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Data-integrated tracer transport simulations in brain tissue: vascular networks, perivascular spaces, extra-vascular tissue

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Tracer experiments are used to assess the transport of solutes and water in brain tissue. Only sparse information is available about the mechanisms and major pathways of water and some solutes entering (infiltration, perfusion) and leaving (clearance) the functional brain tissue. Moreover, there are three main issues with current experimental data when it comes to the quantification of transport: (1) the underlying anatomy and transport pathways are complex (e.g. microvascular networks) but is believed to be crucial in facilitating transport, (2) the measured tracer transport is usually only a proxy of what we are interested in (e.g. water transport), (3) the tracer transport can often not be assessed directly but is to be inferred from a proxy signal (e.g. NMR signal or fluorescence microscope image).

In an attempt to bridge scales, fill in missing data, and connect various data sources, we present a mathematical model to perform virtual tracer perfusion simulations in brain tissue. We consider the architecture of microvascular networks [1] and a parametrization of the model based on a combination of experimental data and computational estimation [2]. The mathematical model is a three-compartment model (vascular, para-vascular, extra-vascular) formulated as a coupled mixed-dimensional system of partial differential equations. Advanced discretization techniques [3] and software [4] for flow and transport in porous media with embedded transport network systems allow for simulating domains with thousands of blood vessels.

In comparison with two-photon microscopy image data in live sleeping and awake mice [5], we discuss the role of compartmentalized molecular diffusion and dispersion driven by arterial pulsations. We show that due to the low volume fraction of the perivascular space, transport into the tissue only appears enhanced if there is a significant mixing effect due to arterial pulsations. We discuss major difficulties arising when comparing simulation results to the image data and demonstrate how image data may be subject to misinterpretation in a lack of careful consideration of supporting information in the imaging process.

Participation

In-Person

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