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# Non-Stationary Model of Cerebral Oxygen Transport with Unknown Sources

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**Abstract:** An inverse problem for a system of equations modeling oxygen transport in the brain is studied. The problem consists of finding the right-hand side of the equation for the blood oxygen transport, which is a linear combination of given functionals describing the average oxygen concentration in the neighborhoods of the ends of arterioles and venules. The overdetermination condition is determined by the values of these functionals evaluated on the solution. The unique solvability of the problem is proven without any smallness assumptions on the model parameters.

**Keywords:** oxygen transport in brain; nonlinear coupled parabolic equations; unique solvability; inverse problem



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## 1. Introduction

Mathematical modeling of cerebral oxygen transport is an interesting and important area of research, since it allows to describe the oxygen distribution in brain tissue and predict some critical situations in oxygen supply. The most popular is an approach where the brain material is considered as a two-compartment structure consisting of blood and tissue fractions. Corresponding mathematical models are represented by coupled partial differential equations describing convection, diffusion, and consumption of oxygen in blood and tissue fractions (see, e.g., [1–3]). Note, however, that the above works do not provide an analysis of the correctness of the corresponding boundary value problems.

A promising direction in modeling cerebral oxygen transport is related to the so-called continuum models obtained using spatial homogenization of the state variables [4,5]. In such continuum models, the blood and tissue fractions occupy the same spatial domain. Although the homogenization of a vascular network does not allow us to observe gradients of the oxygen concentration around blood vessels, this approach gives an opportunity to simulate important processes of oxygen transport, such as diffusion, convection, and consumption of oxygen in relatively large parts of cerebral tissue. Additionally, on the basis of the continuum models, it is possible to estimate the rate of tissue oxygen saturation and study the stabilization of oxygen concentration (see [5]). Additionally, this approach enables carrying out a theoretical analysis of corresponding boundary value and initial boundary value problems using their weak formulations. In [4], a theoretical analysis of the steady-state continuum oxygen transport model is fulfilled. The existence and uniqueness of the solution of the boundary value problem are established, and numerical examples are presented. Theoretical and numerical analyses of the non-stationary continuum oxygen transport model is performed in [5], where the unique solvability of the corresponding initial-boundary value problem is proved and numerical simulations demonstrating the

tissue oxygen saturation after hypoxia are presented. Fast stabilization of the tissue oxygen concentration is shown.

The oxygen supply and its outflow at the ends of arterioles and venules can be described by boundary conditions. For this, in the numerical simulations of [5], it was required to use a perforated computational domain with a large number of small holes corresponding to the ends of arterioles and venules. Another way to take the oxygen supply and its outflow into account is based on the function of sources. In practice, the location of the sources is usually known, but their intensities are unknown. However, additional information about the average blood oxygen concentration in the neighborhoods of the sources can be obtained on the basis of available experimental data. As a result, a non-stationary model of cerebral oxygen transport with unknown intensities of sources can be formulated as an inverse problem with finite-dimensional overdetermination. The non-stationarity of the model is due to the fact that blood oxygen concentration in the neighborhoods of the sources and the corresponding intensities of sources depend on time. For steady-state oxygen transport, the boundary value problem with an unknown intensity of sources is studied in [6], where the existence theorem is proven without assumptions of smallness and the local uniqueness of the solution is established. In particular, the conditions of uniqueness are fulfilled for domains with a sufficiently small thickness. Note that similar inverse problems for various models of heat and mass transfer were also studied in [7–10]. The work [11] is particularly worth mentioning, in which the pressure drop distribution in the homogenized capillary network is described by an inverse problem with finite-dimensional overdetermination.

In the current work, we consider the non-stationary model of cerebral oxygen transport with unknown intensities of sources. The main result of the work is to prove the nonlocal unique solvability of the inverse problem. This is achieved by reducing the inverse problem to a Cauchy problem for an ordinary differential equation with operator coefficients in the corresponding Hilbert space. The result obtained can be used in the future to substantiate numerical algorithms for solving the inverse problem. The paper is organized as follows. In Section 2, the non-stationary model of cerebral oxygen transport is formulated in the form of the Cauchy problem for a nonlinear system with operator coefficients. Further, an inverse problem related to finding the intensities of the sources is posed. In Section 3, the unique solvability of the inverse problem is established by means of a priori estimates and the contraction mapping principle.

