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A new model of red blood cell repartition at small bifurcations

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1. Introduction

In tissues and organs the microvasculature is a complex network of small blood vessels that plays a crucial role in the transport of oxygen and nutrients. The vessel hematocrit represents the volumetric concentration of the RBC phase as the volume fraction occupied by RBCs. However, the local hematocrit can vary along the flow path due to changes in vessel diameters and in velocity of the RBC phase. At the bifurcation, the RBC concentration splits because of the difference in flow resistance between the mother and daughter vessels. This results in a redistribution of RBCs and a change in the hematocrit values in each branch. The vessel hematocrit H_i plays a crucial role in determining the flow behavior and oxygen transport capacity within the microcirculation. Furthermore, the migration of red blood cells (RBCs) downstream at each bifurcation in a vessel network has a significant influence on the distribution of RBCs at a larger network scale. The hematocrit distribution at the bifurcation of vessels is nonlinear with the flow. It has the name of separation phase effect. That is influenced by several factors, including the local flow conditions, the geometry of the vessels, and the local forces on the RBC particles.
For the need of modeling of the microcirculation, including a good repartition of RBC is essential because it impacts local rheology, flow and quantity of oxygen. So models should be capable of predicting the hematocrit distribution at the bifurcation of vessels and in large networks. Over the years, several models have been proposed to describe the distribution of hematocrit at small bifurcations in the microcirculation. The most used of them is based on empirical data (Pries et al. 1996) and others models based on mechanical behaviour (Gould et al. 2015 ; Guibert et al. 2010). We proposed a new model adapted for 0D and 1D models with physical variables and easily adaptable.

2. Method : Bifurcation model

2.1 A model with two factors

We propose a model based on conservation laws for the RBC particles and blood flow at the bifurcation of vessels. In a framework of a reduced modelling for the blood flow (distribution of flow computed by a 0D or 1D model), we propose two factors to model the hematocrit distribution at the bifurcation: one geometrical, the factor a, and a migration factor β which takes into account the local forces on the RBC particles. Most of RBC are in the 'core' region of the vessels because the existence of a cell free l ayer area (CFL) of thickness δ. The geometrical factor a_i takes in account the CFL and, is defined as the ratio between blood core surface and total vessel surface $\alpha_i = \frac{((d_i/2)-\delta)^2}{(d_i/2)^2}$ where d_i is the diameter of the i^{th} vessel which are input geometrical data.
The finite size of red blood cells has also a significant impact on the flow properties of blood rheology in micro-vessels. The assumption that red blood cells follow the flow streamlines in bifurcations is reasonable in vessels with diameters much larger than a single red blood cell (around 7 µm). However, in bifurcations where

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the vessel diameter is comparable to a single cell phase separation becomes more pronounced, challenging this assumption. This effect manifests as the non-sperical particle migrating in the direction of increasing pressure. For including this effect in the proposed model of hematocrit distribution, we follow the ideas of Yen & Fung (1978) for the additional local forces on the red blood cells showing that the resultant force on the particles is proportional to the velocity u_i. So we consider the normalised velocity in another coefficient that takes into account the migration that the particle may undergo $\beta_i = \alpha_i \frac{u_i}{u_0}$. Velocities are data obtained by a numerical resolution of a 0D or 1D model.
We write now the conservation equations for the RBC particles at the bifurcation of volume V_c. The continuum conservation of particles at a junction is governed by the balance between the particle fluxes at the junction boundaries using coefficients a_i and β_i,

$$\int_{V_c} \frac{dn_i}{dt} dV + \int_S \alpha_i \beta_i n_i \bar{u}_i . \bar{n}_i dS = 0$$

2.2 Fractional RBC flux

We defined a fractional RBC flux as $F_{rbc,1} = \frac{\beta_1 \alpha_1 H_1 Q_1}{\beta_0 \alpha_0 H_0 Q_0}$ where indices refers to vessels as it can be seen on Figure 1.A. At stationary state, when considering mass conservation, hematocrit continuity and conservation of particles, we can write the fraction RBC flux as

$$F_{rbc,1} = \frac{1}{1 + K\left(\frac{(1-Q_1)^2}{Q_1^2}\right)} \text{ with } K = \frac{\alpha_2^2 d_1^2}{\alpha_1^2 d_2^2}.$$

Here K englobes all geometrical variables.

