Isogeometric Analysis For The Platelets Role On Shear Stress Effect Over The Cancer Cells Into The Blood Vessel

José A. Rodrigues[1 2]

[1]*Centro de Investigação em Matemática e Aplicações (CIMA)*
Évora, Portugal
[2]*Dept. of Mathematics, Instituto Superior de Engenharia de Lisboa (ISEL), Instituto Politécnico de Lisboa, Lisboa, Portugal*
jose.rodrigues@isel.pt

Abstract. The spread of cancer cells from the original place to another part of the body is known by metastasis. During this processes, cancer cells leave from primary tumor, travel through the blood or lymph system, and form a new tumor in other organs or tissues of the body. Before arrive to new tissues, the cancer cell are subject to the natural body defenses. Once inside the blood vessel, the cancer cells are subject to the shear forces and immune defenses. Recent works induce that platelets play a relevant role in the protection of the cancer cell clusters while in circulation, protecting them from the effects of shear force by forming clumps with the cancer cells.

Using Isogeometric analysis, for modelling complex geometries, we numerical study the shear stress effect over the cancer cells on interstitial medium on later works. With the present work we pretend continue the numerical investigation, through the development and analysis of a mathematical model, for the shear stress effect over the cancer cells into the blood vessel and quantify the platelets protection effect.

Keywords: Isogeometric analysis, Shear stress, Metastasis,Cancer cells, Blood flow, Navier-Stokes equations

1 Introduction

During metastasis, cancer cells must detach from the primary tumor and intravasate into circulation, where tumor cells encounter immune cells and experience fluid shear stress.

Cancer studies suggested the role of platelets in metastasis [1]. When tumor cells detach from the primary tumor and intravasate into the blood vessels, there is a high probability that they will be destroyed due to high shear stress exerted by the blood flow and the endothelium lining the blood vessels, or due to the immune response of the body. However, it has been suggested that because the platelets adhere to circulating tumor cells (CTCs), immune cells cannot recognize CTCs and as a result, the survival rate of CTCs increases.

Additionally, even if leukocytes recognize CTCs by any chance, they do not have access to destroy them because platelets act as a barrier in front of them. Moreover, the platelet shield around CTCs has been proposed to protect CTCs from shear stress by reducing the exerted force [2].

We refer that blood is a non-Newtonian fluid and blood vessels are not rigid tube. Although blood is the non-Newtonian fluid [3], in this study will considered the blood as Newtonian fluid (properties of blood become linear) which is governed by the Navier-Stokes equation and the continuity equation for solving blood flow problems.

With this work, we will continue further work [4] we present the prelimenary results on the study of the effect of shear stress on cancer cell proliferation. We present a numerical study leading to the quantification of the effect of shear stress on CTCs after a platelet aggregation process.

2 Numerical results

We used as a model the Navier-Stokes equations formulated on the velocity $\vec{u} = (u_x, u_y)$ and pressure p, as introduced in [5] , as well as the parameters considered.

With the solution, $\vec{u}$ we evaluate the fluid shear stress. For two-dimensional Newtonian fluid the Stress is written

$$T_{xy} = \frac{\nu}{2}\left(\frac{\partial u_x}{\partial y} + \frac{\partial u_y}{\partial x}\right) \tag{1}$$

wher ν is the viscosity of the fluid.

One use GeoPDEs for the Isogeometric Analysis numerical implementation [6].

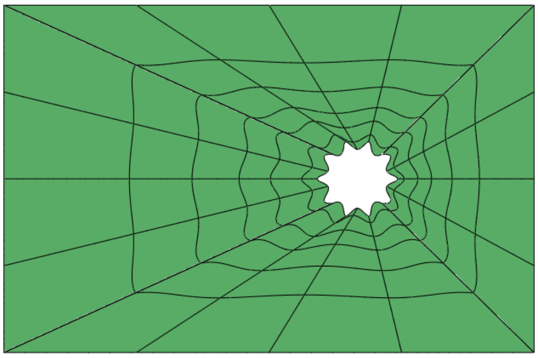

Figure 1. CTCs IGA mesh outline.

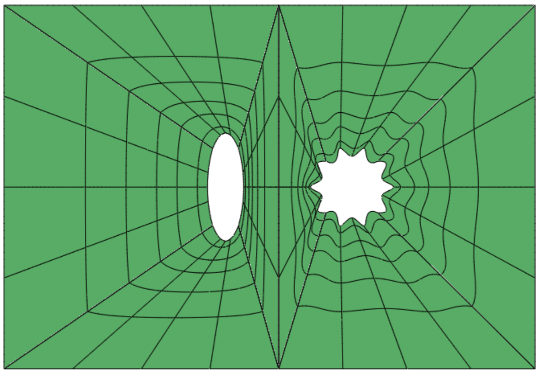

Figure 2. Platelet agglomerate (on the left) CTCs IGA mesh outline (on the right).

