Non-stationary mathematical model of oxygen transport in brain

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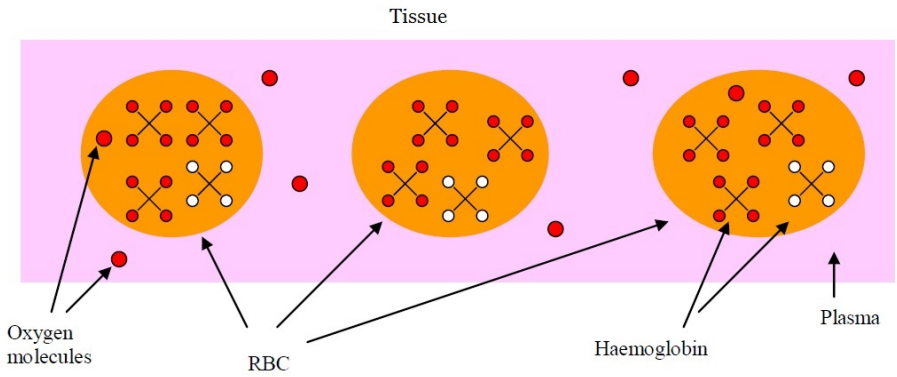
October 10, 2019

Oxygen concentration in the blood (φ), plasma (ϕ), and tissue (θ)



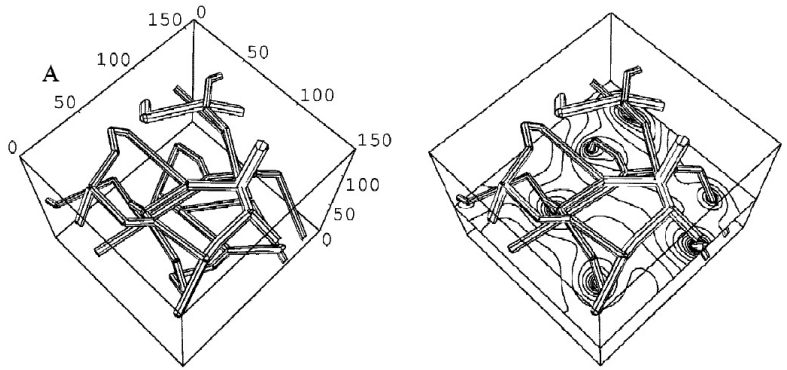
Relation between the blood (φ) and plasma (ϕ) oxygen concentrations:

$$\varphi = f(\phi) := \phi + \frac{b\phi^r}{\phi^r + c}, \quad \text{Hill coefficient}: \ r = 2.73.$$

Relation between the partial pressure of oxygen and concentration:

$$\phi,\, \theta = \text{Soluability} \cdot \mathrm{P_{O2}}.$$

Overview of publications



Numerical simulations under some simplifications: T.W. Secomb et al (1989, 1993, 1994,.. etc.), R. Valabregue et al (2003) etc.

Homogenization the oxygen transport problem

A.-R.A. Khaled, K. Vafai (2003):
The homogenization approach was applied to describe the heat transfer in tissue including the system of blood vessels.

S.-W. Su (2011):
A two phase continuum model the oxygen transport in the brain is proposed.

A.E. Kovtanyuk, A.Yu. Chebotarev et al (2018, 2019):
Convergence of an iterative algorithm for steady-state oxygen transport model is studied and a unique solvability is proven.

Problem formulation

Continuum model of oxygen transport:

$$\partial\varphi/\partial t - \alpha\Delta\varphi + \mathbf{v}\cdot\nabla\varphi = G, \quad \partial\theta/\partial t - \beta\Delta\theta = -\gamma G - \mu, \tag{1}$$

$$\varphi|_{\Gamma_1} = \varphi_b, \quad \theta|_{\Gamma_1} = \theta_b, \quad \partial_n\varphi = \partial_n\theta|_{\Gamma_2} = 0, \tag{2}$$