## 2. Problem Formulation

In the following, the model and the corresponding inverse problem are introduced.

### 2.1. The Model

We consider a two-phase vessel-tissue system consisting of the blood phase with the volume fraction  $\sigma$  and the tissue phase with the volume fraction  $1 - \sigma$ . In the context of a continuum model, we assume that both fractions occupy the same domain  $\Omega$ . Following [5], the oxygen transport in the domain  $\Omega$  within the time interval  $(0, T)$  is described by the following coupled parabolic equations:

$$\partial\varphi/\partial t - \alpha\Delta\varphi + \mathbf{v} \cdot \nabla\varphi = G + S, \quad \partial\theta/\partial t - \beta\Delta\theta = -\kappa G - \mu. \quad (1)$$

Here,  $\varphi$  and  $\theta$  are the blood and tissue oxygen concentrations, respectively,  $\mu$  describes the tissue oxygen consumption,  $G$  is the intensity of oxygen exchange between the blood and tissue fractions,  $\mathbf{v}$  is a given homogenized velocity field in the entire domain  $\Omega$  (obtained by averaging the velocity field of the capillary network),  $\alpha$  and  $\beta$  are diffusivity parameters of the corresponding phases, and  $\kappa = \sigma(1 - \sigma)^{-1}$ . The sources function  $S$  describes the oxygen supply and its outflow at the ends of arterioles and venules.

The homogenized velocity field  $\mathbf{v}$  can be calculated in advance on the basis of the cerebral pressure drop using the approach proposed in [11]. Additionally, it is possible to apply the algorithm from [12] to find the blood velocities in the capillary network with their subsequent homogenization.

The Michaelis Menten equation describes the tissue oxygen consumption rate  $\mu$  as the function of  $\theta$  as follows:

$$\mu = \mu(\theta) := \frac{\mu_0 \theta}{\theta + \theta_{50}},$$

where  $\mu_0$  is the maximum value of  $\mu$ , and  $\theta_{50}$  is the value of  $\theta$  at which  $\mu = 0.5 \mu_0$ .

The transfer rate of oxygen from blood to tissue through vessel walls is given by the formula

$$G = a(\theta - \phi), \quad \phi = f(\phi) := \phi + \frac{b\phi^s}{\phi^s + c},$$

where  $\phi$  is the oxygen concentration in plasma. Note that  $\phi$  can be expressed through  $\varphi$  so that  $\phi$  is not a state variable of the oxygen transport model. The constants  $a, b$ , and  $c$  whose interpretation is given in [4,5] are positive, and  $s > 2$  is the Hill coefficient.

We assume that the oxygen concentrations  $\varphi$  and  $\theta$  satisfy the following conditions on the boundary  $\Gamma = \partial\Omega$ :

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

and the following initial conditions:

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

Here,  $\partial_n$  is the outward (with respect to  $\Omega$ ) normal derivative at points of  $\Gamma$ . The nonnegative functions  $\varphi_b = \varphi_b(x)$ ,  $\gamma = \gamma(x)$ ,  $\delta = \delta(x)$ ,  $x \in \Gamma$ , and the initial functions  $\varphi_0 = \varphi_0(x)$  and  $\theta_0 = \theta_0(x)$ ,  $x \in \Omega$ , are given. The function  $g$  is defined as the inverse of  $f$ .

### 2.2. The Abstract Cauchy Problem

The formulation of the inverse problem relies on a reformulation of the initial boundary value problem (1)–(3) as a Cauchy problem for the equations with operator coefficients.

