Modeling cells in flow: Stream function and vorticity

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Abstract: In this study, we present a phase-field model formulation of two and three dimensional system couple with Navier-Stokes fluid. We apply this formulation to a 3D Poiseuille flow. We study cell interface introducing two stream functions on the procedure. Some morphologies are obtained for 2D case model and properties as the energy and the volume of the cell will be shown.

I. INTRODUCTION

Every human body contains millions of cells. These peculiar objects develop essential functions inside us each second of our entire life. Cells are very complex structures that contains the fundamental molecules of life which composed all living things. In this study we want to focus on a concrete part of them: the cell membrane. Cell membrane show very specific properties which were not shown in any other material (such as non-classical elastic behaviour). This membrane has a high capacity of deformation and it defines the frontier between the interior of the cell and the outside environment.

Canham-Helfrich theory [1]-[2] can describe the free energy of a cell membrane. If we assume there is no homogeneities in the membrane the bending free energy will be:

$$F_b = \frac{\kappa}{2}\int_S H^2 dS, \tag{1}$$

where H is the mean curvature and κ the bending rigidity.

From this point, we will work in a phase-field model. We can describe the phase-field methodology introducing an order parameter in the lines of the Ginzburg-Landau theory. The order parameter describes the two phases: the extracellular ($\phi = +1$) and the intracellular ($\phi = -1$). Following this fundamentals, we can describe the bending energy [3] as a function of the phase-field:

$$F_b[\phi] = \frac{\kappa}{2}\int_V (\Phi)^2 dV \text{ with } \Phi(\phi) = -\phi + \phi^3 - \epsilon^2\nabla^2\phi. \tag{2}$$

The membrane dynamics should be couple to hydrodynamical effects of the surrounding fluid. It is usual to incorporate Navier-Stokes equation to describe the dynamics of the fluid and both equations are coupled describing the interaction membrane-fluid.

It is possible to build the order parameter temporal evolution. This evolution will be essential along the study; we will be able to predict the dynamics of cell membrane. Following with the previous information, we can develop an equation for time evolution adding D as the diffusion coefficient and if we couple it with the velocity field of a Navier-Stokes fluid, the final equations of our model will be:

$$\partial_t\phi = D\nabla^2\mu_m - \overrightarrow{v}\cdot\nabla\phi, \tag{3}$$

$$\rho\left(\partial_t\overrightarrow{v} + \overrightarrow{v}\cdot\nabla\overrightarrow{v}\right) = -\nabla P + \eta\nabla^2\overrightarrow{v} - \phi\nabla\mu_m. \tag{4}$$

where μ_m is the functional derivative of the free energy.

In this paper we focus on the behaviour of red blood cells while flowing in confined channel which is dominated by elasticity and deformity. For this purpose we study the problem on three dimensions to obtain more complete information. The most remarkable novelty is the formulation of the model in 3 dimensions introducing two stream functions. We will obtain the shape of velocity, vorticity and the two stream functions for a 3D flow. Then, we carry on introducing the cell through the phase-field equations on a Navier-Stokes Poiseuille flow to obtain the main equations of the 3D system. Finally we will obtain the initial interface of the 3D cell and results of 2D red blood cells confined in a microchannel will be shown as well as a proof of concept.

II. ADDING A FLUID FLOW INTO A PHASE-FIELD MODEL

First of all, we introduce the chemical potential as [4]:

$$\mu_m = \mu_b + \gamma_1\nabla^2\phi + \gamma_2\cdot(\phi\ (\phi^2-1)) + \gamma_3. \tag{5}$$

where μ_b is the functional derivative of the free energy:

$$\mu_b = \frac{\delta F_b[\phi]}{\delta\phi} = \kappa\ [(3\phi^2-1)\Phi[\phi] - \epsilon^2\nabla^2\Phi[\phi]]. \tag{6}$$

Adding Lagrange multipliers (γ_i) in the bending free energy will let us impose a constant surface area and a constant volume.

