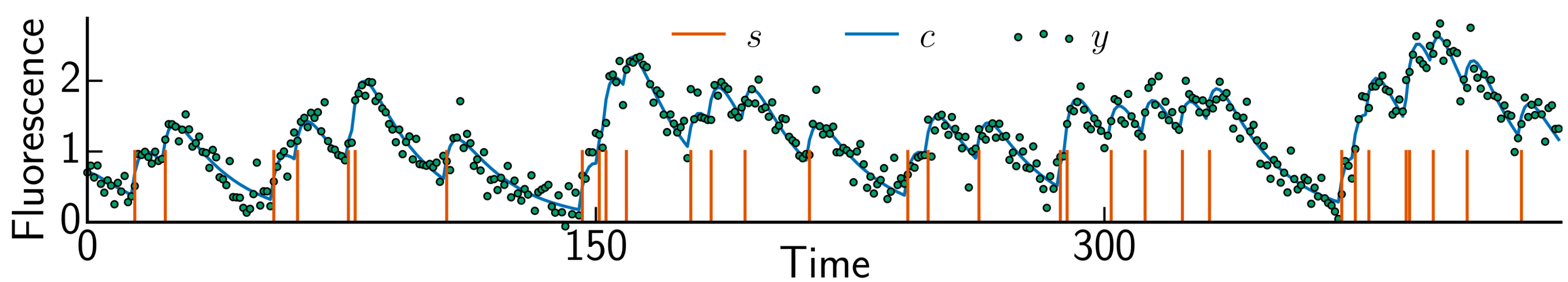
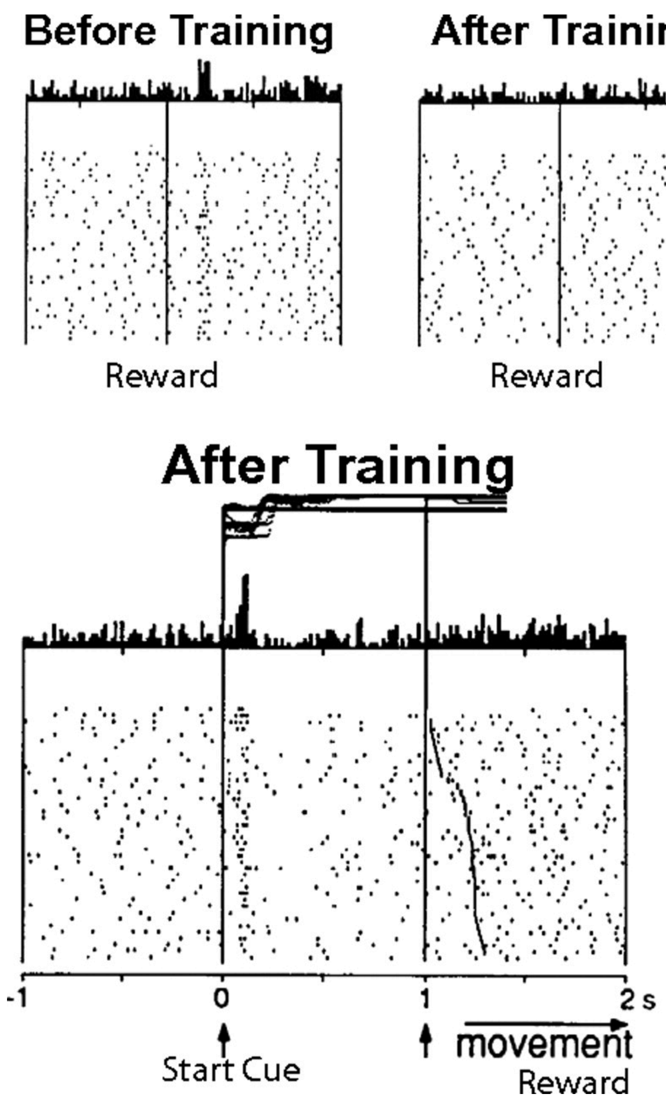
# Exact spike train inference via $\ell_0$ optimization

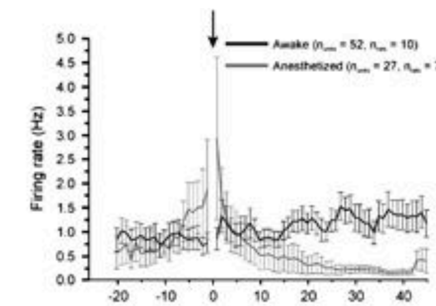
Yiqun Chen,
572 final presentation
05/30/2019

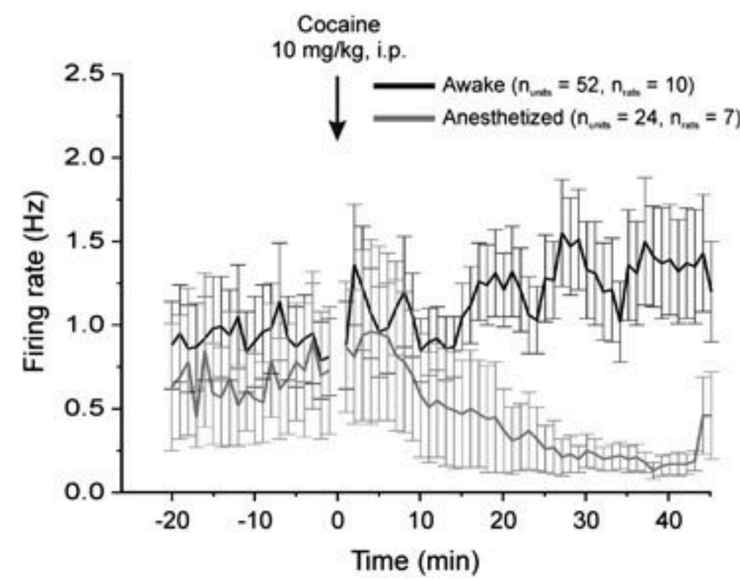


# Spike inference problems (biological)




Glimcher (2011)

