# Dynamical systems for behavioral and neural data


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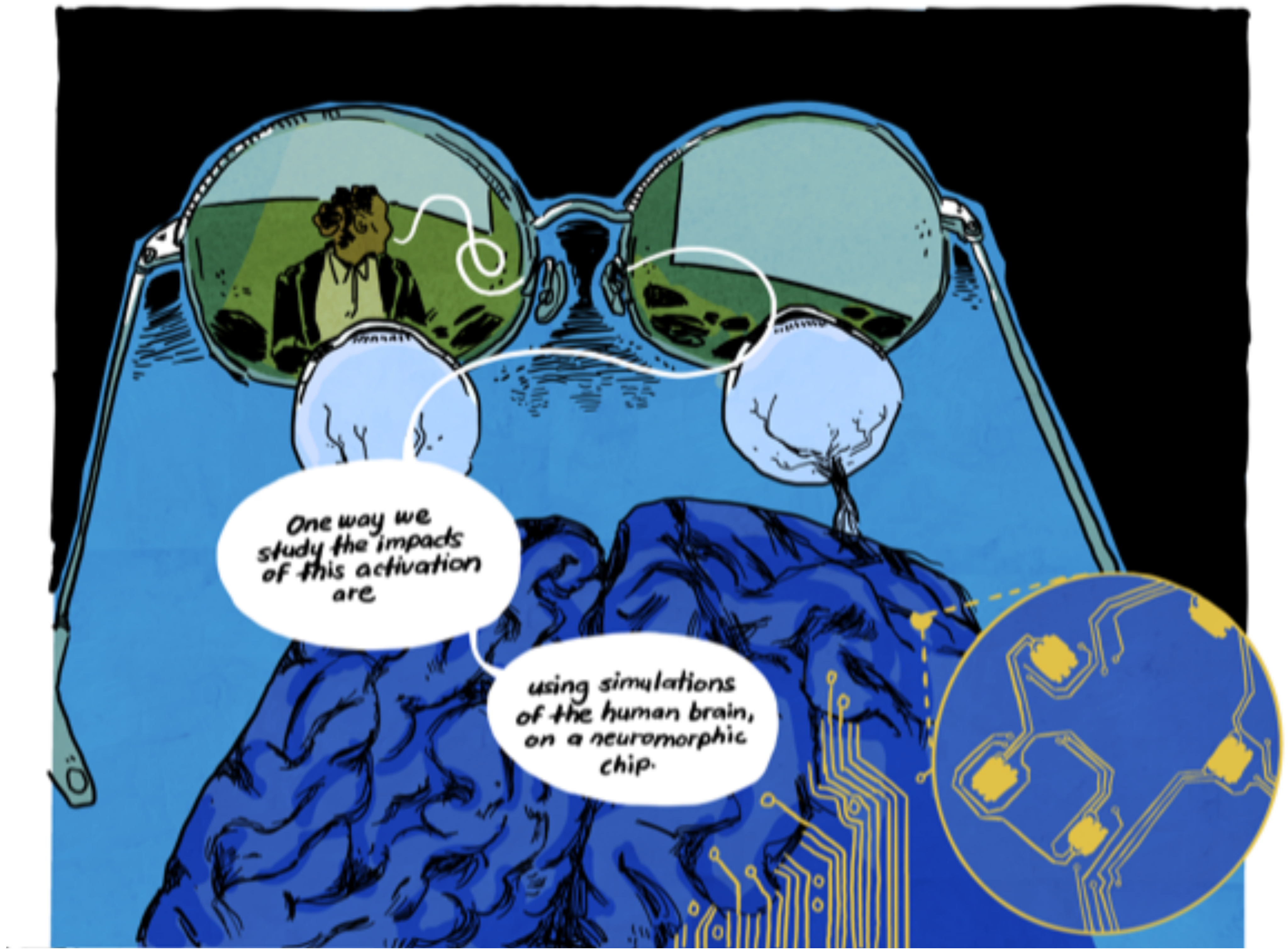


Artwork by Audra McNamee

# Dynamical systems for behavioral and neural data

- TODAY: hidden Markov models, neural data & RNNs:
  - Slides
    - Spontaneous movements - HMM with Autoregressive observations
    - Naturalistic foraging - HMM with Linear Model emissions
    - HMM best practices
  - Live coding session
    - Mystery dataset
    - Fit Linear Model, Mixture of Linear Model
    - Sample and fit data w/ LM-HMM
    - Model selection for # of hidden states

- Neural data
    - Behavior is metastable (Datta) -> Metastable neural activity (Zach)?
        - spike data + HMM tutorial
        - Poisson HMM basics fit to Zach’s session
        - Calculate dimensionality vs shuffled
- RNN
    - Attractor networks
    - HMM fit to attractors

# Cortical computations via metastable activity


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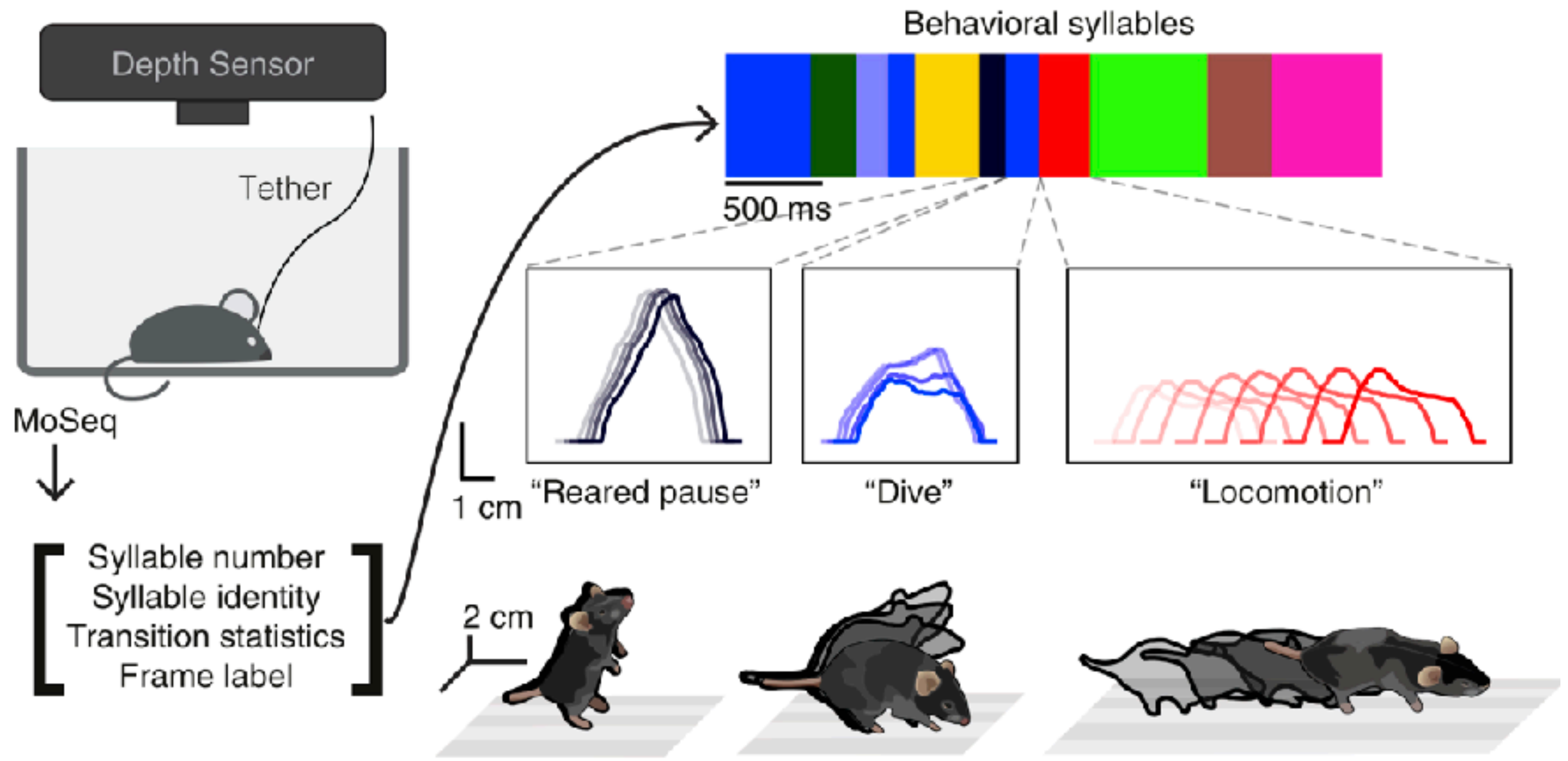
# Complex temporal structure in behavior




Variability sources:

1 - many syllables / actions

2 - many words / sequences

3 - transition times (action duration)

[Wiltschko et al, 2015]
[Markovits et al, 2018]

# Complex temporal structure in behavior

# …originating from neural circuit dynamics?

**Neural mechanisms underlying the temporal organization of naturalistic animal behavior**

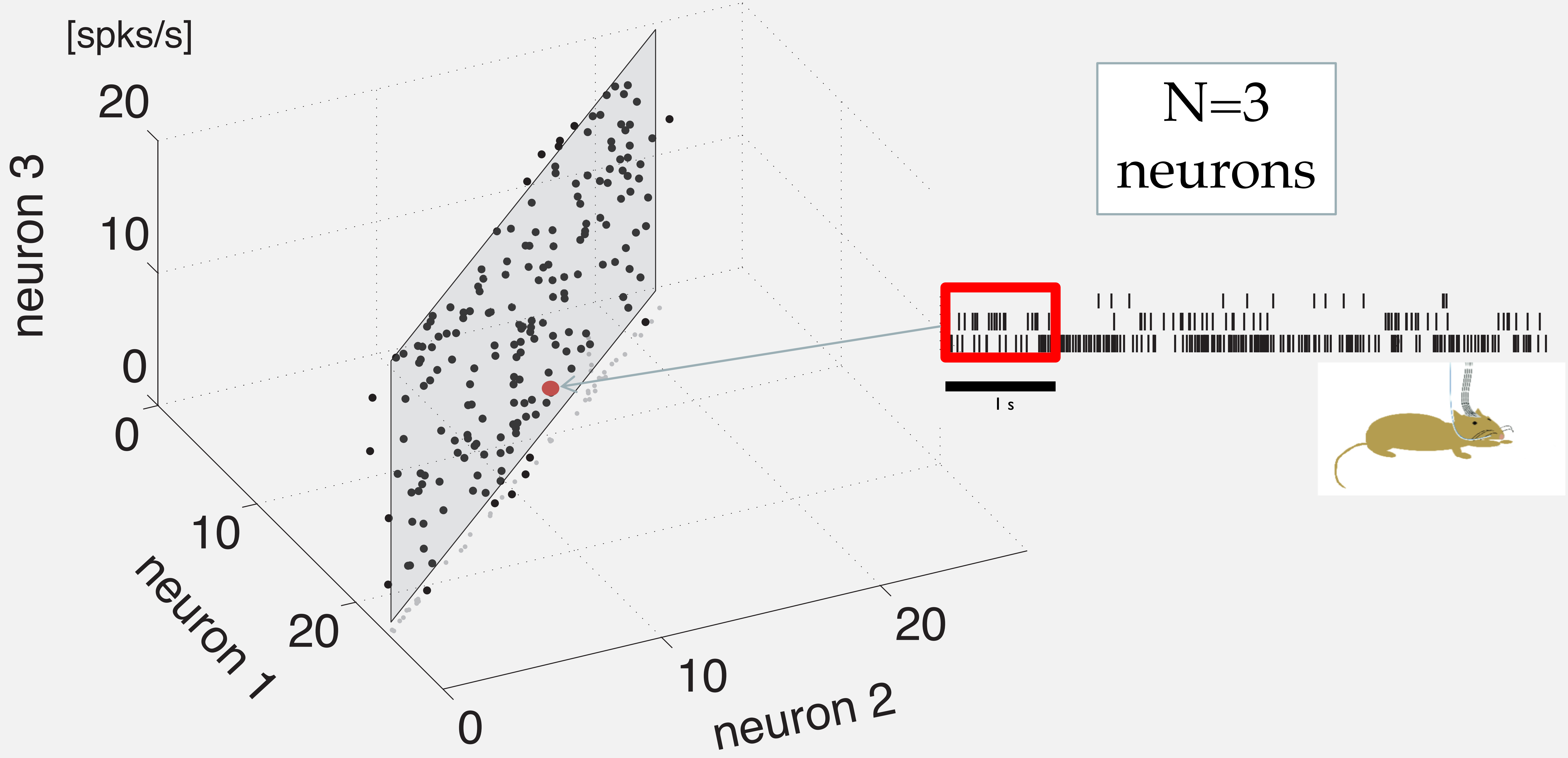
Luca Mazzucato*

eLife

Population activity is a point in N-dimensional space

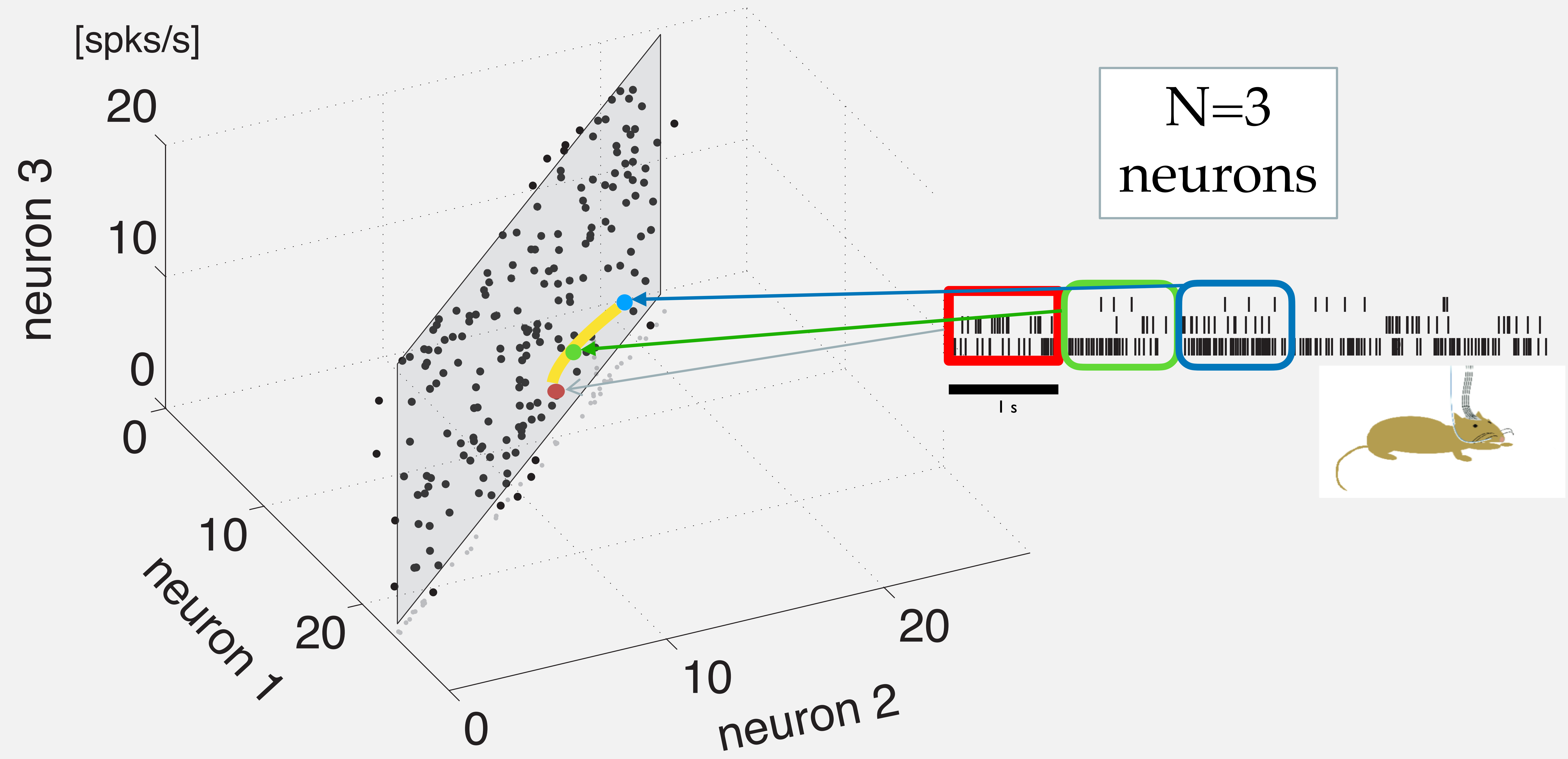
N=3 neurons


$$\overrightarrow{X}(t_1) = [0, 12, 38] \text{ spks/s}$$




N=3
neurons

$d$ = smallest # of coord.
axes accounting for
neural pop. activity

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$d$ = smallest # of coord.
axes accounting for
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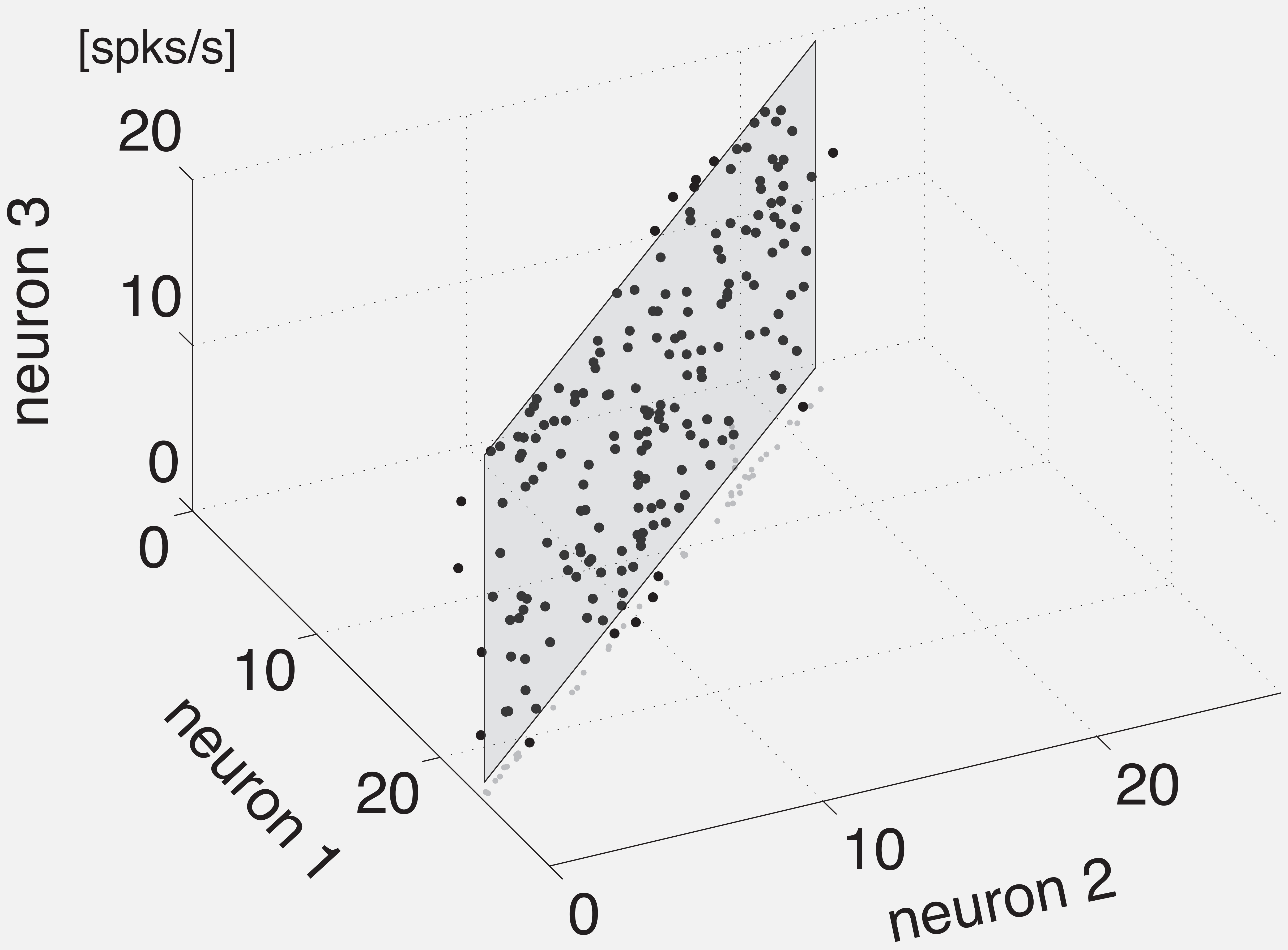
# Neural dimensionality