As we are at very low Reynolds numbers, the velocity and the distances which we are working will be enough

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small to consider a non inertial system. Adding the incompressibility of the fluid to this, we can approximate Eq. 4:

$$Re = \frac{\rho v L}{\eta} \quad \nabla \vec{v} \sim 0 \quad \partial_t \vec{v} \sim 0$$
$$\to \rho \left(\partial_t \vec{v} + \vec{v} \cdot \nabla \vec{v}\right) \sim 0. \tag{7}$$

If we regroup with Eq. 4 and Eq. 7 we finally obtain:

$$0 = -\nabla P + \eta \nabla^2 \vec{v} - \phi \nabla \mu_m, \tag{8}$$

$$\partial_t \phi = D\nabla^2 \mu_m - \vec{v} \cdot \nabla \phi, \tag{9}$$

$$\nabla \cdot \vec{v} = 0. \tag{10}$$

Let focus on Eq. 8. If we take the curl of non zero part of Eq. 8 we find:

$$0 = -\nabla \times (\nabla P) + \eta \nabla \times (\nabla^2 \vec{v}) - \nabla \times (\phi \nabla \mu_m). \tag{11}$$

In our system we will apply a pressure gradient towards only one direction, thus first term of Eq. 11 is 0. In third term, as it deals with scalar functions, we can separate the curl product as $(\nabla \phi) \times (\nabla \mu_m)$. Then, if we manipulate second term a little we finally obtain the main equations of our study:

$$\nabla \times (\nabla \times \vec{\omega}) = -\frac{1}{\eta}(\nabla \phi) \times (\nabla \mu_m),$$
$$\partial_t \phi = D\nabla^2 \mu_m - \vec{v} \cdot \nabla \phi. \tag{12}$$

The aim will be to study the dynamics between the membrane and the fluid through the phase-field model avoiding the explicit calculation of $\vec{v}$. Instead of it, we will use the vorticity $\vec{\omega}$ and it will appear the stream functions.

III. 3D FLOW MODEL

A. Introducing 2 Stream functions

As we know, there are flows that have an axis of symmetry relative to which the velocity field is rotationally invariant. In these cases, we properly know how to obtain the equations of motion using just one stream function if the fluid is incompressible. In our case, due to introduce the phase-field method to describe the cell membrane dynamics and morphology, the symmetry is broken. Thus we will need at least two stream functions. Let us prove that we just need two stream functions to describe our situation:

The continuity equation on 3-D is given by:

$$\frac{\partial v_x}{\partial x} + \frac{\partial v_y}{\partial y} + \frac{\partial v_z}{\partial z} = 0. \tag{13}$$

A theorem by Jacobi [5] shows that Eq. 13 has a general solution given by 2 arbitrary stream functions:

$$\xi_1(x, y, z), \quad \xi_2(x, y, z). \tag{14}$$

Once we have proved that just two stream functions are necessary to work on 3-D, we carry on with the velocity.

Velocity vector from [5] is given by :

$$\vec{v} = \nabla \xi_1 \times \nabla \xi_2, \tag{15}$$

and the vorticity is given by:

$$\vec{\omega} = \nabla \times \vec{v} = \nabla \times \nabla \xi_1 \times \nabla \xi_2. \tag{16}$$

B. Equations with a cell and initial conditions

Through combining equations 12 and 16, we finally obtain the three equations in terms of vorticity, first stream function and second stream function that we will have to try to compute:

$$\partial_t \phi = D\nabla^2 \mu_m - \vec{v} \cdot \nabla \phi = D\nabla^2 \mu_m - (\nabla \xi_1 \times \nabla \xi_2) \cdot \nabla \phi, \tag{17}$$

$$\vec{\omega} = \nabla \times \nabla \xi_1 \times \nabla \xi_2, \tag{18}$$

$$\nabla \times (\nabla \times \vec{\omega}) = -\frac{1}{\eta}(\nabla \phi) \times (\nabla \mu_m), \tag{19}$$

where Eq. 18 and Eq. 19 have 3 components each one.

