FEF Assignment

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1^{st} June 2018

1 Introduction

In this assignment we will try to model the density distribution of F-actin and G-actin in a given domain. We will solve a simplified model of a cell, by means of doing three separate problem:

1. The distribution of F-actin and G-actin under a constant fluid flow
2. The velocity and pressure of the fluid inside the cell
3. The coupling of the evolution of both F-actin and G-actin; and its interaction with the cell's fluid

2 Geometry, material data and boundary conditions

Figure 1 shows the domain that we will consider for this set of problems (units in μm). See how the domain is one ninth $(\frac{1}{9})$ of a circular crown of 25μm and 15μm of outer and inner radius, respectively.

Material parameters for F-actin,G-actin and the fluid are

$$D_F = 5\ \mu m/s;\ \sigma_F = 0.25\ s^{-1} \tag{1}$$

$$D_G = 15\ \mu m/s;\ \sigma_G = 2\ s^{-1}\ \hat{\sigma}_{GF} = 0.5\ s^{-1} \tag{2}$$

$$\nu = 1000\ pN \cdot s/\mu m \tag{3}$$

F-actin density is expected to be constant for $r = 25\mu m$, as well as the velocity in the upper and lower radius. No tractions are considered for the lateral boundaries:

$$\begin{array}{ll} u_r = -0.15;\ u_\theta = 0; & for\ r = 15\mu m \\ u_r = -0.30;\ u_\theta = 0; & for\ r = 25\mu m \\ F = 80\mu M & for\ r = 25\mu m \end{array}$$

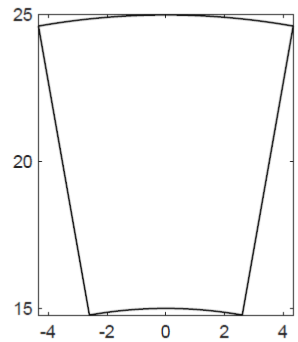


Figure 1: Geometry of the problem

3 TRANSPORT PROBLEM

Considering the following system of partial differential equations

$$\begin{cases} \frac{\partial F}{\partial t} = -\mathbf{u} \cdot \nabla F + D_F \nabla^2 F - \sigma_F F \quad in\ (0, T)\ \times\ \Omega \\ \frac{\partial G}{\partial t} = D_G \nabla^2 G - \sigma_G G + \hat{\sigma}_{GF} F \quad in\ (0, T)\ \times\ \Omega \end{cases}$$

With a velocity field of $\mathbf{u} = -1/1500(rx, ry)$ where r is the radius and x and y the coordinates of the points. Boundary conditions at the upper boundary, and initial condition of $F = 80\ \mu M$ everywhere in the domain.

3.1 Mesh and test parameters

A mesh of bilinear quadrilaterals of 20 elements per side was considered for the solution. In order to reach the steady state, a simulation of 30 seconds was done, with a total of 300 steps, a combination of parameters such that a stable solution could be obtained (maximum $Pe \approx \frac{25^2 0.5}{15005} = 0.417 < 1$)

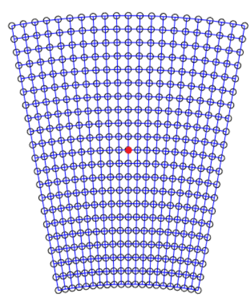


Figure 2: Mesh considered for this problem. 20x20 bilinear quadrilaterals

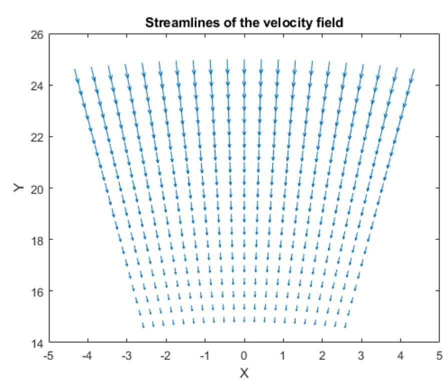


Figure 3: Streamlines of the convection velocity

3.2 Weak form and matrix system

The problem was discretized in space with Galerkin method and in time with Crank-Nicholson. The incremental expression of the weak form for the first equation reads:

$$\begin{aligned}(w,\Delta F)+\frac{\Delta t}{2}(w,\mathbf{u}\cdot\nabla\Delta F)-(w,\nabla\cdot(D_F\nabla\Delta F))+(w,\sigma_F\Delta F))=\\=-\Delta t(w,\mathbf{a}\cdot\nabla F^n)-(w,\nabla\cdot(D_F\nabla F^n))+(w,\sigma_F F^n)\end{aligned}\tag{4}$$

Which can be written in matricial form as

$$(\mathbf{M}+\frac{\Delta t}{2}(\mathbf{C}+\mathbf{K}+\sigma_F\mathbf{M}))\Delta\mathbf{F}=-\Delta t(\mathbf{C}+\mathbf{K}+\sigma_F\mathbf{M})\mathbf{F}^n \tag{5}$$