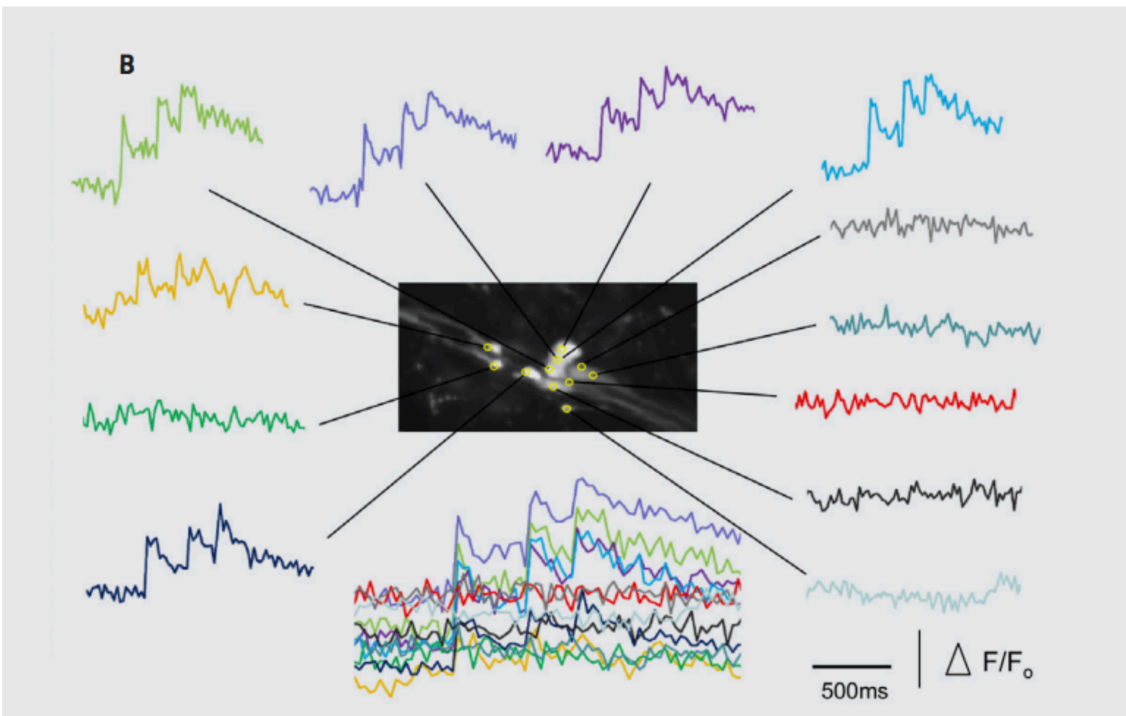


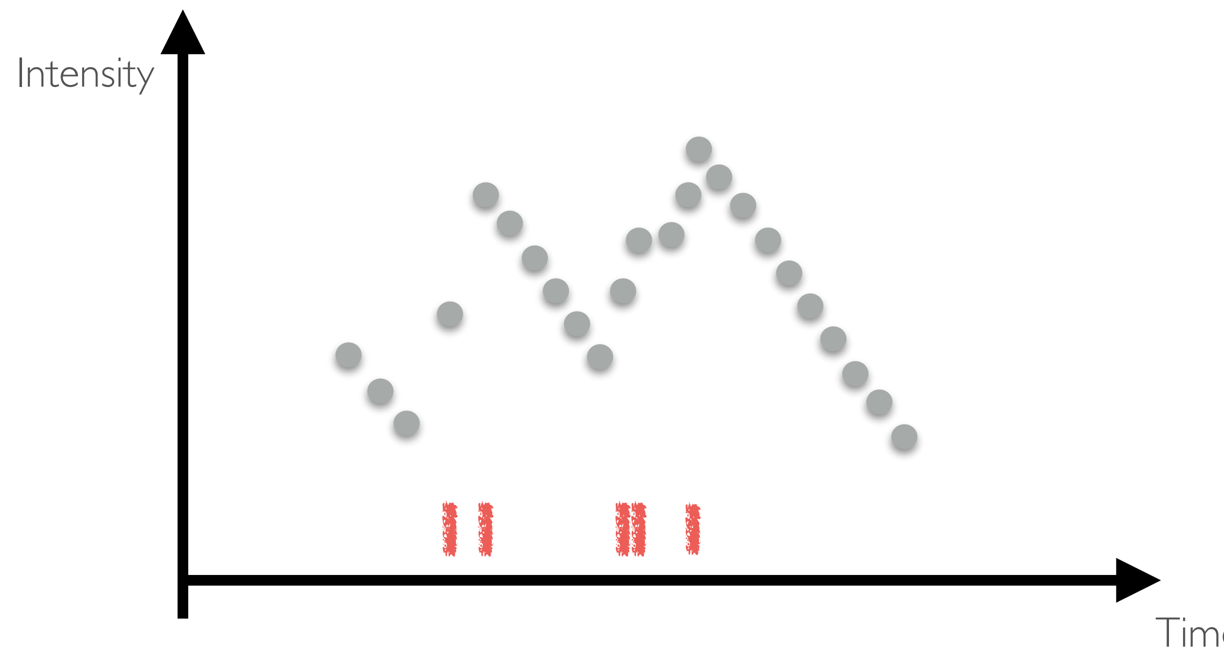



Grace et al. (2009)

Motivation: "spike" is instrumental to understanding neural activities/mechanisms

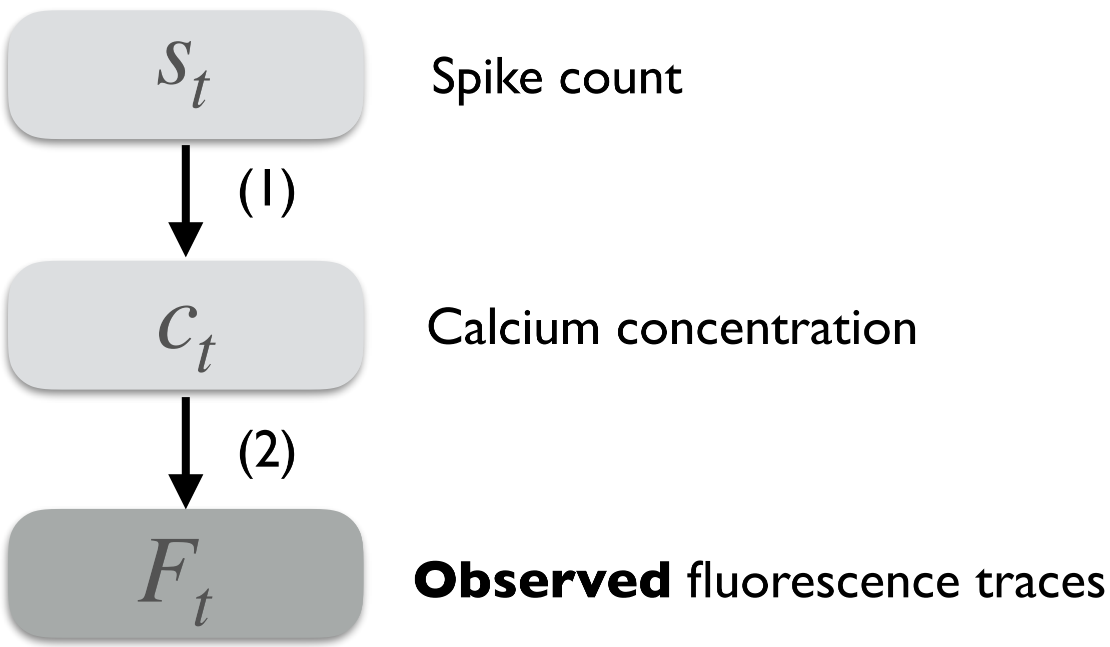
# Spike inference problems (biological)