But if we want to solve this partial derivative equation system, we will need to know the initial conditions without the cell. Thus we should describe very clear everything we need. Imagine we apply a pressure gradient along the channel ΔP in the x direction. L is the channel length and 2R is the channel height (R is the cylindrical radius) [6]:

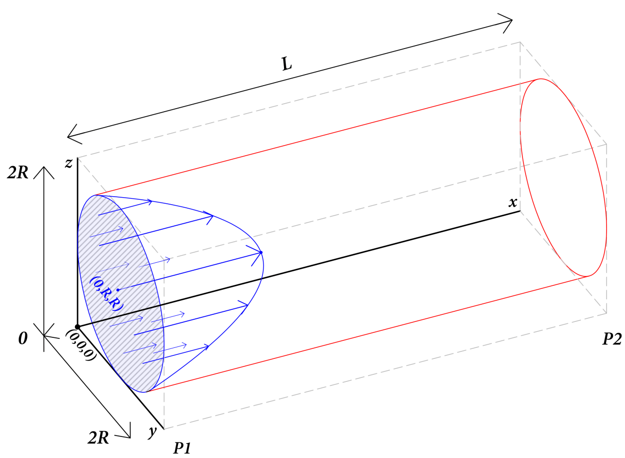

FIG. 1: Poiseuille flow 3D.

If we solve N-S equation without a cell in 3D we obtain:

$$v_x = \frac{\Delta P}{4\eta L}(R^2 - ((z-R)^2 - (y-R)^2), \qquad \omega_y = \frac{-\Delta P(z-R)}{2\eta L} \quad \omega_z = \frac{\Delta P(y-R)}{2\eta L}. \tag{20}$$

Thus, if we try to obtain the two stream functions, we have to solve:

$$\frac{\partial \xi_1}{\partial y}\frac{\partial \xi_2}{\partial z} - \frac{\partial \xi_1}{\partial z}\frac{\partial \xi_2}{\partial y} = \frac{\Delta P}{4\eta L}(R^2 - (z-R)^2 - (y-R)^2), \tag{21}$$

There are infinite solutions if we do not have more equations. Let ξ_1 and ξ_2 be like $\xi = \sum_{i,j,k} a_i x^i + b_j y^j + c_k z^k$. The shape of Eq. 21 will be:

$$\frac{\partial \xi_1}{\partial y}\frac{\partial \xi_2}{\partial z} - \frac{\partial \xi_1}{\partial z}\frac{\partial \xi_2}{\partial y} = Ax^0y^0z^0 + Bx^0y^2z^0 + Cx^0y^0z^2. \tag{22}$$

Let k_1, k_2 the resulting term product of each possible subtraction. In order to have an easy solution we choose for example the cases where the result of the subtraction consists on assume that all the terms (k_1, k_2) are equal to 0 excepting the 3 terms of Eq. 22. I.e., we do not consider cases that $k_1 - k_2 = 0 \;\; where \;\; k_1, k_2 \neq 0$ excepting the terms of Eq. 21 which are non zero:

$$\begin{cases} k_1 x^i y^j z^k - k_2 x^i y^j z^k = 0 & \{i,j,k\} \notin \{2,0,0\} \\ k_1 x^i y^j z^k - k_2 x^i y^j z^k = 0 & \{i,j,k\} \notin \{0,2,0\} \\ k_1 x^i y^j z^k - k_2 x^i y^j z^k = 0 & \{i,j,k\} \notin \{0,0,0\} \end{cases}. \tag{23}$$

Thus the terms that remain are the terms on y^3, z^3, y, z and a constant. Considering this, the stream functions would be like:

$$\xi_i(y,z) = a_i(y-R)^3 + b_i(z-R)^3 + \\ + c_i(y-R) + d_i(z-R) + \xi_i(0,0,0). \tag{24}$$