The weak form of second equation yields

$$\begin{aligned}(w,\Delta G)-\frac{\Delta t}{2}((w,\nabla\cdot(D_G\nabla\Delta G))+(w,\sigma_G\Delta G))=\\=-\Delta t(-(w,\nabla\cdot(D_F\nabla G^n))+(w,\sigma_G G^n)-\frac{1}{2}(w,\hat{\sigma}_{FG}(F^n+F^{n+1})))\end{aligned}\tag{6}$$

And its matricial expression

$$(\mathbf{M}+\frac{\Delta t}{2}(\mathbf{K}+\sigma_G\mathbf{M}))\Delta\mathbf{G}=-\Delta t(\mathbf{K}+\sigma_G\mathbf{M})\mathbf{G}^n+\frac{\Delta t}{2}\sigma_{FG}\mathbf{M}(F^n+F^{n+1}) \tag{7}$$

3.3 Results

The steady distribution of F-actin and G-actin densities can be seen in figures 4 and 5. As it can be assesed by the solution, and given that the geometry, boundary conditions and convective velocity has radial symmetry, the problem can be seen as a 1D problem.

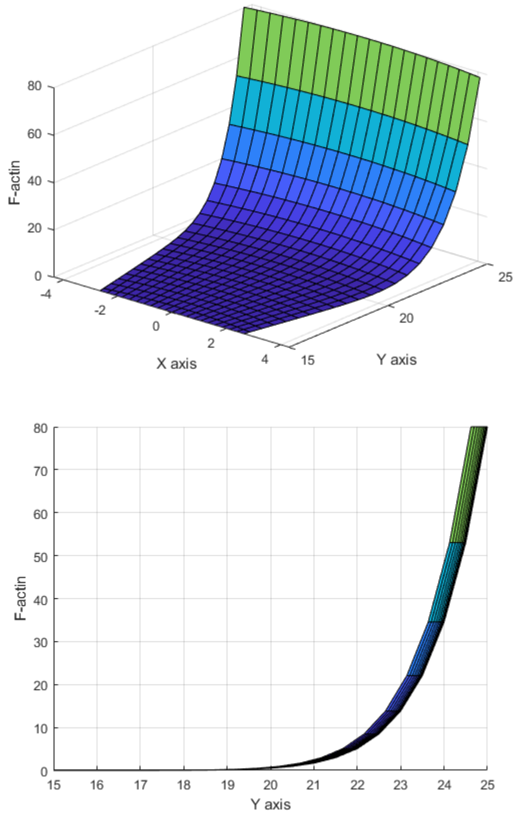


Figure 4: Steady state distribution of F-actin: F-actin is concentrated at the external radius

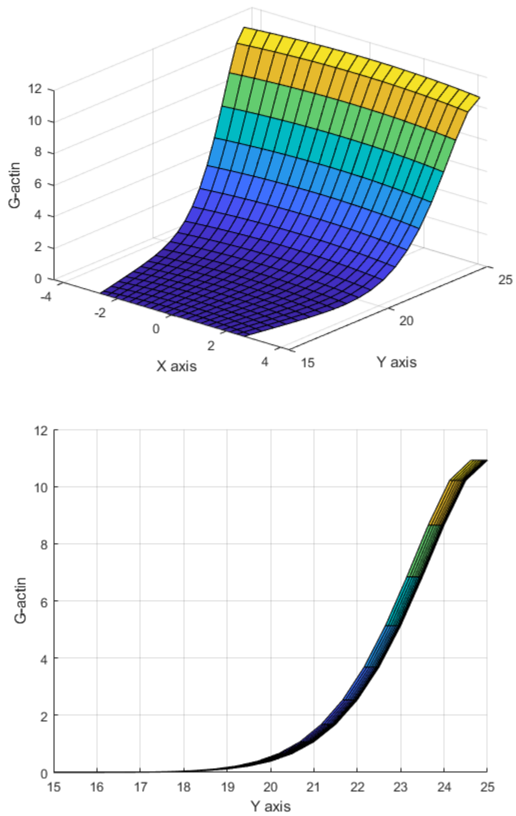


Figure 5: Steady state distribution of G-actin: we can see that if follows the distribution of F-actin

If we follow the evolution of the densities of a point located in the center of the geometry (see red point in figure 2) we can observe that both densities distributions reach the steady state at approximately the same time, and that while F is strictly decreasing (due to the fact that the initial condition considers maximum density of F), G shows a peak of 14.9 μM just at the beginning of the analysis, due to the high amount of F-actin that is reacting. However, both F and G-actin are decreasing at approximately the same rate after their peak value: see table 1 that for the first 5 seconds (50 steps) after peak value both concentrations are reduced in a similar trend, and the same for the next 5 seconds. Final maximum and minimum values are shown in table 2.

step	F-actin	% reduction	step	G-actin	% reduction
0	80	-	10	14.83	-
50	19.45	24.3	60	4.39	29.6
100	4.75	24.4	110	1.27	28.9

Table 1: % reduction of densities for the first 10 seconds after peak value

Maximum values are found on the top boundary, and minimum at the bottom boundary:

Variable	Maximum	Minimum
F-actin	80	$7.18\times10^{-}4$
G-actin	10.9	$5.73\times10^{-}4$

Table 2: Maximum and minimum values of F-actin and G-actin

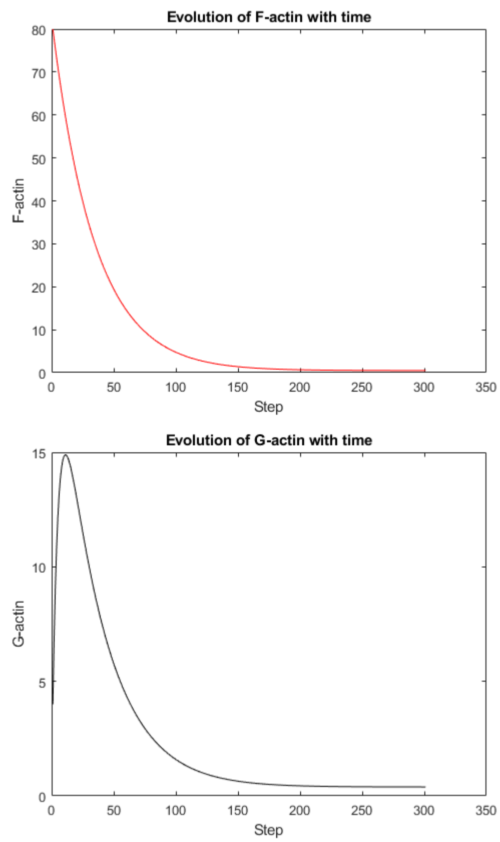


Figure 6: Time evolution of F-actin and G-actin density distribution for the central point of the mesh. We can see that after 30 seconds we have reached the steady state of the solution

4 STOKES PROBLEM

Consider now the following equation for the solution of the fluid's velocity and pressure with boundary conditions in all the boundary.

$$\begin{cases} \nabla \cdot \mathbf{u} & in\ \Omega \\ \nabla \cdot \boldsymbol{\sigma} & in\ \Omega \end{cases}$$

4.1 Mesh and equations

A mesh of 20x20 elements was chosen. For the velocity, quadratic quadrilaterals were considered, while pressure was meshed using bilinear quadrilaterals. This way, we satisfy the LBB condition and don't need regularisation.

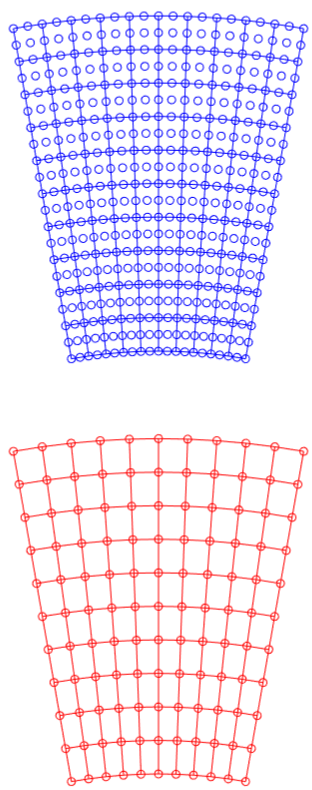


Figure 7: Velocity and pressure meshes of 10x10 Q2Q1 elements for this problem

4.2 Method

As some of the boundary conditions are imposed for the tractions, we'll need to consider the stokes equation in terms of Cauchy stress $\boldsymbol{\sigma}$ instead of pressure. The weak form of the problem shown before can be seen here:

$$\begin{cases} (w, \nabla \cdot \boldsymbol{\sigma}) = 0 \quad in\ \Omega \\ (q, \nabla \cdot v) = 0 \quad in\ \Omega \end{cases}$$

Where w and q are the shape-functions that will be used to discretize velocity and pressure, respectively.

The matricial sytem that arise from this equations is the traditional Stokes problem system:

$$\begin{bmatrix} \mathbf{K} & \mathbf{G}^T \\ \mathbf{G} & 0 \end{bmatrix} \begin{bmatrix} \mathbf{v} \\ \mathbf{p} \end{bmatrix} = \begin{bmatrix} \mathbf{f} \\ \mathbf{h} \end{bmatrix} \tag{8}$$

So we have a partitioned system that will let us solve for velocity and pressure at the same time.

4.3 Results

The results are symmetric with respect to the Y axis. The obtained velocity field shows a little discordance with the drichlet boundary conditions: while the velocities at the superior and lower boundaries are radial, the velocity in the rest of points have both radial and tangential components. As we imposed no tractions on the lateral boundaries, the velocity of the fluid is not directly determined for those points. We should conclude then that the domain boundaries are not a representation of solid boundaries of the cell, but just a portion of its interior. The pressure distribution has an hyperboloid shape, with a minimum at the center of the geometry, a local maximum at the outer radius and a global maximum at the inner one. However, the solution is spoiled at the corners of the geometry.