Let  $\Omega$  be a bounded Lipschitz domain with the boundary  $\Gamma = \partial\Omega$ . Set  $Q = \Omega \times (0, T)$  and  $\Sigma = \Gamma \times (0, T)$ . Denote by  $L^p$ ,  $1 \leq p \leq \infty$ , the space of  $p$ -integrable (essentially bounded if  $p = \infty$ ) functions. Let  $H^n$  be the Sobolev space  $W_2^n$ . The space  $L^p(0, T; X)$  (respectively,  $C([0, T]; X)$ ) consists of  $p$ -integrable on  $(0, T)$  (respectively, continuous on  $[0, T]$ ) functions assuming values in a Banach space  $X$ .

Suppose that the parameters of the model satisfy the following conditions:

- (i)  $\gamma, \delta \in L^\infty(\Gamma)$ ,  $\gamma \geq \gamma_0 > 0$ ,  $\delta \geq \delta_0 > 0$ ,  $\gamma_0, \delta_0 = Const$ ,  $\varphi_b \in L^2(\Sigma)$ ;
- (ii)  $\theta_0, \varphi_0 \in L^2(\Omega)$ ;
- (iii)  $\mathbf{v} \in L^\infty(Q)$ .

Denote  $H = L^2(\Omega)$ ,  $V = H^1(\Omega)$ , and  $V'$  the dual of  $V$ . The space  $H$  is identified with its dual  $H'$  so that  $V \subset H = H' \subset V'$ . Let  $\|\cdot\|$  and  $\|\cdot\|_V$  denote the norms in  $H$  and  $V$ , respectively. Notice that  $(\xi, v)$  is the value of the functional  $\xi \in V'$  on the element  $v \in V$ . If  $\xi \in H$ , then  $(\xi, v)$  coincides with the inner product in  $H$ .

Introduce the inner product in  $V$  by the relation

$$((u, v)) = (u, v) + (\nabla u, \nabla v).$$

Define the following space:

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

where  $v' = dv/dt$ . It is well-known that  $W \subset C([0, T]; H)$  is the continuous embedding.

In accordance with the problem formulation, we introduce strictly increasing odd

functions  $\mu : \mathbb{R} \rightarrow \mathbb{R}$  and  $f : \mathbb{R} \rightarrow \mathbb{R}$  defined by the formulas

$$\mu(\lambda) := \frac{\mu_0 \lambda}{\lambda + \theta_{50}}, \quad f(\lambda) := \lambda + \frac{b \lambda^s}{\lambda^s + c}, \quad \lambda \geq 0.$$

Let  $g : \mathbb{R} \rightarrow \mathbb{R}$  denote the inverse of  $f$ . Note that

$$|\mu(\lambda)| \leq \mu_0, \quad |g(\lambda)| \leq |\lambda|, \quad 0 \leq \mu'(\lambda) \leq \frac{\mu_0}{\theta_{50}}, \quad 0 \leq g'(\lambda) \leq 1, \quad \lambda \in \mathbb{R}. \tag{4}$$

Define the operators  $A_{1,2}: V \rightarrow V'$  and functionals  $g_{1,2} \in L^2(0, T; V')$  using the following relations:

$$(A_1 u, v) = \alpha(\nabla u, \nabla v) + \int_{\Gamma} \gamma u v d\Gamma, \quad (A_2 w, v) = \beta(\nabla w, \nabla v) + \int_{\Gamma} \delta w v d\Gamma,$$

$$(g_1, v) = \int_{\Gamma} \gamma \varphi_b v d\Gamma, \quad (g_2, v) = \int_{\Gamma} \delta g(\varphi_b) v d\Gamma \quad \text{a.e. on } (0, T),$$

where  $u, w, v \in V$  are arbitrary functions. Note that the bilinear forms  $(A_1 y, z)$  and  $(A_2 y, z)$  define the inner products in  $V$ , and the following inequalities hold:

$$(A_1 y, y) \geq k_1 \|y\|_V^2, \quad (A_2 y, y) \geq k_2 \|y\|_V^2, \tag{5}$$

where the positive constants  $k_1$  and  $k_2$  do not depend on  $y \in V$ .

