Bayesian Model Selection for Brain Metabolism

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The inverse problem of estimating metabolic fluxes for brain metabolism is important, among other things, to test the validity of different hypotheses that have been proposed in the literature. The question of how the neuron is supported during neural activity has recently received a lot of attention and two main hypotheses have emerged. The classical hypothesis supports the primacy of glucose as main fuel for active neurons while the astrocyte-neuron lactate shuttle hypothesis (ANLSH) supports the lactate as preferred substrate by neurons. In this talk we will describe a five compartment model of brain metabolism which considers, in addition to the blood compartment, the cytosol and mitochondria of both astrocyte and neuron, including detailed metabolic pathways. We use a recently developed methodology to perform flux balance analysis (FBA) and to test whether one of these hypotheses is more in agreement with measured data. We recast the estimation problem in the form of Bayesian statistical inference and by a Markov Chain Monte Carlo (MCMC) sampling method we estimate simultaneously all the reaction fluxes and transport rates at steady state, under different levels of neural activity. The analysis of the histograms of the posterior distributions provides a useful tool for assessing the validity of different hypotheses and to detect preferred metabolic pathways that are in agrement with experimental data.

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