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Conservative algorithm of substance transport over a closed graph of cardiovascular system

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Abstract — Mathematical models and numerical algorithms of substance transport over a closed graph of a cardiovascular system must satisfy the property of conservativity. A conservative model and a numerical algorithm for calculation of substance transport through a working heart are proposed in the paper. The efficiency of the algorithm considered here is confirmed by test calculations. A method for simulation of substance transport in tissues surrounding vessels is also proposed.

Simulation of transport of substances dissolved in blood (gases, salts, reactants) over a vessel channel is an urgent challenge in physiology and pharmacology. Numerical experiments are often required in the development of new medicines and in studies of oxygen saturability of organs and tissues. An integral part of such experiments is the development of adequate mathematical models and numerical algorithms.

Several research papers have been focused on the construction of models of substance transport in a cardiovascular system. In general, those papers considered either local processes (often in many-dimensional formulation), or a transport of substances over a system of vessels (in one-dimensional or quasi-one-dimensional formulations). An example of the former approach is [13] where transport dynamics of a substance in a separate vessel is studied in a three-dimensional geometry. The latter approach is represented by [1, 3–7, 9–12]. In [5–7], where a quasi-one-dimensional model with a nonlinear diffusion coefficient was used for the calculation of flows in large vessels in the arterial section. A model of substance transport over a branched vascular network without diffusion was considered in [9]. The diffusion of oxygen in a model system consisting of two circles of blood circulation was considered in [10, 11]. In particular, a numerical solution algorithm was developed for quasi-one-dimensional hemodynamic equations combined with oxygen transport equations.

Within the quasi-one-dimensional approach, the authors in [1, 3, 4, 12] use a representation of a cardiovascular system as a whole or its parts as a graph of vessels. Researchers have constructed a model of a cardiovascular system closed through the heart and preserving the total volume of blood. A transport of a substance over a vascular network was also considered and some variants of closure of the model with respect to the transported substance were proposed.

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However, requirements for models and numerical algorithms are becoming stronger. In particular, conservativity is one of such requirements. This is caused by the necessity to adequately represent the influence of dissolved substances on the whole system, because the system may often strongly react even to small concentrations (for example, those of medications), or to the total amount of substances in different groups of vessels [16]. The presence of uncontrolled non-physiological sources of substances may render impossible a correct representation of the corresponding reactions of the organism in numerical calculations.

In this research we propose a conservative model and the corresponding numerical method for the calculation of substance transport through the heart closing the vascular system. The conservativity of the model here means the global preservation of the substance in the whole system under the condition that the blood volume in the considered closed vascular system remains constant.

The paper continues the studies in [3, 4, 12] and is based on the model of closed blood circulation and the calculation algorithm for blood flow parameters developed there. The efficiency of the substance transport algorithm proposed in this paper is confirmed by test calculations. A simulation method for diffusion of substances in tissues surrounding vessels is also proposed.

1. Substance transport over a vascular system closed through the heart

1.1. Substance transport in blood vessels

We associate a vascular system with a graph of elastic vessels. The vessels serve as the graph edges, the nodes are either the points of conjunction of two or more vessels (so-called *branching nodes*), or the heart, organs, and tissues. We consider the model of the two-chamber heart (see [3, 12]) and associate the heart with two nodes corresponding to the left and right ventricles.

We suppose the flow is quasi-one-dimensional in each vessel, i.e., assume that the pressure P, the velocity U, and the flow Q are constant in each cross-section of any vessel (see [1, 12]). In addition, assume that the blood density ρ is constant. Considering the problem of substance transport, we assume that all these values and also the cross-section area S of the vessel are known, because they are calculated by an independent computation module of the CVSS software complex on the base of hemodynamic equations [4, 12, 15].

By $C(x,t)$ we denote the mass concentration of the substance dissolved in blood in the cross-section x of a vessel at some time moment t. The spread of the substance is carried out by convection and diffusion in the axis x directed along the vessel axis. In the case of hemodynamic (subsonic) flows inside each vessel, this spread can be described by the equation (see [4, 12]):

$$\frac{\partial C}{\partial t} + U\frac{\partial C}{\partial x} = D\frac{\partial^2 C}{\partial x^2} \tag{1.1}$$

where D is the diffusion coefficient assumed to be constant within the vessel. Equation (1.1) is parabolic and hence requires boundary conditions at both ends of the

vessel (see [17]). Those are the conjunction conditions at the inner graph nodes and the boundary conditions at the boundary nodes (see [1, 12]).

The conjunction conditions are formed by the requirements of continuity of the concentration C and the volume flow W of the substance at a branching node. This flow has convective and diffusive components (W_c and W_d, respectively) and takes the following form in the quasi-one-dimensional case:

$$W = W_c + W_d = CSU - DS\frac{\partial C}{\partial x}. \tag{1.2}$$

The requirement of the continuity of the flow at a branching node leads to the relation

$$\sum_{i\in{}^{+}(m)} \left(C_i S_i U_i - DS_i \frac{\partial C_i}{\partial x} \right) = \sum_{i\in{}^{-}(m)} \left(C_i S_i U_i - DS_i \frac{\partial C_i}{\partial x} \right) \tag{1.3}$$

where $({}^{+}(m))$ and $({}^{-}(m))$ are the sets of edges incoming to and outgoing from the vertex m. Posing the continuity condition for the concentration at the branching node, we get the system of equalities

$$C_i\big|_m = C_j\big|_m, \qquad i \neq j, \quad i, j \in (m) \tag{1.4}$$

where i and j are all possible numbers of edges from $(m) = {}^{+}(m) + {}^{-}(m)$.