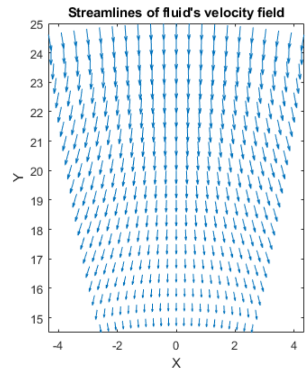


Figure 8: Velocity streamlines: They are vertically symmetric and are pointing outwards at the lateral boundaries of the domain

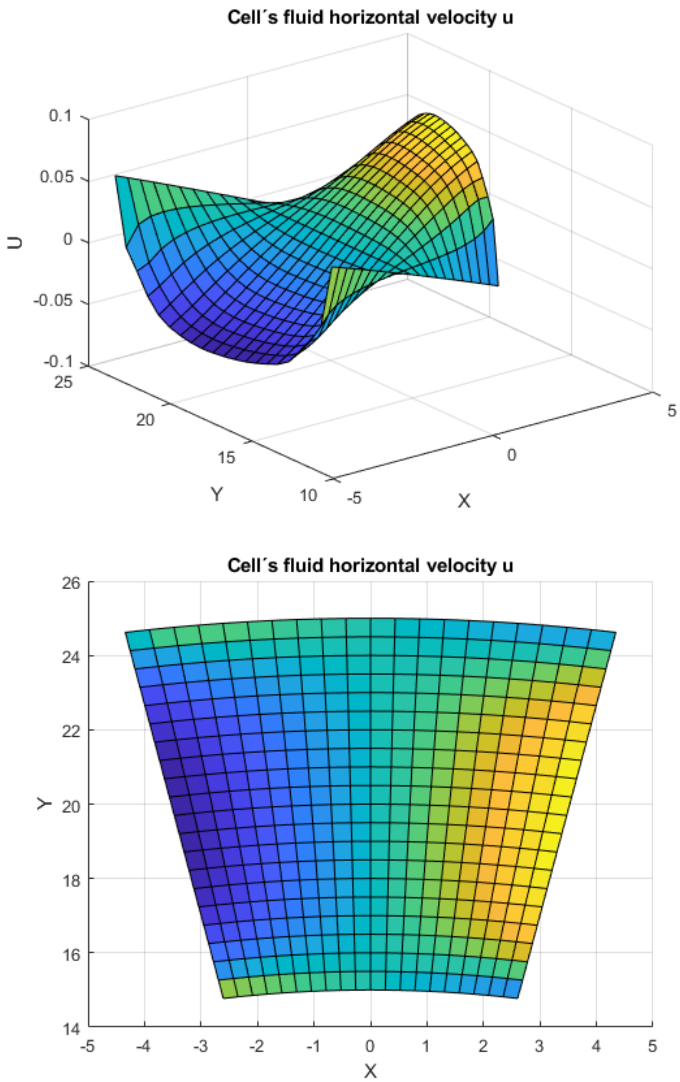
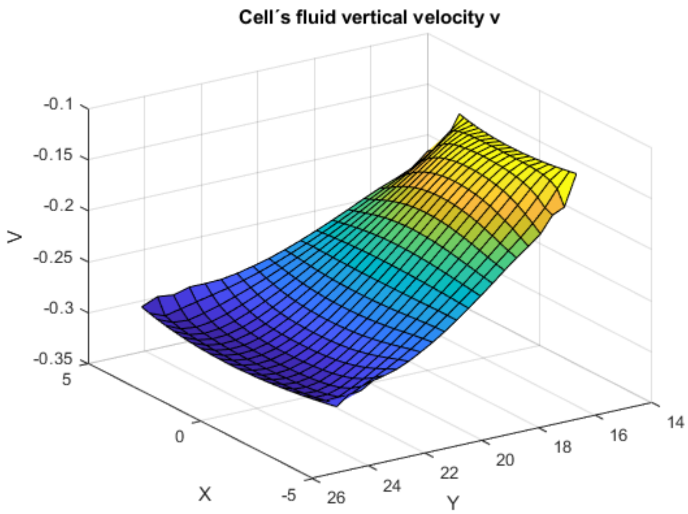


Figure 9: Skewed and top views of vx. See in the top view how the solution is symmetric and it is pointing outwards of the lateral boundaries. The twisted shape of the skewed view is due to the fact that the solution is mirrored, and thus, the sign is different for every side



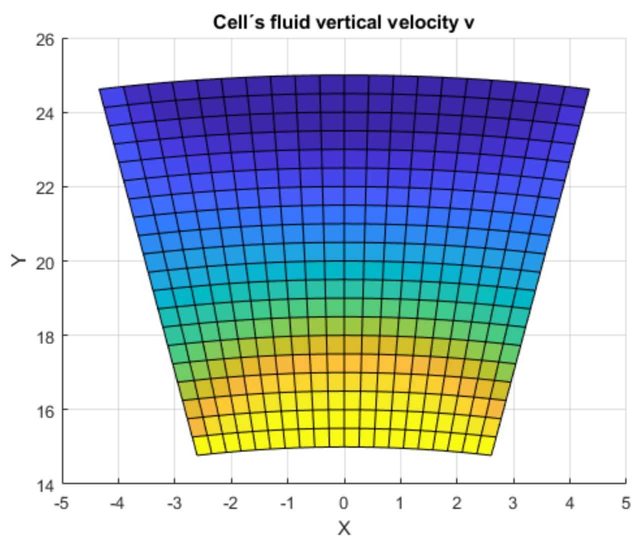


Figure 10: Skewed and top views of vy. See in the top view how the solution is symmetric and it is going from the superior layer to the inferior part of the domain.