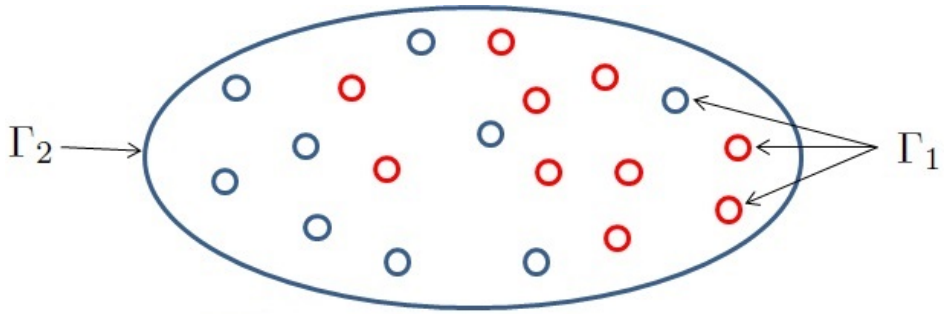
$$\varphi|_{t=0} = \varphi_0, \quad \theta|_{t=0} = \theta_0. \tag{3}$$

μ – tissue oxygen metabolic (consumption) rate
(Michaelis-Menten equation: $\mu = \mu(\theta) := \mu_0\theta/(\theta + \theta_{50})$)

G – local exchange at blood-tissue interface, $G = a(\theta - \phi)$
(Hill equation: $\varphi = f(\phi) := \phi + b\phi^r/(\phi^r + c)$;
$\phi = g(\varphi) := f^{-1}(\varphi)$ – monotonic function)

Problem formalization

Model domain:



Sets and spaces:

$Q = \Omega \times (0, T)$,

$V = H^1(\Omega)$, V' – adjoint space of V,

$W = \{y \in L^2(0, T; V) : y' \in L^2(0, T, V')\}$.

Problem formalization

Suppose that the model data satisfy the following conditions:

$(i)\ \ 0 \le \varphi_b \le M,\ 0 \le \theta_b \le g(M),$

$(ii)\ \exists\, \widetilde{\varphi}, \widetilde{\theta} \in L^\infty(0,T;H^2(\Omega)):$

$$\widetilde{\varphi}_t, \widetilde{\theta}_t \in L^2(Q),\ \ \partial_n \widetilde{\varphi}, \partial_n \widetilde{\theta}|_{\Gamma_2} = 0,\ \ \widetilde{\varphi}|_{\Gamma_1} = \varphi_b,\ \widetilde{\theta}|_{\Gamma_1} = \theta_b,$$

$(iii)\ \mathbf{v} \in L^\infty(0,T;H^1(\Omega)),\ \ \nabla \cdot \mathbf{v} = 0;\ \ \mathbf{v} \cdot \mathbf{n}|_{\Gamma_2} = 0.$

Define operator $A\colon V \to V'$ and functions $f_{1,2} \in L^2(Q)$:

$$(Au, v) = (\nabla u, \nabla v),\ \ \forall u, v \in V; \quad f_1 = -\widetilde{\varphi}_t + \alpha \Delta \widetilde{\varphi}, \quad f_2 = -\widetilde{\theta}_t + \beta \Delta \widetilde{\theta}.$$

Definition *A pair $\varphi = \widetilde{\varphi} + \psi$, $\theta = \widetilde{\theta} + \zeta$ is a weak solution of (1)-(3) if ψ, $\zeta \in W$ and*

$$\psi' + \alpha A\psi + \mathbf{v} \cdot \nabla \varphi + a\,(g(\varphi) - \theta) = f_1 \text{ a.e. on } (0,T), \tag{4}$$

$$\zeta' + \beta A\zeta + \mu(\theta) + \gamma a\,(\theta - g(\varphi)) = f_2 \text{ a.e. on } (0,T), \tag{5}$$

$$\varphi|_{t=0} = \varphi_0,\ \ \theta|_{t=0} = \theta_0. \tag{6}$$

An iterative algorithm

Define the operators $F_1, F_2 : L^\infty(Q) \to W$ such that $\psi = F_1(\zeta)$ if ψ is a solution of the problem

$$\psi' + \alpha A\psi + \mathbf{v} \cdot \nabla\varphi + a\,(g(\varphi) - \theta) = f_1 \text{ a.e. on } (0,T), \quad \psi|_{t=0} = \varphi_0 - \widetilde{\varphi}|_{t=0}, \quad (7)$$

where $\theta = \widetilde{\theta} + \zeta$, $\varphi = \widetilde{\varphi} + \psi$. Accordingly, $\zeta = F_2(\psi)$ if ζ is a solution of the problem

$$\zeta' + \beta A\zeta + \mu(\theta) + \gamma a\,(\theta - g(\varphi)) = f_2 \text{ a.e. on } (0,T), \quad \zeta|_{t=0} = \theta_0 - \widetilde{\theta}|_{t=0}. \quad (8)$$

