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A diffusion-consumption problem for oxygen in a living tissue perfused by capillaries

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Abstract. We study a mathematical model describing the nonlinear diffusion of oxygen in a living tissue, in presence of consumption due to metabolism. The tissue is perfused by a system of parallel capillaries in which oxygen is carried by the blood both in the form of gas freely diffusing in plasma and bound to hemoglobin. We prove global existence of a unique smooth solution to the resulting parabolic-hyperbolic system.

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1 Introduction

It is well known that oxygen is supplied to living tissues through microcirculation of blood. The first attempt to describe the phenomenon in mathematical terms is the classical Krogh's model (see [13], [14]). This model deals with an idealized geometrical arrangement consisting of one capillary of circular cross section con-

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centric with a circular cross section of muscle tissue; the exchange of oxygen is modeled through a law of Robin's type (flux proportional to the jump between partial pressure of O_2 in blood and in the tissue) and a diffusion problem in axial symmetry with a consumption term has to be solved in the region occupied by the tissue.

Many extensions of Krogh's model have been proposed and studied (see [6], [20] for a survey) and several semianalytical or approximated methods have been developed, also to incorporate the effect of the presence of many capillaries.

The number of papers devoted to this subject in last 2-3 decades is really impressive and we will just quote a few of them, referring the interested reader to the literature quoted therein.

We single out three main lines of research: (i) modeling the mechanism of transport/storage of O_2 in microcirculation and of transport/storage/consumption of oxygen in living tissue ([10], [18], [20]); (ii) discussing the boundary conditions that express the exchange across the walls of capillaries ([5], [7], [19], [21]), and (iii) finding approximated solutions often based on the use of line sources to mimic the presence of capillaries and/or on asymptotic expansions ([1], [4], [5], [11], [22]).

Our approach is based on the discussion carried out on topics (i) and (ii) and has the aim of obtaining a rigorous mathematical result on the well-posedness (existence, uniqueness, dependence on the data) of the corresponding analytical problem.

In [16] we already considered the problem of perfusion of living tissue by a bundle of parallel capillaries and we discussed the corresponding homogenization.

In the present paper we release some assumptions that were instrumental for the proofs of [16]: the fact that the transport of O_2 in blood was supposed to be based only on convection and the assumption of instantaneous equilibrium between oxygen in plasma and bound to erythrocytes.

Thus, the model we deal with is more similar to the one presented in [17]. The analysis given there is heavily based on symmetry (just one capillary surrounded by a co-axial cylindrical slab of tissue as in the original Krogh's model, while in our case we have N capillaries of radii R_i, $i = 1, 2 \dots N$), and on the use of classical representation techniques that are clearly inapplicable to our general geometric situation. Our existence and uniqueness results could be compared with the study of smooth solutions for two-scale quasilinear parabolic systems, arising in modeling of catalytic reactors, in [8].

The plan of the paper is the following.

In Section 2 we give the mathematical formulation of the problem, just recalling the basic physiological facts (see [12] for a comprehensive introduction to mathematical physiology), and we prove a simple a-priori estimate; in Section 3 we consider several auxiliary problems which are necessary in the proof of the existence theorem which is given in Section 4 and is based on Schauder's fixed point theorem. The solution is sufficiently smooth, as it will be clear by the arguments. In the last Section we prove the uniqueness.

2 Formulation of the problem and basic assumptions

Let O be a bounded set in $\mathbf{R}^2$ with smooth boundary. Let $\mathbf{x} \equiv (x, y, z)$ and denote by $\Omega \equiv \{\mathbf{x} \equiv (x, y, z) : (x, y) \in O,\ 0 < z < L\}$. For $i = 1, 2, \ldots, N$ denote by $\mathcal{C}_i \equiv \{\mathbf{x} : (x - x_i)^2 + (y - y_i)^2 < {R_i}^2,\ 0 < z < L\}$, and by $\mathcal{C} = \bigcup_{i=1}^{N} \mathcal{C}_i$.

We will assume that the living tissue occupies $\omega = \Omega \setminus \mathcal{C}$, while $\mathcal{C}$ represents the bundle of capillaries. We assume that $\partial\mathcal{C}$ and $\partial\Omega$ have no common parts outside $z = 0$ and $z = L$.

We have to find $2N + 1$ functions: $C(\mathbf{x}, t)$, defined in $\omega \times \mathbf{R}^+$, represents the volumetric concentration of oxygen diffusing in the tissue; $c_i(z, t)$ and $\ell_i(z, t)$, defined on $\mathcal{C}_i \times \mathbf{R}^+$ $(i = 1, 2 \ldots N)$, represent the concentrations of oxygen in the blood flowing in the i-th capillary, respectively dissolved in plasma and bound to hemoglobin.

Oxygen diffuses in the tissue according to mass balance equation:

$$\frac{\partial \mathcal{M}(C)}{\partial t} - D \triangle C = Q(C), \tag{2.1}$$

where D is the diffusion coefficient, $Q \leq 0$ represents, in absolute value, the rate of oxygen consumption, and $\mathcal{M}(C)$ is the total oxygen content of a unit volume of tissue, that is a monotone function of the concentration C of freely diffusing oxygen. To be specific, we can think of a law of type Michaelis-Menten

$$\mathcal{M}(C) = C + \lambda C^p (C^p + k^p)^{-1}, \tag{2.2}$$

where λ and k are positive constants and a typical value for p is 2.5 (see [12], [19]). Assuming (2.2) corresponds to postulate that the mass of oxygen contained in the unit volume of the tissue is the sum of the mass C of the freely diffusing oxygen(e.g. to myoglobin) which is assumed to be in instantaneous equilibrium with the former.

Of course, the equation (2.1) can also include nonlinear diffusivity. Explicit dependence on $\mathbf{x}$ and t will be excluded to avoid additional technical complications.

At the boundaries $\partial\mathcal{C}_i$, i.e. at the walls of capillaries, we assume that oxygen flow is induced by deviations from the osmotic equilibrium (Henri's law) and we write

$$C_i(\theta, z, t) - \nu c_i(z, t) = \beta \frac{\partial C_i}{\partial r},\ i = 1 \ldots N, \tag{2.3}$$

where ν and β are positive constants and we denoted by $C_i(\theta, z, t)$ the value of C at point $(x_i + R_i \cos\theta, y_i + R_i \sin\theta, z)$ and at time t (where θ is an angular coordinate) and by $\frac{\partial C_i}{\partial r}$ its derivative, normal to ∂C_i and pointing toward tissue, at the same point and time.

A generalization of (2.3) in which the normal derivative $\dfrac{\partial C_i}{\partial r}$ is a monotone function of $C_i - \nu c_i$ could be also treated with only minor changes.

