear stationary system describing the transport of solutes dissolved in a fluid circulating in a counter-current tubular architecture, which constitutes a simplified model of a kidney nephron. We prove that for every Lipschitz and monotonic nonlinearity (which stems from active transport across the ascending limb), the dynamic system, a PDE which we study through contraction properties, relaxes toward the unique stationary state. A study of the linearized stationary operator enables us, using eigenelements, to further show that under certain conditions regarding the nonlinearity, the relaxation is exponential. We also describe a finite-volume scheme which allows us to efficiently approach the numerical solution to the stationary system. Finally, we apply this numerical method to illustrate how the counter-current arrangement of tubes enhances the axial concentration gradient, thereby favoring the production of highly concentrated urine.

Key-words: Countercurrent, nonlinear transport equation, ion transport, relaxation toward steady-state, contraction property.

1 Introduction

The main role of the kidney is to maintain fluid and electrolyte homeostasis, by regulating the volume and composition of blood so that it remains clean and chemically balanced. Kidneys receive blood from the renal artery, filter it, and return it to the body via the renal vein while excreting unwanted substances in the urine. The functional units of the kidney, known as nephrons, each consist of several segments arranged in a countercurrent manner so as to maximize the production of concentrated urine.

Our purpose is to develop a simplified mathematical model predicated on a steady-state model describing solute transport in nephrons, to prove that the solution to the dynamic model we defined relaxes toward the solution to the steady-state model, and to compute this solution. In this simplified representation, the nephron consists of 3 water-impermeable tubes that exchange solutes via a common interstitium, as illustrated in Figure 1. There have been other simplified models of renal function based on similar hypotheses [Garner et al., 1978]. In the absence of water fluxes, there is no coupling between the transport of different molecular species except if there are cotransporters or exchangers). Hence, we only consider one generic uncharged solute (e.g., NaCl or urea).

Models that account for the presence of blood vessels usually consider at least 5 tubes (i.e., tubules and vessels). We choose to only represent 3 here so as to keep the presentation and analysis tractable, but the problem formulation and the mathematical methods described herein apply to any number ≥ 3.

Given the solute concentration denoted C at the inlet of tubes 1 and 2, and knowing that $C^3(L) = C^2(L)$ by continuity, our objective is to determine concentration profiles in the three tubes, as well as in the surrounding interstitium.

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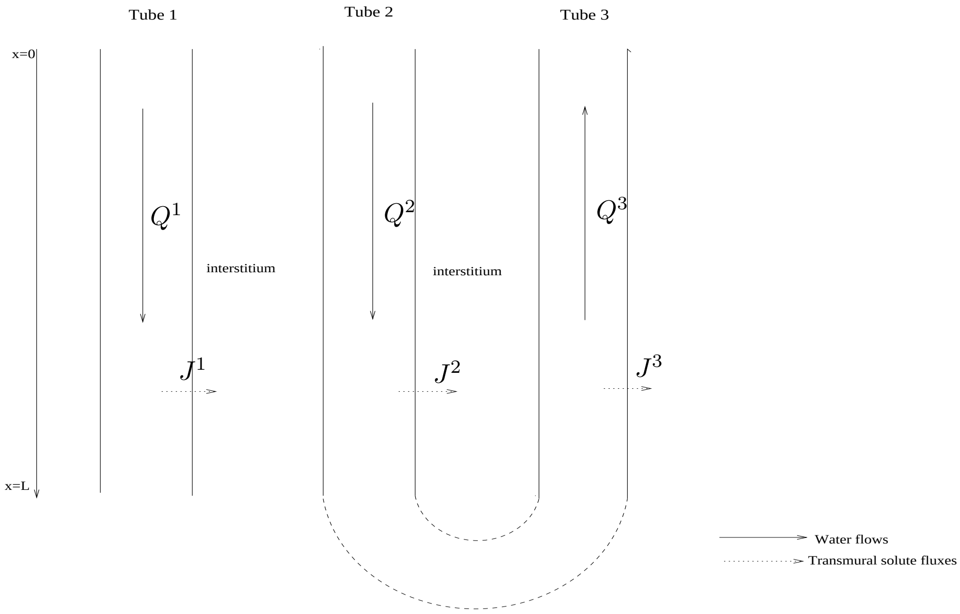

Figure 1: Simplified model of a nephron: Tube 1 represents a descending vasa recta or a collecting duct, tubes 2 and 3 represent descending and ascending limbs. Tubes are water-impermeable but can exchange solutes with the interstitium. These exchanges are quantified by the transmural fluxes J.

In each tube i, the fluid (mostly water) is assumed to circulate at a constant flow Q^i. At steady state, conservation of solute in each tube can be expressed as

$$\begin{cases} Q^1 \dfrac{dC^1(x)}{dx} = J^1(x), \qquad x \in [0, L], \\ Q^2 \dfrac{dC^2(x)}{dx} = J^2(x), \qquad x \in [0, L], \\ Q^3 \dfrac{dC^3(x)}{dx} = J^3(x), \qquad x \in [0, L], \\ \quad C^1(0) = C_0^1, \qquad C^2(0) = C_0^2, \qquad C^3(L) = C^2(L), \end{cases} \tag{1}$$

where C_0^1 and C_0^2 are two given nonnegative values, Q^i is the water flow in tube i and J^i is the transmural flux from the interstitium into the tube i.

In the absence of transversal water movement, the main driving force for solute transport is diffusion. In some kidney tubules there is also active transport, across energy-consuming pumps that carry some solutes against their concentration gradient. We assume the presence of such a pump in only tube 3 (which is meant to represent the thick ascending limb), so that

$$\begin{cases} J^1(x) = 2\pi R^1(x) P^1(x) (C^{int}(x) - C^1(x)), \\ J^2(x) = 2\pi R^2(x) P^2(x) (C^{int}(x) - C^2(x)), \\ J^3(x) = 2\pi R^3(x) P^3(x) (C^{int}(x) - C^3(x)) - F(C^3(x), x), \end{cases} \tag{2}$$

where R^i and P^i respectively denote the radius and solute permeability of tube i, C^{int} is the interstitial concentration, and $F(C^3, x) > 0$ is a nonlinear term representing active transport which is usually described using Michaelis-Menten kinetics:

$$F(C^3, x) = V_m(x) \frac{C^3}{1 + C^3}. \tag{3}$$

In order to simplify the notations, we assume that the effective solute permeability of each tube ($2\pi RP$) is equal to 1. We also assume that the flow Q is equal to 1 in tubes 1 and 2, and -1 in tube 3 where the flow is in the reverse direction. The resulting equations can be viewed as nondimensional, in the specific case where flows, radii, and permeabilities are taken to be constant and equal everywhere. Summarized in Table 1 are symbol definitions.

Table 1: Definition of frequently used symbols

Parameter	Description
$C^i(x)$	Solute concentration in tube i at depth x
$C^{int}(x)$	Solute concentration in the interstitium at depth x
C_0^1, C_0^2	Concentrations at the inlet of tubes 1 and 2 (assumed to be known)
$J^i(x)$	Transmural flux of solute through the wall of tube i at depth x
$Q^i(x)$	Water flow in tube i at depth x
$R^i(x)$	Radius of tube i at depth x
$P^i(x)$	Solute permeability of the wall of tube i at depth x

Axial convection and diffusion are thought to be negligible in the renal interstitium. Since there is no accumulation of solute therein, we have

$$J^1(x) + J^2(x) + J^3(x) = 0. \tag{4}$$

This condition enables us to calculate the interstitium concentration explicitly

$$\forall x \in [0, L], \qquad C^{int}(x) = \frac{1}{3}\Big[C^1(x) + C^2(x) + C^3(x) + F(C^3(x), x)\Big].$$

The goal of the study is to analyze and solve the following nonlinear boundary value problem set for $x \in [0, L]$

$$\begin{cases} \dfrac{dC^1(x)}{dx} = \dfrac{1}{3}\Big[C^1(x) + C^2(x) + C^3(x) + F(C^3(x), x)\Big] - C^1(x), \\ \dfrac{dC^2(x)}{dx} = \dfrac{1}{3}\Big[C^1(x) + C^2(x) + C^3(x) + F(C^3(x), x)\Big] - C^2(x), \\ -\dfrac{dC^3(x)}{dx} = \dfrac{1}{3}\Big[C^1(x) + C^2(x) + C^3(x) + F(C^3(x), x)\Big] - C^3(x) - F(C^3(x), x), \\ C^1(0) = C_0^1, \qquad C^2(0) = C_0^2, \qquad C^3(L) = C^2(L). \end{cases} \tag{5}$$

For this purpose, we introduce the dynamic problem set for $t \geq 0$ and $x \in [0, L]$,

$$\begin{cases} \dfrac{\partial C^1}{\partial t}(x,t) + \dfrac{\partial C^1}{\partial x}(x,t) = \dfrac{1}{3}\Big[C^1(x,t) + C^2(x,t) + C_3(x,t) + F(C^3(x,t), x)\Big] - C^1(x,t), \\ \dfrac{\partial C^2}{\partial t}(x,t) + \dfrac{\partial C^2}{\partial x}(x,t) = \dfrac{1}{3}\Big[C^1(x,t) + C^2(x,t) + C^3(x,t) + F(C^3(x,t), x)\Big] - C^2(x,t), \\ \dfrac{\partial C^3}{\partial t}(x,t) - \dfrac{\partial C^3}{\partial x}(x,t) = \dfrac{1}{3}\Big[C^1(x,t) + C^2(x,t) + C^3(x,t) + F\big(C^3(x,t), x\big)\Big] - C^3(x,t) - F(C^3(x,t), x), \\ C^1(0,t) = C_0^1, \qquad C^2(0,t) = C_0^2, \qquad C^3(L,t) = C^2(L,t), \end{cases} \tag{6}$$

which we complete with nonnegative initial concentrations $C^1(x,0)$, $C^2(x,0)$, $C^3(x,0)$. Implicite in this dynamic system is the assumption that the interstitium equilibrates immediately with it surrounding. In this study, we first prove that the solution to (6) converges, as t tends to ∞, to the solution to (5) and that, under certain conditions, the convergence is exponential. We then use a finite volume scheme to solve (6) and thus approach the solution to (5). The numerical solution is subsequently employed to examine the effects of the countercurrent architecture on concentration gradients.

2 Main Results

The main objective of this section is to study the long time convergence of the dynamic solution to the stationary solution. For this purpose, we describe the mathematical structure of the dynamic and stationary systems, state the natural properties of the dynamic solution, and infer a priori bounds for the latter solution which are time-independent. The proofs of the theorems outlined below are given in section 3.

We use the notation C for the vector function (C^1, C^2, C^3).

2.1 Existence, uniqueness and a priori bounds

To ensure that the dynamic solution exists, we must make some assumptions regarding the nonlinear term representing active transport. We assume that the (smooth) function F satisfies for some (smooth) function $\mu(x) \geq 0$

$$F(C^3, x) \geq 0, \qquad F(0, x) = 0, \qquad 0 \leq F_C(C^3, x) \leq \mu(x) \leq \mu_M. \tag{7}$$

The Michaelis-Menten equation (3) which is generally used to represent active transport in the thick ascending limb can readily be shown to satisfy these 3 assumptions. The first one means that the pump can only transport the solute in one direction, from the lumen of the thick ascending limb toward the interstitium. The second one describes the fact that there is no transport in the absence of solute. Lastly, the third assumption expresses the fact that the pump can be saturated because the number of carriers is limited.

Initial ($t = 0$) solute concentrations are positive. We further assume that, for $i = 1$, 2 or 3,

$$C^i(t = 0) \geq 0, \qquad C^i(t = 0) \in L^1(0, L), \qquad \frac{d}{dx}C^i(t = 0) \in L^1(0, L). \tag{8}$$

Another possible assumption is that the initial data are 'well-prepared', that is to say they match the boundary conditions

$$C^1(0, t = 0) = C_0^1, \qquad C^2(0, t = 0) = C_0^2, \qquad C^3(L, t = 0) = C^2(L, t = 0).$$

We do not use this assumption and thus handle possibly discontinuous solutions.

