## Predicting the Growth of Glioblastoma Multiforme Spheroids using a Multiphase Porous Media Model

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## ABSTRACT

Recently, a computational model based on the thermodynamically constrained averaging theory [1] has been proposed to predict tumor growth and its interaction with the host tissue [2,3].

Inspired by this work, herein we present a simplified version of the original model, adapted for tumor spheroids growth and its experimental validation. In the framework of porous media theory, we model tumor cells (TC) and interstitial fluid (IF) to fill the voids left by the extracellular matrix (ECM), which represents the solid skeleton of the porous medium. The evolution of a nutrient species (nl) is also taken into account, allowing the TC to become necrotic after the exposure to low level of nutrient. A constitutive relationship from [4] is also adapted to close the system of equations, and the numerical problem is solved by finite differences.

Moreover, a set of experiments with multicellular tumor spheroids (MTS) is performed to validate the model *in vitro*. Our results point out that there exists a characteristic asymptotic value for the MTS radius and, by a combination of numerical and analytical techniques, we can derive an expression for predicting this value, which is in quantitative good agreement with the experimental observations. Finally, we study the effects of the parameters that appear in this expression on the growth of the tumor, and we look for conditions that may inhibit tumor expansion.

As it is becoming increasingly clear that the interactions between the tumor and its environment affect critically the growth of the malignant mass [5,6], future developments of the model will be addressed to investigate these interactions and their effect on tumor behavior.

## REFERENCES

[1] Gray, W. G., & Miller, C. T. (2005). Thermodynamically constrained averaging theory approach for modeling flow and transport phenomena in porous medium systems: 1. Motivation and overview. *Advances in Water Resources*, 28(2), 161–180. doi:10.1016/j.advwatres.2004.09.005

- [2] Sciumè, G., Shelton, S., Gray, W. G., Miller, C. T., Hussain, F., Ferrari, M., ... Schrefler, B. a. (2013). A multiphase model for three-dimensional tumor growth. *New Journal of Physics*, 15(1), 015005. doi:10.1088/1367-2630/15/1/015005
- [3] Sciumè, G., Gray, W. G., Hussain, F., Ferrari, M., Decuzzi, P., & Schrefler, B. a. (2013). Three phase flow dynamics in tumor growth. *Computational Mechanics*, 53(3), 465–484. doi:10.1007/s00466-013-0956-2
- [4] Byrne, H., & Preziosi, L. (2003). Modelling solid tumour growth using the theory of mixtures. Mathematical Medicine and Biology, 20(4), 341–66. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/14969384
- [5] Chauhan, V. P., & Jain, R. K. (2013). Strategies for advancing cancer nanomedicine. Nature Materials, 12(11), 958–62. doi:10.1038/nmat3792
- [6] Delarue, M., Montel, F., Caen, O., Elgeti, J., Siaugue, J., Vignjevic, D., & Prost, J. (2013). Mechanical Control of Cell flow in Multicellular Spheroids, 138103(March), 1–5. doi:10.1103/PhysRevLett.110.138103