And if we solve this we finally obtain two possible stream functions:

$$\xi_1(y,z) = \sqrt{\frac{\Delta P}{12L\eta}}((y-R) + (z-R)) + \xi_1(0,0,0),$$
$$\xi_2(y,z) = \sqrt{\frac{\Delta P}{12L\eta}}((y-R)^3 - (z-R)^3 + (y-R) \\ + (1+3R^2)(z-R)) + \xi_2(0,0,0). \tag{25}$$

These expressions give us a specific solution of the two stream functions. Combining equations 25 and 20 we finally acquire the initial conditions. Through these important results we will be able to solve the partial derivative equation system of the phase field (Eq. 17) and study the vorticity and cell evolution.

C. Discussion of current 3D results

Here we present some results of the 3 dimensional system of the formation of the cell interface without coupling fluid flow:

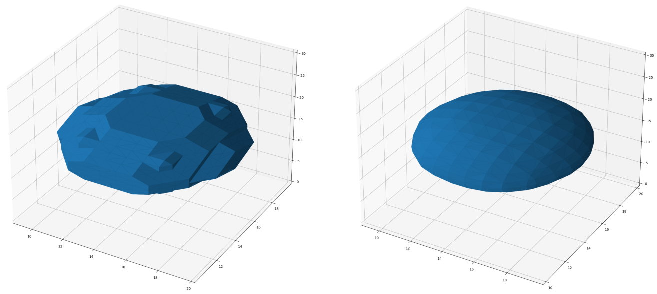

FIG. 2: Interface 3D cell formation with Δt = 50 where each Δt are 2500 steps.

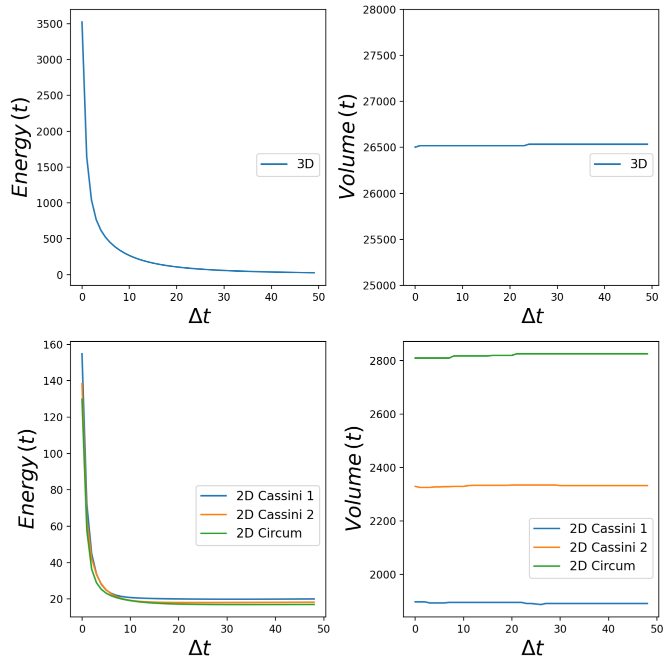

FIG. 3: Comparison of energy and volume evolution on 2D (beyond) and 3D (above) model through Δt = 50.

The figure 2 shows the formation of the interface in absence of fluid. This part of the simulation is essential to create the correct initial conditions. Apart from the evolution of the shape, we also can study the evolution of the energy and the volume. To compute the energy of the membrane we define the energy as:

$$E = \int_V \mu_m dV. \tag{26}$$

As we can observe in Fig. 3 the volume maintains constant. This was a requirement for the cell model that is being fulfilled. Meanwhile if we focus on the energy evolution (Fig. 3) we obtain that it tends to stationary state. This shows us that the diffuse interface is formed.