Theorem 1 (Existence and uniqueness of the dynamic problem solution)**.** *With assumptions* (7) *and* (8)*, there is a weak solution (defined in Appendix A) to the initial value problem* (6)*, which lies in* $BV([0, L]\times[0, T])$. *For two initial data* $C(x, 0)$ *and* $\widetilde{C}(x, 0)$*, the weak solutions satisfy the weak contraction property and the comparison principle*

$$\int_0^L [\, |C^1 - \widetilde{C}^1| + |C^2 - \widetilde{C}^2| + |C^3 - \widetilde{C}^3| \,](x, t)dx \leq \int_0^L [\, |C^1 - \widetilde{C}^1| + |C^2 - \widetilde{C}^2| + |C^3 - \widetilde{C}^3| \,](x, 0)dx, \tag{9}$$

$$\int_0^L [\, |C^1 - \widetilde{C}^1|_+ + |C^2 - \widetilde{C}^2|_+ + |C^3 - \widetilde{C}^3|_+ \,](x, t)dx \leq \int_0^L [\, |C^1 - \widetilde{C}^1|_+ + |C^2 - \widetilde{C}^2|_+ + |C^3 - \widetilde{C}^3|_+ \,](x, 0)dx. \tag{10}$$

For the latter inequality, we can assume that $\widetilde{C}$ *is only a supersolution. The contraction property implies the uniqueness of the solution.*

Theorem 2 (Stationary supersolution)**.** *There is a family of supersolutions to* (5)*, as large as needed, that are continuous functions* U *such that*

$$\begin{cases} \dfrac{dU^1(x)}{dx} + \dfrac{2}{3}U^1(x) - \dfrac{1}{3}\Big[U^2(x) + U^3(x)\Big] - \dfrac{1}{3}F(U^3(x), x) \geq 0, & (i) \\ \dfrac{dU^2(x)}{dx} + \dfrac{2}{3}U^2(x) - \dfrac{1}{3}\Big[U^1(x) + U^3(x)\Big] - \dfrac{1}{3}F(U^3(x), x) \geq 0, & (ii) \\ -\dfrac{dU^3(x)}{dx} + \dfrac{2}{3}U^3(x) + \dfrac{2}{3}F(U^3(x), x) - \dfrac{1}{3}\Big[U^1(x) + U^2(x)\Big] \geq 0, & (iii) \\ U^1(0) \geq C_0^1, \qquad U^2(0) \geq C_0^2, \qquad U^3(L) \geq U^2(L). \end{cases} \tag{11}$$

For initial data $C^i(x, 0) \leq U^i$*, then* $C^i(x, t) \leq U^i$ *for all* $t \geq 0$.

Theorem 3 (Uniform a priori estimates)**.** *The weak solution to* (6) *satisfies*

$$\int_0^L [\, |\frac{\partial}{\partial t}C^1| + |\frac{\partial}{\partial t}C^2| + |\frac{\partial}{\partial t}C^3| \,](x, t)dx \leq A^0, \tag{12}$$

$$\sup_{0 \leq x \leq L} [C^1 + C^2 + C^3](x, t) \leq A^1, \tag{13}$$

$$\int_0^L [\, |\frac{\partial}{\partial x}C^1| + |\frac{\partial}{\partial x}C^2| + |\frac{\partial}{\partial x}C^3| \,](x, t)dx \leq A^2, \tag{14}$$

for some constants A^i *depending only on the initial values* $C^i(0, x)$ *and their derivatives but not on* t.

2.2 Long time behavior. Stationary problem

Our next results concern the problem of interest for us, that is the steady state and its stability. We begin with the

Theorem 4 (Existence of the stationary problem solution)**.** *With assumptions* (7)*, there is a unique solution to* (5) *which is* C^1 *and nonnegative.*

With the uniform bounds in Theorem 3, we can study the time convergence to this steady state

Theorem 5 (Long time behavior and uniqueness of the stationary problem solution)**.** *With assumptions* (7)*,* (8)*, the solution* C *to* (6) *converges to the unique solution* $\overline{C}$ *to* (5) *in* L^1*,*

$$\|C(x,t) - \overline{C}(x)\|_{L^1} \underset{t\to\infty}{\searrow} 0.$$

Physiologically, this means that, whatever the initial solute concentrations, the system reaches the same steady-state, that is, stationary concentration profiles are independent of initial values.

We can go further and study the rate of convergence toward the stationary solution. This requires some further notations and assumptions. For $\mu(x)$ defined in (7), we use the notations in appendix C for the eigenelements $\phi = (\phi^1, \phi^2, \phi^3)$, $k(\mu)$ and $\Lambda(\mu)$. We assume

$$\sup_{x\in[0,L]} \big(2 - k(\mu)\big)_+ [\mu(x) - F_C(C,x)] < \Lambda(\mu). \tag{15}$$

When $F(C,x) = \mu(x)C$, this condition is obviously satisfied and thus it expresses a smallness condition on the second derivative in C.

When $F(C^3,x) = V_m(x)\frac{C^3}{1+C^3}$, the condition simplifies to

$$\sup_{x\in[0,L]} \big(2 - k(V_m)\big)_+ V_m(x) < \Lambda(V_m), \tag{16}$$

which is a smallness condition on V_m since $\Lambda(0) > 0$.

With this assumption, we can state the

Theorem 6 (Exponential convergence)**.** *With assumptions* (7)*,* (8) *and* (15)*, the solution to the problem* (6) *converges exponentially with* t *to the unique solution to* (5) *in the space*

$$L^1(\phi) = \left\{ f : [0,L] \to \mathbb{R}^3,\ \int_{[0,L]} \Big(|f^1(x)|\phi^1(x) + |f^2(x)|\phi^2(x) + |f^3(x)|\phi^3(x)\Big)dx < \infty \right\}.$$

that is to say:

$$\|C(x,t) - \overline{C}(x)\|_{L^1(\phi)} \le e^{-\mu t}\|C(x,0) - \overline{C}(x)\|_{L^1(\phi)}.$$

This theorem expresses a narrower result: if the maximal pump velocity V_m is small enough, the system reaches steady-state at an exponential rate which depends on V_m.

3 Proof of existence and a priori bounds

Because it is closely related to our numerical algorithm, we choose an approach based on the semi-discrete scheme.

3.1 Existence of a solution to the semi-discrete problem

Consider a discretisation parameter $\Delta x = L/N > 0$ with N an integer. The semi-discrete scheme associated with (6) is defined, for $k \in [1, N]$, as

$$\begin{cases} \dfrac{dC_k^1}{dt}(t) + \dfrac{C_k^1(t) - C_{k-1}^1(t)}{\Delta x} = \dfrac{1}{3}\Big[C_k^1(t) + C_k^2(t) + C_k^3(t) + F_k(C_k^3(t))\Big] - C_k^1(t), \\ \dfrac{dC_k^2}{dt}(t) + \dfrac{C_k^2(t) - C_{k-1}^2(t)}{\Delta x} = \dfrac{1}{3}\Big[C_k^1(t) + C_k^2(t) + C_k^3(t) + F_k(C_k^3(t))\Big] - C_k^2(t), \\ \dfrac{dC_k^3}{dt}(t) - \dfrac{C_{k+1}^3(t) - C_k^3(t)}{\Delta x} = \dfrac{1}{3}\Big[C_k^1(t) + C_k^2(t) + C_k^2(t) + F_k(C_k^3(t))\Big] - C_k^3(t) - F(C_k^3(t)), \end{cases} \tag{17}$$

with the boundary conditions $C_0^1 > 0$ and $C_0^2 > 0$ given in (6) and $C_{N+1}^3 = C_N^2$. We also choose the initial data

$$C_k^i(0) = \frac{1}{\Delta x}\int_{(k-1)\Delta x}^{k\Delta x} C^i(x,0)dx, \quad i = 1,\ 2,\ 3, \quad k = 1, ..., N. \tag{18}$$

Because (17) is a system of differential equations, it has a unique smooth solution and it is nonnegative. In order to link the continuous model to this discrete equation, we reconstruct three piecewise constant functions $C_{\Delta x}^i(x,t)$, from the discrete values, as

$$C_{\Delta x}^i(x,t) = C_k^i(t), \quad \text{for} \quad x \in ((k-1)\Delta x, k\Delta x), \quad i = 1,\ 2,\ 3. \tag{19}$$

To simplify the notation, we sometimes merely write C instead of $C_{\Delta x}$. We next prove that $C_{\Delta x}$ converges to the continuous solution.

Our proof is divided in several steps. We first recall some preliminary estimates on $C_k^i(0)$. Secondly we derive several uniform (in Δx) a priori bounds on the semi-discrete solutions. In a third , we use these estimates to prove that the solution converges when Δx goes to 0 to a weak solution to (6). Then, still using a priori bounds, we find some additional properties of the solution. These are enough to pass to the limit and recover a weak solution to (6).

First step. Preliminary controls. Given our assumptions (8), we derive using a classic approach (see [Bouchut, 2004, Godlewski and Raviart, 1996, LeVeque, 2002]) the following initial bounds at the discrete level

$$\|C_{\Delta x}(t=0)\|_{L^1} \le K^0 := \sum_{i=1}^{3} \|C^i(t=0)\|_{L^1}, \tag{20}$$

$$\sum_{i=1}^{3}\sum_{k=1}^{N} \|C_k^i(t=0) - C_{k-1}^i(t=0)\|_{L^1} \le K^1 := \sum_{i=1}^{3} \|\frac{d}{dx}C^i(t=0)\|_{M^1}, \tag{21}$$

$$\|\frac{d}{dt}C_{\Delta x}(t=0)\|_{L^1} \le K^2, \tag{22}$$

for a constant K^2, obtained from the equation and using (20)–(21), which only depends on the initial data but not on Δx. Indeed, from (17), we deduce that for $k \in [1, N]$ we have

$$\begin{cases} \Big|\dfrac{dC_k^1}{dt}(0)\Big| \le \dfrac{1}{\Delta x}\Big|C_k^1(0) - C_{k-1}^1(0)\Big| + \dfrac{2}{3}\Big|C_k^1(0)\Big| + \dfrac{1}{3}\Big|C_k^2(0)\Big| + \dfrac{1}{3}\Big|C_k^3(0)\Big| + \dfrac{1}{3}\Big|C_k^3(0)\Big|\mu(x), \\ \Big|\dfrac{dC_k^2}{dt}(0)\Big| \le \dfrac{1}{\Delta x}\Big|C_k^2(0) - C_{k-1}^2(0)\Big| + \dfrac{1}{3}\Big|C_k^1(0)\Big| + \dfrac{2}{3}\Big|C_k^2(0)\Big| + \dfrac{1}{3}\Big|C_k^3(0)\Big| + \dfrac{1}{3}\Big|C_k^3(0)\Big|\mu(x), \\ \Big|\dfrac{dC_k^2}{dt}(0)\Big| \le \dfrac{1}{\Delta x}\Big|C_k^2(0) - C_{k+1}^2(0)\Big| + \dfrac{1}{3}\Big|C_k^1(0)\Big| + \dfrac{1}{3}\Big|C_k^2(0)\Big| + \dfrac{2}{3}\Big|C_k^3(0)\Big| + \dfrac{2}{3}\Big|C_k^3(0)\Big|\mu(x). \end{cases}$$

We multiply each line by Δx and add them to obtain

$$\|\frac{dC}{dt}(0)\|_{L^1} \le \sum_{k=1}^{N}|C_k^1(0) - C_{k-1}^1(0)| + \sum_{k=1}^{N}|C_k^2(0) - C_{k-1}^2(0)| + \sum_{k=1}^{N}|C_k^3(0) - C_{k+1}^3(0)| + K_\mu\|C(0)\|_{L^1} \tag{23}$$

because μ is bounded on $[0, L]$ by a constant K_μ.

