

A Physical Model of Blood Platelets Shape and its Effect on Light Scattering

Alexander E. Moskalensky^{*†}, Alyona L. Litvinenko^{*†}, Vyacheslav M. Nekrasov^{*†}, and Maxim A. Yurkin^{*†}

^{*}Novosibirsk State University, Novosibirsk, Russia

[†]Voevodsky Institute of Chemical Kinetics and Combustion, Novosibirsk, Russia

e-mail: sunmosk@mail.ru

Abstract— Quantitative description of blood platelet shape and its dramatic change during activation is necessary for the correct interpretation of light-scattering data, routinely measured in diagnostic laboratories. We propose the model of platelet shape, based on the known information on the cell cytoskeleton. The model geometry is characterized by two parameters: the cell volume and the overcurvature of the internal microtubule bundle, which changes during platelet activation. We describe the procedure for the construction of a cell shape given the volume and overcurvature, and also the way for simulation of light scattering by such objects.

I. INTRODUCTION

Blood is the entirely indispensable tissue of the human body. Happily, it has an invaluable ability to protect itself from outflow. In the case of vessel damage, it changes from a liquid to a gel, forming a blood clot. Coagulation begins with the involvement of blood platelets – small, disk-shaped corpuscles that are able to sense physical and chemical signals of vessel wall injury. These signals causes platelets activation and aggregation, which leads to the formation of mechanical plug and prevention of bleeding.

Disorders of platelet activation and aggregation leads to serious pathologies [1]. There are several methods of platelet function testing, including light-transmission aggregometry [2], [3] and flow cytometry [4], [5]. Both techniques rely on the scattering of light by individual cells or their suspension. However, little is known about the geometry of blood platelets, which hinders the interpretation of light scattering data. Moreover, the activation includes reorganization of the cell cytoskeleton and dramatic shape change from highly flattened object to a rounded one. This effect precedes aggregation and alter the light transmission of platelet suspension, which indeed interferes with its change due to aggregation [6].

In the present work, we propose novel model of platelet shape, based on the latest discoveries of the cell structure [7]–[9]. The model is based on two parameters: the cell volume and the overcurvature of the internal microtubule bundle. The latter is supposed to change continuously during platelet activation, which gives the opportunity to describe both resting and activating platelets by the same family of

geometries. We describe the procedure for the construction of a cell shape given the volume and overcurvature, and for simulation of light scattering by such objects.

II. MODELING OF PLATELETS SHAPE

A. Basic Assumptions

Resting platelets have discoid shape due to microtubule ring (“marginal band”) along its equator [10]. During activation, the marginal band is coiled to 3-dimensional rounded structure observed in [8]. The proposed model is based on the following assumptions:

1. The curvature of marginal bang is constant along its length. On the other words, it forms an “overcurved circle” [11] – a space curve whose curvature is greater than that of flat ring with the same length by the factor called “overcurvature” (Fig. 1a);
2. Microtubules form a rigid frame, which is not affected by membrane tension and other factors. This follows from the characteristic energy of microtubule bundling and intermediate filaments stretching.
3. Membrane stretches over the overcurved circle of microtubules to have minimal surface area with given cell volume. This actually means that the cell membrane is tensioned by the intermediate filaments which seek to reduce its area by forming a convoluted surface [12]; thus, the whole membrane with filaments can be described as a film having surface tension.

The latter leads to the analogy between the proposed model and the soap bubble formed on an overcurved circle.

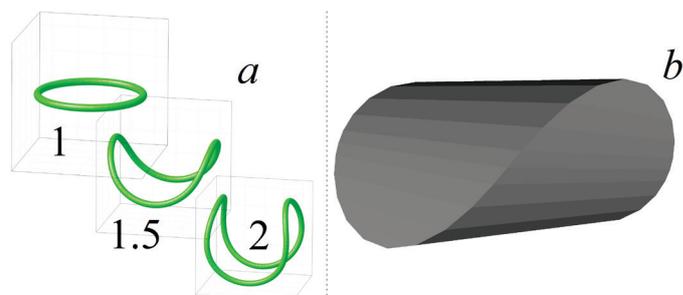


Fig. 1 (a) Examples of overcurved circles. Numbers denote the values of the overcurvature. (b) An example of the initial surface mesh for the optimization with the Surface Evolver.

B. Construction of the Platelet Shape

We constructed overcurved circles by implementing equations from [11] into LabVIEW program. Several examples of generated curves are shown in Fig. 1a. They are indeed very similar to the observations of coiled marginal band of microtubules in activated platelets [8].

The initial surface mesh were made by joining the opposite points of curve (Fig. 1b). It was saved in an appropriate format for further optimization with the Surface Evolver [13], which was used for the minimization of the surface area with given volume. The initial surface mesh were refined several times during optimization. Examples of the resulting shapes are shown in Fig. 2. They represent a catalogue of possible platelets geometries with dimensionless size; each of them can be scaled to provide the desired cell volume. These simulations were validated by the repeating with finer initial discretization. Some of the models were also implemented manually using wire contour and soap film and agreed well with the simulations.