Mass balance of oxygen in each $\mathcal{C}_i$ will include convection (with given speed $u(t)$ of the blood, say in the positive z direction) for both ℓ_i and c_i, diffusion in axial direction for c_i, and exchange with the surrounding tissue. If α and $1-\alpha$ represent the volume fraction of the blood occupied by plasma and erythrocytes, respectively, and d is the diffusivity of oxygen in plasma, we will write

$$\alpha\{\frac{\partial c_i}{\partial t} + u(t)\frac{\partial c_i}{\partial z} - d\frac{\partial^2 c_i}{\partial z^2}\} + (1-\alpha)\{\frac{\partial \ell_i}{\partial t} + u(t)\frac{\partial \ell_i}{\partial z}\} = \tag{2.4}$$

$$= \frac{D}{\pi {R_i}^2}\int_0^{2\pi} \frac{\partial C_i}{\partial r} R_i d\theta,\ i = 1\dots N.$$

From now on, we will assume that $u(t)$ is a given positive C^1-function. Finally, we will have to postulate a relationship between ℓ_i and c_i. In [16] we assumed a law of instantaneous equilibrium $\ell_i = \gamma(c_i)$, γ being a monotone increasing function with $\gamma_i(0) = 0$. Here, we make the more general assumption that a relaxation mechanism toward equilibrium is given: so that a positive constant τ and a monotone function Φ ($\Phi(0) = 0$) exist, so that:

$$\tau\{\frac{\partial \ell_i}{\partial t} + u(t)\frac{\partial \ell_i}{\partial t}\} = \Phi(\gamma(c_i) - \ell_i),\ i = 1\dots N. \tag{2.5}$$

The problem is completed by prescribing the following conditions:

(i) initial conditions:

$$\begin{cases} C(\mathbf{x}, 0) = C^0(\mathbf{x}), & \mathbf{x} \in \omega, \\ c_i(z, 0) = {c_i}^0(z), & z \in (0, L),\ i = 1\dots N, \\ \ell_i(z, 0) = {\ell_i}^0(z), & z \in (0, L),\ i = 1\dots N; \end{cases} \tag{2.6}$$

(ii) inlet/outlet boundary conditions for the capillaries:

$$\begin{cases} c_i(0, t) = c_{i0}(t), & t > 0,\ i = 1\dots N, \\ c_i(L, t) = c_{iL}(t), & t > 0,\ i = 1\dots N, \\ \ell_i(0, t) = \ell_{i0}(t), & t > 0,\ i = 1\dots N; \end{cases} \tag{2.7}$$

(iii) boundary conditions for the tissue, that we will take simply as homogeneous Neumann conditions:

$$\frac{\partial C}{\partial n} = 0, \text{ on } \partial\Omega \setminus \partial\mathcal{C},\ t > 0. \tag{2.8}$$

We note that, incorporating α and $1-\alpha$ in the definition of c_i and ℓ_i and renormalizing variables, the problem reduces to the following, where the same symbols have been used to save notation:

$$\frac{\partial \mathcal{M}(C)}{\partial t} - \triangle C = Q(C) \text{ in } \omega \times \mathbf{R}^+ \tag{2.9}$$

$$C_i(\theta, z, t) - c_i(z, t) = \beta \frac{\partial C_i(\theta, z, t)}{\partial r} \text{ on } \partial \mathcal{C}_i \times \mathbf{R}^+ \tag{2.10}$$

$$\frac{\partial c_i}{\partial t} + u\frac{\partial c_i}{\partial z} - d\frac{\partial^2 c_i}{\partial z^2} + \frac{\partial \ell_i}{\partial t} + u\frac{\partial \ell_i}{\partial z} = \frac{K}{\pi R_i}\int_0^{2\pi} \frac{\partial C_i}{\partial r} d\theta, \text{ in } \mathcal{C}_i \times \mathbf{R}^+ \tag{2.11}$$

$$\frac{\partial \ell_i}{\partial t} + u\frac{\partial \ell_i}{\partial z} = \Phi(\gamma(c_i) - \ell_i), \text{ in } \mathcal{C}_i \times \mathbf{R}^+ \tag{2.12}$$

where $i = 1, 2 \dots N$ in (2.10)-(2.12) and the initial and boundary conditions are given by (2.6)-(2.8).

We make the following assumptions on functions $\mathcal{M}$, Q, Φ, γ appearing in (2.9)-(2.12).

(H1) $\mathcal{M}$ is a positive strictly increasing locally Lipschitz continuous function defined on $[0, +\infty)$.

(H2) Q is a non-positive locally Lipschitz continuous function defined on $[0, +\infty)$, $Q(0) = 0$.

(H3) Φ is an increasing locally Lipschitz continuous function defined on $(-\infty, +\infty)$, $\Phi(0) = 0, \Phi'(0) > 0$.

(H4) γ is a strictly increasing locally Lipschitz continuous function defined on $[0, +\infty)$, $\gamma(0) = 0$.

Concerning the notations and the functional spaces, we follow the reference [15] .

We prove the following a-priori estimate.

Proposition 2.1 *Assume that initial and boundary data for c_i and C are strictly positive and smaller than a constant E. Then, if*

$$E_1 = \gamma(E), \tag{2.13}$$

and if data for ℓ_i are strictly positive and less than E_1, any classical solution of problem (2.6)-(2.12) is such that

$$0 < C(\mathbf{x}, t) < E, \quad \mathbf{x} \in \omega,\, t > 0; \tag{2.14}$$

$$0 < c_i(z, t) < E, \quad z \in [0, L],\, t > 0,\, i = 1 \dots N; \tag{2.15}$$

$$0 < \ell_i(z, t) < E_1, \quad z \in [0, L],\, t > 0, i = 1 \dots N. \tag{2.16}$$

We could allow positive quantities β and K to depend on i.

Proof. We confine ourselves to prove the upper bound. If the second inequality is violated in any of (2.14)-(2.16), then a $t_0 > 0$ should exist such that for $t < t_0$ they hold and one of the following cases occur:

(a) $\ell_i(z_0, t_0) = E_1$ for some z_0 and i, while
$C(\mathbf{x}, t_0) < E$, $\mathbf{x} \in \omega$ and $c_i(z, t_0) < E$ in $(0, L) \forall i$;

(b) $c_i(z_0, t_0) = E$ for some z_0 and i, while
$C(\mathbf{x}, t_0) < E$, $\mathbf{x} \in \omega$ and $\ell_i(z, t_0) \leq E_1$ in $(0, L) \forall i$.

(c) $C(\mathbf{x_0}, t_0) = E$ for some $\mathbf{x_0}$ and
$\ell_i(z, t_0) \leq E_1$, $c_i(z, t_0) \leq E$, $z \in (0, L)$, $\forall i$.

