Fast nonnegative spatiotemporal calcium smoothing in dendritic trees

Eftychios A. Pnevmatikakis*, Columbia University, eftychios@stat.columbia.edu
Keith Kelleher*, University of Houston, keith.kelleher@gmail.com
Rebecca Chen, University of Houston, rlchen83@gmail.com
Krešimir Josić, University of Houston, josic@math.uh.edu
Peter Saggau, Baylor College of Medicine, psaggau@bcm.tmc.edu
Liam Paninski, Columbia University, liam@stat.columbia.edu

* Equal contributions

Summary

Understanding what triggers synaptic strength modifications *in vivo* remains a key problem in cellular neuroscience. Recent fast scanning multi-photon microscopy techniques [1] support the role of calcium as a key biochemical effector, signaling the coincident occurrence of back-propagating action potentials (bAPs) and excitatory post-synaptic potentials (EPSPs), which is a key tenet of models of STDP [2]. However, determining the entire spatio-temporal pattern of calcium influx is difficult since the available experimental techniques are noisy, sub-sampled observations of the true underlying calcium signals. It is therefore necessary to use statistical methods to infer details of calcium transients. Optimal spatiotemporal smoothing of the calcium profile on a dendritic tree given local noisy measurements remains a computationally hard problem, due to the high dimensionality and complex structure of dendritic trees.

Here we take a functional approach: The evolution of calcium concentration on the whole tree is determined from a smaller set of hidden variables that govern the calcium dynamics and incorporate possible calcium bumps due to bAPs, EPSPs or external stimulation. The observations are then expressed as linear, noisy measurements of the hidden variables. Using a state-space approach, our problem reduces to the maximum a-posteriori estimation of these hidden states and can be efficiently solved, if the prior distributions of the calcium activity and measurement noise are log-concave as a function of the hidden states. The complexity of the estimation algorithm scales linearly both with the number of time steps T over which we infer the underlying signal and with the number of hidden states d (i.e., the size of the tree), leading to a tractable overall complexity of $O(dT)$. We apply our algorithm to real reconstructed dendritic trees and find that the filtered output can quite accurately interpolate and denoise the subsampled, noisy observed spatiotemporal data.

Methods

The calcium activation is modeled as a linear combination of localized spatial functions (e.g. splines or diffusion kernels) weighted by hidden, temporal variables. As a result, the calcium profile on the whole tree is given by the multiplication of the hidden variables with a sparse tree-banded matrix. The temporal dynamics are modeled by an auto-regressive process driven by non-negative inputs that model calcium bumps. The distribution over the inputs models our prior knowledge about calcium influx and local correlations, and can be chosen to be log-concave in general. In our data the measurements, taken from a fast three-dimensional scanning microscope, have the form of emitted light at certain positions and are corrupted with highly non-gaussian, yet log-concave, noise. The MAP estimate of the hidden variables is the solution of an optimization problem, which due to log-concavity can be found efficiently using standard interior-point algorithms. Our model is of first order hidden markov form, and therefore the Hessian of the log-posterior is a block tridiagonal matrix which can be inverted in $O(d^3T)$ time and space using a forward-backward recursion (e.g. the LDL^T decomposition). As the number of compartments can often be quite large, it is important to seek methods with complexity that does *not* scale superlinearly with d. By exploiting the tree-banded structure of the problem, we find that each matrix in the LDL^T recursion is sparse and approximately tree-banded. Consequently, the complexity and space requirement can be further reduced to $O(dT)$, and therefore applied to arbitrarily complex dendritic structures and arbitrarily long experiments.

References

[1] Reddy GD et al, Nature neuroscience, 11(6):713-720, 2008.
[2] Sjöström PJ, Nelson SB, Current opinion in neurobiology, 12(3):305-314, 2002.