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SIMULATION OF COAGULABLE MIXTURES DYNAMICS IN INCOMPRESSIBLE LIQUID CONSIDERING CLOT CLUSTER FORMATION

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Abstract: one of the key problems associated with COVID-19 is blood circulation impairment, particularly caused by thrombosis. The impairment significantly reduces the blood flow and restricts oxygen delivery to the entire body. The paper covers the simulation model for the coagulable mixture dynamics in an incompressible liquid considering clot cluster formation. Simulation models for the thrombosis and coagulation processes in the human cardiovascular system will help efficiently manage these phenomena. The study proposes a simulation model of the coagulation processes in disperse systems, i.e., the thrombosis process. The paper presents the numerical solution results and the visualization of the analytical solution. The key thrombosis properties such as impurity concentration distribution in the liquid, and the pressure field distribution, were estimated. The simulation model can become a foundation for developing a multi-tier clot formation system in the cardiovascular system: from the microscopic level to the macroscopic structures. Besides, the model can estimate the efficiency of anticoagulants administered to COVID-19 positive patients at emergency care departments.

Keywords: simulation, thrombosis, hydrodynamics, disperse systems, crystal systems.
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О МАТЕМАТИЧЕСКОМ МОДЕЛИРОВАНИИ ДИНАМИКИ КОАГУЛИРУЮЩИХ СМЕСЕЙ В НЕСЖИМАЕМОЙ ЖИДКОСТИ С УЧЕТОМ ЯВЛЕНИЯ ФОРМИРОВАНИЯ КЛАСТЕРОВ-ТРОМБОВ

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Аннотация: одной из ключевых проблем, на решение которой направлены ресурсы общества по преодолению заболевания, вызванного новым коронавирусом COVID-19, является проблема нарушения кровотока, связанная, в частности, с процессом тромбообразования. Это явление существенно ограничивает кровоток, снижая доставку кислорода в целом по всему организму. В статье рассмотрены результаты создания математической модели динамики коагулирующих смесей в несжимаемой жидкости с учетом явления формирования кластеров-тромбов. Создание математических моделей процессов коагуляции и тромбообразования в сердечно-сосудистой системе человека обеспечит разработку эффективного управления этими явлениями. В статье описана математическая модель для процессов коагуляции в дисперсных системах — тромбообразования. Представлены результаты численного решения задачи и визуализация аналитического решения задачи, включая такие важнейшие параметры для тромбообразования, как распределение концентрации примеси в жидкости и распределение поля давления. Указанная модель может служить основой для построения иерархической системы образования тромбов в сердечно-сосудистой системе от микроскопического уровня до макроскопических структур. В том числе модель позволит сделать выводы об эффективности использования антикоагулянтов при поступлении пациентов в отделения неотложной помощи и при положительном результате теста на COVID-19.

Ключевые слова: математическое моделирование, тромбообразование, гидродинамика, дисперсные системы, кристаллические структуры.

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Introduction

One of the key problems to which society's resources are directed in addressing the disease caused by the new coronavirus COVID-19 is the problem of impaired blood flow, associated in particular with the process of thrombosis. This phenomenon significantly limits blood flow, reducing oxygen delivery throughout the whole organism. A mathematical study of coagulation and clot fragmentation processes in the human cardiovascular system will provide the development of effective management of these phenomena. It is important to develop a model of the flow of multiphase dispersed media in the human cardiovascular system, as well as in capillaries and porous media (in a more general problem statement), taking into account the time-varying flow region. This class of problems is characterized by the complex geometry of the flow manifold, the time-varying structure of the considered region, the combination of hydrodynamics and coagulation kinetics problems of the formed cluster-thrombi. The description of the dynamics of such processes is based on a combination of problems for the Smoluchowski-Boltzmann equation of the kinetic theory of coagulation in a spatially heterogeneous branched spatial structure of the porous medium type and hydrodynamics described by the Navier-Stokes equations. It should be taken into account that the density of distribution of the mixture components changing in time and space due to their mutual reactions changes the flow field of the medium, i.e., the diffusion coefficients that determine the fluctuations of the hydrodynamic field of transport velocities change. In the simplest approximation of the description of thrombosis, the model should include the Navier-Stokes equations for a viscous incompressible fluid with viscosity coefficients depending on the distribution density of the coagulating components carried in it, considered as an impurity. It is assumed that the admixture influences the hydrodynamic field as a set of microscopic scattering centers similar to Brownian particles in the well-known classical Smoluchowski-Fokker-Planck-Langevin-Kolmogorov models [1].

However, it should be emphasized at once that the mentioned models of Brownian motion should be considered for many different stochastic influences with averaging of results (canonical ensemble in molecular dynamics), which is a very resource-intensive task. Therefore, in this paper, we will limit ourselves to a heuristic model aimed at highlighting the essential relationships, which, naturally, will require further detail and microphysical justification.

An empirical investigation in physical and biological environments is limited due to high demands on time resources, patient safety, and small spatial scales. An equally important component for the medical staff is the need for high-quality visualization of the development of clot formation. There is a gap between specialized software aimed at solving scientific research and software for the end-user. This often does not allow mass implementation of developments in practical medicine. Creation of software for modeling and visualization of complex structures, including blood flow in vessels and coagulation (including thrombus formation) in humans on high-performance computing systems will form the basis for modeling processes occurring in physical and biological environments, having practical application in industry and medicine.