In case (a), first we note that $z_0 \neq 0$, $z_0 \neq L$ so that $\ell_{iz}(z_0, t_0) = 0$. Hence (2.12) implies

$$\Phi(\gamma(c_i(z_0, t_0)) - E_1) \geq 0, \tag{2.17}$$

but since $c_i < E$, $\gamma(c_i) < E_1$ and (2.17) contradicts (H3).
In case (b), again $z_0 \neq 0$, $z_0 \neq L$, so that $c_{iz} = 0$, $c_{izz} \leq 0$, $c_{it} \geq 0$. Moreover, from (2.12):

$$\ell_{it} + u\ell_{iz|_{z_o,t_o}} = \Phi(\gamma(E) - \ell_i) \geq 0. \tag{2.18}$$

Consequently, from (2.11) $\int_0^{2\pi} C_{ir|_{z_o,t_o}} d\theta \geq 0$, which is in contradiction with (2.10) and (b).
Finally, maximum principle applied to (2.9) ensures that if C attains a maximum value in $\omega \times (0, t_0]$, it should be attained at some point of $\partial\mathcal{C}_i \times \{t_0\}$ where C_{ir} has to be strictly negative, according to boundary point principle. But this contradicts (2.10). □

Corollary 2.2 *Let (H1)-(H4) and the assumptions of Proposition 2.1 hold. Then functions $\mathcal{M}$, Q, γ, Φ in (2.9), (2.12) can be truncated, i.e. there is no loss of generality in assuming that*

(H5) Functions $\mathcal{M}$, $|Q|$, $|\Phi|$, γ are Lipschitz continuous and bounded by a constant $\hat{M}$.

3 Preliminary results

Denote by $S_T = \{(z, t) : 0 < z < L, 0 < t < T\}$ and consider the following

Problem A. For any given non-negative $w \in H^{\alpha, \alpha/2}(S_T) \cap C(\overline{S}_T)$, find $\ell(z, t) \in C(\overline{S}_T)$ and satisfying

$$\ell_t + u(t)\ell_z = \Phi(\gamma(w) - \ell) \quad \text{in } S_T, \tag{3.1}$$

In fact its material derivative corresponding to the velocity $u(t)\vec{e}_z$ is also continuous.

$$\ell(z,0) = \ell^0(z) \geq 0, \quad 0 < z < L, \tag{3.2}$$

$$\ell(0,t) = \ell_0(t) \geq 0, \quad 0 < t < T. \tag{3.3}$$

We prove

Proposition 3.1 *Let the chain of data (3.2), (3.3) be continuous , and denote by $\ell_{0\,MAX}$ its maximum. Then* Problem A *has a unique solution; moreover*

$$0 \leq \ell \leq \gamma(W), \quad \text{in } S_T, \tag{3.4}$$

where

$$W = \max(\|w\|_{C(S_T)}, \gamma^{-1}(\ell_{0\,MAX})). \tag{3.5}$$

Furthermore, if the chain of data is Hölder continuous with the exponent $\alpha \in (0,1)$, the solution is Hölder continuous with exponent $\alpha/2$.

Proof. To find $\ell(z,t)$ it is sufficient to integrate an ordinary differential equation along the characteristics $z - \int_0^t u(\tau)d\tau$ =const. Hence $\ell(z,t)$ is continuously differentiable along the tangential direction to the characteristics. The normal direction enters as a parameter and inherits the smoothness of the chain of data. Estimate (3.4) follows at once using assumptions (H3) and (H4). □

Next, we want to investigate how the solution $\ell[w]$ of *Problem A* depends on w and we prove

Proposition 3.2 *Under the same assumptions, there exists a constant $k > 0$ such that*

$$\|\ell[w^{'}] - \ell[w^{''}]\|_{L^\infty(0,T;L^2(0,L))} + \sqrt{\min_{0\leq t\leq T} u(t)}\|\ell[w^{'}] - \ell[w^{''}]\|_{L^2(0,T;L^\infty(0,L))}$$
$$\leq k\,\|w^{'} - w^{''}\|_{L^\infty(0,T;L^2(0,L))}. \tag{3.6}$$

Proof. For given $w^{'}$ and $w^{''}$ find $\ell[w']$ and $\ell[w'']$ solving *Problem A* and let $\overline{\ell} = \ell[w'] - \ell[w'']$. Then $\overline{\ell}(z,t)$ solves

$$\overline{\ell}_t + u(t)\overline{\ell}_z = [\Phi(\gamma(w') - \ell') - \Phi(\gamma(w') - \ell'')] + [\Phi(\gamma(w') - \ell'') - \Phi(\gamma(w'') - \ell'')] \tag{3.7}$$

with zero initial and boundary data. Multiply (3.7) by $\overline{\ell}$ and note that the first term on the r.h.s. of the equation so obtained is negative, while the second term is dominated by $\Lambda^2|w' - w''||\overline{\ell}|$, where Λ is the largest of the Lipschitz constants of Φ and of γ. Integrating over S_T concludes the proof. □

As usual, by this expression we mean that data themselves are continuous and zero-order compatibility conditions are satisfied (in this case $\ell^0(0) = \ell_0(0)$).

Remark 3.3 The calculations as in Proposition 3.2 are justified by regularization. For such calculations in the theory of the first order semi-linear hyperbolic equations see e.g. [2] . Using the technique from [2] it is straightforward to prove that for $\ell_0 \in BV(0,T)$ and $\ell^0 \in BV(0,L)$ we have $\ell \in L^\infty(0,T;BV(0,L))$ and

$$\|\ell\|_{L^\infty(0,T;BV(0,L))} \le C\big\{\|\ell_0\|_{BV(0,T)} + \|\ell^0\|_{BV(0,L)} + \|\partial_z w\|_{L^1((0,L)\times(0,T))}\big\} \quad (3.8)$$

We note that this regularity doesn't require the compatibility of ℓ^0 and ℓ_0.

Next, for $i = 1,\, 2 \dots N$ we consider the following

Problem B. For any w_i as in *Problem A* and for any given positive constant λ_i and any non-negative function $A_i \in H^{\beta,\beta/2}(S_T) \cap C(\overline{S}_T)$ find $c_i \in W_q{}^{2,1}(S_T)$ $\cap\, C(\overline{S}_T)$ $(\forall q \in [2,+\infty))$ such that

$$c_{it} + u(t)c_{iz} - dc_{izz} = -\Phi(\gamma(c_i) - \ell[w_i]) + A_i(z,t) - \lambda_i c_i, \text{ in } S_T, \quad (3.9)$$

$$c_i(z,0) = c_i{}^0(z) \ge 0, \quad 0 < z < L, \quad (3.10)$$

$$c_i(0,t) = c_{i0}(t) \ge 0, \quad 0 < t < T, \quad (3.11)$$

$$c_i(L,t) = c_{iL}(t) \ge 0, \quad 0 < t < T. \quad (3.12)$$

From now on we drop index i for simplicity. We prove

Proposition 3.4 *Let the chain of the data (3.10)-(3.12) be Hölder continuous and denote by $c_{0\,MAX}$ its maximum. Then* Problem B *has a unique solution $c \in \overset{0}{V}{}^{1,0}_{2,2}(S_T) \cap H^{\alpha,\,\alpha/2}(\overline{S}_T)$, where*

$$\overset{0}{V}{}^{1,0}_{2,2} \equiv \{\, \varphi \in L^\infty(0,T;L^2(0,L)) \,:\, \varphi_z \in L^2(S_T), \\ \int_0^T h^{-2}\|\varphi(z,t+h) - \varphi(z,t)\|^2_{L^2(S_{T-h})}\, dh < +\infty\}.$$

Moreover

$$0 \le c \le M \quad \text{in } S_T \quad (3.13)$$

where

$$M = \max(c_{0\,MAX},\, W,\, \|A\|_{C(S_T)}/\lambda). \quad (3.14)$$

If, in addition $c_i(\cdot,0) \in C^2[0,L]$, $c_i(0,\cdot)$ and $c_i(L,\cdot) \in C^1[0,T]$, and the zeroth order compatibility conditions are satisfied, then $c \in W^{2,1}_q(S_T)$, $\forall q < \infty$.

