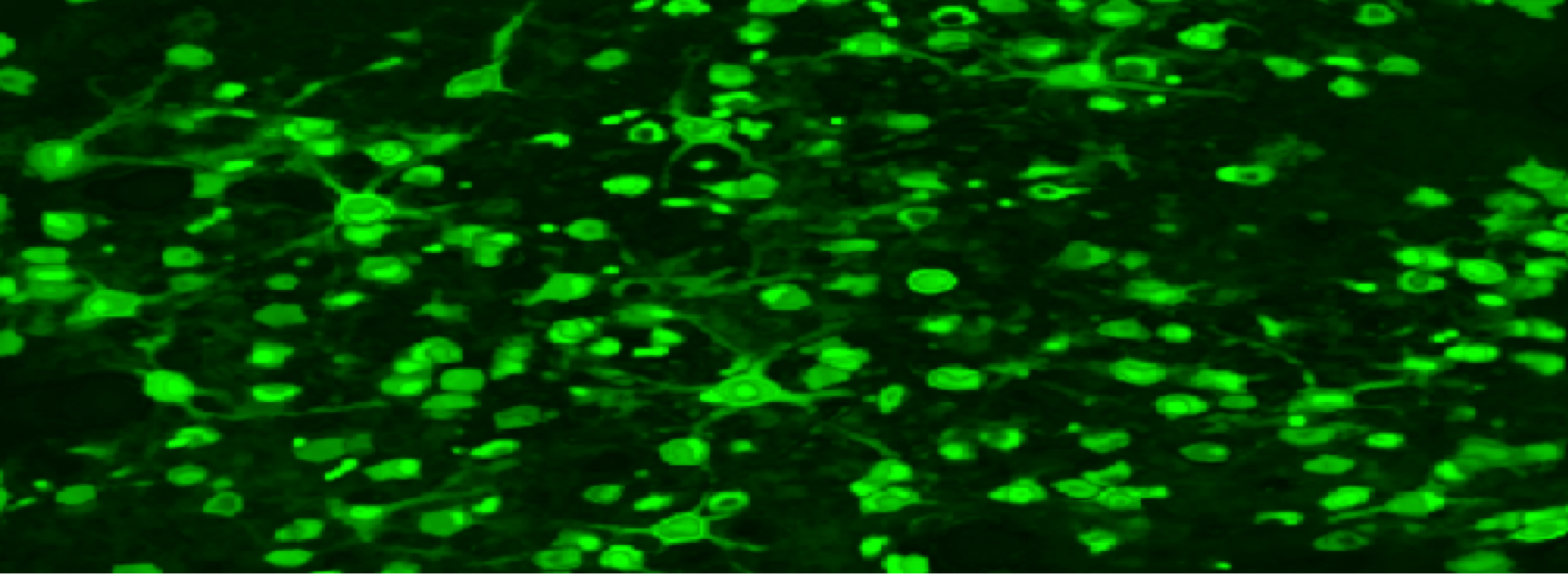

Learning Spatially-correlated Temporal Dictionaries For Calcium Imaging

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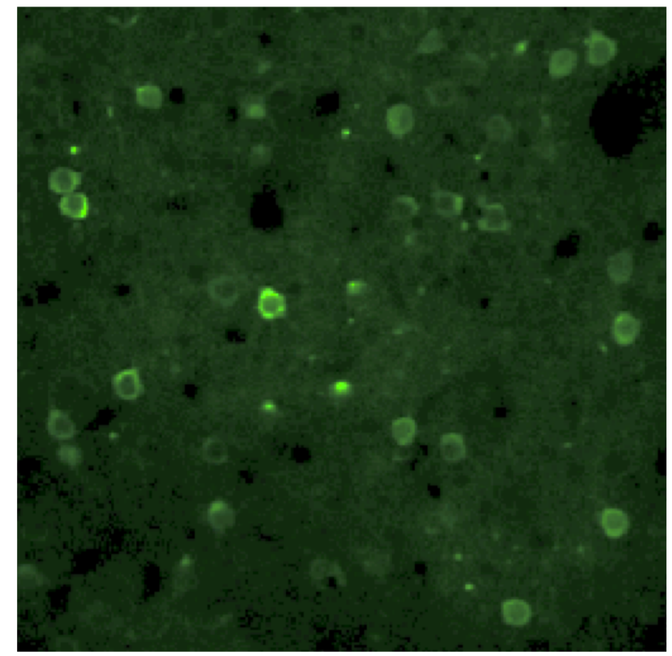
Applied Mathematics, Yale

Joint work with Adam Charles

ICASSP 2019

Calcium imaging

- Records **hundreds** of neurons *in vivo*
- Tracks same population across days
- Sub-cellular spatial resolution
- Temporal resolution at behavioral time-scales
- Extract neural activity from complex large-scale imaging and behavioral data



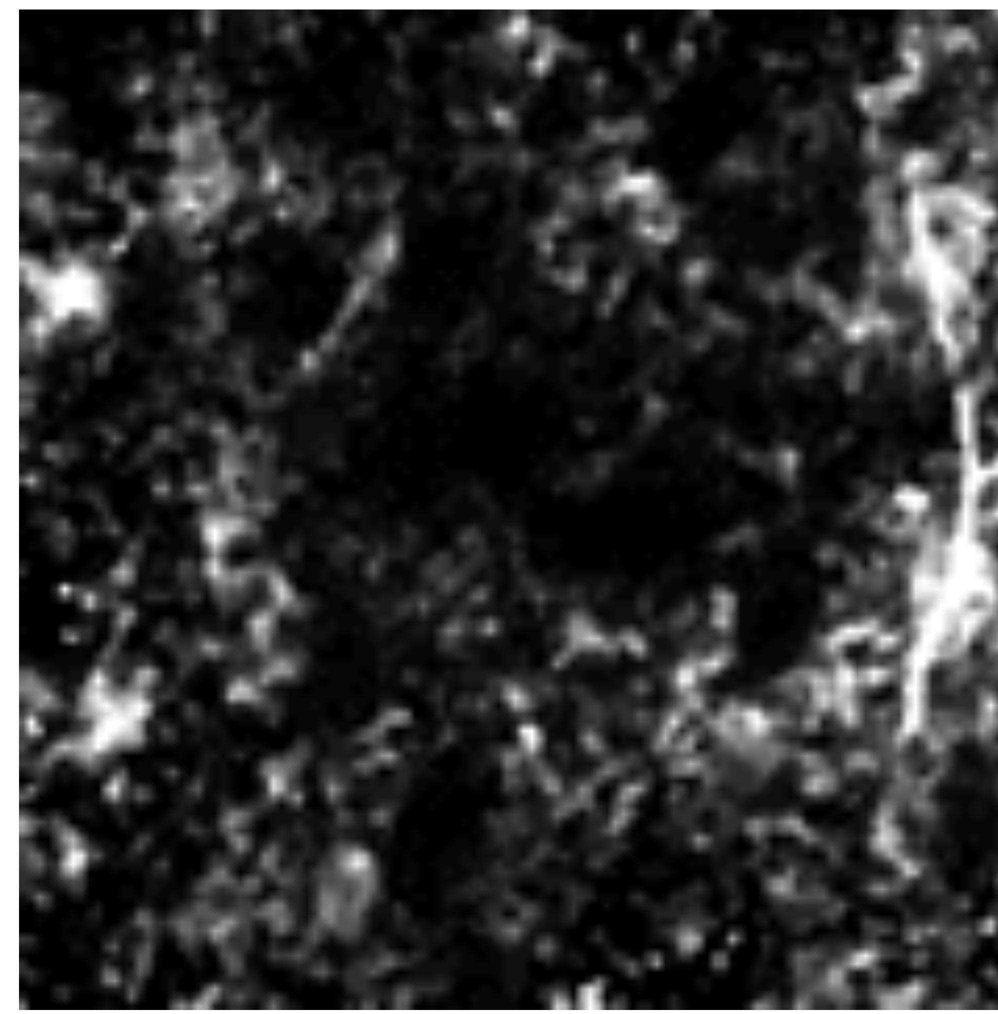
Calcium imaging analysis

Goals:

- Identify individual **cells** and dendrites
- Calculate corresponding **time traces**