Models of Disperse Systems and Coagulation

Multicomponent medium-mixtures are widespread and used in many areas of human activity. Models of multicomponent media are considered for gas-dynamic mixtures in [2]. Conditions are formulated, under which the model of multi-velocity interacting continuums follows a model of turbulent mixing. The equations describing generation, dissipation and diffusion of turbulence for each component are proposed. For mixtures of isothermal and polytropic gases, analytical solutions on the structure of rarefaction and shock waves are given.

In the problems of describing thrombosis, it is important to take into account the processes of coagulation (merging or, in other words, inelastic collision) of mixture components in the hydrodynamic flow, which can serve as a source of formation of spatiotemporal structures in the medium flow field similar to the Belousov–Zhabotinsky reactions [3–7]. The first model of the Belousov-Zhabotinsky reaction was obtained in 1967 by Zhabotinsky and Korzukhin based on the selection of empirical relations correctly describing oscillations in the system, see [8]. The paper [8] is further considered in the "brusselator-type" models in the works of Prigozhine I. R. [9].

The inelastic collision of elements of complex systems affects a great deal in our daily lives, an example of this is the phenomenon of blood coagulation (coagulation) during cuts (lack of blood coagulation is lethal, as is its excessive intensity leading to the formation of blood clots with subsequent blockage of blood vessels!), the curdling of the milk and the formation of sour milk are also coagulation; polymerization processes, i.e. the very intense coagulation of particles, underlie the production of polymeric threads used in the manufacture of modern materials. Similar phenomena can be observed in the establishment of communications in the telephone network, in the transmission of messages over the Internet.

In many physical processes, mixtures can arise in systems in which they did not initially exist, in particular, due to the instability and breakdown of contact boundaries under dynamic loads. In other cases, dynamic loads can lead to the opposite effect: separation of the components of the pre-created mixture.

One of the main mechanisms of the evolution of dispersed systems is the mechanism of coagulation (fusion) of system particles. It should be emphasized that usually research works are devoted to the study of the behavior of already prepared mixtures and do not touch the issues of their formation.

Coagulation (merging) of particles is one of the main causes of the evolution of spatially heterogeneous disperse systems, which are understood as a mechanical mixture of medium (gaseous or liquid) with particles of the dispersed phase (solid or liquid), and the properties of phases significantly depend on the transfer of substance between different points of coordinate space. It is important to emphasize the presence of dispersion of transfer rates for particles in different states; otherwise, by replacing the system of spatial and temporal coordinates, the description is reduced to a model similar to the spatially homogeneous case. It should be emphasized that the presence of spatial inhomogeneity significantly complicates the investigation of mathematical models of coagulation. In particular, it is caused by a new effect (as compared to spatially homogeneous problems), namely by the emergence of non-differentiated features of solution on spatial and temporal variables. These features, in turn, generate spatial and temporal zones in which the conservation relation for the Smoluchowski collision operator turns into the dissipation relation (these regions can be interpreted as zones of intense precipitation formation not interacting with the dispersed phase).

Mathematical issues of the correctness of problems of the kinetic theory of coagulation are very complicated and most of the results refer, as a rule, to the theory of spatially homogeneous systems or close to them. Spatially inhomogeneous problems, especially those related to the free transfer of particles carried out through a one-parameter shift group on a spatial variable, are the most difficult from the mathematical point of view.

The Mathematical Model

Let in a viscous medium $\mathbb{R}_3 = \{x = (x_1,x_2,x_3)\}$ filled with particles of different masses $\mu \in \mathbb{R}^+$ with the distribution of concentration $f(\mu,x,t)$, moving under the action of a hydrodynamic field of the external medium, there is a process of coagulation during pair collisions of particles with intensity $\Phi(\mu, \mu_1,x,t) \geq 0$, or particle impacts at the $\Psi(\mu,\mu_1,x,t) \geq 0$ rate, where μ and μ_1 the are masses of interacting particles. (Below we will omit possible dependence of collision and fragmentation rates on the spatial and temporal coordinates x,t for simplicity. Still, the dependence on the masses is essential.) In this case, the dependence on the masses is essential. For the transfer rate of particles, for example, for homogeneous spheres with masses μ, falling in a viscous medium under the action of gravitation according to Stokes's law, a power dependence is valid:

$$\mathrm{V}(\mu) \sim \mu^{2/3}.$$

If in this case, the particles move in a locally uniform hydrodynamic flow of the external medium with velocity $V(,x,t) = (v_1,v_2,v_3) \in \mathbb{R}_3$ and experience Brownian wandering with the diffusion coefficient $\mathrm{D}(\mu,x,t)$, then the accepted mathematical model of the above process is the kinetic Smoluchowski equation for continuous masses [10–12]:

$$\frac{\partial f(\mu,x,t)}{\partial t} + \mathrm{div}_x[\mathrm{V}(\mu,x,t)f(\mu,x,t)] - \mathrm{div}_x[\mathrm{D}(\mu,x,t)\nabla_x f(\mu,x,t)] = S(f) + q(\mu,x,t), \\ x,\mu \geq 0, \quad t > 0, \tag{1}$$

where $S(f)$ is the particle collision operator, which acts on the unknown function (concentration) f by the variable μ, usually without affecting its spatial and temporal arguments x,t, $q(\mu,x,t) \geq 0$ is the given intensity of the particle sources:

$$S(f) = S_c(f) + S_b(f).$$

For the Smoluchowski model of coagulating systems consisting of particles with a continuous mass spectrum, the operator of inelastic collisions $S_c(f)$ local on x,t has the following form [1]:

$$S_c(f) = \frac{1}{2}\int_0^{\mu} \Phi(\mu-\mu_1,\mu_1)f(\mu-\mu_1,x,t)f(\mu_1,x,t)\,d\mu_1 - f(\mu,x,t)\int_0^{\infty}\Phi(\mu,\mu_1)f(\mu_1,x,t)\,d\mu_1. \tag{2}$$