Proof. From Theorem 6.4 and Theorem 6.7 of [15] chapter V it follows that *Problem B* has a solution such that

$$c \in \overset{0}{V}{}^{1,0}_{2,2}(S_T) \cap H^{\alpha,\,\alpha/2}(\overline{S}_T), \quad \alpha > 0, \tag{3.15}$$

Moreover, with additional regularity of the data, $c \in W^{2,1}_q(S_T)$ for any $q > 1$ (see [15], Chapter 4, and recall boundedness of Φ and A) we have

$$c_z \in H^{\lambda,\,\lambda/2}(S_T), \quad \forall \lambda < 1. \tag{3.16}$$

To prove uniqueness, denote by c' and c'' two possible solutions and let

$$\overline{c}(z,t) = c'(z,t) - c''(z,t). \tag{3.17}$$

We have

$$\overline{c}_t + u\overline{c}_z - d\overline{c}_{zz} + \lambda\overline{c} = \Phi(\gamma(c'') - \ell[w]) - \Phi(\gamma(c') - \ell[w]), \tag{3.18}$$

with $\overline{c} = 0$ on the parabolic boundary of S_T. Multiply (3.18) by $\overline{c}$ and integrate over S_T. Using (H3) and (H4) we conclude that $\overline{c} \equiv 0$. Next, use maximum principle noting that the r.h.s. of (3.9) is non-negative for $c = 0$ and non-positive for $c = M$. □

It is clear that, for fixed A and λ, solving *Problem A* for any w and then *Problem B* for $\ell[w]$ defines a mapping

$$c = c[w]. \tag{3.19}$$

According to Proposition (3.1) and (3.4), if

$$|w| \le \max\{\gamma^{-1}(\ell_{0\,\mathrm{MAX}}),\, c_{0\,\mathrm{MAX}},\, \|A\|_{C(S_T)}/\lambda\} \equiv \overline{M} \tag{3.20}$$

then

$$|c[w]| \le \overline{M}. \tag{3.21}$$

Hence $c[w]$ maps the ball with radius $\overline{M}$ of $C(S_T)$ into itself.
Moreover, since

$$\|c_z\|_{H^{\lambda,\,\lambda/2}} \le k \tag{3.22}$$

where k only depends on $\overline{M}$, the mapping is compact. To prove that the mapping is continuous we take a sequence $\{w^m\}$ and study the corresponding $c^m = c[w^m]$. Since

$$\|c^m_z\|_{H^{\lambda,\,\lambda/2}(S_T)} + \|c^m\|_{W^{2,1}_q} \le k, \tag{3.23}$$

there is a subsequence c^r converging to $\hat{c}(z,t)$ uniformly and converging weakly in $W_q^{2,1}$. Hence, passing to the limit (along the subsequence) in the equation satisfied by $c[w^r]$ we obtain that $c[w^r] \to c[w]$. Using Schauder fixed point theorem gives us the existence theorem for the following

Problem C. For any given $\lambda_i > 0$ and non-negative $A_i \in H^{\beta,\beta/2}(S_T) \cap C(\overline{S}_t)$ solve *Problem B* with $\ell[w_i]$ replaced by $\ell[c_i]$.

Now (dropping again index i) we investigate the dependence of c upon A and prove

Proposition 3.5 *Let c' and c'' be solutions of* Problem C *corresponding to A' and A'' respectively. Then, for any $t \in (0,T)$ it is:*

$$\int_0^L |c'(z,t) - c''(z,t)|\, dz \le k\, \|A' - A''\|_{L^1(S_T)}. \tag{3.24}$$

Proof. Writing again $\overline{c} = c' - c''$, it is

$$\overline{c}_z + u(t)\overline{c}_z - d\overline{c}_{zz} + \lambda\overline{c} = \Phi(\gamma(c'') - \ell[c'']) - (\Phi(\gamma(c') - \ell[c']) + A' - A''. \tag{3.25}$$

Testing (3.25) with regularized sign$(\overline{c})$ we get

$$\int_o^L |\overline{c}(z,t)|dz + \lambda \iint_{S_t} |\overline{c}|dzd\tau + \iint_{S_t} (\Phi'' - \Phi')\text{sign } \overline{c} \le \iint_{S_T} |A' - A''|dzd\tau, \tag{3.26}$$

(the meaning of Φ' and Φ'' is obvious).

Now, proceeding as in the proof of Proposition 3.2, the integral containing $\Phi'' - \Phi'$ is estimated in terms of $\iint_{S_t} |\ell[c''] - \ell[c']|dz\, d\tau$. Then using Proposition (3.2) the proof is concluded. □

Therefore we have

Corollary 3.6 *Solution to* Problem C *is unique.*

Now, we state and solve our last auxiliary problem.

Problem D. For any given n-tuple $\underline{\varphi} \equiv \{\varphi_1 \ldots \varphi_N\}$ of non-negative functions $\varphi_i \in L^\infty(S_T)$ find $C \in L^\infty(Q_T) \cap V_2^{1,1/2}(Q_T)$ $(Q_T = \omega \times (0,T))$, such that

$$\frac{\partial}{\partial t}\mathcal{M}(C) - \Delta C = Q(C) \quad \text{in } Q_T, \tag{3.27}$$

$$C(\mathbf{x},0) = C^0(\mathbf{x}), \quad \mathbf{x} \in \omega, \tag{3.28}$$

$$\frac{\partial C}{\partial n} = 0, \quad \text{on } \partial\Omega \setminus \partial\mathcal{C} \times (0,T), \tag{3.29}$$

$$[C - \beta C_r]_i = \varphi_i, \quad \text{on } \partial\mathcal{C}_i \times (0,T), \tag{3.30}$$

where we wrote for simplicity $[C - \beta C_r]_i$ to indicate that the quantity in bracket has to be evaluated for $x = x_i + R_i \cos\theta$, $y = y_i + r_i \sin\theta$.