Using the introduced operators and functionals, a weak formulation of the initial-boundary value problem (1)–(3) is derived using standard techniques. To do this, each of Equation (1) is multiplied by the test function  $v \in V$  and integrated over the domain  $\Omega$ . For integrals containing the Laplacians of unknown functions, the integration by parts formula is used. Then, taking into account the boundary conditions, the definitions of the operators  $A_1, A_2$  and the functionals  $g_1, g_2$ , the problem (1)–(3) can be rewritten as the following Cauchy problem for a system of equations with operator coefficients.

**Definition 1.** Let  $S \in L^2(0, T; V')$ . A pair  $\{\varphi, \theta\} \in W \times W$  is a weak solution of the problem (1)–(3) if

$$\varphi' + A_1 \varphi + \mathbf{v} \cdot \nabla \varphi + a(g(\varphi) - \theta) = g_1 + S \quad \text{a.e. on } (0, T), \tag{6}$$

$$\theta' + A_2 \theta + \mu(\theta) + \kappa a(\theta - g(\varphi)) = g_2 \quad \text{a.e. on } (0, T), \tag{7}$$

$$\varphi|_{t=0} = \varphi_0, \quad \theta|_{t=0} = \theta_0. \tag{8}$$

In [5], a priori estimates of the solution to the problem (6)–(8) for  $S = 0$  were obtained and the unique solvability of (6)–(8) was proved.

### 2.3. The Inverse Problem

To formulate the inverse problem, consider a linearly independent system of functionals  $\{f_1, f_2, \dots, f_m\}$  in  $V'$ . Denote by  $V_m$  their linear hull and assume that the function  $S : (0, T) \rightarrow V_m$  is unknown, but the values of the functionals mentioned above are given on the solution component  $\varphi(t)$  for every  $t \in (0, T)$ . Thus, we have the following problem.

**Problem 1.** Find the vector  $\mathbf{q} = \{q_1, q_2, \dots, q_m\} \in L^2(0, T)$  and functions  $\{\varphi, \theta\} \in W \times W$  satisfying

$$\varphi' + A_1 \varphi + \mathbf{v} \cdot \nabla \varphi + a(g(\varphi) - \theta) = g_1 + \sum_{j=1}^m q_j f_j, \tag{9}$$

$$\theta' + A_2 \theta + \mu(\theta) + \kappa a(\theta - g(\varphi)) = g_2, \tag{10}$$

$$\varphi(0) = \varphi_0, \quad \theta(0) = \theta_0, \tag{11}$$

$$(f_j, \varphi(t)) = r_j(t), \quad j = 1, \dots, m, \quad t \in (0, T). \tag{12}$$

Here,  $\varphi_0 \in H$ ,  $\theta_0 \in H$ , and the functions  $r_j \in H^1(0, T)$  are given.

**Example 1.** Let  $\Omega_j \subset \Omega$ ,  $j = 1, \dots, m$ , be disjoint subdomains;  $f_j(x) = 1$  if  $x \in \Omega_j$ , and  $f_j(x) = 0$  if  $x \in \Omega \setminus \Omega_j$ . In this case, the inverse problem consists in finding the coefficients  $q_1(t), q_2(t), \dots, q_m(t)$  and solutions  $\varphi$  and  $\theta$  of (9)–(11) such that

$$\int_{\Omega_j} \varphi(x, t) dx = r_j(t), \quad j = 1, 2, \dots, m; \quad t \in (0, T). \tag{13}$$

That is, the values  $r_j(t)$ ,  $j = 1, 2, \dots, m$ , are the average values of the blood concentration on the subdomains  $\Omega_j$ .