N=3
neurons

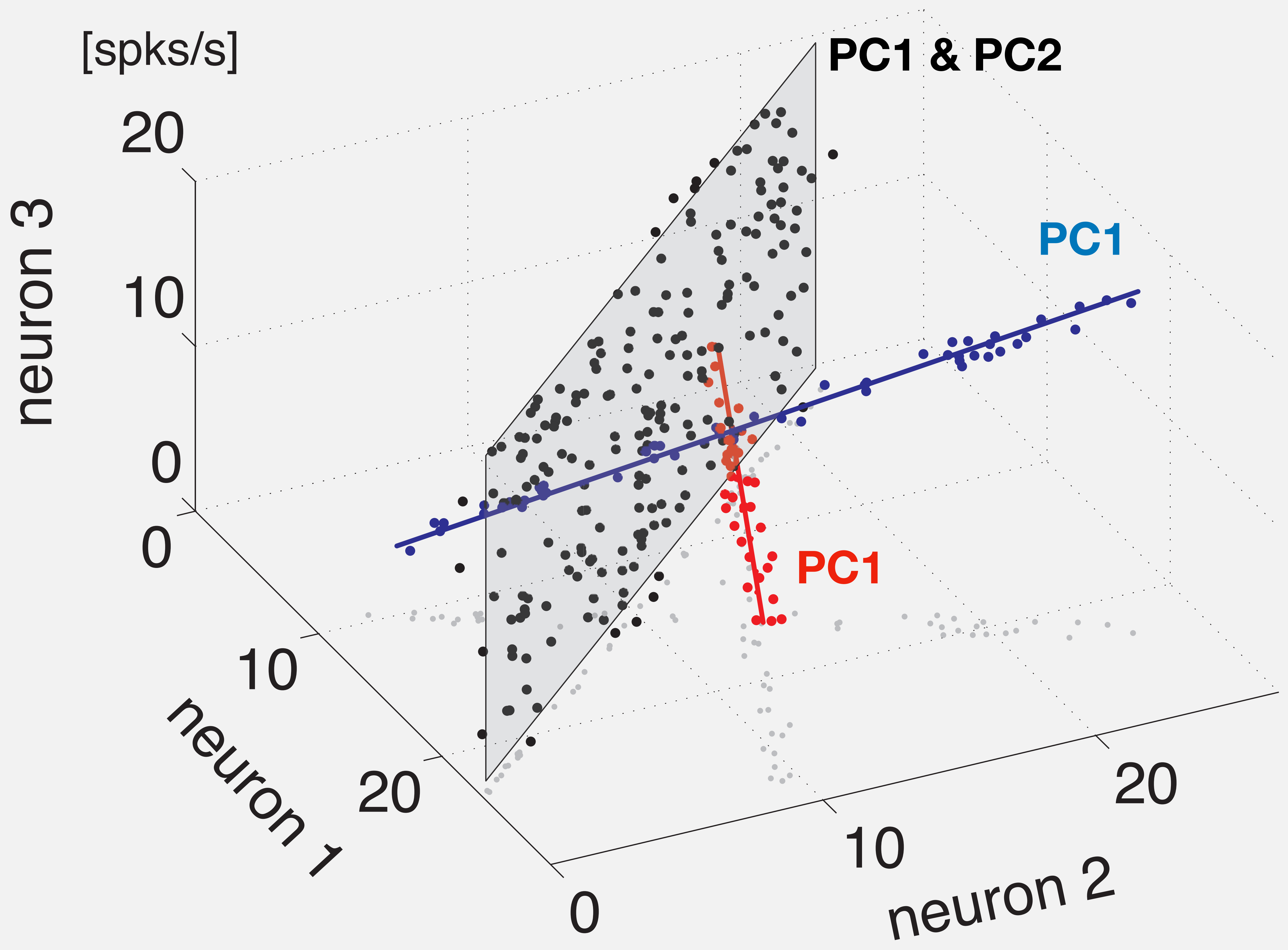
2 coordinate axes
required:

$d = 2$

$d$ = smallest # of coord. axes accounting for neural pop. activity

# Neural dimensionality

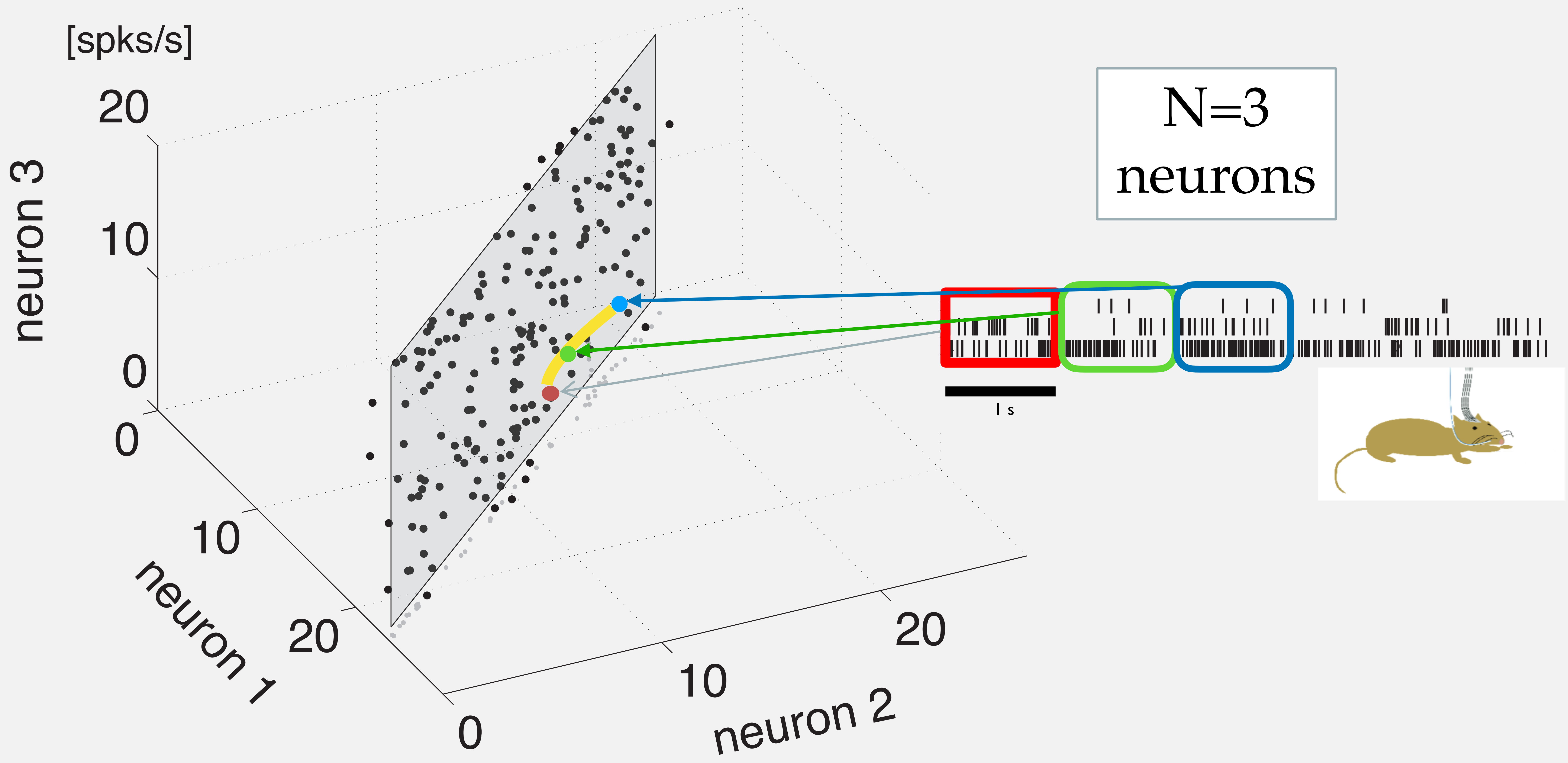
**Principal Component Analysis (PCA)**




N=3
neurons

- ongoing d=2
- stimulus A d=1
- stimulus B d=1

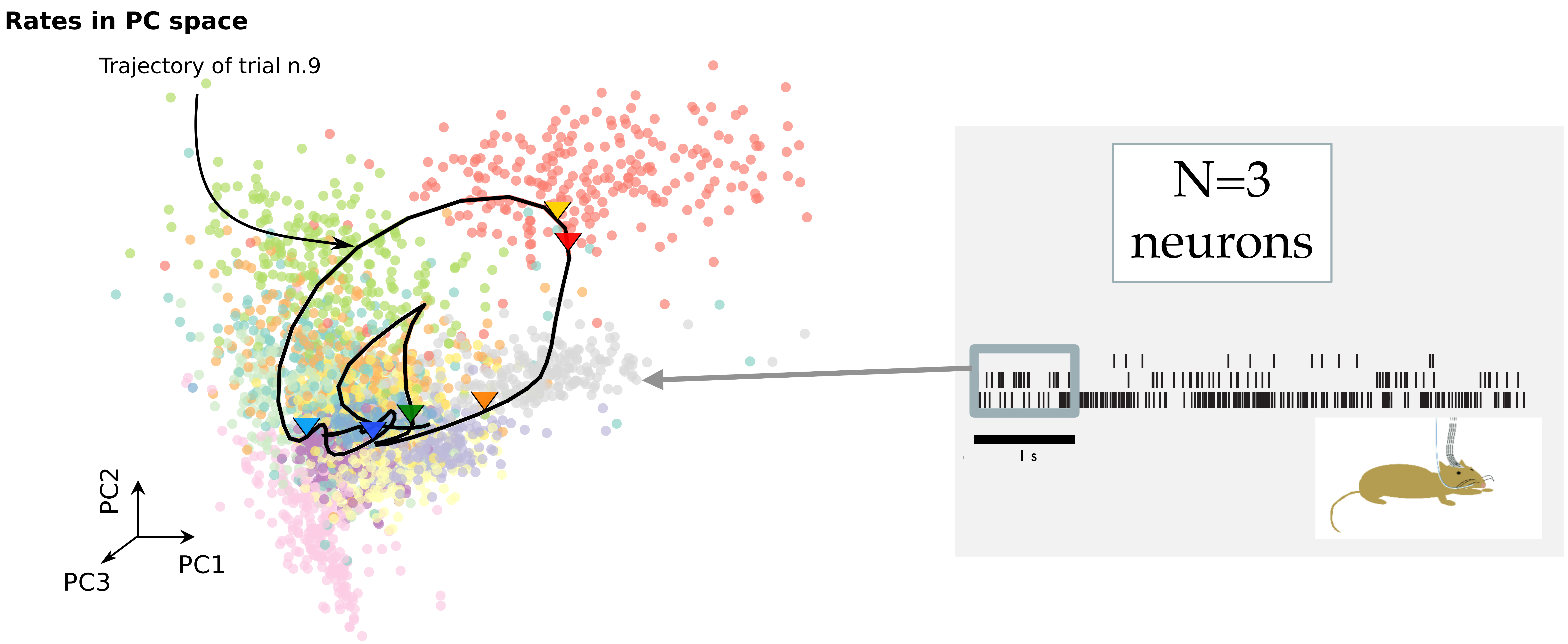
$d$ = smallest # of coord. axes accounting for neural pop. activity




N=3
neurons

$d$ = smallest # of coord. axes accounting for neural pop. activity

# Population activity



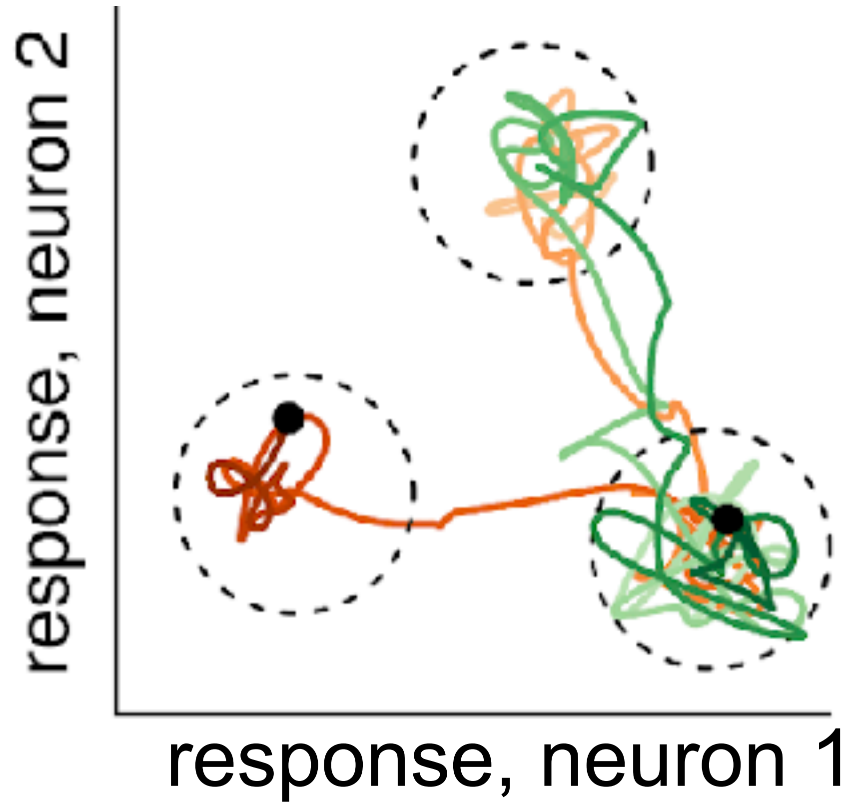
# Temporal dynamics in neural circuits

Dynamical repertoires:

Nonlinear

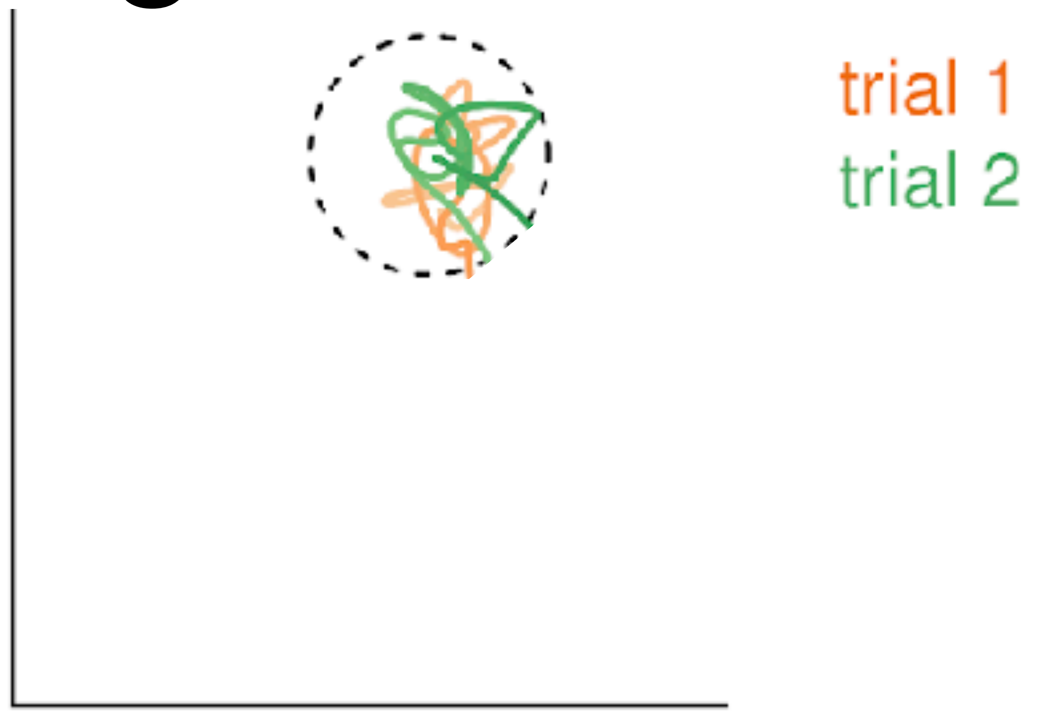
Linear

Multi-attractor

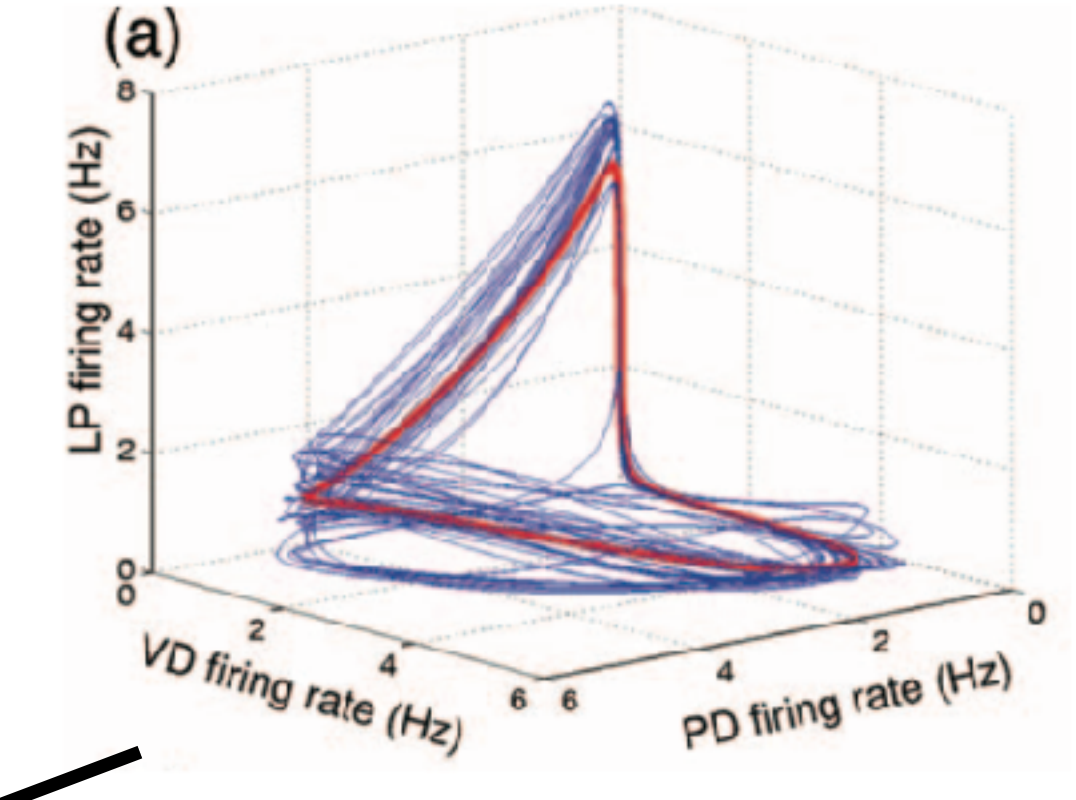



Chaos

Single-attractor




Oscillation

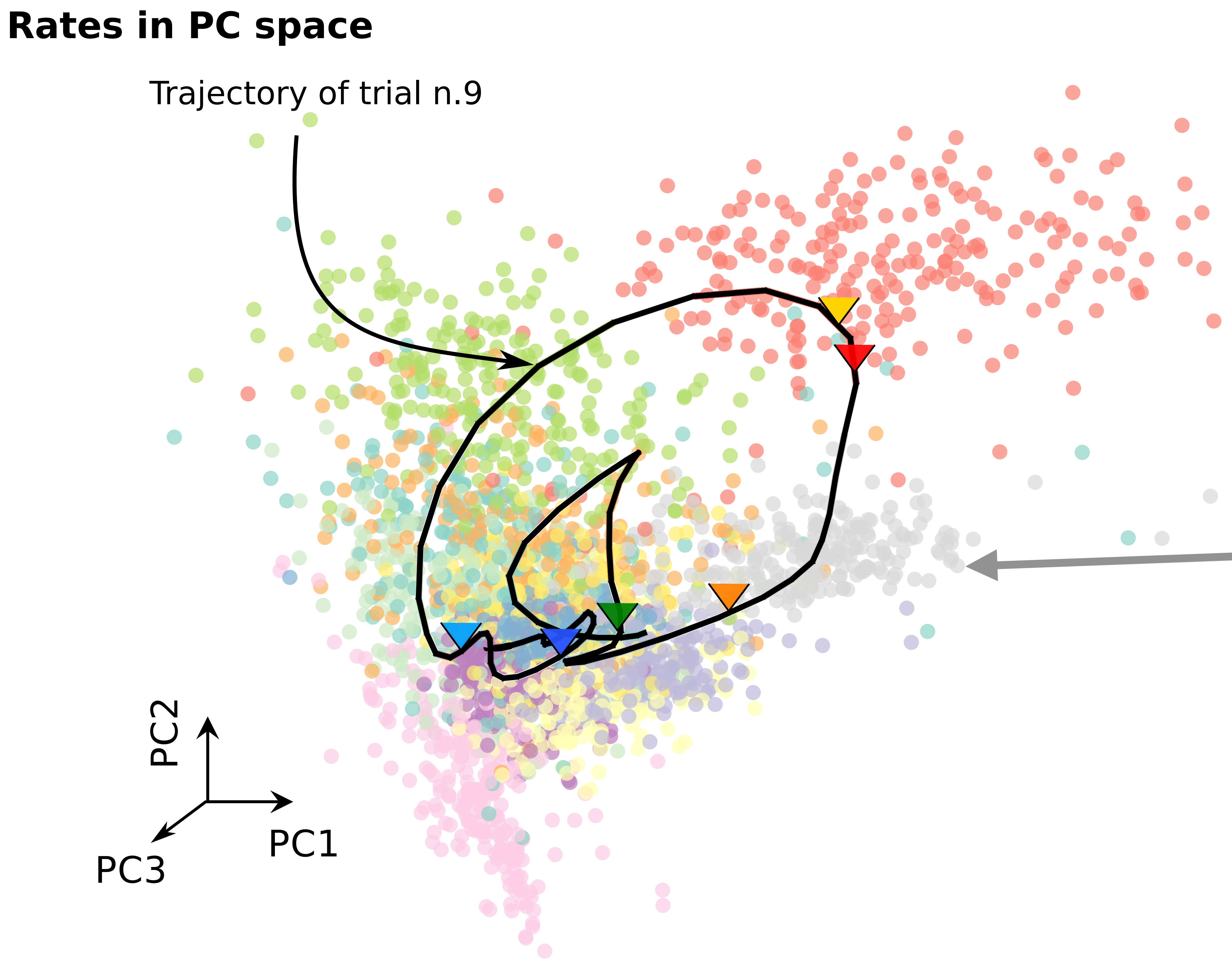


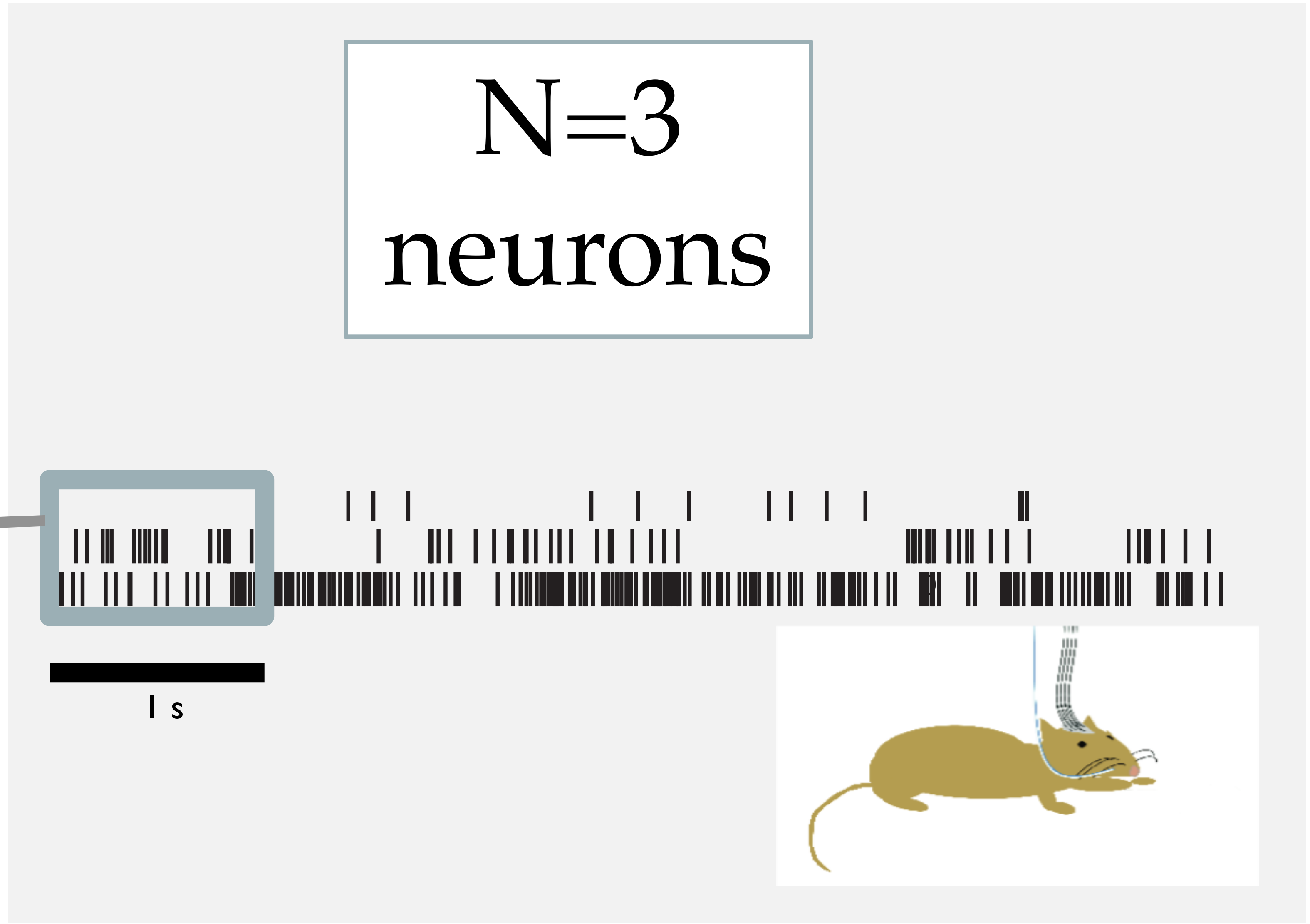

Jumping

Varying smoothly

[Rabinovich et al, 2006]
[Hennequin et al, 2018]

# Population activity



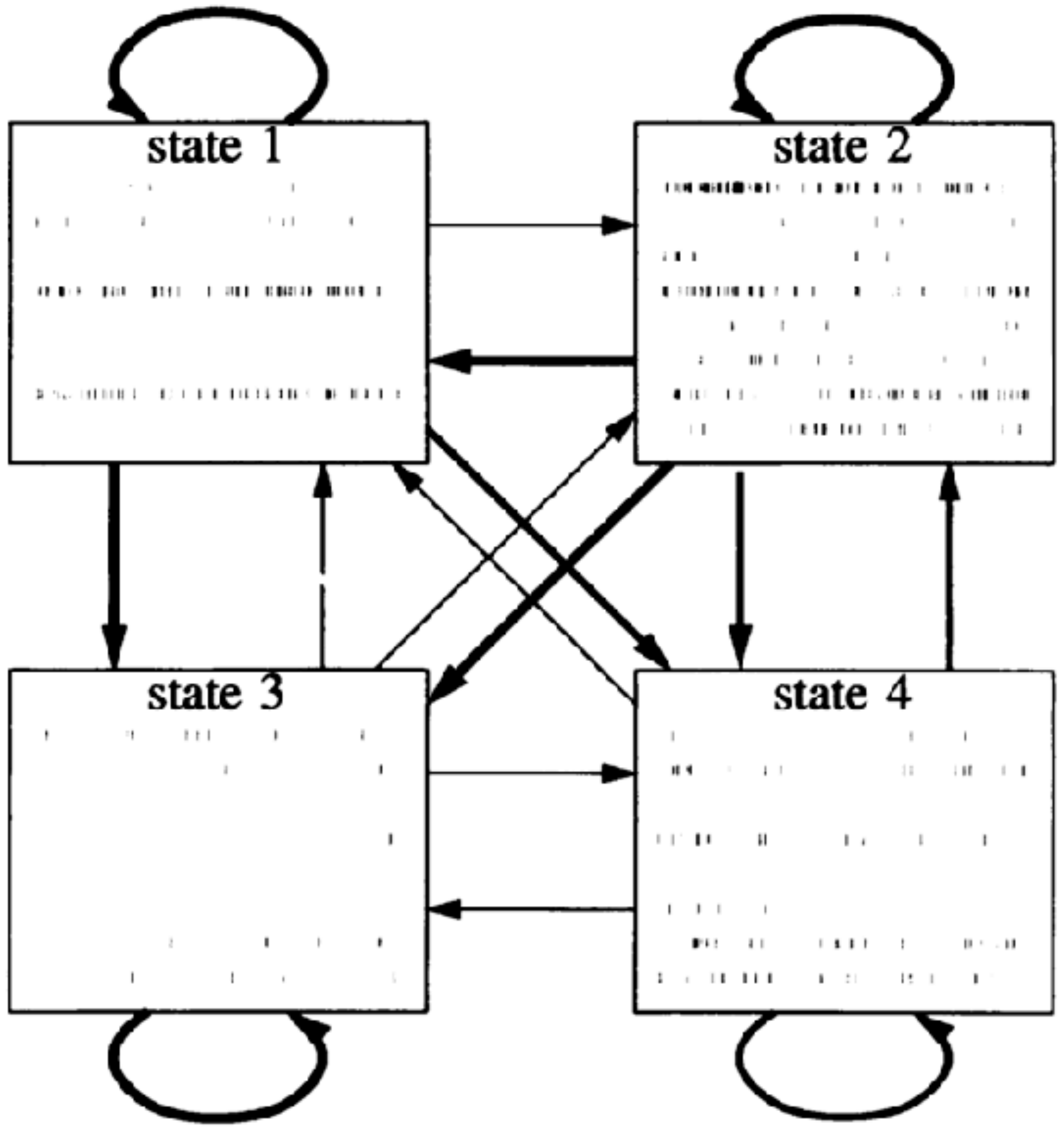
# Metastable activity

*Proc. Natl. Acad. Sci. USA*
Vol. 92, pp. 8616–8620, September 1995
Neurobiology

## Cortical activity flips among quasi-stationary states

**(single-unit activity/behaving monkeys/hidden Markov models)**

Moshe Abeles*†, Hagai Bergman*, Itay Gat‡, Isaac Meilijson§, Eyal Seidemann§, Naftali Tishby‡, and Eilon Vaadia*



# Goals

**Part I - Theory**

- **Metastable activity in cortical circuits**
- **Hidden Markov Models fit to metastable activity**
- **Modeling metastable activity with attractor networks**

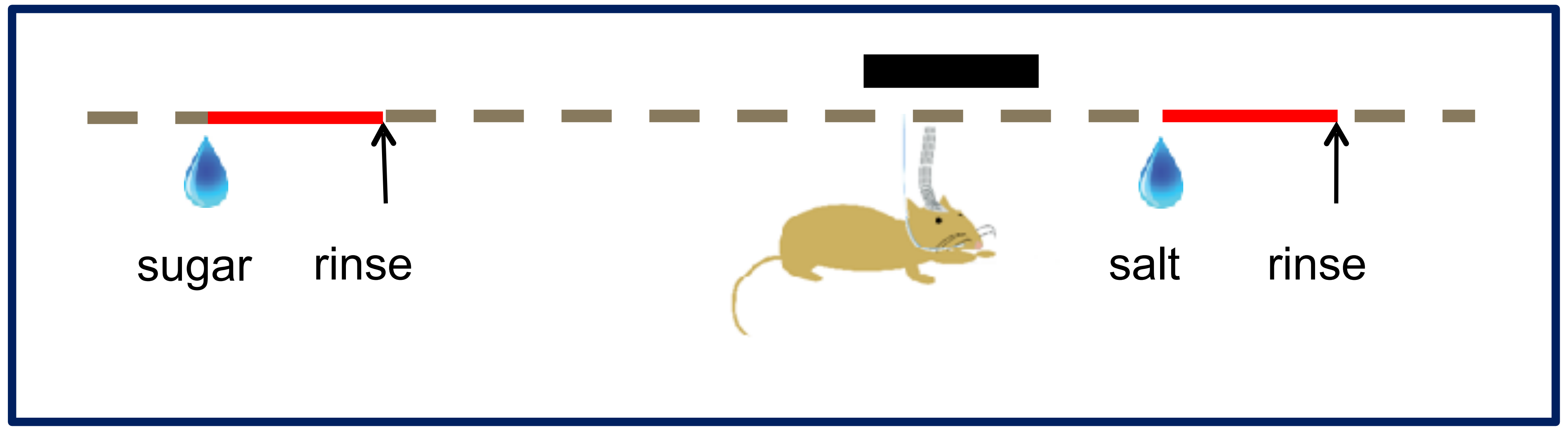
**Part II - Exercise**

- **HMM: model selection with gaussian emissions**
- **Fit Poisson-HMM to spike trains**
- **Challenge: A model of arousal in attractor networks**

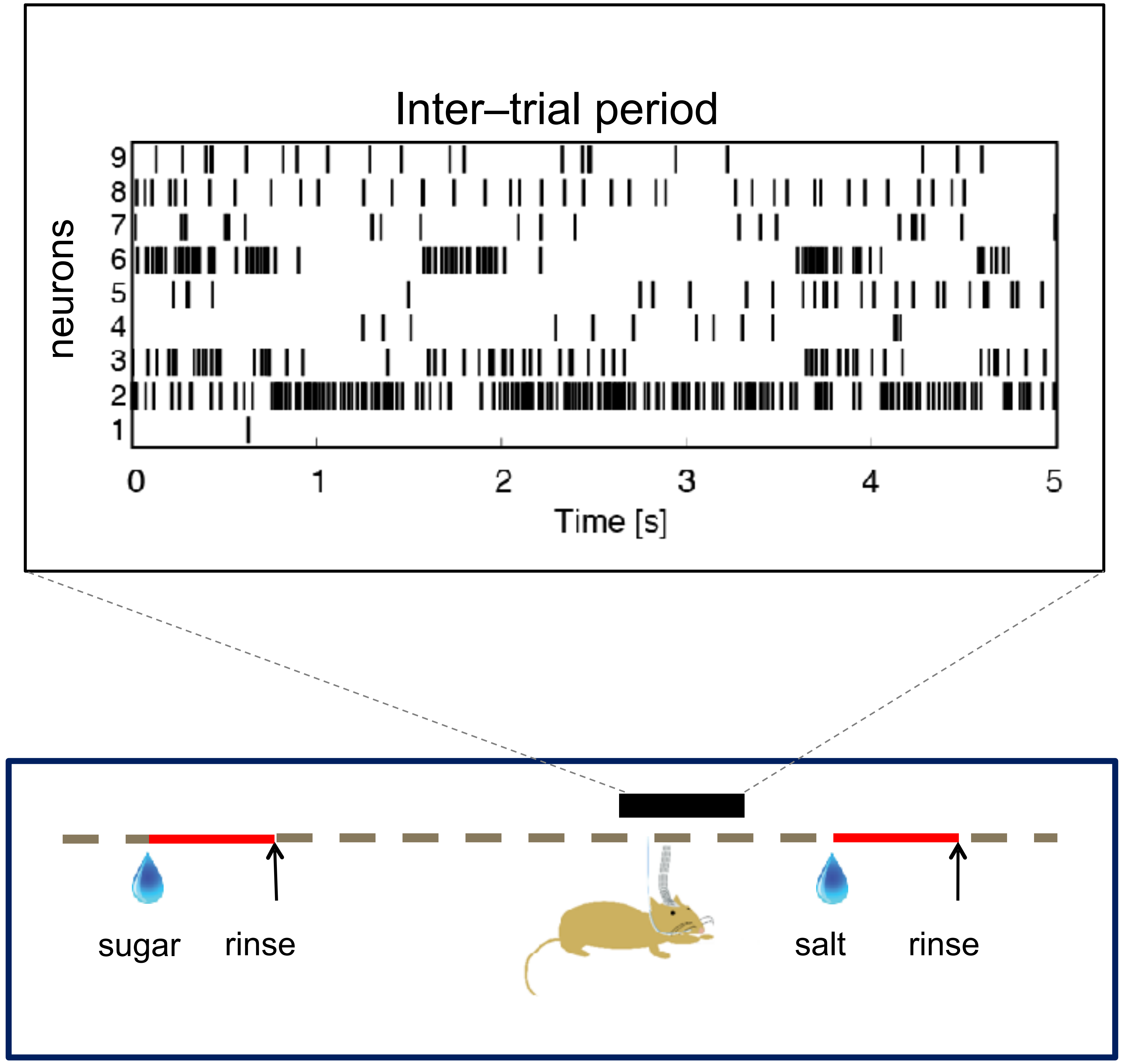
Fit Hidden Markov Models
to neural spike trains…