1.2. Model of the heart

A heart is considered as a pump providing in its normal condition a periodic inflow of blood into the aorta and then into the whole vascular system. In the two-chamber point model, the heart consists of a ventricle pushing out blood into the aorta and an auricle through which blood gets into the ventricle from the venous vessels. The work of the heart is cyclic, and each cycle consists of the period of blood accumulation in the ventricle (*diastole*) and the period of blood output into the aorta (*systole*). In this case the blood is not released into arterial vessels in diastole and does not come to the ventricle from the venous part of the vascular system (auricle) during the systole.

The heart is represented by two vertices in the graph of vessels, these vertices serve as the 'input' and 'output' of the circle of blood circulation. There exist different methods to simulate the cardiac function. We use the model coordinated in its flows and described in detail in [1, 12]. This model states the following dependence of the blood volume in the heart ventricle V_H on time:

$$V_H(t) = \begin{cases} V_H(0) - \displaystyle\int_0^t Q_A(\tau)\mathrm{d}\tau, & 0 \leqslant t \leqslant \tau_s \\ V_H(\tau_s) + \displaystyle\int_{\tau_s}^t Q_V(\tau)\mathrm{d}\tau, & \tau_s \leqslant t \leqslant \tau_s + \tau_d \end{cases} \tag{1.5}$$

where τ_s, τ_d are the durations of the systole and diastole, respectively; $V_H(0)$ means the blood volume in the ventricle at the beginning of the current cardiac cycle; Q_A and Q_V correspond to the cardiac output into the aorta and the inflow into the ventricle from the auricle. The volume V_H is bounded by the values $V_{\min}$ and $V_{\max}$. If V_H reaches the value $V_{\max}$ in the course of blood accumulation, the diastole stops and the systole begins. Similarly, if V_H reaches the value $V_{\min}$ in the process of blood release, then the systole is replaced by the diastole. Thus, generally speaking, the values τ_s and τ_d are not constant, but the model blood circulation system considered here is closed and the total blood volume is preserved.

The flow $Q_A(t)$ is specified explicitly (a typical form of dependence was presented in [12]), the values $Q_V(t)$ and $V_H(t)$ are calculated in the solution of the system of hemodynamic equations ([2, 4]), and in the substance transport problem we assume these values to be known.

1.3. Substance transport through the heart

We assume that the substance carried by blood is uniformly distributed inside the ventricle and has the concentration $C_H(t)$. A variation of C_H in the systole can occur only due to the inflow of the substance from the auricle. By W_V and W_A we denote the flows of the substance from (1.2) at the entrance to the heart in the venous part of the system and at the outlet from the heart at the beginning of the aorta. Then in the systolic period ($0 \leqslant t \leqslant \tau_s$) we have

$$\begin{aligned} C_H(t)V_H(t) &= C_H(0)V_H(0) - \int_0^t W_A(\tau)\mathrm{d}\tau \\ W_V(t) &= 0. \end{aligned} \tag{1.6}$$

Similarly, in the diastole ($\tau_s \leqslant t \leqslant \tau_d$) we have

$$\begin{aligned} C_H(t)V_H(t) &= C_H(\tau_s)V_H(\tau_s) + \int_{\tau_s}^t W_V(\tau)\mathrm{d}\tau \\ W_A(t) &= 0. \end{aligned} \tag{1.7}$$

In both cases the volume $V_H(t)$ can be calculated by formula (1.5). The formulation of the problem within the model described here is the following: *determine the function $C(x,t)$ on the graph of vessels with the heart so that it satisfies equation* (1.1) *at the inner points of each vessel, conditions* (1.3) *and* (1.4) *hold at the branching nodes, relations* (1.6) *hold in the systole, and relations* (1.7) *hold in the diastole.*

1.4. Difference problem

In order to solve numerically the problem formulated here, we use the method of finite differences. Introduce the uniform grid $\omega_h = \{x_i = ih,\ i = 0,\ldots,N\}$ in each

vessel. Assume that the step in time τ is constant. Along with the 'integer' points x_i, we consider 'half-integer' points $x_{i+1/2} = x_i + h/2,\ i = 0,\dots,N-1$. Instead of the functions C, U, S, W of a continuous argument, we consider their grid analogues c, u, s, w. Construct difference approximations for all conditions of the problem.