The spontaneous particle fragmentation operator $S_b(f)$ with a spectrum $\Psi(\mu,\mu_1)$ of the distribution of decay products on the values of masses $\mu \geq 0$ formed from a fissile particle with a mass $\mu_1 \geq \mu$ provided that this process is Markovian) is given by the expression [13]:

$$S_b(f)(\mu,x,t) = \int_0^{\infty}\Psi(\mu,\mu_1)f(\mu+\mu_1,x,t)\,d\mu_1 - \frac{1}{2}f(\mu,x,t)\int_0^{\mu}\Psi(\mu-\mu_1,\mu_1)d\mu_1. \tag{3}$$

The $S_c(f)$ and $S_b(f)$ operators look similar for the spectra of $f^{(\omega)}$ particles with discrete masses $\omega \in \mathbb{N}$ [14]:

$$S_c^{(\omega)}(f^{(.)}) = \frac{1}{2}\sum_{\omega'=1}^{\omega-1}\Phi(\omega-\omega',\omega')f^{(\omega-\omega')}f^{(\omega')} - f^{(\omega)}\sum_{\omega'=1}^{\infty}\Phi(\omega,\omega')f^{(\omega')}, \quad \omega \in \mathbb{N} \tag{4}$$

$$S_b^{(\omega)}(f) = \sum_{\omega'=1}^{\infty}\Psi(\omega,\omega')f^{(\omega+\omega')} - \frac{1}{2}f^{(\omega)}\sum_{\omega'=1}^{\omega-1}\Psi(\omega-\omega',\omega'). \quad \omega \in \mathbb{N}. \tag{5}$$

Expressions in the above operators written with the minus sign set the "death" of particles in the spectrum, while the remaining non-negative terms set their "birth". The heuristic method of writing them is based on the local law of conservation of mass. (For the Smoluchowski collision operator these are balance relations of birth and death of particles in the process of their paired instantaneous interaction.) The mathematical justification of the coagulation model is very time-consuming, refer to [14].

In their physical content, the above models of interaction of particles in the external medium flow correspond to the Boltzmann approach in the kinetic theory of gases [15].

When considering the mathematical model, we will impose the following assumptions of physical nature:

- of particles is large enough that we can apply the particle number mass distribution function
- the particles of the system form a locally chaotic set.

The above class of Boltzmann-type models for locally interacting particles (in pairwise collisions) is joined by models with nonlocal interactions, which include, first of all, the plasma theory equations (Vlasova A.A.) [16]. In particular, the Vlasov-type kinetic equation was proposed in [17] to simulate the growth of crystal structures in the volume of a supercooled melt.

The state of such a system at each time moment t is described by the probability density of the distribution of particles *f(m,t)* by the masses m. At the initial moment, the state of the system is given by the probability density of distribution f_0. New particles can enter our system due to a source, which acts with intensity *q(m,t)*. In practice, the source can be, for example, inhomogeneity of the medium. That is, if we place ions of some substance in our system, the melt immediately condenses on them and new particles are formed. The function Φ is the intensity of particle collisions.

The coagulation equation of the Vlasov type [18–19] in the space of masses $m \geq 0$ has the form:,

$$\frac{\partial f(m,t)}{\partial t} + \frac{\partial \dot{m} f(m,t)}{\partial m} = -\frac{1}{2} f(m,t) \int_0^\infty \Phi(m,y) f(y,t) dy + q(m,t), \ \ t > 0, \tag{6}$$

where

$$\dot{m} = \frac{1}{2} \int_0^\infty \Phi(m,y) f(y,t) y dy.$$

The hypotheses, based on which equation (6) is written down, assume that in the process of interaction there is a paired interaction of particles, i.e. the particle field is quite rarefied, which corresponds to the initial stage of crystallization (thrombosis).

This equation for the dynamics of the spectrum in the space of values of continuous masses of interacting particles is directly related to the problems of creating and operating nuclear reactor facilities with heavy liquid metal coolant (HLMC) lead-bismuth or lead, one of the key problems of operation of which is the problem of freezing-defrosting of HLMC in the primary circuit. During freezing, heating and cooling of liquid metal coolant in a solid state, significant mechanical impacts on structures may occur due to inconsistency of movements of coolant volumes with movements of structures and commensurability of mechanical properties of coolant in a solid state with properties of structural materials.

Modeling of multiple mergers is a significantly more complex model of coagulation and is based on the kinetic approach. But even such simplified models demonstrate the extreme complexity of the problem related to the dissipative phenomena investigated in the simplest models of "brusselator" type by Prigozhine I.R. [9].