…and investigate metastable activity

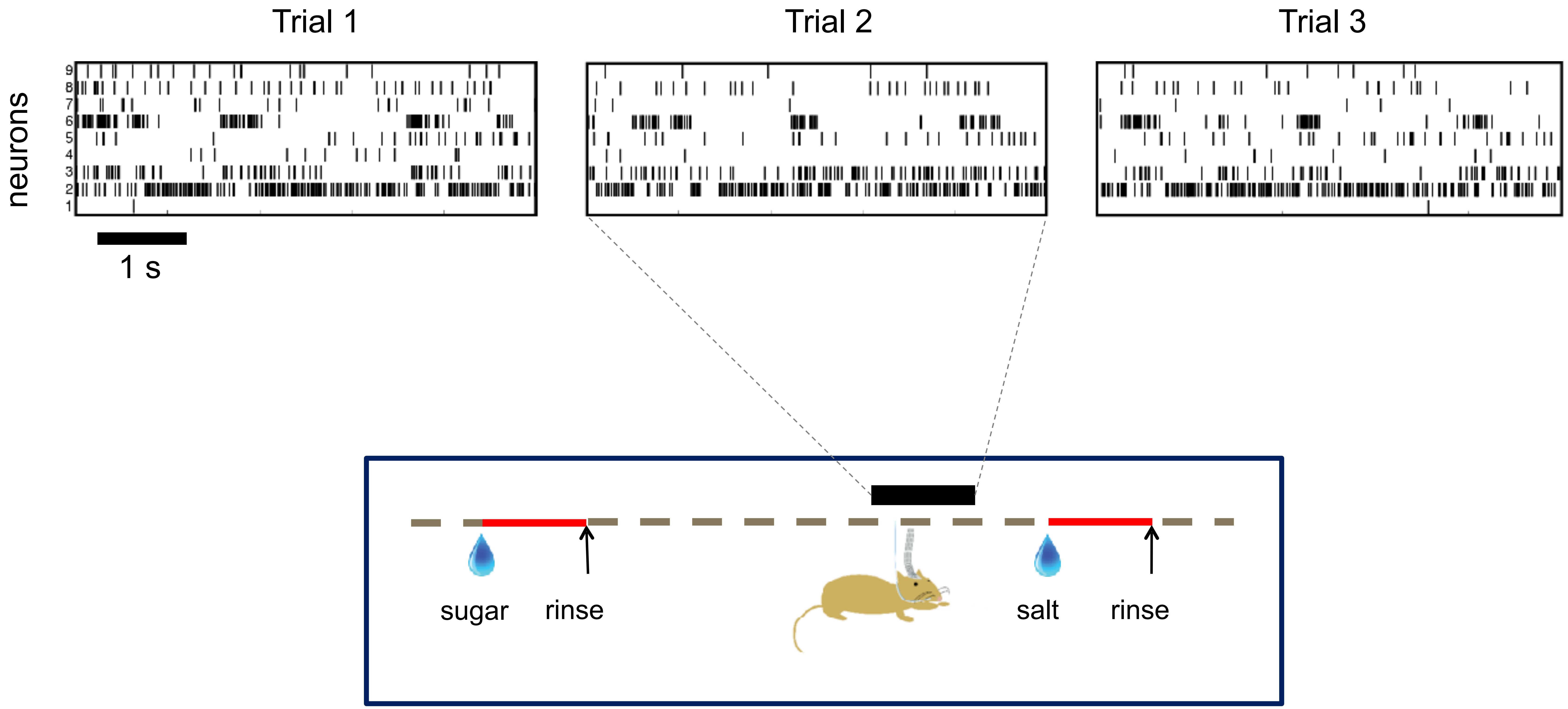
# HMM for neural spike trains



# HMM for neural spike trains

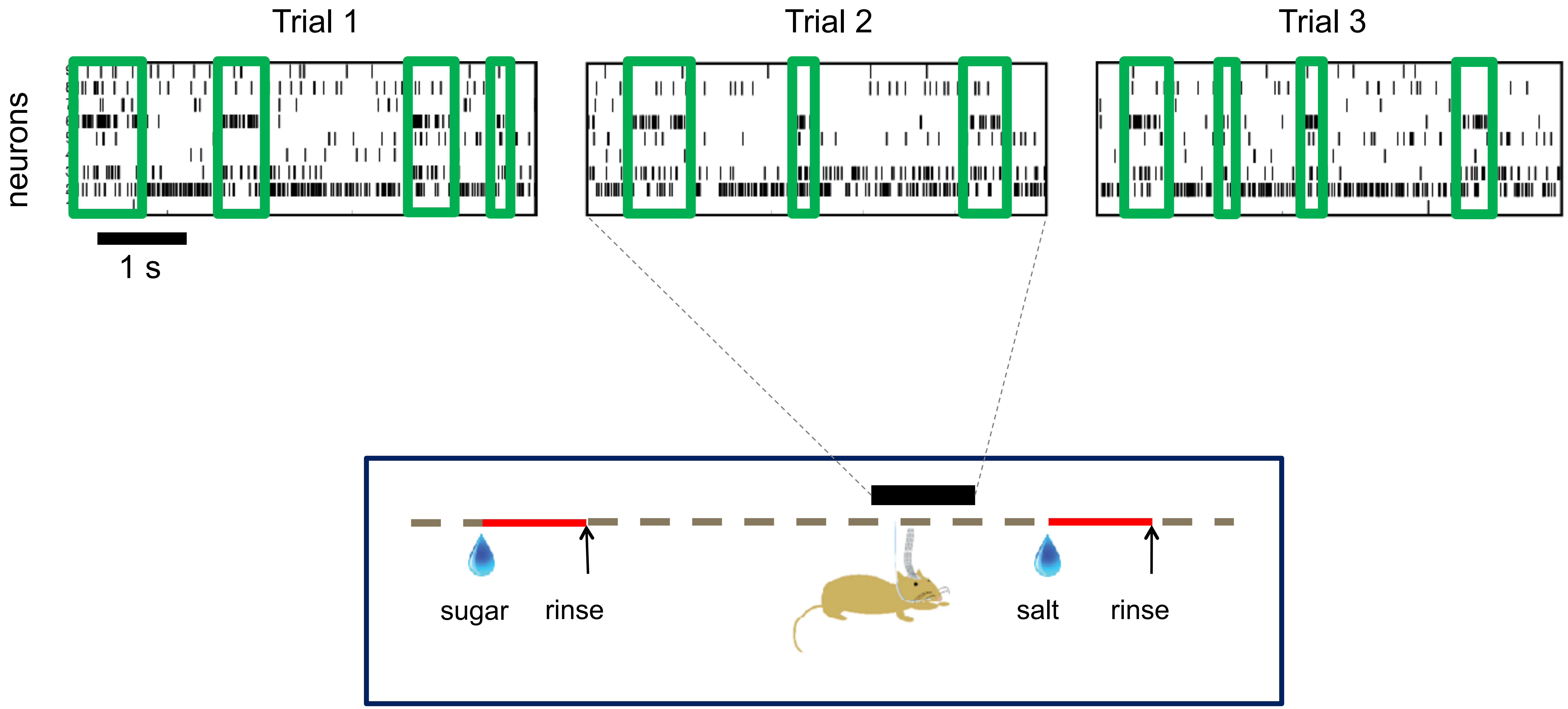


# HMM for neural spike trains



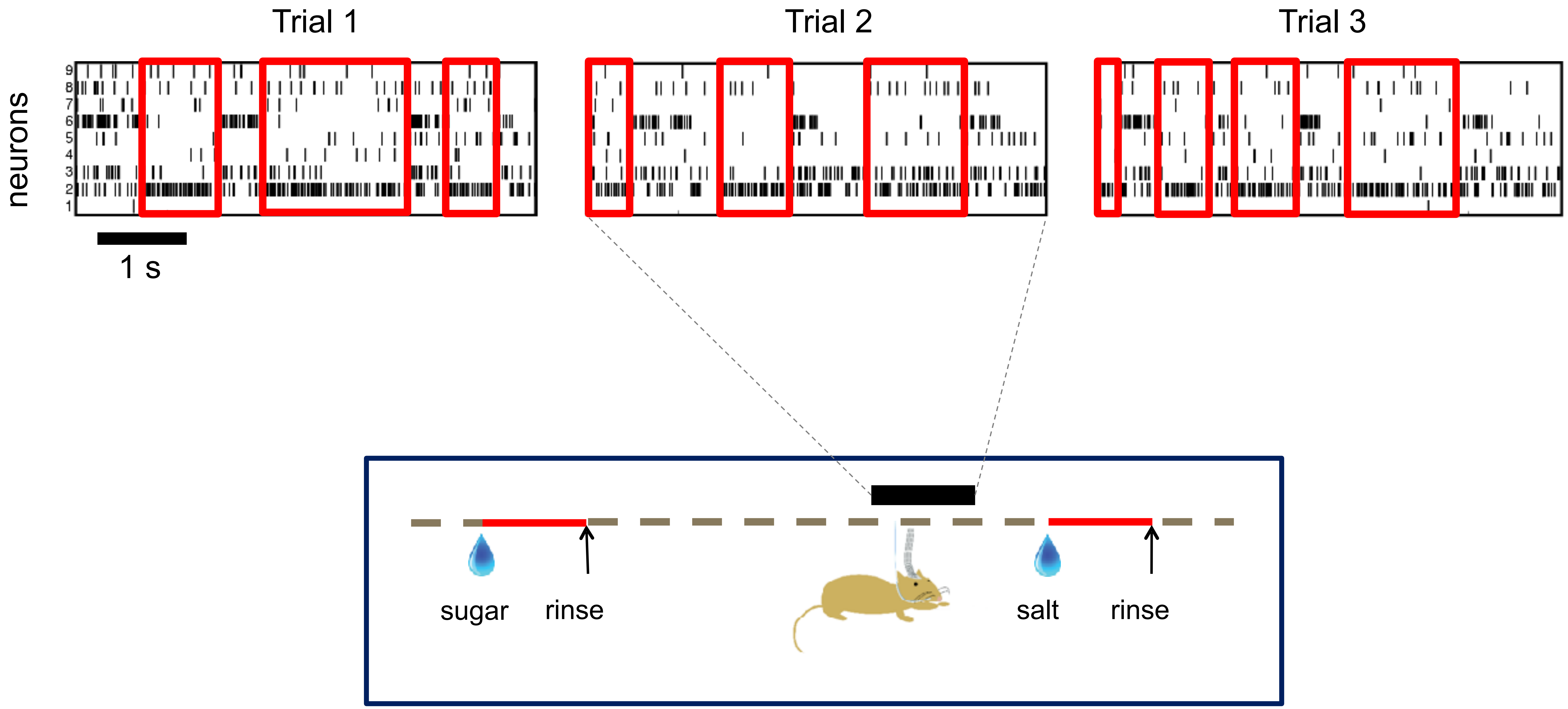

[Mazzucato et al., 2015, 2016]

# HMM for neural spike trains




[Mazzucato et al., 2015, 2016]

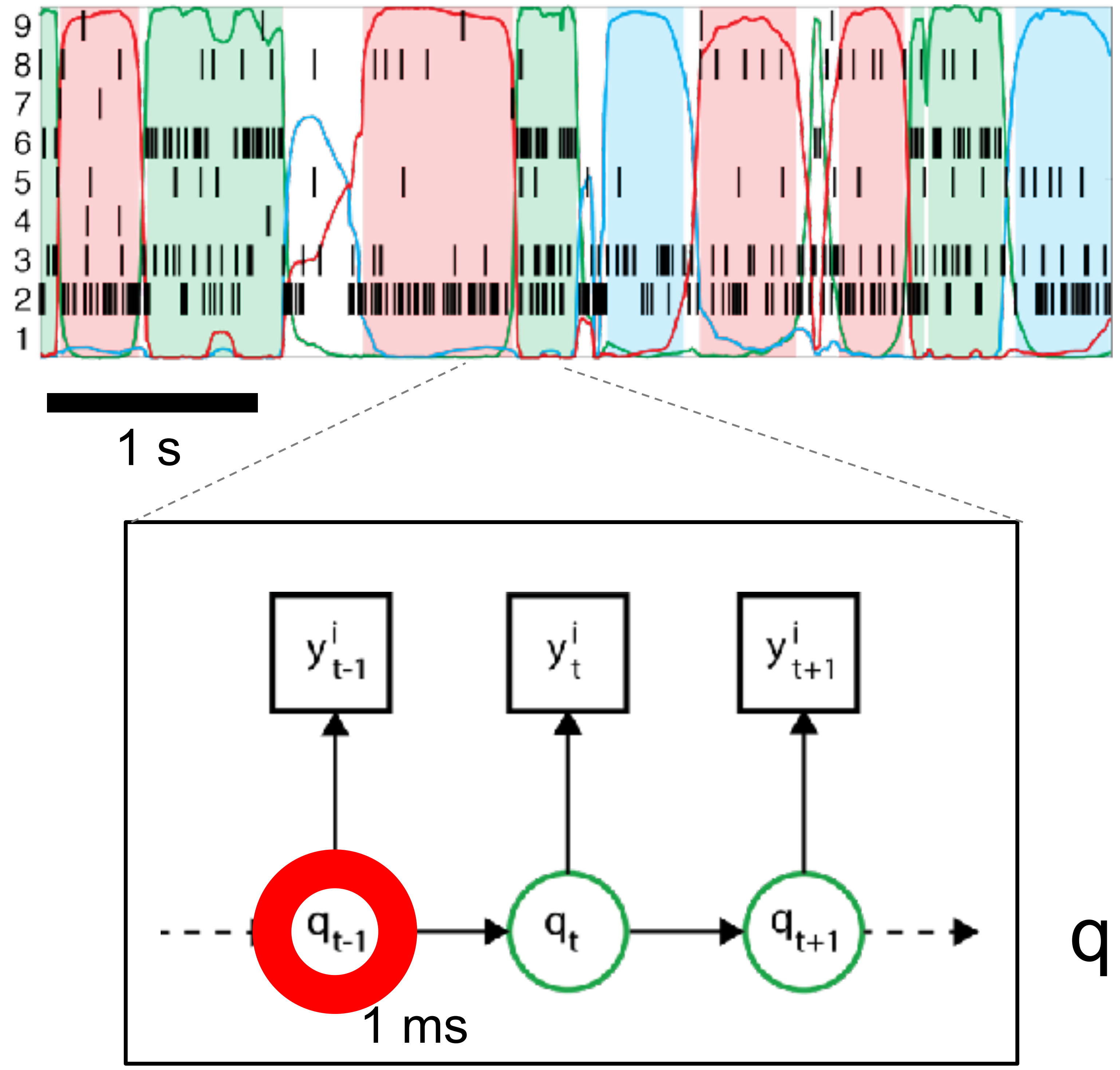
# HMM for neural spike trains




[Mazzucato et al., 2015, 2016]

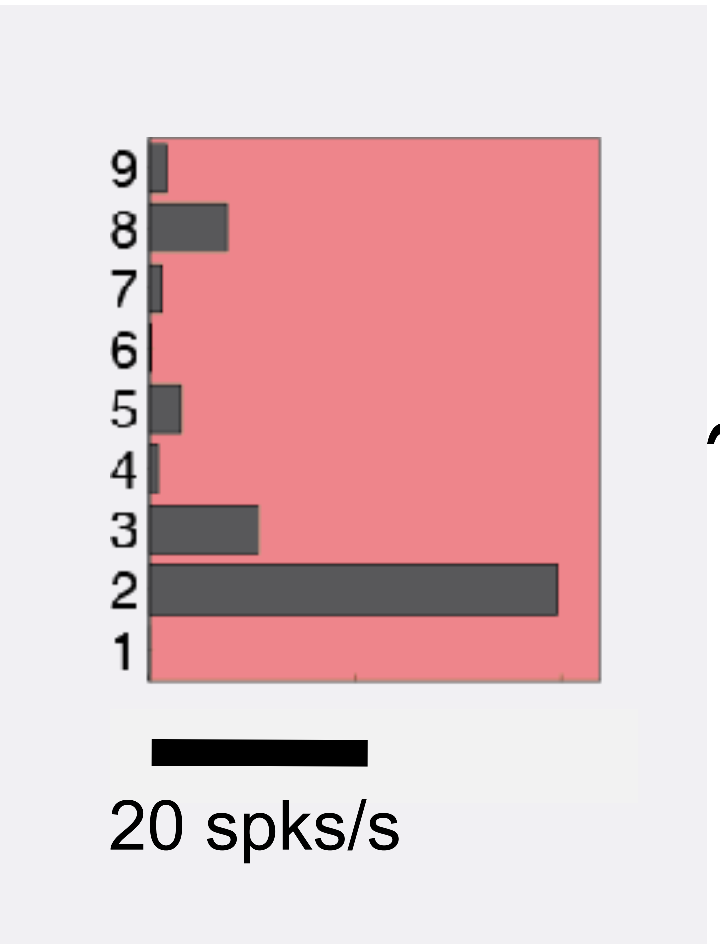
# HMM for neural spike trains

- Hidden Markov Model fit




q = hidden state

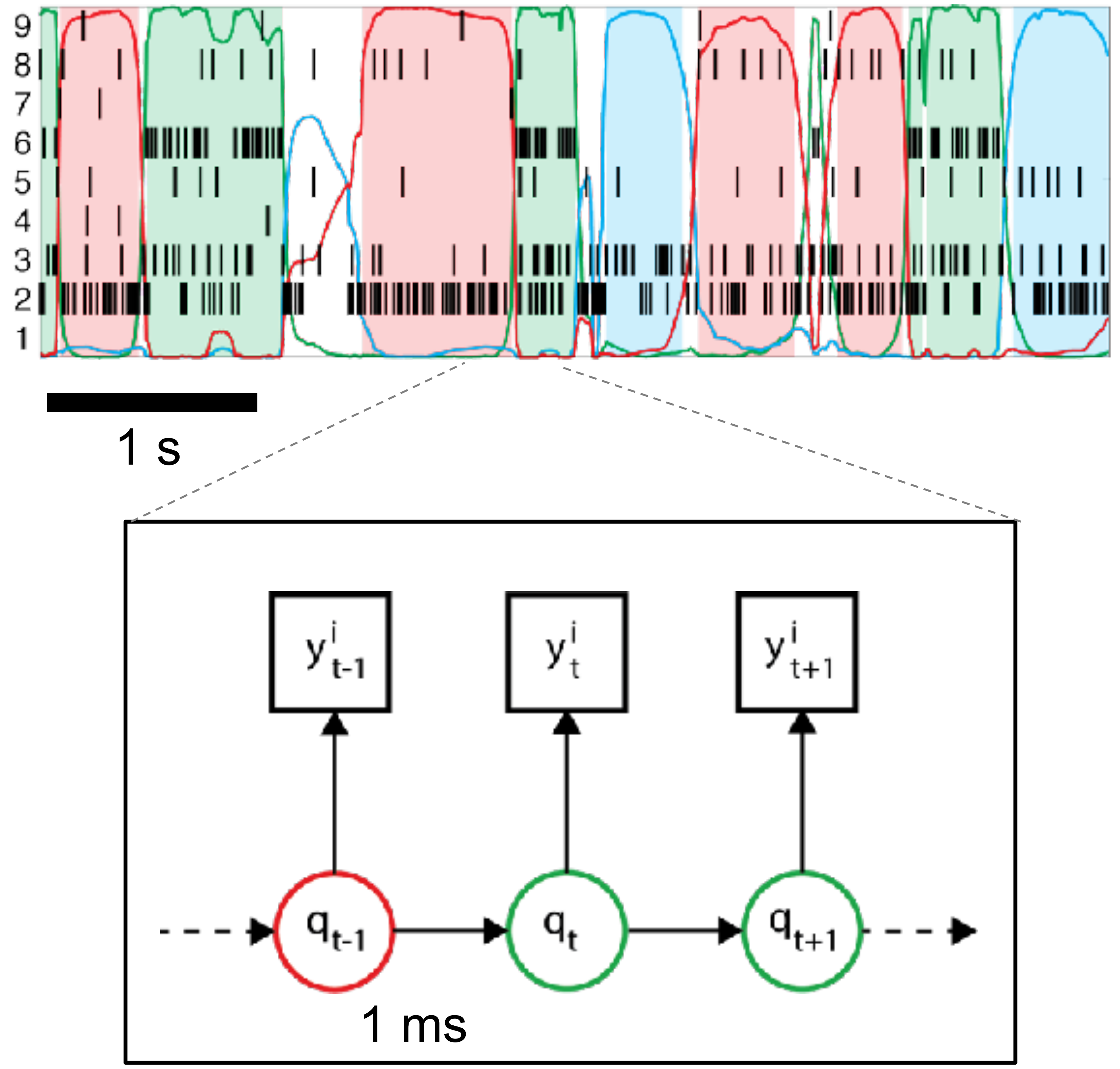
Firing rate vector $r_i$

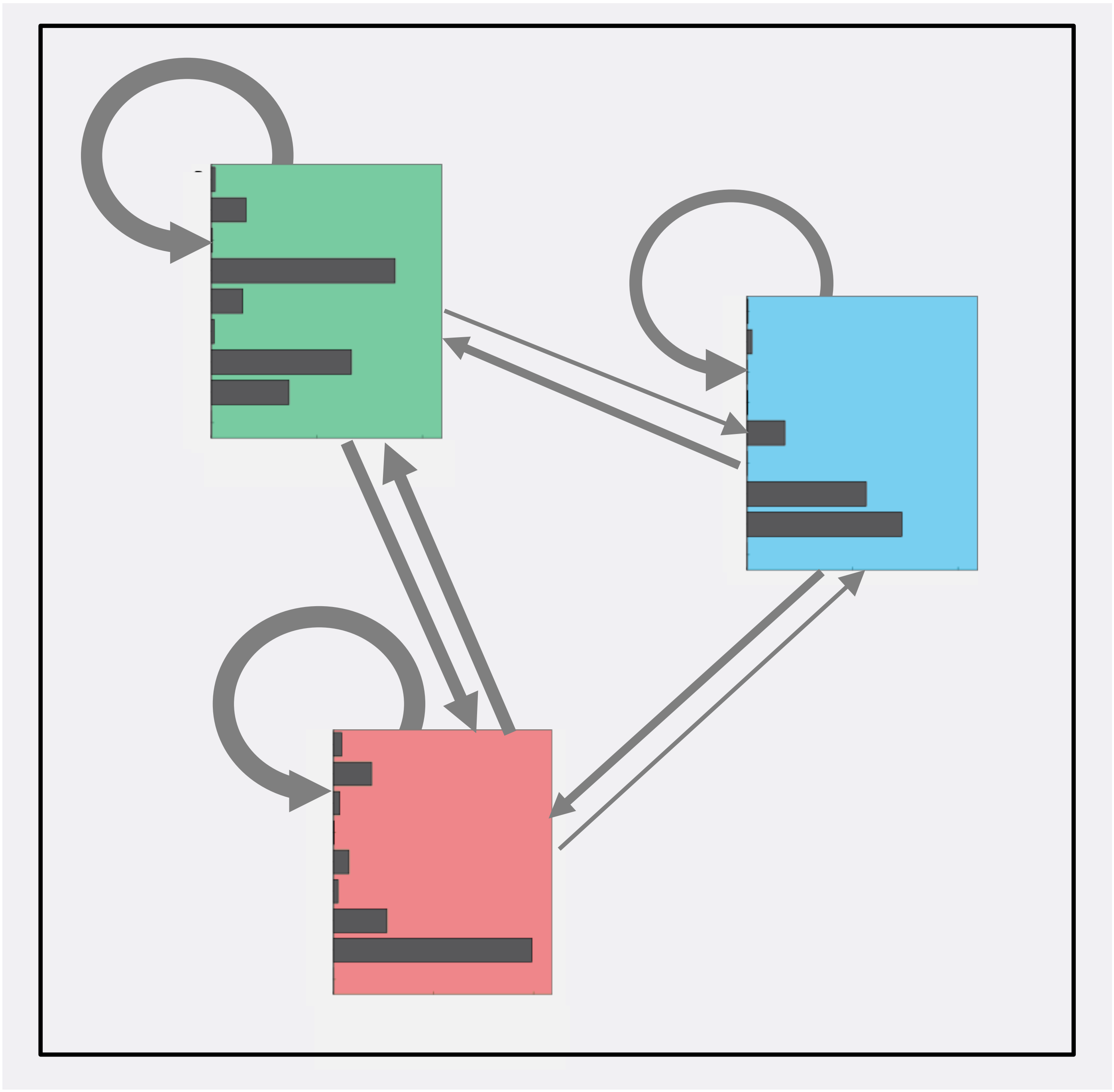



$$\sim y^i_t = \begin{bmatrix} 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \\ 1 \\ 0 \end{bmatrix}$$

# HMM for neural spike trains

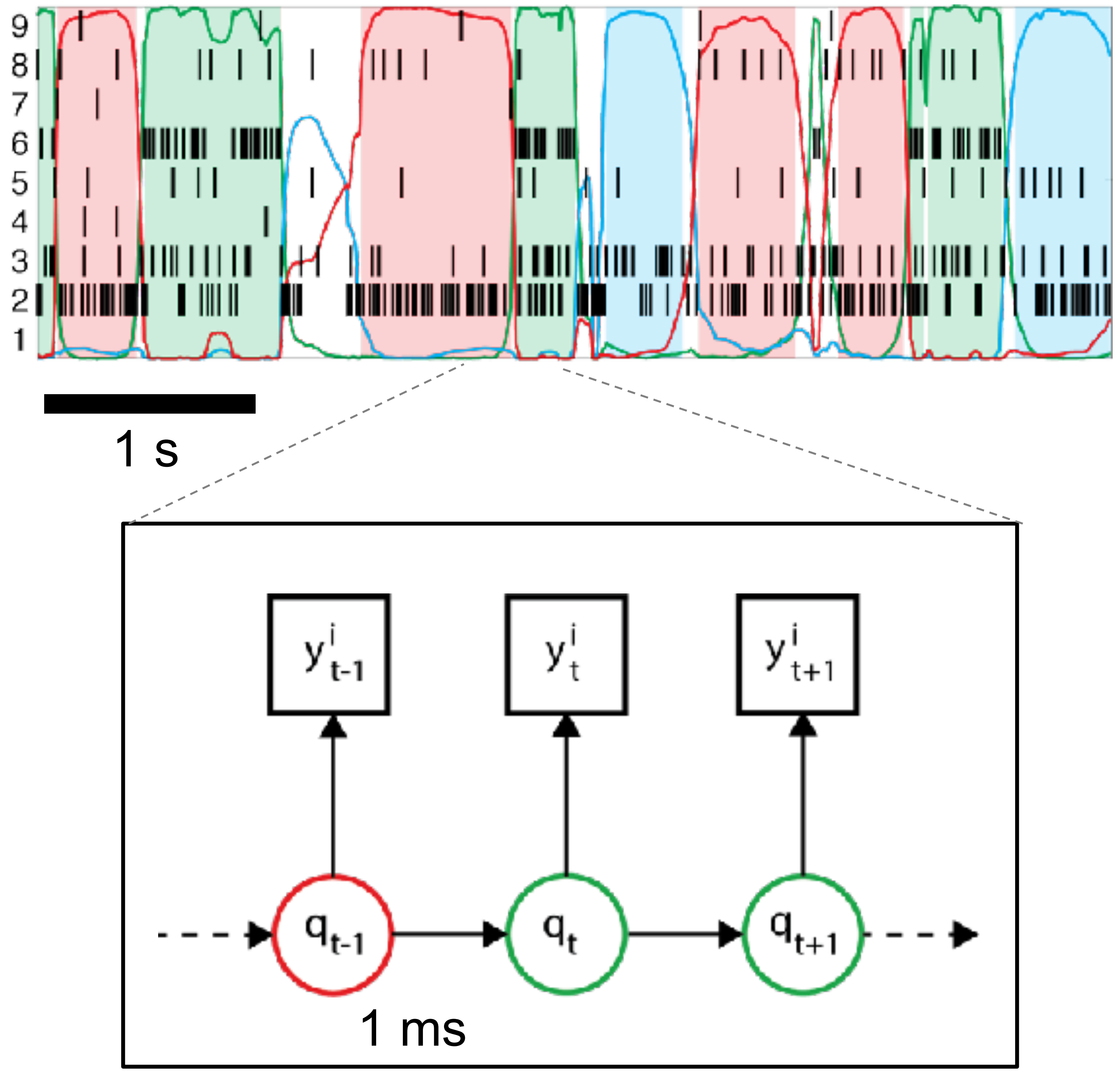
- Hidden Markov Model fit



# HMM for neural spike trains

- Hidden Markov Model fit




- Binning spikes $\Delta t$=1-5 ms
- Tradeoff: speed vs. accuracy:

Poisson $p(y_i(t) = k | S_t = m) = \frac{(\nu_i(m)dt)^k e^{-\nu_i(m)dt}}{k!},$

Bernoulli $p(y_i(t) = 1 | S_t = m) = 1 - e^{\nu_i(m)dt}.$

- “Poisson” HMM → “Bernoulli” HMM

# HMM for neural spike trains

## Model selection

How do we choose the number of hidden states?