The following approximation is used for equation (1.1) fulfilled at the inner points of a vessel:

$$\frac{\hat{c}_i - c_i}{\tau} + u_i c_{\overset{\circ}{x},i}^{(\sigma_c)} = D c_{\overline{x}x,i}^{(\sigma_d)}, \qquad i = 1,\dots,N-1 \tag{1.8}$$

where $\hat{c}_i$ and c_i are approximate values of the function C at the point x_i on the upper and lower time layers, respectively, and, according to [14], we use the notations

$$c_{\overset{\circ}{x},i} = \frac{c_{i+1} - c_{i-1}}{2h}, \qquad c_{\overline{x}x,i} = \frac{c_{i+1} - 2c_i + c_{i-1}}{h^2}, \qquad c^{(\sigma)} = \sigma\hat{c} + (1-\sigma)c.$$

In order to construct an approximation of the boundary conditions at branching nodes (conjunction conditions), we use the following approximations for the flows:

$$w_0 = \hat{c}_0 s_0 u_0 - D\frac{s_0 + s_1}{2} \cdot \frac{\hat{c}_1 - \hat{c}_0}{h} \tag{1.9a}$$

$$w_N = \hat{c}_N s_N u_N - D\frac{s_N + s_{N-1}}{2} \cdot \frac{\hat{c}_N - \hat{c}_{N-1}}{h}. \tag{1.9b}$$

Introduce the notations

$$E = \begin{cases} 0 & \text{if } m \text{ corresponds to } x_0 \\ N & \text{if } m \text{ corresponds to } x_N, \end{cases} \qquad z_i = \begin{cases} -1 & \text{if } E = 0 \text{ on the edge } l_i \\ 1 & \text{if } E = N \text{ on the edge } l_i. \end{cases}$$

Under these notations, the conditions of continuity of the flows and concentrations are written in the following way [8]:

$$\sum_{i \in (m)} z_i w_E\big|_{l_i} = 0 \tag{1.10}$$

$$\hat{c}_E\big|_{l_i} = \hat{c}_E\big|_{l_j}, \qquad i, j \in (m), \quad i \neq j. \tag{1.11}$$

1.5. Approximation of boundary conditions on the heart

Systems of equalities (1.8), (1.10)–(1.11) give $l(N+1) - 2$ conditions, whereas the number of all unknowns, including $\hat{c}_H$ is equal to $l(N+1)+1$ (l means here the number of the edges of the graph). We have to supplement the system with three more conditions. However, relations (1.6), (1.7) contain only two equations both for the systole and the diastole. These equations describe the balance of the concentrations in the heart and in the vessel adjacent to the heart valve closed at the moment (the aorta in diastole and the venous sinus in systole). Therefore, it is necessary to describe separately the balance of the substance at the end of the vessel communicating with the heart at that moment.

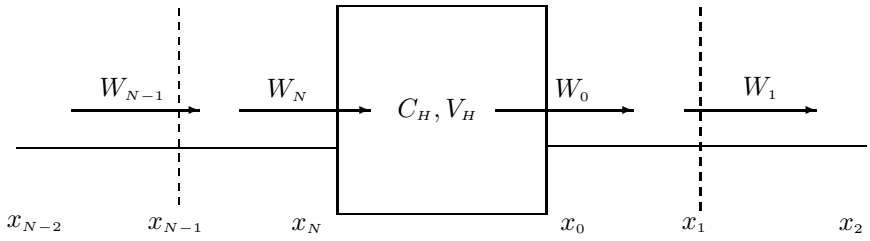


Figure 1. Heart and adjacent vessels. Flows of substance.

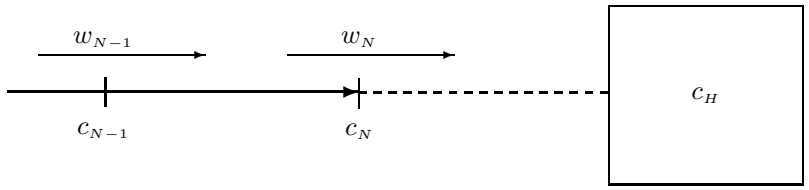


Figure 2. Heart and auricle in diastole.

1.5.1. Balance of substance at the heart interface. Consider a part of the blood vascular system containing the heart and the ends of the adjacent vessels (see Fig. 1).

For definiteness sake, let the coordinate axis of the adjacent vessel be directed to the heart in the auricle and from the heart in the aorta.

The balance of the substance in the venous part in the segment $[x_{N-1}, x_N]$ is determined in the time period $[t_1, t_2]$ in the *diastole* by the following integral equation:

$$\int_{x_{N-1}}^{x_N} SC\Big|_{t_1}^{t_2} \mathrm{d}x = \int_{t_1}^{t_2} (W_{N-1} - W_N)\mathrm{d}t.$$

The balance equation in the segment $[x_0, x_1]$ in the aorta in the *systole* is similar:

$$\int_{x_0}^{x_1} SC\Big|_{t_1}^{t_2} \mathrm{d}x = \int_{t_1}^{t_2} (W_0 - W_1)\mathrm{d}t.$$

Consider a technique of approximation of these integral relations.

Auricle. Consider the condition valid in the diastole in the venous part of the vascular system. Approximate the integral at the left-hand side by the quadrature formula

$$\int_{x_{N-1}}^{x_N} SC\Big|_{t_1}^{t_2} \mathrm{d}x \approx (\hat{c}_\gamma - c_\gamma) s_\gamma h. \tag{1.12}$$

Here we have used the notation $f_\gamma = \gamma f_N + (1-\gamma) f_{N-1}$ for the grid functions c and s. The choice of γ determines a particular quadrature and, generally speaking, influences the order of approximation of the integral at the left-hand side of (1.12)

(see [8]). For $\gamma = 1/2$ the approximation used here has the third order, and in the general case the second order of approximation is attained. Below we consider the values of γ from the segment $[0,1]$.