The unique solvability of the problem (7) for given ζ and of the problem (8) for given ψ takes place due to the monotonicity of nonlinearities (Lions J.L., 1969).

Notice that if $\varphi_* = \widetilde{\varphi} + \psi_*$, $\theta_* = \widetilde{\theta} + \zeta_*$ is a weak solution of the problem (1)–(3), then $\psi_* = F_1(F_2(\psi_*))$ and $\zeta_* = F_2(F_1(\zeta_*))$.

An iterative algorithm

Lemma 1 *Let the conditions (i)–(iii) hold. Then*

$$0 \le \varphi \le M \ \text{ if } \ 0 \le \theta \le g(M); \quad 0 \le \theta \le g(M) \ \text{ if } \ 0 \le \varphi \le M.$$

Lemma 2 *Let the conditions (i)–(iii) hold. Then*

$$F_1(\zeta_1) \le F_1(\zeta_2) \ \text{ if } \ \zeta_1 \le \zeta_2; \quad F_2(\psi_1) \le F_2(\psi_2) \ \text{ if } \ \psi_1 \le \psi_2.$$

An iterative algorithm

Define the functional sequences in a recurrent way:

$$\theta_k = \widetilde{\theta} + \zeta_k, \quad \varphi_k = \widetilde{\varphi} + \psi_k,$$
$$\zeta_0 = -\widetilde{\theta}, \quad \psi_k = F_1(\zeta_k), \quad \zeta_{k+1} = F_2(\psi_k), \quad k = 0, 1, 2, \dots . \tag{9}$$

Due to Lemma 1, the following inequality holds: $0 = \theta_0 \le \theta_1$. Therefore, $\theta_1 = \widetilde{\theta} + F_2(F_1(\theta_0 - \widetilde{\theta})) \le \widetilde{\theta} + F_2(F_1(\theta_1 - \widetilde{\theta})) = \theta_2$ and then accordingly

$$0 \le \theta_k \le \theta_{k+1} \le g(M), \ k = 0, 1, 2, \dots$$

Analogously, $\varphi_0 = \widetilde{\varphi} + F_1(\theta_0 - \widetilde{\theta}) \le \widetilde{\varphi} + F_1(\theta_1 - \widetilde{\theta}) = \varphi_1$, and then

$$0 \le \varphi_k \le \varphi_{k+1} \le M, \ k = 0, 1, 2, \dots$$

An iterative algorithm

From the monotonicity and boundedness of the sequences φ_k, θ_k, from the Levi's theorem, it follows the existence of the functions θ_*, $\varphi_* \in L^\infty(Q) \cap W$ such that

$$\theta_k \to \theta_*, \quad \varphi_k \to \varphi_* \text{ a.e. in } Q, \quad \text{weakly in } W. \tag{10}$$

