TIME-DEPENDENT PLATELET ADHESION

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INTRODUCTION

The first stage of thrombogenesis is platelet adhesion on a surface followed by aggregation and the formation of platelet mural thrombi (Friedman and Leonard 1971). The resulting thrombosis and/or embolisation from diseased arteries produces a wide variety of clinical scenarios; myocardial infarction, strokes and gangrene. Vascular geometry, can now be regarded as a risk factor, due to the influence of that geometry on local haemodynamic effects. In particular it is extremely important to gain a thorough understanding of the relationship between vascular geometry, blood flow and the onset of thrombus formation in both the natural and diseased arteries. Although the formation of thrombi and platelet activation in stasis is fairly well understood the influence of blood flow characteristics has yet to be fully investigated. Fluid dynamic studies of blood flow, in models of arteries, suggests a set of fluid dynamic conditions which appear to predispose thrombus formation (platelet adhesion), principally at arterial bifurcations, T-junctions and curved sections.

Numerical models have been developed which include the integration of computational fluid dynamics with relatively complex kinetic mechanisms (Sorensen, Burgreen et al. 1999; Sorensen, Burgreen et al. 1999).

The presented work puts forward a boundary layer type model for time-dependent platelet adhesion with simple kinetics. This model is applicable to axi-symmetric flows, commonly found in the neighbourhoods of stagnation points and 2D flows where, in both cases, the wall shear stress is known a priori. The model has the ability to cover a large range of kinetic rates, from reaction controlled through intermediate kinetics to diffusion controlled systems. We investigate the role of time-dependency on the adhesion of platelets and we compare the results with experiment.

THEORY

By choosing appropriate length and velocity scales, L and U respectively the constant density conservation equation for the mass fraction of platelets, ϕ, can be written in the boundary layer type form of

$$u\frac{\partial \phi}{\partial x}+v\frac{\partial \phi}{\partial y}=\frac{1}{Pe}\frac{\partial^2 \phi}{\partial y^2} \qquad (1)$$

Pe , the Peclet number is defined as

$$Pe=\frac{UL}{D}$$

D is of the order $10^{-13}m^2s^{-1}$, thus the Peclet number is correspondingly high.

We wish to investigate the temporal affect on platelet adhesion using a time-dependent model. We choose a non-dimensional time t defined as

$$\tau=\omega t \qquad (2)$$

and write the corresponding Peclet number as

$$Pe=\frac{\omega L^2}{D} \qquad (3)$$

Since the Peclet number is high, for physiological ω, we assume that the mass transfer boundary layer thickness is much smaller than the associated viscous boundary layer and hence the velocity profile can be approximated by a linear function. Using a non-dimensional wall shear stress $\sigma_w(x,\tau)$, known a priori, we can write the conservation of species equation in the form

$$\frac{\partial^2 \phi_i}{\partial \eta^2}+3\eta^2\frac{\partial \phi_i}{\partial \eta}=\frac{\omega Pe}{\left(\beta(x,\tau)\right)^2}\left\{\frac{\partial \phi_i}{\partial \tau}+\frac{\eta}{V_*}\frac{\partial V_*}{\partial \tau}\frac{\partial \phi_i}{\partial \eta}\right\} \qquad (4)$$

where

$$\eta = \beta(x,\tau)\, y; \quad V_*^2(x,\tau) = \sigma_w(x,\tau)$$

$$\beta(x,\tau) = \frac{\{V_*(x,\tau)\}(\mathrm{Re}\,Pe)^{\frac{1}{3}}}{\left[9\int_{x_0}^{x}\{V_*(\gamma,\tau)\}d\gamma\right]^{\frac{1}{3}}}$$

It is assumed that no aggregation occurs in the blood and that platelet adhesion is represented by a simple reaction boundary condition. Adhered platelets are modelled as being part of the surface and, once adhered, stay in that state. A boundary condition at the surface of the following form is used

$$\frac{\partial \phi_{pl}}{\partial y} = \kappa \phi_{wall} \Rightarrow \frac{\partial \phi_{pl}}{\partial \eta} = \kappa \frac{\phi_{wall}}{\beta(x,\tau)} \qquad (5)$$

Far away from the reaction surface the concentration of species is a constant.

$$\eta \to \infty; \quad \phi_{pl}(\eta,\tau) \to \phi_{pl\,\infty}, \quad \forall\ \tau \geq 0 \quad (6)$$

The initial conditions are given by

$$\phi(x,\tau=0) = 1.0, \quad x \in [0,10] \qquad (7)$$

To maintain simplicity $V_*(x,\tau)$ is defined by a simple step function leading to $V_{S*}(x)$ the steady state wall shear stress function.