Problem: estimate "spikes"/changepoints given observed fluorescence

# Spike inference problems (statistical)




$$\forall t \in [T]$$

$$s_t \overset{i.i.d.}{\sim} Poisson(\theta)$$

$$c_t = \gamma c_{t-1} + s_t \qquad (1)$$

$$F_t = c_t + \epsilon_t, \epsilon_t \overset{i.i.d}{\sim} \mathcal{N}(0,\sigma^2) \qquad (2)$$

## Goal: estimate $s_t$ given $F_t$

Questions:

1. How many spikes?
2. Where are the spikes (how precise are they)?
3. Computational efficiency?
4. Model selection?

……

Generative model → optimization problem

$$G(T) = \min_{c_1,\cdots,c_T} \frac{1}{2}\sum_{t=1}^{T}(F_t - c_t)^2 + \lambda \sum_{t=2}^{T} \mathbf{1}\{c_t \neq \gamma c_{t-1}\}$$

Seemingly intractable → Dynamic programming $O(T^2)$

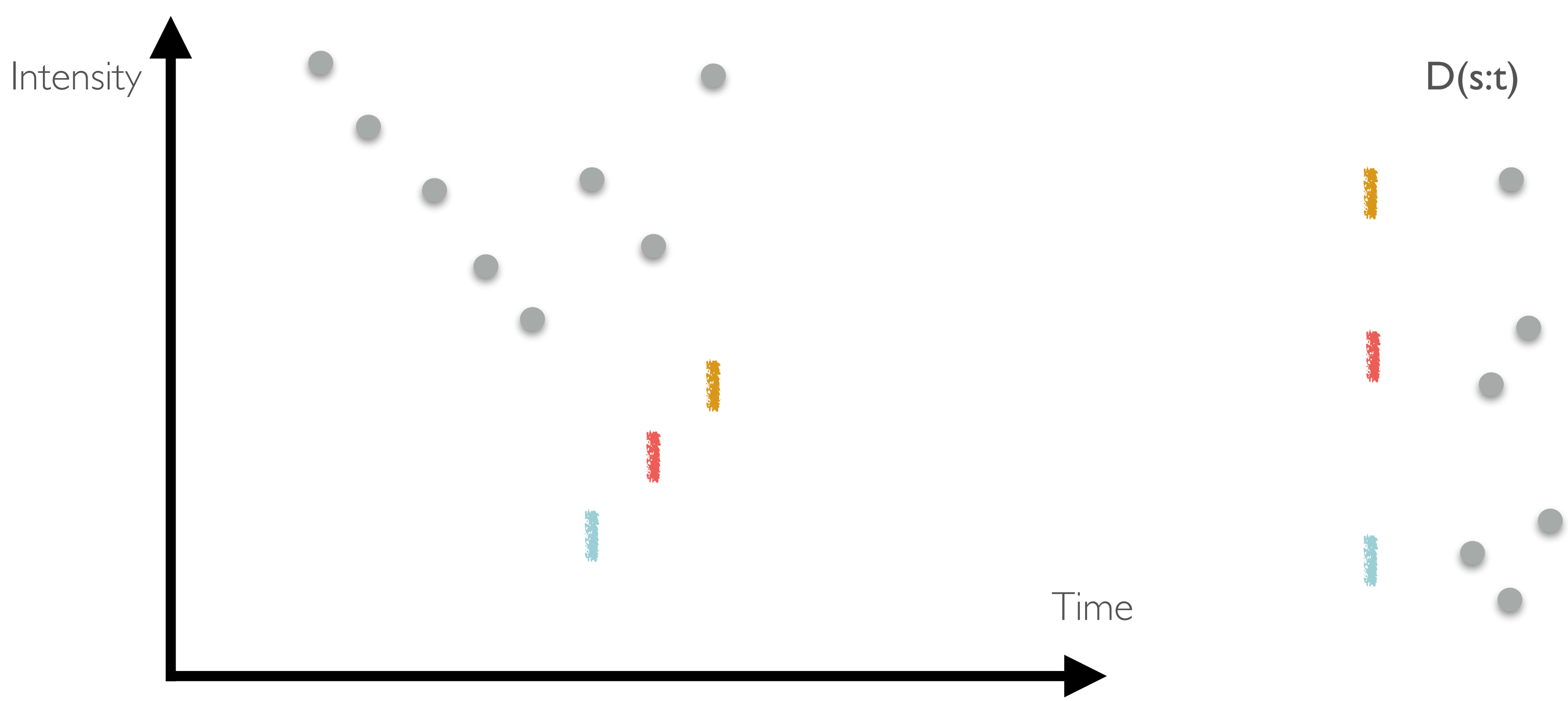
$$G(t) = \min_{s<t}\left\{ G(s) + \mathbf{D}(s:t) + \lambda \right\}$$