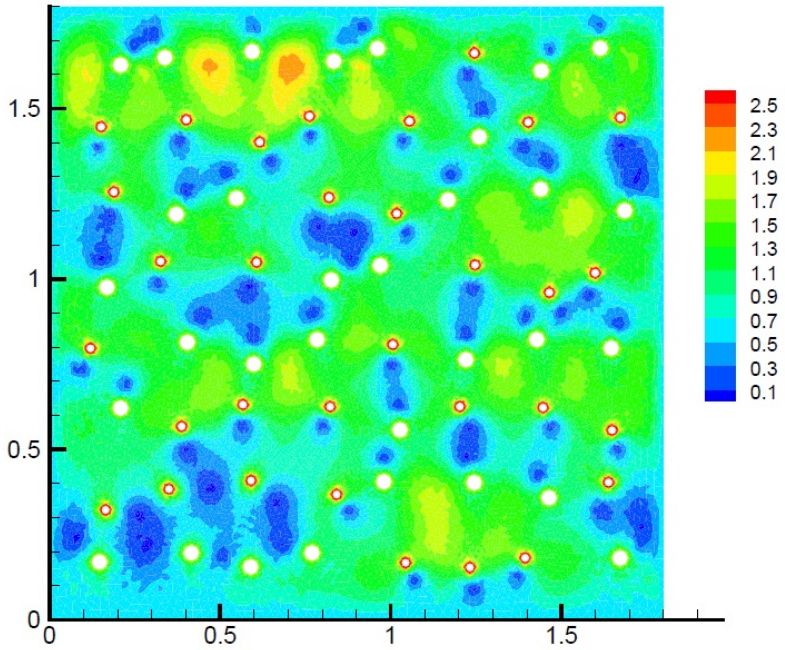
The convergence results (10) make it possible in the standard way to pass to the limit in the equalities defining φ_k, θ_k. The passage to the limit in nonlinear terms is guaranteed by their monotonicity. Thus, we conclude that φ_*, θ_* is a weak solution of the problem (1)–(3). Moreover, it is possible to prove the uniqueness of the solution.

Theorem *Let the conditions (i)–(iii) hold. Then the non-decreasing sequence $\{\varphi_k, \theta_k\}$ defined by (9) converge a.e. in Q to a unique weak solution of the problem (1)–(3).*

Numerical experiments

Numerical example involves a 2D square domain with the area of 1.8mm $\times$ 1.8mm. It contains 64 holes corresponding to 32 inlets and 32 outlets that are interpreted as arteriolar and venular ends of the capillary network.

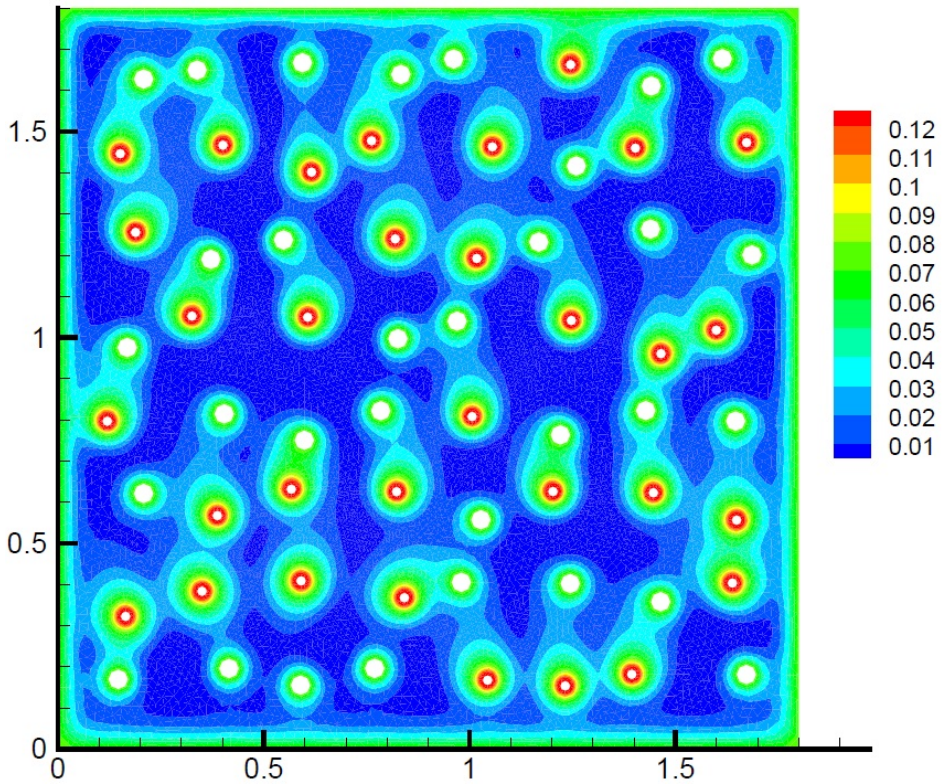
The absolute velocity (mm/s)



The velocity field $\mathbf{v}$ is computed in advance using the Stokes equation. To solve the Stokes equation, following Rosenblum (1969), velocities of 3.4 mm/s and 1.7 mm/s are set at the ends of arterioles and venules, respectively. Note that we use the Stokes equation to obtain an example of velocity field satisfying the specified boundary conditions in the considered complex domain. Nevertheless, in most of the domain, the velocity norm computed lies in the range of acceptable values (from 0.3 to 1.7 mm/s), which is necessary for normal functioning of brain cells (see Ivanov et al. (1981)).

