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Flow of a capsule through a constriction : application to cell filtration

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Abstract. — The motion of a freely suspended capsule (liquid drop surrounded by a deformable membrane) forced to squeeze through an axisymmetric constriction smaller than its initial dimensions is studied by means of a numerical model based on boundary integrals. The flow is driven by a constant pressure difference. The suspending liquid and internal capsule viscosities are equal. It is found that the maximum energy loss is due to entrance effects rather than to the flow in the pore itself. The role of the membrane rigidity can be predicted.

1. Introduction.

In filtration or duct flow experiments conducted on particulate suspensions, the absence of an appropriate model makes it difficult to relate quantitatively and unambiguously the measured pressure drop to the intrinsic properties of the suspended particles. When the particles are deformable, as in two phase flow through porous media or in blood microcirculation, the problem is even more complicated since the bulk flow properties of the suspension depend on the deformation of the particles. Such a situation is considered here where a capsule (a generic name for liquid drops surrounded by a deformable membrane) is flowing through a pore.

The difficulties encountered in designing such a model result from an interplay of complicated mechanical effects : viscous forces due to the motion of both the internal and external fluids and elastic forces exerted by the membrane under large deformations. The objective of this paper is to show that a numerical modelling using an integral formulation of the flow of a capsule through a constriction is possible, and then, to illustrate how such a model may help in understanding the mechanics of this type of flow and in interpreting filtration experiments conducted on dilute suspensions of red blood cells (RBCs).

2. Problem statement.

2.1 DEFINITION OF THE MODEL. — Although transient in nature, the very low Reynolds number filtration flows may be considered as quasi-steady at any moment and are therefore described by the Stokes equations. Rather than solving these equations in their differential

form, an integral formulation is used. The model matches the experimental conditions shown by Drochon *et al.* [1] to improve the discriminating power of filtration experiments, i.e., the Newtonian and incompressible internal fluid of the capsule and suspending liquid have the same viscosity μ . The capsule membrane (M) is infinitely thin, has no bending resistance and has a neo-hookean constitutive law characterized by a surface shear elastic modulus E_s .

A fully axisymmetric configuration, where an ellipsoidal capsule is freely suspended in a hyperbolic constriction having the same revolution axis, is chosen. Such a channel corresponds to a short pore. The total pressure drop across the pore is kept constant (as in many filtration devices), and thus the flow rate $Q(t)$ varies with time as the capsule flows along. At each time step, the unperturbed velocity field $\mathbf{v}^{np}(\mathbf{x}, t)$, that would exist if no capsule were present is a function of $Q(t)$ and of the pore geometry, given by Happel & Brenner [2].

The internal domain of the capsule is bounded by M. The external domain, denoted Ω_e , is bounded by M, by the solid wall of the constriction B and by the entrance and exit sections, respectively E_1 and E_2 . In the following, $(B \cup E_1 \cup E_2)$ is denoted by $\partial\Omega_e$. The radius of the constriction throat is denoted r_t and the angle of the hyperbola asymptote with the revolution axis is $\arcsin(\zeta_0)$.

Non-dimensional quantities are used throughout, using r_t for lengths, E_s for elastic tensions, V^{np} , the initial mean velocity at the throat of the constriction in the absence of a capsule, for velocities and $\mu V^{np}/r_t$ for viscous stresses.

The boundary conditions associated with the Stokes equations describing the flows in the internal and external domain of the capsule are as follows :

No-slip condition on the solid boundaries of the constriction :

$$\mathbf{v}(\mathbf{x}, t) = 0 \quad \text{for } \mathbf{x} \text{ on } B. \quad (1)$$

The entrance and exit sections, E_1 and E_2 , are chosen sufficiently far away from the capsule, for the flow field to have regained its unperturbed value :

$$\mathbf{v}(\mathbf{x}, t) = \mathbf{v}^{np}(\mathbf{x}, t) \quad \text{and} \quad p(\mathbf{x}, t) = \text{Const.} \quad \text{for } \mathbf{x} \text{ on } E_1 \text{ or } E_2. \quad (2)$$

