Tokarev et al. (2011) — "Platelet Adhesion from Shear Blood Flow is Controlled by Near-Wall Rebounding Collisions with Erythrocytes"

March 28, 2017; rev. March 29, 2018

Andrew Watson

1 Introduction

Hematocrit and wall shear rate are both known to affect platelet adhesion. Transport of platelets to the vessel wall involves platelet-platelet collisions, platelet-RBC collisions, and Brownian diffusion. The claim that previous models of platelet transport and adhesion only account for Brownian diffusion and model adhesion as a one-step process. The authors developed a model that more explicitly included platelet diffusion in the bulk due to collisions with other blood cells, and using a multi-step model of platelet adhesion to the wall. Their goal was to describe platelet adhesion as a function of hematocrit, wall shear rate, and RBC and platelet size.

Their model describes an experimental setup where whole blood is perfused through a flow chamber at a prescribed shear rate, and on the bottom of the flow chamber is some immobilized agonist. Then the mean surface density of platelets is measured as a function of time.

Their model describes the following processes:

1. Transport within the flow—both advection in the direction of fluid flow, and diffusion due to collisions with blood cells
2. Near-wall and wall processes:
   (a) Collision of a platelet in the RBC depleted zone with an RBC at the edge of the DZ, pushing the platelet into the wall
   (b) Capture of the platelet on the wall (i.e. formation of GP1b-vWF bonds)
   (c) Deceleration of the captured platelet relative to the flow (although later they will assume the deceleration to 0 velocity is instantaneous)
   (d) Either detachment of the platelet, or stable adhesion

2 Mathematical Model

They assume 2D Poiseuille flow between stationary plates at a distance of $2H$ (equations (1) and (2)). Platelet concentration is P, and is advected in the direction of the flow, and diffuses according to a nonlinear diffusion term (equation (3)).

The platelet diffusion coefficient includes terms that describe collisions with RBCs, collisions with other platelets, and Brownian diffusion. In equation (4), d_{RBC} and d_P are the RBC and platelet diameters, and Φ_{RBC} and $V_P P$ are the RBC and platelet volume fractions (parameter values are given in Tables S1 and S2 of the Supporting Material). They cite Ref. 32 in their paper for the first two terms of this diffusion coefficient. They also assume that Φ_{RBC} is constant throughout the domain, which they justify in Supplement 1. Essentially their argument is that the RBC DZ is small enough to ignore, and throughout the rest of the blood vessel RBC volume fraction is constant.

They assume that $D\nabla P \cdot n = 0$ along the top wall and at the outflow. They assume that $P = P_0$ at the inflow, and equation (5) gives the BC at the active wall ($y = 0$). $M(x)$ is the concentration of stably adhered platelets, and is governed by equation (7). Here $R(x)$ is the surface concentration of captured platelets and k_{bind} is the adhesion rate constant.

They model R with the advection reaction equation (8). Note $R(x)$ is not a function of y, and only applies at $y = 0$. w is the velocity of a captured platelet, $J(x)$ is the platelet flux toward the wall, $\Omega(x)$ is the proportion of uncovered surface, and α is the probability that a platelet colliding with the wall is captured.

They then argue that w is small, and the timescale of adhesion is much shorter than the timescale of the experiment, and so they assume that R is in quasi-steady-state (equation (9)). Their expression for J (given in equations (10) and (11)) is derived in Supplement 2.

They assumed that α was independent of $\dot{\gamma}_w$, and that k_{bind} was a decreasing linear function of $\dot{\gamma}_w$ (equation (12)). They also assumed that k_{det} is proportional to $\dot{\gamma}_w$. Then using equations (7), (9), (12), and (13) they found an effective binding rate constant k_{eff} that depends on $\dot{\gamma}_w$, Φ_{RBC}, d_{RBC}, and d_P. The surface availability function is given by equation (16). For most of their analysis, they averaged M over the length of the channel, and assumed that it was independent of x.

They also came up with a reduced model where they :

1. ignored platelet movement in the bulk and just used $P|_{y=0} = P_0$
2. assumed $\Omega(x) \equiv 1$
3. eliminated the second term in Q, that is they ignored flux of platelets to the surface due to collisions with other platelets.

Equations (17)–(19) describe the reduced model. In the reduced model, M^0 grows linearly in time, proportional to P_0 and k^0_{eff} which is the reduced k_{eff} parameter.

The parameters given in Tables S1 and S2 are fixed in the model. The parameters they estimated were α, $k_a = \frac{k^0_{\mathit{bind}}}{\delta}$, $\xi = \frac{\beta}{\delta}$, k_1 and k_2.

Reference

Tokarev, A. A., Butylin, A. A., and Ataullakhanov, F. I. (2011). Platelet adhesion from shear blood flow is controlled by near-wall rebounding collisions with erythrocytes. *Biophysical Journal*, pages 799–808.