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# Numerical modeling of thrombus formation dynamics with the rheological properties of blood

**Abstract.** In this paper, the dynamics of blood clotting is numerically simulated when blood viscosity changes. Blood was considered as an incompressible fluid, the initial equations were the Navier-Stokes equations supplemented by equations for the dynamics of blood clotting. Two cases for modeling blood viscosity are considered: viscosity as a constant and as a function characterizing non-Newtonian effects. The effects of the Reynolds and Peclet numbers on the process of thrombus formation are studied. As the Reynolds number increases, an increase in shear stress is observed. Increasing of platelet activation tends to thrombus formation. For the lower Reynolds number the better the transport of oxygen and nutrients prevents thrombus formation. Comparing the results obtained using the Cross model (viscosity is considered as a function of the velocity shear) with the results in the case of constant viscosity, it was found how increased blood viscosity leads to an increase in flow resistance, which requires a larger pressure gradient to maintain normal blood flow. High viscosity promotes platelet aggregation, increasing the likelihood of thrombus formation. Changing the Peclet number significantly affects the balance between convection and diffusion, which in turn affects the distribution of thrombin in the blood. The study of the rheological properties of blood and the blood coagulation process provides important information for improving medical diagnostics and treatment methods. The results of the work contribute to a deeper understanding of the influence of rheological properties of blood on the blood coagulation process, improving diagnostic and therapeutic methods in medical practice.
**Key words**: thrombus formation, Navier-Stokes equations, viscosity, rheological properties, blood coagulation.

## Introduction

The blood system plays an important role in maintaining homeostasis and normal functioning of the body, supplying essential substances, protecting against infections and controlling bleeding. The main objective of the work is numerical modeling of blood coagulation with its rheological properties. Blood coagulation is a biological process necessary to stop bleeding after damage to blood vessels. This process consists of several stages: adhesion and aggregation of platelets, formation of a fibrin mesh and interaction of blood coagulation factors. Impaired coagulation can lead to pathological conditions such as thrombosis and bleeding [1], so a deep understanding of this process is important. Currently, in many countries, it is one of the main causes of death – thrombosis – myocardial infarction (heart attack), stroke (apoplexy), pulmonary embolism, deep vein thrombosis, peripheral arterial disease, post-thrombotic syndrome, thrombophlebitis, chronic thromboembolic pulmonary hypertension, retinal thrombosis, placental insufficiency. The occurrence and development of these diseases are directly related to the rheological properties of blood, especially its viscosity and the coagulation process. Therefore, a deeper understanding of the rheological properties and coagulability of blood is an important scientific task [2]. The ability to study, predict and control the complex dynamics of biological systems increases with the help of modeling methods. In addition, mathematical modeling allows improving the methods of diagnosis and treatment of diseases in medicine. These methods help to understand the mechanisms of disease development, plan a treatment strategy and increase the effectiveness of medical interventions [3]. A detailed description of blood flow in large vessels is carried out using the Navier-Stokes equations in a three-dimensional or two-dimensional approximation [4]. The authors of [5] proposed a model of the growth of a thrombus separated from the vessel wall in the near-wall flow,

 

with not only the influence of hydrodynamic flows on chemical reactions occurring in the system, but also the influence of a growing thrombus against the flow pattern. In this paper, we use the Navier-Stokes equations and differential equations of chemical reactions to model the blood coagulation process.

**Description of Blood Coagulation**

The results of the phenomenological model study show that the blood coagulation process and the dynamics of thrombus formation are observed during the interaction of two interacting concentration waves – an activator and an inhibitor [6]. Some predictions of the model analysis have found experimental confirmation [7]. In [8], the modeling of the spatio-temporal dynamics of blood coagulation was conserved by numerically solving differential equations.