The dynamic equilibrium of the membrane (3) and the continuity of the velocity between the liquids and the membrane material points (4) are imposed :

$$\varepsilon(\sigma^{\text{ext}}(\mathbf{x}) - \sigma^{\text{int}}(\mathbf{x})) \cdot \mathbf{n}(\mathbf{x}) = \mathbf{F}_M(\mathbf{x}) \quad \text{for } \mathbf{x} \text{ on } M \quad (3)$$

$$\mathbf{v}^{\text{ext}}(\mathbf{x}) = \mathbf{v}^{\text{int}}(\mathbf{x}) = \partial\mathbf{x}/\partial t \quad \text{for } \mathbf{x} \text{ on } M \quad (4)$$

where σ^{ext} and σ^{int} are the stress tensors and \mathbf{v}^{ext} and \mathbf{v}^{int} the velocities of points situated in the external and internal domains, respectively. The load vector \mathbf{F}_M exerted by the fluids on the membrane is determined in terms of the membrane deformation by means of the classical theory of thin elastic shells undergoing large deformations. This is possible as long as the characteristic law of the membrane is known. The integration of the continuity condition (4) allows to compute the membrane deformation once the velocity fields have been determined.

An important parameter of the model, the capillary number ε , appears in (3) through the non-dimensionalization process. It measures the ratio between the viscous forces which tend to deform the membrane and the elastic forces which tend to restore its initial shape :

$$\varepsilon = \mu V^{np}/E_s,$$

The higher ε the smaller E_s and therefore, the more deformable the capsule.

2.2 INTEGRAL FORMULATION. — The integral equation expressing the velocity of any point on M , B , E_1 and E_2 as a function of the forces exerted by these boundaries on the internal and external fluids is obtained following the same steps as Martinez & Udell [3] for the related problem of the motion of a liquid droplet through a cylindrical tube. The fact that the internal and external liquids have the same viscosity results in a significant simplification of the equations due to the vanishing contribution of the double layer potentials on the membrane. Further simplifications of the equation arise when the non-perturbed velocity of the flow in the domain bounded by B , E_1 and E_2 is subtracted off. In particular, using boundary conditions (1) and (2), and following a simple asymptotic analysis, it is possible to show that the double layer potentials on B , E_1 and E_2 resulting from the subtraction of v^{np} vanish. After these simplifications, the velocity of a point x taken in Ω_e or on $\partial\Omega_e$ is given by :

$$\frac{v(x)}{\alpha} = \frac{v^{np}(x)}{\alpha} - \frac{1}{8\pi} \int_M J(x-y) \cdot \frac{F_M(y)}{\varepsilon} dS(y) + \frac{1}{8\pi} \int_{\partial\Omega_e} J(x-y) \cdot \Delta F(y) dS(y) \quad (5)$$

where $\alpha = 1$ when x is on M and $\alpha = 2$ when x is on $\partial\Omega_e$. Use has been made of boundary condition (3), since the jump in viscous stresses across M has been replaced by F_M/ε . The kernels J correspond to single layer potentials and are known functions of $(x-y)$ given in [4]. The perturbation of the force exerted by the boundaries of Ω_e on the fluid, due to the presence of the capsule in the constriction, is ΔF . When applied to E_1 or E_2 , ΔF is simply the pressure perturbation $\Delta P_1 \mathbf{n}$ or $\Delta P_2 \mathbf{n}$, respectively. In the axisymmetric case considered here, equation (5) can be integrated once over the angle of revolution and then rewritten in a meridian plane (O, x, r) of a cylindrical reference frame centered on the axis of revolution $[O, x[$ of the constriction.

2.3 NUMERICAL SOLUTION. — The capsule is injected in the flow at time $t = 0$, all the membrane points have initially the unperturbed fluid velocity and F_M is zero. At any time t , the position of the membrane points is obtained by integration of (4) with an Eulerian explicit scheme. The membrane state of deformation being known, it is easy to determine the load vector F_M . Equation (5) is then used to express the velocity on B , E_1 , E_2 and M and solve the system defined by boundary conditions (1), (2), (3), and (4). This yields a new velocity of membrane points from which their new position may be determined.