Challenges

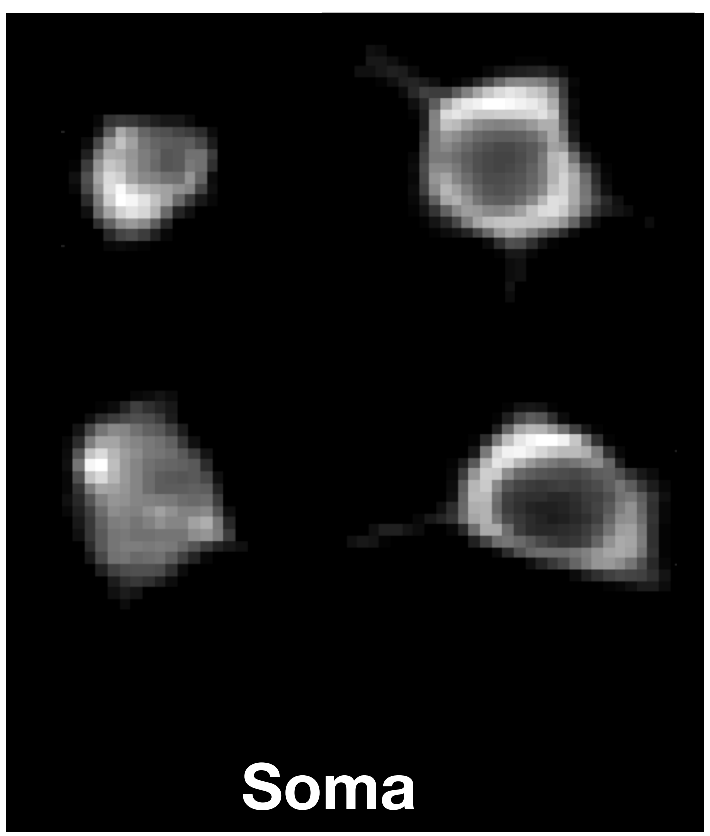
- **Overlapping** cells
- Varying **dynamic range**
- Challenging noise conditions:
  - Noisy heterogeneous background
  - Measurement noise
  - Movement artifacts
- **Large scale** (typical size: 512x512x10k)



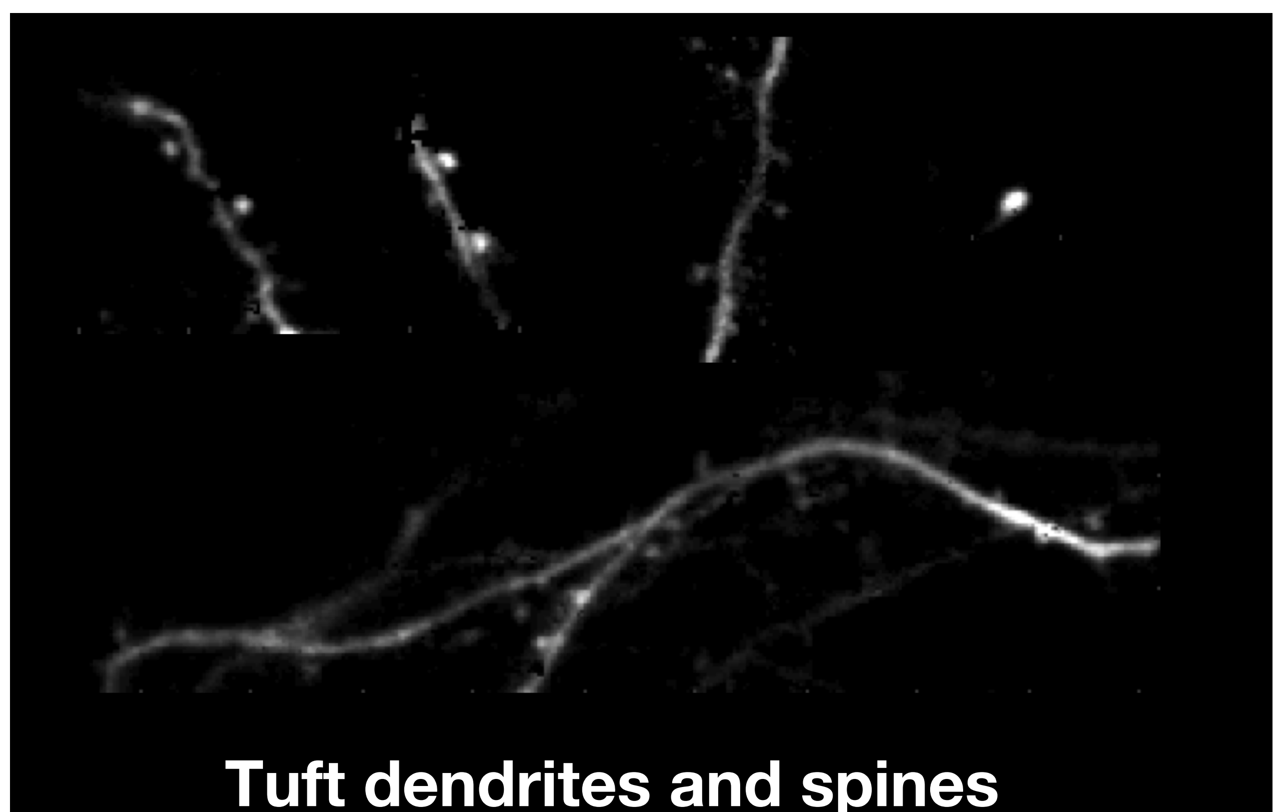
Functional imaging

Need for flexible methods to handle:

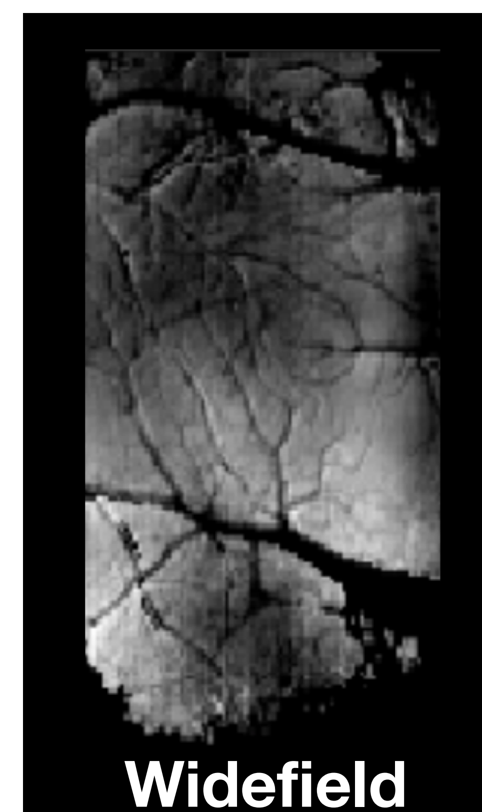
- Different scales: population, dendritic, widefield
- Indicators: calcium, voltage, …
- Acquisition modalities: 1p/2p/3p, head-fixed / microendoscopy,…