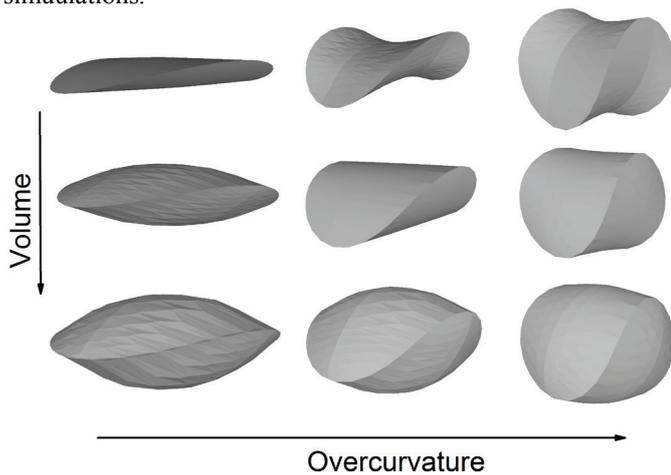


Fig. 2 Examples of the platelet shape model.

III. LIGHT SCATTERING SIMULATION

We saved the optimized structure from the Surface Evolver to .obj file and then used "Point in Polyhedron" tool that transforms .obj files into DDSCAT7 shape format [14]. In order to create the dipole set, this algorithm first creates a cubic bounding box around the object, and scans every coordinate to see whether the point is inside or outside the object. For the points inside the object, a dipole is set at that position. Examples of the constructed configuration of dipoles are shown in Fig. 3. The discretization level was chosen to provide 10 dipoles per the wavelength.

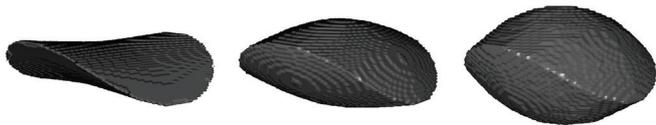


Fig. 3 Examples of targets for light scattering simulation.

The discrete dipole approximation, implemented in the code ADDA v 1.3b4 [15] was used for the simulation of light scattering by the obtained target. It is important to note that the

proposed model is not axisymmetric (it belongs to D_{2d} symmetry group); therefore, all three Euler angles of particle orientation would affect the simulation results.

Examples of the distribution of scattered light intensity (S_{11} element of the Mueller matrix [16]) versus polar and azimuthal scattering angles for the oblate spheroid and the novel platelet shape model in different orientations are shown in Fig. 4. The volumes of particles are $4 \mu\text{m}^3$, refractive index 1.03, wavelength used was 660 nm. The lack of axial symmetry of the proposed model leads to light scattering patterns substantially different from that of oblate spheroid, especially for the lower particle.

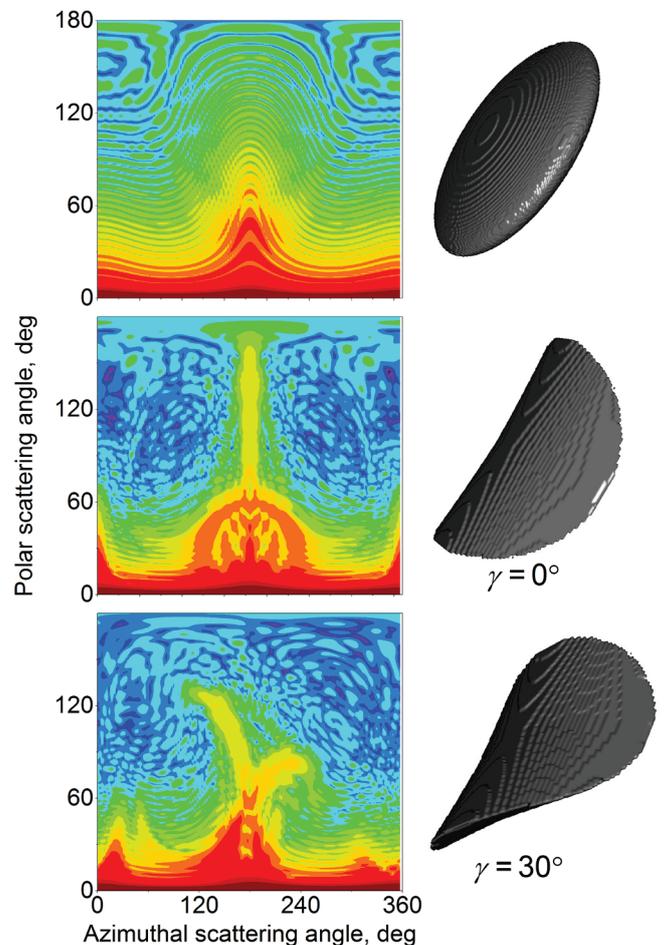


Fig. 4 Distribution of the intensity of scattered light (S_{11} element of Mueller matrix) for the oblate spheroid (aspect ratio 3.7) and the novel platelet model. Particle volumes are $4 \mu\text{m}^3$, wavelength 660 nm, refractive index 1.03, and Euler angles of orientation (α, β, γ) equal $(0^\circ, 60^\circ, 0^\circ)$ for first two particles and $(0^\circ, 60^\circ, 30^\circ)$ for the lower one.

IV. CONCLUSION

We proposed a physical model of platelet shape and described a procedure for its construction. Although actual platelets may have deviations from that shape, e.g., outgrowths of membrane, this is the first attempt to take into account the layout of marginal band of microtubules. The novel model predicts that platelets shape has no axial symmetry; instead, it belongs to D_{2d} symmetry group. In particular, this makes light scattering patterns of the proposed model differ significantly

from that of oblate spheroid, a geometry used previously for modeling of platelets [5], [17], [18]. With the detailed platelet model, the interpretation of light scattering techniques for the analysis of platelets would be more accurate. However, the proposed model needs to be proven to accurately describe the actual platelet shape. Single-particle scattering experiments, e.g., with the scanning flow cytometry [19], are needed for this purpose.

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