Optimal objective

Objective of most recent spike

Cost of fitting the non-spike dots using least square

Cost of putting a spike



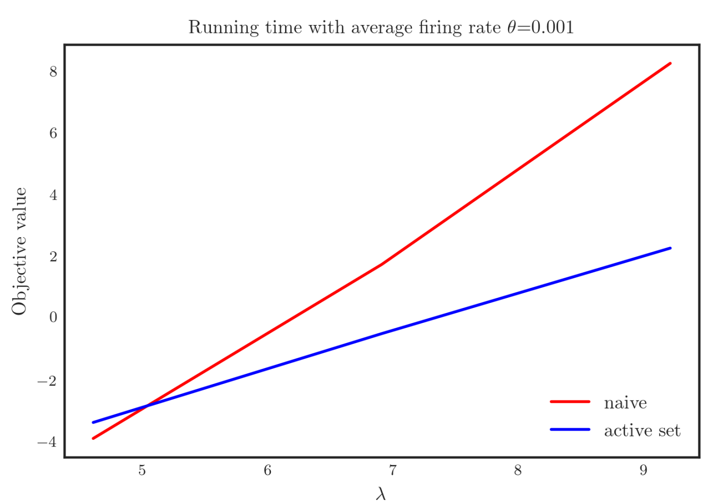
# Result 1: pruning of the active sets

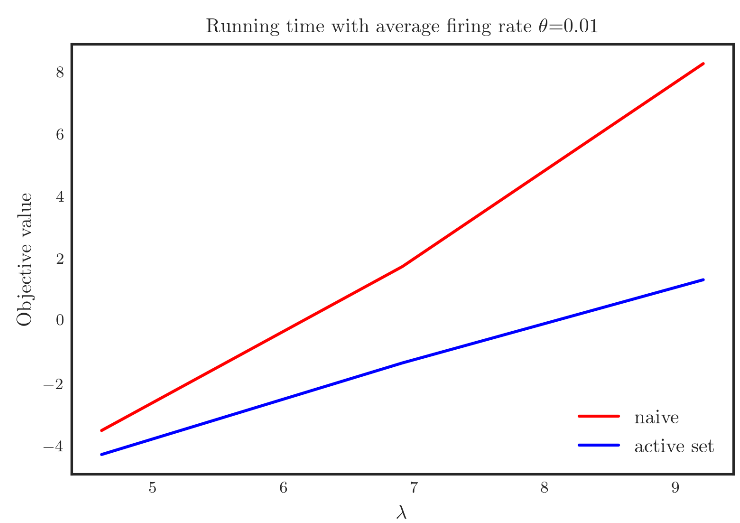
$$G(t) = \min_{s<t} \left\{ G(s) + \mathbf{D}(s:t) + \lambda \right\}$$

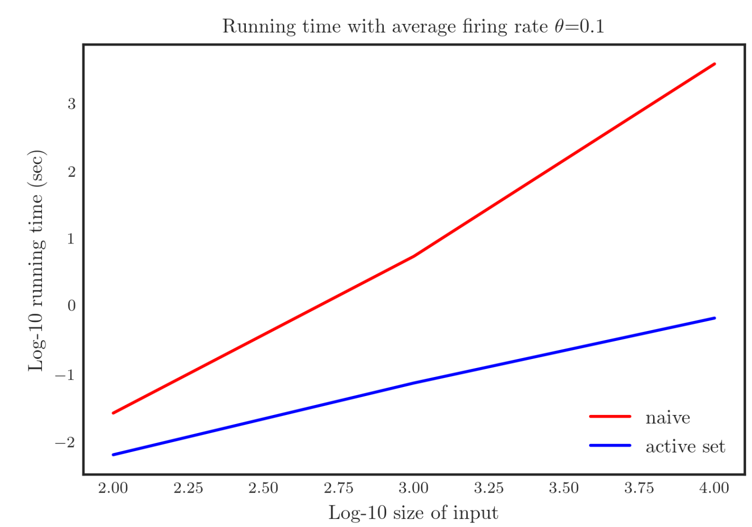
Maybe we don't need to do it for all t possible candidates…

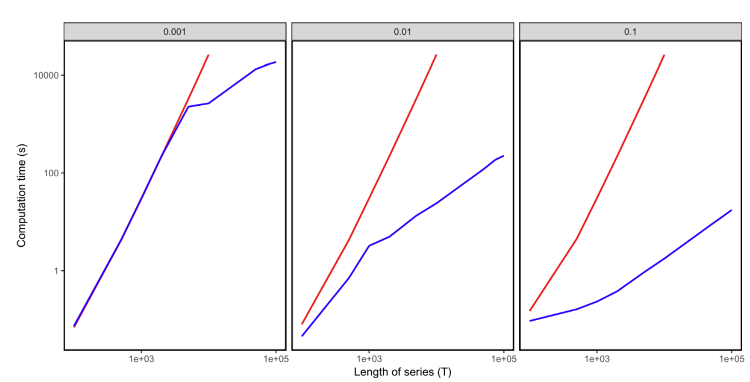
$$G(t) = \min_{s \in \mathscr{E}_s} \left\{ G(s) + \mathbf{D}(s:t) + \lambda \right\}$$

$$\mathscr{E}_{s+1} = \{ \tau \in \{ \mathscr{E}_s \cup s \} : G(\tau) + \mathbf{D}(y_{\tau+1:s}) < G(s) \}$$