A collocation method is used: the discretization of each of the boundaries B , E_1 , E_2 and M into n_B , n_E and n_M points, respectively, allows the boundary integrals to be evaluated numerically by means of a Simpson's rule for unequally spaced points. A system of $2 * n_B + 2$ linear scalar equations obtained by writing (1) and (2) at each collocation point on B and at only one location in E_1 and E_2 is then solved. This system of Nystrom equations resulting from the repeated three-point Simpson's integration scheme applied to the integrals of the single layer potentials can be represented as follows :

$$A \cdot F(t) = S(t)$$

where $F(t)$ is a vector containing $2 * n_B + 2$ unknowns (the radial and axial coordinates of ΔF at each collocation point of B plus ΔP_1 and ΔP_2), where $S(t)$ is a vector consisting of the integrals on M of the load vector F_M , and where A is a dense matrix which is a function of the fixed geometry of the problem and is therefore inverted only once. In the case of a constant pressure drop situation, the additional pressure drop $\Delta P_{add} = \Delta P_1 - \Delta P_2$ needed to force the capsule through the constriction is then used to adjust the flow rate and compute the corresponding velocity v^{np} that will be used in (5) for integration at time $t + \Delta t$. The whole process is then repeated.

The kernels J in equation (5) are singular, although logarithmically convergent, whenever the current point along one of the boundaries approaches the point at which the velocity is computed. These singular cases are treated using the classical method which consists in subtracting the asymptotic expression of the kernel in the numerical integrals of the singular terms and then, in adding its analytical sum. Consequently, the initially singular integral is split into a sum of non-singular expressions.

Extensive numerical testing of the model has been conducted in order to validate the numerical methods used. This validation is based upon the perturbation of the different parameters involved, such as the density of points on the boundaries, the position of E_1 and E_2 , the initial position of the capsule and the value of the time step. As a by product, this study resulted in the determination of optimum densities of points on the boundaries. This search for optimality is based on a balance between the need for numerical precision and the necessity to limit c.p.u. time consumption. A parameter was considered optimum as soon as any further change in its value produced a difference of less than 5 % in the results obtained. The most sensitive numerical parameter is the number of points on B. As shown by Delves & Mohamed [5], Nystrom type solution schemes for Fredholm equations of the first kind, such as (5) when ΔF is to be determined, may become divergent when the discretization of the boundaries is made finer. However, as pointed out by Pozrikidis [6], the first kind Fredholm equations arising from Stokes flows have shown to be particularly stable through this type of procedure. Our findings confirm that statement. Typical values of the numerical parameters are, in the particular case of a spherical capsule with radius $R/r_t = 1.2$ and $\varepsilon = 0.5$: initial position of the capsule $x_G(t=0) = -6$, position of E_1 . $x_{E_1} = -30$, position of E_2 . $x_{E_2} = +30$, $n_B = 207$, $n_E = 125$, $n_M = 45$, $\Delta t = 5 \times 10^{-4}$. Details of the numerical scheme and of the different validation tests performed may be found in [7].

3. Results and discussion.

The results presented in figure 1 and figure 2 are obtained for a spherical capsule of radius 1.2 flowing in a hyperbolic constriction with $\zeta_0 = 0.7$ under a constant pressure difference between the entrance and exit sections. This configuration was chosen to match the conditions

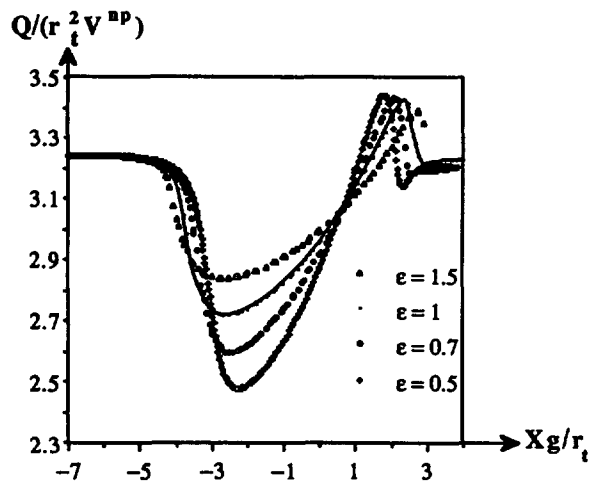


Fig. 1. — Evolution of the non-dimensional flow rate as a function of the capsule position, for different values of ε .