Activators and inhibitors of blood coagulation closely interact to maintain homeostasis. Violation of the balance between them can lead to such serious diseases as thrombosis or hemophilia. Blood is a multicomponent mixture with complex rheological characteristics. Studies have shown that blood has non-Newtonian properties such as shear thinning, viscoelasticity, thixotropy and yield strength. It has been proven that the rheology of blood is associated with its microscopic structures such as the deformation of blood cells and platelets. The presence of blood cells means that blood cannot be considered as a Newtonian fluid, as a continuous medium. The characteristics of blood as a continuous medium of complex rheology are presented in [9]. In this case, it is necessary to solve a variational problem to model the movement of fluid through a vessel [10]. Solving such a problem presents significant difficulties. The development of computer technology and the availability of resources make it possible to consider blood as a suspension of a large number of deformable particles. In the bloodstream, the predominant non-Newtonian effect is blood thinning under shear. Almost all physiological fluids have non-Newtonian properties, that is, their viscosity changes depending on the shear rate. Blood viscosity depends on the shear rate, temperature, and hematocrit level [11]. There are many studies using non-Newtonian models in hemodynamics; in [12], the flow of the vascular system was modeled using non-Newtonian models. There are many models describing viscosity, some of which are presented in Figure 1.

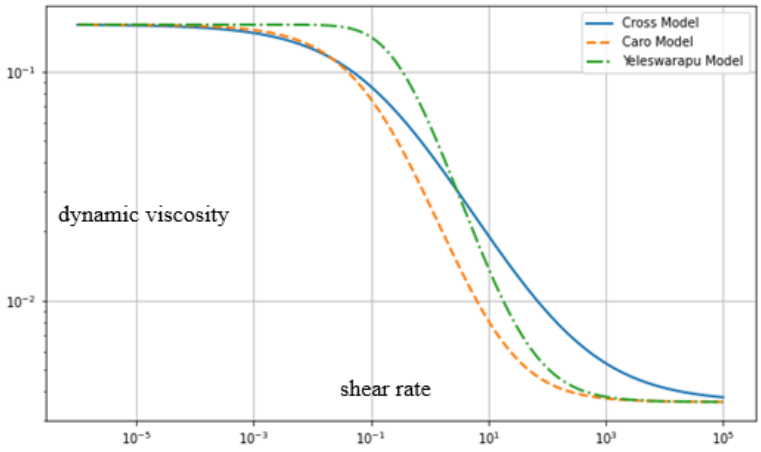


**Figure 1** – Relationship between dynamic viscosity and shear rate

**Statement of the problem and initial boundary conditions**

Blood was considered as an incompressible fluid in order to modelling of thrombin formation during blood coagulation. Two cases of blood viscosity were considered: a constant and a function characterizing non-Newtonian effects.

The blood flow is described by non-stationary Navier-Stokes equations:

$$divV = 0 \qquad (1)$$

$$\rho\left(\frac{\partial V}{\partial t} + (V \cdot \nabla)V\right) = -\nabla p + \mu \Delta V \qquad (2)$$

To describe the dynamics of blood coagulation, the factors involved in the activation process (tissue factor (TF), factor VIIa, factor VIIIa, factor Xa, factor Va) are called activators, and the factors involved in the inactivation process (antithrombin III (antithrombin III), AT III, protein C and protein S, tissue factor inhibitor (TFPI)) are called inhibitors. We will use the following equations [12]:

Equation for the activator:

$$\frac{\partial \theta}{\partial t} = D_1 \Delta\theta - div(V\theta) + \\ + \frac{\alpha\theta^2}{\theta + \theta_0} - \gamma\theta\phi - \chi_1 \quad (3)$$

Equation for the inhibitor:

$$\frac{\partial \phi}{\partial t} = D_2 \Delta\phi - div(V\phi) + \\ + \beta\theta\left(1 - \frac{\phi}{C}\right)\left(1 + \frac{\phi^2}{\phi_0^2}\right) - \chi_2 \quad (4)$$

Equation for fibrin:

$$\frac{\partial \psi}{\partial t} = k \quad (5)$$

здесь: where

- $D_1, D_2$ –diffusion coefficients;
- $V$ –velocity vector;
- $\alpha, \beta, \chi_1, \chi_2$ –kinetic parameters;
- $\theta_0, \phi_0$ –initial concentrations.

Domain of the blood coagulation process under consideration is shown in Fig. 5. The vessel wall is damaged, and the coagulation process occurs in the damaged area.