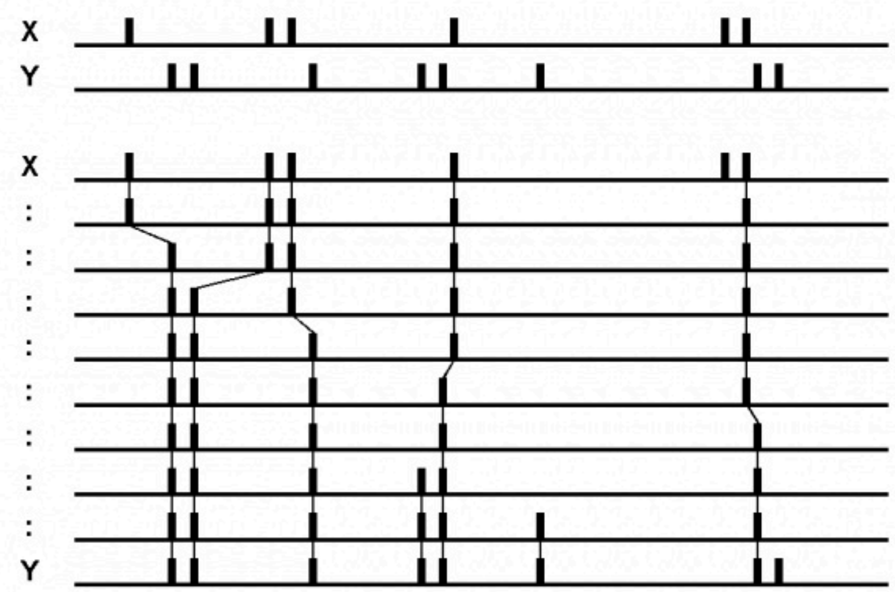


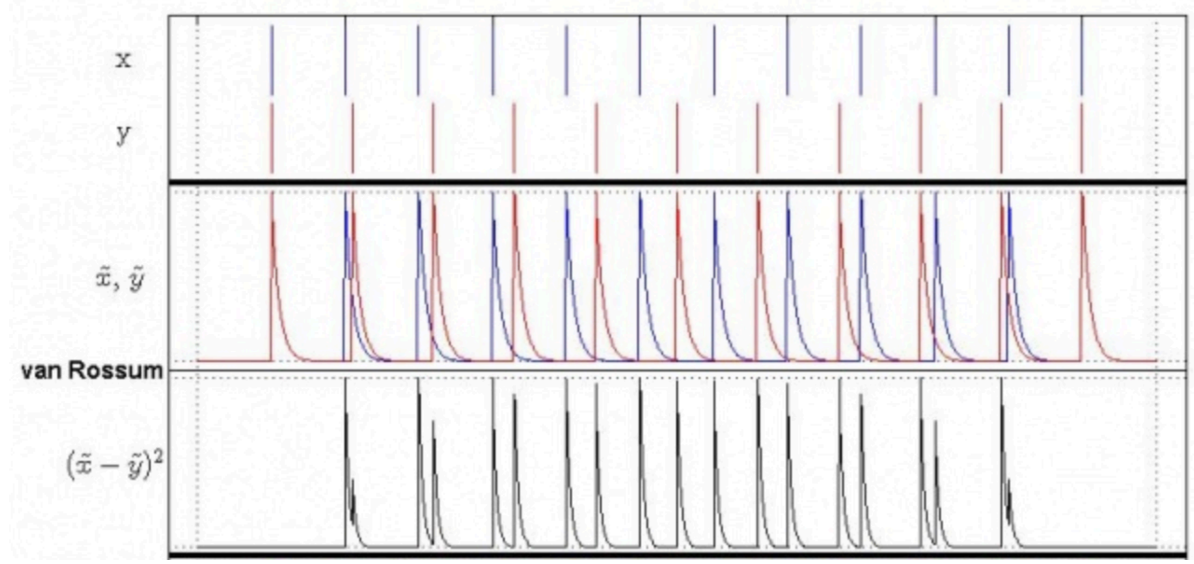



# Spike distance




Victor-Purpura distance




Van Rossum distance

$$c_t = \gamma c_{t-1} + s_t$$

$$F_t = c_t + \epsilon_t, \epsilon_t \overset{i.i.d}{\sim} \mathcal{N}(0,\sigma^2)$$

1. How to estimate $\gamma$?

   a. Estimate from a segment of exponentially decaying data (eye-ball test)
   b. (Follow-up paper) $\gamma = 1 - \frac{\Delta_t}{\phi}$

2. How to choose $\lambda$?

2-fold Cross-validation to minimize MSE of estimated $Ca^{2+}$,e.g. ,

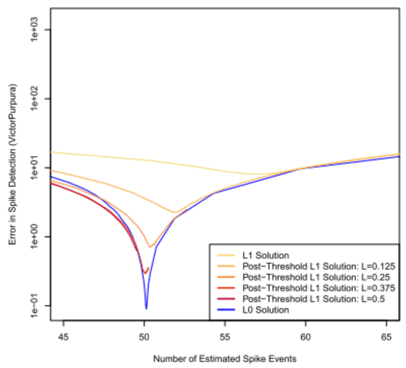
$$\hat{c}_2 = \frac{1}{2}(\hat{c}_1 + \hat{c}_3)$$

3. In reality, $F_t = \beta_1 c_t + \beta_0 + \epsilon_t$ or $F_t = c_t + \beta_{0,t} + \epsilon_t$

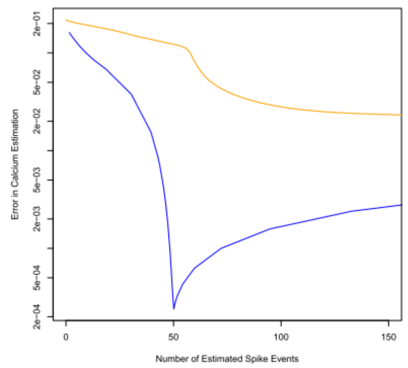
Reformulate the optimization problem and/or try a grid of intercept values via CV and pick the best fit

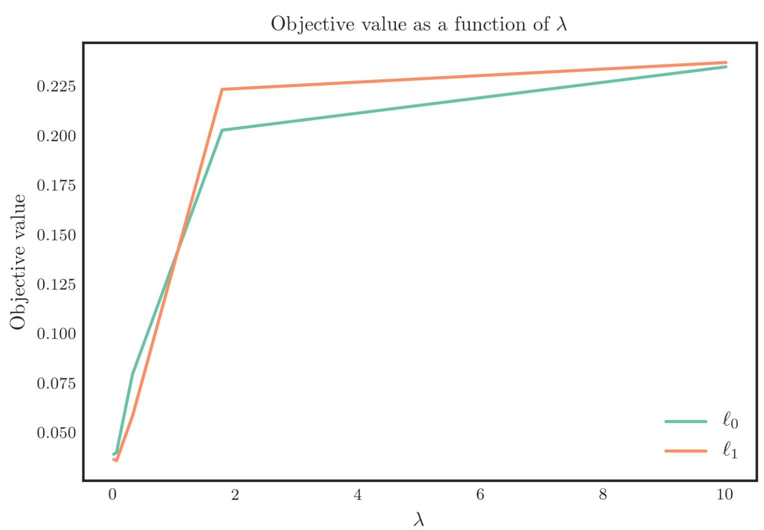
# Result 2: $\ell_0$ versus $\ell_1$ (under AR-1 generative process)

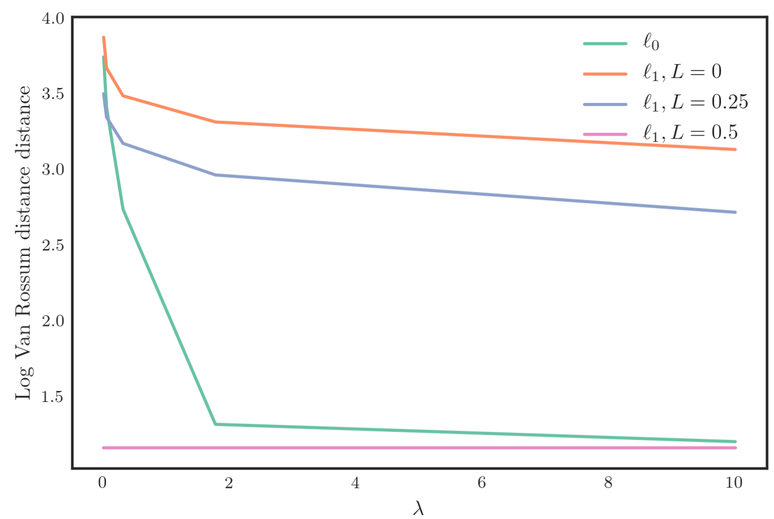
(b)