1. Information criterion (AIC, BIC)
2. Cross-validation

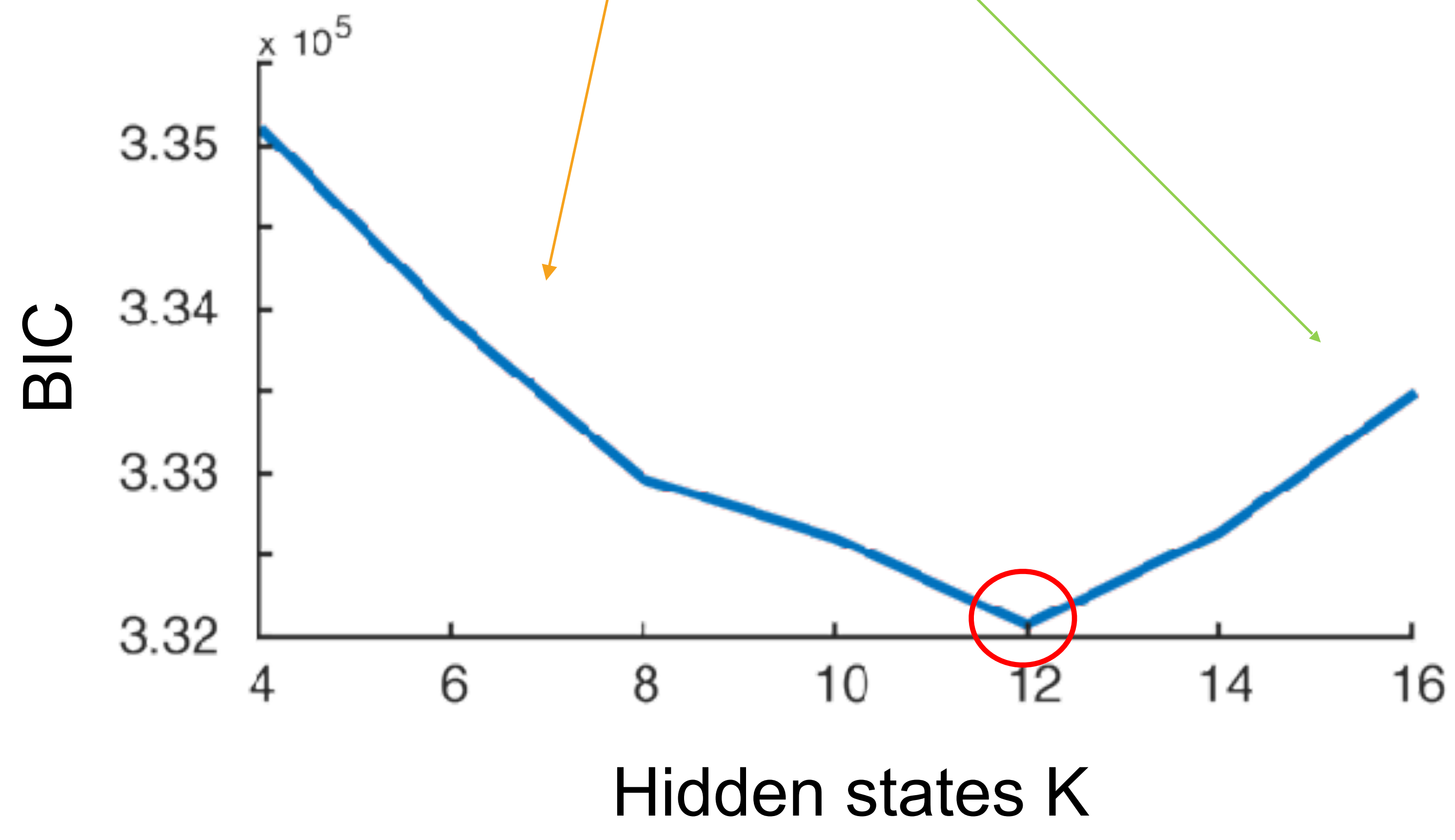
# HMM for neural spike trains

- Information criterion:
  # of HMM parameters: $p(K)=K(K-1)+KN$

K=states
N=neurons

$$\text{BIC} = -2\,\boxed{\text{LL(K)}} + \boxed{\text{p(K)}}\,\log(\text{T})$$

T=# of datapoints



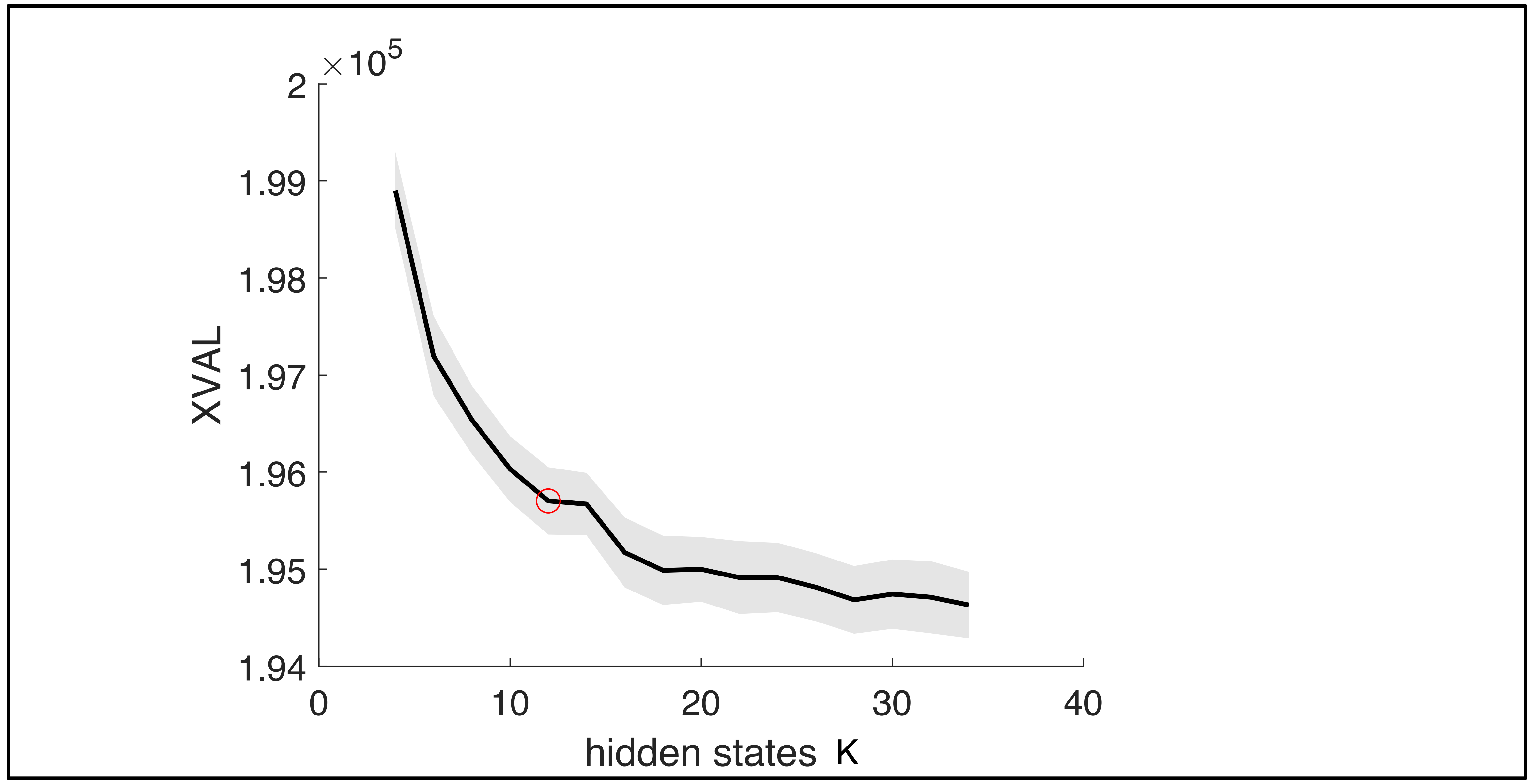

[Recanatesi et al., 2020]
[Sadacca et al., 2016]
[Engel et al., 2016]

# HMM for neural spike trains

- Cross-validation:

1. Randomly split trials in training set $S_1$ and test set $S_2$
2. Fit HMM with $K$ states on $S_1$
3. Estimate log-likelihood of test set $L(S_2|K)$

Select point with largest curvature (2nd deriv.)

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# HMM for neural spike trains

How do we choose the number of hidden states?

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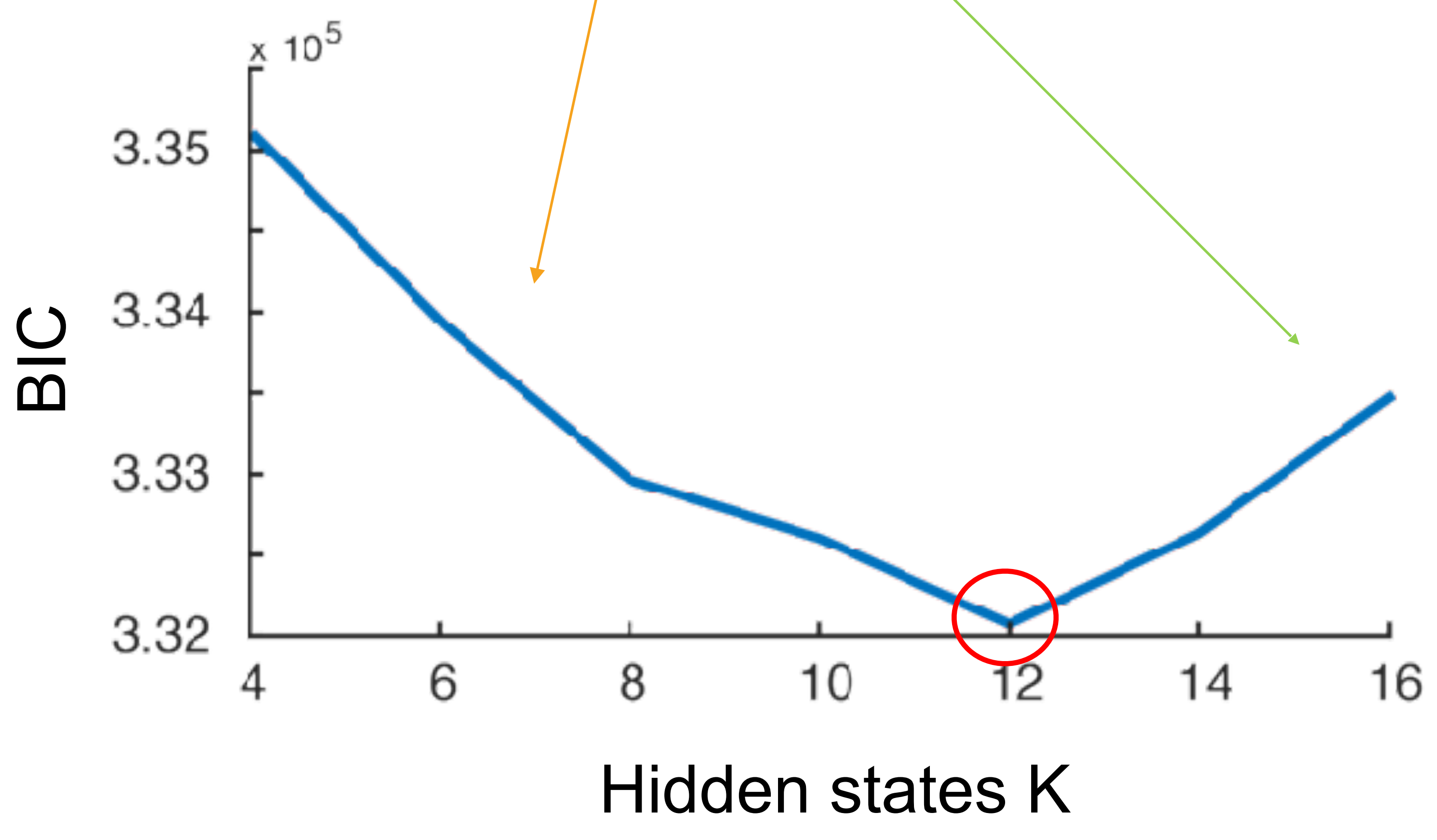
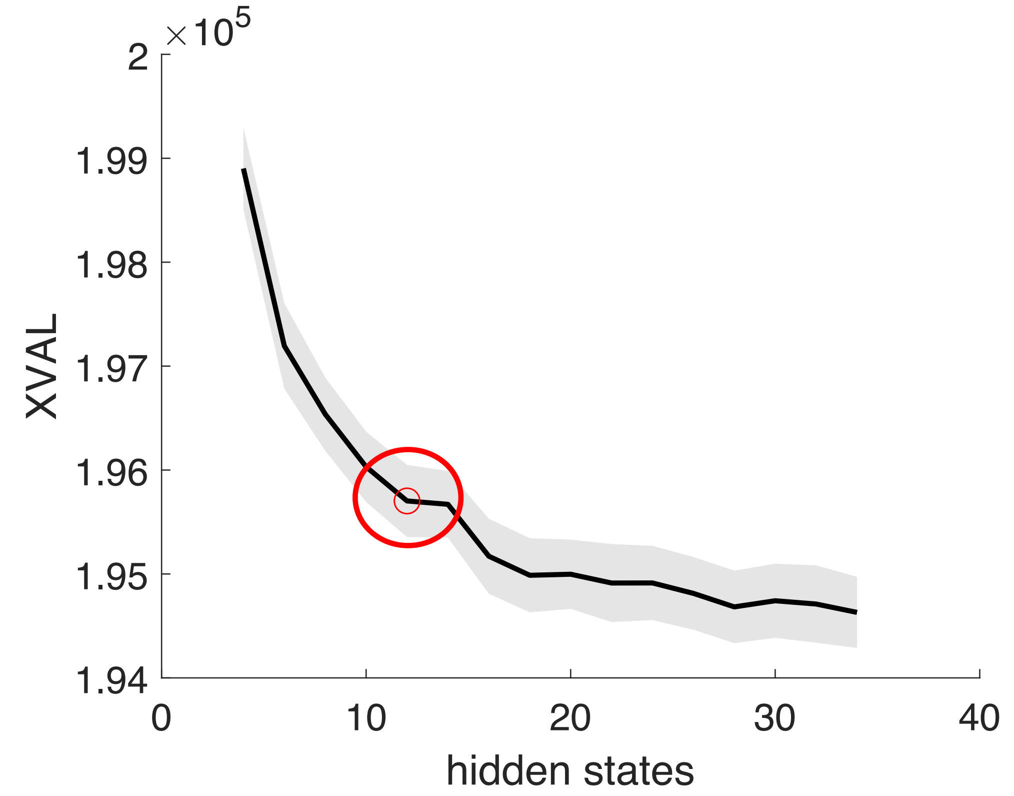
$$\mathrm{BIC} = -2\,\boxed{\mathrm{LL}(K)} + \boxed{p(K)}\,\log(T)$$




XVAL

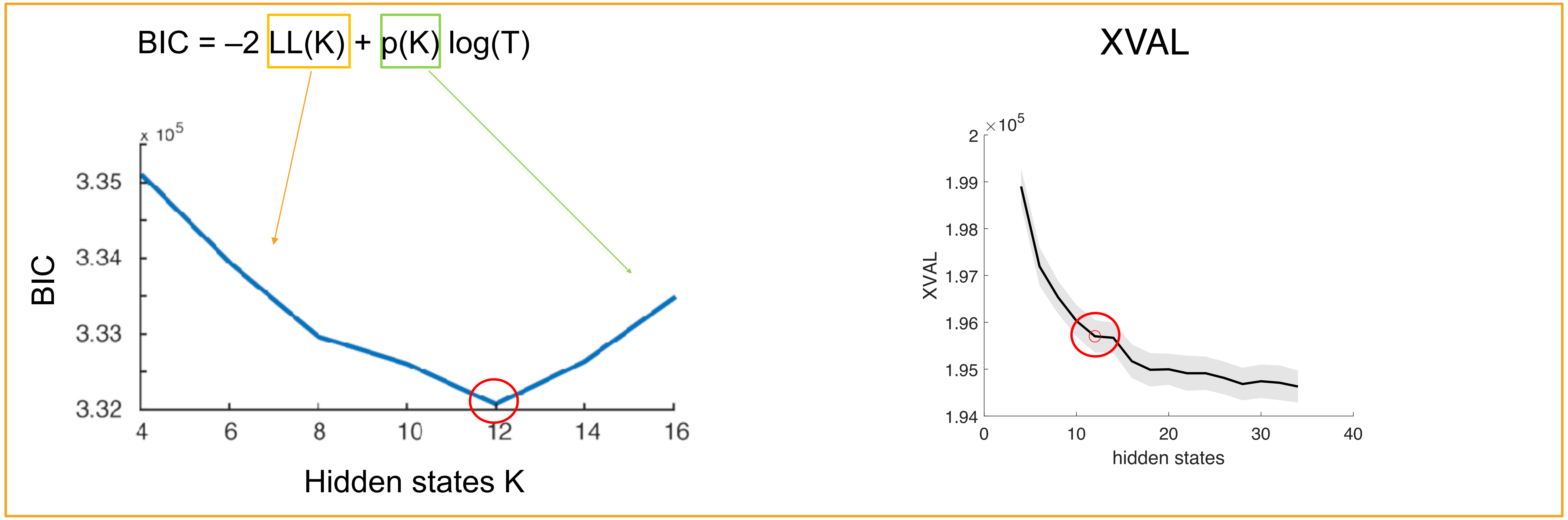



[Recanatesi et al., 2020]
[Sadacca et al., 2016]
[Engel et al., 2016]

# HMM for neural spike trains

## Local minima

- Transition and emission matrices optimized via Expectation-Maximization
- Not convex —> many local minima
- Run several times with random initial conditions, pick best run.