**Figure 2** – Computational domain

Initial conditions:

$$u(0, x, z) = 1, w(0, x, z) = \\ = 0, 0 \le x \le L, 0 \le z \le H \quad (6)$$

Initial conditions for pressure:

$$p(0, x, z) = 0, 0 \le x \le L, 0 \le z \le H \quad (7)$$

Boundary conditions for velocity for x=0:

$$u(t, 0, z) = 1, w(t, 0, z) = \\ = 0, t > 0, x = 0, 0 \le z \le H \quad (8)$$

Boundary conditions for pressure:

$$p(t, 0, z) = 1, t > 0, x = 0, 0 \le z \le H \quad (9)$$

For x=L the following conditions used:

$$\frac{\partial g}{\partial x} = 0, g = (u, w, p), x = L \quad (10)$$

Boundary conditions for the lower and upper walls:

$$u(t, x, 0) = 0, w(t, x, 0) = \\ = 0, t > 0, z = 0, 0 \le x \le L \quad (11)$$

$$\frac{\partial \mathrm{p}}{\partial x} = 0, t > 0, z = 0, 0 \le x \le L \quad (12)$$

Initial conditions for the activator and inhibitor:

$$\theta(0, x, z) = 1, \phi(0, x, z) = 0 \quad (13)$$

To satisfy the boundary conditions in the obstacle region, the fictitious region method is used which was described in [14]. Then the initial equations can be rewritten:

$$\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + w\frac{\partial u}{\partial z} = -\frac{\partial P}{\partial x} + \\ + \nu\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial z^2}\right) - K(u - u_0) \quad (14)$$

$$\frac{\partial w}{\partial t} + u\frac{\partial w}{\partial x} + v\frac{\partial w}{\partial z} = -\frac{\partial P}{\partial z} + \\ + \nu\left(\frac{\partial^2 w}{\partial x^2} + \frac{\partial^2 w}{\partial z^2}\right) - K(w - w_0) \quad (15)$$

where $K(x,z)=\begin{cases}0,(x,z)\in D\\ \varepsilon^{-2},(x,z)\in D_0\end{cases}$, $\varepsilon$ – small value, $u_0, w_0$ – flow velocity values at the lower boundary.

**Calculation algorithm**

The method of splitting by physical processes [14] was used to solve this problem. The backward difference scheme was used for approximating of the convective terms in order to increase of the stability of the computational algorithm.

Intermediate velocities values were determined using the following equations:

$$\frac{\tilde{u}-u}{\Delta t}=-u\frac{\partial u}{\partial x}-w\frac{\partial u}{\partial z}+ +\nu\left(\frac{\partial^2 u}{\partial x^2}+\frac{\partial^2 u}{\partial z^2}\right)-K(u-u_0) \quad (16)$$

$$\frac{\tilde{w}-w}{\Delta t}=-u\frac{\partial w}{\partial x}-w\frac{\partial w}{\partial z}+ +\nu\left(\frac{\partial^2 w}{\partial x^2}+\frac{\partial^2 w}{\partial z^2}\right)-K(w-w_0) \quad (17)$$

In the second stage, the pressure values were determined using the Laplace equation, obtained from the continuity equation:

$$\frac{\partial^2 p^{n+1}}{\partial x^2}+\frac{\partial^2 p^{n+1}}{\partial z^2}=\frac{1}{\Delta t}\left(\frac{\partial \tilde{u}}{\partial x}+\frac{\partial \tilde{w}}{\partial z}\right) \quad (18)$$

At the third stage, the final velocities values were determined:

$$\frac{u^{n+1}-\tilde{u}}{\Delta t}=-\frac{\partial p^{n+1}}{\partial x} \quad (19)$$

$$\frac{w^{n+1}-\tilde{w}}{\Delta t}=-\frac{\partial p^{n+1}}{\partial z} \quad (20)$$