The specific feature of the models considered in this work is their substantially large (unbounded) dimensionality on the mass spectrum of the interacting particles, which may be the source of a new class of phenomena – spontaneous structure formation in the coagulating system, similar to the process of formation of shock fronts in gas dynamics [20–22].

In essence, the above mathematical models are analogous to the processes of thrombosis in the blood system due to the coagulation of clots formed in blood. In particular, the same processes were investigated for the phenomenon of crystal growth by a mathematical model of crystallization in the volume of supercooled melt based on the kinetic approach [23]. Equation (1) belongs to the "reaction-diffusion" type family [24–25] with a continuum of components. It is known that the formation of periodic space-time structures is possible for three-component families [9].

In multicomponent systems of coagulating mixtures with a stationary source, similar phenomena have been predicted, see [26].

Equation (1) for $t = 0$ in the spatial domain $G \subseteq \mathbb{R}_3$ is supplemented with initial data:

$$f(\mu,x,0) = f^{(0)}(\mu,x), \quad \mu,x \in \Pi_0 = \mathbb{R}_1^+ \times G. \tag{7}$$

Additional conditions at the boundary ∂G of the region G are discussed below.

Within the framework of the simplified model under consideration, as a first approximation, let us assume that the transport of particles obeys a system of Navier-Stokes equations for a viscous incompressible fluid with a flow velocity field $\mathrm{V}(x,t) = \{\mathrm{V}^{(i)}\} \in \mathbb{R}_N, \ x \in \mathbb{R}_N, \quad t > 0$ and pressure $p(x,t)$:

$$\frac{\partial}{\partial t}\mathrm{V}^{(i)} + \sum_{j=1}^{N} \mathrm{V}^{(j)} \frac{\partial}{\partial x_j}\mathrm{V}^{(i)} + \rho^{-1}\frac{\partial}{\partial x_i}\rho^{-1}p = \rho^{-1}R^{(i)} + \mathrm{div}_x[v(\mathrm{n},T)\nabla_x \mathrm{V}^{(i)}], \quad x \in G, \ \ t > 0, \\ i = 1,2,\ldots,N, \tag{8}$$

$$\mathrm{div}_x \mathrm{V} = 0, \tag{9}$$

$$\mathrm{n}(\mu,x,t) = \int_0^\infty f(\mu,x,t) d\mu, v(\mathrm{n}) \geq 0. \tag{10}$$

It is assumed that in the region G the fluid has constant density $\rho > 0$, $\nu = \eta\rho^{-1}$ is the kinematic viscosity of the fluid, η is the dynamic viscosity. In the general case, given the law of conservation of energy, equations of motion (1) should be considered in conjunction with the fluid temperature dynamics $T(x,t)$, on which the kinematic viscosity depends [27–28].

Here $R^{(i)} = R^{(i)}(x,t)$ are the density components of the field of external forces applied to the mixture (note that for potential forces, their influence leads only to the additive addition of the potential of forces to the value of pressure in the problem without their action, while the velocity field $\mathrm{V}(x,t)$ remains unchanged). It is assumed that the constituent parts of the mixture are captured by the medium flow, instantly acquiring its local velocity $\mathrm{V}(x,t)$, affecting the dynamics of the fluid composing the mixture through its integral local concentration $\mathrm{n}(\mu,x,t)$. This hypothesis of the influence of the mixture concentration on the flow field assumes that the mixture components are scattering centers, which through their local Brownian wandering change the mean value of the isotropic viscosity coefficient of the medium $v(\mathrm{n},T)$. When building more detailed models of the mixture dynamics, one should take into account the possibility of changing the flow field in time $G(t)$ [29].

Including the effects of inertia effects for particles with positive mass μ, which change the configuration of the flow field with an explicit dependence $\mathrm{V}(\mu,x,t)$ the same applies to viscosity coefficients), should be taken into account. Moreover, the presence of extended sizes of coagulating particles in the flow can lead to a complex phenomenon – the meshing effect, see [13], when "an inertialess non-Brownian particle, generally speaking, should bypass a large particle... However, streamlined particles have finite sizes. And since at a distance of the order of particle radius from surface of a large particle the normal component of velocity ... is finite, at convective transport "meshing" of a small particle with a large particle is possible" [13]. There is also an effect of inertial deposition. "Since the hydrodynamic field of a large particle is inhomogeneous, movement of small particles in this field is always influenced by their inertia. The influence of inertia is manifested in the reduction of curvature of particle trajectories in some areas of flow as compared with the curvature of medium flow lines. There are two different modes of motion of particles under the influence of inertia in a heterogeneous field of the medium: subcritical when the trajectories of particles and the medium current lines do not coincide, but their behavior is similar, and supercritical when the influence of inertia is so great that the trajectories of particles cross the surface of large particles. In the first case, particle inertia either enhances or reduces the effect of other coagulation mechanisms, such as the entanglement effect. In supercritical mode, there is a new mechanism of coagulation acting independently – inertial deposition" [13]. Given the extreme complexity of accounting for such effects, we will limit ourselves to consideration of the above-mentioned simplified model, in which we can analyze the influence of joint factors: processes of coagulation, fragmentation of point particles and their interaction in the external weakly perturbed hydrodynamic field of incompressible liquid with viscosity coefficient, depending on the integral concentration of the mixture.

In particular, this paper assumes that the flow region G is constant in time and that adhesion conditions or no-flow conditions for the velocity field $\mathrm{V}(x,t)$ are set at its boundary, the values of concentrations and temperatures, or their incoming fluxes along the normal to the boundary of the region are also set.