On the other hand (21) holds true with M^1 the Banach space of bounded measures. The notation $\|\cdot\|_{M^1}$ includes a Dirac mass at $x = 0$ for $i = 1,\ 2$, when the initial data does not match the boundary condition. Indeed, applying (8) to C^1, we have

$$\sum_{k=1}^{N}|C_k^1(0) - C_{k-1}^1(0)| = \frac{1}{\Delta x}\sum_{k=2}^{N}\Big|\int_{(k-1)\Delta x}^{k\Delta x} C^1(x,0)dx - \int_{(k-2)\Delta x}^{(k-1)\Delta x} C^1(x,0)dx + \int_0^{\Delta x}(C^1(x,0) - C_0^1)dx\Big|$$

and based upon (18), we can write

$$
\begin{aligned}
\sum_{k=1}^{N}|C_k^1(0)-C_{k-1}^1(0)| &= \sum_{k=2}^{N}\frac{1}{\Delta x}\Big[\Big|\int_{(k-1)\Delta x}^{k\Delta x}[C^1(x,0)dx-C^1(x-\Delta x,0)]dx+\int_0^{\Delta x}(C^1(x,0)-C_0^1)dx\Big|\Big]\\
&= \sum_{k=2}^{N}\frac{1}{\Delta x}\Big[\Big|\int_{(k-1)\Delta x}^{k\Delta x}\int_{x-\Delta x}^{x}\frac{d}{dx}C^1(z,0)dz]dx\Big|\Big]+\int_0^{\Delta x}\int_0^x\Big|\frac{d}{dx}C^1(z,0)dzdx\Big|\\
&= \sum_{k=2}^{N}\frac{1}{\Delta x}\Big[\int_{(k-1)\Delta x}^{k\Delta x}\int_0^{\Delta x}\Big|\frac{d}{dx}C^1(x+u-\Delta x,0)du\Big|dx\Big]+\int_0^{\Delta x}\int_0^x\Big|\frac{d}{dx}C^1(z,0)dz\Big|dx\\
&\le \frac{1}{\Delta x}\Big[\int_0^{\Delta x}\int_{\Delta x}^{L}\Big|\frac{d}{dx}C^1(x+u-\Delta x,0)\Big|dx\;du\Big]+\int_0^{\Delta x}\int_0^x\Big|\frac{d}{dx}C^1(z,0)dz\Big|dx\\
&\le \frac{1}{\Delta x}\Big[\int_0^{\Delta x}\int_x^{L+x-\Delta x}\Big|\frac{d}{dx}C^1(z,0)\Big|dz\;dx\Big]+\int_0^{\Delta x}\int_0^x\Big|\frac{d}{dx}C^1(z,0)dz\Big|dx\\
&\le \frac{1}{\Delta x}\int_0^{\Delta x}\int_0^{L+x-\Delta x}\Big|\frac{d}{dx}C^1(z,0)\Big|dz\;dx\\
&\le \|\frac{d}{dx}C^1(t=0)\|_{L^1}.
\end{aligned}
$$

□

Second step. Control in time. We first prove a uniform control on time derivatives

$$\|\frac{dC_{\Delta x}}{dt}(t)\|_{L^1}\le\|\frac{dC_{\Delta x}}{dt}(0)\|_{L^1}\le K^2,\qquad \forall t>0. \tag{24}$$

To prove this, we differentiate (17) with respect to t and find

$$
\begin{cases}
\frac{d}{dt}\Big(\frac{dC_k^1}{dt}\Big)+\frac{d}{dt}\Big(\frac{C_k^1-C_{k-1}^1}{\Delta x}\Big)=-\frac{2}{3}\frac{d}{dt}C_k^1+\frac{1}{3}\frac{d}{dt}C_k^2+\frac{1}{3}\frac{d}{dt}C_k^3+\frac{1}{3}\frac{d}{dt}C_k^3\frac{\partial F}{\partial C},\\
\frac{d}{dt}\Big(\frac{dC_k^2}{dt}\Big)+\frac{d}{dt}\Big(\frac{C_k^2-C_{k-1}^2}{\Delta x}\Big)=\frac{1}{3}\frac{d}{dt}C_k^1-\frac{2}{3}\frac{d}{dt}C_k^2+\frac{1}{3}\frac{d}{dt}C_k^3+\frac{1}{3}\frac{d}{dt}C_k^3\frac{\partial F}{\partial C},\\
\frac{d}{dt}\Big(\frac{dC_k^3}{dt}\Big)+\frac{d}{dt}\Big(\frac{C_k^3-C_{k+1}^3}{\Delta x}\Big)=\frac{1}{3}\frac{d}{dt}C_k^1+\frac{1}{3}\frac{d}{dt}C_k^2-\frac{2}{3}\frac{d}{dt}C_k^3-\frac{2}{3}\frac{d}{dt}C_k^3\frac{\partial F}{\partial C}.
\end{cases}
\tag{25}
$$

We multiply each line i by $\text{sign}(\frac{d}{dt}C_k^i)$ and find

$$
\begin{cases}
\frac{d}{dt}\Big|\frac{dC_k^1(t)}{dt}\Big|+\frac{1}{\Delta x}\Big[\Big|\frac{d}{dt}C_k^1(t)\Big|-\Big|\frac{d}{dt}C_{k-1}^1(t)\Big|\Big]\le-\frac{2}{3}\Big|\frac{d}{dt}C_k^1\Big|+\frac{1}{3}\Big|\frac{d}{dt}C_k^2\Big|+\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|+\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|\frac{\partial F}{\partial C},\\
\frac{d}{dt}\Big|\frac{dC_k^2(t)}{dt}\Big|+\frac{1}{\Delta x}\Big[\Big|\frac{d}{dt}C_k^2(t)\Big|-\Big|\frac{d}{dt}C_{k-1}^2(t)\Big|\Big]\le\frac{1}{3}\Big|\frac{d}{dt}C_k^1\Big|-\frac{2}{3}\Big|\frac{d}{dt}C_k^2\Big|+\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|+\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|\frac{\partial F}{\partial C},\\
\frac{d}{dt}\Big|\frac{dC_k^3(t)}{dt}\Big|+\frac{1}{\Delta x}\Big[\Big|\frac{d}{dt}C_k^3(t)\Big|-\Big|\frac{d}{dt}C_{k+1}^3(t)\Big|\Big]\le\frac{1}{3}\Big|\frac{d}{dt}C_k^1\Big|-\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|+\frac{2}{3}\Big|\frac{d}{dt}C_k^2\Big|-\frac{1}{3}\Big|\frac{d}{dt}C_k^3\Big|\frac{\partial F}{\partial C}.
\end{cases}
$$

We sum on the lines and on the indices k to obtain

$$\frac{d}{dt}\sum_{k=1}^{N}\sum_{i=1}^{3}\Delta x|\frac{d}{dt}C_k^i(t)|\le-|\frac{d}{dt}C_N^1(t)|+|\frac{d}{dt}C_0^1|-|\frac{d}{dt}C_N^2(t)|+|\frac{d}{dt}C_0^2|+|\frac{d}{dt}C_{N+1}^3(t)|-|\frac{d}{dt}C_1^3|. \tag{26}$$

Knowing that C_0^1 and C_0^2 are independent on t, we have $\frac{d}{dt}C_0^1=0$, $\frac{d}{dt}C_0^2=0$. In addition, since $C_{N+1}^3(t)=C_N^2(t)$, we have $\frac{d}{dt}C_{N+1}^3(t)=\frac{d}{dt}C_N^2(t)$. Altogether, we arrive at

$$\frac{d}{dt}\sum_{k=1}^{N}\Delta x\Big[|\frac{d}{dt}C_k^1(t)|+|\frac{d}{dt}C_k^2(t)|+|\frac{d}{dt}C_k^3(t)|\Big]\le 0. \tag{27}$$

That proves our first estimate (24).

Third step. Bounds on $C_{\Delta x}$. Our purpose here is to prove that we also have for all $t\ge 0$

$$\|C_{\Delta x}(t)\|_{L^1}\le K^0+K^3t,\qquad \text{with}\;\; K^3=C_0^1+C_0^2. \tag{28}$$

To do so, using (17), we sum on the lines and on the indices and find

$$\frac{d}{dt}\sum_{k=1}^{N}\Delta x\Big[C_k^1(t)+C_k^2(t)+C_k^3(t)\Big]\le C_0^2+C_0^1 \tag{29}$$

and the result follows.

Fourth step. Uniform bounded variations on $C_{\Delta x}$. We want to prove the uniform BV control

$$\sum_{k=1}^{N}|C_k-C_{k-1}|(t)\le K^4(1+t) \qquad \forall t>0. \tag{30}$$

Note that an uniform bound follows directly from this BV control. For all $t\ge 0$,

$$C_k^i\le C_0^i+K^4(1+t),\ i=1,\ 2, \qquad C_k^3\le C_0^2+2K^4(1+t). \tag{31}$$

We prove it for C^1 only. We deduce from (17) that

$$\begin{aligned}\sum_{k=1}^{N}|C_k^1-C_{k-1}^1|(t) &\le \sum_{k=1}^{N}\Delta x|\frac{d}{dt}C_k^1(t)|+\sum_{k=1}^{N}\frac{\Delta x}{3}\Big[2|C_k^1|+|C_k^2|+(1+K_\mu)|C_k^3|\Big](t)\\ &\le K^4(1+t)\end{aligned}$$

using the estimates (28) and (24).

Fifth step. Convergence of the semi-discrete solution. Because we have proved that $C_{\Delta x}$ is uniformly bounded in $BV([0,T]\times[0,L])$, according to the Rellich-Kondrachov compactness theorem (see [Evans, 1998, Demengel and Demengel, 2007, Dafermos, 2005]), there is a subsequence which converges in $L^1\big((0,T)\times(0,L)\big)$ to a function $C(x,t)\in L^1\big((0,T)\times(0,L)\big)$. Then, after further extracting a subsequence we obtain

$$C_{\Delta x}(x,t)\underset{\Delta x\to 0}{\longrightarrow} C(x,t), \qquad a.e.$$

Consequently we also have, because F is continuous in C^3,

$$F(C_{\Delta x}^3(x,t),x)\underset{\Delta x\to 0}{\longrightarrow} F(C^3(x,t),x).$$

To check that this limit is a weak solution to (6), we introduce the set V of test-functions

$$V=\left\{\Phi\in\Big(C^1(\mathbb{R}^+\times[0,L])\Big)^3, \qquad \Phi^1(L,t)=\Phi^3(0,t)=0, \qquad \Phi^3(L,t)=\Phi^2(L,t)\right\}. \tag{32}$$

It is easy to pass to the limit in the zero order terms because, using the dominated convergence theorem, we have, for all $\Phi\in V$,

$$\int_0^T\int_0^L C_{\Delta x}^j(x,t)\Phi^j(x,t)dxdt\underset{\Delta x\to 0}{\longrightarrow}\int_0^T\int_0^L C^j(x,t)\Phi^j(x,t)dxdt,$$

$$\int_0^T\int_0^L F(C_{\Delta x}^3(x,t),x)\Phi^j(x,t)dxdt\underset{\Delta x\to 0}{\longrightarrow}\int_0^T\int_0^L F(C^3(x,t),x)\Phi^j(x,t)dxdt.$$

To recover the terms with x-derivative is more difficult. After a change of variable, we write

$$\begin{aligned}&\int_0^T\int_{\Delta x}^L\frac{C_{\Delta x}^1(x,t)-C_{\Delta x}^1(t,x-\Delta x)}{\Delta x}\Phi^1(x,t)dxdt\\ &=\int_0^T\int_{\Delta x}^L\frac{C_{\Delta x}^1(x,t)}{\Delta x}\Phi^1(x,t)dxdt-\int_0^T\int_0^{L-\Delta x}\frac{C_{\Delta x}^1(x,t)}{\Delta x}\Phi^1(t,x+\Delta x)dxdt\\ &=-\int_0^T\int_0^{\Delta x}\frac{C_{\Delta x}^1(x,t)}{\Delta x}\Phi^1(t,x)dxdt+\int_0^T\int_0^{L-\Delta x}C_{\Delta x}^1(x,t)\frac{\Phi^1(x,t)-\Phi^1(t,x+\Delta x)}{\Delta x}dxdt\\ &\quad+\int_0^T\int_{L-\Delta x}^L\frac{C_{\Delta x}^1(x,t)}{\Delta x}\Phi^1(x,t)dxdt.\end{aligned}$$

Using again the dominated convergence theorem, we have

$$\int_0^T \int_{\Delta x}^{L-\Delta x} C^1_{\Delta x}(x,t) \frac{\Phi^1(x,t) - \Phi^1(t, x+\Delta x)}{\Delta x} dxdt \underset{\Delta x \to 0}{\longrightarrow} - \int_0^T \int_0^L C^1(x,t) \frac{\partial \Phi^1(x,t)}{\partial x} dxdt,$$

$$- \int_0^T \int_0^{\Delta x} \frac{C^1_{\Delta x}(x,t)}{\Delta x} \Phi^1(t, x+\Delta x) dxdt \underset{\Delta x \to 0}{\longrightarrow} - \int_0^T \Phi^1(0,t) C^1(0,t),$$

$$\int_0^T \int_{L-\Delta x}^L \frac{C^1_{\Delta x}(x,t)}{\Delta x} \Phi^1(x,t) dxdt \underset{\Delta x \to 0}{\longrightarrow} \int_0^T \Phi^1(L,t) C^1(L,t) = 0.$$