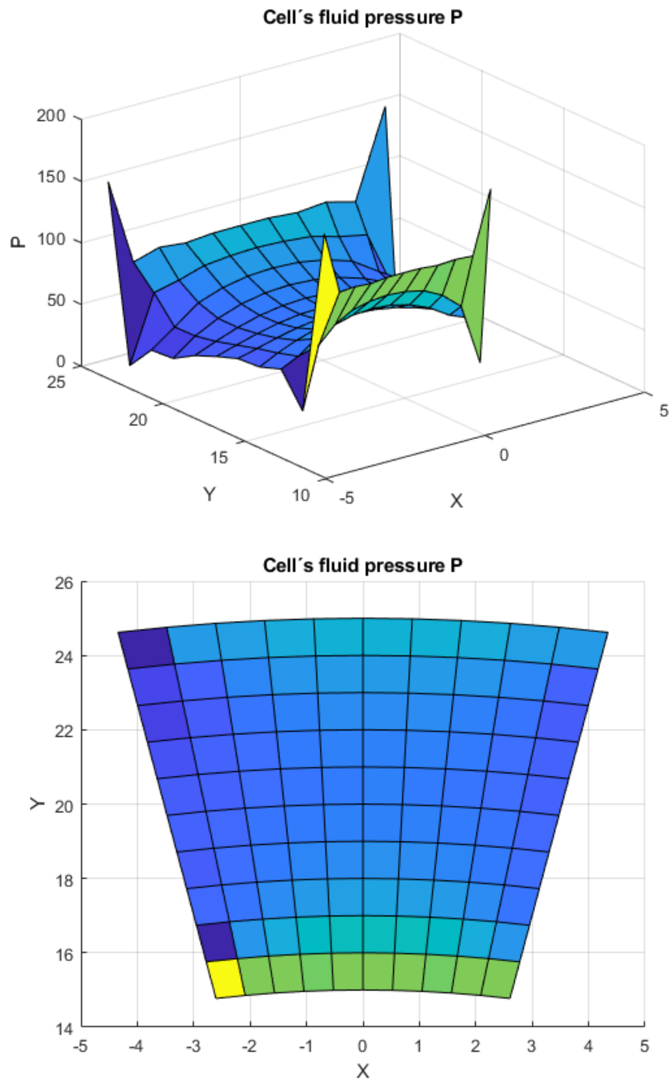


Figure 11: Skewed and top views of pressure p. Solution is spolied at the corners and is symmetric with respect to the Y axis(assesed in its top view)

5 COUPLED PROBLEM

The last step to take is the coupling of the equations shown in the previous sections. However, the stokes equations will be modified in order to neglect the pressure and the convective terms. The resulting problem (after including forces at the boundary) is

$$\begin{cases} \nu\nabla\cdot(\nabla\mathbf{u}) + \nabla\cdot\boldsymbol{\sigma}_m(F) + \mathbf{T}_m(\mathbf{u}) \quad in\ \Omega \\ \frac{\partial F}{\partial t} = -\mathbf{u}\cdot\nabla F + D_F\nabla^2 F - \sigma_F F \quad in\ (0,T)\ \ \Omega \\ \frac{\partial G}{\partial t} = D_G\nabla^2 G - \sigma_G G + \hat{\sigma}_{GF} F \quad in\ (0,T)\ x\ \Omega \end{cases}$$

With all the boundary conditions and parameters given in the first section of this document. As initial condition, we will consider F to have a density of 80 μM in the whole domain, G will be 0 everywhere and the velocity will be in equilibrium with the initial F-actin.