3. Results and discussion

3.1 Result on a junction

We compute the RBC flow for experimental data of Pries et al. (1996). The diameters, see *Figure 1.A*, are $d_0 = 9\mu m$; $d_1 = 8\mu m$; $d_2 = 6\mu m$, the hematocrit $H_o = 0{,}45$, and the entry dimensionless blood flow $Q_o = 1$. We present the numerical results for the hematocrit distribution at the bifurcation in Figure 1.
Figure 1.B shows the results for the fractional RBC flux $F_{rbc,1}$ as a function of the fractional flux $F_1 = \frac{Q_1}{Q_0}$ for branch 1 and 2. The results are in agreement with the data from Pries et al. (1996).
We also show result for the relative hematocrit $Hc = \frac{H_1}{H_0}$ which can be rewritten as $Hc = \frac{F_{rbc,1}}{Q_1}$ in our problem.

3.2 Model for the cell-free layer thickness δ

In-vitro microfluidic experiment shows that the cell-free layer does not have a constant thickness (Tateishi et al. 1994). So, we try different types of function for the variation of the CFL thickness δ depending on the diameter of the vessel. Results with an increasing CFL with the diameter shows better agreement with experimental *in-vivo* repartition data (Pries 1996) compared to a constant δ. So, results from the model are also coherent with *in-vitro* data from Tateishi et al. (1994) and others measurements of CFL. This provides a numerical evidence that the cell free layer has a significant impact on the hematocrit distribution at the bifurcation.

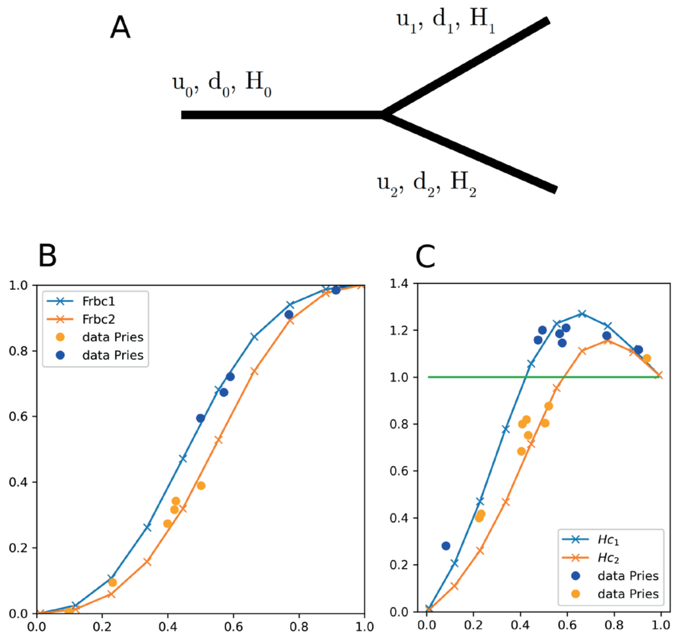

Figure 1. (A) Scheme of a junction. (B) Fractional RBC flux in function of the fractional flux at a junction. (C) Relative hematocrit in function of the fractional flux for branch 1 (blue) and branch 2 (orange). Data from Pries (1996) are superimposed.

Credit: J.-M. Fullana.

4. Conclusions

We have presented a model for the hematocrit distribution at the bifurcation of vessels. The theoretical model does not require any fitting parameters, just the thickness of the CFL and the viscosity is not explicitly included in the model. The model predicts the hematocrit distribution at the bifurcation as function solely of the blood flow and the geometrical factors a and β.

The model is validated using experimental data, and we have shown that the presence and the thickness of the cell-free layer significantly influences the hematocrit distribution at the bifurcation. The model is simple but effective, and can be easily adapted to both 0D and 1D approaches, making it versatile for different modeling scenarios.

Conflict of interest statement

No conflict of interest to declare.

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