Soma

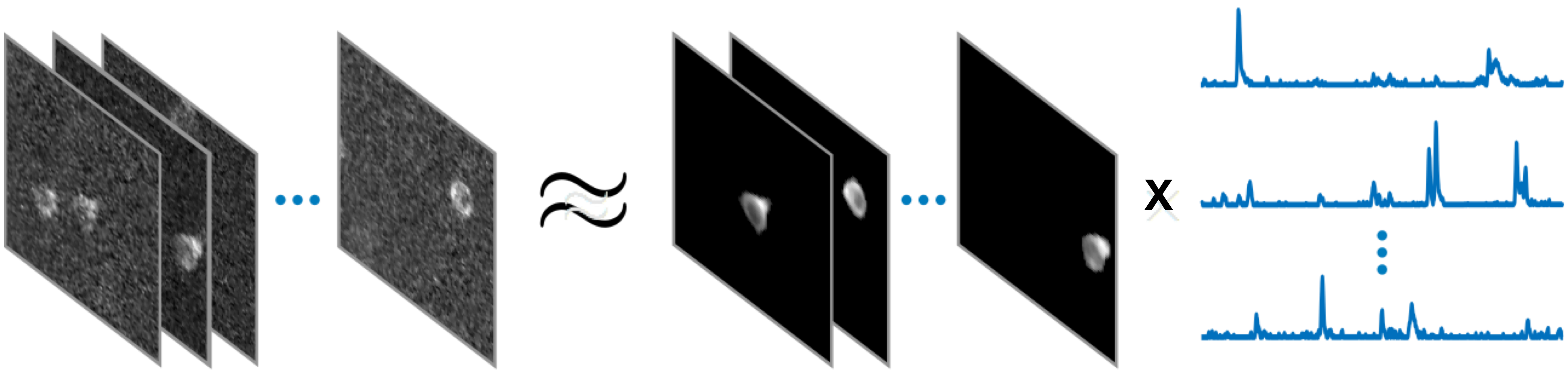


Tuft dendrites and spines



Widefield

Matrix Factorization



Data		Spatial profiles		Time traces
Y	$\approx$	A	x	Φ

Manual segmentation still commonplace

[Deigo-Andilla and Hamprecht 2014
Maruyama et al. 2014,
Pnevmatikakis et al. 2013 & 2016,
Pachitariu et al. 2016
Petersen et al. 2018, …]

Additional constraints:

- **Spatial sparsity**
- **Temporal sparsity**
- **Non-negativity**
- **Calcium dynamics**

Matrix Factorization

- Cost function:

$$\widehat{\boldsymbol{\Phi}}, \widehat{\boldsymbol{A}} = \arg\min_{\boldsymbol{\Phi} \geq 0} \|\boldsymbol{Y} - \boldsymbol{A}\boldsymbol{\Phi}\|_F^2 + \mathcal{R}\left(\boldsymbol{\Phi}, \boldsymbol{A}\right)$$

Data fidelity

regularization (sparse, connected)

- Spatial solution typically involves

$$\widehat{\boldsymbol{A}} | \widehat{\boldsymbol{\Phi}} = \arg\min_{\boldsymbol{A}} \|\boldsymbol{Y} - \boldsymbol{A}\widehat{\boldsymbol{\Phi}}\|_F^2 + \mathcal{R}(\boldsymbol{A})$$

- Overlaps and initialization sensitivity can induce bias in this step [Gauthier et al. 2018].

- Does not readily extend to different spatial scales.

Dictionary learning

- Learns features under a sparse mixture model

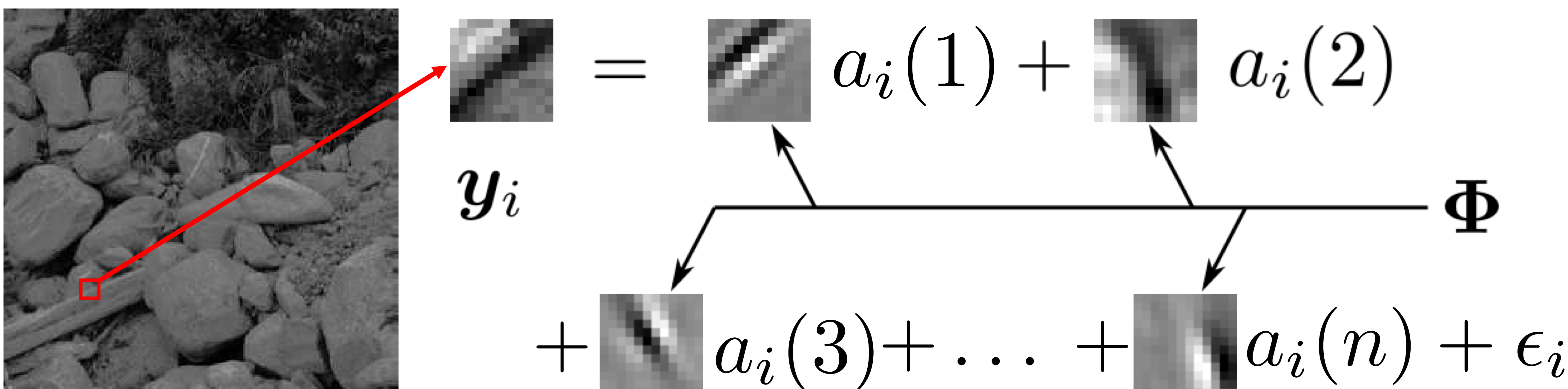
dictionary matrix

$$\boldsymbol{y}_i = \boldsymbol{\Phi}\boldsymbol{a}_i + \epsilon_i$$

sparse

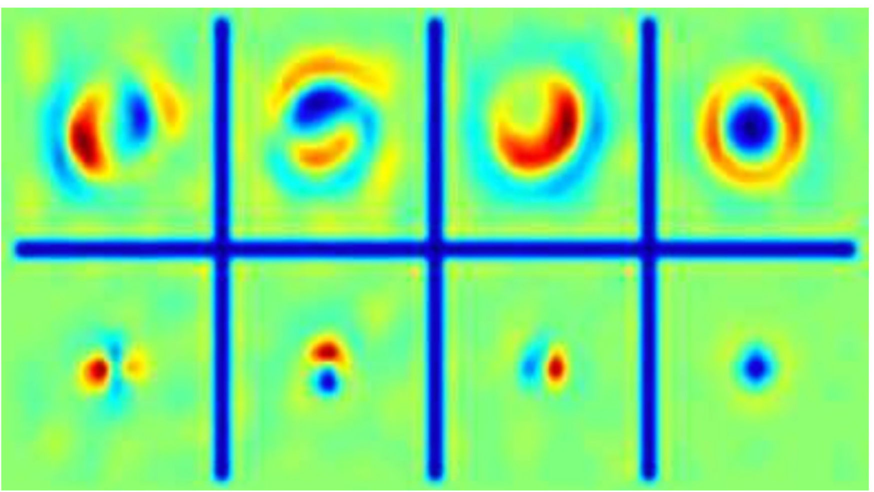
"noise"

- Traditionally used in image processing:

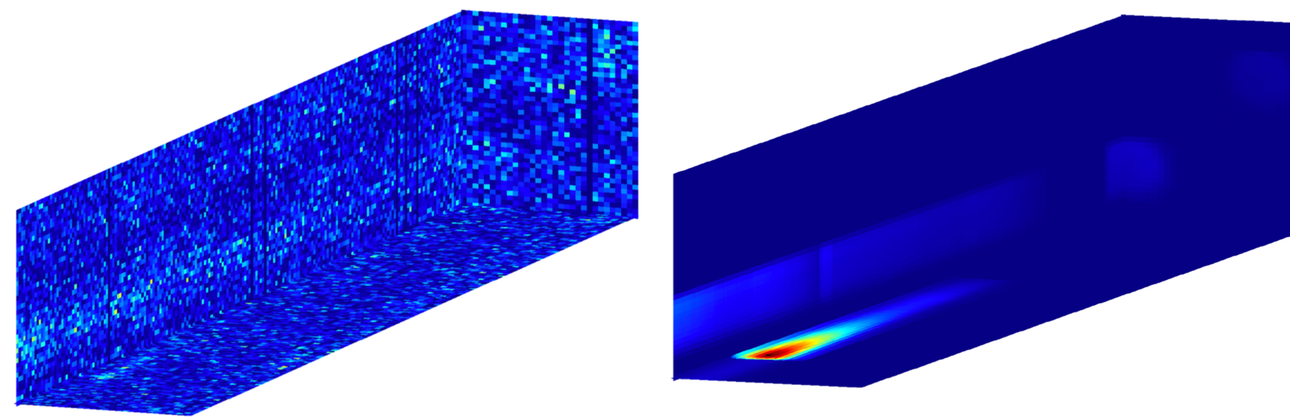


Dictionary learning in calcium imaging

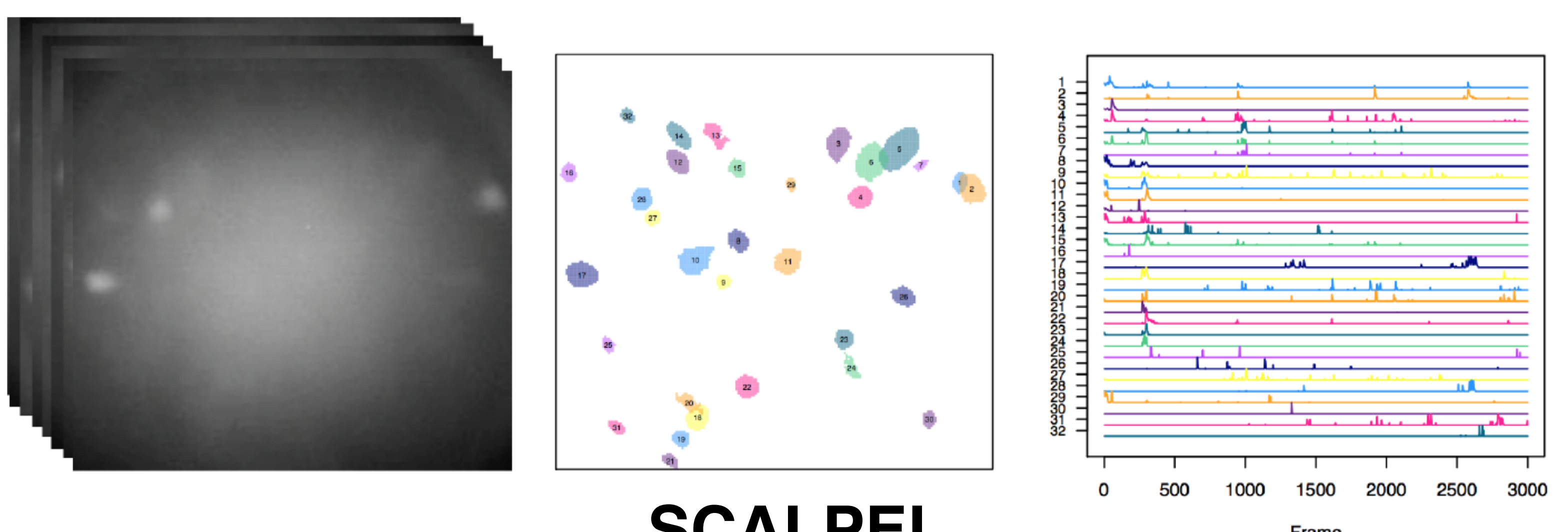
- Prior work focuses on spatial dictionary:



Convolutional sparse block coding,
[Pachitari et al. 2013]



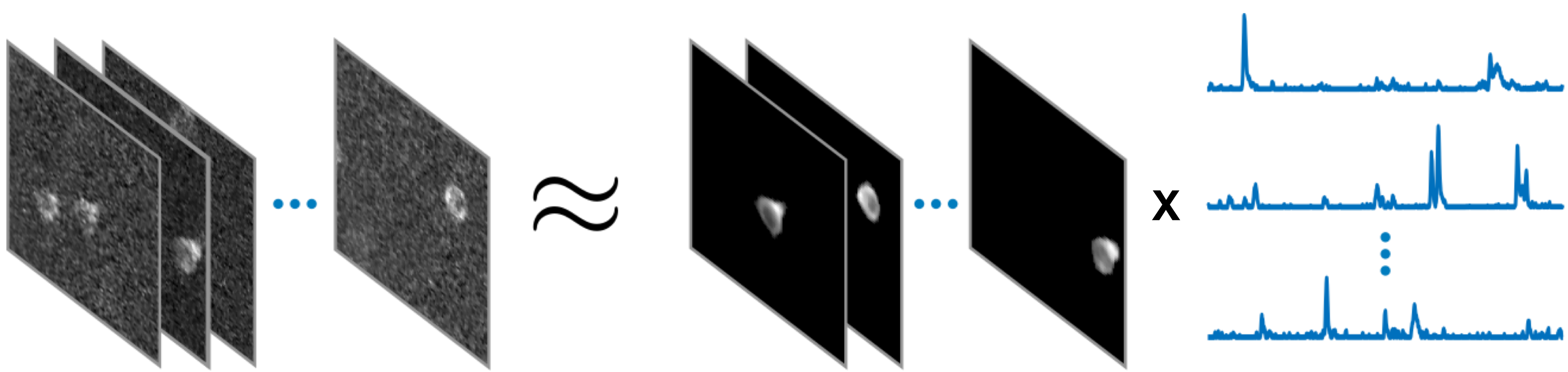
Sparse space-time deconvolution
[Diego & Hamprecht 2014]



SCALPEL
[Petersen, Simony, & Witten 2018]

Temporal dictionary learning

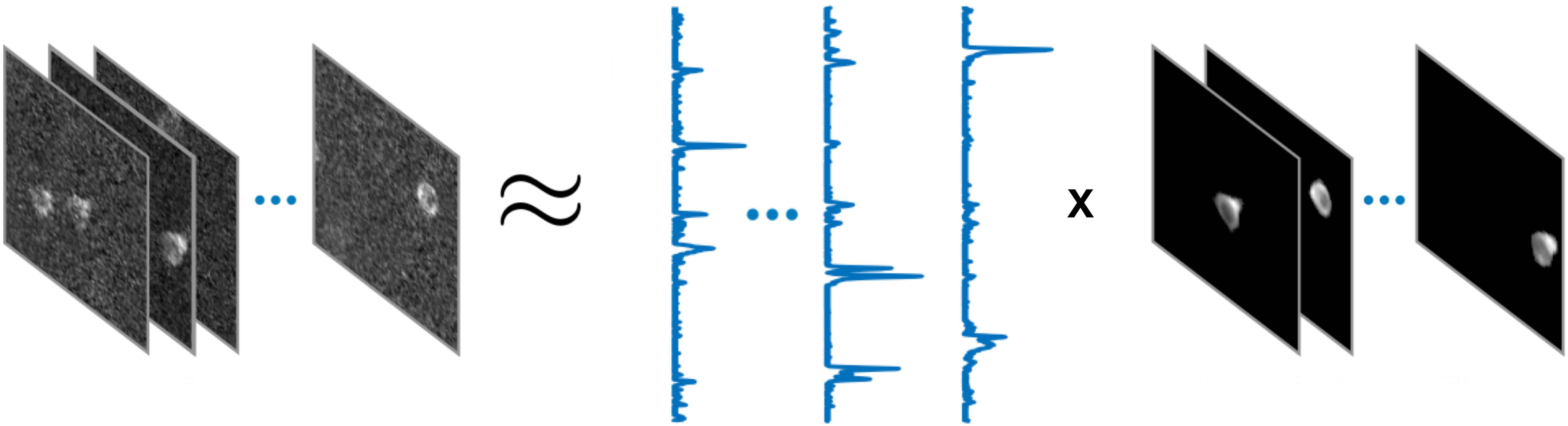
- Matrix factorization model $\boldsymbol{Y}^T = \boldsymbol{A}\boldsymbol{\Phi}^T + \boldsymbol{E}^T$



Temporal dictionary learning

- Our solution: flip the model!

$$\boldsymbol{Y} = \boldsymbol{\Phi}\boldsymbol{A}^T + \boldsymbol{E}$$



- Find temporal dictionary time-traces
- Sparse coefficients are spatial profiles

Temporal dictionary learning

We add regularization terms to learning the dictionary to better model the data:

$$\widehat{\boldsymbol{\Phi}} = \arg\min_{\boldsymbol{\Phi}\geq 0}\{\|\boldsymbol{Y} - \boldsymbol{\Phi}\boldsymbol{A}\|_F^2$$

- Fidelity

$$+ \lambda_1\|\boldsymbol{\Phi}\|_F^2$$

- Frobenius (implicitly infer # of components)

$$+ \lambda_2\|\boldsymbol{\Phi} - \widehat{\boldsymbol{\Phi}}\|_F^2$$

- Continuation (stable convergence)

$$+ \lambda_3||\Phi^T\Phi - \mathrm{diag}(\Phi^T\Phi)||_{sav}\}$$

- Penalize correlated traces

Sparse spatial coefficients

Sparse spatial coefficients inferred via reweighted L1 with spatial filtering [Charles & Rozell 2014]