Integrating by part, we obtain

$$\int_0^T \int_0^L \frac{\partial C^1_{\Delta x}(x,t)}{\partial t} \Phi^1(x,t) dxdt = \int_0^T \int_0^L C^1_{\Delta x}(x,t) \frac{\partial \Phi^1(x,t)}{\partial t} dxdt$$

$$+ \int_0^L \Phi^1(x,T) C^1_{\Delta x}(x,T) dx - \int_0^L \Phi^1(x,0) C^1_{\Delta x}(x,0) dx$$

$$\underset{\Delta x \to 0}{\longrightarrow} - \int_0^T \int_0^L C^1(x,t) \frac{\partial \Phi^1(x,t)}{\partial t} dxdt$$

$$+ \int_0^L \Phi^1(x,T) C^1(x,T) dx - \int_0^L \Phi^1(x,0) C^1(x,0) dx$$

We are now ready to pass to the limit in the equations. We argue independently for each component of the system. The equation satisfied by $C^1_{\Delta x}$ is,

$$\begin{cases} \frac{\partial C^1_{\Delta x}}{\partial t}(x,t) + \frac{C^1_{\Delta x}(x,t) - C^1_{\Delta x}(t, x-\Delta x)}{\Delta x} = -\frac{2}{3} C^1_{\Delta x}(x,t) + \frac{1}{3} \Big[C^2_{\Delta x}(x,t) + C^3_{\Delta x}(x,t) + F(C^3_{\Delta x}(x,t), x) \Big], \; x \in]\Delta x, L], \\ \frac{\partial C^1_{\Delta x}}{\partial t}(x,t) + \frac{C^1_{\Delta x}(x,t) - C^1_0}{\Delta x} = -\frac{2}{3} C^1_{\Delta x}(x,t) + \frac{1}{3} \Big[C^2_{\Delta x}(x,t) + C^3_{\Delta x}(x,t) + F(C^3_{\Delta x}(x,t), x) \Big], \quad x \in]0, \Delta x], \\ C^1_{\Delta x}(0,t) = C^1_0, \qquad x = 0 \end{cases} \tag{33}$$

Thus, we prove that C satisfies the following weak formulation. For $\Phi \in V$ (see (32)) we have

$$\begin{aligned} &\int_0^T \int_0^L \frac{\partial \Phi}{\partial t} . C(x,t) dxdt + \int_0^T \int_0^L \frac{\partial \Phi}{\partial x} . C(x,t) dxdt = \frac{2}{3} \int_0^T \int_0^L \Phi . C(x,t) dxdt \\ &\quad + \frac{2}{3} \int_0^T \int_0^L \Phi^3 . F(C^3, x)(x,t) dxdt - \frac{1}{3} \int_0^T \int_0^L \Big[\Phi^1 (C^2 + C^3 + F(C^3, x))(x,t) \Big] dxdt \\ &\quad - \frac{1}{3} \int_0^T \int_0^L \Big[\Phi^2 (C^1 + C^3 + F(C^3, x))(x,t) \Big] dxdt - \frac{1}{3} \int_0^T \int_0^L \Big[\Phi^3 (C^1 + C^2)(x,t) \Big] dxdt \\ &+ \int_0^T \Phi^1(0,t) C^1(0,t) dt + \int_0^T \Phi^2(0,t) C^2(0,t) dt + \int_0^L \Phi(x,T) C(x,T) dx - \int_0^L \Phi(x,0) C(x,0) dx \end{aligned} \tag{34}$$

The equations for C^2 and C^3 are treated similarly, because the boundary conditions are related and cancel out when adding the equations.

We subsequently prove that the first line of (33) converges to a weak equation, and deduce the weak equation satisfied by C.

3.2 Properties of limit

In the limit process, we keep the a priori bounds that we record here from (24), (28), (30),

$$\int_0^L [C^1 + C^2 + C^3](x,t) dx \leq K^0 + K^3 t, \qquad \forall t \geq 0, \tag{35}$$

$$\int_0^L \Big[\, |\frac{\partial}{\partial t} C^1| + |\frac{\partial}{\partial t} C^2| + |\frac{\partial}{\partial t} C^3| \, \Big](x,t) dx \leq K^2, \qquad \forall t \geq 0, \tag{36}$$

$$\|\frac{\partial C}{\partial x}(t)\|_{L^1[0,L]} \le K^4(1+t) \qquad \forall t \ge 0. \tag{37}$$

Moreover, we can prove that C is uniformly continuous in time. Indeed, $\forall t < 0, h > 0$,

$$\begin{aligned}\|C(x,t+h) - C(x,t)\|_{L^1[0,L]} &\le \int_0^L \Big| \int_0^h \frac{\partial}{\partial t} C(x,t+s)ds \Big| dx \\ &\le \int_0^h \|\frac{d}{dt} C(x,t+s)\|_{L^1[0,L]} ds \le K^0 h. \qquad \square\end{aligned}$$

This proves that for all $T > 0$ the regularity holds also

$$C^i \in C\Big([0,T]; L^1[0,L]\Big) \cap BV\Big([0,T] \times [0,L]\Big).$$

The drawback of estimates (35) and (37) is that they are time-dependent. This is improved in section 3.4.

3.3 The contraction property and the comparison principle

We continue this section with the contraction property (9). We use the notations

$$d^i(x,t) := |C^i(x,t) - \widetilde{C}^i(x,t)|, \qquad i = 1,\ 2,\ 3.$$

$$G(x,t) := |F\big(C^3(x,t),x\big) - F\big(\widetilde{C^3}(x,t),x\big)| \le \mu(x)\ d^3(x,t).$$

We substract the lines i in (6) for C and $\widetilde{C}$. We multiply them by sign $\big(C^i(x,t) - \widetilde{C^i}(x,t)\big)$, (see [Allaire, 2007, Perthame, 2007] and the references therein). We obtain the inequalities

$$\begin{cases} \dfrac{\partial d^1}{\partial t} + \dfrac{\partial d^1}{\partial x} \le -\dfrac{2}{3} d^1 + \dfrac{1}{3}(d^2 + d^3 + G), \\ \dfrac{\partial d^2}{\partial t} + \dfrac{\partial d^2}{\partial x} \le -\dfrac{2}{3} d^2 + \dfrac{1}{3}(d^1 + d^3 + G), \\ \dfrac{\partial d^3}{\partial t} - \dfrac{\partial d^3}{\partial x} \le -\dfrac{2}{3}(d^3 + G) + \dfrac{1}{3}(d^2 + d^1). \end{cases} \tag{38}$$

The third line uses the fact that, because we assume F is nondecreasing in C (assumption (7))

$$\text{sign}\left(C^3(x,t) - \widetilde{C^3}(x)\right) \Big[F\big(C^3(x,t),x\big) - F\big(\widetilde{C^3}(x),x\big)\Big] = \Big|F\big(C^3(x,t),x\big) - F\big(\widetilde{C^3}(x),x\big)\Big|.$$

From these inequalities we conclude that

$$\frac{d}{dt}\int_0^L [d^1 + d^2 + d^3]dx \le -d^1(L,t) - d^3(0,t) \le 0, \tag{39}$$

which implies

$$\int_0^L [d^1(x,t) + d^2(x,t) + d^3(x,t)]dx \le \int_0^L [d^1(x,0) + d^2(x,0) + d^3(x,0)]dx. \tag{40}$$

This is the contraction property (9). $\square$

The variant (10) can be proved following the same calculation, multiplying line i by $\text{sign}_+\Big(\widetilde{C}^i(x,t) - C^i(x,t)\Big)$, defined by $\text{sign}_+(f) = \text{sign}\Big(\max(f,0)\Big)$. Because sign_+ is increasing, it is enough to work with a supersolution $\widetilde{C}^i(x,t)$.

3.4 Proof of theorem 3 and supersolution

We first build the family of stationary supersolutions, then we derive the uniform bounds on $C(x,t)$.

First step. A family of supersolution to (5)**.** Our goal is to build nonnegative functions U^1, U^2, U^3 such that $U^3(x) = U^1(x) + U^2(x)$ and U^1, U^2 satisfy

$$\begin{cases} \dfrac{dU^1(x)}{dx} + \dfrac{1}{3}U^1(x) - \dfrac{2}{3}U^2(x) - \dfrac{1}{3}F(U^1(x)+U^2(x),x) = 0, \\ \dfrac{dU^2(x)}{dx} + \dfrac{1}{3}U^2(x) - \dfrac{2}{3}U^1(x) - \dfrac{1}{3}F(U^1(x)+U^2(x),x) = 0, \\ U^1(0) \geq C_0^1, \qquad U^2(0) \geq C_0^2. \end{cases} \tag{41}$$

which is clearly sufficient to have a supersolution to (5).

For U^3, summing the equations on U^1 and U^2, we obtain

$$\frac{d}{dx}\Big[U^1(x)+U^2(x)\Big] - \frac{1}{3}\Big[U^1(x)+U^2(x)\Big] - \frac{2}{3}F(U^1(x)+U^2(x),x) = 0,$$

so that we also have

$$-\frac{dU^3(x)}{dx} + \frac{2}{3}U^3(x) + \frac{2}{3}F(U^3(x),x) - \frac{1}{3}\Big[U^1(x)+U^2(x)\Big] = 0,$$

which implies that the correct equation holds. The boundary condition is also satisfied as a supersolution because $U^3(L) = U^2(L) + U^1(L) \geq U^2(L)$.

To build a supersolution to (41), we choose $U^1 = U^2 = \frac{1}{2}H$, where H satisfies

$$\frac{dH(x)}{dx} - \frac{1}{3}H(x) - \frac{2}{3}F(H(x),x) = 0, \qquad H(0) = 2\max(C_0^1, C_0^2). \tag{42}$$

We conclude the proof because (42) is solved by the Cauchy-Lipschitz theorem. Note that the boundary condition $H(0) = H^0$ in place of $2\max(C_0^1, C_0^2)$ allows us to find U^1 and U^2 (and thus U^3) as large as we want. □

Second step. Uniform L^∞ bounds on $C^i(x,0)$. From the comparison principle (10), we conclude that $C(x,t) \leq U^i(x)$ choosing, as indicated above, $U^i \geq C^i(x,0)$. This proves (13).

From this uniform a priori bound, we also deduce 14 which improves (37). □

3.5 Proof of theorem 4 (existence of a solution to the stationary problem)

We prove the existence of a solution to (5). To do so, we use an auxiliary boundary value problem which is studied in Appendix B,

$$\begin{cases} \dfrac{dC^1(x)}{dx} + \dfrac{2}{3}C^1(x) = \dfrac{1}{3}\Big[C^2(x) + C^3(x) + F(C^3(x),x)\Big], \\ \dfrac{dC^2(x)}{dx} + \dfrac{2}{3}C^2(x) = \dfrac{1}{3}\Big[C^1(x) + C^3(x) + F(C^3(x),x)\Big], \\ -\dfrac{dC^3(x)}{dx} + \dfrac{2}{3}\Big[C^3(x) + F(C^3(x),x)\Big] = \dfrac{1}{3}\Big[C^1(x) + C^2(x)\Big], \\ C^1(0) = C_0^1 > 0, \qquad C^2(0) = C_0^2 > 0, \qquad C^3(L) = C_L^3 \geq 0. \end{cases} \tag{43}$$

For theorem 4, it is enough to prove that there is a positive value C_L^3 such that the solution to (43) satisfies $C^3(L) = C^2(L)$. To do so, we define the continuous mapping

$$g : C_L^3 \longmapsto C^2(L) - C^3(L)$$

We claim that $g(0) > 0$ and that $g(\infty) < 0$, which gives us that g vanishes on $\mathbb{R}^+$ and concludes the proof.

- $g(0) > 0$. By the maximum principle, the $C^i(\cdot)$ are nonnegative and since C_0^2 is positive, so is $C^2(L)$.
- $g(\infty) < 0$. We want to prove that for C_L^3 large enough $C^2(L) < C_L^3$. It is enough to prove that

$$C^1(L) + C^2(L) < C^3(L). \tag{44}$$

Because solutions to (43) satisfy

$$\frac{d}{dx}\Big[C^1 + C^2 - C^3\Big] = 0,$$

proving (44) is equivalent to prove

$$C_0^1 + C_0^2 < C^3(0). \tag{45}$$

But this is obvious because, since the C^is are nonnegative, we have $C^3(x) \geq C^3(L)\exp(-2(1+\mu_M)(L-x)/3)$. This concludes the existence proof.

Uniqueness follows by monotonicity of g by the maximum principle for the transport equations. □

3.6 Proof of theorem 5 (large time limit)

Our proof is organized as follows. We consider the case where the initial data is a sub or a supersolution to the steady state equation (5); we prove that the solutions are monotonic in time and, because they are bounded as stated in theorem 3, they converge to the steady state. This is enough because for a general initial data, we can always use theorem 2 and find a supersolution U_0 such that

$$0 \leq C^i(x,0) \leq U_0^i(x) \qquad \forall i,\ \forall x \in [0,L].$$

According to the comparison principle, calling V and U the solutions to (6) with respective initial conditions taken to be $V_0 = 0$ (a subsolution!) and U_0, we obtain

$$V^i(x,t) \leq C^i(x,t) \leq U^i(x,t) \qquad \forall i,\ \forall x \in [0,L],\ \forall t > 0.$$

As U and V converge toward the steady state, so does C.

With this argument we are reduced to proving theorem 5 with an initial data C_0 which is supersolution to (5); indeed the same argument holds for subsolutions with the only modification to replace the $|\frac{\partial C}{\partial t}|_+$ by $|\frac{\partial C}{\partial t}|_-$.