We prove

Proposition 3.7 *If $C^0 \in L^\infty(\omega)$ is a given non-negative function, then* Problem D *is uniquely solvable in Q_T. Moreover, if C^0 is in addition Hölder continuous, then*

$$0 \le C \le \max\{\max C^0, \max_i \|\varphi_i\|_{L^\infty(S_T)}\}, \tag{3.31}$$

and there exist positive constants δ, k_1 and k_2 such that

$$\|C\|_{V_2^{1,1/2}(Q_T)} + \|C\|_{H^{\delta,\delta/2}(\overline{Q}_T)} \le k_1 \sum_i \|\varphi_i\|_{L^\infty(S_T)} + k_2, \tag{3.32}$$

where

$$\|C\|_{V_2^{1,1/2}(Q_T)} = \| \bigtriangledown C\|^2_{L^2(Q_T)} + \int_0^{T-h} dt \int_\omega h^{-1} |C(\mathbf{x}, t+h) - C(\mathbf{x}, t)|^2 \, dx.$$

Proof. Using the classical theory of linear parabolic equations with discontinuous coefficients from [15], together with the Schauder fixed point theorem, we arrive at solvability of the *Problem D*. The membership of C in $V_2^{1,1/2}(Q_T)$ and estimate (3.32) follow from classical theory of parabolic equations.
Uniqueness is obtained by the theory of entropy solutions (see [3]).
It can also be seen that constants k_1 and k_2 exist such that

$$\|C\|_{H^{\delta,\delta/2}(\overline{Q}_T)} \le k_1 \sum_i \|\varphi_i\|_{L^\infty(S_T)} + k_2. \tag{3.33}$$

For more details we refer to [15], pages 418-423. From maximum principle and assumptions (H1), (H2), it is immediately seen that $C \ge 0$.
Moreover, since Q is non-positive, and $\beta > 0$ the upper bound for C is obtained at once. $\square$

Corollary 3.8 *Let $C^0(\mathbf{x}) \in C^2(\bar{\omega})$ and that its normal derivative vanishes on $\partial\omega \setminus \mathcal{C}$; moreover let $\varphi \in C[\overline{S}_T]$, $\varphi_{iz} \in H^{\beta,\beta/2}$ be chosen so that (3.30) holds initially. Then the problem (3.27)-(3.30) has a unique solution $C \in H^{2+\beta,1+\beta/2}\,(Q_T)$.*

Proof. From Theorem 7.4 page 491 of [15] we find that under our assumptions a solution of *Problem D* exists in the class specified. $\square$

Remark 3.9 Having stated the problem in a class of very smooth functions, we require lot of smoothness on the data. Some generalizations are however possible. Par example, we could study the problem in the class of bounded elements of $V_2^{1,1/2}(\omega \times (0,T)) \times \overset{0}{V}{}^{1,0}_{2,2}(\mathcal{C}_i \times (0,T))^N \times L^\infty(0,T; BV(\mathcal{C}_i))^N$ and then only the zeroth order compatibility conditions, with minimal regularity, should be imposed.

4 Existence theorem

Denote by $K(M,T)$ the set of all n-tuple of functions $\varphi_i \in C(\overline{S}_T)$ and such that

$$0 \le \varphi_i(z,t) \le M, \quad i = 1, \dots N,\ z \in S_T. \tag{4.1}$$

Solve *Problem D* with this choice of $\boldsymbol{\varphi} \equiv \{\varphi_1,\ \varphi_2 \dots \varphi_N\}$ and let

$$A_i(z,t) = \frac{\lambda_i}{2\pi} \int_0^{2\pi} C(x_i + R_i \cos\theta,\ y_i + R_i \sin\theta,\ z,\ t)\, d\theta, \quad i = 1,\ 2, \dots N. \tag{4.2}$$

Now, for each i, solve *Problem C* and find an n-tuple $\mathbf{c} \equiv \{c_1, \dots, c_N\}$.

Thus, we have defined a mapping

$$\mathbf{c} = \mathcal{T}[\boldsymbol{\varphi}], \tag{4.3}$$

and we have

Proposition 4.1 *Let $\lambda_i = \frac{2K}{\beta R_i}$. If $\underline{\hat{c}}$ is a fixed point of mapping (4.3)*

$$\underline{\hat{c}} = \mathcal{T}[\hat{c}],$$

then our problem is solved by the $2N+1$ functions

$$\hat{\mathbf{c}},\ \boldsymbol{\ell}[\hat{\mathbf{c}}],\ C[\hat{\mathbf{c}}]$$

where $\boldsymbol{\ell}[\hat{\mathbf{c}}] \equiv \{\ell_1[\hat{c}_1],\ \ell_2[\hat{c}_2], \dots, \ell_N[\hat{c}_N]\}$ is obtained solving Problem A *and $C[\hat{\mathbf{c}}]$ is obtained solving* Problem D.

In order to prove that the mapping $\mathcal{T}$ has a fixed point we should establish its properties. First we prove

Proposition 4.2 *There exists $M > 0$ such that*

$$\boldsymbol{\varphi} \in K_{M,T} \Rightarrow \mathcal{T}[\boldsymbol{\varphi}] \in K_{M,T} \tag{4.4}$$

for any given $T > 0$.

Proof. Take

$$M > \max\{\, \|C^0\|_{C(\bar{\omega})},\ c_{0MAX},\ \gamma^{-1}(\ell_{0MAX})\} \tag{4.5}$$

and recall (3.4), (3.13), (3.21), (3.31). □

Now we prove

Proposition 4.3 *$\mathcal{T}$ maps $K_{M,T}$ into a compact subset.*

Proof. Proposition 3.7 guarantees that (3.31) and (3.32) are satisfied. This ensures that $C[\boldsymbol{c}]$ belongs to a set $\mathcal{A}$ which is compact in $L^2(0,T;H^\alpha(\omega))$ for any $\alpha < 1$. Then $\mathcal{T}[\boldsymbol{c}]$ is uniformly bounded in $W_q^{2,1}$ (recall (3.23)) and hence compact in $K_{M,T}$ for $q > 3$. □

Proposition 4.4 *$\mathcal{T}$ is continuous.*

Proof. Let $\mathbf{c}_m \to \mathbf{c}$ in $K_{M,T}$. Then the set $\mathcal{A}$ is compact in $L^2(0,T,H^\alpha(\omega))$ for any $\alpha < 1$ as seen above and $C[\boldsymbol{c}_m]$ contains a subsequence converging strongly in $L^2(0,T;H^\alpha(\omega))$, weakly in $V_2^{1,1/2}(Q_T)$ and weak* in $L^\infty(Q_T)$ to a solution C of *Problem D*. Because of the uniqueness, the whole sequence converges.
Moreover, from Proposition 3.2 we have that $\boldsymbol{\ell}[\mathbf{c}_m]$ converges in $L^1(S_T)$ and $\mathcal{T}[\mathbf{c}_n]$ are uniformly bounded in $W_q^{2,1}(S_T)$ so that they converge uniformly and weakly in $W_q^{2,1}$.
Finally, $\mathbf{w} = \lim \mathcal{T}[\boldsymbol{c}_n]$ satisfies *Problem C* and, because of uniqueness, the whole sequence converges. □