5.1 Mesh

Given that there is no more accounting for both velocity and pressure, we don't need to have two different meshes, one for each kind of variable. For this reason, we will consider the same mesh of 20x20 bilinear quadrilaterals, so that we have the same interpolation for **u** and **F** and we can use the given MatLab function. *boundaryMatrices.m*

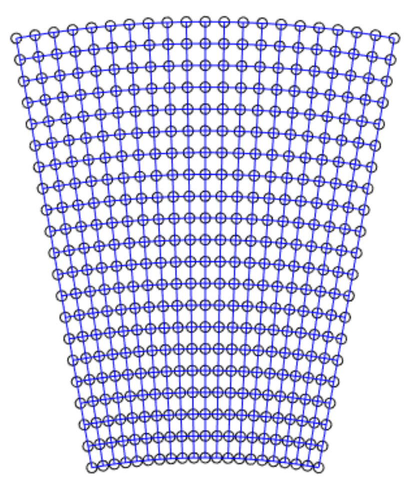


Figure 12: Mesh of 20x20 bilinear quadrilaterals for the coupled problem

5.2 Method

The weak form of the equations for $\mathbf{u}$:

$$(w, \nu\nabla^2 v) - (w, \mathbf{T}_m) = (w, \nabla \cdot \boldsymbol{\sigma_m}) \tag{9}$$

For F-actin

$$\begin{aligned}(w, \Delta\mathbf{F}) + \frac{\Delta t}{2}(w, \mathbf{u} \cdot \nabla\Delta\mathbf{F}) - (w, \nabla \cdot (D_F \nabla\Delta\mathbf{F})) + (w, \sigma_F \Delta\mathbf{F})) = \\ = -\Delta t(w, \mathbf{a} \cdot \nabla\mathbf{F}^n) - (w, \nabla \cdot (D_F \nabla\mathbf{F}^n)) + (w, \sigma_F \mathbf{F}^n)\end{aligned} \tag{10}$$

and for G-actin

$$\begin{aligned}(w, \Delta\mathbf{G}) - \frac{\Delta t}{2}((w, \nabla \cdot (D_G \nabla\Delta\mathbf{G})) + (w, \sigma_G \Delta\mathbf{G})) = \\ = -\Delta t(-(w, \nabla \cdot (D_F \nabla\mathbf{G}n)) + (w, \sigma_G \mathbf{G}^n) - \frac{1}{2}(w, \hat{\sigma}_{FG}(\mathbf{F}^n + \mathbf{F}^{n+1})))\end{aligned} \tag{11}$$

And in matricial form:

$$\begin{cases} \nu\mathbf{K}_v\mathbf{u} - \mathbf{T}_U\mathbf{u} = \mathbf{T}_F\mathbf{F} \\ (\mathbf{M} + \frac{\Delta t}{2}(\mathbf{C} + \mathbf{K} + \sigma_F\mathbf{M}))\Delta\mathbf{F} = -\Delta t(\mathbf{C} + \mathbf{K} + \sigma_F\mathbf{M})\mathbf{F}^n \\ (\mathbf{M} + \frac{\Delta t}{2}(\mathbf{K} + \sigma_G\mathbf{M}))\Delta\mathbf{G} = -\Delta t(\mathbf{K} + \sigma_G\mathbf{M})\mathbf{G}^n + \frac{\Delta t}{2}\sigma_{FG}\mathbf{M}(\mathbf{F}^n + \mathbf{F}^{n+1}) \end{cases}$$

Due to the fact that the equations are coupled, in order to solve them for the step n+1 we will perform an iterative process per every timestep. Starting with a guess for the velocity field $\mathbf{u}$, we will iteratively compute the F-actin density $\mathbf{F}$ (second equation) to update $\mathbf{u}$ until the increment between trials is lower than 10^{-6}. This way, we will be sure that our final velocity field gives for the step n+1 the correct F-actin density.

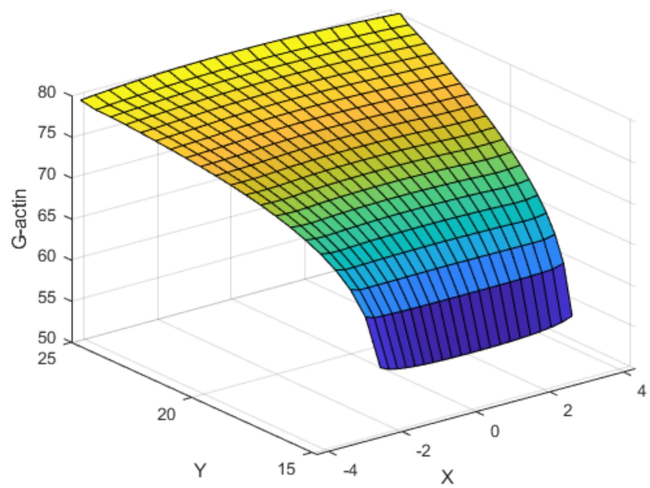
This iterative scheme will look like:

FOR EVERY TIMESTEP

1. $v^k_{guess} \rightarrow F^{n+1}_{guess} \rightarrow v^{k+1}_{guess}$
2. while $\|v^k_{guess} - v^{k+1}_{guess}\| \geq 10^{-6}$ GO TO 1
3. else $\rightarrow v^{n+1} = v^{k+1}_{guess} \rightarrow F^{n+1} \rightarrow G^{n+1}$

5.3 Results

The results of the computation are unexpectedly far from those found on the previous points. With respect to the density of F-actin, results can be seen in figure 13, The distribution is more or less constant if compared to the solution in figure 4. While in the first case F-actin rapidly went to zero, in this case it has values between 80 μM and μM. Because of these high concentrations of F, the distribution of G is dramatically changed, too. If in previous results maximum values were under 12 μM, in this case they are around 180 μM.