First step. In the same way we established the first inequality of theorem 3, we can differentiate (6) with respect to t, multiply each line i by $\text{sign}_+(\frac{\partial C^i}{\partial t})$ (defined in section 3.3), and sum on the lines. We obtain the variant of (12)

$$\frac{d}{dt}\int_0^L \Big[\Big(\frac{\partial C^1}{\partial t}\Big)_+ + \Big(\frac{\partial C^2}{\partial t}\Big)_+ + \Big(\frac{\partial C^3}{\partial t}\Big)_+\Big](x,t)dt \leq 0. \tag{46}$$

Second step. As $C(.,t=0)$ is a supersolution, we have $\Big(\frac{\partial C^i}{\partial t}(x,0)\Big)_+ = 0$ for all i, $x \in [0,L]$. Using (46), we conclude that

$$\Big(\frac{\partial C^i}{\partial t}(x,t)\Big)_+ = 0 \qquad \forall i,\ \forall x \in [0,L],\ \forall t > 0,$$

which means that $C(.,t)$ is a supersolution of (5) for all $t > 0$ and that each component is monotonically decreasing.

Therefore we can pass to the limit pointwise as $t \to \infty$ and $C_i(x,t)$ converges to a function $\overline{C}_i(x)$ which is a steady state and thus coincides with that built in theorem 4.

This establishes theorem 5 for initial data which are supersolutions and thus concludes the proof. □

4 Numerical method

Since, at least for small nonlinearities, the solution to the dynamic problem converges exponentially toward the steady state solution, we propose to approach numerically the solution to (5) by computing the solution to (6) for large times. For simplicity, we only treat the Michaelis-Menten form of the active transport term (3). Also, as is usually done with in transport equations we use a finite volume method (see [Bouchut, 2004, LeVeque, 2002, Godlewski and Raviart, 1996]).

4.1 The finite volume scheme

We use a time step Δt and a mesh of size $\Delta x = L/N$ with N the number of cells $Q_k = (x_{k-1/2}, x_{k+1/2})$ (that means $x_{1/2} = 0$ and $x_{N+1/2} = L$). The discrete times are denoted by $t^n = n\Delta t$. To guarantee that the discrete solution remains nonnegative as shown later, we use the CFL condition

$$\Delta t \leq \frac{3\Delta x}{3 + 2\Delta x + 2\Delta x V_m}. \tag{47}$$

The principle of finite volumes is to enforce numerical conservation of quantities that are physically conserved and thus to approximate quantities by their average. For instance the discrete initial states are, as before,

$$C_k^{j,0} = \frac{1}{\Delta x}\int_{Q_k} C^j(x,0)dx, \qquad i = 1,\ 2,\ 3, \quad k = 1, ..., N. \tag{48}$$

We call $C_k^{j,n}$ the discrete solution at time t^n in tube i that approximates equation (6), for $k \in [0, N]$. We use the scheme

$$\begin{cases} C_k^{1,n+1} = & C_k^{1,n} - \dfrac{\Delta t}{\Delta x}(C_k^{1,n} - C_{k-1}^{1,n}) + \Delta t J_k^{1,n}, \\ C_k^{2,n+1} = & C_k^{2,n} - \dfrac{\Delta t}{\Delta x}(C_k^{2,n} - C_{k-1}^{2,n}) + \Delta t J_k^{2,n}, \\ C_k^{3,n+1} = & C_k^{3,n} + \dfrac{\Delta t}{\Delta x}(C_{k+1}^{3,n} - C_k^{3,n}) + \Delta t J_k^{3,n}, \end{cases} \tag{49}$$

with the notations

$$\begin{cases} C_k^{int,n} = \dfrac{1}{3}\Big[C_k^{1,n} + C_k^{2,n} + C_k^{3,n} + V_m \dfrac{C_k^{3,n}}{1 + C_k^{3,n}}\Big], \\ J_k^{1,n} = C_k^{int,n} - C_k^{1,n}, \qquad J_k^{2,n} = C_k^{int,n} - C_k^{2,n}, \\ J_k^{3,n} = C_k^{int,n} - C_k^{3,n} - V_m \dfrac{C_k^{3,n}}{1 + C_k^{3,n}}. \end{cases} \tag{50}$$

For boundary conditions, at each time we choose: $C_0^{1,n} = C_0^1$, $C_0^{2,n} = C_0^2$, $C_{N+1}^{3,n} = C_N^{2,n}$.

Because this is an explicit scheme, departing from (48), we obtain directly the solution $C_k^{1,n+1}$ at time t^{n+1} from that at time t^n.

Derivation of the CFL condition. In order to guarantee that the discrete solution remains nonnegative, under the assumptions that the boundary conditions and the initial conditions are nonnegative we assume that

$$\forall i \in [1, 2, 3], \forall k \in [1, N], C_k^{i,n} \geq 0.$$

We seek to have the same property for the following step of time:

$$\forall i \in [1, 2, 3], \forall k \in [1, N], C_k^{i,n+1} \geq 0.$$

We begin with $C_k^{1,n+1}$ and we write (49) as

$$C_k^{1,n+1} = \Big[1 - \frac{2}{3}\Delta t - \frac{\Delta t}{\Delta x}\Big]C_k^{1,n} + \frac{\Delta t}{\Delta x}C_{k-1}^{1,n} + \frac{\Delta t}{3}C_k^{2,n} + \frac{\Delta t}{3}C_k^{3,n} + \frac{\Delta t}{3}V_m \frac{C_k^{3,n}}{1 + C_k^{3,n}}.$$

To insure that $C_k^{1,n+1}$ is a positive combination of positive terms, we have to impose $1 - \frac{2}{3}\Delta t - \frac{\Delta t}{\Delta x} \geq 0$, that is to say

$$\Delta t \leq \frac{3\Delta x}{2\Delta x + 3}. \tag{51}$$

The same argument holds for C^2. For C^3, we write

$$C_k^{3,n+1} = \Big[1 - \frac{2}{3}\Delta t - \frac{\Delta t}{\Delta x} - \frac{2}{3}V_m \frac{\Delta t}{1 + C_k^{3,n}}\Big]C_k^{3,n} + \frac{\Delta t}{\Delta x}C_{k+1}^{3,n} + \frac{\Delta t}{3}C_k^{2,n} + \frac{\Delta t}{3}C_k^{1,n}.$$

Here we have to impose that

$1-\frac{2}{3}\Delta t-\frac{\Delta t}{\Delta x}-\frac{2}{3}V_m\frac{\Delta t}{1+C_k^{3,n}}\geq 0$, that is to say

$$\Delta t\leq\frac{3\Delta x}{3+2\Delta x+2\Delta xV_m}\leq\frac{3\Delta x}{2\Delta x+3}. \tag{52}$$

Finally, to satisfy both (51) and (52), it is sufficient to impose (47). □

The arguments developed for the continuous model can be used at the discrete level to prove that the numerical solutions remain bounded, as we now describe.

Stability of the scheme. We want to guarantee, under the CFL condition, the stability of the scheme under the form:

$$0\leq C_k^{i,n}\leq M,\qquad\forall k\in[1,N],\qquad\forall n\in[0,\infty[,\qquad i=1,\ 2,\ 3. \tag{53}$$

First step. Existence of a family of discrete supersolutions. We build a nonnegative vector $U=(U_1^1,\dots,U_N^1,U_1^2,\dots,U_N^2,U_1^3,\dots,U_N^3)$ such that

$$\begin{cases}U_k^1-U_{k-1}^1\geq\dfrac{\Delta x}{3}\Big[U_k^2+U_k^3-2U_k^1+V_m\dfrac{U_k^3}{1+U_k^3}\Big], & k\in[1,N],\\ U_k^2-U_{k-1}^2\geq\dfrac{\Delta x}{3}\Big[U_k^1+U_k^3-2U_k^2+V_m\dfrac{U_k^3}{1+U_k^3}\Big], & k\in[1,N],\\ \Big(U_{k+1}^3-U_k^3\Big)\geq\dfrac{\Delta x}{3}\Big[U_k^1+U_k^2-2U_k^3-2V_m\dfrac{U_k^3}{1+U_k^3}\Big], & k\in[1,N],\\ U_0^1>C_0^1,\qquad U_0^2>C_0^2,\qquad U_{N+1}^3=U_N^2, & \end{cases} \tag{54}$$

and

$$U_k^i\geq C_k^{i,0},\qquad\forall k\in[1,N],\qquad i=1,\ 2,\ 3, \tag{55}$$

We define the matrix $A=A_{\Delta x}$ such that solving (54) is equivalent to finding U which satisfies

$$AU\geq 0. \tag{56}$$

A is irreducible [Prasolov, 1994], and

$$\exists\ j_0\text{ such as }a_{j_0,j_0}-\sum_{\substack{1\leq i\leq 3N\\ i\neq j_0}}a_{i,j_0}>0,\qquad(j_0=2N+1)$$

Using the M-matrix theory, A is invertible and A^{-1} is positive (that is to say all its coefficients are positive). We then choose $x>0,\ x\in\mathbb{R}^{3N}$. We have $A^{-1}x=y>0$, so $Ay=x$. We can choose α such that

$$\alpha y\geq C^0,\qquad\alpha y_1\geq C_0^1,\qquad\alpha y_{N+1}\geq C_0^2. \tag{57}$$

Thus, $U=\alpha y$ satisfies (54) and (55).

Second step. The induction. Assuming that for a given n

$$C_k^{i,n}\leq U_k^i\qquad\forall k\in[1,N]\qquad i=1,\ 2,\ 3. \tag{58}$$

Then,

$$\begin{aligned}C_k^{1,n+1}=&\Big[1-\frac{2}{3}\Delta t-\frac{\Delta t}{\Delta x}\Big]C_k^{1,N}+\frac{\Delta t}{\Delta x}C_{k-1}^n+\frac{\Delta t}{3}C_k^{2,n}+\frac{\Delta t}{3}C_k^{3,n}+\frac{\Delta t}{3}\frac{C_k^{3,n}}{1+C_k^{3,n}},\\ \leq&\Big[1-\frac{2}{3}\Delta t-\frac{\Delta t}{\Delta x}\Big]U_k^{1,N}+\frac{\Delta t}{\Delta x}U_{k-1}^n+\frac{\Delta t}{3}U_k^{2,n}+\frac{\Delta t}{3}U_k^{3,n}+\frac{\Delta t}{3}\frac{U_k^{3,n}}{1+U_k^{3,n}},\\ \leq&U_k^1.\end{aligned}$$

The same calculation holds for $C_k^{2,n+1}$ and $C_k^{3,n+1}$. Since (55) holds true, we deduce (53) with $M=\max\{U_k^i,\ k\in[1,N],i=1,\ 2,\ 3\}$.

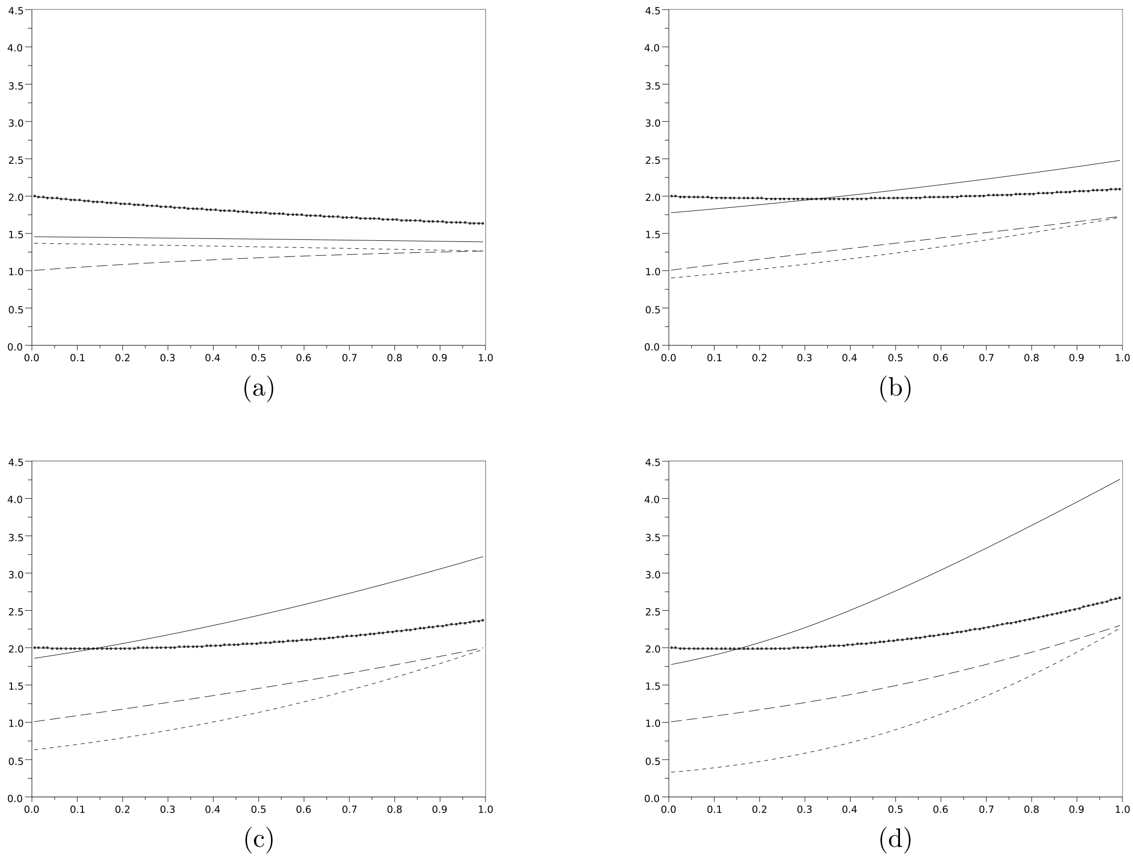

Figure 2: Concentration profiles at steady state in different tubes. The thin solid curve represents C^1, the thick curve C^{int}, the dashed curve C^2, and the dotted curve C^3. Parameters: $C_0^1 = 2$ and $C_0^2 = 1$, $L = 1$, $\Delta x = 0.01$, $Nc = 0.99$, where $Nc = \frac{\Delta t}{\Delta x}$. The pump velocity V_m is taken as 0 (a), 3 (b), 5 (c), and 8 (d). The profiles are obtained after 1000 time iterations.

