Computational analysis of energy metabolism at different scales

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We develop a three-dimensional spatially distributed model of cellular brain energy metabolism and investigates how the locus of the synaptic activity in reference to the capillaries and diffusion affects the behavior of the model, a type of analysis which is impossible to carry out in spatially lumped models, which are shown to be consistent spatially averaged approximations of the distributed model. To avoid a geometrically detailed modeling of the complex structure of the tissue consisting of different cell types and the extracellular space, inspired by the bi-domain approach to describing the electric properties of cardiac tissue, the distributed model is based on a novel multi-domain formulation of reaction-diffusion equations, accounting also for separate mitochondria. The model reduction relating the spatially distributed model and lower dimensional reduced models, including the well-mixed spatially lumped compartment model, is carefully explained. We illustrate the effects of losing the spatial resolution with a computed example which is based on a reduced one-dimensional distributed radial model, and looks into how the model behaves when the locus of the synaptic activity in reference to the capillaries is changed. By averaging the fluxes and concentrations in the distributed radial model to correspond to quantities in a lumped model, and further by estimating the parameters in the lumped, we conclude that varying the locus of the synaptic activity in reference to the capillaries alters significantly the lumped model parameters. This observation seems to be consequential for parameter estimation procedures from data when the spatial resolution is insufficient to determine the locus of the activity, indicating that the model uncertainty is an inherent feature of lumped models.