Following the figures 3-5, we observe the evident protection provided by the platelet agglomerate to the set of CTCs.

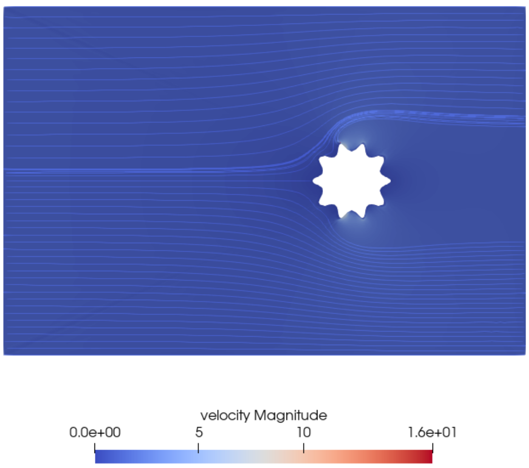

Figure 3. The velocity representation with stream lines without platelet aggregation.

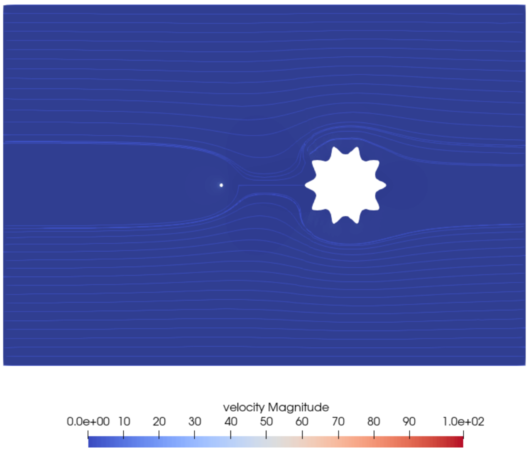

Figure 4. The velocity representation with stream lines with the platelets occupying the area $3.1\mu^2$.

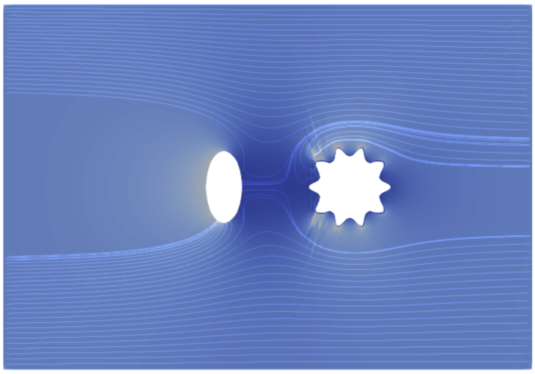

Figure 5. The velocity representation with stream lines with the platelets occupying the area $6.2\mu^2$.

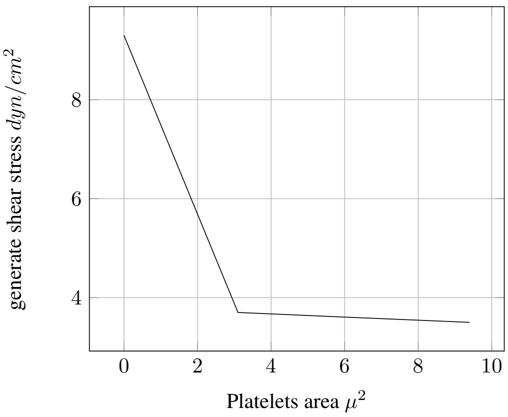

Figure 6. Comparison of the evolution of the area occupied by platelets with the shear stress effect.

The agglutination of platelets together with the CTCs induces a certain protection against the shear stress effect. In Figures 3 to 5, the CTCs are represented on the left, with natural roughness, which favors the shear stress effect. The increasing agglutination of platelets is represented on the right, in the same sequence of figures. In figure 6 we see the evolution of the shear stress effect depending on the area occupied by the platelets. It is noteworthy that the membrane of cancer cells collapses when shear stress reaches $0.55\ dyn/cm^2$ [4].

3 Conclusions

With these numerical results we obtained a quantification of the effect of platelet agglomeration on CTCs. Extraordinary platelet production and subsequent agglutination to CTCs evidence the need for protection of tumor cells. Preliminary results encourage further quantification of this platelet-CTC relationship.

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