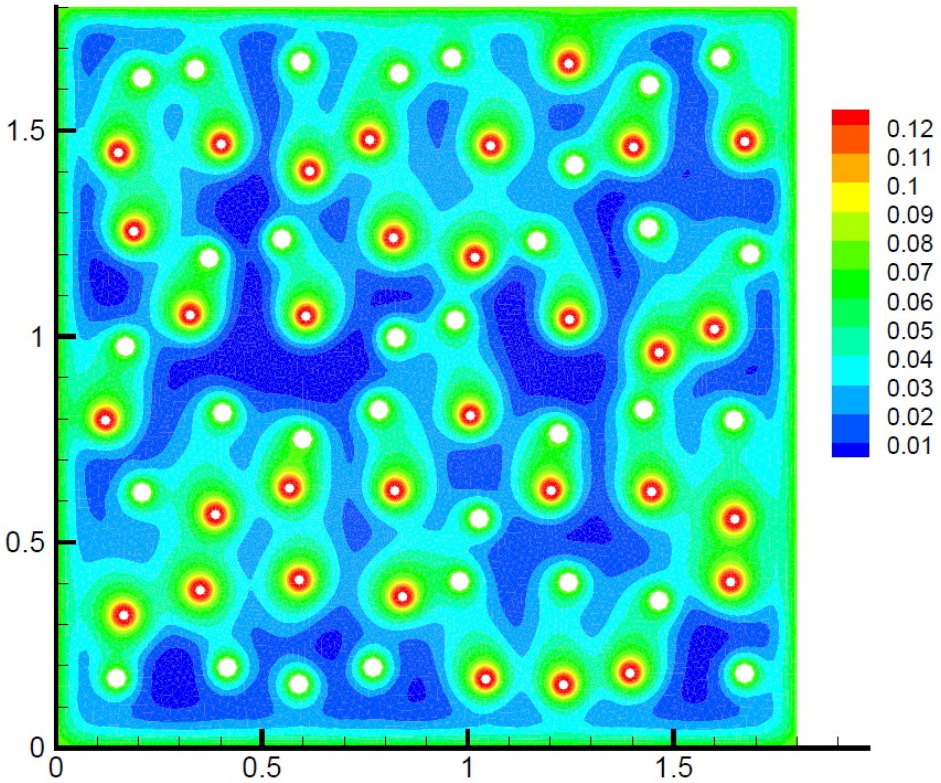
Numerical experiments

The tissue oxygen concentration at 1 s (mM)