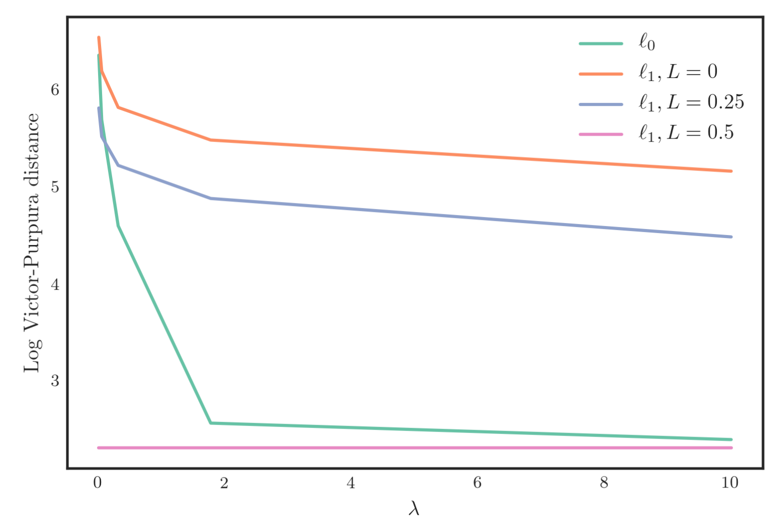



(c)



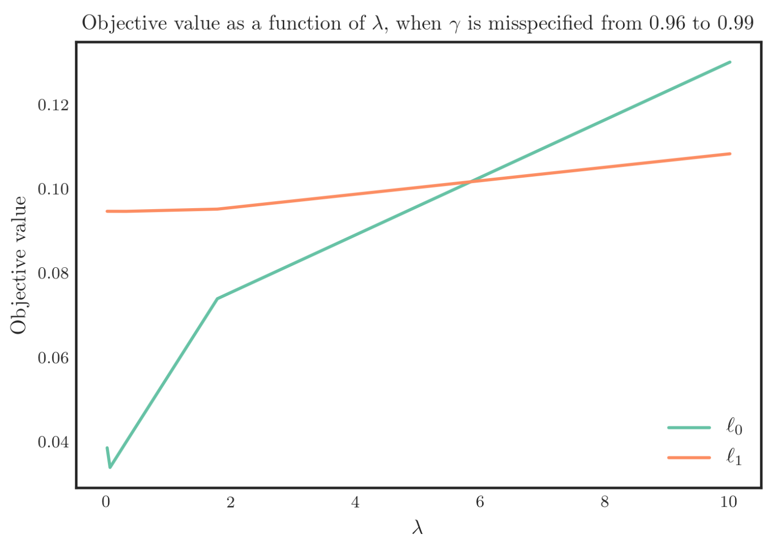



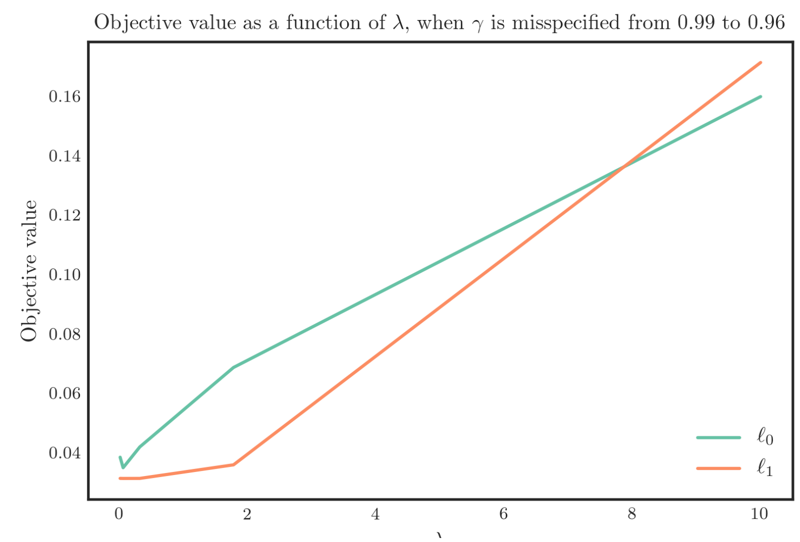



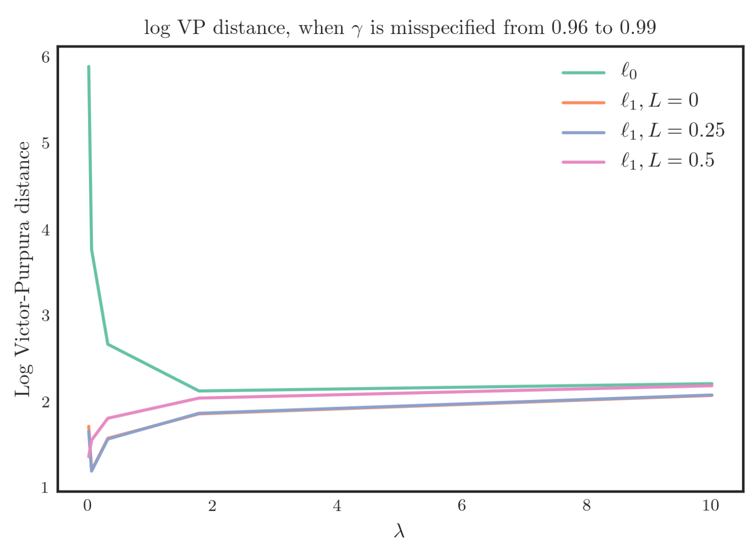

Our proposed algorithm does pretty well!

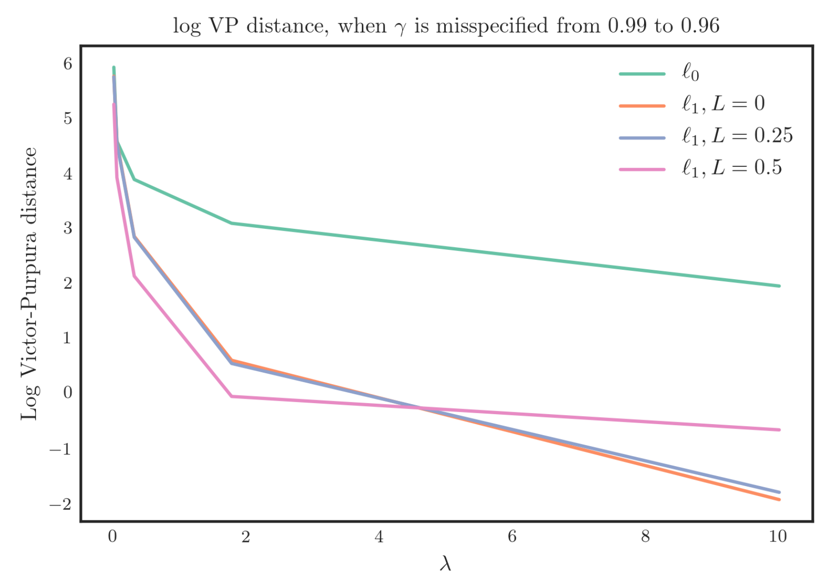
# Brownie point:

## How sensitive are $\ell_0$ and $\ell_1$ to the specification of $\gamma$



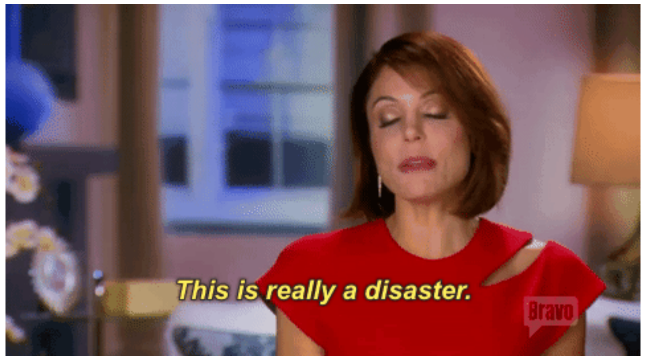



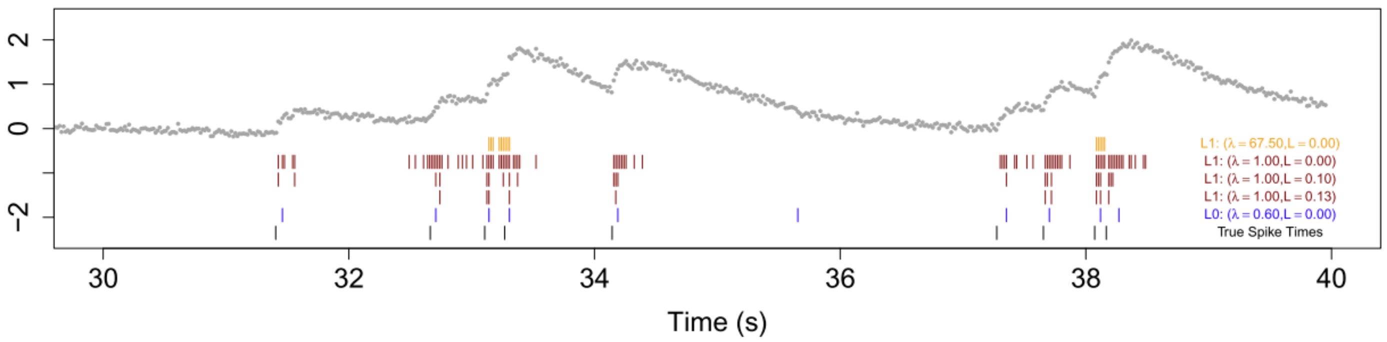




Underestimate decay

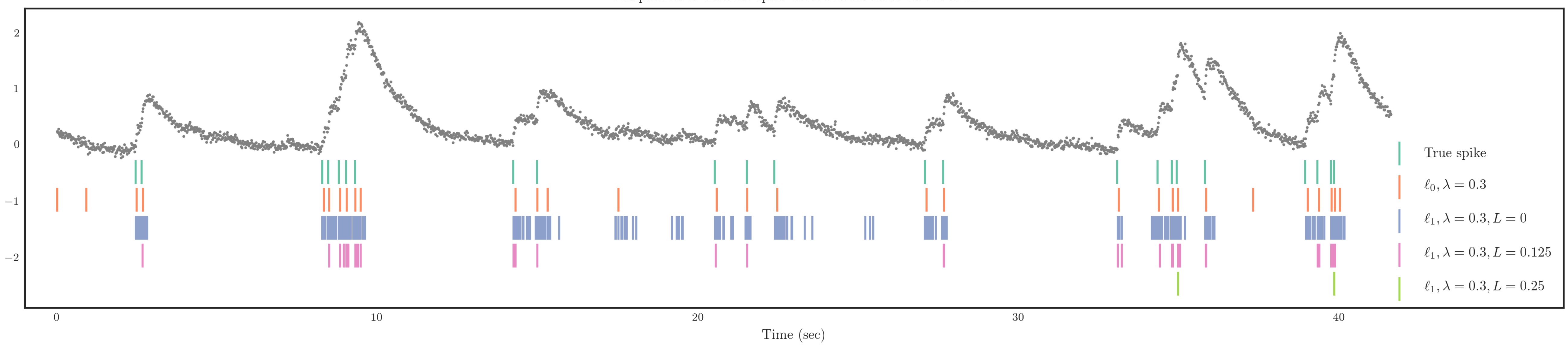
Overestimate decay



# Result 3: $\ell_0$ versus $\ell_1$ on Chen et al. dataset



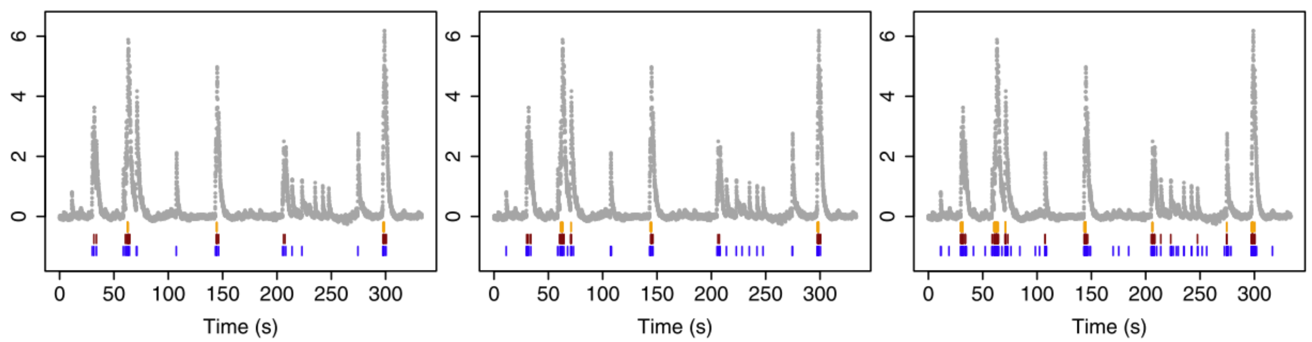

Comparison of different spike detection methods on cell 2002




Observations:

1. L0 does well! - why this cell; is it generalizable?
2. Why no metric is reported?
3. The way paper chooses the hyper-parameter on this data is more *ex post facto* than systematic