Now consider the right-hand side of the balance equation. We use the following approximations for the flows:

$$w_{N-1} = s_{N-1}\,u_{N-1}\,c_{N-1} - D\,s_{N-1}\,\frac{c_N - c_{N-1}}{h}$$
$$w_N = s_N\,u_N\,c_N - D\,s_N\,\frac{c_H - c_N}{h}.$$

In this case the boundary condition in the auricle takes the following form (not taking into account the weight multipliers):

$$\begin{aligned} h s_\gamma(\hat{c}_\gamma - c_\gamma) = \tau &\left(s_{N-1}\,u_{N-1}\,c_{N-1} - D\,s_{N-1}\,\frac{c_N - c_{N-1}}{h} \right) \\ &- \tau \left(s_N\,u_N\,c_N - D\,s_N\,\frac{c_H - c_N}{h} \right), \qquad \gamma \in [0,1]\,. \end{aligned} \tag{1.13}$$

The expression for the flow w_N corresponds to the part of the venous channel at the boundary with the heart presented in Fig. 2. In this representation, the value c_H is associated with the fictitious point $x_{N+1} = x_N + h$.

Now we get an approximation of the first equation of system (1.7). It follows from (1.5) that in the diastole we have

$$V_H(t+\Delta t) = V_H(t) + \int_t^{t+\Delta t} S(x_N,\tau)U(x_N,\tau)\,\mathrm{d}\tau$$

which can be approximated by the relation

$$\hat{V}_H = V_H + \tau s_N u_N.$$

Similarly, from (1.7) we get

$$C_H(t+\Delta t)V_H(t+\Delta t) = C_H(t)V_H(t) + \int_t^{t+\Delta t} W_N(\tau)\,\mathrm{d}\tau.$$

This relation can be approximated in the following way:

$$\hat{c}_H = \frac{V_H c_H + \tau \left(s_N u_N c_N - D s_N \dfrac{c_H - c_{N-1}}{h} \right)}{V_H + \tau s_N u_N}. \tag{1.14}$$

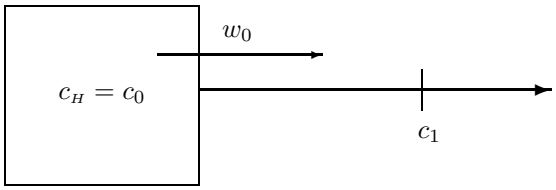


Figure 3. Heart and aorta in systole.

Aorta. Consider the ventricle-aorta zone in the systole (see Fig. 3). The model is based on the equality

$$\hat{c}_0 = c_H. \tag{1.15}$$

We calculate the flow w_0 from the heart to the aorta by the formula

$$w_0 = s_0 u_0 c_H - D s_0 \frac{c_1 - c_H}{h}.$$

Similar to formula (1.14), from (1.5) we get that the balance of the substance inside the ventricle in the systole takes the form

$$\hat{c}_H = \frac{V_H c_H - \tau \left(s_0 u_0 c_H - D s_0 \dfrac{c_1 - c_H}{h} \right)}{V_H - \tau s_0 u_0}. \tag{1.16}$$

Closed heart valve. Let us obtain an approximation of the boundary conditions appearing in the auricle in systole and in the aorta in diastole, i.e., in the periods when these vessels do not communicate with the heart. The grid functions w_0 and w_N are used as approximate values of W_0 and W_N, these functions are defined by formulas (1.9). Then, according to relations (1.6), (1.7), the missing boundary conditions have the form

$$\hat{c}_0 s_0 u_0 - D \frac{s_0 + s_1}{2} \frac{\hat{c}_1 - \hat{c}_0}{h} = 0 \tag{1.17a}$$

$$\hat{c}_N s_N u_N - D \frac{s_N + s_{N-1}}{2} \frac{\hat{c}_N - \hat{c}_{N-1}}{h} = 0. \tag{1.17b}$$

The relations obtained above supplement the set of boundary conditions for the heart in the diastole and systole, respectively.

Difference scheme. The difference scheme constructed here includes:

- equations (1.8) at the inner points of vessels;
- relations (1.11) and (1.10) at the branching nodes;

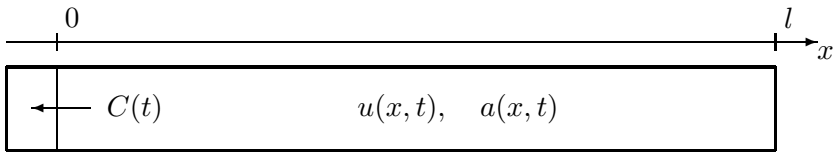


Figure 4. Diffusion of substance in vessel-tissue system: one-dimensional model.

- boundary conditions (1.16), (1.17b), and (1.15) for the heart in the systole;
- boundary conditions (1.14), (1.17a), and (1.13) for the heart in the diastole.