Let us dwell on the phenomenon of internal friction in a viscous incompressible fluid [27, 28, 30, 31], which for large-scale flows can affect the thermal and electrical phenomena at large values of viscosity ν, changing the characteristics of the flow, and in some cases – lead to phase transitions, electrical breakdowns, etc. This may entail the overestimation of operating modes in reservoir management. Similar problems are associated with hemodynamics control, in particular, with thermoelectric processes during flow in porous media, typical for warm-blooded organisms, as well as with optimization problems of controlled swimming in a viscous incompressible fluid.

It follows from the law of conservation of energy that dissipative processes due to internal friction determine the equation for the temperature field of a viscous incompressible fluid [28, 30]:

$$\frac{\partial}{\partial t}T(x,t) + \sum_i \mathrm{V}^{(i)}\frac{\partial}{\partial x_i}T(x,t) = \chi\Delta T(x,t) + \frac{\varepsilon}{c_p}, t > 0, x \in G, \tag{11}$$

where $\chi = \kappa\rho^{-1}c_p^{-1}$ is the coefficient of thermal conductivity of the medium, c_p is the heat capacity. The last term in the right part of Equation (11) describes the total warming of the medium, caused by the internal friction of the liquid. Type of dissipative internal heat source is determined by the following expression:.

$$\varepsilon = \frac{1}{2}\nu \sum_{i,j} (\frac{\partial}{\partial x_i} \mathrm{V}^{(j)} + \frac{\partial}{\partial x_j} \mathrm{V}^{(i)})^2.$$

Direct calculations show a significant influence of this heat source for liquids with large viscosity coefficients ν, which is a direct analog of the Joule-Lenz law in electric circuits. There is experimental evidence [32] of the influence of such viscous heat generation in oil bearings. Note that the same nature has the effect of throttling the viscous fluid flow in a porous medium. In particular, in [33] there is a table of heat release values of petroleum products, water and methyl alcohol during throttling motion at a given pressure drop. The same heat release effects take place during the initiation of volumetric explosions when a porous catalyst is introduced into viscous fluids [34], described by functional solutions of systems of conservation laws [14].

Visualization and Numerical Solutions

An example of visualization of the exact solution of the equations of three-dimensional hydrodynamics in a porous medium consisting of a filamentary grid of vertical obstacles ∂G, which are located with a period $\lambda > 0$orthogonal to the plane $x_3 = 0$, is shown below. It is assumed that the sticking conditions in the obstacles are fulfilled $\mathrm{V}|_{\partial G} = 0$. The family of exact solutions of these equations, including the temperature $T(x,t)$ and admixture $n(x,t)$ fields determined by constant parameters $\alpha,\beta,\chi,\lambda,\mu,\nu$, has the following form:

$$\mathrm{V} = \begin{pmatrix} \exp(\mu x_3)\sin\lambda x_2 \\ \exp(-\mu x_3)\sin\lambda x_1 \\ 0 \end{pmatrix} \exp\left(\left(\mu^2 - \lambda^2\right)\nu t\right);$$

$$p = \exp\left(2\nu\left(\mu^2 - \lambda^2\right)t\right)\cos(\lambda x_1)\cos(\lambda x_2);$$

$$n = \exp\left(\left(\mu^2 - \lambda^2\right)\chi t\right)\left(\exp(-\mu x_3)\cos(\lambda x_1) - \exp(\mu x_3)\cos(\lambda x_2)\right) + \\ + \exp\left(\mu^2 \chi t\right)\left[\alpha \exp(-\mu x_3) + \beta \exp(-\mu x_3)\right].$$

The temperature field $T(x,t)$ in the absence of internal heat generation is similar to the impurity field $n(x,t)$.

Below are graphs of different cross-sections of the flow and impurity fields. (Visualization of the fields was made by Dubovik A.O., Institute for System Research, Russian Academy of Sciences.)

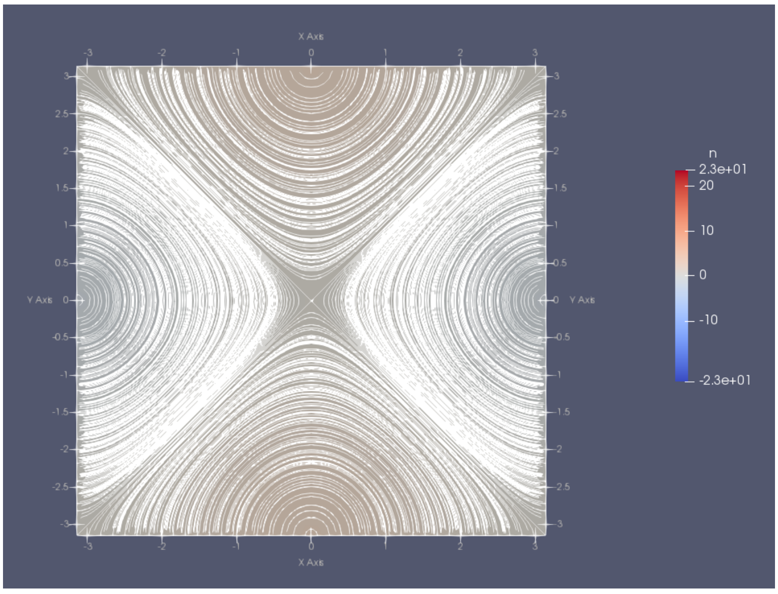

Figure 1. *Spatial distribution of impurity concentrations $n(x,t)$, cross section $x_3 = 0$*