Hence we have proved the following result

Corollary 4.5 *Let us suppose hypothesis (H1)-(H5). Let C^0 be a non-negative bounded function. Let $c^0 \in C^2[0,L]$ and $c_0, c_L \in C^1[0,T]$ be non-negative vector valued functions satisfying zero-order compatibility condition. Let ℓ^0 and ℓ_0 be non-negative vector functions of bounded variation. Then there is $M > 0$ such that the mapping $\mathcal{T}$ has at least one fixed point $\hat{c} \in K_{M,T}$. Furthermore, $\{\hat{\boldsymbol{c}}, \boldsymbol{\ell}[\hat{\boldsymbol{c}}], C[\hat{\boldsymbol{c}}\} \in W_q^{2,1}(\mathcal{C}_i \times (0,T))^N \times L^\infty(0,T;BV(\mathcal{C}_i))^N \times V_2^{1,1/2}(\omega \times (0,T))$, $\forall q \geq 2$.*

Supposing a bit more of regularity, we find that solution is very regular :

Theorem 4.6 *Let the assumptions of Corollary 4.5 be satisfied and let in addition $C^0 \in C^3(\bar{\omega})$ and let chain of data (3.2)-(3.3) be Hölder continuous, with exponent $\lambda \in (0,1)$. Furthermore, let the compatibility condition (3.30) be satisfied at $t = 0$. Then the problem (2.6)-(2.12) has a non-negative solution $\{\hat{\boldsymbol{c}}, \boldsymbol{\ell}[\hat{\boldsymbol{c}}], C[\hat{\boldsymbol{c}}\} \in W_q^{2,1}(\mathcal{C}_i \times (0,T))^N \times H^\lambda(\bar{\mathcal{C}}_i \times [0,T])^N \times H^{2+\beta,1+\beta/2}(\omega \times (0,T))$, $\forall q \geq 2$ and $\beta \in (0,1)$.*

Remark 4.7 Let in addition $c^0 \in C^3[0,L]$ and $c_0, c_L \in C^2[0,T]$ be non-negative vector valued functions satisfying zero and first-order compatibility condition. Then $\hat{\boldsymbol{c}} \in H^{2+\lambda,1+\lambda/2}(\mathcal{C}_i \times (0,T))^N$.

5 Uniqueness theorem

The uniqueness theorem is somehow unexpected, except with very high regularity. We note that even for a special case of our model, studied in [17], no uniqueness result was obtained. In fact for the uniqueness we don't really need classical solutions. The regularity $V_2^{1,1/2}(\omega\times(0,T))\times \overset{0}{V}{}^{1,0}_{2,2}(\mathcal{C}_i\times(0,T))^N\times L^\infty(0,T;BV(\mathcal{C}_i))^N$ is enough, but we have to balance carefully the corresponding " energy " terms. It should be noted that the presence of $\mathcal{M}$ makes the calculations with the time derivatives and time differences tricky. Only optimal arrangement of the terms from 3 equations gives the right conclusion.

Theorem 5.1 *The problem (2.6)-(2.12) has a unique bounded non-negative solution* $\{C,c,\ell\}\in V_2^{1,1/2}(\omega\times(0,T))\times \overset{0}{V}{}^{1,0}_{2,2}(\mathcal{C}_i\times(0,T))^N\times L^\infty(0,T;BV(\mathcal{C}_i))^N$.

Proof. Let us suppose that there exist two solutions for the problem (2.6)-(2.12). Then the difference of the solutions, denoted by $\{C,c,\ell\}$, is once more in $V_2^{1,1/2}(\omega\times(0,T))\times \overset{0}{V}{}^{1,0}_{2,2}(\mathcal{C}_i\times(0,T))^N\times L^\infty(0,T;BV(\mathcal{C}_i))^N$. We note that there are N capillary tubes $\mathcal{C}_i$ of the length L and consequently functions c and ℓ are vector valued with N components.

We proceed in several steps.

$\boxed{\text{1. STEP}}$ We integrate the equation (2.9) in time and get

$$\mathcal{M}(C_1(x,t))-\mathcal{M}(C_2(x,t))-D\Delta\int_0^t C(x,\xi)\,d\xi=\int_0^t\big(Q(C_1)-Q(C_2)\big)\,d\xi \tag{5.1}$$

Consequently for every $\varphi\in H^1(\omega)$ we have

$$\begin{aligned}&\int_\omega(\mathcal{M}(C_1(x,t))-\mathcal{M}(C_2(x,t)))\,\varphi\,dx+D\int_\omega\nabla\Big(\int_0^t Cd\xi\Big)\nabla\varphi\,dx+\\&\frac{D}{\beta}\sum_{i=1}^N\int_0^L\int_{\{r=R_i\}}\left(\int_0^t Cd\xi\right)\varphi\,dSdz=\int_\omega\left(\int_0^t(Q(C_1)-Q(C_2))\,d\xi\right)\varphi\,dx\\&\quad+\frac{D}{\beta}\sum_{i=1}^N\int_0^L\int_{\{r=R_i\}}\left(\int_0^t c\,d\xi\right)\varphi\,dSdz\end{aligned} \tag{5.2}$$

We take $\varphi=C$ as a test function and get

$$\begin{aligned}&\int_0^t\int_\omega(\mathcal{M}(C_1(x,\xi))-\mathcal{M}(C_2(x,\xi)))\,C\,dxd\xi+\frac{D}{2}\int_\omega|\nabla\left(\int_0^t C\,d\xi\right)|^2\,dx\\&\quad+\frac{D}{2\beta}\sum_{i=1}^N\int_0^L\int_{\{r=R_i\}}\left(\int_0^t C\,d\xi\right)^2dSdz\end{aligned}$$

$$-\frac{D}{\beta}\sum_{i=1}^{N}\int_0^t\int_0^L\int_{\{r=R_i\}} C(\xi)\left(\int_0^\xi c\ d\eta\right)\ dSdzd\xi$$
$$=\int_0^t\int_\omega\left(\int_0^\xi (Q(C_1)-Q(C_2)\ d\eta)C(\xi)\right)\ dxd\xi \tag{5.3}$$