[Recanatesi et al., 2020]
[Sadacca et al., 2016]
[Engel et al., 2016]

# HMM for neural spike trains

In practice:

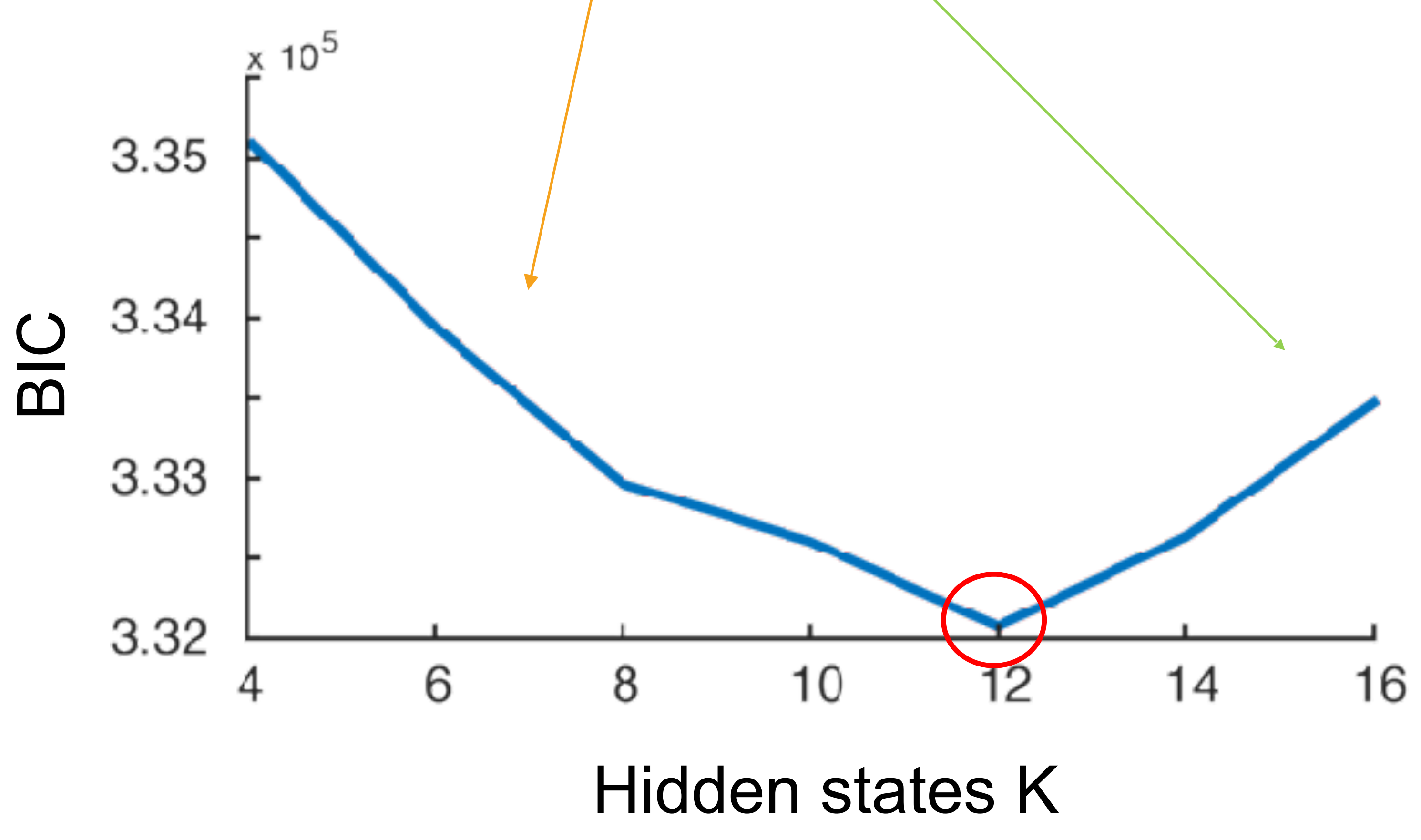
• Most “extra states” have very low posterior probabilities *p*($S_t$=*m*|*data*) in all trials

→ post-hoc state admission criterion:

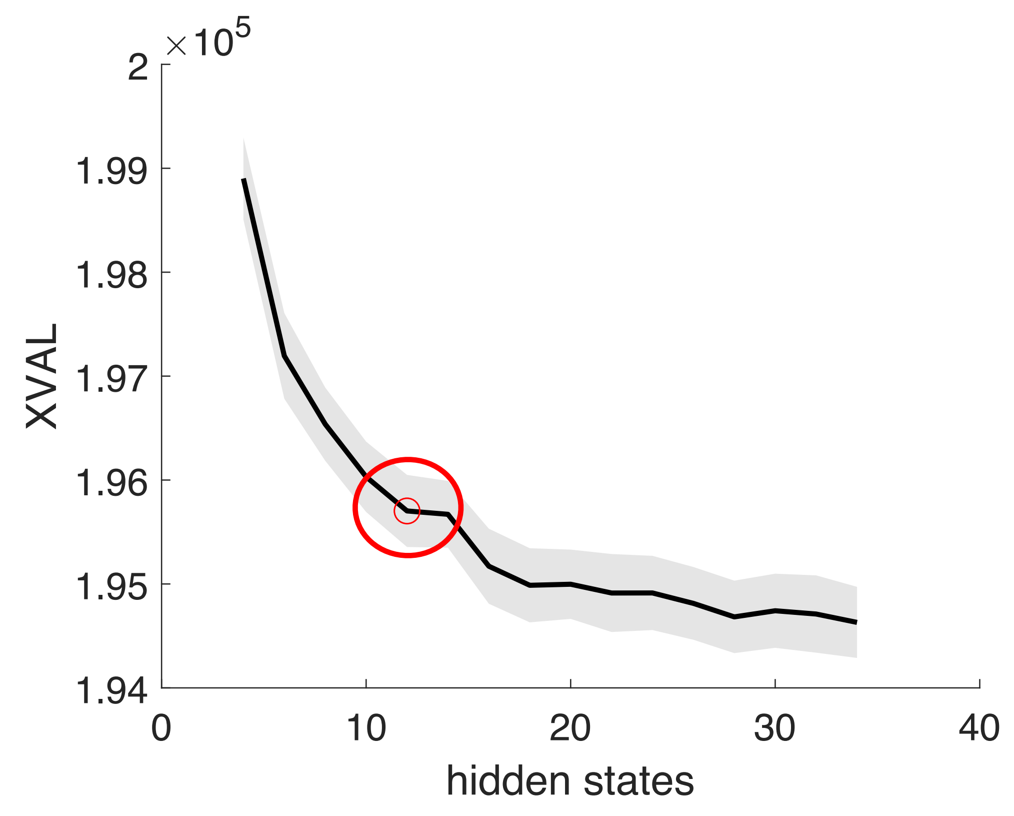
A state is detected at time *t* if it ***p*($S_t$=*m*|*data*)>80% for at least one 50 ms bins**

→ ***only keep “admissible states” for the rest of the analyses***

BIC = –2 $\boxed{\text{LL(K)}}$ + $\boxed{\text{p(K)}}$ log(T)




XVAL




[Recanatesi et al., 2020]
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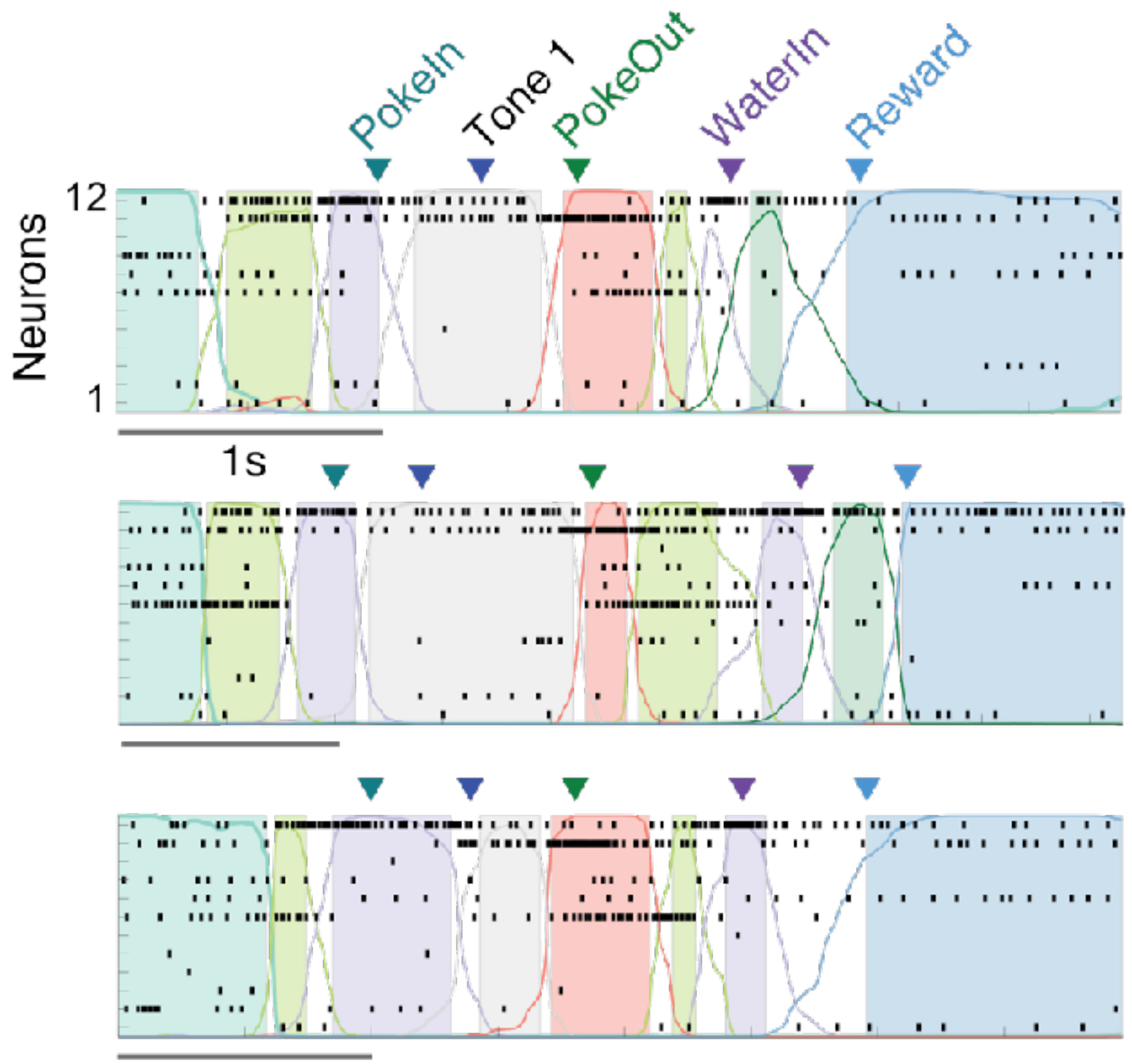
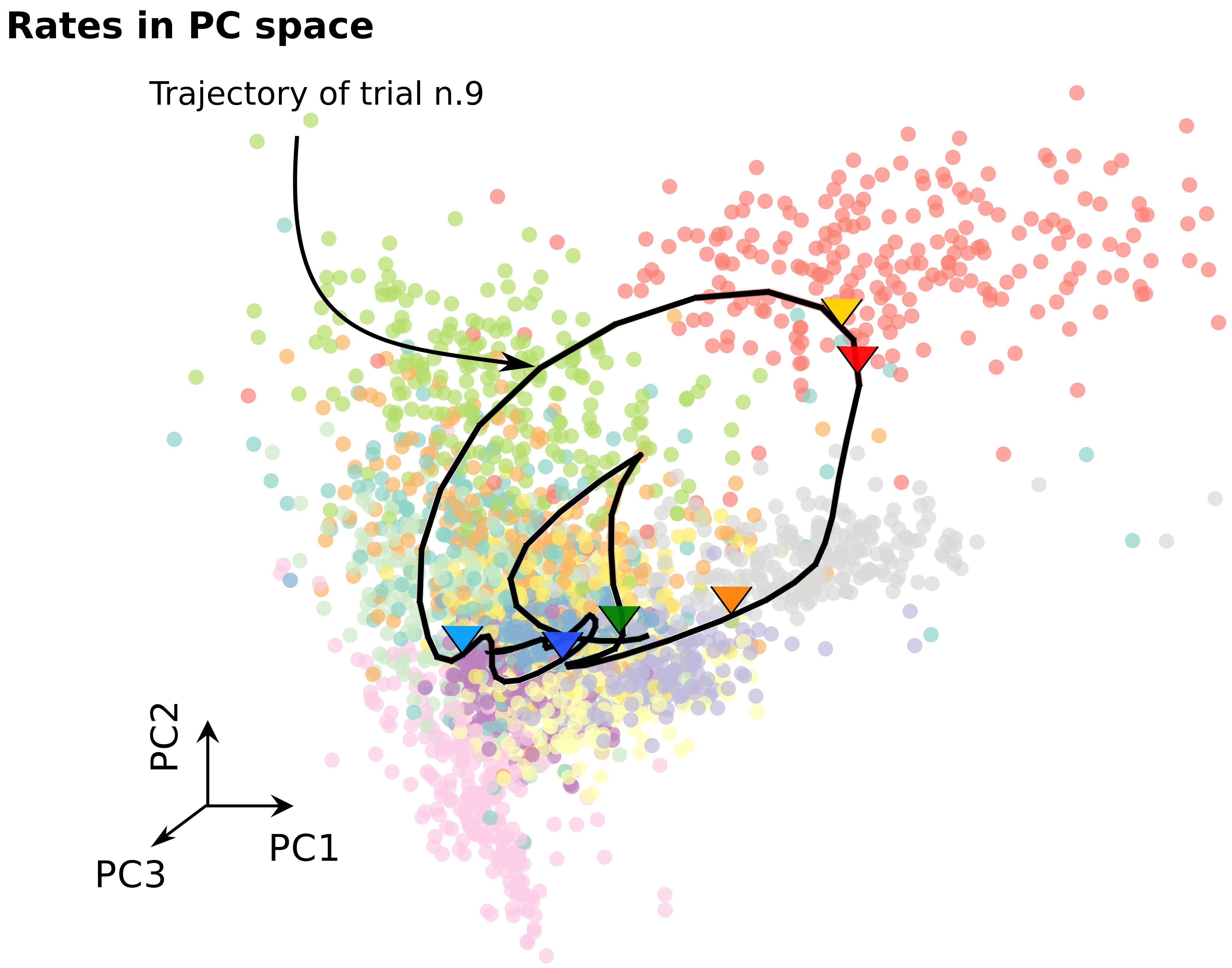
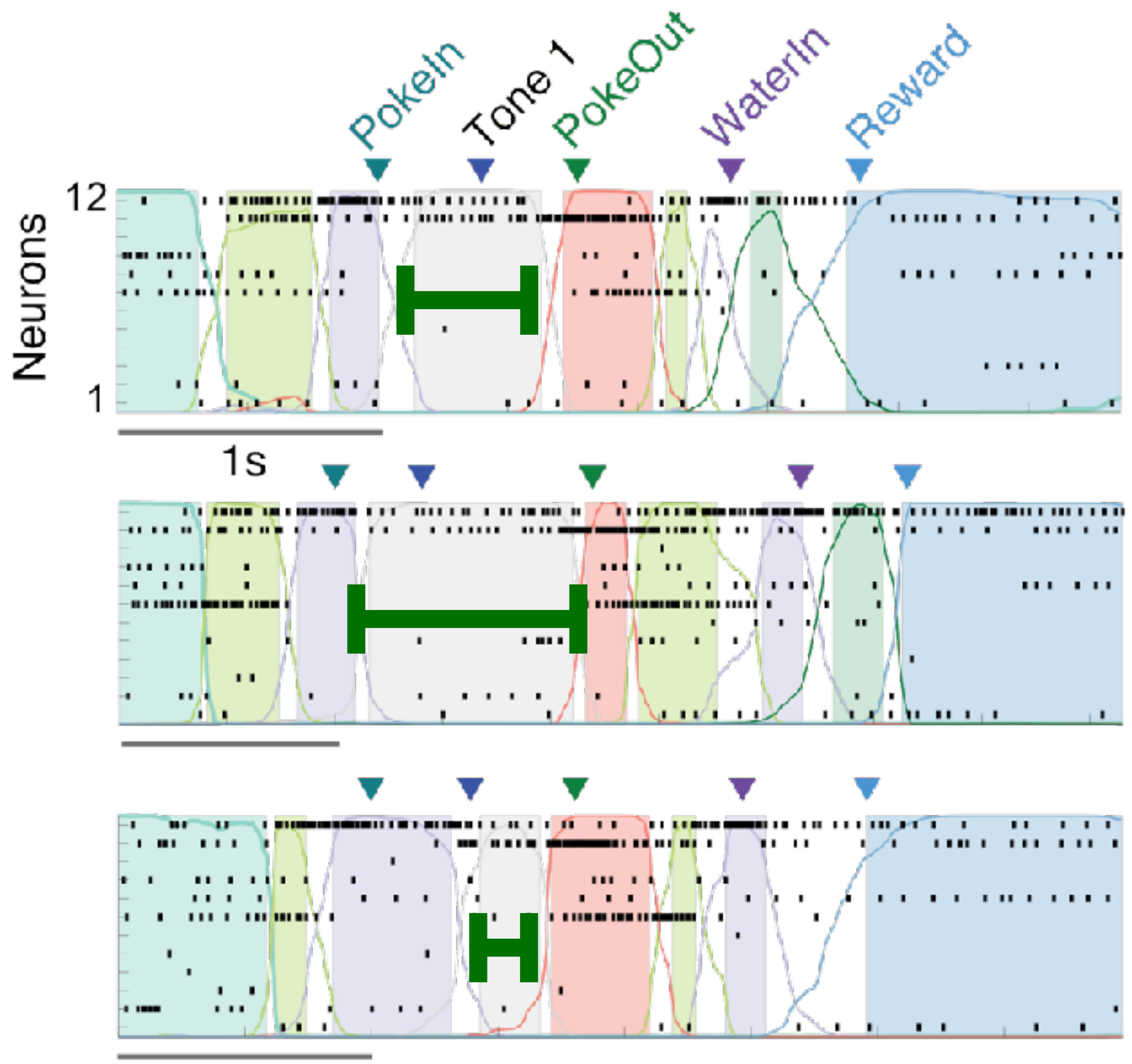
# Secondary motor cortex - sequences of attractors



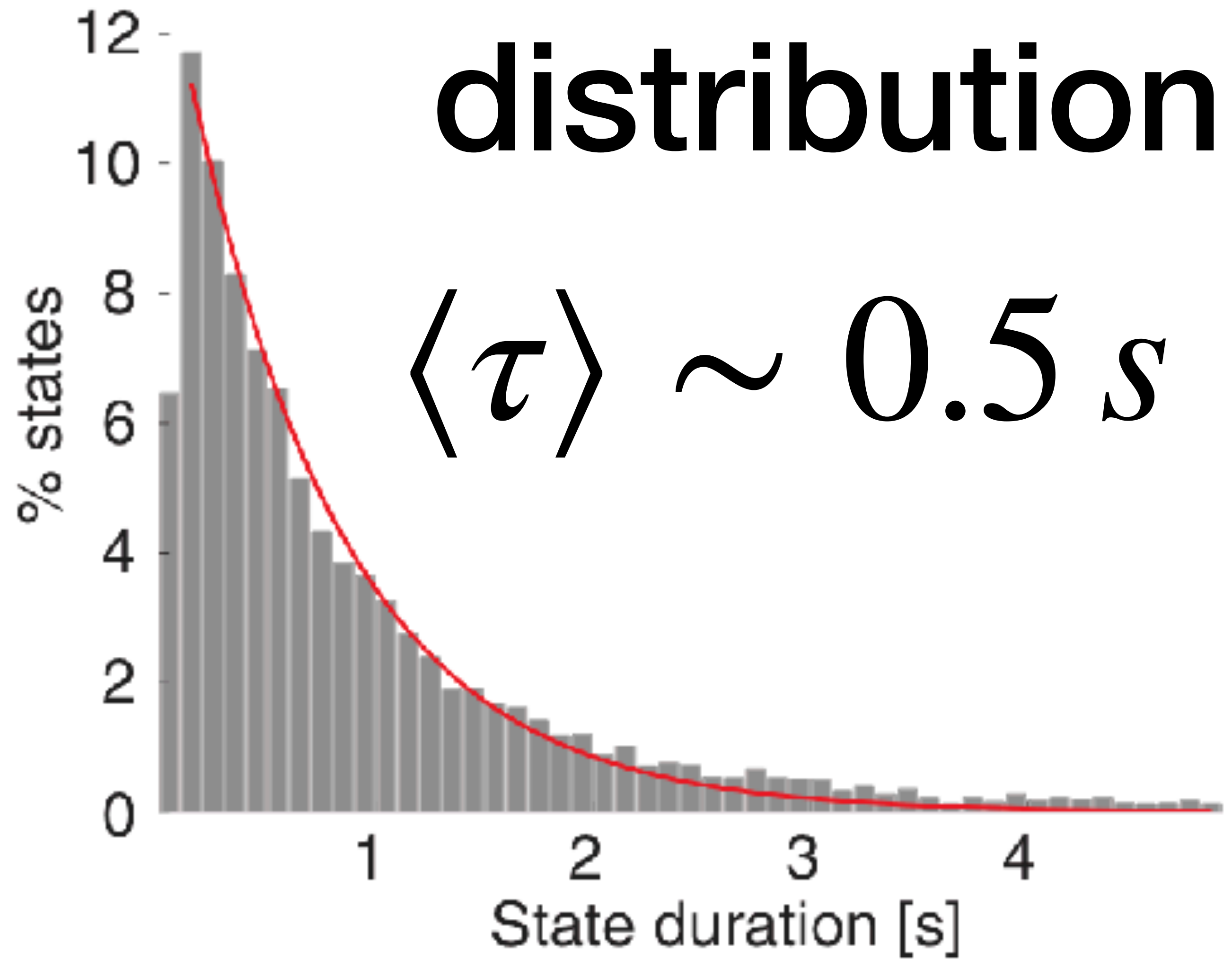

[Recanatesi et al., 2020]