- Solve for every pixel separately

$$\widehat{\boldsymbol{a}}_{i,j} = \arg\min_{\boldsymbol{a}\geq 0} \frac{1}{2\sigma_y^2} \left\|\boldsymbol{y}_{i,j} - \boldsymbol{\Phi}\boldsymbol{a}\right\|_2^2 + \sum_k \lambda_{i,j,k}|a_{i,j,k}|$$

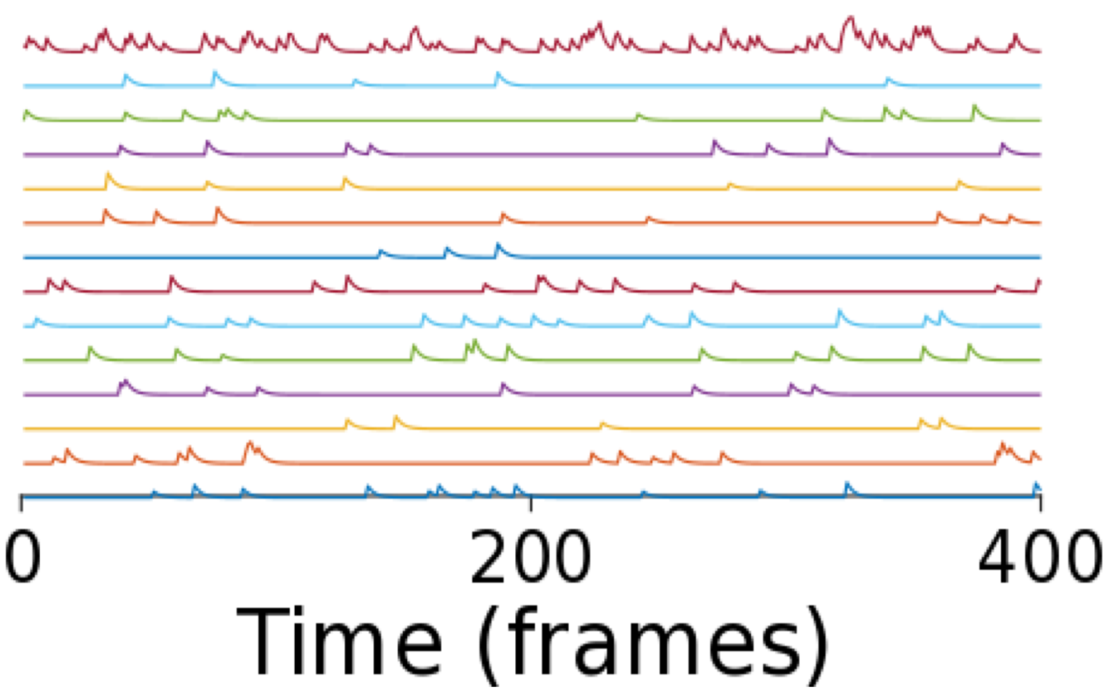
- Reweighting introduces spatial cohesion

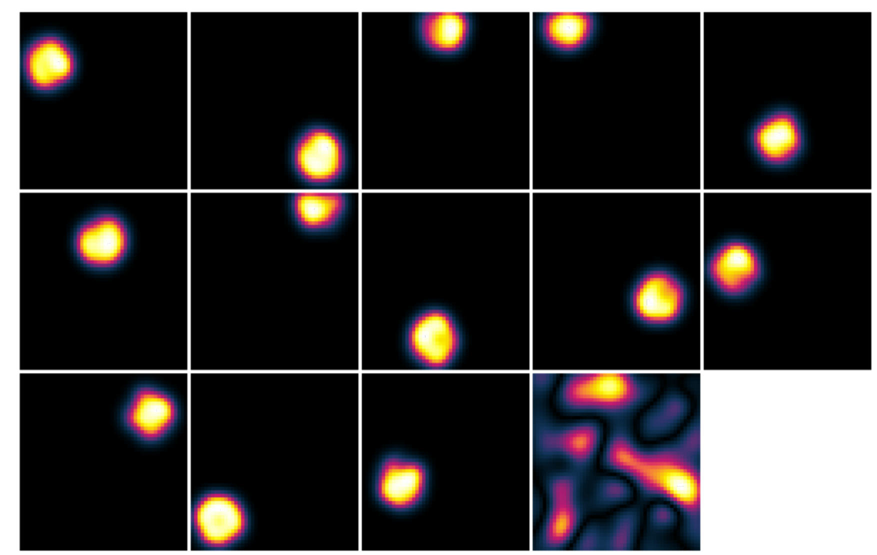
$$\lambda_{i,j,k} = \frac{\xi}{\beta + |a_{i,j,k}| + \left[|\boldsymbol{W} * \widehat{\boldsymbol{A}}_k|\right]_{i,j}}$$

