Rank-penalized nonnegative spatiotemporal deconvolution and demixing of calcium imaging data

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Summary

Calcium imaging is an increasingly powerful and popular technique for studying large neuronal ensembles. However, data interpretation remains challenging; the fast spiking of neurons is indirectly observed through a noisy slower calcium signal, obtained at a low imaging rate. FOOPSI [1] and "peeling" [2] are two algorithms for extracting spikes from imaging data using nonnegative sparse deconvolution. They both use a simple linear model in each pixel: upon each spike, the calcium signal increases by a fast stereotypical transient and then it decays slowly towards a baseline concentration. Although effective, these methods are typically applied on a pixel-by-pixel basis (or summed across the full ROI) and do not combine information optimally across pixels.

Here we extend FOOPSI to derive an efficient spatiotemporal deconvolution and demixing algorithm. Our key insight is that under this linear model, the spatiotemporal calcium evolution matrix has rank equal to the (unknown) number of underlying neurons. Our problem can be cast as a rank-penalized estimation of a structured matrix and solved in a relaxed form using convex optimization. Our algorithm can be parallelized by considering nonoverlapping ROIs and scales linearly with time and quadratically with the number of pixels in each ROI. Moreover, we develop a highly optimized GPU implementation.

Our algorithm leads to dramatic denoising compared to non-spatial approaches. We can further apply a nonnegative structured matrix factorization to simultaneously deconvolve and demix the spike trains, even in the presence of spatially overlapping neurons. We introduce a method-of-moments approach to fitting the model parameters that is quicker and more robust than the previous approximate expectation-maximization methods. We also derive and compare several model selection strategies (e.g., BIC, AIC, Cp). We apply our methods to simulated and in-vitro spinal cord data, for which ground truth is available via antidromic stimulation, with promising results.

Additional Details

If d is the total number of pixels, our spatiotemporal model can be described by the following equations:

noiseless, baseline-subtracted image:	$F(t) = \sum_{i=1}^{N} a_i C_i(t),$	$a_i \in \mathbb{R}^d,$ location vector for neuron i.
observed noisy image:	$Y(t) = F(t) + b + \varepsilon,$	$b, \varepsilon \in \mathbb{R}^d, b$: baseline vector, $\varepsilon \sim \mathcal{N}(0, \Sigma)$
underlying 1-d calcium signals:	$\frac{dC_i(t)}{dt} = -\frac{C_i(t)}{\tau} + n_i(t),$	τ : time constant, n_i : spiking of neuron i.

Note that this simple model can be readily extended to model multi-exponential dynamics (e.g. non-instantaneous rise times). Using this notation, we estimate the d-by-T matrix F of the spatiotemporal dynamics by solving:

$$\begin{aligned} \underset{F}{\text{minimize}} \;\; & \frac{1}{2}\|\Sigma^{-1/2}(Y - b1_T^T - F)\|^2 + \sum_{i=1}^{N} \frac{1}{\lambda_i} \sum_{t=1} n_i(t) + \lambda_{NN}\|F\|_* \\ \text{subject to} \;\; & F(1) \geq 0, n_i(t) \geq 0, \; i = 1, \ldots, N, \; t = 1, \ldots, T. \end{aligned} \tag{P1}$$

Here 1_T is a vector of ones of length T, λ_i are the firing rates of the neurons, $\|\cdot\|_*$ denotes the nuclear norm of a matrix, i.e., the sum of its singular values, and λ_{NN} is the regularization parameter. The nuclear norm penalizes the