### 3. The Existence and Uniqueness of the Solution of Problem 1

Define the space

$$V_0 = \{z \in V : (f_j, z) = 0, \quad j = 1, 2, \dots, m\},$$

and denote by  $H_0$  the closure of  $V_0$  with respect to the norm of  $H$ . Let  $\{z_j\}_{j=1}^m \subset V$  be a biorthogonal set to the system of functionals  $\{f_j\}_{j=1}^m$ , that is,  $(f_i, z_j) = \delta_{ij}$ . Using them, we define the function

$$r = \sum_{j=1}^m r_j z_j.$$

**Remark 1.** Note that, since  $C^\infty(\overline{\Omega})$  is dense in the space  $H^1(\Omega) = V$ , the functions  $z_j$  can be chosen from  $C^\infty(\overline{\Omega})$ .

Let a triple  $\{\mathbf{q}, \varphi, \theta\}$  be a solution of the Problem 1. We write  $\varphi$  in the form  $\varphi = r + \psi$ , where  $\psi \in L^2(0, T; V_0)$  and  $\psi' \in L^2(0, T; V'_0)$ . Then the following equality holds:

$$\psi' + A_1\psi + \mathbf{v} \cdot \nabla\psi + a(g(\varphi) - \theta) = g_1 + \zeta \quad \text{in } V'_0.$$

Here,

$$\zeta = -(r' + A_1r + \mathbf{v} \cdot \nabla r) \in L^2(0, T; V')$$

and  $\psi(0) = \psi_0 = \varphi_0 - r(0) \in H_0$ .

In what follows, we will use the spaces  $X = H \times H, Y = V_0 \times V$ , in which the norms of  $y = \{\psi, \theta\}$  are defined by the equalities

$$\|y\|_X^2 = \|\psi\|^2 + \|\theta\|^2, \quad \|y\|_Y^2 = \|\psi\|_V^2 + \|\theta\|_V^2.$$

Further, define the mappings  $A(t) : Y \rightarrow Y', t \in (0, T), B : Y \rightarrow Y', F \in L^2(0, T; Y')$ , using the following equalities which are valid for all  $y = \{\psi, \theta\}, z = \{w, v\} \in Y$ :

$$\langle A(t)y, z \rangle = (A_1\psi, w) + (A_2\theta, v) + (\mathbf{v}(t) \cdot \nabla\psi, w) + a(\theta, \kappa v - w),$$

$$\langle B(y), z \rangle = (\mu(\theta), v) + a(g(r + \psi), w - \kappa v),$$

$$\langle F, z \rangle = (g_1 + \zeta, w) + (g_2, v).$$

Here,  $\langle \cdot, \cdot \rangle$  denotes the pairing of  $Y'$  and  $Y$ .

**Lemma 1.** A triple  $\{\mathbf{q}, \varphi, \theta\}$  is a solution of the Problem 1 iff  $\varphi = r + \psi$ ,

$$q_j = (\varphi' + A_1\varphi + \mathbf{v} \cdot \nabla\varphi + a(g(\varphi) - \theta) - g_1, z_j), \quad j = 1, 2, \dots, m, \tag{14}$$

and  $y = \{\psi, \theta\} \in L^2(0, T; Y)$  satisfies the problem

$$y' + Ay + B(y) = F, \quad y(0) = y_0 = \{\psi_0, \theta_0\}. \tag{15}$$

**Proof of Lemma 1.** Let  $y = \{\psi, \theta\}$  be a solution of the problem (15). Notice that

$$w - \sum_{j=1}^m (f_j, w) z_j \in V_0 \quad \forall w \in V.$$

From the equality  $\langle y' + Ay + B(y) - F, z \rangle = 0$ , where

$$z = \{w - \sum_{j=1}^m (f_j, w) z_j, v\} \in Y,$$

we obtain (10) and (11). Moreover,

$$\langle \varphi' + A_1\varphi + \mathbf{v} \cdot \nabla \varphi + a(g(\varphi) - \theta) - g_1, w - \sum_{j=1}^m (f_j, w) z_j \rangle = 0.$$

Taking into account (14), it follows from the last inequality that

$$\varphi' + A_1\varphi + \mathbf{v} \cdot \nabla \varphi + a(g(\varphi) - \theta) = g_1 + \sum_{j=1}^m q_j f_j.$$

Thus, the triple  $\{\mathbf{q}, \varphi, \theta\}$  is a solution of the Problem 1.