Spatial convolution

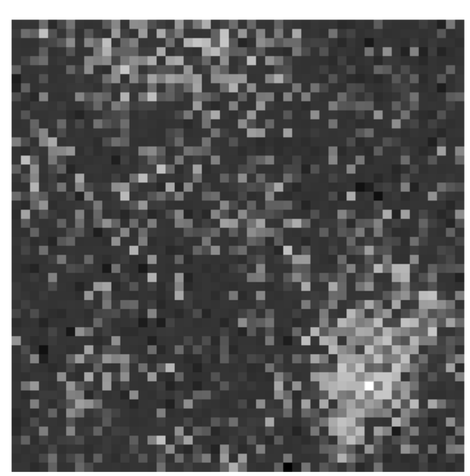
Experimental results

- Synthetic data: generate time-traces + spatial maps

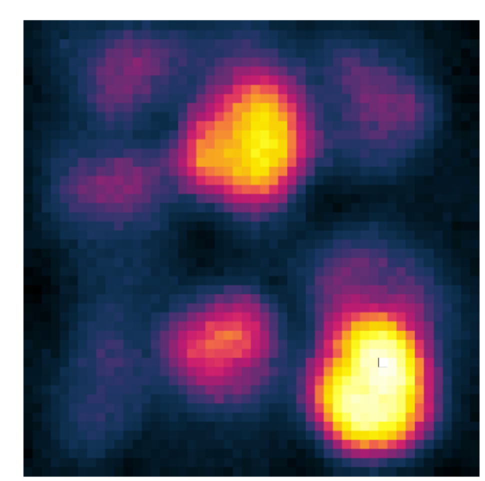




A



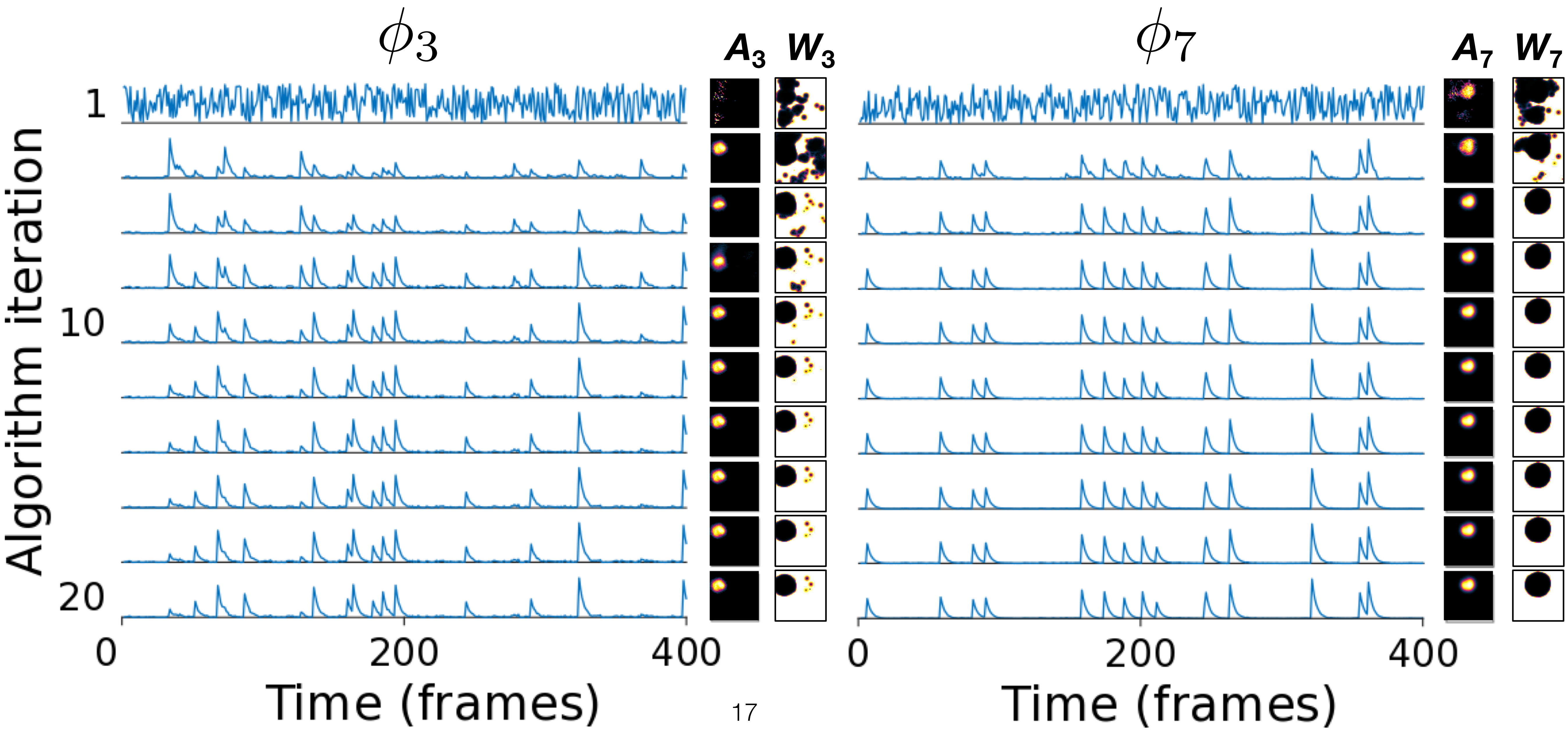
Video



Temporal mean

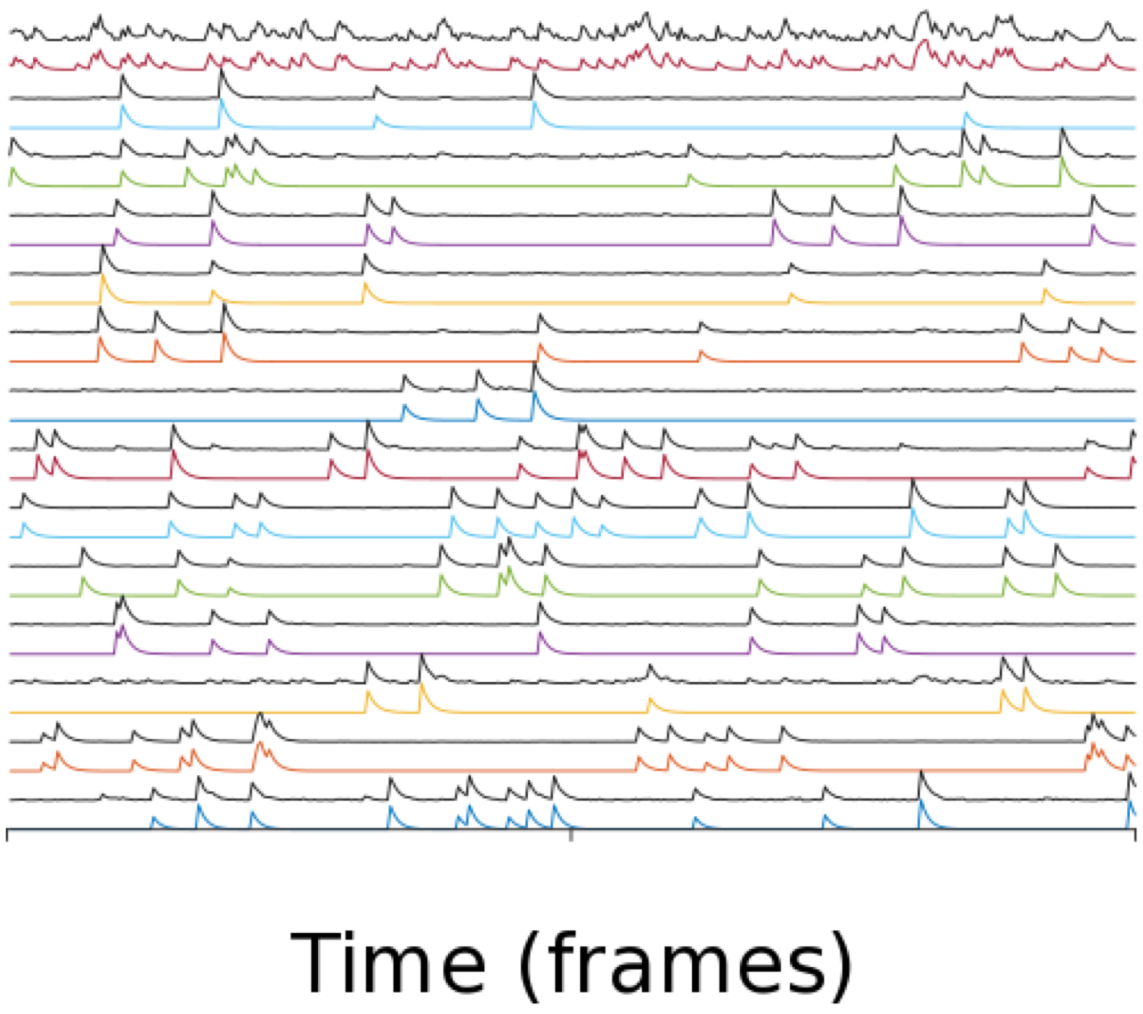
Learning time-traces

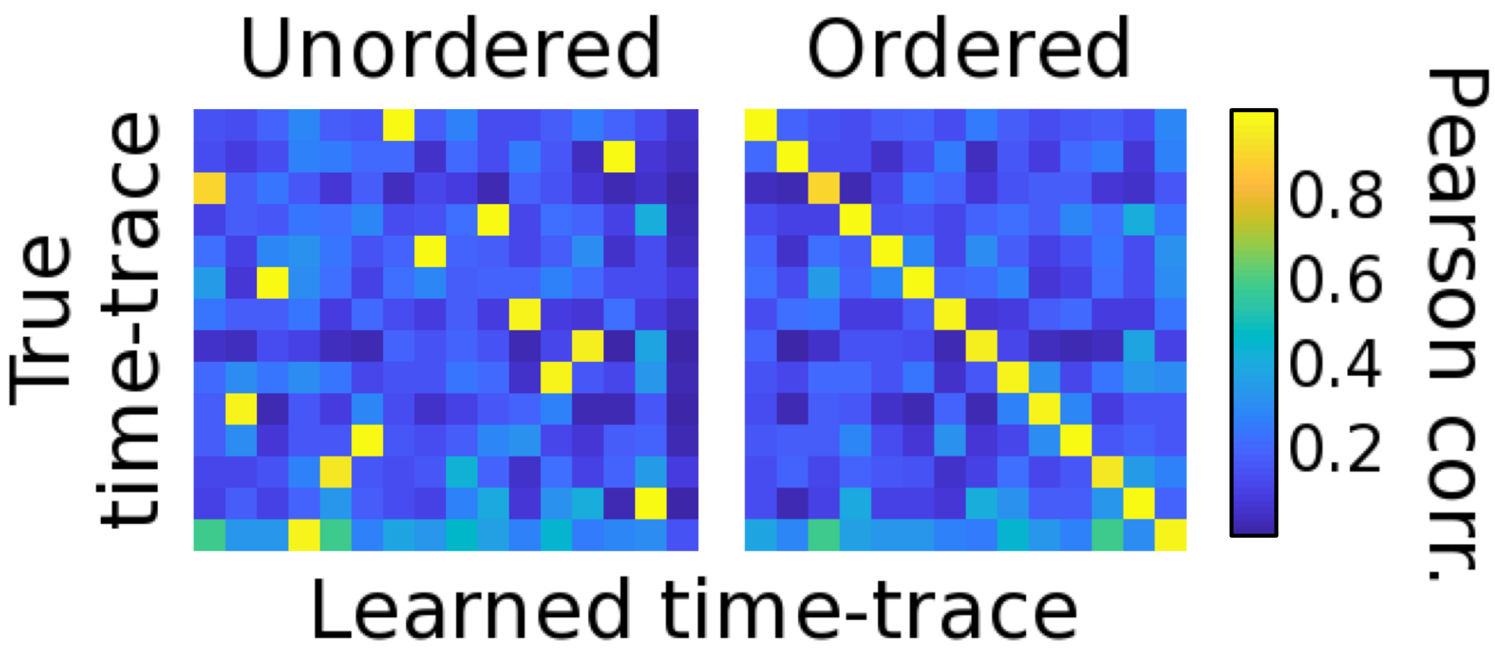
- Dictionary initialized with random traces
- Algorithm converges quickly