The maximum time step is determined by the following stability conditions:

$$0{,}25(|u|+|w|))^2\Delta t\, Re\le 1$$

және $\Delta t/(Re\Delta x^2)\le 0{,}25$

|Initial equations were rewritten in dimensionless form to solve the problem numerically [12] by following dimensionless parameters:

$$u'=\frac{u}{u_0}, w'=\frac{w}{u_0}, x'=\frac{x}{L}, z'=\frac{z}{L},$$

$$\theta'=\frac{\theta}{\theta_0}, \varphi'=\frac{\varphi}{\varphi_0}, p'=\frac{P}{u_0^2}, \psi'=\frac{\psi}{\psi_0},$$

$$t'=\frac{t}{T}=\frac{tu_0}{L}, \mu'=\frac{\mu}{\mu_0}$$

The following equations were obtained:

$$\frac{\partial\theta}{\partial t}=\frac{1}{Pe}\Delta\theta-div(V\theta)+ +\frac{1}{M}\left(\frac{\theta(\theta-\widetilde{\chi_1}}{\theta+1}-\bar{\gamma}\theta\phi\right) \quad (21)$$

$$\frac{\partial\phi}{\partial t}=\frac{1}{Pe}\Delta\theta-div(V\varphi)+ +\frac{1}{M}(b\theta(1-\varepsilon\varphi)(1+\varphi^2)-X_2\varphi \quad (5.28)$$

$$\frac{\partial\psi'}{\partial t}=k\theta' \quad (22)$$

Where:

$$M=\frac{V}{\alpha_* L}, Pe=\frac{LV}{D}, \chi_1=\alpha_*\overline{\chi_1},$$

$$\chi_2=\alpha_*\overline{\chi_2}, b=\frac{\beta\theta_0}{\phi_0\alpha_*}, c=\frac{\phi_0}{\varepsilon}, Re=\frac{LV}{\nu}$$

Below are the models of blood viscosity [16]-[18]:

Cross Model:

$$\mu=\mu_\infty/\mu_0+\frac{1-\mu_\infty/\mu_0}{1+\alpha D^n} \quad (23)$$

Carro model:

$$\mu=\mu_\infty/\mu_0+\frac{1-\mu_\infty/\mu_0}{(1+(Cu)^2D^2)^{\frac{2}{n-1}}} \quad (24)$$

Yeleswarapu Model:

$$\mu=\mu_\infty/\mu_0+\frac{(1-\mu_\infty/\mu_0)\big(1+ln(1+\alpha D)\big)}{1+\alpha D} \quad (25)$$

The fractional step method was used to numerically solve the velocity equation.

**Numerical Results Analysis**

The numerical studies were performed on an 86x86 grid on a quadrilateral domain of size L=7, H=1. The time step was Δt=0.001.

The Reynolds number is important for modeling and understanding blood flow, especially laminar flow and thrombus formation. The effect of changing the Reynolds number is shown in Figure 3-5.

As is known, laminar flow occurs at low Reynolds numbers. This shows that the blood layers move in parallel without mixing, and also reduce mechanical loads on the vessel walls, ensuring the stability of the distribution of blood coagulation factors. As the Reynolds number increases, the shear stress increases, the activation of platelets increases and, accordingly, the probability of thrombus formation increases. The lower the Reynolds number, the better the transport of oxygen and nutrients, which prevents thrombus formation.

Figure 5 shows the dynamics of fibrin changes for the Cross viscosity model, where $\mu_0 = 0.364$, $\mu_\infty = 0.0345, \alpha = 0.38, N = 1.45$.