2. Transport of substance in the vessel-tissue system

Consider one- and two-dimensional models of distributed diffusion through a vessel wall into a tissue adjacent to the vessel for a substance carried by blood. Within a one-dimensional approximation, the concentration of the carried substance is assumed to be the same in the whole vessel and also at the points of the tissue equidistant from the vessel wall. For example, it is convenient to use such model for the study of propagation of a substance in vessels of a small length or for a small variation of the concentration along the vessel. Within a two-dimensional approximation, the values are assumed to be different not only at increasing distances from the vessel, but also along the vessel itself, which allows us to take into account the specificity of the concentration profile in the vessel.

Note that in this paper a tissue is considered in a rectangular geometry.

2.1. One-dimensional model

Consider a vessel of a blood vascular system together with the adjacent tissue (see Fig. 4). Direct the coordinate axis along the tissue, associate the point $x = 0$ with the wall of the vessel adjacent to the tissue. The point $x = l$ bounds the tissue from the other side. A substance with the volume concentration $C(t)$ is contained inside the vessel. We assume that the concentration is a known function. The tissue is considered as a porous sorbing medium where we point out two types of concentrations: the concentration $u(x,t)$ of the substance contained in the pores of the sorbent and the quantity of the substance absorbed by a unit volume of the sorbent denoted by $a(x,t)$ (see [17, 18]).

We study the propagation dynamics of the substance in this system assuming that a two-way exchange takes place between the vessel and the tissue; the intensity and direction of this exchange depend on the difference between the concentrations $u(0,t)$ and $C(t)$. In addition to sorption and desorption, we have the diffusion of the free substance $u(x,t)$. The coefficient of diffusion is assumed to be constant.

Write the balance equation for the transported substance in the following differential form [8, 17]:

$$\frac{\partial}{\partial t}u = D\frac{\partial^2 u}{\partial x^2} - \beta(u - \gamma a) - f_{\text{tiss}}. \tag{2.1}$$

In order to describe the sorption-desorption directly, we use the sorption kinetic equation with the Henry isotherm [17]:

$$\frac{\partial a}{\partial t} = \beta(u - \gamma a) + f_{\text{tiss}}. \tag{2.2}$$

The coefficient γ here specifies the point of equilibrium between u and a: in the case $u > \gamma a$ the value a grows, i.e., we have absorption of the substance by the sorbent, and if $u < \gamma a$, then the quantity of the bound substance decreases. The multiplier β called the kinetic coefficient is responsible for the intensity of absorption, or release of the substance by the sorbent. By f_{tiss} we have denoted here the external volume flow of the substance. For example, it may correspond to the absorption of oxygen or glucose by a working muscle, to the release of CO_2 into the blood vascular system in the process of work of muscles and organs, or may take into account chemical reactions with the sorbed substance, etc.

The following equation is taken as the boundary condition for the free concentration $u(x,t)$ on the boundary with the vessel ($x = 0$):

$$\frac{\partial u}{\partial x}(0,t) = \varkappa_u(t)\big(\alpha_u(t)u(0,t) - C(t)\big) \tag{2.3}$$

it describes the exchange of the substance between the tissue and the blood vascular system. The equilibrium point is set by the coefficient α_u ($\alpha_u u = C$) and the exchange rate is governed by the value $\varkappa_u$.

We supplement system of equations (2.1)–(2.3) with the following second-order homogeneous boundary conditions:

$$\frac{\partial u}{\partial x}(l,t) = \frac{\partial a}{\partial x}(l,t) = \frac{\partial a}{\partial x}(0,t) = 0 \tag{2.4}$$

expressing the absence of the corresponding flows of the substance through the boundaries. In addition, we assume the initial conditions

$$a(x,0) = a_0(x), \quad u(x,0) = u_0(x). \tag{2.5}$$

Within the model described above, the formulation of the problem is the following: *find the functions* $u(x,t)$, $a(x,t)$ *determined in the domain* $\{0 \leqslant x \leqslant l, t \geqslant 0\}$ *satisfying equations* (2.1), (2.2) *inside the domain and boundary and initial conditions* (2.3)–(2.5) *on its boundaries.*

2.2. Two-dimensional model

We consider a blood vessel with adjacent tissue represented as a two-dimensional rectangular domain (see Fig. 5).

As before, direct the axis x along the tissue and the axis y along the vessel. In the coordinates introduced in this way, the tissue occupies the domain $[0, l_x] \times [0, l_y]$, the vessel has the length l_y and is placed along the straight line $x = 0$.

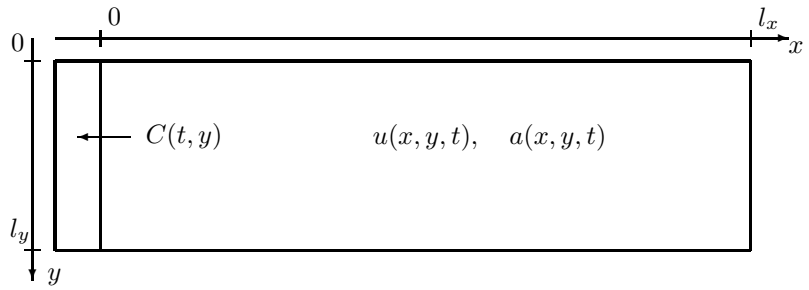


Figure 5. Diffusion of substance in vessel–tissue system, two-dimensional model.