4.2 Steady states

We then use this method to compute a numerical solution to (5), iterating the scheme for n large enough with the initial data $C^j(x,0) = 1$ for $j = 1$, 2 and 3.

Figure 2 depicts the concentration profiles at steady state for different values of V_m. We observe that if V_m is large enough, there is a longitudinal gradient of concentration, as observed physiologically.

In order to assert the exponential convergence of the algorithm (as predicted by the theory), we define for each time step n the indicator

$$c(n) = \max_{k\in[1,N]} \|C_k^n - C_k^{n-1}\|_\infty.$$

Displayed in Figure 3 is the plot of $log(c(n))$ as a function of the number of time iterations n. Our results indicate that the exponential convergence holds true even for large values of V_m, even though the decay rate is then slower. A physiological interpretation could be that the higher V_m, the more significant the concentration gradient, and the longer the time needed to reach equilibrium.

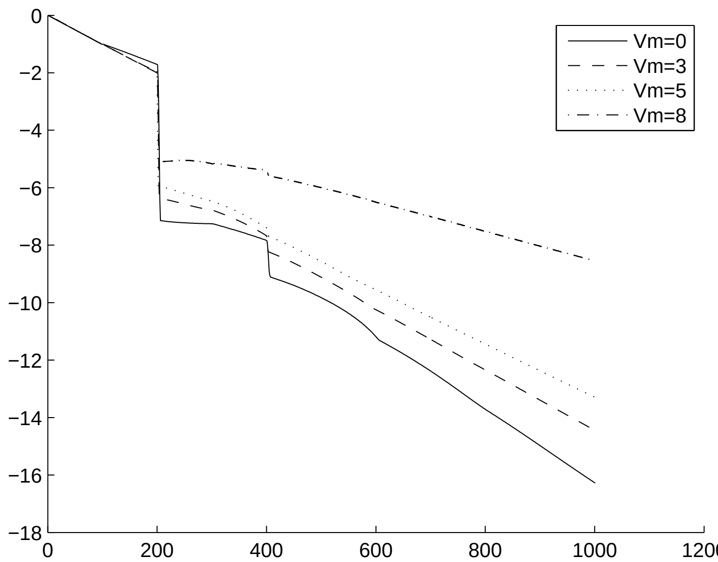

Figure 3: Log-convergence of the dynamic problem toward the steady-state solution, for different values of V_m. The parameters are the same as those used in Figure 2.The convergence slows down as V_m increases.

4.3 The linear case $V_m = 0$

If we ignore active transport, the system becomes linear. In this case we prove that the convergence toward the equilibrium state is of order $e^{-\lambda t}$ with λ the first eigenvalue as described in Appendix C.

For different values of L, on one hand, we calculate the eigenvalue λ in (73) using the power algorithm, and on the other hand, we compute the logarithmic rate of convergence for the numerical solution to (6) as t grows. The theoretical and numerical values are compared in Table 2.

Table 2: Comparison between the first eigenvalue λ of the differential operator (73) and the value γ of the numerical gradient of the logarithmic convergence. The two values are obtained as described in the text in the linear case $V_m = 0$.

L	0.1	0.5	1	2	3	6
λ	25.530	3.299	1.3044	0.509	0.296	0.125
γ	25.166	3.234	1.3044	0.517	0.292	0.109

5 Countercurrent exchange across 2 tubes

The counter-current arrangement of tubules and vessels in the kidney has long been known to improve the production of concentrated urine (for a review, see [Stephenson, 1992]). The concentrating capacity of the kidney is reflected by the increase in fluid osmolality (or concentration) along the collecting duct and can therefore be quantified by the interstitial axial concentration gradient. In order to assess the extent to which the counter-arrangement architecture enhances concentration gradients, we then consider a simpler system consisting of two tubes only. Note first that if there were no pump (i.e., no active transport of solute out of one the tubes), the concentration of solute would remain constant, independent of x, in both tubes (results not shown). In other words, the pump creates a transversal concentration gradient (referred to as the "single effect"), which in turn generates an axial osmolality gradient [Hargitay and Kuhn, 2001], [Stephenson, 1992]. The multiplication of the single effect in the axial direction concentrates the fluid flowing downwards. Our simple 2-tubule model illustrates why multiplication of the single effect is greater in counter-current flows than in cocurrent flows.

5.1 Countercurrent versus cocurrent exchange

Garner et al. Garner et al. [1978] undertook a similar study, in which they solved analytically the time-dependent linear system relative to (59), using a Laplace transform which was numerically inverted. In this study, we solve analytically (59) and (60) to compare the steady state solutions of a countercurrent and a cocurrent architecture, assuming a linear rate for the pump. We then solve numerically the corresponding dynamic system using the finite volume scheme. The advantages of our numerical method are that it can be extended to n tubes ($n \geq 2$), and that we could assume a nonlinear term for active transport.

The countercurrent flows. When the tubes are arranged in a counter-current manner, the conservation equations can be written as

$$\begin{cases} \dfrac{dC^1(x)}{dx} = J^1(x), \ -\dfrac{dC^2(x)}{dx} = J^2(x), \qquad x \in [0, L], \\ C^1(0) = C_0^1, \qquad C^2(L) = C^1(L). \end{cases} \tag{59}$$

The fluxes are given by

$$J^1(x) = C^{int}(x) - C^1(x), \ J^2(x) = C^{int}(x) - C^2(x) - V_m C^2(x).$$

with the condition

$$J^1 + J^2 = 0.$$

We infer from this condition that

$$C^{int}(x) = \frac{1}{2}\Big[C^1(x) + C^2(x) + V_m C^2(x)\Big], \ C^1(x) - C^2(x) = constant.$$

Knowing that $C^1(L) = C^2(L)$, we conclude that $C^1 = C^2$. Then the system reduces to a single equation

$$\begin{cases} \dfrac{dC^1(x)}{dx} = \dfrac{1}{2} V_m C^1(x), \quad C^1(0) = C_0^1. \\ C^2(x) = C^1(x). \end{cases}$$

We can calculate the analytical solution

$$C^1(x) = C_0^1 e^{\frac{V_m}{2} x}.$$

The cocurrent flows. In a cocurrent architecture, the equations are

$$\begin{cases} \dfrac{dC^3(x)}{dx} = J^3(x), \qquad \dfrac{dC^4(x)}{dx} = J^4(x), \\ C^3(0) = C_0 = C^4(0). \end{cases} \tag{60}$$

The fluxes are still given by

$$J^3(x) = C^{int}(x) - C^3(x), \qquad J^4(x) = C^{int}(x) - C^4(x) - V_m C^4(x).$$

With similar arguments, we obtain the solution

$$\begin{cases} C^3(x) = 2C_0\Big[\dfrac{1+V_m}{2+V_m} - \dfrac{V_m}{2(2+V_m)}e^{(-1-\frac{V_m}{2})x}\Big], \\ C^4(x) = 2C_0\Big[\dfrac{1}{2+V_m} + \dfrac{V_m}{2(2+V_m)}e^{(-1-\frac{V_m}{2})x}\Big]. \end{cases}$$

In both configurations, there is a gradient of concentration in the first tubes (tubes 1 and 3). In the countercurrent configuration, the gradient is exponential in both tubes, with parameter $\frac{V_m}{2}$, where V_m quantifies the single-effect. In the cocurrent configuration, the gradient is lower, and in the best case (L and V_m very large), $C^3(L)$ tends toward $2C_0$ whereas $C^4(L)$ falls near 0.

Shown in figure 4 are concentration profiles solution to (59) and (60).

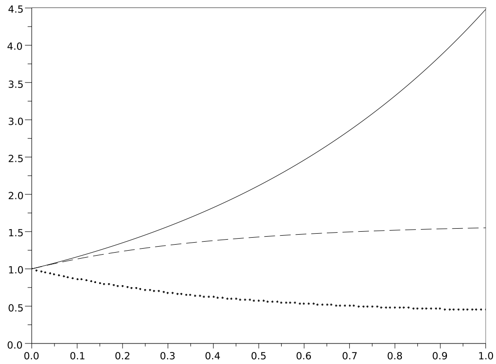

Figure 4: The solid curve represents the steady-state concentration profile ($C^1 = C^2$) for the countercurrent arrangement. The dashed curve (C^3) and the dotted curve (C^4) represent steady-state concentration profiles in the cocurrent arrangement. The pump term is taken to be linear here.

5.2 Visualization of the dynamic of a countercurrent-flows system relaxing toward the steady state

To visualize the evolution of concentration profiles with time, we consider the dynamic problem with countercurrent flows, assuming as the initial condition that the concentration is equal to C_0 all along the tubes. We display some curves of concentration profiles at different times and see them evolve toward the equilibrium state. We introduce the equation describing this dynamic problem

$$\begin{cases} \dfrac{\partial C^1}{\partial t}(x,t) + \dfrac{\partial C^1}{\partial x}(x,t) = J^1(x,t), & x \in [0,L],\ t>0, \\ \dfrac{\partial C^2}{\partial t}(x,t) - \dfrac{\partial C^2}{\partial x}(x,t) = J^2(x,t), & x \in [0,L],\ t>0, \\ \qquad C^1(0,t) = C^1_0, \qquad C^2(L,t) = C^1(L,t). \end{cases} \tag{61}$$

which we complete with nonnegative initial concentrations $C^1(x,0), C^2(x,0)$. The fluxes are given by:

$$J^1(x,t) = C^{int}(x,t) - C^1(x,t),$$
$$J^2(x,t) = C^{int}(x,t) - C^2(x,t) - V_m C^2(x,t),$$

with the condition:

$$J^1(x,t) + J^2(x,t) = 0.$$

Shown in Figure 5 are concentration profiles at different times in 2 tubes arranged in a counter-current manner, with a pump in the ascending tube, solution to (61) obtained using a finite volume scheme.