IV. 2D FLOW MODEL

In this section, we will briefly introduce the model on 2 dimensions and we will study some shapes as the Cassini oval and circumference shape. It is well known that in 2-dimensional flows the velocity can be related to just one stream function, ξ, that satisfies [7]:

$$v_x = \partial_y \xi, \quad v_y = -\partial_x \xi, \tag{27}$$

$$\overrightarrow{A} = (0, 0, \xi(x, y)), \quad \overrightarrow{v} = \nabla \times \overrightarrow{A}. \tag{28}$$

The vorticity is given by:

$$\overrightarrow{\omega} = \nabla \times \overrightarrow{v} = \nabla \times (0, 0, \xi(x, y)) = -\nabla^2 \xi \ \hat{k}. \tag{29}$$

And we can simplify the equation 19:

$$\nabla \times (\nabla \times (0, 0, \omega)) = -\nabla^2 \omega \ \hat{k} = -\frac{1}{\eta}(\nabla\phi) \times (\nabla\mu_m) \ \hat{k}. \tag{30}$$

We finally obtain the three main equations of our system which depends on stream function and vorticity. As we can observe, the solution of it is based on two scalar Poisson equations [8]:

$$\partial_t \phi = D\nabla^2 \mu_m - (\frac{\partial \xi}{\partial y}\frac{\partial \phi}{\partial x} - \frac{\partial \xi}{\partial x}\frac{\partial \phi}{\partial y}), \tag{31}$$

$$\nabla^2 \omega = \frac{1}{\eta}(\frac{\partial \phi}{\partial x}\frac{\partial \mu_m}{\partial y} - \frac{\partial \phi}{\partial y}\frac{\partial \mu_m}{\partial x}), \tag{32}$$

$$\nabla^2 \xi = -\omega. \tag{33}$$

A. Results for a Poiseuille flow

Imagine we apply a pressure gradient ΔP along the channel with a $d/2$ radius and length L in the x direction:

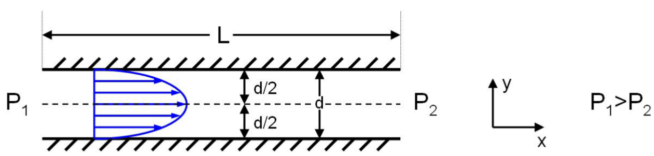

FIG. 4: Poiseuille flow 2D. $V_y = V_z = 0$.

We can use the Navier-stokes solution for a Poiseuille flow as initial conditions (without cell):

$$v_x(y) = -\frac{\Delta P}{\eta L} y(d-y) \rightarrow \begin{cases} \omega = \dfrac{\Delta P}{\eta L}(d-2y) \\ \\ \xi = \dfrac{\Delta P}{6L\eta} y^2(2y-3d) \end{cases} . \tag{34}$$

But we need the boundary conditions to compute the code to display the different morphologies of the cell motion evolution through the flow. These are given by:

$$\begin{aligned} \omega(y=0) &= \frac{\Delta P}{\eta L}h, & \omega(y=h) &= -\frac{\Delta P}{\eta L}h, \\ \xi(y=0) &= 0, & \xi(y=h) &= -\frac{\Delta P}{6\eta L}h^3. \end{aligned} \tag{35}$$

Let show the different figures obtained from several conditions:

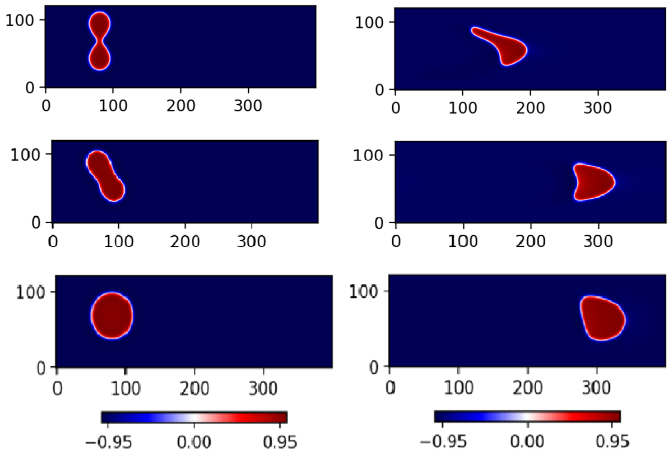

FIG. 5: Evolution of circumference shape and different Cassini oval shape cell. Δt is 50 and the velocity is 0.8 in units of length/units of time.