The vessel contains a substance of the concentration $C = C(y,t)$, and the tissue is a sorbing medium where we consider the concentrations $\big(u(x,y,t)\big)$ and $\big(a(x,y,t)\big)$ of the free substance and the substance bound by the sorbent, respectively. As before, we assume that diffusion of the free substance u (with the constant coefficient D) takes place in the tissue in addition to sorption/desorption, and the exchange between the vessel and the tissue is two-way and depends on the difference between the concentrations $u(0,y,t)$ and $C(y,t)$.

By the analogy with the one-dimensional case, we can write the differential equation describing the balance of the substance in the tissue

$$\frac{\partial}{\partial t}(a+u) = D\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right). \tag{2.6}$$

As above, we use the sorption kinetic equation with Henry isotherm (2.2). In the two-dimensional case, the boundary condition for u on the boundary $x = 0$ takes the form

$$\frac{\partial u}{\partial x}(0,y,t) = \varkappa_u(y,t)\big(\alpha_u(y,t)\,u(0,y,t) - C(y,t)\big). \tag{2.7}$$

Supply the system of equations with the following second-order homogeneous boundary conditions:

$$\frac{\partial u}{\partial x}(l_x,y,t) = \frac{\partial a}{\partial x}(0,y,t) = \frac{\partial a}{\partial x}(l_x,y,t) = 0 \tag{2.8a}$$

$$\frac{\partial u}{\partial y}(x,0,t) = \frac{\partial u}{\partial y}(x,l_y,t) = \frac{\partial a}{\partial y}(x,0,t) = \frac{\partial a}{\partial y}(x,l_y,t) = 0. \tag{2.8b}$$

In addition, we assume the initial conditions

$$u(x,y,0) = u_0(x,y), \quad a(x,y,0) = a_0(x,y). \tag{2.9}$$

Within the model described here, the formulation of the differential problem is the following: *find the functions* $u(x,y,t)$, $a(x,y,t)$ *determined in the domain* $\{[0,l_x]\times[0,l_y], t \geqslant 0\}$ *satisfying equations* (2.6), (2.2) *inside the domain and boundary and initial conditions* (2.7)–(2.9) *on its boundaries.*

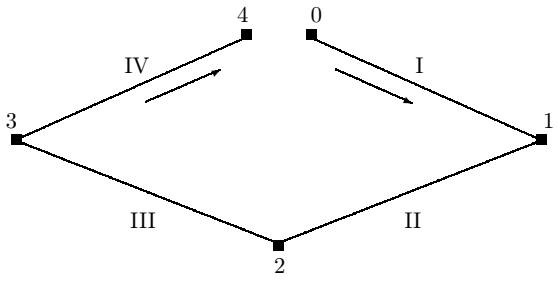


Figure 6. Model graph of vessels.

3. Test calculations

The calculations of hemodynamic parameters were performed with the use of the CVSS software package (CardioVascular Simulating System, the package for calculation of hemodynamic flows developed by the researchers of the Department of Mathematical Methods, Computational Mathematics and Cybernetics Faculty of the Lomonosov Moscow State University) [4]. The algorithm described in this paper was implemented according to the standards of this package and was integrated into it. The following model graph of the blood vascular system was used for test calculations (see Fig. 6). The circle of blood circulation is formed by four vessels I, II, III, IV. Nodes $1,2,3$ correspond to the points of the vessel conjunctions, nodes 0 and 4 are boundary for the graph and correspond to the heart (edge I is considered as the aorta and edge IV is considered as the venous sinus). The arrows indicate the typical direction of the blood flow.

The graph was taken with a small number of edges for simplicity of analysis and visible clarity of calculation results.

The initial conditions on edge III (of length L) were specified by the function

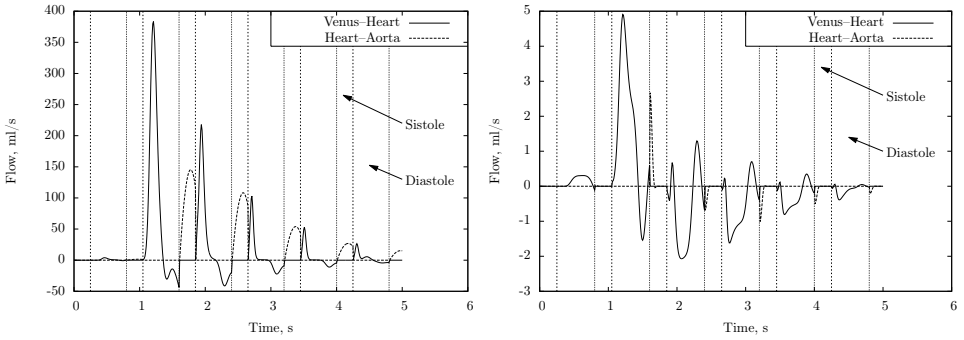
$$C(x,0) = \frac{1}{2}\left[\cos\left(\pi\left(2\frac{x}{L}-1\right)\right)+1\right], \quad x \in [0,L] \tag{3.1}$$

taking the value 0 at the ends of the segment $[0,L]$ together with its first derivative. The initial concentrations on the other edges and in the heart were taken equal to 0.

