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Data Driven Tumor Growth Modelling: mechanics of multiphase systems and model reduction for personalized medicine

Trade-off between machine learning and physics-based modelling in oncology

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We seek a PhD student jointly between University of Luxembourg and ENSAM.
In Luxembourg, the student will join the Computational and Data Science Doctoral Programme, along with over 40 other candidates from multi-disciplinary backgrounds and a dynamic team of computational mechanics researchers. In France he/she will enrol in the doctoral school '*Sciences des Métiers de l'Ingénieur*' of ENSAM, a leading French engineering school for mechanics, energetics and industrial design; this joint doctorate agreement allows for delivering of the Luxembourgish and French PhD degrees.

Abstract

Advances in oncological research have clearly shown that beyond chemical and biological factors, mechanics and physics have a substantial role in tumor growth. The tumor mass is indeed a thermodynamical system interacting with the host tissue and its vascular and lymphatic system with which it exchanges mass and energy [1, 2]. For these reasons, over the past decade, an increasing number of mathematicians, physicists and research engineers is becoming involved in oncology research, which is nowadays, especially in the US, profoundly multidisciplinary.

Within this context, mathematical modeling of tumor growth plays a key role in the development of new therapeutic strategies. A new scientific research domain is emerging: "transport oncophysics".

A mathematical model for tumor growth has been recently developed by **the prospective PhD supervisor** G. Sciumè et al. [3-8] (I2M-Bordeaux). In this model tumor tissue and its microenvironment are treated as a deformable porous medium permeated by three immiscible complex fluids (healthy tissue cells, cancer cells, and interstitial fluid). The proposed model is very general, and with its specificities, is currently one of the most complete tools existing in literature. Some of the constitutive equations used in this theory have been derived exploiting **strong mathematical formulation analogies** between the problem of tumor growth and that of flows in soils and / or geomaterials [9].

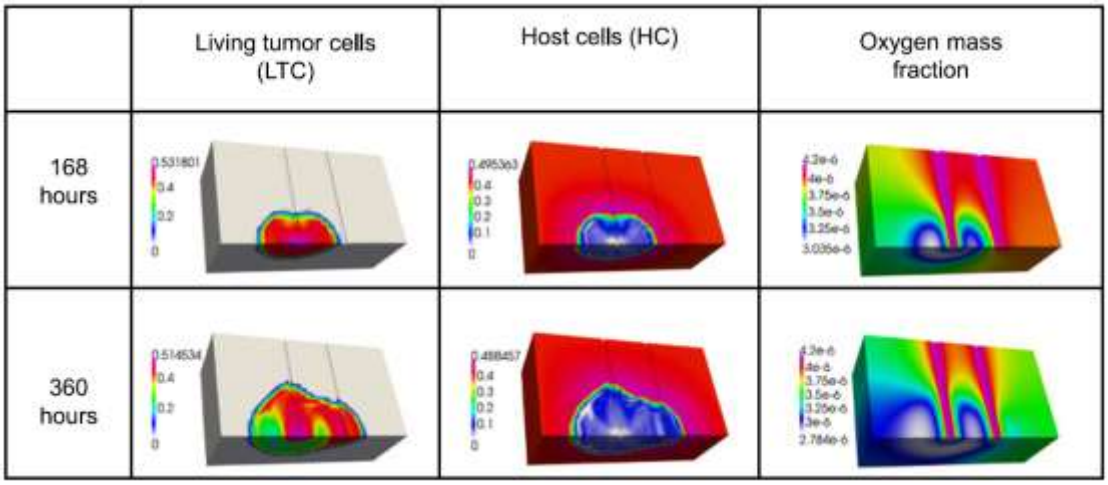

Figure 1 – Tumor growing in proximity of two healthy blood vessels

Employing recent mechanistic experimental results (*e.g.* [10]) and fresh data on tumor growth in confined environments (research team of P. Nassoy at Optics Institute of Aquitaine), the first objective of the PhD thesis is therefore to study - and improve when necessary - the consistency of adopted constitutive laws. Attention will be paid on identifying the physical and biological properties that have a major influence on tumor growth and invasion. Moreover, the PhD candidate will investigate the tradeoff between "data-driven prediction" based on machine learning algorithms, and "physics-based modelling" where tumor growth is modelled from first principles.

In parallel with the validation/improvement of the cell migration model, setting up the model and associated methodologies for clinical use is the second objective of the PhD thesis. Machine learning, Bayesian inverse problems for parameter identification and model order reduction for the free boundary problem of interest will be implemented by the PhD student. This will be facilitated by the collaboration between the Legato Team led by S. Bordas (http://legato-team.eu partner team in this project) and the research team of W. Skalli and PY Rohan of the l'Institut de Biomécanique Humaine Georges Charpak (IBHGC).