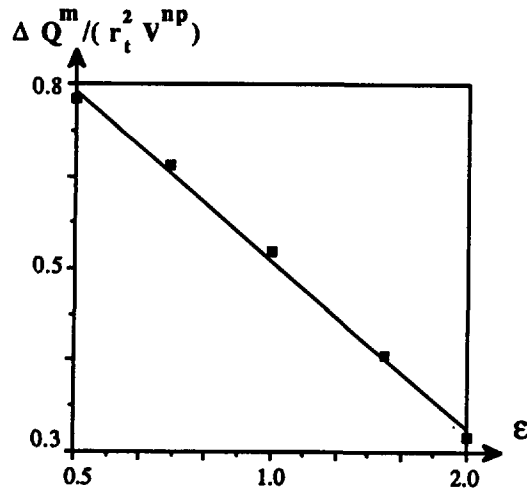


Fig. 2. — Evolution of the non-dimensional maximum flow rate perturbation as a function of ε .

of RBC filtration experiments (1.2 is the ratio between the radius of a sphere having the same volume as a RBC and the radius of a filter pore).

Figure 1 shows the evolution of the non-dimensional flow rate as a function of the position of the capsule center of mass Xg , for different values of ε . As a result of the choice of scales, the initial non-dimensional value of the flow rate is π . As the capsule passes through the constriction, the flow rate decreases to reach a minimum value at a position Xg which depends on ε . The smaller ε , the less deformable the capsule and the greater the decrease in flow rate, i.e., the more the capsule plugs the constriction. The minimum value of flow rate is reached upstream of the throat and is nearer the throat for smaller values of ε . Indeed, it takes longer for less deformable capsules to reach a deformed shape which minimizes the flow perturbation. The maximum energy expenditure therefore occurs during entrance phenomena. The flow rate then slowly increases again until it reaches the initial, non perturbed value for a position of Xg somewhere between 1 and 2, depending on the value of ε . Then, the flow rate becomes larger than the non-perturbed value with a perturbation which increases as ε decreases. This shows that, owing to its elastic properties, the capsule recoils, sucking some fluid downstream of the throat. It also shows that the higher E_s , the more efficient the aspiration of fluid through the constriction. This interpretation is confirmed by the negative values of F_M (force exerted by the fluids on the membrane) which are observed for capsules situated just downstream of the throat. Finally, the flow rate regains its initial value.

Figure 2 shows the evolution of the non-dimensional value of the maximum flow rate reduction (ΔQ^m) as a function of ε . A regression conducted for this set of points leads to :

$$\Delta Q^m / (r_t^2 V^{np}) = 0.5 \varepsilon^{-0.61}$$

This correlation can be used to interpret the filtration experiments of Drochon *et al.* [1] which are conducted on dilute suspensions of RBCs. Normal and diamide treated RBCs are suspended in a dextran solution with a viscosity of order 8 mPas so that the viscosity ratio between this external medium and the internal haemoglobin solution is roughly equal to unity. The effect of the diamide treatment is to rigidify the cell membrane, the elastic modulus of which is roughly doubled (as measured with a micropipette). The suspensions are passed through a filter with pores of 4.7 μm diameter and 11 μm length. Under a given pressure head,

through a single pore, the flow rate reduction ΔQ between the buffer and the suspension is measured :

$$\Delta Q = Q(\text{buffer}) - Q(\text{suspension}) .$$

The ratio between the values of ΔQ obtained experimentally for normal and for diamide treated cells is found to be :

$$\frac{\Delta Q(\text{normal})}{\Delta Q(\text{diamide})} = 0.67 \pm 0.15 .$$

The model predicts that this ratio should be equal to $(2)^{-0.61}$, i.e., 0.66. The agreement is of course satisfactory and indicates that the membrane rigidification is properly taken into account by the model. However, the absolute values of E_s predicted by the model are much larger than the physiological values. This is probably due to the Mooney-Rivlin law used for the membrane. Indeed, a constitutive law taking into account the membrane incompressibility would be more appropriate. It follows that, presently, only relative variations of E_s can be predicted.

4. Conclusion.

This study gives an insight into the investigating possibilities offered by the model of a capsule flowing through a constriction. Owing to the consistency of the results obtained in this first set of numerical experiments, further tests should be conducted in order to investigate the influence of parameters such as the size ratio between the capsule and the constriction throat or the shape of the capsule. Different types of constriction should also be studied, starting with various shapes of hyperbolic constrictions, and noting that any channel shape can actually be treated with the model as long as the non-perturbed velocity of the flow can be computed. This work will undoubtedly help to determine and understand RBC mechanical properties and their rheological behavior when they flow through filter pores or narrow capillaries of the body.

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