6 Conclusion and perspectives

Using a simplified model of solute exchange across 3 kidney tubules, in which the latter were taken to all be impermeable to water, we demonstrated the existence and uniqueness of the stationary state. In

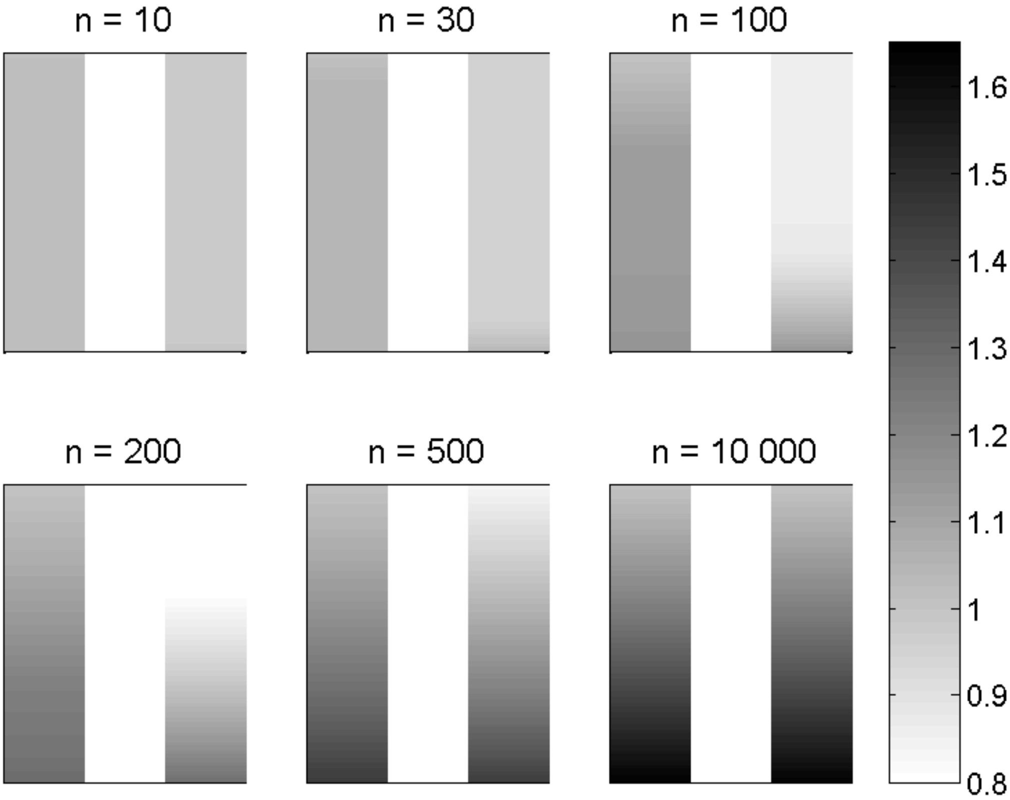

Figure 5: Concentration profiles at different time iterations n in 2 tubes arranged in a countercurrent manner, with a pump in the ascending one. The pump rate is taken to increase linearly with the concentration C, see (61). Parameters: $L = 1,\ C^0 = 1,\ V_m = 1,\ \Delta x = 0.01,\ ; \Delta t = 0.0099$.

addition, we showed that the dynamic solution converges toward the steady-state solution, and that the convergence is exponential if the maximum rate of the pump mediating active transport in one of the tubes is not too high. Finally, our results illustrate how the counter-current arrangement of tubules enhances the axial concentration gradient, thereby favoring the production of highly concentrated urine.

Under physiological conditions, water and solute flows are tightly coupled in the kidney: osmosis (i.e., transmembrane concentration gradients) is the main driving force for water exchange, and solute movement is partly driven by convection. Hence, the system of nonlinear differential equations yielding solute and water flows must generally be solved numerically. In this study, we chose to make some simplifying assumptions (such as that of water-impermeable tubules) in order to better characterize this system of differential equations, and to determine the existence and uniqueness of the solution. To the best of our knowledge, there have been very few previous attempt to do so in a comparable system. Layton [Layton, 1987] showed that for sufficiently low or sufficiently large rates of NaCl active transport, there exists a unique solution to the Peskin model[Layton, 1986]. The latter model also considers three tubules surrounded by a common interstitium, but it differs significantly from ours in that it assumes that solute concentration is equal in the descending limb (i.e., tube 2 in our representation), the collecting duct (i.e., tube 1), and the interstitium at each level. For the model considered in the present study, we showed that the steady-state solution exists and is unique for any given value of V_m (i.e., the maximum rate of NaCl active transport out of the ascending limb). We also demonstrated that the solution to the dynamic model always converges toward the steady-state solution. Moreover, if Vm is small enough, namely if condition (13) is satisfied, then the convergence is exponential with time.

It was recognized early on, as reviewed by Stephenson ([Stephenson, 1992]), that the formation of a large axial concentration gradient in the kidney is made possible by the fact that tubules (1) exhibit differential permeabilities and (2) are arranged in a counterflow manner. To assess the degree to which the counter-current architecture increases the axial concentration gradient, relative to the cocurrent configuration, we used a 2 tube system and derived an analytical solution for solute concentration profiles. Our results suggest that solute concentration increases exponentially with x in the former case (with an exponential factor that is proportional to V_m), whereas it is bounded independently of V_m in the latter case.

A similar exponential concentration increase was predicted for the single loop cycling model with constant water flows [Garner et al., 1978] . The investigators used Laplace transforms to obtain numerical solutions for two limiting cases: when the pump is either saturated (i.e., the active transport rate is a constant) or very far from saturation (i.e., the rate is a linear function of concentration). Their study cannot be easily extended to account for nonlinear rates, and for more than two tubes, as calculations would then become impracticable. In contrast, the method we developed could be extended to consider more tubules, and could apply to nonlinear rates.

A more realistic representation of kidney function would require accounting for transversal water movement. Whether the existence and uniqueness of steady-state solutions to such problems can then be proven remains to be determined.

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A Definition of weak solutions

A weak solution to (6) is a function $C \in C\Big([0,T], L^1[0,L]\Big)^3$ such that for all $\Phi \in V$ defined in (32), we have

$$\begin{aligned}\int_0^T\int_0^L \frac{\partial \Phi}{\partial t}.C(x,t)dxdt + \int_0^T\int_0^L \frac{\partial \Phi}{\partial x}.C(x,t)dxdt = \frac{2}{3}\int_0^T\int_0^L \Phi.C(x,t)dxdt\\ + \frac{2}{3}\int_0^T\int_0^L \Phi^3.F(C^3,x)(x,t)dxdt - \frac{1}{3}\int_0^T\int_0^L \Big[\Phi^1(C^2+C^3+F(C^3,x))(x,t)\Big]dxdt\\ - \frac{1}{3}\int_0^T\int_0^L \Big[\Phi^2(C^1+C^3+F(C^3,x))(x,t)\Big]dxdt - \frac{1}{3}\int_0^T\int_0^L \Big[\Phi^3(C^1+C^2)(x,t)\Big]dxdt\\ + \int_0^T \Phi^1(0,t)C^1(0,t)dt + \int_0^T \Phi^2(0,t)C^2(0,t)dt + \int_0^L \Phi(x,T)C(x,T)dx - \int_0^L \Phi(x,0)C(x,0)dx. \quad (62)\end{aligned}$$

For (5), the definition of a weak solution $C \in (L^1[0,L])^3$ uses test functions $\Phi \in W$ with

$$W = \{\Phi \in \Big(C^1([0,L])\Big)^3, \qquad \Phi^1(L) = \Phi^3(0) = 0, \qquad \Phi^3(L) = \Phi^2(L)\},$$

and reads

$$\begin{aligned}\int_0^L \frac{d\Phi}{dx}.C(x)dx = \frac{2}{3}\int_0^L \Phi.C(x,t)dx + \frac{2}{3}\int_0^L \Phi^3.F(C^3,x)(x)dx - \frac{1}{3}\int_0^L \Big[\Phi^1(C^2+C^3+F(C^3,x))(x)\Big]dx\\ - \frac{1}{3}\int_0^L \Big[\Phi^2(C^1+C^3+F(C^3,x))(x)\Big]dx - \frac{1}{3}\int_0^L \Big[\Phi^3(C^1+C^2)(x)\Big]dx - \Phi^1(0)C^1(0) - \Phi^2(0)C^2(0).\end{aligned} \quad (63)$$

B Existence of a solution to (43)

In subsection 3.5, we have used that there are nonnegative solutions to

$$\begin{cases} \dfrac{dC^1(x)}{dx} + \dfrac{2}{3}C^1(x) = \dfrac{1}{3}\Big[C^2(x) + C^3(x) + F(C^3(x),x)\Big],\\ \dfrac{dC^2(x)}{dx} + \dfrac{2}{3}C^2(x) = \dfrac{1}{3}\Big[C^1(x) + C^3(x) + F(C^3(x),x)\Big],\\ -\dfrac{dC^3(x)}{dx} + \dfrac{2}{3}\Big[C^3(x) + F(C^3(x),x)\Big] = \dfrac{1}{3}\Big[C^1(x) + C^2(x)\Big],\\ \qquad C^1(0) = C_0^1 > 0, \qquad C^2(0) = C_0^2 > 0, \qquad C^3(L) = C_L^3 \geq 0. \end{cases} \quad (64)$$

and that they are monotonic with respect to the boundary values. We prove these statements here.

First step. A regularized problem. For every $\alpha > 0$, we prove that the following system has a solution C which is nonnegative

$$\begin{cases} \dfrac{dC^1(x)}{dx} + \dfrac{2}{3}C^1(x) + \alpha C^1(x) = \dfrac{1}{3}\Big[C^2(x) + C^3(x) + F(C^3(x), x)\Big], \\ \dfrac{dC^2(x)}{dx} + \dfrac{2}{3}C^2(x) + \alpha C^2(x) = \dfrac{1}{3}\Big[C^1(x) + C^3(x) + F(C^3(x), x)\Big], \\ -\dfrac{dC^3(x)}{dx} + \dfrac{2}{3}\Big[C^3(x) + F(C^3(x), x)\Big] = \dfrac{1}{3}\Big[C^1(x) + C^2(x)\Big], \\ \qquad C^1(0) = C^1_0 > 0, \qquad C^2(0) = C^2_0 > 0, \qquad C^3(L) = C^3_L \geq 0. \end{cases} \tag{65}$$

To do so, we use the Banach-Picard theorem in the Banach space

$$X = L^1([0, L], \mathbb{R}^+) \times L^1([0, L], \mathbb{R}^+), \qquad \|(C^1, C^2)\|_X = \int_0^L \Big(C^1(x) + C^2(x)\Big)dx$$

For $(D^1, D^2) \in X$, we define (C^1, C^2) the solution to

$$\begin{cases} \dfrac{dC^1(x)}{dx} + \dfrac{2}{3}C^1(x) + \alpha C^1(x) = \dfrac{1}{3}\Big[D^2(x) + C^3(x) + F(C^3(x), x)\Big], \\ \dfrac{dC^2(x)}{dx} + \dfrac{2}{3}C^2(x) + \alpha C^2(x) = \dfrac{1}{3}\Big[D^1(x) + C^3(x) + F(C^3(x), x)\Big], \\ -\dfrac{dC^3(x)}{dx} + \dfrac{2}{3}\Big[C^3(x) + F(C^3(x), x)\Big] = \dfrac{1}{3}\Big[D^1(x) + D^2(x)\Big], \\ \qquad C^1(0) = C^1_0 > 0, \qquad C^2(0) = C^2_0 > 0, \qquad C^3(L) = C^3_L \geq 0. \end{cases} \tag{66}$$

Then, we claim that the operator

$$\mathcal{B} : (D^1, D^2) \longmapsto (C^1, C^2) := \mathcal{B}(D^1, D^2)$$

has a unique fixed point in X_+ (the cone of nonnegative functions), which follows from the two properties

$$(a)\ B : X_+ \longrightarrow X_+, \qquad\qquad (b)\ B \text{ is a strong contraction.}$$

Second step. The fixed point. To prove (a), we check that (C^1, C^2) are nonnegative functions. The Cauchy Lipschitz theorem tells us that there is a unique C^3, which is a nonnegative continuous solution to the third equation of (66) (here we use assumption (7)). Then, we again apply the Cauchy Lipschitz theorem to the first two equations of (66) to obtain that C^1 and C^2 are continuous and positive functions.