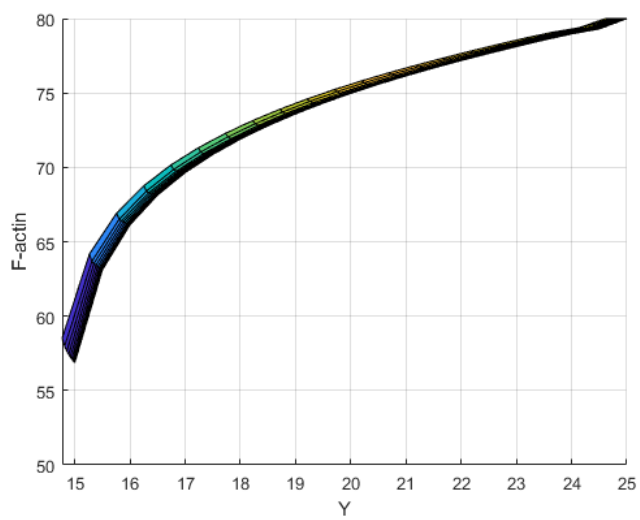


Figure 13: Skewed and side views of F-actin density. Values range from 80 to 57 μM

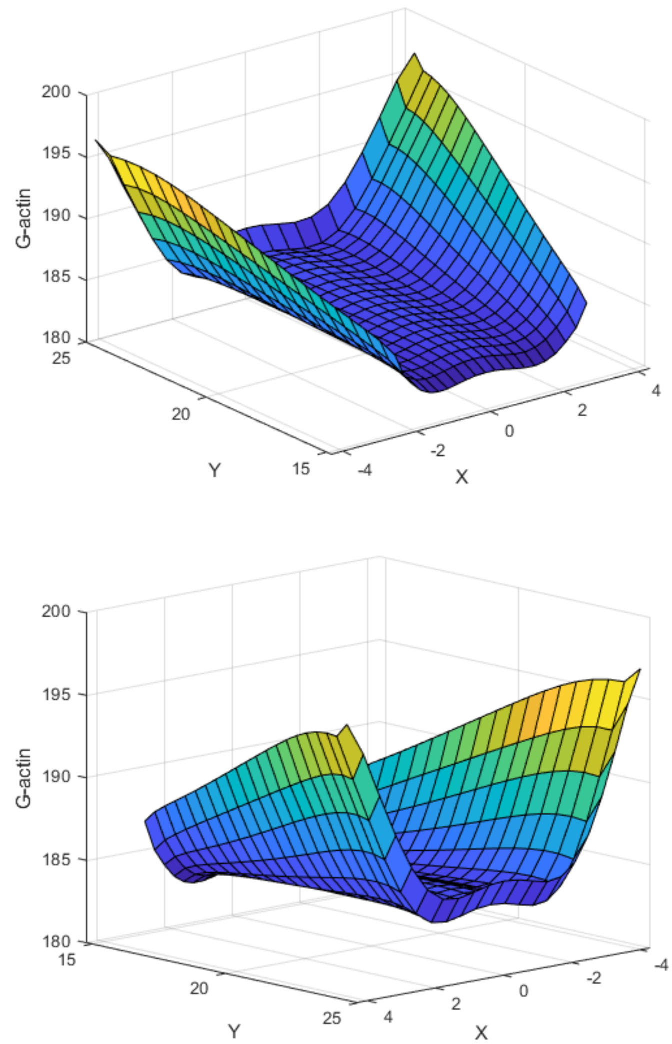


Figure 14: Skewed and side views of F-actin density. Given the high amount of F-actin that was computed, the values are completely different from the previously calculated

