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Blood Sedimentation: A Model of an Active Colloidal System

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Abstract—A model of an active colloidal system with particle properties changing in the course of sedimentation is proposed. Simulational calculations has been performed for sedimentation of blood cells, with erythrocyte aggregation/disaggregation and interaction of the resultant structures with leukocytes (white blood cells) taken into account.

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The erythrocyte sedimentation rate (ESR) within 1 h is one of the diagnostic parameters based on blood cell sedimentation that are most widely used in clinical practice. To date, there is no substantiated interpretation of processes in the settling cell mass or their relationship with the final integrated index (ESR).

Erythrocyte sedimentation is usually explained by models describing the behavior of a dense suspension of electrically charged macroparticles (erythrocytes) and their aggregates in a viscous medium with a complex composition [1]. These models mostly use the same parameters characterizing viscosity, density, hematocrit, concentrations of some proteins, etc. and attempt to approximate the sedimentation by smooth functions [2]. None of these models can explain the experimentally observed nonlinearity of erythrocyte sedimentation revealed by analysis of the sedimentation curve [3].

Earlier data showed that erythrocyte sedimentation was a multistage process depending not only on the physicochemical characteristics of the system, but also on the preserved metabolic activity of blood cells. For example, it was demonstrated that addition of microquantities of substances that did not change the physicochemical characteristics of the system but specifically affected the metabolism of white blood cells (neutrophils) to the settling blood considerably decelerated the sedimentation of the entire cell mass [4].

We developed a basic model of an active colloidal system in which the properties of the settling particles change in the course of sedimentation. Simulated sedimentation of blood cells with intercellular interactions in the process taken into account was used as a first approximation.

Our model of sedimentation is based on the following assumptions on the behavior of blood cells:

(1) Platelets are considered to be neutral agents with respect to sedimentation and are regarded as plasma in calculations.

(2) All leukocytes (white, immunocompetent blood cells) behave as neutrophils.

(3) The sedimentation rate of erythrocytes depends on their saturation with oxygen: the higher the oxygen saturation, the slow the sedimentation. This assumption is based on the experimentally observed higher sedimentation rate of erythrocytes saturated with carbon monoxide (CO) [5].

(4) Leukocytes receive oxygen necessary for their vital activity from plasma only if there are erythrocytes close to them. This assumption is based on the experimentally found movement of neutrophils on polymeric gel along the oxygen gradient accompanied by release of enzymatic systems into the medium [6]; therefore, the fewer are erythrocytes in the vicinity of a neutrophil, the slower the neutrophil sedimentation. Correspondingly, if there is a leukocyte close to an erythrocyte, the oxygen content of the erythrocyte decreases.

(5) Erythrocytes aggregate forming “rouleaux” or branched structures [7]. Presumably, erythrocytes with a decreased oxygen content tend to move closer to one another and form a cluster, which simulates their aggregation.

(6) Leukocytes settle more slowly than erythrocytes and are not included in the “rouleaux.” The approximation is used: if there are two or more erythrocytes near a neutrophil, then the latter “floats up”; i.e., it moves against gravity. This assumption is based on the formation of a Braunberger layer at the blood plasma–blood cell interface, which has been experimentally shown to accompany blood sedimentation when the ESR is

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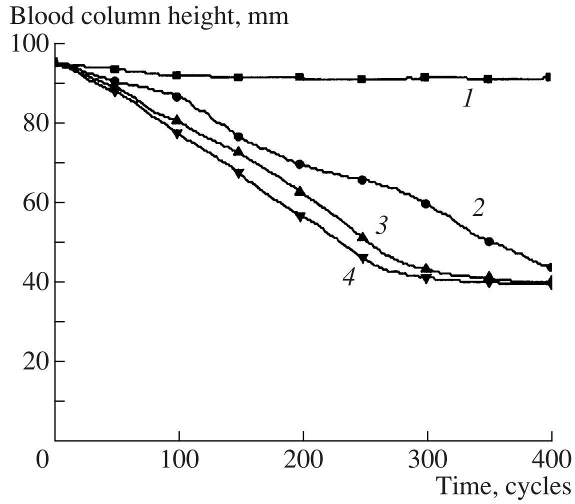

Fig. 1. The effect of varying the amount of white blood cells. The ESR dramatically increases with an increase in the proportion of white blood cells (*1*, 0.01; *2*, 0.02; *3*, 0.03; *4*, 0.04).

measured. This is a layer of neutrophils under which there is a dark layer of erythrocytes containing less oxygen than the other erythrocytes do [5].

The ESR test is performed as follows. Blood stabilized with an anticoagulant (sodium citrate) is aspirated into a standard capillary to a height of 100 mm (the inner diameter of the capillary is 1.0 ± 0.1 mm). The capillary is set vertically, and the height of the column of plasma above the settling red blood is determined after 1 h of sedimentation. This height is taken to be the mean ESR. It is assumed that ESRs higher than 12 mm/h in men and 15 mm/h in women suggest inflammation or another pathological process in the body [8].

The computer simulation of this process was carried out as follows. The capillary containing the settling blood was simulated by a $5 \times 5 \times 100$ three-dimensional array of the spatial positions of cells. The ratio between the white and red blood cells corresponded to the relative amounts of leukocytes (0.01) and erythrocytes (0.42) in the human blood. At the initial moment of time, blood cells were randomly distributed over the volume of the sample, and 70% of erythrocytes were saturated with oxygen [9]. For each cell, the probability of random movements was calculated. Each cell, within the framework of the model, could perform definite types of movements (one movement per calculation cycle) depending on the type of the cell.