The converse: if  $\{\mathbf{q}, \theta, \varphi\}$  is a solution of Problem 1, then assuming  $\psi = \varphi - r$ , from the definitions of the space  $V_0$ , the system  $\{z_j\}_{j=1}^m$ , the operators  $A$  and  $B$ , and the function  $F$ , we obtain the equalities (14) and (15).  $\square$

**Lemma 2.** Let the conditions (i) and (iii) hold. Then for all  $y \in Y$ , the following inequalities are true:

$$\langle Ay, y \rangle \geq k_3 \|y\|_Y^2 - k_4 \|y\|_X^2, \quad \langle B(y), y \rangle \geq -k_5 \|y\|_X^2 - k_6. \tag{16}$$

Here,

$$k_3 = \min\{k_1/2, k_2\}, \quad k_4 = \frac{a}{2} + \frac{\|\mathbf{v}\|_{L^\infty(Q)}^2}{2k_1}, \quad k_5 = a \max\{2, \kappa^2\}, \quad k_6 = a \|r\|^2.$$

**Proof of Lemma 2.** For  $y = \{\psi, \theta\} \in Y$ , the following inequality holds:

$$\begin{aligned} \langle Ay, y \rangle &= (A_1\psi, \psi) + (A_2\theta, \theta) + (\mathbf{v} \cdot \nabla \psi, \psi) + a(\theta, \kappa\theta - \psi) \geq \\ &\geq k_1 \|\psi\|_V^2 + k_2 \|\theta\|_V^2 - \|\mathbf{v}\|_{L^\infty(Q)} \|\psi\| \|\psi\|_V - a \|\psi\| \|\theta\|. \end{aligned}$$

Since

$$\|\mathbf{v}\|_{L^\infty(Q)} \|\psi\| \|\psi\|_V \leq \frac{1}{2k_1} \|\mathbf{v}\|_{L^\infty(Q)}^2 \|\psi\|^2 + \frac{k_1}{2} \|\psi\|_V^2, \quad \|\psi\| \|\theta\| \leq \frac{\|\psi\|^2 + \|\theta\|^2}{2},$$

the first estimate in (16) is true.

Further, taking into account (4) and the oddness of the function  $\mu$ , we obtain

$$\begin{aligned} \langle B(y), y \rangle &= (\mu(\theta), \theta) + a(g(r + \psi), \psi - \kappa\theta) \geq -a \|r + \psi\| \|\psi - \kappa\theta\| \geq \\ &\geq -a(2\|\psi\|^2 + \kappa^2 \|\theta\|^2 + \|r\|^2) \geq -k_5 \|y\|_X^2 - k_6. \end{aligned}$$

The lemma is proved.  $\square$

Let us obtain a priori estimates for a solution of the problem (15).

**Lemma 3.** *Let the conditions (i)–(iii) hold. If  $y \in L^2(0, T; Y)$  is a solution of the problem (15), then  $y \in L^\infty(0, T; X)$  and the following estimate is true:*

$$\|y\|_{L^\infty(0,T;X)} + \|y\|_{L^2(0,T;Y)} \leq C, \tag{17}$$

where  $C > 0$  depends only on  $k_3, k_4, k_5, k_6, \|y_0\|_X, T$ , and  $\|F\|_{L^2(0,T;Y')}$ .

**Proof of Lemma 3.** From the equality

$$\langle y' + Ay + B(y) - F, y \rangle = 0,$$

taking into account the inequalities (16), we obtain

$$\frac{d}{2dt} \|y\|_X^2 + k_3 \|y\|_Y^2 \leq (k_4 + k_5) \|y\|_X^2 + k_6 + \frac{k_3}{2} \|y\|_Y^2 + \frac{1}{2k_3} \|F\|_{Y'}^2,$$

and

$$\begin{aligned} \|y(t)\|_X^2 + k_3 \int_0^t \|y(\tau)\|_Y^2 d\tau \leq \\ \|y_0\|_X^2 + \int_0^t \left( 2(k_4 + k_5) \|y(\tau)\|_X^2 + 2k_6 + \frac{1}{k_3} \|F(\tau)\|_{Y'}^2 \right) d\tau. \end{aligned}$$

