On the Mathematical Model of Delayed Activation of Platelets

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Abstract

This paper introduces a general concept of Eulerian reformulation of Langrangian particle tracking methods in evaluation of platelet damage and activation. It is applied to formulation of a new multistage algorithm describing the delayed activation of platelets due to excessive exposure to supra-critical stress. This new class of multistage Eulerian activation models allows for numerous extensions and generalizations, while preserving its simplicity and flexibility.

The main motivation for this work was an attempt to solve a complex macroscopic blood coagulation model in flowing blood. This continuous model originally presented in [1, 2] based on coupled set of advection-diffusion-reaction equations was solved numerically in [3, 4]. One of the model components omitted in these numerical simulations is the Lagrangian platelet activation model based on [5]. This activation model assumes that the platelets are activated after accumulating certain amount of supra-critical stress along their pathlines. The activation is however not immediate, but it takes some time t_{act} , i.e. the actual activation is delayed.

Implementation of this (Lagrangian) platelet activation model into (Eulerian) blood coagulation model would be rather difficult and numerically inefficient. The Eulerian reformulation of the activation model is possible, however there remains the problem of delayed activation that was not treated in the Eulerian framework so far. The sequential Eulerian modeling approach presented in this talk is attempting to address these issues.

The proposed model can be summarized as a set (sequence) of coupled equations.

$$\frac{\mathrm{D}A}{\mathrm{D}t} = Q(\tau)\mathcal{H}(\tau - \tau_c) \tag{1}$$

$$\frac{\mathrm{D}B}{\mathrm{D}t} = \mathcal{H}(A - A_c) \tag{2}$$

$$C = \mathcal{H}(B - B_c) \tag{3}$$

The local stress magnitude is denoted by τ and $\mathcal{H}$ stands for Heaviside function. The local activation state $C(\boldsymbol{x}, t)$ is the final product of a sequence of activation indicators based on accumulated supracritical ($\tau > \tau_c$) stress ($A(\boldsymbol{x}, t)$) and delay time count ($B(\boldsymbol{x}, t)$) in this case. For detailed description of the model see [6].

The newly formulated model can be seen as a prototype of a much wider class of multistage (sequential) models applicable to simulations of various phenomena in many branches of science. Here it has allowed us to reformulate the classically Lagrangian platelet damage models into the Eulerian framework, and easily include the delayed activation. This framework offers a great flexibility and variability while keeping the simplicity and convenience of Eulerian fluid flow description. This makes the model easy to implement as a straightforward extension of existing CFD codes and underlying mathematical models.

Keywords: blood flow, platelet, stress, activation

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