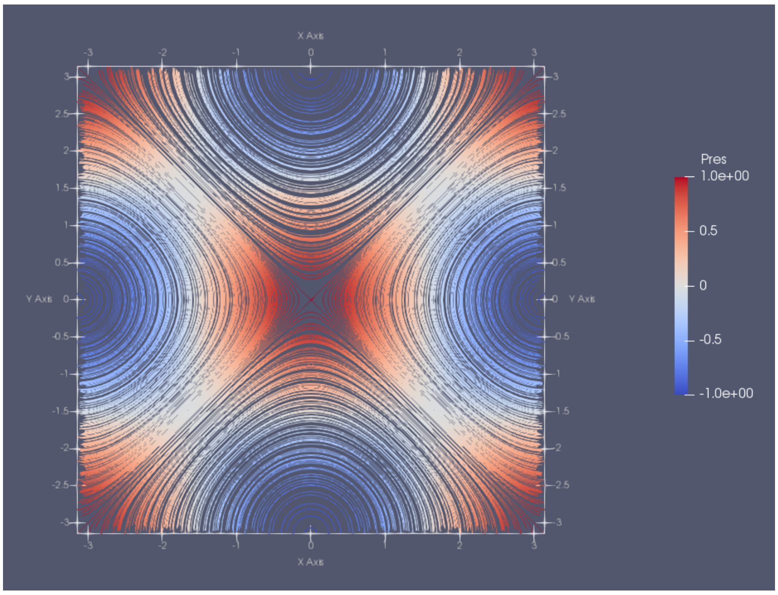

Figure 2. *Spatial distribution of the pressure field* $p(x,t)$*, cross section* $x_3 = 0$

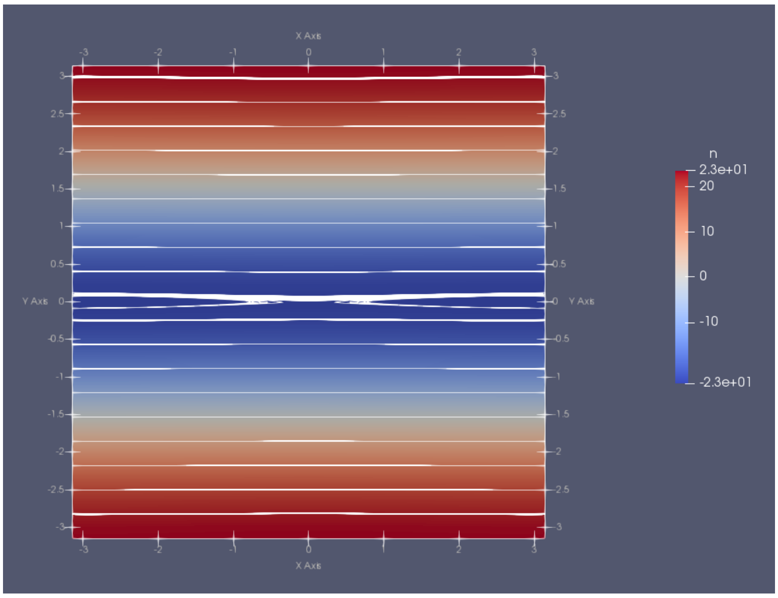

Figure 3. *Spatial distribution of the impurity concentration field* $n(x,t)$*, cross section* $x_3 > 0$

The following example of stationary hydrodynamics concerning the coagulation process indicates the possibility of the appearance of macroscopic structure in a one-dimensional flow of the coagulating substance:

$$\begin{aligned} &\mathrm{V}(\mu)\frac{\partial f(\mu,x)}{\partial x} = \frac{1}{2}\int_0^{\mu} f(\mu-\mu_1,x)f(\mu_1,x)\,d\mu_1 - f(\mu,x)\int_0^{\infty} f(\mu_1,x)\,d\mu_1, \qquad x \geq 0, \\ &f(\mu,0) = f_0(\mu), \end{aligned} \tag{12}$$

where the values of spatial transport velocity $\mathrm{V}(\mu) > 0$ are assumed to be a given function of the mass of the particles coagulating in the flow $\mu \geq 0$. At the inlet $x = 0$ of a one-dimensional flow channel located along the axis $x \geq 0$, a given stationary incoming particle flow $\mathrm{J}_0(\mu) = \mathrm{V}(\mu)f_0(\mu) \geq 0$. is supplied. Assuming the new unknown value of the flow $\mathrm{J}(\mu,x) = \mathrm{V}(\mu)f(\mu,x)$, for J we obtain the Cauchy problem