Now, we check (b). By substractions of solutions, say (C^1, C^2) and $(\overline{C^1}, \overline{C^2})$ for two different D, say (D^1, D^2) and $(\overline{D^1}, \overline{D^2})$, we obtain

$$\begin{cases} \dfrac{d(C^1 - \overline{C^1})}{dx}(x) + (\dfrac{2}{3} + \alpha)(C^1 - \overline{C^1}) = \dfrac{1}{3}\Big[(D^2 - \overline{D^2})(x) + (C^3 - \overline{C^3})(x) + F(C^3(x), x) - F(\overline{C^3}(x), x)\Big], \\ \dfrac{d(C^2 - \overline{C^2})}{dx}(x) + (\dfrac{2}{3} + \alpha)(C^2 - \overline{C^2}) = \dfrac{1}{3}\Big[(D^1 - \overline{D^1})(x) + (C^3 - \overline{C^3})(x) + F(C^3(x), x) - F(\overline{C^3}(x), x)\Big], \\ -\dfrac{d(C^3 - \overline{C^3})}{dx}(x) + \dfrac{2}{3}\Big[(C^3 - \overline{C^3})(x) + F(C^3(x), x) - F(\overline{C^3}(x), x)\Big] = \dfrac{1}{3}\Big[(D^1 - \overline{D^1})(x) + (D^2 - \overline{D^2})(x)\Big], \\ \qquad (C^1 - \overline{C^1})(0) = 0, \qquad (C^2 - \overline{C^2})(0) = 0, \qquad (C^3 - \overline{C^3})(L) = 0. \end{cases} \tag{67}$$

We use the notation

$$\delta^i(x) := (C^i(x) - \overline{C}^i(x)), \qquad i = 1,\ 2,\ 3.$$

As in subsection 3.3 and using the same notations, we obtain the following inequalities

$$\begin{cases} \dfrac{d|\delta^1|}{dx} + (\dfrac{2}{3} + \alpha)|\delta^1| = \dfrac{1}{3}\,\mathrm{sign}(\delta^1)(D^2 - \overline{D^2} + \delta^3 + F(C^3) - F(\overline{C^3})), \\ \dfrac{d|\delta^2|}{dx} + (\dfrac{2}{3} + \alpha)|\delta^2| = \dfrac{1}{3}\,\mathrm{sign}(\delta^2)(D^1 - \overline{D^1} + \delta^3 + F(C^3) - F(\overline{C^3})), \\ -\dfrac{d|\delta^3|}{dx} + \dfrac{2}{3}(|\delta^3| + G) = \dfrac{1}{3}\,\mathrm{sign}(\delta^3)(D^1 - \overline{D^1} + D^2 - \overline{D^2}). \end{cases} \tag{68}$$

Integrating these inequalities, we conclude that

$$
\begin{aligned}
|\delta^1(L)|+|\delta^2(L)|+|\delta^3(0)|+\int_0^L(\alpha+\frac{2}{3})|\delta^1|+\int_0^L(\alpha+\frac{2}{3})|\delta^2|\\
+\frac{1}{3}\int_0^L\Big[2\,\mathrm{sign}(\delta^3)-\mathrm{sign}(\delta^1)-\mathrm{sign}(\delta^2)\Big](\delta^3+F(C^3)-F(\overline{C^3}))\\
=\frac{1}{3}\int_0^L\Big[\mathrm{sign}(\delta^2)+\mathrm{sign}(\delta^3)\Big](D^1-\overline{D^1})+\frac{1}{3}\int_0^L\Big[\mathrm{sign}(\delta^1)+\mathrm{sign}(\delta^3)\Big](D^2-\overline{D^2}), \quad (69)
\end{aligned}
$$

which gives us

$$\int_0^L(\alpha+\frac{2}{3})(|\delta^1|+|\delta^2|)\leq\frac{2}{3}\int_0^L\Big[|D^1-\overline{D^1}|+|D^2-\overline{D^2}|\Big]. \quad (70)$$

In terms of the Banach space under consideration, this is to say

$$\|(C^1,C^2)-(\overline{C^1},\overline{C^2})\|_X\leq\frac{2}{2+3\alpha}\|(D^1,D^2)-(\overline{D^1},\overline{D^2})\|_X,$$

and we have obtained the strong contraction property, and thus the existence of a solution to (65).

Third step. The limit $\alpha=0$. Until now, we denote the solution to (65) as $C_\alpha=(C^1_\alpha,C^2_\alpha,C^3_\alpha)$; it is Lipschitz continuous because F is. We prove here that the familiy $(C_\alpha)_{\alpha>0}$ is equicontinuous on $[0,L]$. Then we may apply Ascoli theorem to obtain a strongly convergent subsequence and conclude the proof.

From (65), we deduce that

$$\frac{d}{dx}(C^1_\alpha(x)+C^2_\alpha(x)-C^3_\alpha(x))\leq 0, \quad (71)$$

which tells us that

$$C^1_\alpha(L)+C^2_\alpha(L)+C^3_\alpha(0)\leq C^1_\alpha(0)+C^2_\alpha(0)+C^3_\alpha(L)=C^1_0+C^2_0+C^3_L.$$

We deduce that $C^1_\alpha(L),C^2_\alpha(L)$ and $C^3_\alpha(0)$ are uniformly bounded in α. Then, using that the endpoints are controled, (71) tells us that the function h defined as

$$h(x)=C^1_\alpha(x)+C^2_\alpha(x)-C^3_\alpha(x) \quad (72)$$

is uniformly bounded in α too. Inserting this in the third line of (65), we write

$$-\frac{d}{dx}C^3_\alpha+\frac{2}{3}\Big(C^3_\alpha+F(C^3_\alpha)\Big)=\frac{C^3_\alpha+h}{3},$$

so that C^3_α is uniformly bounded in α. Using the first and second lines of (65), we also conclude that $(C^1_\alpha+C^2_\alpha)$ are uniformly bounded in α, and so do C^1_α and C^2_α.

Fourth step. The comparison principle. As it was done in the Second step, and using again the argument of subsection 3.3 (replacing the absolute value by the positive part), one obtains that $C^1_0\geq\overline{C}^1_0$, $C^2_0\geq\overline{C}^2_0$ and $C^3_L\geq\overline{C}^3_L$ implies that $C^i(x)\geq\overline{C}^i(x)$ for all $x\in[0,L]$ and $i=1$, 2 and 3.

C Existence of eigenelements

As often in nonlinear problems, the eigenelements for the linear problem play an important role in the understanding of nonlinear effects. We state the first eigenelement problem and recall some properties here. For a given continuous function $\mu(x)>0$, this consists in finding $\big(\Lambda(\mu),N(x;\mu)\geq 0,\phi(x,\mu)\geq 0\big)$ solutions to the direct and dual problems defined as

$$
\begin{cases}
\dfrac{dN^1(x)}{dx}=\dfrac{1}{3}\big[N^2(x)+(1+\mu(x))N^3(x)\big]+(\Lambda-\dfrac{2}{3})N^1,\\
\dfrac{dN^2(x)}{dx}=\dfrac{1}{3}\big[N^1(x)+(1+\mu(x))N^3(x)\big]+(\Lambda-\dfrac{2}{3})N^2,\\
-\dfrac{dN^3(x)}{dx}=\dfrac{1}{3}\big[N^1(x)+N^2(x)\big]+\big(\Lambda-\dfrac{2}{3}(1+\mu(x))\big)N^3,\\
N^1(0)=0,\qquad N^2(0)=0,\qquad N^3(L)=N^2(L).
\end{cases} \quad (73)
$$

$$
\begin{cases}
-\dfrac{d\phi^1(x)}{dx} = \dfrac{1}{3}\big[\phi^2(x)+\phi^3(x)\big] + (\Lambda - \dfrac{2}{3})\phi^1, \\
-\dfrac{d\phi^2(x)}{dx} = \dfrac{1}{3}\big[\phi^1(x)+\phi^3(x)\big] + (\Lambda - \dfrac{2}{3})\phi^2, \\
\dfrac{d\phi^3(x)}{dx} = \dfrac{1+\mu(x)}{3}\big[\phi^1(x)+\phi^2(x)\big] + \big(\Lambda - \dfrac{2}{3}(1+\mu(x))\big)\phi^3, \\
\phi^1(L)=0, \qquad \phi^3(0)=0, \qquad \phi^2(L)=\phi^3(L).
\end{cases} \tag{74}
$$

It is also standard to normalize the eigenfunctions as

$$
\int_0^L (N^1+N^2+N^3) = 1, \qquad \int_0^L (N^1\phi^1 + N^2\phi^2 + N^3\phi^3) = 1. \tag{75}
$$

Finally we use the notation $k(\mu)$:

$$
k := k(\mu) \ \text{ is the biggest real number such that } \qquad \phi^1+\phi^2 \geq k\phi^3. \tag{76}
$$

The standard result *à la* Krein-Rutman is

Proposition 1. *For $\mu > 0$ there is a (smooth) solution with $\Lambda(\mu) > 0$. Moreover we have: $N^1(x) > 0$, $N^2(x) > 0$ for $x > 0$, $N^3 > 0$ and $\phi^1(x) > 0$ for $x < L$, $\phi^3(x) > 0$ for $x > 0$, $\phi^2 > 0$.*

Strategy of the proof. We consider the implicit scheme with space step h associated to (73). We call A_h the matrix of the scheme. We can prove that A_h is invertible and that its inverse is positive. Thus, the Perron Frobenius theorem yields the existence of $\lambda_h > 0, N_h \geq 0, \phi_h \geq 0$, solution to the eigenproblem

$$
A_h N_h = \lambda_h N_h, \ {}^tA_h\phi_h = \lambda_h \phi_h.
$$

Since $(\lambda_h)_h$ is bounded by $1 + spec(A)$, there is a subsequence (λ_h) such that

$$
\lim_{h\to 0} \lambda_h = \lambda > 0.
$$

From the discrete functions N_h and ϕ_h we build, as in section 3, continuous piecewise functions. Applying the Ascoli theorem to the bounded and equicontinuous families $(N_h)_h$ and $(\phi_h)_h$, we also prove that there are subsequences $(\lambda_h), (\phi_h)$ such as

$$
\lim_{h\to 0} N_h = N \geq 0, \ \lim_{h\to 0} \phi_h = \phi \geq 0,
$$

with N and ϕ satisfying the condition (75). Then, we prove that λ, N, ϕ satisfy (73), (74).

Proof of the exponential convergence. We define, with the notation of section 2.2

$$
M(t) = \int_0^L \Big[d^1(x,t)\phi_1(x) + d^2(x,t)\phi_2(x) + d^3(x,t)\phi_3(x)\Big]dx.
$$

The usual duality argument (see [Perthame, 2007]) gives, with G defined in section 3.3

$$
\begin{aligned}
\frac{d}{dt}M(t) &\leq -\lambda M(t) + \frac{1}{3}\int_0^L (G-\mu(x)\ d^3)(\phi_1(x)+\phi_2(x)-2\phi_3(x)dx \\
&\leq -\lambda M(t) + \frac{(k-2)}{3}\int_0^L (G-\mu(x)\ d^3)\phi_3(x)dx
\end{aligned}
$$

because $G \leq \mu(x)\ d^3$.

If, in (76), $k(\mu) \geq 2$, the result follows from the Gronwall lemma.

Otherwise $k-2<0$ and we write, treating only the case $C^3 \leq \overline{C^3}$ to simplify

$$
(2-k)[\mu(x)d^3 - G] = \int_{C^3}^{\overline{C^3}} [\mu(x) - F_C(c,x)]dc \leq d^3[\Lambda - \delta]
$$

with $\delta > 0$ given by the difference between the right and left hand sides in (15). From this we conclude that

$$
\frac{d}{dt}M(t) \leq -\delta M(t)
$$

and the exponential convergence again follows from the Gronwall lemma. □

References

Grégoire Allaire. *Numerical analysis and optimization.* Numerical Mathematics and Scientific Computation. Oxford University Press, Oxford, 2007. An introduction to mathematical modelling and numerical simulation, Translated from the French by Alan Craig.

F. Bouchut. *Nonlinear stability of finite volume methods for hyperbolic conservation laws and well-balanced schemes for sources.* Frontiers in Mathematics. Birkhäuser Verlag, Basel, 2004.

C. M. Dafermos. *Hyperbolic conservation laws in continuum physics*, volume 325 of *Grundlehren der Mathematischen Wissenschaften [Fundamental Principles of Mathematical Sciences].* Springer-Verlag, Berlin, second edition, 2005.

F. Demengel and G. Demengel. *Espaces fonctionnels.* Savoirs Actuels (Les Ulis). [Current Scholarship (Les Ulis)]. EDP Sciences, Les Ulis, 2007. Utilisation dans la résolution des équations aux dérivées partielles. [Application to the solution of partial differential equations].

L. C. Evans. *Partial differential equations*, volume 19 of *Graduate Studies in Mathematics.* American Mathematical Society, Providence, RI, 1998.

J. L. Garner, K. S. Crump, and J. B. Stephenson. Transient behaviour of the single loop solute cycling model of the renal medulla. *Bull. Math. Biol.*, 40:273–300, 1978.

E. Godlewski and P.-A. Raviart. *Numerical approximation of hyperbolic systems of conservation laws*, volume 118 of *Applied Mathematical Sciences.* Springer-Verlag, New York, 1996.

B. Hargitay and W. Kuhn. The Multiplication Principle as the Basis for Concentrating Urine in the Kidney (with comments by B. Hargitay and S. R. Thomas). *J. Am. Soc. Nephrol.*, 12(7):1566–1586, 2001.

H. E. Layton. Distribution of henle's loops may enhance urine concentrating capability. *Biophysical Journal*, 49:1033–1040, 1986.

H. E. Layton. Existence and uniqueness of solutions to a mathematical model of the urine concentrating mechanism. *Math. Biosci.*, 84:197–210, 1987.

R. J. LeVeque. *Finite volume methods for hyperbolic problems.* Cambridge Texts in Applied Mathematics. Cambridge University Press, Cambridge, 2002.

B. Perthame. *Transport equations in biology.* Frontiers in Mathematics. Birkhäuser Verlag, Basel, 2007.

V. V. Prasolov. *Problems and theorems in linear algebra*, volume 134 of *Translations of Mathematical Monographs.* American Mathematical Society, Providence, RI, 1994. Translated from the Russian manuscript by D. A. Leĭtes.

J. L. Stephenson. *Handbook of Physiology. Section 8. Renal Physiology*, chapter Urinary concentration and dilution: Models, pages 1349–1408. Oxford University Press, Bethesda, MD, 1992.