Since

$$|\int_0^t\int_\omega\left(\int_0^\xi (Q(C_1)-Q(C_2))\ \ d\eta\right) C(\xi)\ dxd\xi = |\int_0^t\int_\omega (Q(C_1(\eta))-$$
$$Q(C_2(\eta)))\left(\int_\eta^t C(\xi)\ d\xi\right)\ dxd\eta|$$
$$\leq \|Q'\|_\infty|\int_0^t\int_\omega |C(\eta)|\left(\int_\eta^t |C(\xi)|\ d\xi\right)\ dxd\eta| =$$
$$\frac{t}{2}\|Q'\|_\infty\int_\omega\left(\int_0^t |C(\xi)|\ d\xi\right)^2\ dx \leq \frac{t^2}{2}\|Q'\|_\infty\int_0^t\int_\omega C^2\ dxd\xi \tag{5.4}$$

and

$$\frac{D}{\beta}\sum_{i=1}^{N}\int_0^t\int_0^L\int_{\{r=R_i\}} C(\xi)(\int_0^\xi c\ d\eta)\ dSdz$$
$$=\frac{D}{\beta}\sum_{i=1}^{N}\int_0^L\int_{\{r=R_i\}}\left(\left(\int_0^t C\ d\xi\right)\left(\int_0^t c\ d\xi\right)\right.$$
$$\left.-\int_0^t (c(\xi)\left(\int_0^\xi C(\eta)\ d\eta\right)\ d\xi)\right)dSdz \tag{5.5}$$

we get

$$\left(\min\mathcal{M}'-\frac{t^2}{2}\|Q'\|_\infty\right)\int_0^t\int_\omega C^2\ dxd\xi+\frac{D}{2}\int_\omega |\nabla(\int_0^t C\ d\xi)|^2\ dx$$
$$+\frac{D}{2\beta}\sum_{i=1}^{N}\int_0^L\int_{\{r=R_i\}}(\int_0^t C\ d\xi)^2\ dSdz-\frac{D}{\beta}\sum_{i=1}^{N}\int_0^L\int_{\{r=R_i\}}$$
$$\big((\int_0^t C\ d\xi)(\int_0^t c\ d\xi)-\int_0^t (c(\xi)(\int_0^\xi C(\eta)\ d\eta)\ d\xi)\big)\ dSdz \leq 0 \tag{5.6}$$

$\boxed{\text{2. STEP}}$ Next we study the equation for c :

$$\frac{\partial c}{\partial t}+u(t)\frac{\partial c}{\partial z}-d\frac{\partial^2 c}{\partial z^2}+\frac{2K}{\beta R_i}c=-\Big(\Phi(\gamma(c_1)-\ell_1)-\Phi(\gamma(c_2)-\ell_2)\Big)$$
$$+\frac{K}{\beta\pi R_i}\int_0^{2\pi} C|_{r=R_i}\ d\vartheta \quad \text{in } (0,L)\times(0,T) \tag{5.7}$$

We integrate (5.7) from 0 to t and test the obtained equation by c. Then we have

$$\int_0^t \int_0^L c^2 \, dzd\xi + \int_0^t \int_0^L c(\xi)(\int_0^\xi u(\eta)\frac{\partial c}{\partial z} \, d\eta) \, dzd\xi + \frac{d}{2}\int_0^L |\frac{\partial}{\partial z}\int_0^t c \, d\eta|^2 \, dz$$
$$+\frac{K}{\beta R_i}\int_0^L (\int_0^t c \, d\xi)^2 \, dz - \frac{K}{\pi\beta R_i^2}\int_0^t \int_0^L (\int_{\{r=R_i\}} \int_0^\xi C \, d\xi) \, dS)c(\xi) \, dzd\xi$$
$$\leq \|\Phi'\|_\infty \Big(\frac{t}{2}\|\gamma'\|_\infty \int_0^t \int_0^L c^2 \, dzd\xi + \int_0^t \int_0^L |c(\xi)| \, (\int_0^\xi |\ell(\eta)| \, d\eta) \, dzd\xi\Big) \tag{5.8}$$

Clearly, we should first take care of the transport term :

$$|\int_0^t \int_0^L c(\xi)(\int_0^\xi u(\eta)\frac{\partial c}{\partial z} \, d\eta) \, dxd\xi|$$
$$= |\int_0^t \int_0^L \Big(\partial_\xi(\int_0^\xi u(\eta)\frac{\partial c}{\partial z} \, d\eta \int_0^\xi c(\eta) \, d\eta)$$
$$-u(\xi)\frac{\partial c}{\partial z}(\xi)\int_0^\xi c\Big) \, dxd\xi| \leq \frac{d}{4}\Big(\int_0^L |\frac{\partial}{\partial z}\int_0^t c(\eta) \, d\eta|^2 \, dz$$
$$+\frac{2\|u\|_\infty^2}{d}\int_0^t \int_0^L |\frac{\partial}{\partial z}\int_0^\xi c \, d\eta|^2 \, dzd\xi\Big)$$
$$+(\frac{t\|u\|_\infty^2}{d} + 1/2)\int_0^t \int_0^L c^2 \, dzd\xi \tag{5.9}$$

After inserting (5.9) into (5.8), multiplication by $\dfrac{D\pi R_i^2}{K}$ and summation over i, we get

$$\frac{D}{2K}\Big(1 - t(\|\Phi'\|_\infty\|\gamma'\|_\infty + \frac{2\|u\|_\infty^2}{d})\Big)\sum_{i=1}^N \int_0^t \int_{\mathcal{C}_i} c^2 \, dxd\xi$$
$$+\frac{Dd}{4K}\sum_{i=1}^N \int_{\mathcal{C}_i} |\frac{\partial}{\partial z}\int_0^t c \, d\xi|^2 \, dx$$
$$+\frac{D}{2\beta}\sum_{i=1}^N \int_0^L \int_{\{r=R_i\}} \Big((\int_0^t c \, d\xi)^2 - 2(\int_0^t c(\xi)(\int_0^\xi C(\eta) \, d\eta) \, d\xi)\Big) \, dSdz$$
$$\leq \frac{D}{K}\|\Phi'\|_\infty \sum_{i=1}^N \int_{\mathcal{C}_i} \int_0^t |c(\xi)| \, (\int_0^\xi |\ell(\eta)| \, d\eta) \, dx$$
$$+\frac{D\|u\|_\infty^2}{2K}\int_0^t \sum_{i=1}^N \int_{\mathcal{C}_i} |\frac{\partial}{\partial z}\int_0^\xi c \, d\eta|^2 \, dxd\xi \tag{5.10}$$

$\boxed{\text{3. STEP}}$ Now we study the equation for ℓ :

$$\frac{\partial \ell}{\partial t} + u(t)\frac{\partial \ell}{\partial z} = (\Phi(\gamma(c_1) - \ell_1) - \Phi(\gamma(c_2) - \ell_2)) \quad \text{in } (0,L) \times (0,T) \tag{5.11}$$

By testing this equation by regularized ℓ and after arguing as in Proposition 3.2, we get

$$\frac{1}{2}\int_0^L \ell(t)^2 \, dz \leq \|\Phi'\|_\infty \|\gamma'\|_\infty \int_0^t \int_0^L |c||\ell| \, dz d\xi \tag{5.12}$$

Hence we have

$$\int_0^t \int_0^L \ell^2 \, dz d\xi \leq (2\|\Phi'\|_\infty \|\gamma'\|_\infty t)^2 \int_0^t \int_0^L c^2 \, d\xi dz \quad \text{for every i} \tag{5.13}$$

