The effect of extracellular volume on the energy balance of neurons

Extracellular space is a largely unexplored domain of neuroscience, even though it is the site of many pathologies, such as the deposition of proteins in neuro-degenerative diseases. Remarkably, its volume seems not to be constant but to expand and contract during sleep. The goal of this project is to build and simulate computer models to predict the change in energy balance accompanying these changes in the volume of extracellular space (as compared to the intra-cellular volume of neurons and glial cells).

Neurons, like other cell types, generate ionic concentration gradients across their cell membrane by accumulating K^+ inside and extruding Na^+ outside. This pumping process consumes more than half of a neuron's metabolic energy. Maintenance of this gradient is essential for the electrical signalling between neurons, and for brain function in general.

An open but intriguing question is how much of the energy stored in the ionic concentration gradients can be retrieved during periods of stress (neuron hyperactivity during epileptic seizures, oxygen deficiency during stroke, etc.). Understanding the mechanisms involved in this energy retrieval would lead to the development of new therapies.

A number of studies have modelled the membrane pumps, ion channels and transporters involved in this energy balance (see references below), but most of these studies considered only intra-neuronal ionic homeostasis, assuming in contrast that extracellular space is an infinite reservoir of constant ionic composition. Actual interstitial space, however, occupies only 20 % of the brain's volume, and theoretical calculations by our group show that the size of its volume may considerably affect the amount of energy that can be stored and retrieved.

This project requires a good knowledge of electrophysiology (membrane potential, ion channels, etc.) and the underlying physics, basics of biochemistry and thermodynamics (Gibbs free energy), and programming skills in a major computer language.

This work will be conducted in the Bio-computation Research Group of the Department of Physics, Engineering and Computer Science at the University of Hertfordshire (College Lane campus).

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