RESULTS

Figure 1 shows the resulting deposition of adhered platelets after 300 seconds. This time corresponds with the data of (Sorensen, Burgreen et al. 1999). The similarity solution given by equation (4) with simple first order kinetics agrees very well with the complex kinetic CFD model of (Sorensen, Burgreen et al. 1999). A large majority of the change in platelet concentration occurs at the initial stages from the onset of the flow where the geometric function β has a particular influence (close to the upstream edge of the parallel plate). Further downstream the concentration changes with time over a longer period.

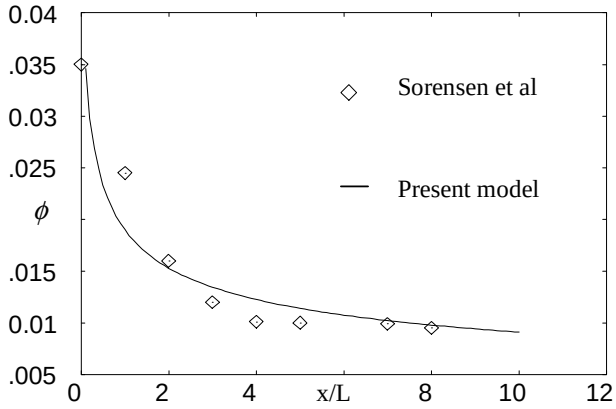
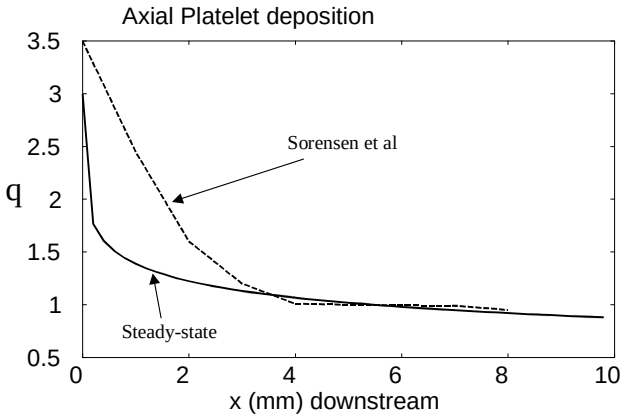


Fig 1 deposition of adhered platelets after 300 secs.

We are thus able to find a single kinetic rate which encompasses the reaction mechanism of platelet adhesion.

Comparison with the steady-state results shown in Figure 2 indicates that the factor $\omega Pe(\beta(x,\tau))^{-2}$ has a particular influence. More complex geometric configurations such as bifurcations and arterial junctions will therefore have a predominant role in the adhesion of platelets as shown in the steady-state model (David and Walker 2001).



In particular if the shear stress varies as a function of time (physiologically in a pulsatile mode) then adhesion distribution could well be significantly different from the steady-state case.

Further work will encompass the role of spatially varying wall shear stress, for example at stagnation points and arterial bifurcations as well as more complex time-dependencies where $\frac{\partial}{\partial \tau} V_*(x,\tau)$ becomes non zero.

Fig 2. Comparison of steady-state model and results of (Sorensen, Burgreen et al. 1999)

CONCLUSIONS

A time-dependent model for platelet adhesion has been developed. Results how a difference between the present model and that of the steady-state. The model is generally applicable to a range of 2D, and axi-symmetric wall shear stress profiles which can be found in the human arterial system. In addition pulsatile flow can be easily incorporated and provides an additional spatially scaled convective term to the governing conservation equation .

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