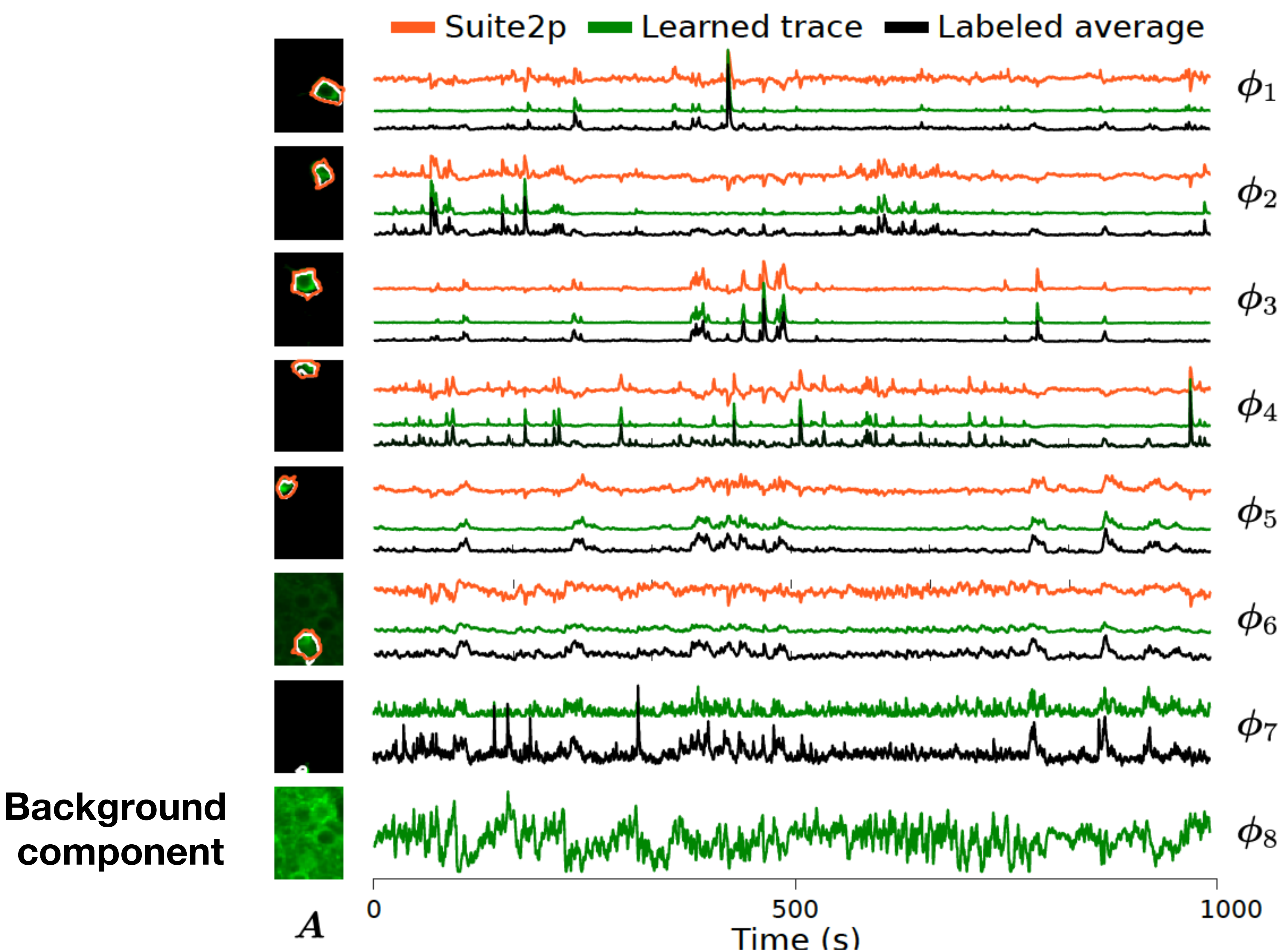
Learning time-traces

- Empirical recovery of ground truth time-traces



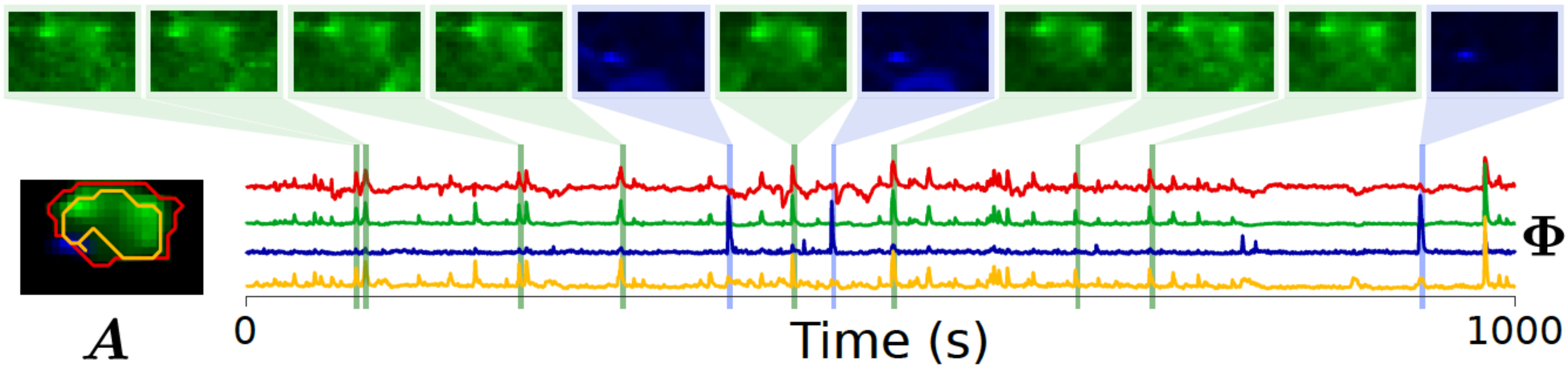


Experimental results: Neurofinder

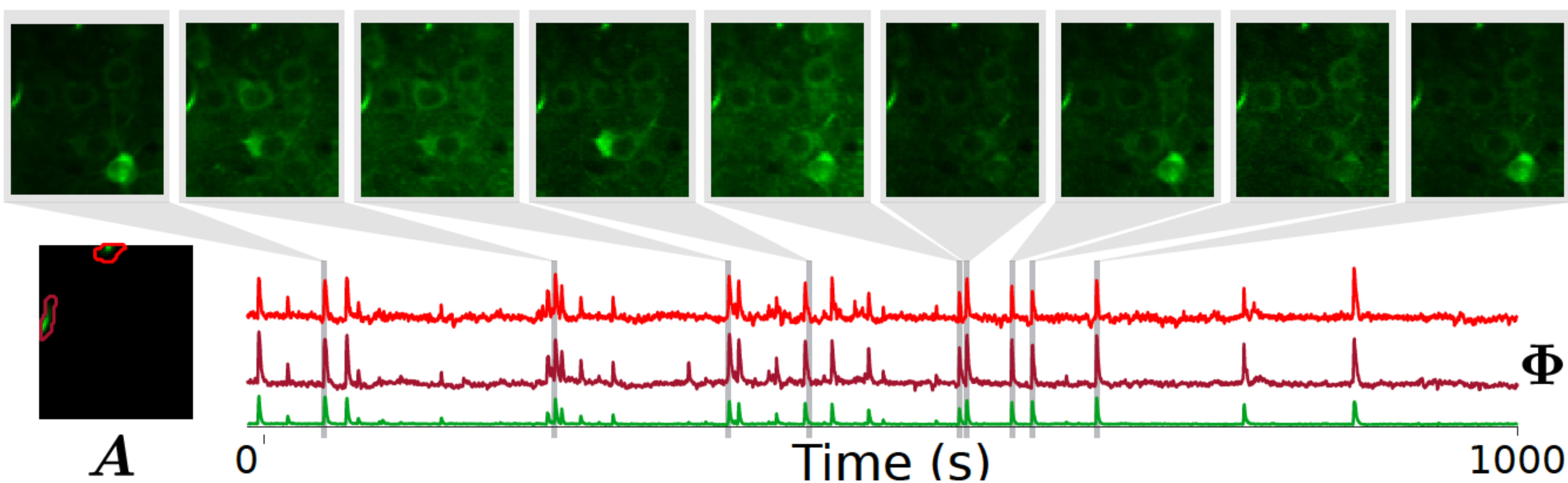


Experimental results: Neurofinder

Detecting apical dendrites



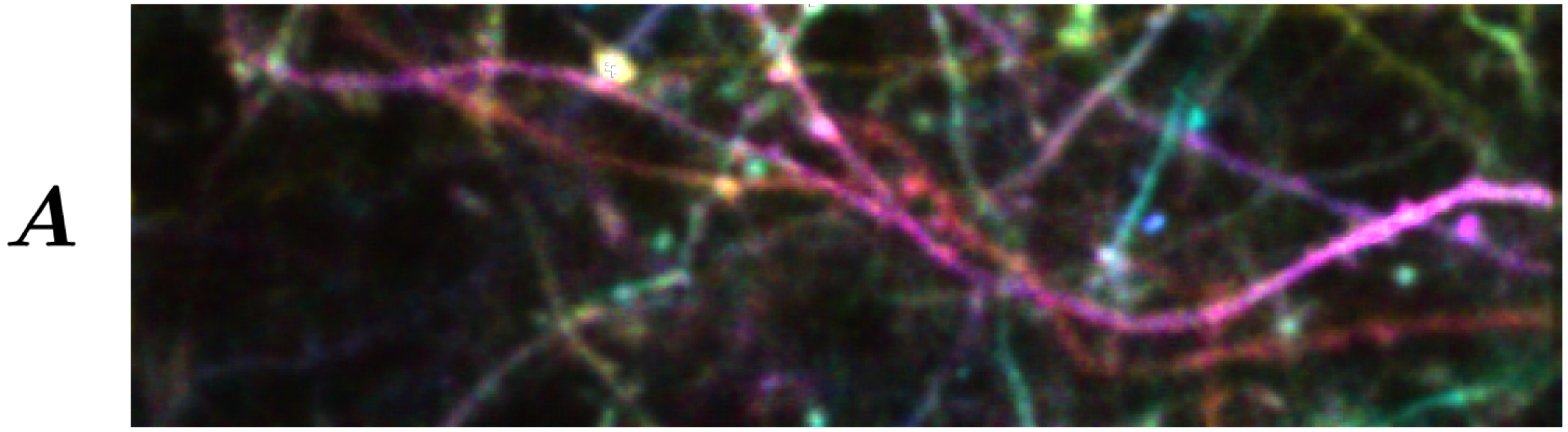
Detecting dendrites with “occlusions”

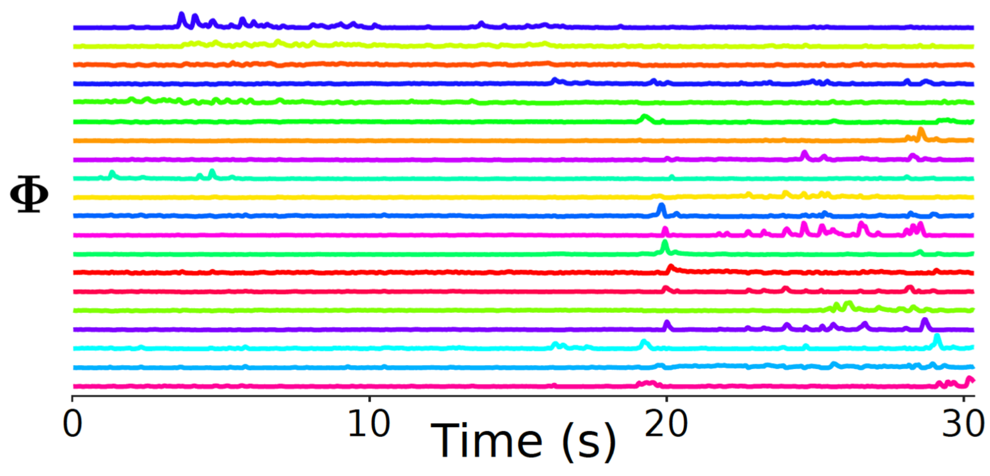