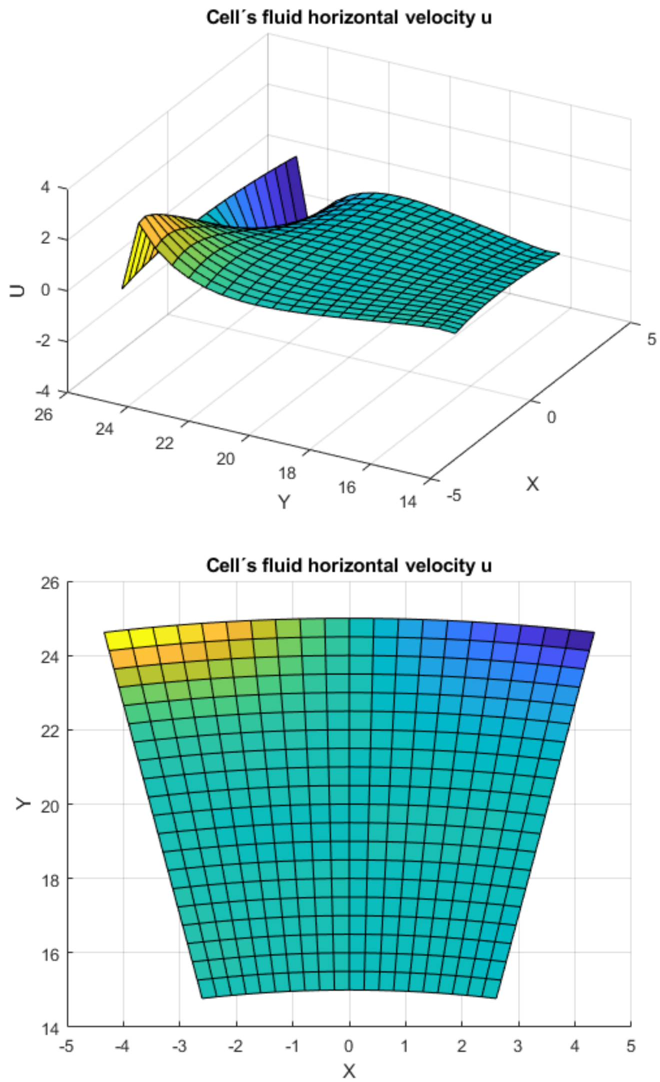


Figure 15: Skewed and top views of horizontal velocity

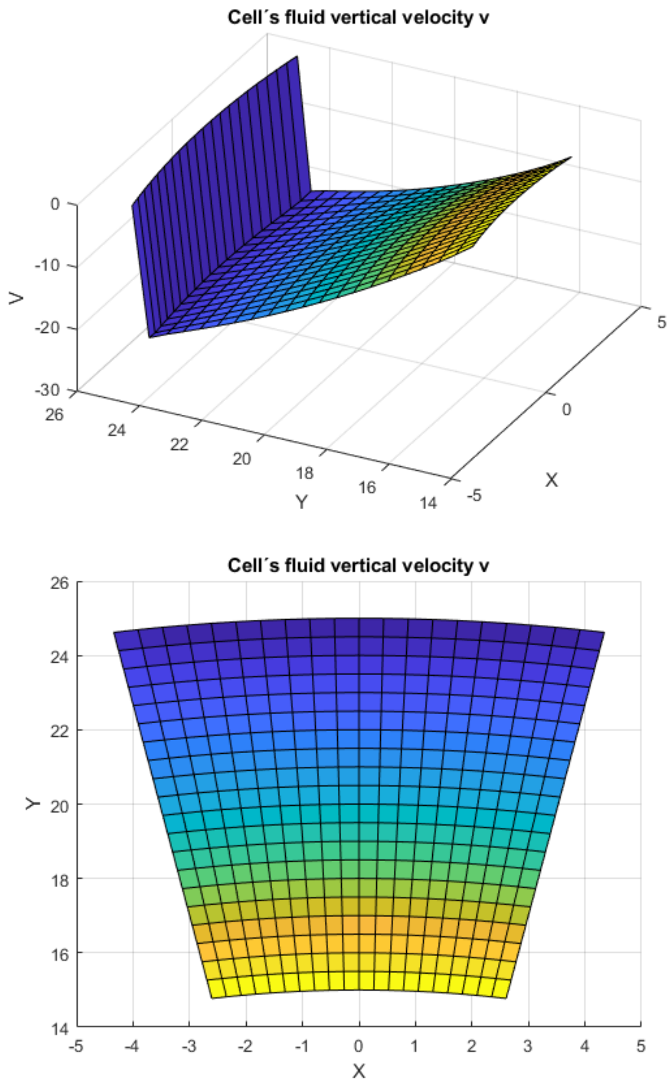


Figure 16: Skewed and top views of horizontal velocity

The velocity field is rapidly stabilized, due to the short time with which F-actin is arriving to the steady state. Figures 15 and 16 show the velocity field, that is constant for the whole analysis. Notice how it is also different from the field in section **4: STOKES PROBLEM**. In this case is almost in the direction of the Y axis and there is a huge jump between velocity at the top boundary and the rest of the domain.

6 Conclusions

For the first two exercises, the analysis show that the actin density gradient goes in the opposite direction of the cell's fluid. Also, and given the model's simple geometry, we can reduce the size of the problem by applying symmetry conditions: For a radial velocity field, we have a 1D problem, and if not, we can always apply symmetry with respect to the Y axis.
With respect to the distribution of actin (1^{st} problem), we can see that G, whose changes depend on the concentration of F, follows its evolution in time. The velocity and specially the pressure (2^{nd} problem) suffer from boundary effects. The velocity shows a sudden change in its horizontal direction and the pressure values at the corners are completely spoiled.
The coupling of the problems yields a solution incompatible with the previous results, and it can be reasonabily considered invalid. Not only the actin densities are completely different from the other results, but the velocity is around 100 times higher in a vast part of the domain. Also, the coupled problem reaches the steady state almost instantaneously, a result which again is quite different from the other problems'. We can consider that we failed to solve this third problem and that our solution for this one should not be taken into account.
When looking at the solution, it is sensible to think on the velocity solver as the main cause of discrepancies between solutions, as the rest of the equations have not been modified.