# Secondary motor cortex - sequences of attractors




Exponential dwell time distribution

$$\langle \tau \rangle \sim 0.5\, s$$




[Recanatesi et al., 2020]

# Goals

**Part I - Theory**

- Metastable activity in cortical circuits
- Hidden Markov Models fit to metastable activity
- Modeling metastable activity with attractor networks

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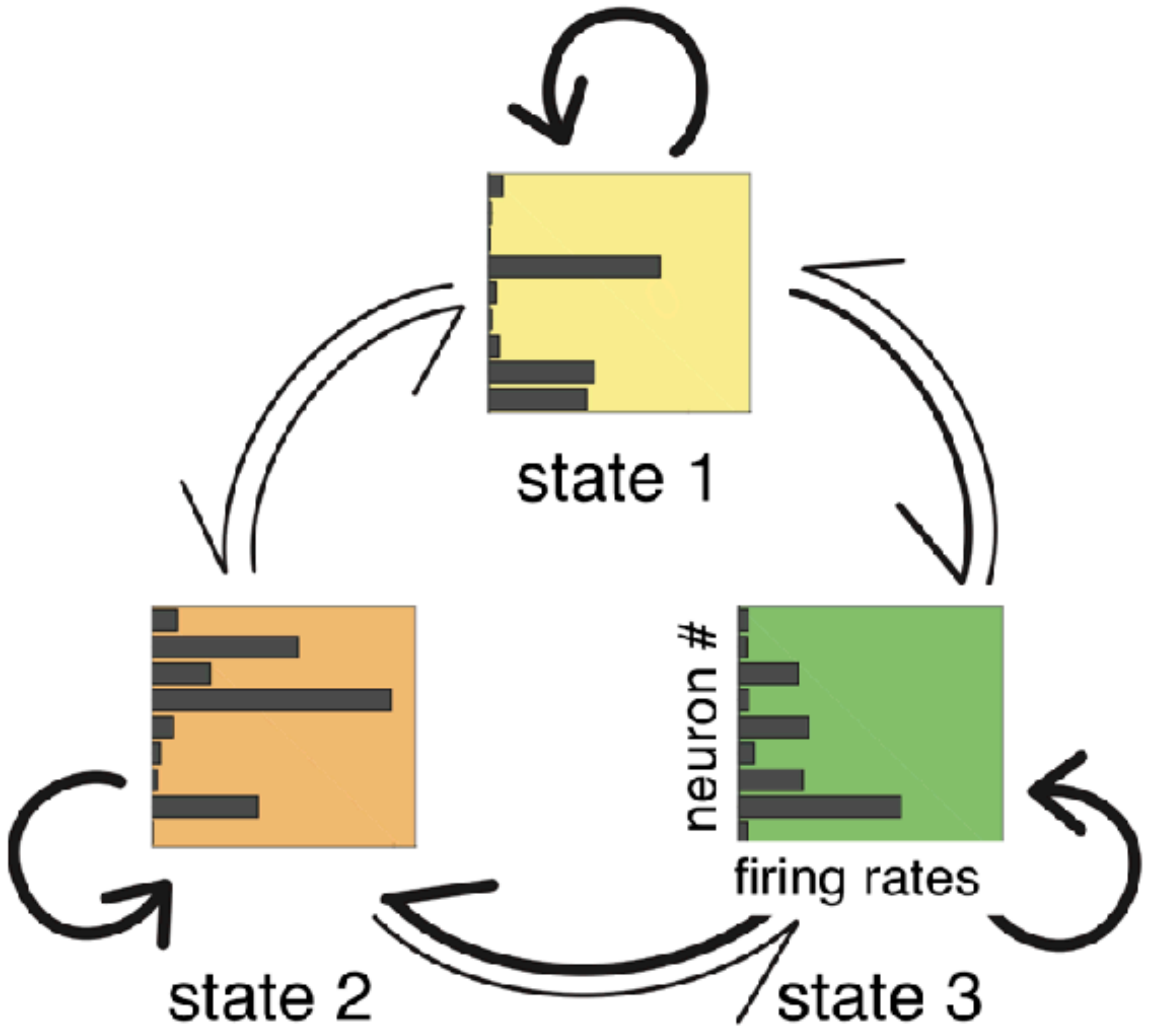
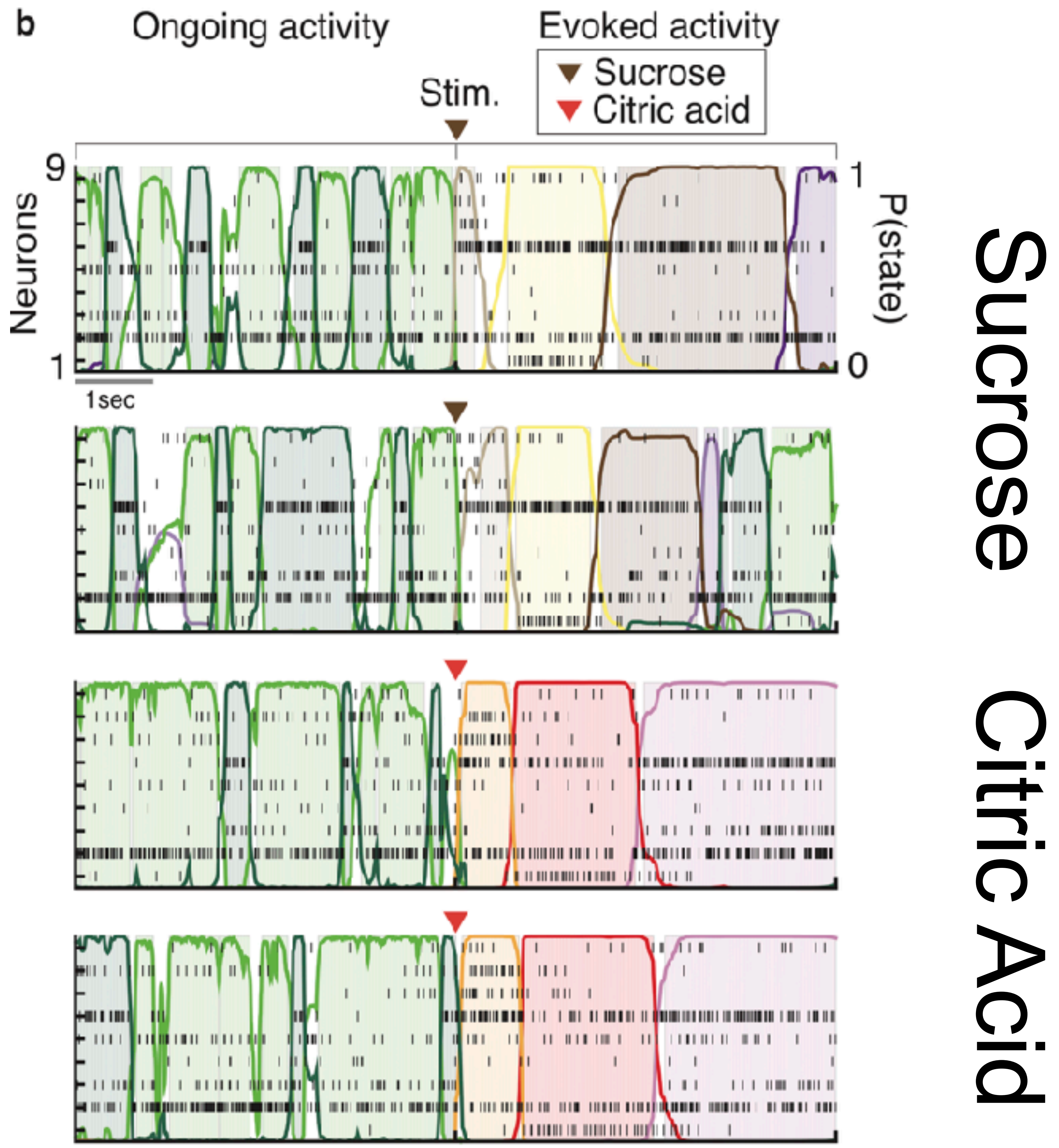
# Metastable activity: sensory processing

**Poisson-Hidden Markov Model**

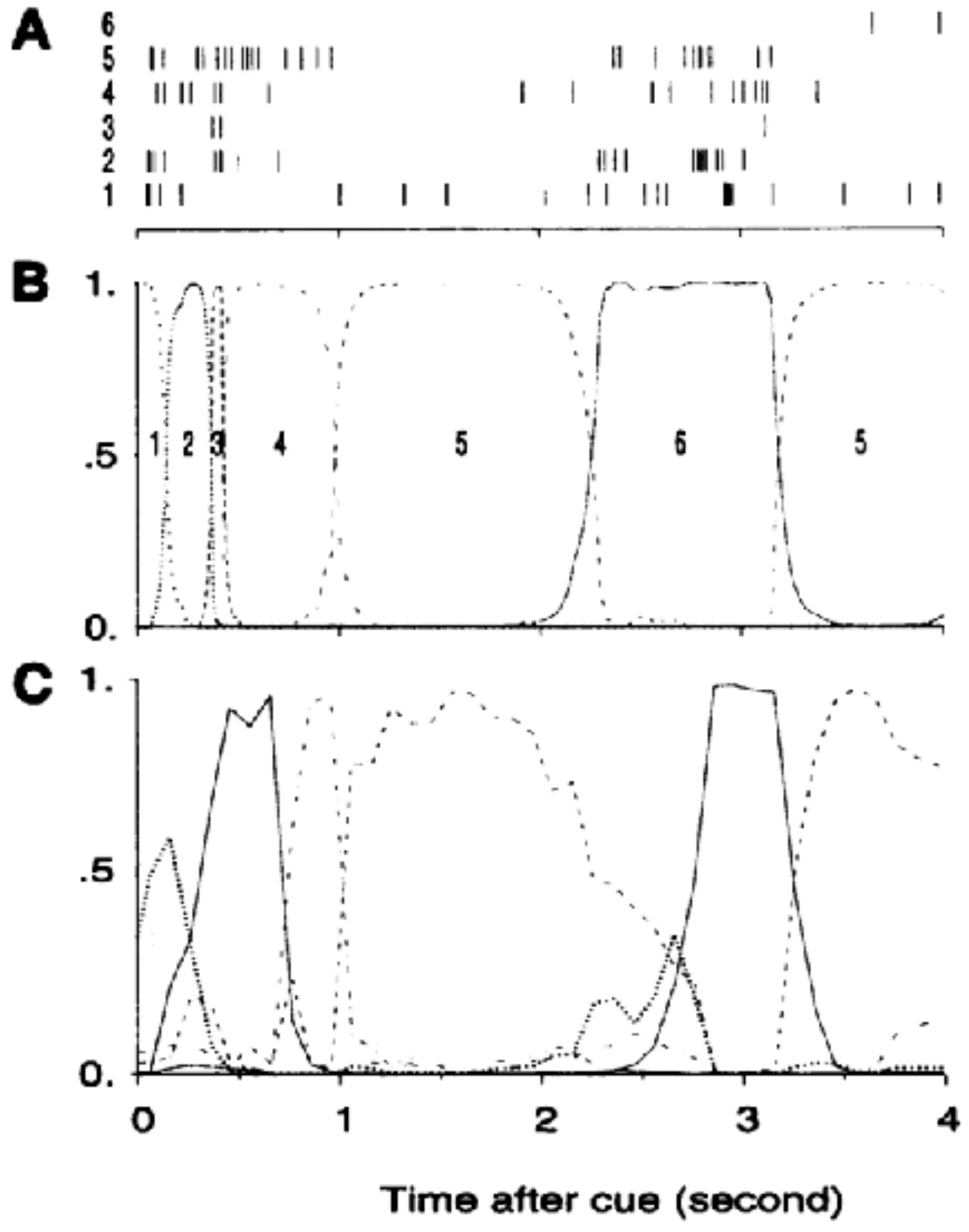



[Mazzucato et al., 2015]

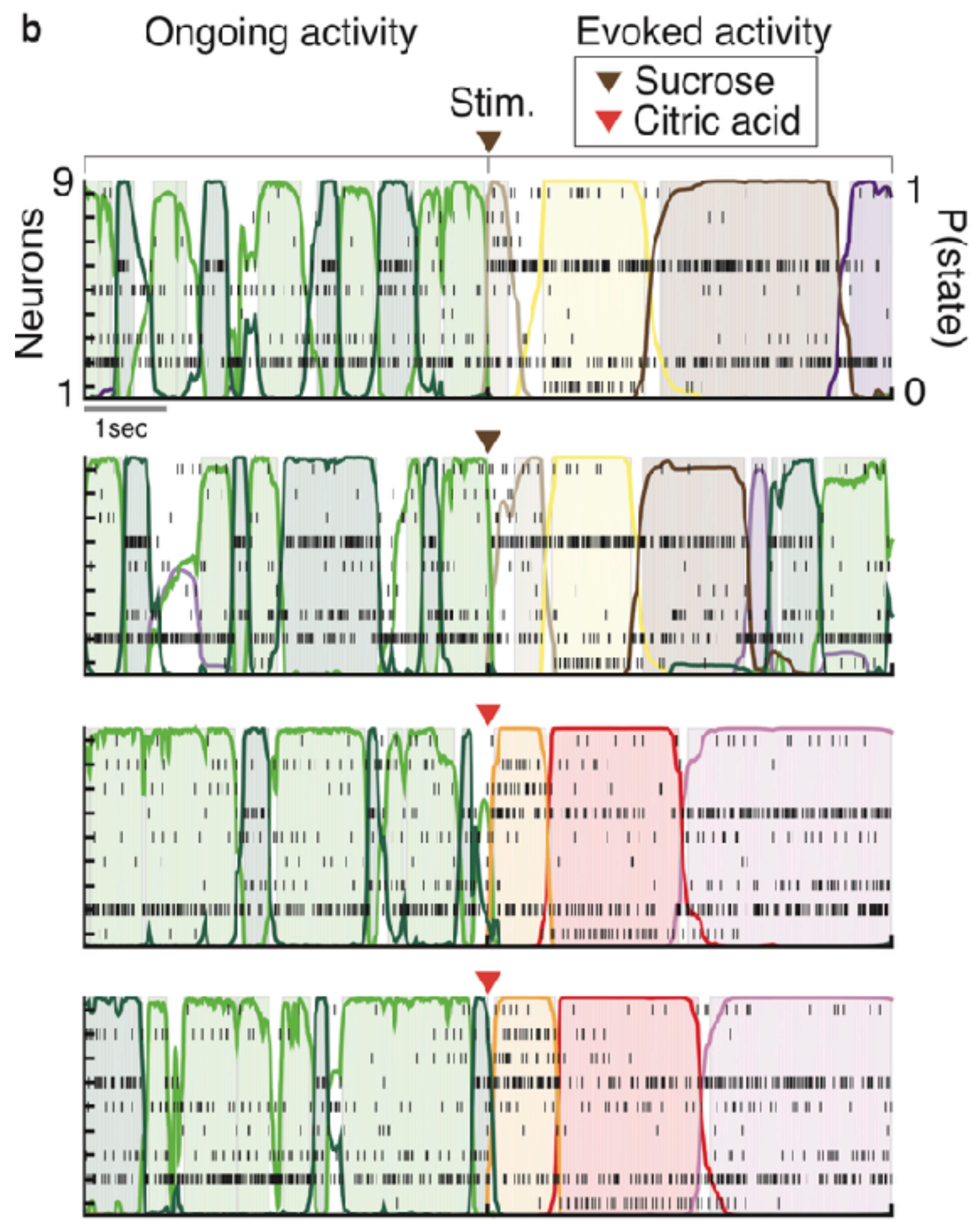
# Metastable activity: sensory processing

## Visual (in PFC)



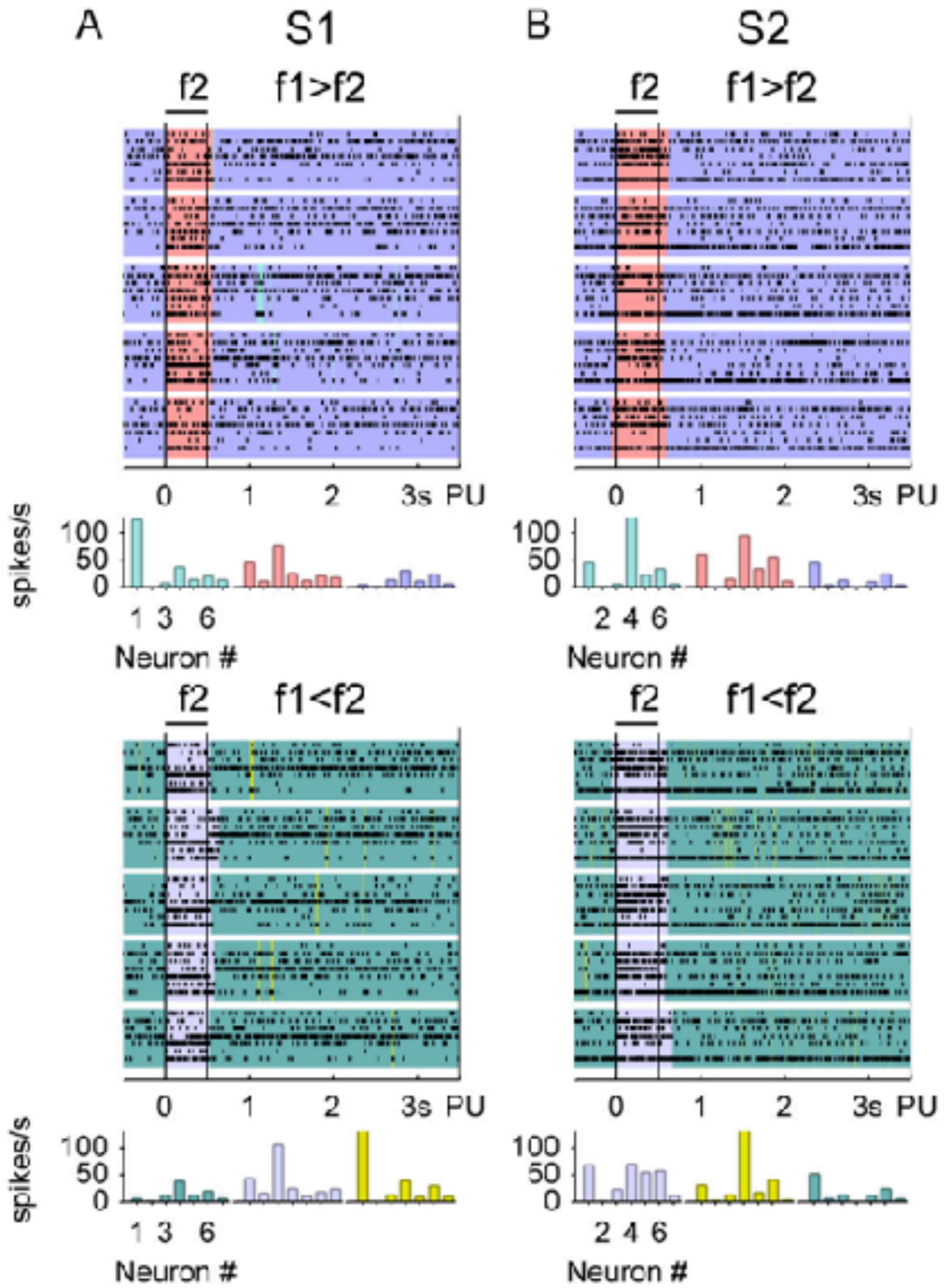

[Abeles et al, 1995]

## Gustatory




[Jones et al, 2007]
[Mazzucato et al, 2015]