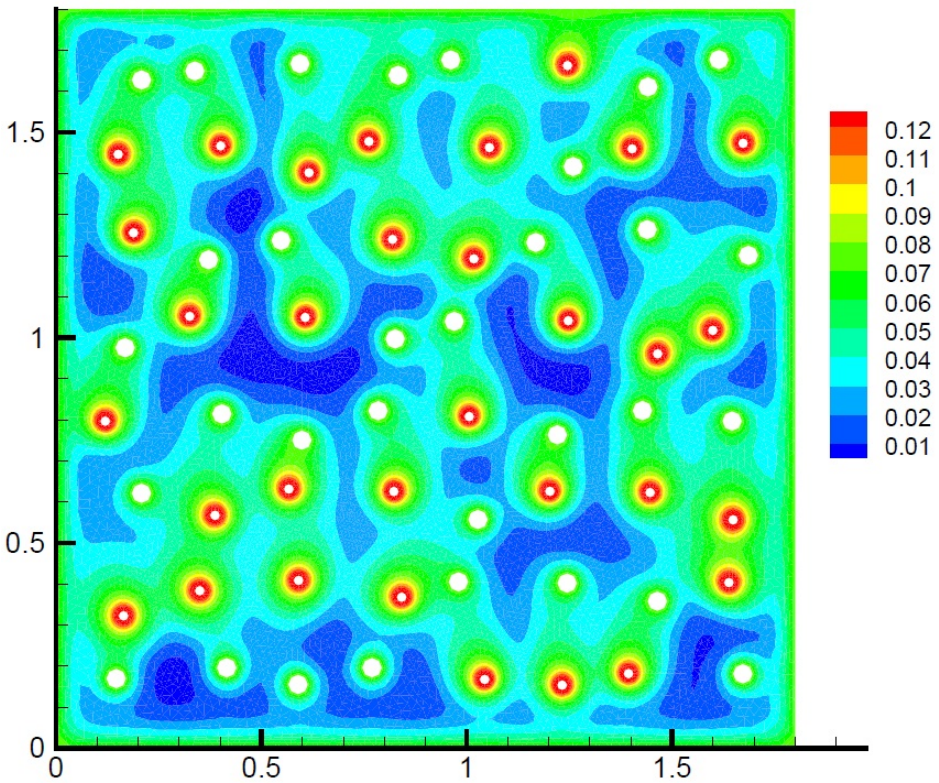
Numerical experiments

The tissue oxygen concentration at 2 s (mM)



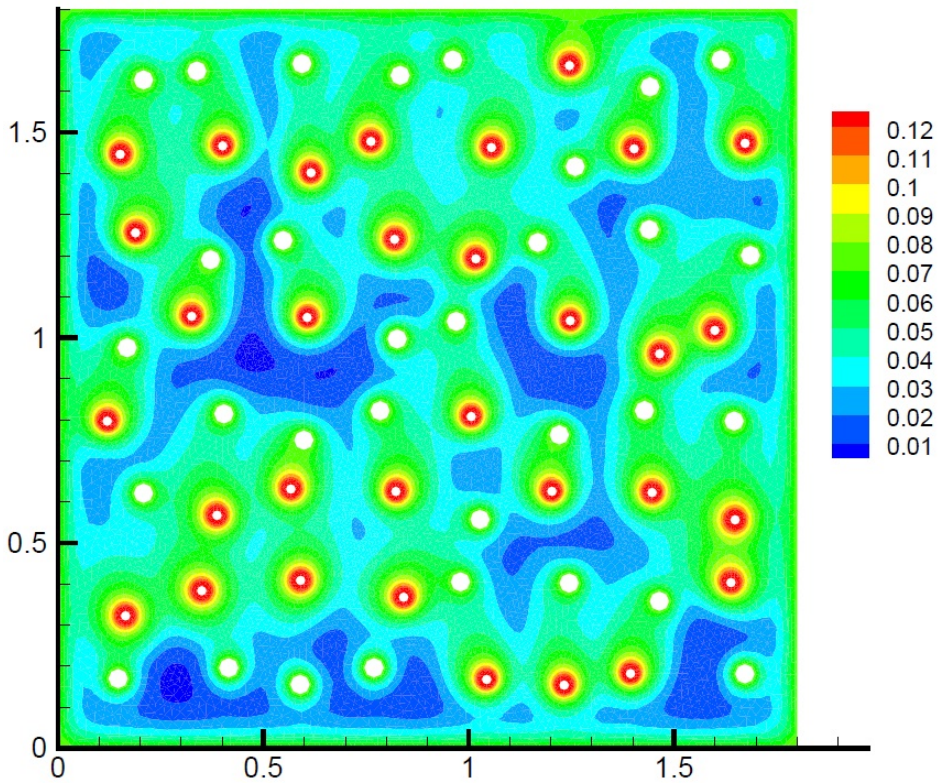
Numerical experiments

The tissue oxygen concentration at 3 s (mM)



Numerical experiments

The tissue oxygen concentration at 7 s (mM)



Conclusion

1. Convergence of the iterative algorithm for finding a solution of the initial boundary-value problem is proven.

2. Numerical analysis was conducted. Convergence and fast stabilization* are demonstrated.

* A rapid stabilization (within 6-7 seconds) of oxygen distribution in tissue is observed. More fast stabilization (within 3-4 seconds) occurs in the blood fraction.

THANK YOU FOR ATTENTION!