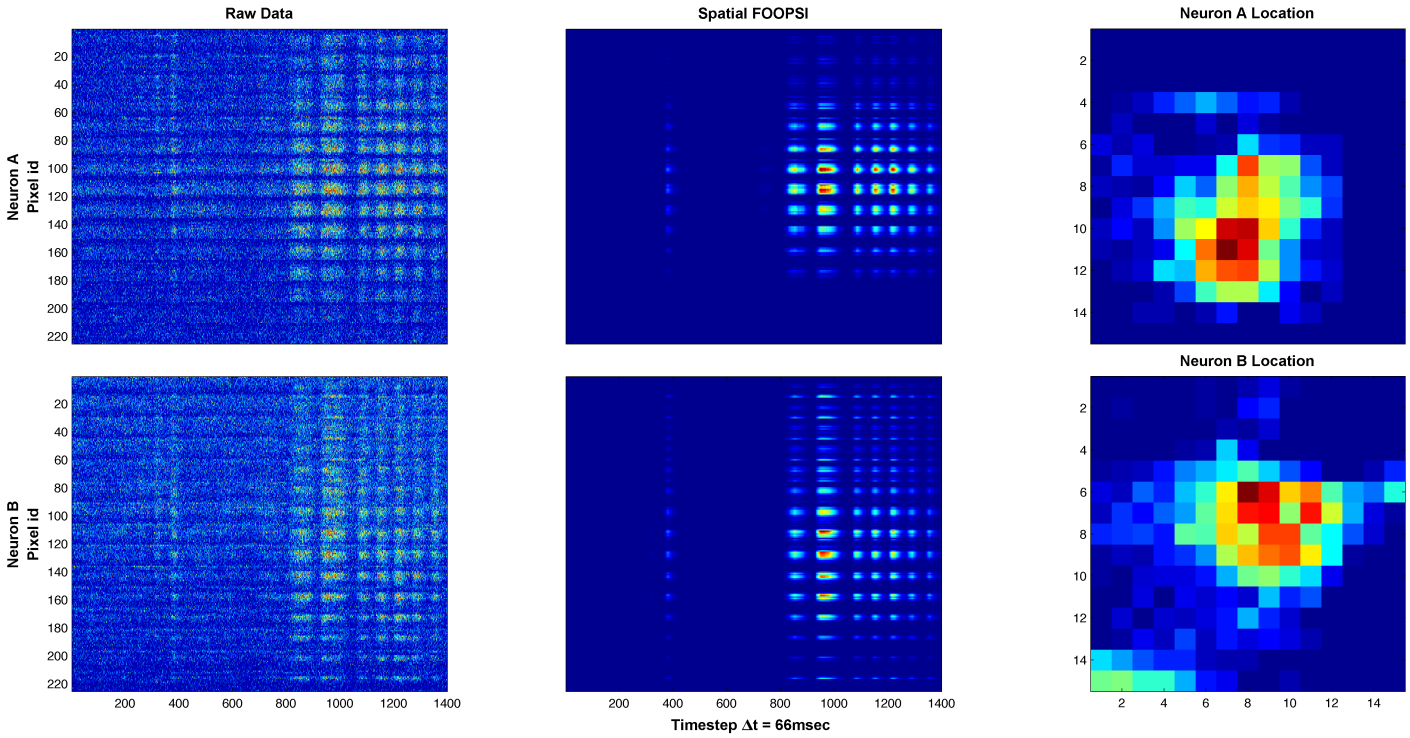

Figure 1: Application of our algorithm to in-vitro spinal cord data using the genetically encoded calcium indicator GCaMP3 . The algorithm was applied to data from two 15-by-15 patches containing each a single neuron. The 225 pixels on the y-axis in the left and middle panels correspond to the 15-by-15 patches vectorized column-by-column. Our algorithm leads to substantial denoising and produces estimates of both the spikes (not shown) and the spatial locations of the neurons (right panels). The results are best viewed in movie format. For more info please visit: `http://www.stat.columbia.edu/~eftychios/Home/Cell_Separation.html`

rank of the inferred matrix since it is the convex envelope of the non-convex rank function. Note that the number of neurons N is in general unknown. However, since $a_i \geq 0$ pointwise, nonnegativity constraints $n_i(t) \geq 0$ can be directly expressed as $F(t) - \gamma F(t-1) \geq 0$, where $\gamma = 1 - \Delta t/\tau$, is the discretized time constant. The problem (P1) is convex and can be solved efficiently using the ADMM method [3] in $O(d^2 T)$ time.

After solving (P1) we obtain an estimate of N by thresholding the singular values of F. By forming the matrices $A = [a_1, \ldots, a_N]$ and $C = [C_1, \ldots, C_N]$ of size d-by-N and T-by-N respectively. We can then obtain explicit estimates of the spatial locations A and the calcium traces C by solving the problem (P2) using standard nonnegative matrix factorization methods.

$$\begin{aligned} \underset{A,C}{\text{minimize}} \quad & \frac{1}{2}\|\Sigma^{-1/2}(Y - b1_T^T - AC^T)\|^2 + \sum_{i=1}^{N} \frac{1}{\lambda_i} \sum_{t=1} n_i(t) \\ \text{subject to} \quad & A \geq 0, C(1) \geq 0, n_i(t) \geq 0, \ i = 1, \ldots, N, \ t = 1, \ldots, T. \end{aligned} \tag{P2}$$

References

[1] Vogelstein J. et al, *Journal of Neurophysiology,* 104(6):3691-3704, 2010.
[2] Grewe F. et al, *Nature Methods,* 7(5):399-405, 2010.
[3] Boyd S. et al, *Foundations and Trends in Machine Learning,* 3(1):1-122, 2011.