In Fig. 5 we display a curious shape named Cassini Oval [9] and a circumference shape cell. We have to remember that the cell is inside a Poiseuille flow. Just like in [8], we can observe that with this chosen velocity (0.8), the velocity field in the channel is the dominant mechanism of deformation. Depending on the geometrical properties of the cell, the symmetry will be broken along one axis or another, creating a parachute or slipper morphology (Fig. 5). Two different Cassini ovals with different Area-Volume relation give two different final shapes: slipper and parachute shape [8].

As seen in Fig. 3 for the two dimensional the volume remains constant fulfilling physical constraints.

We can compare Fig. 5 with real experiment in Fig. 6.

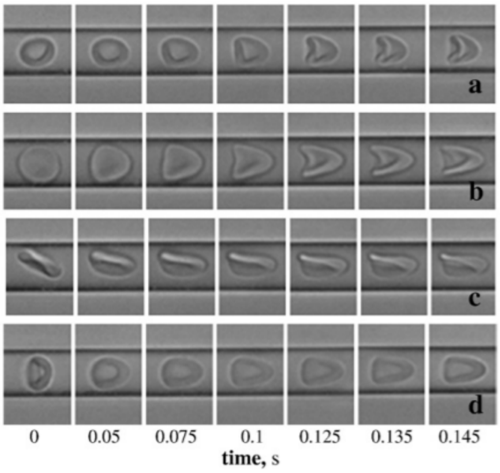

FIG. 6: Evolution of a real experiment adapted from Tomaiuolo [10].

In this figure, we can observe the mentioned morphologies. Circumference shape obtained in Fig. 5 belongs to first states of sequence b. First Cassini Oval of Fig. 5 presents similarities with final stages of sequence a. This shape presents slipper shape. Second Cassini Oval of Fig. 5 can be matched with final stages of sequence b. It gets a parachute shape.

V. CONCLUSIONS AND FUTURE WORK

The expansion into the three dimensions of the phase-field model coupled with Navier-Stokes gives us a way to study the deformation of the cell membrane. Through the cutting-edge technology of nowadays studies on 3 dimensions are essential for the understanding of biological processes. The formulation of Navier-Stokes equations using vorticity and stream functions bring us a phase-field model without some hard mathematical calculations. Through this improvement, we have been able to compute the model hence there is still many theoretical research to improve the implementation code.

We have defined the velocity in terms of two stream functions and we have coupled with a Navier-Stokes fluid ensuring the maintenance of area and volume of the cell. This formulation allows to calculate explicitly the surrounding conditions of the membrane in each temporal step of the simulation.

The shape sequences of membranes of [10] give us an opportunity to compare our numerical results with experimental results. We can check that slipper and parachute shape are not only a numerical result, they can be obtained through a microscope and present some coincidence.

Observing the parameters of the interface formation in Fig. 3, we see that the energy evolves to a stationary state and the cell volume maintains constant. The same results occur in 2D model. Thus the model predicts the same behaviour in the interface creation. We can observe some differences on the scale of the parameters as well. This happens because there is difference on the system size.

However, next step will be include entirely the complete equations in our simulation that we obtained coupling a Navier-Stokes fluid (Eq. 17, 18 and 19) into the phase-field model. With this progress, in the future we will simulate the interaction between two attached red blood cells inside a fluid flow.

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