Computational models for fluid exchange and bio-chemical transport between microcirculation and tissue interstitium. A study of drug delivery strategies to target tumors

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Starting from the fundamental laws of filtration and transport in biological tissues, we develop a mathematical model able to capture the interplay between blood perfusion, fluid exchange with the interstitial volume, mass transport in the capillary bed, through the capillary walls and into the surrounding tissue. These phenomena are accounted at the microscale level, where the capillary bed and the interstitial volume are viewed as two separate regions. The capillary bed is described as a network of vessels carrying blood flow.

We apply the model to study drug delivery to tumors. Owing to its general foundations, the model can be adapted to describe and compare various treatment options. In particular, we consider drug delivery from bolus injection and from nanoparticles, which are in turn injected into the blood stream. The computational approach is prone to perform a systematic quantification of the treatment performance, enabling the analysis of interstitial drug concentration levels, drug metabolization rates, cell surviving fractions and the corresponding timecourses. Our study shows that for the treatment based on bolus injection, the drug dose is not optimally delivered to the tumor interstitial volume. Using nanoparticles as intermediate drug carriers overrides the shortcomings of the previous delivery approach.

The present work shows that the proposed theoretical and computational framework represents a promising tool to compare the efficacy of different treatments of cancer based on chemotherapy. Being directly derived from the fundamental laws of flow and transport, the model may be adapted in future to study different types of cancer, provided that suitable metrics are available to quantify the transport properties of a specific tumor mass.