We used the following scheme with the condition on the auricle differing from formula (1.13) by the presence of weight factors:

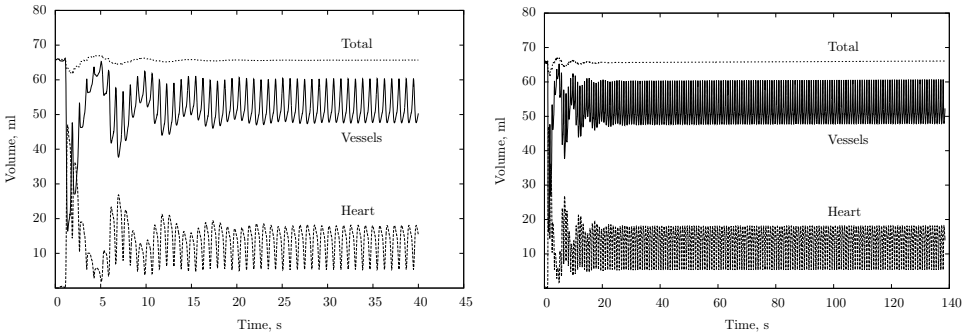
$$\begin{aligned} hs_\gamma(\hat{c}_\gamma - c_\gamma) = {} & \tau\left(s_{N-1}u_{N-1}c_{N-1}^{(\sigma_1)} - Ds_{N-1}\frac{c_N - c_{N-1}}{h}\right) \\ & - \tau\left(s_N u_N c_N^{(\sigma_2)} - Ds_N\frac{c_H - c_N}{h}\right), \qquad \gamma \in [0,1]. \end{aligned} \tag{3.2}$$

The calculations were performed according to the implicit variant of the algorithm, $\sigma_1 = \sigma_2 = 1$. The illustrations presented below correspond to the calculations with $\gamma = 3/4$.



(a) Convective flows (b) Diffusive flows

Figure 7. Convective and diffusive flows on the boundary with the heart.



(a) Volumes of substance for small time periods (b) Volumes of substance for large time periods

Figure 8. Volumes of substance for $\gamma = 3/4$.

Flows of substance on the heart boundary. As is seen from Fig. 7a, convective flows take both positive and negative values, which indicates the appearance of reverse flows. The absolute magnitudes of the convective flows have the order 10^1 ml/s for large time periods.

Diffusive flows are presented in Fig. 7b. These flows become negligibly small in comparison with the convective ones (of order 10^{-3} ml/s). It is seen from the graph that the diffusive transport of substance between the heart and the aorta in the systole stops after some period of time, which is caused by the the fact that the substance concentrations in the heart and at the beginning of aorta become equal. Note also that the diffusive and convective flows are absent in the part of the blood vascular system where the heart valve is closed (in the auricle in the systole and at the beginning of the aorta in the diastole).

Total volume of transported substance. The total volumes of the substance in the vessels, in the heart, and in the whole system are presented in Fig. 8. The volume

in the heart (lower curve) and in the vessels (middle curve) are changed quasi-periodically. We can point two types of oscillations. Oscillations of the first type have the period of order 0.8 s and are related to the accumulation and release of the substance within a single cardiac cycle. Oscillations of the second type are well visible for small time periods (about 10–15 s), their period is about 5 s. These oscillations are caused by the presence of a concentration wave in the system. Its advance through the heart ventricle causes an overall increase of the substance in the heart (with continuing oscillations of the first type) and its similar decrease in the vessels. Both types of oscillations of the substance volume in the heart are in the antiphase to the oscillations of the substance volume in the vessels. The total volume of the substance in the system is changed for small time periods. This is caused by the fact that, from the viewpoint of hemodynamics, these calculations begin from zero, i.e., from the state of the system when the blood flow velocities and pressures are not coordinated (as a rule, equal to zero). The computational algorithm has to bring the system into a working state. The system of hemodynamic equations for the graph (forming the base of the solution of the substance transport problem) is essentially nonlinear, and an iterative process is used at each time step for its solution. This calculation stage, which is the most difficult from the computational viewpoint, contains iterations not completely convergent, which inevitably implies a disbalance of the total blood volume, large gradients of the functions, etc. Until the system comes to a mathematically or physically adequate mode (the stabilization of the total blood volume is the indicator of such mode), i.e., while the iterations on time steps do not converge, the errors are essential in calculations of hemodynamic parameters (and hence in concentrations), and the whole stage is considered as a specific iterative process. A solution to this problem will be the subject of further studies.

When the system attains the stationary mode (25–30 s), the total volume of the substance is preserved and remains the same in prolonged calculations. Thus, the algorithm proposed here is a conservative model of a diffusive substance transport.