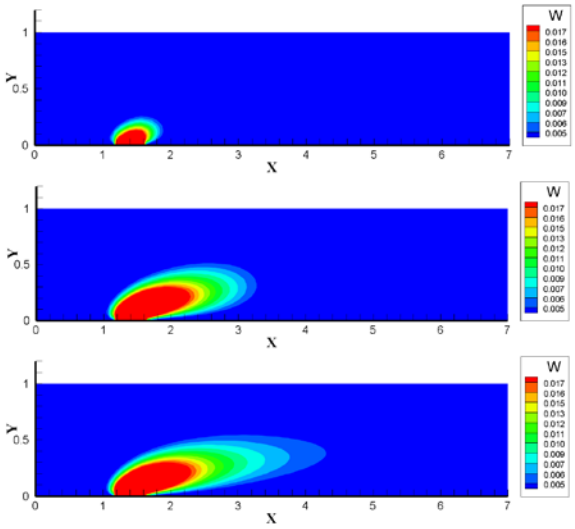


**Figure 3 –** Re=0.01, μ = const: a) n=100, в) n=300, c) n=600

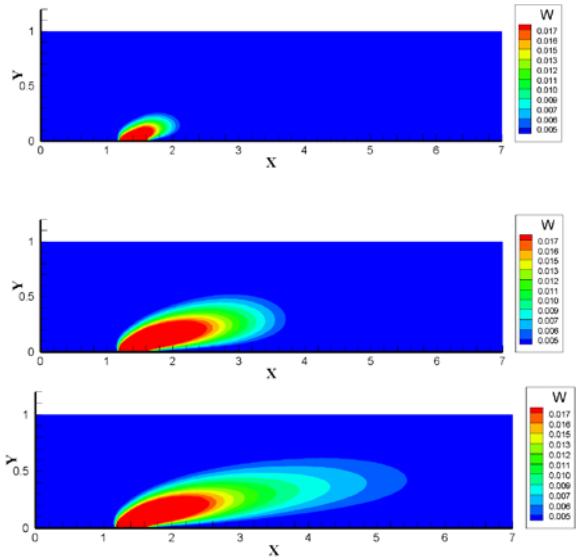


**Figure 4** – Re=3.1, μ = const: a) n=100, в) n=300, c) n=600

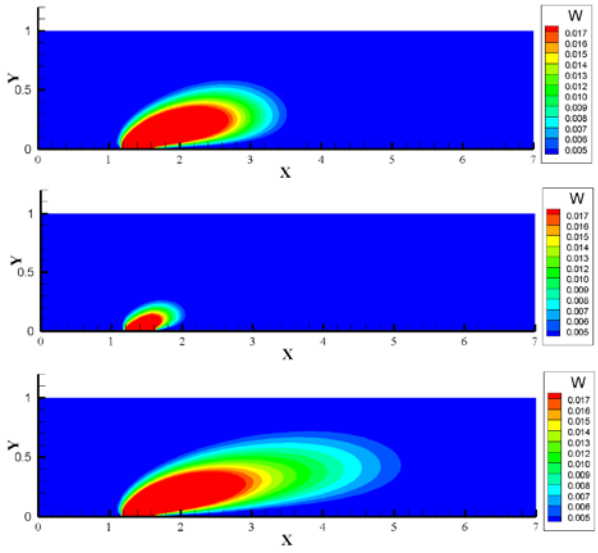


**Figure 5** – model Crossa. a) n=100, b) n=300, c) n=600

Comparing the results obtained using the Cross model with the results in the case of constant viscosity, we can see, that increased blood viscosity leads to increased flow resistance, which requires a larger pressure gradient to maintain normal blood flow. High viscosity promotes platelet aggregation,

increasing the likelihood of thrombus formation. In the case of increased viscosity, blood can stagnate, especially in the capillaries. This can lead to an increase in the contact time of platelets with the damaged vessel wall, which contributes to the formation of thrombi. Due to high viscosity, internal resistance to blood flow increases, so the thrombus impedes blood flow and stimulates platelet activation.

The Peclet number (Pe=LV/D) is a dimensionless number used to evaluate convection and diffusion during transport. Changes in the Peclet number (Pe) significantly affect the distribution of thrombin in the blood. Convection and diffusion are the two main processes that affect the distribution of substances in a fluid. Figure 6 shows the effect of changing the Peclet number on the thrombus formation process using the Carreau model [15].

Figure 6(a) with a Peclet number of 4 shows a relatively compact and concentrated thrombin distribution. The lower Pe number indicates the important role of thrombin diffusion. Convective transport of the substance (flow transport) has a smaller effect than diffusion. As a result, thrombin is distributed uniformly around the starting point. In Figure 6(b), with a Peclet number of 8, the influence of convection increases, and thrombin spreads in the direction of the flow along the X-axis. A Peclet number of 18 indicates the dominance of convection (Figure 6(c)). Thrombin is rapidly transported downstream, creating a narrow and elongated distribution. Diffusion has virtually no effect on the horizontal distribution of thrombin, and the substance is concentrated in the direction of the flow.

The change in the Peclet number significantly affects the balance between convection and diffusion, which in turn affects the distribution of thrombin in the blood. The influence of the convection-diffusion balance on the distribution of thrombin was reported in [19], and our results confirmed the conclusions of this work. Knowledge of this is important for understanding and modeling the processes of thrombus formation and the distribution of biomolecules in the circulatory system. Blood viscosity changes significantly in the presence of thrombin due to the activation of platelets and the conversion of fibrinogen to fibrin.

