



## A multiphase porous media model for transport oncophysics

Cancer is an extraordinarily complex disease. It is now recognized that methods commonly used in physics can help to reduce the complexity of cancer to a manageable set of underlying principles and phenomena. Physical properties of biological barriers control cell, particle, and molecule transport across tissues and this transport and its deregulation play an overarching role in cancer physics and drug delivery. Transport Oncophysics views hence cancer as a disease of multiscale mass transport deregulation involving biological barrier. Computational Transport Oncophysics provides the computational tools which, together with imaging, analysis and quantification, will contribute to rationalize the delivery of therapeutic agents and to evaluate their efficiency, forming an oncophysical modeling framework. This framework should comprise a tumor growth model within the local tumor environment, coupled with a patient specific biodistribution model. For the first one we present a very general multiphase flow model in an extracellular matrix (ECM), dealt with as a deforming porous solid which may undergo remodeling; it comprises three fluid phases, i.e. tumor cells (TCs), divided into living and necrotic cells, healthy cells (HCs) and interstitial fluid (IF). The IF transports chemical species such as tumor angiogenic factor (TAF), nutrients and therapeutic agents. Transport of these species within extravascular space takes place by convection and diffusion. Coopted blood vessels are included as line elements with blood flow exchanging nutrients and therapeutic agents with the IF. Angiogenesis is represented by the blood vessel density (density of newly created endothelial cells). The model accounts not only for growth and necrosis but also for migration of cells through the ECM, for different stiffness of the cell population with respect to the ECM, build-up of cortical tension between healthy and tumor tissues and possible invasion of the tumor tissue by the healthy tissue or vice versa, mediated by these cortical tensions. Further it allows for modeling lysis, adhesion of the cells to their ECMs as well as adhesion among cells and possible detachment. Several examples show the possibilities offered by such a model.

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