Future work

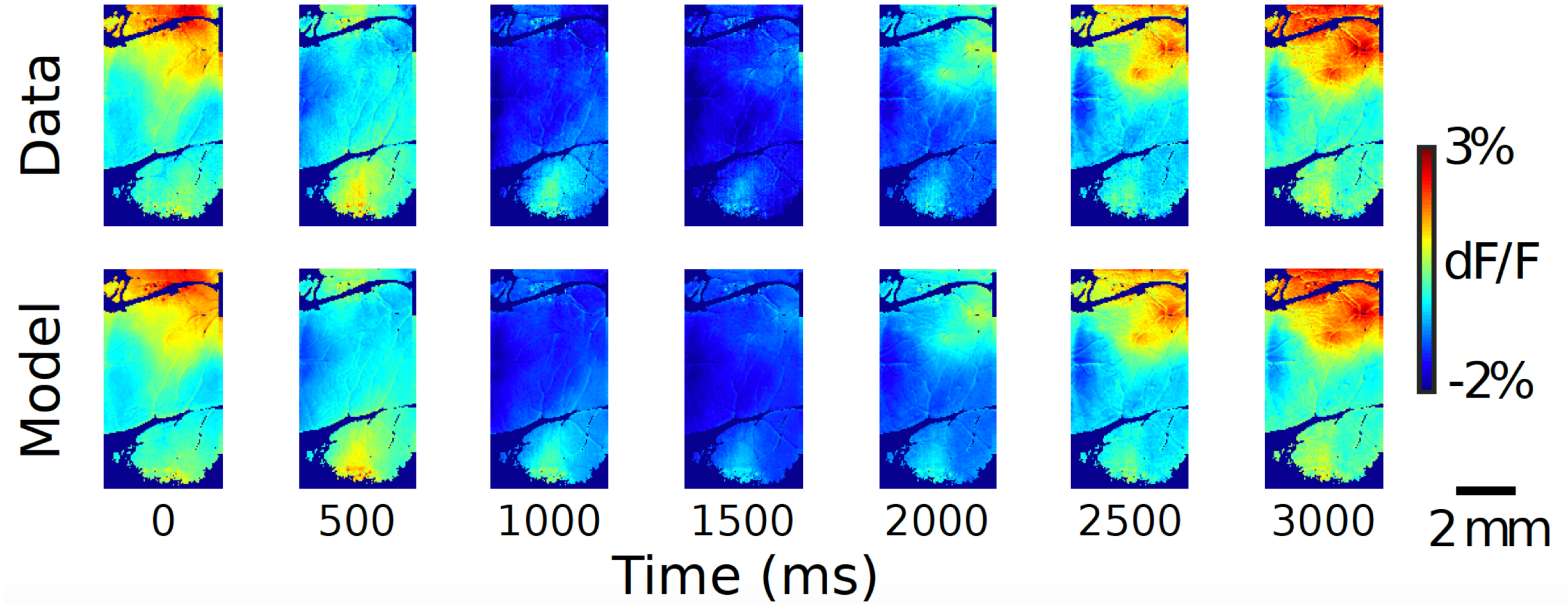
Dendritic imaging

* Data courtesy of Schiller lab





Widefield imaging



*Data from [Scott et al. 2018]

Conclusions

- New model for calcium imaging source segmentation
- Flexible: works across scales
- Robust: can handle disconnected and nested components
- Number of components implicitly inferred

Funding: NIH (NINDS, NIBIB)