Consequently, we have

$$\frac{D}{K}\|\Phi'\|_\infty \sum_{i=1}^N \int_{\mathcal{C}_i} \int_0^t |c(\xi)| \, (\int_0^\xi |\ell(\eta)| \, d\eta) \, dx \leq \frac{D}{4K}\sum_{i=1}^N \int_{\mathcal{C}_i} \int_0^t c^2 \, d\xi dx +$$

$$\|\Phi'\|_\infty^2 \frac{Dt^2}{2K} \sum_{i=1}^N \int_{\mathcal{C}_i} \int_0^t \ell^2 \, d\xi dx \leq \left(\frac{D}{4K} + \|\Phi'\|_\infty^4 \frac{2Dt^4}{K}\right) \sum_{i=1}^N \int_{\mathcal{C}_i} \int_0^t c^2 \, d\xi dx \tag{5.14}$$

$\boxed{\text{4. STEP}}$ Now we insert (5.14) into (5.10) and add the resulting inequality and (5.6). We get

$$\begin{aligned}
&\left(\min \mathcal{M}' - \frac{t^2}{2}\|Q'\|_\infty\right) \int_0^t \int_\omega C^2 \, dx d\xi + \frac{D}{2}\int_\omega |\nabla(\int_0^t C \, d\xi)|^2 \, dx \\
&+ \frac{D}{2\beta}\sum_{i=1}^N \int_0^L \int_{\{r=R_i\}} (\int_0^t (C-c) \, d\xi)^2 \, dS dz + \frac{Dd}{4K}\sum_{i=1}^N \int_{\mathcal{C}_i} |\frac{\partial}{\partial z}\int_0^t c \, d\xi|^2 \, dx \\
&+ \frac{D}{2K}\left(\frac{1}{2} - t(\|\Phi'\|_\infty \|\gamma'\|_\infty + \frac{2\|u\|_\infty^2}{d} + 4T^3\|\Phi'\|_\infty^3)\right) \sum_{i=1}^N \int_0^t \int_{\mathcal{C}_i} c^2 \, dx d\xi \\
&\leq \frac{D\|u\|_\infty^2}{2K} \int_0^t \sum_{i=1}^N \int_{\mathcal{C}_i} |\frac{\partial}{\partial z}\int_0^\xi c \, d\eta|^2 \, dx d\xi
\end{aligned} \tag{5.15}$$

For $t \leq T_0 = \min\{T, \sqrt{\frac{\min \mathcal{M}'}{\|Q'\|_\infty}}, \frac{1}{4(\|\Phi'\|_\infty \|\gamma'\|_\infty + \frac{2\|u\|_\infty^2}{d} + 4T^3\|\Phi'\|_\infty^3)}\}$ and by using Gronwall's inequality , we conclude that $c(x,t) = 0$ and $C = 0$. ℓ are also zero.

Therefore we have uniqueness on a small time interval with length independent of the data. By repeating this procedure a finite number of times, we get uniqueness on $(0,T)$. $\square$

References

[1] C. BOS, L. HOOF and T. OOSTENDORP, Mathematical model of erytrocytes as point-like sources, *Math. Biosci.* **125** (1995), 165–189.

[2] C. BOURDARIAS, Sur un système d'E.D.P. modélisant un processus d'adsorption isotherme d'un mélange gazeux, M^2AN Mathematical Modelling and Numerical Analysis, Vol. **26** (1992), 867–892.

[3] J. CARRILLO, Entropy Solutions for Nonlinear Degenerate Problems, Arch. Rational Mech. Anal., **147** (1999), 263–361.

[4] A. DUTTA and A. S. POPEL, A Theoretical analysis of intracellular oxygen diffusion, J. Theoret. Biol. **176** (1995), 165–174.

[5] C. D. EGGLETON, A. VARDAPALLI, T. K. ROY and A. S. POPEL, Calculation of intracapillary oxygen tension distribution in muscle, Math.Biosci., **167** (2000), 123–143.

[6] J. E. FLETCHER, Mathematical modeling of the microcirculation, Math. Biosci. **38** (1978), 155–202.

[7] J. E. FLETCHER and R. W. SHUBERT, On the computation of substrate levels in perfused tissues, Math. Biosci. **62** (1982), 75–106.

[8] A. FRIEDMAN and A. TZAVARAS, A Quasilinear Parabolic System Arising in Modelling of Catalytic Reactors, J. of Differential Equations, **70** (1987), 167–196.

[9] J. GONZALEZ - FERNANDEZ and S. ATTA, Transport and consumption of oxygen in capillary-tissue structure, Math. Biosci. **2** (1968), 225-261.

[10] L. HOOFD, Calculation of oxygen pressures in tissue with anisotropic capillary orientation, Math. Biosci. **129** (1995), 1–23.

[11] R. HSU, T. W. SECOMB, A Green's function method for analysis of oxygen delivery to tissue by microvascular networks, Math. Biosci. **96** (1989), 61-78.

[12] J. KEENER and J. SNEYD, Mathematical Physiology, Interdisciplinar Appl. Math. **8** Springer Verlag, 1998.

[13] A. KROGH, The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue, J. Physiol. (London) **52** (1919), 409–415.

[14] A. KROGH, The Anatomy and Physiology of Capillaries, Yale Univ. Press, New Haven 1929.

[15] O. A. LADYŽENSKAYA, V. A. SOLONNIKOV and N. N. URAL'CEVA, Linear and Quasi-Linear Equations of Parabolic Type, Translations of Mathematical Monographs Vol. 23, American Mathematical Society, Providence, 1968.

[16] A. MIKELIĆ and M. PRIMICERIO, Oxygen exchange between multiple capillaries and living tissues: An homogenization study, Rend. Mat. Acc. Lincei, Vol. **13** (2002), 149–164.

[17] C. V. PAO, Stability analysis of a coupled diffusion-transport system for oxygen transport in blood and tissue, *Nonl. Anal. Th. Met. App.* **9** (1985), 1037–1059.

[18] A. S. POPEL, Analysis of capillary-tissue diffusion multicapillary system, *Math. Biosci.* **35** (1978), 187–211.

[19] A. S. POPEL, Mathematical modelling of oxygen transport near a tissue surface: effect of the surface P_{O_2}, *Math. Biosci.* **55** (1981), 231–246.

[20] A. S. POPEL, Theory of oxygen transport to tissue, *Crit. Riv. Biomed. Engrs.*, **17** (1989), 257–321.

[21] E. P. SALATHÉ, T. C. WANG and J. F. GROSS, Mathematical analysis of oxygen transport to tissue, *Math. Biosci.* **51** (1980), 89–115.

[22] M. S. TITICOMBE, M. J. WARD, An asymptotic study of oxygen transport from multiple capillaries to skeletral muscle tissue, *SIAM J. Appl. Math.*, **60** (2000), 1767–1788.

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