Using Gronwall’s inequality, we have

$$\|y(t)\|_X^2 \leq k_7 := \exp(2T(k_4 + k_5)) \left( \|y_0\|_X^2 + 2k_6T + \frac{1}{k_3} \int_0^T \|F(\tau)\|_{Y'}^2 d\tau \right).$$

As a result,

$$k_3 \int_0^T \|y(\tau)\|_Y^2 d\tau \leq 2((k_4 + k_5)k_7 + k_6)T + \frac{1}{k_3} \int_0^T \|F(\tau)\|_{Y'}^2 d\tau.$$

The lemma is proven.  $\square$

Further, let us formulate the main result regarding the unique solvability of the considered inverse problem of oxygen transport in the brain.

**Theorem 1.** *Let the conditions (i)–(iii) hold. Then, the Problem 1 is uniquely solvable on any finite time interval  $[0, T]$ ,  $0 < T < \infty$ .*

**Proof of Theorem 1.** Let us prove the unique solvability of the problem (15). By virtue of Lemma 1, this will mean the unique solvability of Problem 1. First, using the principle of contraction mappings, we prove the time-local solvability. Since the a priori estimate (17) does not depend on the length of the interval of existence of the local solution, the local solution can be extended to the entire interval  $[0, T]$ .

Let  $0 < T_1 \leq T$ . Define the operator  $\mathcal{P}: C([0, T_1]; X) \rightarrow C([0, T_1]; X)$  such that if  $\hat{y} \in C([0, T_1]; X) \cap L^2(0, T_1; Y)$ , then  $\hat{y} = \mathcal{P}(z)$  is a solution of the following linear problem on  $(0, T_1)$ :

$$\hat{y}' + A\hat{y} = F - B(z), \quad \hat{y}(0) = y_0. \tag{18}$$

The unique solvability of this problem with monotone nonlinearity is well-known (Theorem 4.1, Chapter 3 in [13]).

Let  $\hat{y}_1 = \mathcal{P}(z_1)$  and  $\hat{y}_2 = \mathcal{P}(z_2)$ , where  $z_1 = \{\eta_1, \zeta_1\}$ ,  $z_2 = \{\eta_2, \zeta_2\}$ ,  $\hat{y}_1 = \{\hat{\psi}_1, \hat{\theta}_1\}$ , and  $\hat{y}_2 = \{\hat{\psi}_2, \hat{\theta}_2\}$ . Denote

$$\hat{y} = \hat{y}_1 - \hat{y}_2 = \{\hat{\psi}, \hat{\theta}\} \quad \text{and} \quad z = z_1 - z_2 = \{\eta, \zeta\}.$$

Taking into account the equality

$$\langle \hat{y}' + A\hat{y} + B(z_1) - B(z_2), \hat{y} \rangle = 0$$

and estimates (16), we obtain

$$\frac{d}{2dt} \|\hat{y}\|_X^2 + k_3 \|\hat{y}\|_Y^2 \leq k_4 \|\hat{y}\|_X^2 + \langle B(z_2) - B(z_1), \hat{y} \rangle. \tag{19}$$

Using (4), the last term in the right-hand side of (19) can be estimated as follows:

$$\begin{aligned} \langle B(z_2) - B(z_1), \hat{y} \rangle &= (\mu(\zeta_2) - \mu(\zeta_1), \hat{\theta}) + a(g(r + \hat{\eta}_2) - g(r + \hat{\eta}_1), \hat{\psi} - \kappa\hat{\theta}) \leq \\ &\leq \frac{\mu_0}{\theta_{50}} \|\zeta\| \|\hat{\theta}\| + a\|\eta\|(\|\hat{\psi}\| + \kappa\|\hat{\theta}\|) \leq \frac{k_8}{2} \|\hat{y}\|_X^2 + \frac{k_9}{2} \|z\|_X^2. \end{aligned}$$

Here,  $k_8 = \max\{a, \mu_0/\theta_{50} + a\kappa\}$ ,  $k_9 = \max\{a(1 + \kappa), \mu_0/\theta_{50}\}$ .