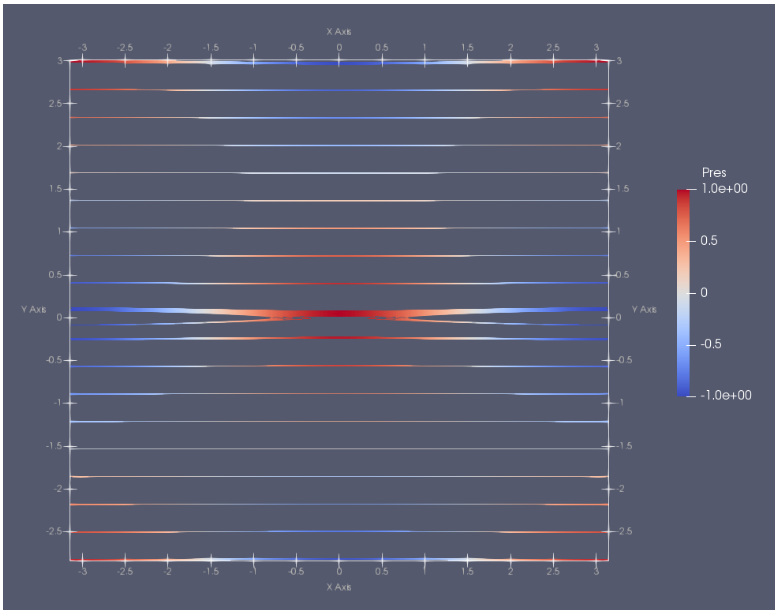

Figure 4. *Spatial distribution of the pressure field* $p(x,t)$*, cross section* $x_3 > 0$

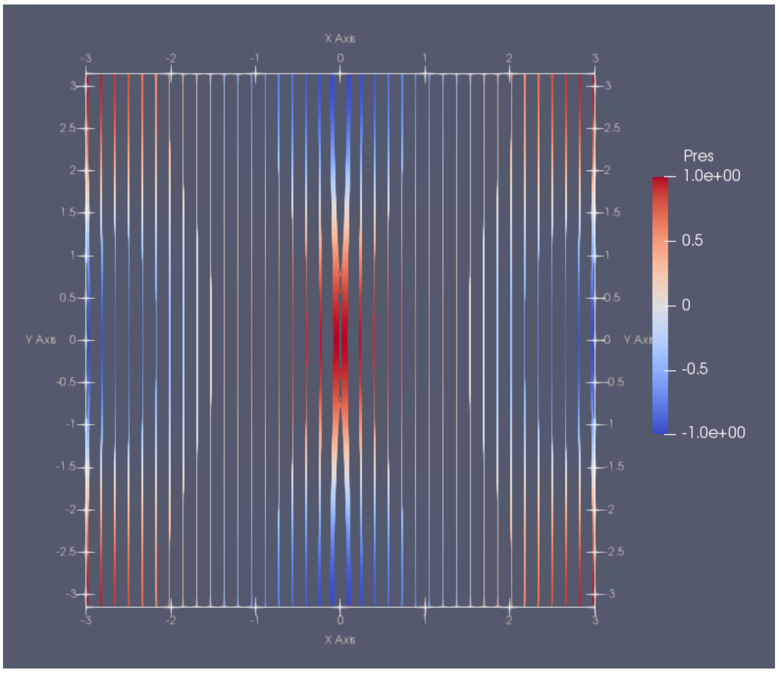

Figure 5. *Spatial distribution of the pressure field* $p(x,t)$*, cross section* $x_3 < 0$

for the Smoluchowski equation:

$$\begin{aligned} &\frac{\partial \mathrm{J}(\mu,x)}{\partial x} = \frac{1}{2}\int_0^{\mu} \Phi(\mu-\mu_1,\mu_1)\mathrm{J}(\mu-\mu_1,x)\mathrm{J}(\mu_1,x)\,d\mu_1 - \mathrm{J}(\mu,x)\int_0^{\infty} \Phi(\mu,\mu_1)\mathrm{J}(\mu_1,x)\,d\mu_1, \\ &x \geq 0, \ \ \mu \geq 0, \\ &\mathrm{J}(\mu,0) = \mathrm{J}_0(\mu), \quad \Phi(\mu,\mu_1) \equiv \mathrm{V}^{-1}(\mu)\mathrm{V}^{-1}(\mu_1). \end{aligned} \tag{13}$$

Assuming

$$\mathrm{V}(\mu) \equiv \mu^{-1} \tag{14}$$

at $\mu > 0$, we obtain a classical example of solutions with dissipative structure [23, 24]. In this case, macroscopic precipitation for values of spatial coordinates is released from the coagulation flow:

$$x \geq x_c = \frac{1}{\int\limits_0^\infty \mu^2 \mathrm{J}_0(\mu) d\mu > 0}.$$

It should be emphasized that the integral mass flux value of coagulating particles $\int\limits_0^\infty \mu_1 \mathrm{J}(\mu_1, x)\, d\mu_1$ is a constant value equal $\int\limits_0^\infty \mu_1 \mathrm{J}_0(\mu_1) d\mu_1$ at $0 \leq x \leq x_c$, and at $x \geq x_c$, this value monotonically decreases, tending to zero at $x \to +\infty$, due to precipitation along the flow channel of macroscopic sediment not interacting with microparticles in the flow [10].

Additional hypotheses and studies are required to describe the flow characteristics of the released macrostructure and its effect on the flow structure [35, 23].