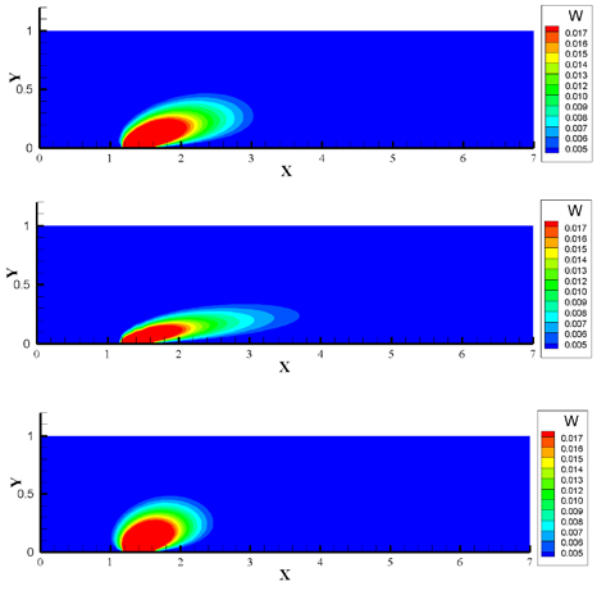


**Figure 6 –** Carreau model. *Gu=5.2,* а) *Pe=4,* в) *Pe=8,* с) *Pe=18*

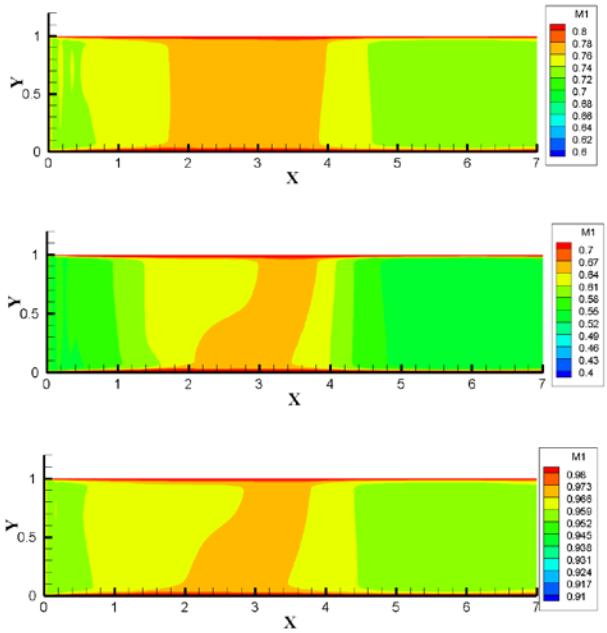


**Figure 7** – Change in viscosity near thrombin according to models a) Cross, b) Carreau, c) Yeleswarapu

From Figure 7, it can be seen that the viscosity increases in the region of thrombin formation. This is because platelets stick to each other, forming clots that increase the viscosity of the blood.

## Conclusion

In this study, the effect of blood rheological properties on the blood coagulation process was

numerically studied. The Navier-Stokes equations and differential equations of chemical reactions were used to create models of blood flow and the blood coagulation process. Viscosity was considered as a function of shear rate. Numerical results showed that at low shear rates, blood coagulates rapidly in a vessel. Modeling the coagulation process allowed us to describe the distribution of thrombin and the formation of a fibrin network. These models help to understand and predict pathological conditions in the circulatory system. The modeling results show that disruption of the blood coagulation process can lead to pathological conditions such as thrombosis and bleeding. At low Reynolds numbers, laminar flow is maintained, indicating parallel movement of blood layers without disrupting the linearity of the blood flow. High Peclet numbers indicate that thrombin is rapidly transported downstream. A decrease in blood flow velocity contributes to the formation of thrombi. The study of rheological properties of blood and the blood clotting process provides important information for improving medical diagnostics and treatment methods. The results of the work contribute to a deeper understanding of the rheological properties of blood and the blood clotting process, improving diagnostic and therapeutic methods in medical practice. In the future, these studies can be continued to further improve the models and study the possibility of their clinical application. This research work is an important step towards finding new ways to treat and prevent cardiovascular diseases.

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