AN INVERSE PROBLEM OF OXYGEN TRANSPORT IN BRAIN

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Abstract. A continuum steady-state model of oxygen transport in brain is studied. The problem is considered as an inverse problem with unknown sources. The unique solvability of the inverse problem is proven, and an algorithm to find solutions is proposed.

Key words Boundary-value problem, inverse problem, unique solvability, oxygen transport in brain.

1. Introduction

Delivery of a sufficient amount of oxygen to cerebral cells is the most important requirement for functioning of the brain. The lack of oxygen can lead to irreversible neuronal damage within a few minutes. Therefore, mathematical models of oxygen transport in brain substance are important for simulation of dangerous situations arising from impaired cerebral circulation.

The most promising approach is that the brain material is considered as a twocompartment (blood and tissue) structure, and coupled equations describe convection of oxygen in blood as well as its diffusion and consumption in tissue (Secomb et. al., 2000; Payne, Lucas, 2018; Su, 2011).

A perspective approach to modeling oxygen transport is associated with spatial homogenization of state variables. There, the homogenization is being performed under the assumption that the tissue and blood fractions occupy the same spatial region. In (Khaled, Vafai, 2003), this approach was applied to a model of heat transfer in tissue comprising a network of blood vessels. A similar approach to studying oxygen transport process in brain was used in (Su, 2011), where a two-phase continuum model describing coupled oxygen transport in tissue and blood is considered. A coupled system of equations arises here as the result of homogenization of a two-phase model of oxygen transport in a media contained blood and tissue fractions. Numerical simulations for a simplified domain were conducted, and the comparison with simulations based on the original (non-homogenized) model was done.

In (Kovtanyuk et. al., 2018), a theoretical analysis of steady-state oxygen transport model is fulfilled. A priori estimates of solutions, implying the unique solvability of the problem under some conditions, are obtained. An iterative numerical procedure for finding solutions is proposed, along with the proof of its convergence. In (Kovtanyuk et. al., 2019), the investigation of the steady-state continuum model was continued, the existence and uniqueness of solutions for the boundary-value problem were established, and numerical examples illustrated the theoretical analysis were presented.

In the present work, the boundary-value problem of oxygen transport is considered as an inverse problem with unknown sources. The unique solvability of the inverse problem is proven and numerical algorithm to find a solution is proposed.

2. Problem formulation

A two-compartment (blood and tissue) model of oxygen transport is considered. It is assumed that the both compartments occupy the same spatial region $\Omega \subset \mathbb{R}^3$ and have different volume fractions for the blood and tissue compartments, σ and $1 - \sigma$, respectively. Following (Su, 2011; Kovtanyuk et. al., 2018; Kovtanyuk et. al., 2019), oxygen transport can be described by the following coupled equations:

$$-\alpha\Delta\varphi + \mathbf{v}\cdot\nabla\varphi = G, \ -\beta\Delta\theta = -\kappa G - \mu, \ x \in \Omega.$$

Here, φ is the oxygen concentration in blood; θ the oxygen concentration in tissue; μ the tissue oxygen metabolic (consumption) rate associated with brain functioning; $G = c(\theta - \psi)$ the local exchange at the blood-tissue interface, where ψ is the plasma oxygen concentration; $\kappa = \sigma(1 - \sigma)^{-1}$, where σ is the volume fraction of blood; v a given velocity field in the domain Ω ; and α and β are diffusion coefficients for blood and tissue, respectively.

There is a nonlinear monotonic dependence of the tissue oxygen metabolic rate, μ , on the tissue oxygen concentration, θ , and of the plasma oxygen concentration on the blood oxygen concentration, φ . To simplify the model, the following linear approximations: $\mu = p\theta + s$ and $\psi = a\varphi + b$, where a, p > 0, will be used.

In (Kovtanyuk et. al., 2018), a perforated model domain was considered to simulate the ends of arterioles and venules. The concentrations corresponding to the ends of arterioles and venules were set at the boundaries of the holes.

In the present work, we will use another approach to simulate the ends of arterioles and venules. Let $\Omega_j \subset \Omega$, j = 1, ..., m, be disjoint subdomains. The oxygen transport will be described by the following system of elliptic equations:

$$-\alpha\Delta\varphi + \mathbf{v}\cdot\nabla\varphi = G + \sum_{j=1}^{m} q_j f_j, \quad -\beta\Delta\theta = -\kappa G - \mu + \sum_{j=1}^{m} p_j f_j, \quad x \in \Omega.$$
(1)

Here, f_i is the characteristic function of the subdomain Ω_i .

Equations (1) are supplemented by the following boundary conditions imposed on $\Gamma := \partial \Omega$:

$$\alpha \partial_n \varphi + \gamma (\varphi - \varphi_b)|_{\Gamma} = 0, \quad \beta \partial_n \theta + \delta (\theta - \theta_b)|_{\Gamma} = 0.$$
 (2)

The inverse problem consists in finding intensities $r = (q_1, ..., q_m, p_1, ..., p_m) \in \mathbb{R}^{2m}$ and the corresponding solution $y = \{\varphi, \theta\}$ of the boundary-value problem (1) and (2) with the following integral overdetermination:

$$\int_{\Omega_j} \varphi dx = Q_j, \quad \int_{\Omega_j} \theta dx = P_j, \quad j = 1, 2, \dots, m.$$
(3)

Here, Q_j and P_j are the prescribed averaged values of the functions φ, θ with respect to subdomains Ω_j .