Taking into account the last inequality, it follows from (19) that

$$\frac{d}{dt} \|\hat{y}\|_X^2 \leq (2k_4 + k_8) \|\hat{y}\|_X^2 + k_9 \|z\|_X^2.$$

Further,

$$\|\hat{y}(t)\|_X^2 \leq (2k_4 + k_8) \int_0^t \|\hat{y}(\tau)\|_X^2 d\tau + k_9 \int_0^t \|z(\tau)\|_X^2 d\tau. \tag{20}$$

Let  $(2k_4 + k_8)T_1 \leq 1/2$ . Then, from (20), we obtain the estimate

$$\|\hat{y}\|_{C([0, T_1]; X)}^2 \leq 2k_9 T_1 \|z\|_{C([0, T_1]; X)}^2.$$

Hence, the operator  $\mathcal{P}$  is a contraction if  $2k_9 T_1 < 1$ .

Thus, there is a unique fixed point  $\theta$  of the operator  $\mathcal{P}$  which is a solution of the problem (15) on  $(0, T_1)$ . The a priori estimate (17) does not depend on the length  $T_1$  of the interval of existence of the local solution, and therefore the local solution can be continued over the entire interval  $[0, T]$ .

Let us prove the uniqueness of the solution. Let  $y_1$  and  $y_2$  be solutions of the problem (15). Note that  $y_1 = \mathcal{P}(y_1)$  and  $y_2 = \mathcal{P}(y_2)$ . From estimate (20), it follows that

$$\|y_1(t) - y_2(t)\|_X^2 \leq (2k_4 + k_8 + k_9) \int_0^t \|y_1(\tau) - y_2(\tau)\|_X^2 d\tau.$$

Based on Gronwall's lemma, we conclude that  $y_1 = y_2$ .  $\square$

#### 4. Conclusions

The considered inverse problem can be interpreted as an alternative approach with respect to the corresponding initial-boundary value problem to describe the oxygen transport in brain tissue. In contrast to the steady-state case, in which the uniqueness of the solution is shown under additional conditions (e.g., on the thickness of the model domain), the unique solvability for the non-stationary problem is proven without any smallness assumptions on the model parameters. It is worth mentioning the importance of the obtained result on the unique solvability of the inverse problem for the substantiation of the numerical algorithm which reduces to solving the following extremal problem based on the idea of Tikhonov regularization:

$$J(\mathbf{q}, \varphi, \theta) = \frac{1}{2} \sum_{j=1}^m \int_0^T \left( (f_j, \varphi(t)) - r_j(t) \right)^2 + \lambda q_j^2(t) dt \rightarrow \inf,$$

where  $\lambda > 0$  is the regularization parameter and the triple  $\{\mathbf{q}, \varphi, \theta\}$  satisfies the equalities (9)–(11). Note that the estimates for the solution of the direct problem (6)–(8) allow us to establish the solvability of the extremal problem.

Using the proven unique solvability of Problem 1, similarly to [10], it is easy to verify that the sequence of solutions to the optimal control problem converges to the exact solution of the inverse problem as  $\lambda \rightarrow +0$ , which is the basis for choosing a numerical algorithm.

The proposed approach makes it possible to estimate the intensities of the sources corresponding to the ends of arterioles and venules, with the subsequent calculation of the distribution of oxygen concentrations for sufficiently large brain regions.

Another application of the obtained results is the formulation of the inverse problem in the form of the Cauchy problem for an ordinary differential equation with operator coefficients. Using this formulation, it is possible to construct a numerical algorithm for solving the inverse problem by means of an explicit scheme with respect to the time variable. The method of reducing the inverse problem to the Cauchy problem can be used to analyze various inverse problems for nonlinear parabolic systems.

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