For visual analysis of the solution of equations (12, 13) when condition (14) for particle transport velocities in one-dimensional flow (14) is satisfied, let us consider an example with the following particle distribution at the channel inlet $x = 0$:

$$f_0(\mu) = \exp(-\mu), \quad \mu \geq 0.$$

Solving these equations, taking into account the requirement of adjacency of the solution to the initial function, we have:

$$\mathrm{J}(\mu, x) = \begin{cases} \mu^{-2} x^{-1/2} I_1(2\mu x^{-1/2}) \exp[-\mu(1+x)], & \mu \geq 0, \quad 0 \leq x \leq x_c = 1, \\ \mu^{-2} x^{-1/2} I_1(2\mu x^{-1/2}) \exp[-2\mu x^{-1/2}], & \mu \geq 0, \quad x > x_c, \end{cases}$$

where I_1 is the Bessel function of the imaginary argument. The position of the critical point x_c, to the right of which the mass release of sediment along the flow of coagulating particles begins, is determined by equality $x_c = 1$. The corresponding equations for the integral mass flow of the coagulating substance along the channel $\mathrm{O}x = \{x \geq 0\}$ are as follows:

$$\bar{\mathrm{J}}_{micro}(x) \equiv \int\limits_0^\infty \mu_1 \mathrm{J}(\mu_1, x)\, d\mu_1 = \begin{cases} 1, & 0 \leq x \leq x_c = 1, \\ x^{-1/2}, & x > x_c. \end{cases} \tag{15}$$

,

Accordingly, under the law of mass conservation, the flux of matter in the form of a deposit $\bar{\mathrm{J}}_{macro}(x)$ (macrostructure-polymer) released along the channel $\mathrm{O}x$ and does not interact with the flow of coagulating particles (microphase of matter) is determined by the following equations:

$$\bar{\mathrm{J}}_{macro}(x) = \begin{cases} 0, & 0 \leq x \leq x_c = 1, \\ 1 - x^{-1/2}, & x > x_c. \end{cases} \tag{16}$$

Equations (15), (16) were tested by direct modeling method for the mentioned process and satisfactory agreement of Monte Carlo results with analytical solution and calculations according to the difference scheme was obtained, see Fig. 6.

Conclusion

The specified model can serve as a basis for the construction of a hierarchical system of thrombus formation in the cardiovascular system from the microscopic level to macroscopic structures. In particular, in [36] the specialists of Mount Sinai Medical Complex in New York emphasize: “The use of agents that reduce blood clotting – anticoagulants – can increase the chances of COVID-19 patients for survival”. The researchers analyzed records of 2,773 patients with COVID-19 admitted to hospitals between March 14 and April 11, 2020. They paid particular attention to the survival rates of patients who received anticoagulants. The researchers also took into account certain risk factors, including age, ethnicity, chronic disease, etc. Anticoagulants were given to 28% of patients. They were given a dose higher than the prophylactic dose: high concentrations of drugs are used when blood clots are detected or suspected to have formed. The

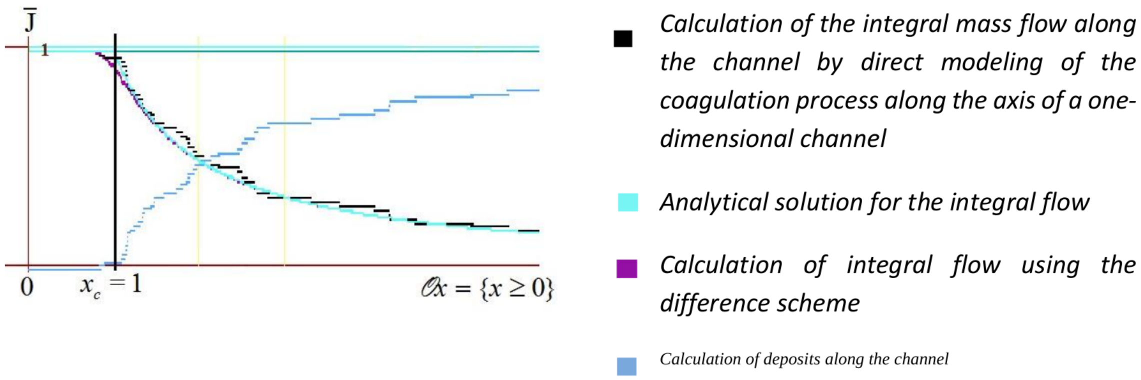

Figure 6. *Integral values of the amount of precipitation from the flow of coagulating particles along the flow channel* Ox

use of anticoagulants was associated with improved survival in COVID-19 patients both in and out of the ICU. Among the patients who died, those who received anticoagulants survived 21 days. Those who were not receiving anticoagulants lasted 14. Taking anticoagulants was associated with increased survival among ventilated patients: 62.7% of patients who did not receive the drugs died in the group, and half as many patients who did, 29.1%. All patients were given blood tests on admission to the hospital, which also showed various inflammatory markers. Analysis of these records showed that the patients who received anticoagulants had higher inflammatory markers than the others. This may indicate that patients in the more severe condition may have received anticoagulants at an early stage. However, patients who received anticoagulants were more likely to have bleeding of various types, from intracerebral to gastric, hemorrhage in the eyes and blood in the urine, which was 3%. In the group that did not receive anticoagulants, bleeding and hemorrhage occurred in 1.9%. This study demonstrates that anticoagulants taken orally, subcutaneously, or intravenously can play an important role in the care of patients with COVID-19 and can prevent possible fatal outcomes associated with coronavirus, including heart attack, stroke, and pulmonary embolism. The use of anticoagulants should be considered when patients are admitted to emergency departments and when they test positive for COVID-19.

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