Erythrocytes (Red Blood Cells)

An erythrocyte settles along the gravity gradient; remains at the same place but changes its oxygen saturation level (by releasing oxygen into plasma) in the presence of a closely located neutrophil; or moves horizontally if there is a leukocyte "below."

Leukocytes (White Blood Cells)

A leukocyte goes down along the gravity gradient; goes up if there is a vacant place; or remains immobile if there is an erythrocyte above it or if an erythrocyte located near the leukocyte has changed its oxygen saturation.

A cycle (step) of calculation consisted in a single traversal of all cells in a different (random) order at every next step. A total of 100–1000 steps were performed, after which the sedimentation ceased (the calculated sedimentation curve plateaued). The probabilities of different types of movements for erythrocytes were calculated on the basis of the following assumptions.

Movement along the gravity gradient in the absence of interactions between particles is independent and is governed by Stokes' and Einstein's laws. The probability of sedimentation is proportional to $1/(1 + \alpha\varphi)$, where φ is the particle concentration, and α is a coefficient depending on the particle shape.

Absence of movement. The probability of oxygen release from an erythrocyte into plasma is proportional to the total number of closely located neutrophils. Since enzymatic processes occur in a diffuse manner, the effect of neutrophils on erythrocytes is assumed to be inversely proportional to the squared distance between them [6].

Sideway movement. The probability that an erythrocyte will be involved in aggregation is proportional to the total number of closely located erythrocytes. The effectiveness of this process is assumed to be inversely proportional to the squared distance between erythrocytes.

The probability of random movement of an erythrocyte (caused by plasma currents not taken into account in the model) is assumed to be constant and equal to 0.1.

The probability of each type of movement was calculated on the following assumptions: (1) the probability of a neutrophil movement against the gravity is proportional to the total number of closely located erythrocytes; (2) the effectiveness of this process is assumed to be inversely proportional to the squared distance between erythrocytes and neutrophils.

RESULTS AND DISCUSSION

Figure 1 shows the calculated sedimentation curves for different relative amounts of leukocytes (white blood cells) at a constant amount of erythrocytes. As can be seen in the figure, the ESR in the system increases with an increase in the number of white blood cells, although all other parameters of interactions included in the model remain unchanged. This confirms that the proposed approach is correct, because an increase in the number of leukocytes in the blood, e.g., at early stages of inflammation, is known to increase the ESR [1].

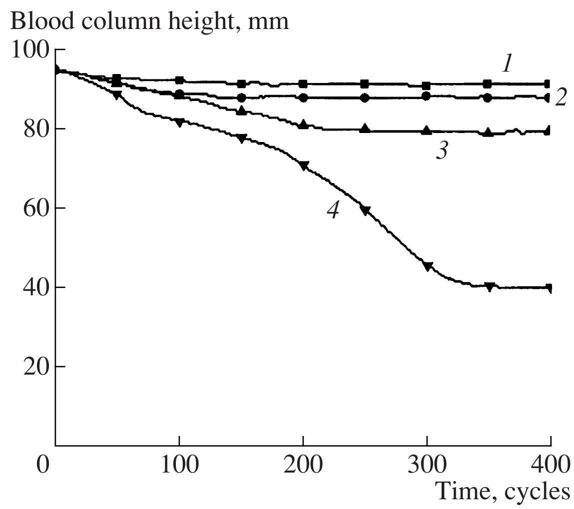

Fig. 2. The effect of varying the probability of erythrocyte deoxygenation. The ESR increases with an increase in this probability (*1*, 0.1; *2*, 0.2; *3*, 0.3; *4*, 0.4).

If the number of white blood cells is decreased, and other parameters of the calculation remain unchanged, the ESR in the system is decreased. This situation simulates allergy, when part of immunocompetent cells (neutrophils) is spent on phagocytosis of allergen particles [5].

Figure 2 shows the calculated sedimentation curves for different values of the parameter of leukocyte–erythrocyte interaction at a constant composition of blood cells. Apparently, this variant can be actualized if white blood cells are subjected to a targeted action. This may occur in the case of allergy and may be simulated by artificial changes in leukocyte activity induced by chemical or physical factors [4].

Thus, our basic model of behavior of the blood as an active colloidal system, where erythrocyte aggregation/disaggregation and interaction of the resultant structures with leukocytes are taken into consideration, qualitatively describes the trends of changes in the ESR observed in clinical practice.

REFERENCES

1. Chizhevskii, A.L., *Biofizicheskie mekhanizmy reaktsii osedaniya eritrotsitov* (Biophysical Mechanisms of Erythrocyte Sedimentation), Novosibirsk, 1980.
2. Fabry, T.L., *Blood*, 1987, no. 5, p. 1572.
3. Kuo, C.D., Bai, J.J., Chang, I.T., Wang, J.H., and Chien, S., *J. Biomech. Eng.*, 1988, no. 4, p. 392.
4. Voeikov, V.L., Gurfinkel', Yu.I., Dmitriev, A.Yu., and Kondakov, S.E., *Dokl. Akad. Nauk*, 1998, no. 5, p. 686.
5. Berchanu, Sh., *Klinicheskaya gematologiya* (Clinical Hematology), Bucharest, 1985.
6. Kindzelskii, A.L., Zhou, M.-H., Haugland, R.P., Boxer, L.A., and Petty, H.A., *Biophys. J.,* 1998, no. 1, p. 90.
7. Fahraeus, R., *Acta Med. Scand.*, 1958, p. 151.
8. *Rukovodstvo po gematologii* (A Handbook on Hematology), Vorob'ev, A.I., Ed., Moscow, 2005, vol. 3.
9. Fok, M.V., Zaritskii, A.R., Prokopenko, G., and Lobchenko, I.M., *Zh. Obshch. Biol.*, 1994, no. 1, p. 84.