3. Problem formalization.

Let $H = L^2(\Omega), V = H^1(\Omega), V \subset H = H' \subset V'; W = V \times V$, and $W' = V' \times V'$. By (f, v) (respectively ((F, z))) we denote a value of the functional $f \in V'$ at the element $v \in V$ (respectively $F \in W'$ at the element $z \in W$) wich coincide with the inner product in H (respectively in $H \times H$) if $f \in H$ (respectively $F \in H \times H$). Denote $||f||^2 = (f, f)$.

Let the follwing conditions hold:

 $(i) \quad \gamma, \delta \in L^{\infty}(\Gamma), \ \gamma \geq \gamma_0 > 0, \ \delta \geq \delta_0 > 0, \ \varphi_b, \theta_b \in L^{\infty}(\Gamma);$

(ii) $\mathbf{v} \in H^1(\Omega)$, $\nabla \cdot \mathbf{v} = 0$, $\gamma + 0.5 \mathbf{v} \cdot n \ge 0$ on Γ .

Define the following operators and functionals:

$$\begin{split} A: W \to W', \quad B: W \to W', \quad F_j \in W', \quad j = 0, 1, \dots, 2m; \\ ((Ay, z)) &= \alpha(\nabla \varphi, \nabla \psi) + \int_{\Gamma} \gamma \varphi \psi d\Gamma + \beta(\nabla \theta, \nabla \zeta) + \int_{\Gamma} \delta \theta \zeta d\Gamma; \\ ((By, z)) &= (v \cdot \nabla \varphi - c(\theta - a\varphi), \psi) + (p\theta + \kappa c(\theta - a\varphi), \zeta); \\ ((F_0, z)) &= \int_{\Gamma} \gamma \varphi_b \psi d\Gamma + \int_{\Gamma} \delta \theta_b \zeta d\Gamma - bc(1, \psi) + (\kappa bc - s)(1, \zeta); \\ ((F_j, z)) &= (f_j, \psi), \quad j = 1, 2, \dots, m; \\ ((F_j, z)) &= (f_{j-m}, \zeta), \quad j = m + 1, \dots, 2m. \end{split}$$

These equalities are valid for any $y = \{\varphi, \theta\}$, $z = \{\psi, \zeta\} \in W$. Using these operators, the inverse problem (1)–(3) can be rewritten in the following form.

Problem (P). Find $y = \{\varphi, \theta\} \in W$ and a vector $r = (r_1, r_2, \dots, r_{2m}) := (q_1, \dots, q_m, p_1, \dots, p_m)$ such that

$$Ay + By = F_0 + \sum_{j=1}^{2m} r_j F_j,$$
 (4)

$$((F_j, y)) = R_j, \text{ where } R_j = \begin{cases} Q_j, & j = 1, 2, ..., m, \\ P_j, & j = m + 1, ..., 2m. \end{cases}$$
 (5)

4. Reducing the Problem (P) to a system of linear algebraic equations.

The following auxiliary results are true. Lemma 1. For any $F \in W'$, there exists a unique solution of the problem

$$Az + Bz = F, \quad z \in W. \tag{6}$$

Let $y_j \in W$, j = 0, 1, ..., 2m, and moreover

$$Ay_j + By_j = F_j, \quad j = 0, 1, \dots, 2m.$$
 (7)

Then for a solution of the equation (4) the following presentation is true:

$$y = y_0 + \sum_{j=1}^{2m} r_j y_j.$$
 (8)

From the overdetermination conditions (5), we conclude that the intensities r_j , j = 1, 2, ..., 2m, are solutions of the following system of linear algebraic equations:

$$\sum_{j=1}^{2m} ((F_k, y_j)) r_j = R_k - ((F_k, y_0)), \quad k = 1, 2, \dots, 2m.$$
(9)

Lemma 2. The system of linear algebraic equations (9) is uniquely solvable.

Thus, accounting for Lemmas 1 and 2, the following final result with respect to unique solvability of Problem (P) is true.

Theorem. Problem (P) is uniquely solvable. Moreover, its solution $y \in W$, $r \in \mathbb{R}^{2m}$ is defined by formula (8), where $r = (r_1, r_2, ..., r_{2m})$ are solutions of the system of linear algebraic equations (9).

5. Conclusion.

A new approach to find a solution of the boundary-value problem of oxygen transport in brain is proposed. The problem is considered as an inverse problem with finite overdetermination. The inverse problem is reduced to finding a solution of a system of linear algebraic equations.

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References

Khaled A.-R.A., Vafai K. The role of porous media in modeling flow and heat transfer in biological tissues // Int. J. Heat Mass Transf. 2003. V. 46. P. 4989–5003.

Kovtanyuk A.E., Chebotarev A.Yu., Dekalchuk A.A., Botkin N.D., Lampe R. Analysis of a mathematical model of oxygen transport in brain // Proc. Int. Conf. Days on Diffraction 2018. 2018. P. 187–191.

Kovtanyuk A.E., Chebotarev A.Yu., Botkin N.D., Turova V.L., Sidorenko I.N., Lampe R. Continuum model of oxygen transport in brain // J. Math. Anal. Appl. 2019. V. 474. P. 1352–1363.

Payne S.J., Lucas C. Oxygen delivery from the cerebral microvasculature to tissue is governed by a single time constant of approximately 6 seconds // Microcirc. 2018. V. 25. e12428.

Secomb T.W., Hsu R., Beamer N.B., Coull B.M. Theoretical simulation of oxygen transport to brain by networks of microvessels: Effects of oxygen supply and demand on tissue hypoxia // Microcirc. 2000. V. 7. P. 237–247.

Su S.-W. Modelling blood flow and oxygen transport in the human cerebral cortex. PhD Thesis. Oxford, Depart. Eng. Sci., 2011. 248 p.