SIMULATION OF ANGIOGENESIS DURING TUMOUR GROWTH PROLIFERATION

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Introduction

During tumour growth, when tumours achieve a critical size, their growth tends to stop due to poor blood supply, as it is dependent on a direct supply of nutrients [1, 2]. In these situations, tumour cells become capable of secreting tumour angiogenic growth factors that stimulate endothelial cells to initiate the process of angiogenesis [3]. During this process, endothelial cells proliferate and migrate towards the tumour cells, creating a new vessel network that will supply them and support their continued growth [1, 3]. The development of new mathematical and computational models to describe tumour-induced angiogenesis increased in the last years and currently, researchers seek to increase their accuracy by making them able to cover a growing number of biological phenomena [5]. As predictable tools of these phenomena, they have already proven their potential [6]. Different numerical methods have been used to solve these models. One popular example is the Smoothed Particle Hydrodynamics (SPH), a meshless discrete method [7]. The present work aimed to implement the process of angiogenesis in a previously developed 3D algorithm that simulates cell proliferation. This process was activated by VEGF concentration and different values and different locations for the focus of concentration were tested in order to see their influence on the growth of new vessels.

Methods

To discretize the domain, the SPH resorts to particles without a pre-established connection and uses them to obtain the approximation functions and to approximate the field function [7]. The algorithm combines four different types of particles: cell, extracellular matrix, boundary and blood vessel. The particle at the center of the domain was defined as cell and, after obtaining the initial velocity, internal pressure and acceleration of all particles, the cell was allowed to grow and divide, generating new cells in the domain, following an exponential growth. A VEGF gradient was also initially defined along the whole domain and the main concentration was defined in the area occupied by the cells. As the cell proliferates, and following the focus of VEGF concentration, a blood vessel was created.

Results

To verify the viability of the algorithm, different simulations were performed in order to verify if correct vessel growth was achieved along the iterations and following the growth of the cells. In all cases, the vessel grew towards the direction of the cells, which were defined as the source of concentration of VEGF. This growth was controlled by the growth of the cells so it did not occur in all iterations but only in specific ones. Different concentrations of VEGF and different positions of the focus of concentration were tested in order to verify their influence in the process of angiogenesis, namely, in the direction of the growth of the vessel. It tended to grow in the direction of areas where the concentration of VEGF was higher, which represented the location of the different focuses of concentration that were defined in each simulation.

Discussion

The process of angiogenesis was simulated in combination with the process of cell proliferation in a single algorithm. The new part of the algorithm, i.e. the angiogenesis process, was dependent on cell proliferation since the cells were the source of VEGF, which is the factor that stimulates vessel growth. Such is in accordance with what is defined in the literature. The direction of the growth was also coherent with the focus of concentration, as defined in the algorithm. The obtained results were satisfactory even if there is still room for improvement for the algorithm in future work.

References

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Acknowledgements

The authors acknowledge the funding provided by Ministério da Ciência, Tecnologia e Ensino Superior – Fundação para a Ciência e a Tecnologia (Portugal), under grants: SFRH/BD/146272/2019, and by LAETA, under project UIDB/50022/2020.