Concentration profile. The dynamics of the substance transport over a model blood vascular system is presented in Fig. 9. At the initial time moment we have substance distribution (3.1) specified in vessel III. In the course of one cardiac cycle, the perturbation reaches the heart. In this case the amplitude of the concentration wave decreases, but the total length of vascular channels containing the transported substance is increased. The passage of the substance through the heart takes several cardiac cycles. Thus, for example, for $t = 3.4$ s the transported substance is present both in the venous and arterial parts of the blood vascular system. The release of the substance from the heart into the aorta produces a new concentration wave going through all vessels of the vascular system until it reaches the heart. The transported substance is distributed over all parts of the vessel channel due to diffusion, and a concentration background is formed ($t = 5.27$ s). The substance accumulated in the auricle passes through the heart. A new concentration wave is generated ($t = 6.65$ s) and the process is repeated. The convection and diffusion result in a uniform distribution of the transported substance over the blood vascular system (approximately

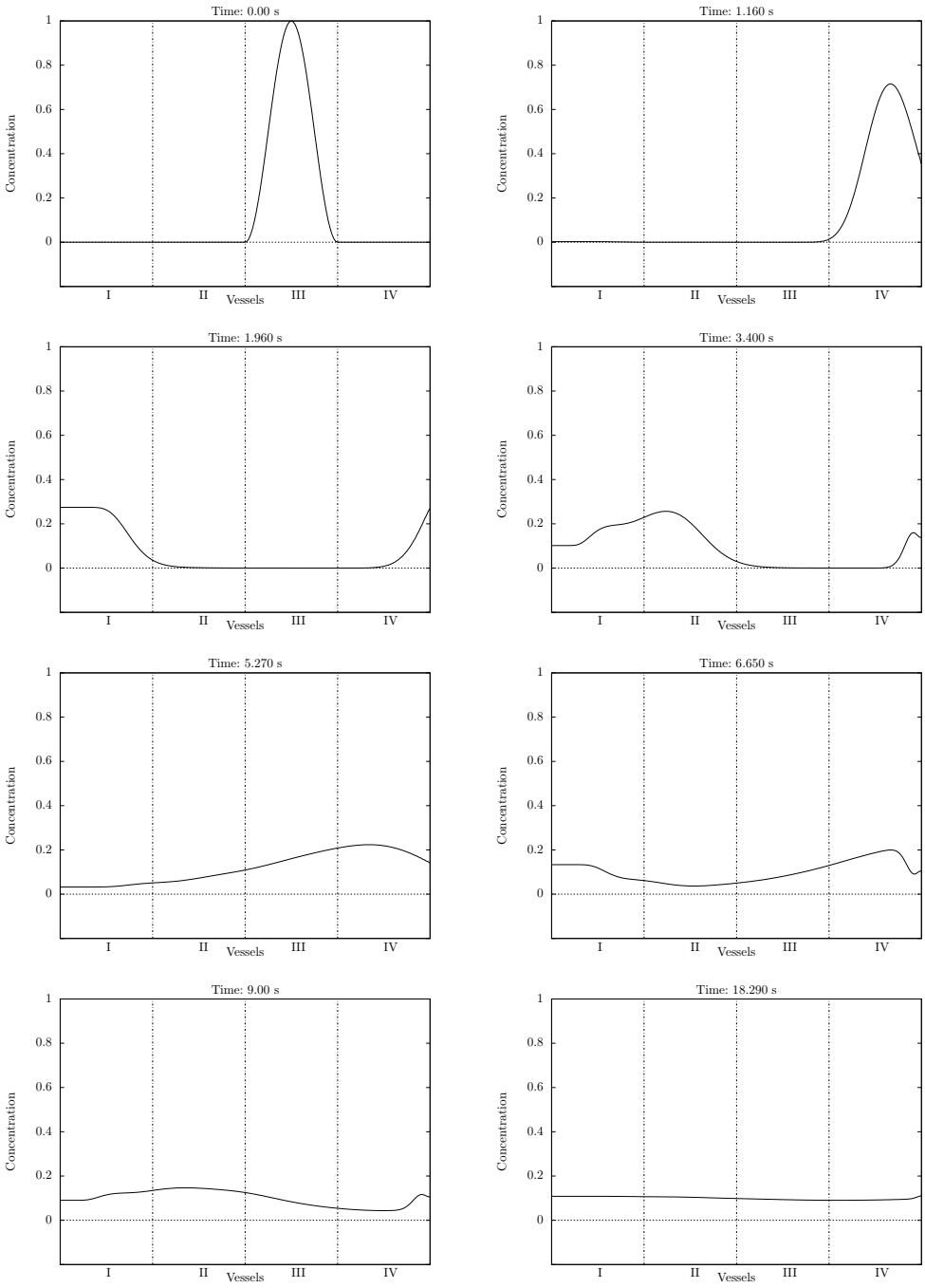


Figure 9. Variation of substance concentration profile in vessels.

by 25–30 s). The effect of the actual disappearance of diffusive substance transport is related to this fact.

The process described here corresponds to the physiology of the spread of a substance introduced locally (for example, by injection) over the cardiovascular system.

Conclusion

A model of diffusive transport of a dissolved substance over a system of vessels closed through the heart and models of distributed diffusion of a substance in tissues are proposed in the paper. The model is conservative, i.e., it preserves the total amount of the substance in the system under the conservation of the total blood volume. The corresponding numerical algorithms are implemented in the standard of the CVSS package (software complex for calculation of hemodynamic flows developed by researchers of the Department of Mathematical Methods of the Computational Mathematics and Cybernetics Faculty of the Lomonosov Moscow State University) and are integrated into this software package. Test calculations have confirmed the efficiency of the proposed algorithms.

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