This work will give to the model the needed flexibility for use in personalized/precision medicine by striking the required balance between physics-based modelling and machine learning algorithms. The relevance of the developed approach will be tested on cases of tumor growth in bone tissue. Clinical and experimental data will be provided by partner university-hospital teams in Paris and Bordeaux and processed by the doctoral student jointly with a research master student at IBHGC. These data will allow characterizing material and geometry and to build the personalized FE mesh at the macroscopic level. A major issue will be to establish the correct degree of detail of the model by identifying the phenomena/factors having a predominant impact on tumor growth and those that can be disregarded. This will be done using recent work performed at the Legato Team. A multi-scale model based on a structural zoom can be also considered.

REFERENCES

[1] Michor F., Liphardt J., Ferrari M. & Widom J.(2011). What does physics have to do with cancer? *Nature Reviews Cancer*.

[2] Ferrari M, (2010). Frontiers in cancer nanomedicine: directing mass transport through biological barriers. *Trends in Biotechnology*.

[3] Sciumè G, (2013). THCM model of concrete at early ages and its extension to tumor growth numerical analysis. *PhD Thesis Univ. of Padua & ENS-Cachan*.

[4] Sciumè G., Shelton S., Gray W. G., Miller C. T., Hussain F., Ferrari M., Decuzzi P., Schrefler B. A. (2012). Tumor Growth Modeling from the Perspective of Multiphase Porous Media Mechanics. *Molecular & Cellular Biomechanics.*

[5] Sciumè G, Shelton S., Gray W. G., Miller C. T., Hussain F., Ferrari M., Decuzzi P., Schrefler B. A. (2013). A multiphase model for three-dimensional tumor growth. *New Journal of Physics.*

[6] Sciumè G., Gray W. G., Ferrari M., Decuzzi P., Schrefler B. A. (2013). On Computational modeling in tumor growth. *Archives of Computational Methods in Engineering.*

[7] Sciumè G., Gray W.G., Hussain F., Ferrari M, Decuzzi P, Schrefler B. A. (2014). Three phase flow dynamics in tumor growth. *Computational Mechanics.*

[8] Sciumè G., Santagiuliana R., Ferrari M., Decuzzi P., Schrefler B. A. (2014). A tumor growth model with deformable ECM. *Physical Biology*.

[9] Sciumè G., Ferrari M., Schrefler B.A. (2015) Saturation–pressure relationships for two- and three-phase flow analogies for soft matter. *Mechanics Research Communications*.

[10] Nia H., Liu H., Seano G. et al. (2016) Solid stress and elastic energy as measures of tumour mechanopathology. *Nature Biomedical Engineering*.

[11] Pottecher P, Engelke K, Duchemin L, Museyko O, Moser T, Mitton D, Vicaut E, Adams J, Skalli W, Laredo JD, Bousson V. (2016) Prediction of Hip Failure Load: In Vitro Study of 80 Femurs Using Three Imaging Methods and Finite Element Models-The European Fracture Study (EFFECT). *Radiology 280(3):837-47*.

[12] Vardakastani V, Saletti D, Skalli W, Mary P, Allain JM, Adam C. (2014) Increased intra-cortical porosity reduces bone stiffness and strength in pediatric patients with osteogenesis imperfecta. *Bone 69:61-7*.

[13] Sapin-de Brosses E, Jolivet E, Travert C, Mitton D, Skalli W. (2012) Prediction of the vertebral strength using a finite element model derived from low-dose biplanar imaging: benefits of subject-specific material properties. *Spine 37(3):E156-62*.

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PROJET INFORMATIONS – JOINT DOCTORATE

Scientific consortium	ENSAM (I2M - IBHGC) & Université du Luxembourg (*Legato Team*)
Involved Persons	Giuseppe SCIUME (ENSAM / I2M) Wafa SKALLI (ENSAM / IBHGC) Pierre-Yves ROHAN (ENSAM / IBHGC) Stéphane BORDAS (Université du Luxembourg) Paul HAUSEUX (Université du Luxembourg)
Scientific domain	Transport oncophysics, multiphase modeling, optimization, model order reduction, uncertainties quantification, clinical biomechanics
Suitable applicant	Skills in Continuum Mechanics and Applied Mathematics
Starting date PhD	October 2018
Research Collaborations	• *Laboratoire de l'Angiogénèse et du Microenvironnement des Cancers* (Inserm U1029) (Andreas Bikfalvi & Thomas Daubon) • *Institut d'Optique d'Aquitaine* (Pierre Nassoy) • Professor Thomas SAUTER and Dr Marco ALBRECHT, Life Science Research Unit, University of Luxembourg • Dr. Davide BAROLI, Legato Team, Institute of Computational Engineering Sciences, University of Luxembourg.

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