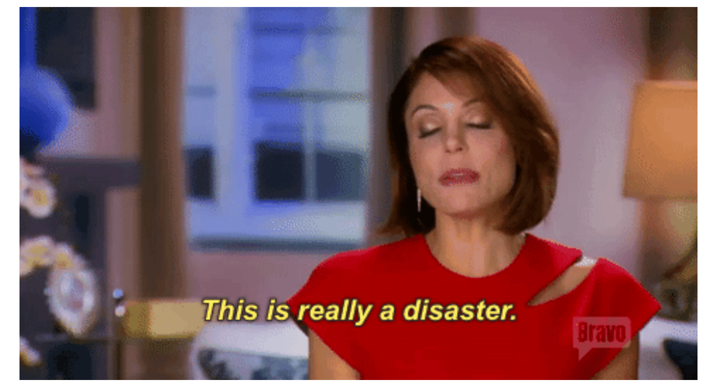
# Result 3: $\ell_0$ versus $\ell_1$ on Allen Institute data

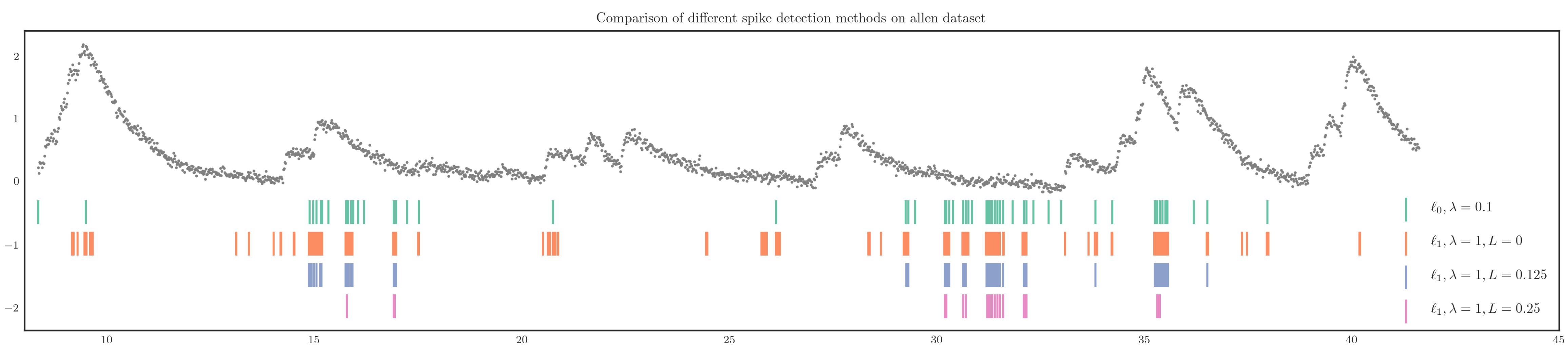


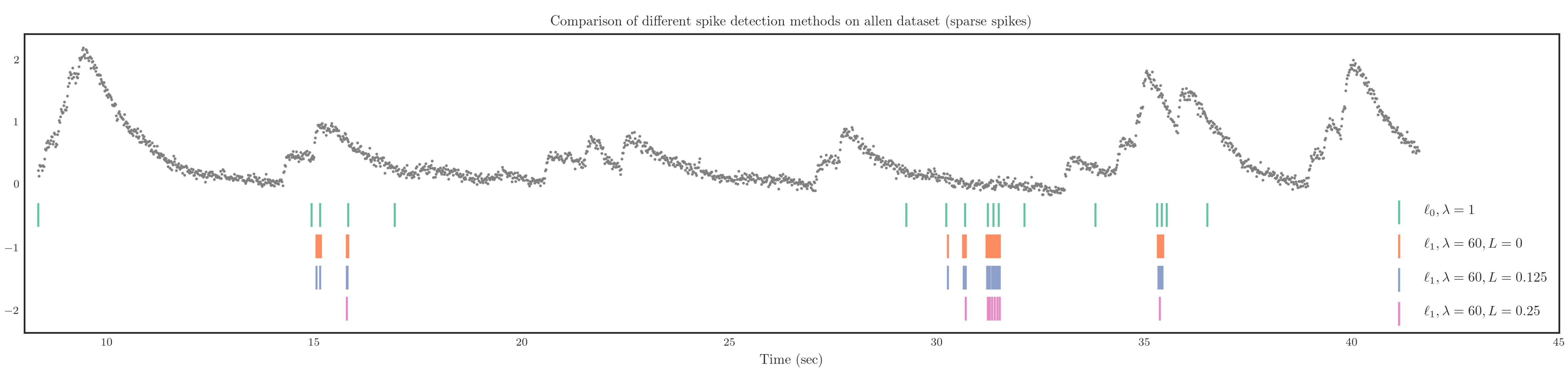

(a) 27 spikes. (b) 49 spikes. (c) 128 spikes.

Observations:

1. L0 is not perfect :(
2. Can one do better than eyeball testing for validation on unlabeled data?



# Reference:

Thanks!!!


Glimcher, P.W. (2011). Understanding dopamine and reinforcement learning: the dopamine reward prediction error hypothesis. Proceedings of the National Academy of Sciences of the United States of America, 108 Suppl 3, 15647–15654. https://doi.org/10.1073/pnas.1014269108

Koulchitsky, S., De Backer, B., Quertemont, E., Charlier, C., & Seutin, V. (2012). Differential effects of cocaine on dopamine neuron firing in awake and anesthetized rats. Neuropsychopharmacology: Official Publication of the American College of Neuropsychopharmacology, 37(7), 1559–1571. https://doi.org/10.1038/npp.2011.339

Paladini, C. A., Robinson, S., Morikawa, H., Williams, J.T., & Palmiter, R. D. (2003). Dopamine controls the firing pattern of dopamine neurons via a network feedback mechanism. Proceedings of the National Academy of Sciences of the United States of America, 100(5), 2866–2871. https://doi.org/10.1073/pnas.0138018100

Chen, T.-W., et al. (2013). Ultra-sensitive fluorescent proteins for imaging neuronal activity. Nature

Friedrich, J., Zhou, P., & Paninski, L. (2017). Fast online deconvolution of calcium imaging data. PLoS Computational Biology, 13(3), e1005423.

Jewell, S., & Witten, D. (2018). EXACT SPIKE TRAIN INFERENCE VIA $\ell 0$ OPTIMIZATION. The Annals of Applied Statistics, 12(4), 2457–2482.

Vogelstein, J.T., et al. (2010). Fast nonnegative deconvolution for spike train inference from population calcium imaging. Journal of Neurophysiology, 104(6), 3691–3704.