Modeling Neuron-Astrocyte Metabolic Interactions: From Hodgkin-Huxley to the BOLD Signal

Renaud Jolivet\textsuperscript{1,2}, and Pierre J. Magistretti\textsuperscript{1,2}

\textsuperscript{1}Ecole polytechnique fédérale de Lausanne, Switzerland
\textsuperscript{2}Université de Lausanne, Switzerland

In recent years, accumulating evidences have shown that astrocytes play a critical role at synapses and in providing energy substrates for neurons\cite{1}. Despite the ongoing revolution regarding their role in the nervous system, astrocytes have attracted only very little attention from the computational neuroscience community.

In order to study how neurons and astrocytes modulate imaging signals like the BOLD signal, we developed a mathematical model of the metabolic neuron-astrocyte interactions. Our model is based on recent work by Aubert and Costalat connecting the principal metabolic pathways to the cerebral blood flow\cite{2}. The novelty is that our model is the first to bridge the gap between these approaches and the Hodgkin-Huxley model of neuronal membrane excitability. To constrain the model, it was fitted on experimental data assuming a specific steady-state. Parameters for which no precise measure is available were numerically optimized so that our model quantitatively reproduces recent results of NADH fluorescence dynamics\cite{3}.

Interestingly, the only acceptable parameter set resulting from this optimization procedure yields a model that strongly supports the astrocyte-neuron lactate shuttle hypothesis. Namely, the astrocyte continuously releases lactate that is consumed as an energy substrate by the neuron and thus even in the basal state. Moreover, the model successfully explains various experimentally observed behaviors like the biphasic dynamics of tissue lactate, the dynamics of tissue oxygen and the reduction of the oxygen-glucose index following stimulation. We propose that lactate could be used as an important vasoregulator signal potentially explaining why not all the consumed glucose is oxidized by the brain. Finally, the model allows us to decipher the contribution of the different cell types to the BOLD signal and supports the recent finding that an important part of energy demand and consequent metabolic response is linked to astrocytic activity\cite{4}.

Our results bring support for an active and central role of the astrocytes in brain energy metabolism. More important, our approach gives us the unique and novel opportunity to embrace the full range of observables and provides mechanistic insights into the existing coupling between astrocytes, pre and postsynaptic neuronal activities, cerebral blood flow and metabolism.

References

\begin{enumerate}
\item Interaction between astrocytes and neurons studied using a mathematical model of compartmentalized energy metabolism, A. Aubert and R. Costalat, \textit{JCBFM} 25:1476-1490, 2005.
\end{enumerate}