## Somatosensory

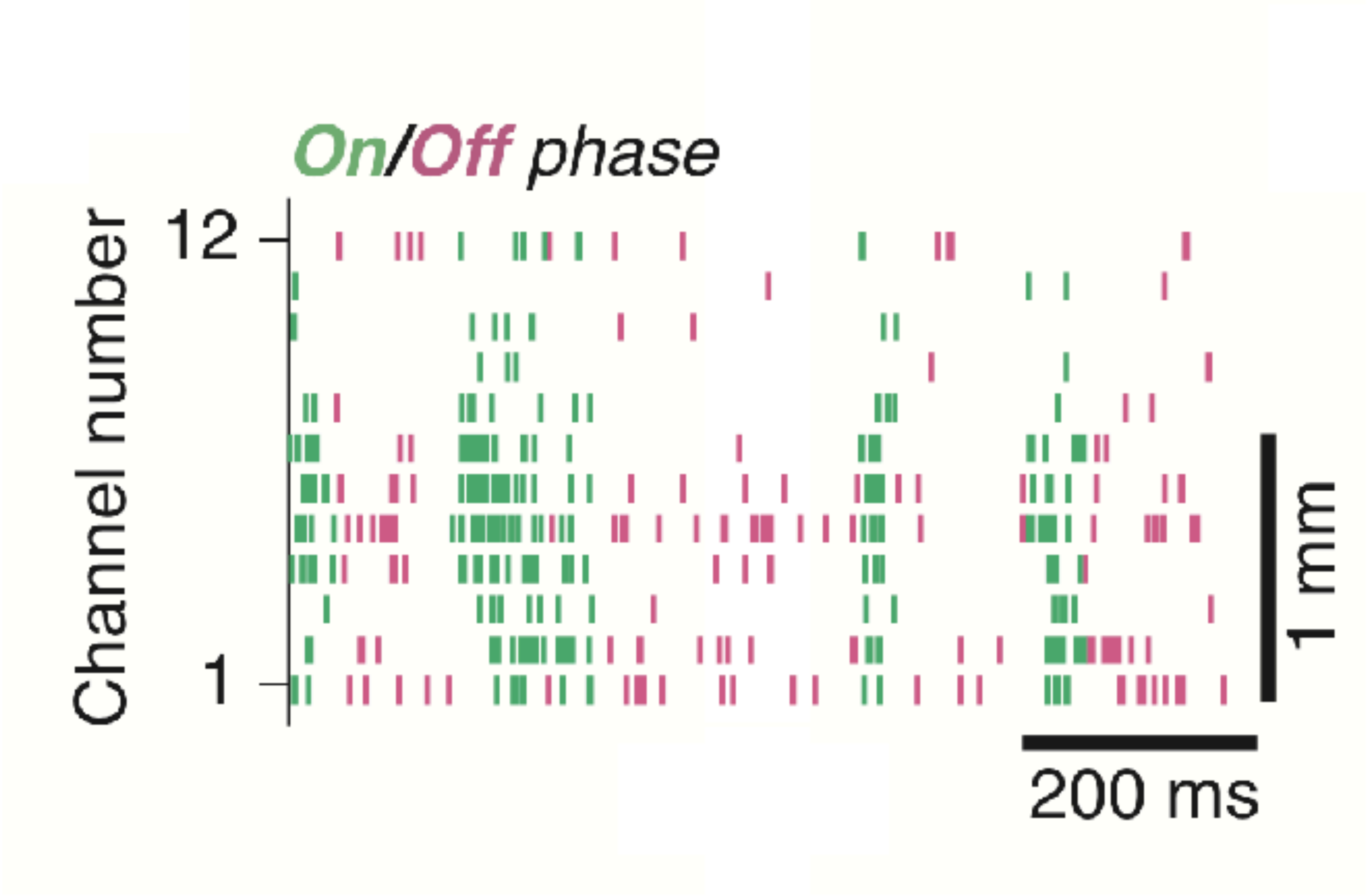


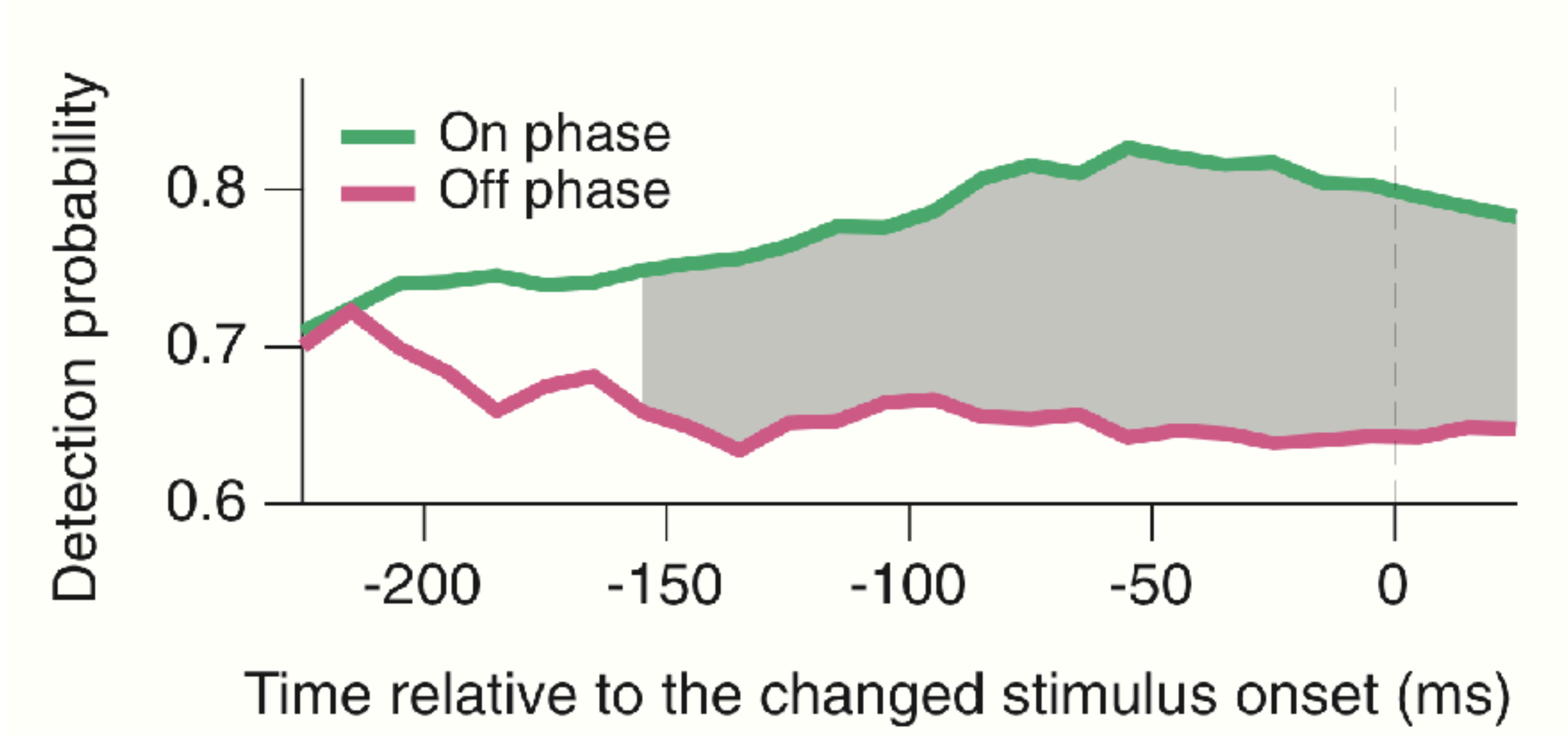

[Ponce-Alvarez et al, 2012]

# Metastable activity: cognition

Selective attention task in V4 (monkey)

*Better task performance during On*



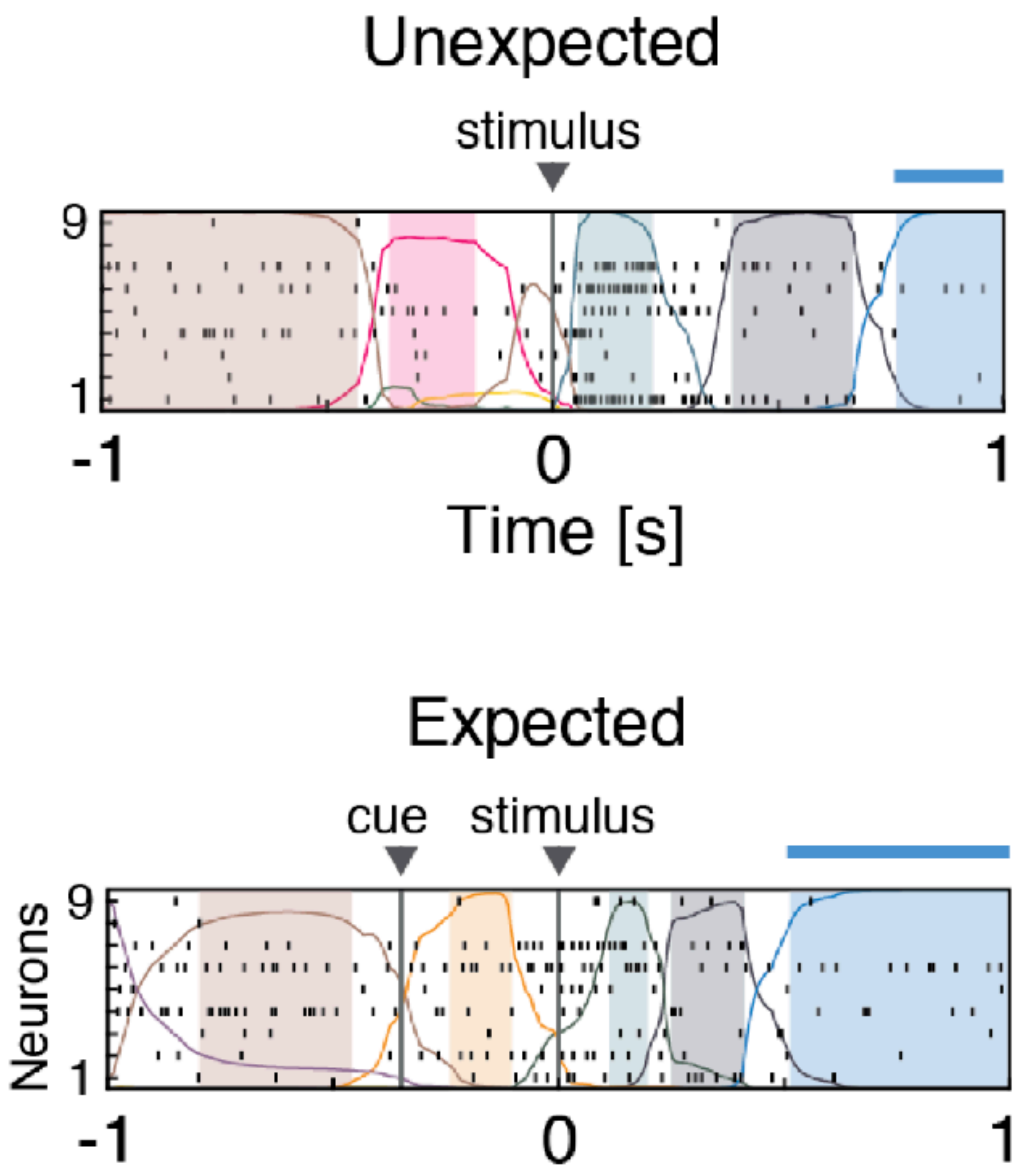

[Engel et al, 2016]

# Metastable activity: cognition

Expectation of taste

in gustatory cortex

**Expected** stimuli
are recognized **faster**
than unexpected ones




[Mazzucato et al, 2019]

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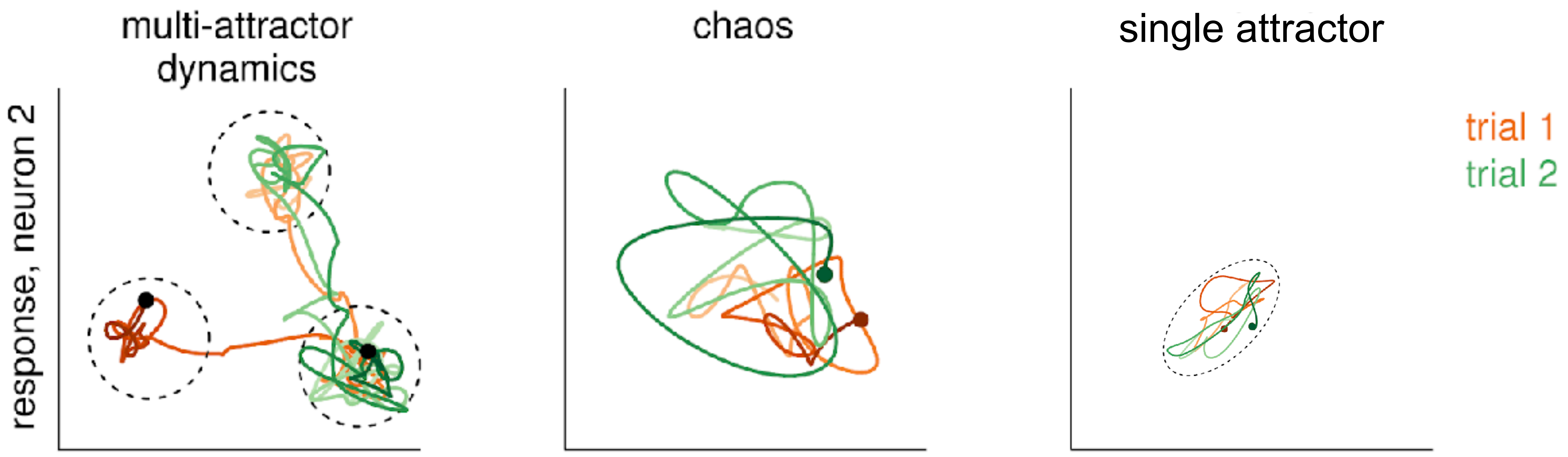
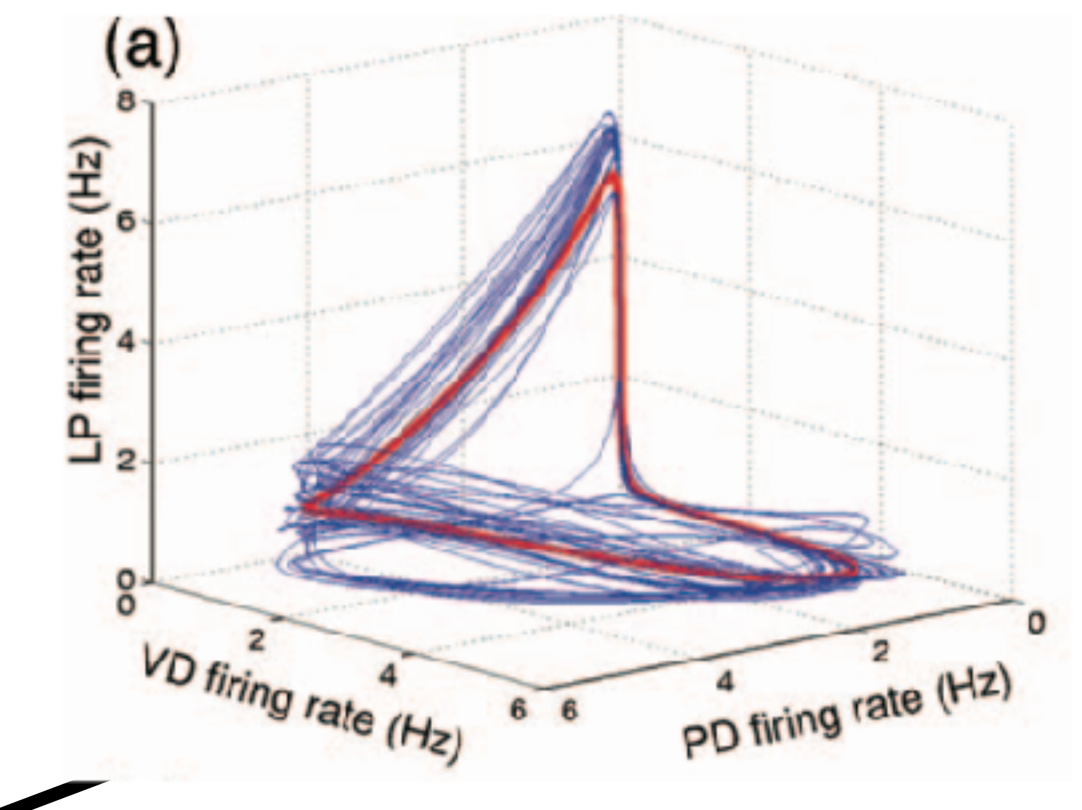
# Modeling metastable neural activity with attractor networks

# Temporal dynamics in neural circuits

Dynamical repertoires:




oscillations




Jumping

Varying smoothly

[Rabinovich et al, 2006]
[Hennequin et al, 2018]

# Clustered networks of leaky-integrate-and-fire neurons

# LIF neuron

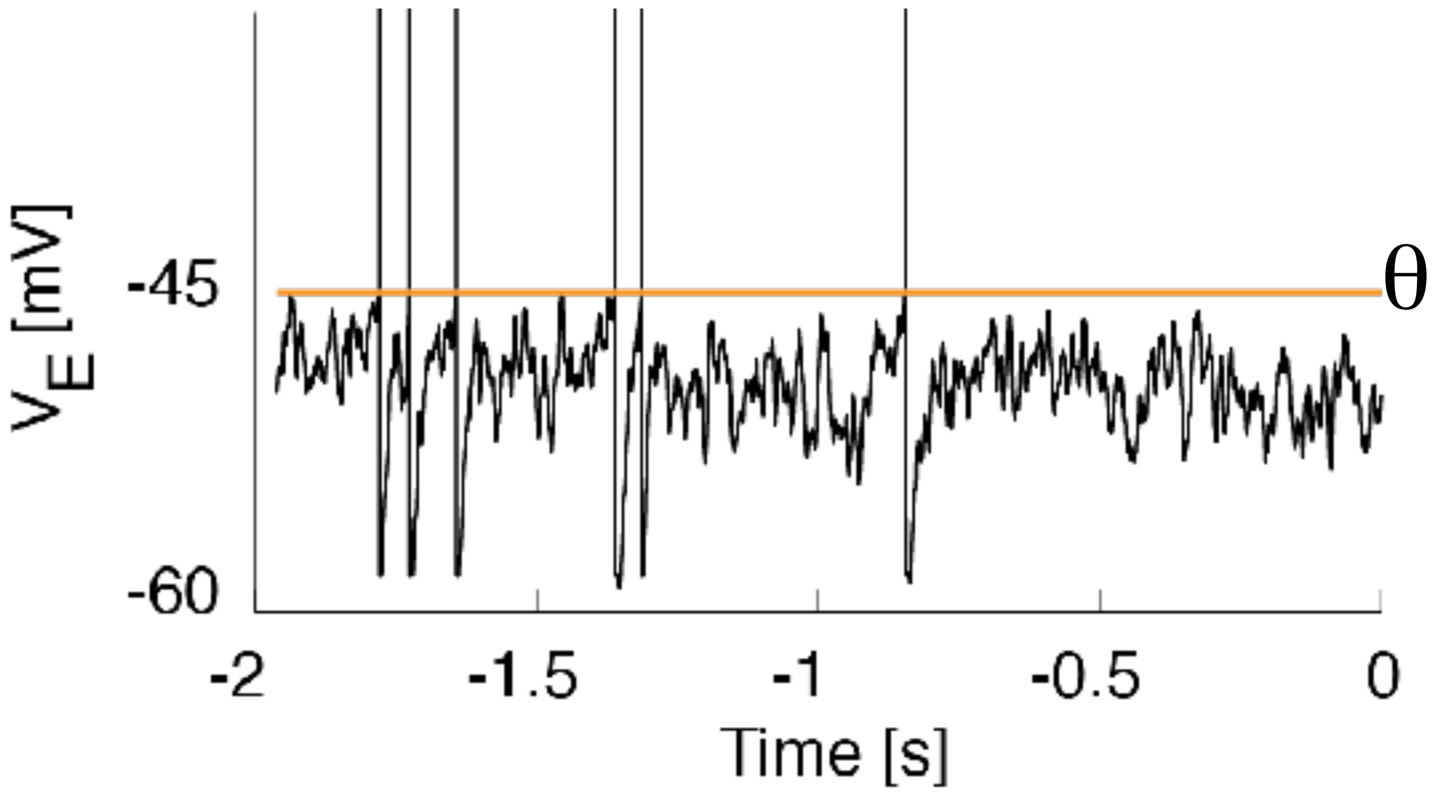
PSC: $$\tau_s \frac{dI_i}{dt} = -I_i + I_{ext}(t) + \sum_j^{pre} J_{ij} \sum_n^{spikes} \delta(t - t_j^{(n)})$$

Potential: $$\tau_m \frac{dV_i}{dt} = V_L - V_i + I_i(t)$$

b.c.: $V(t^*) = \theta$

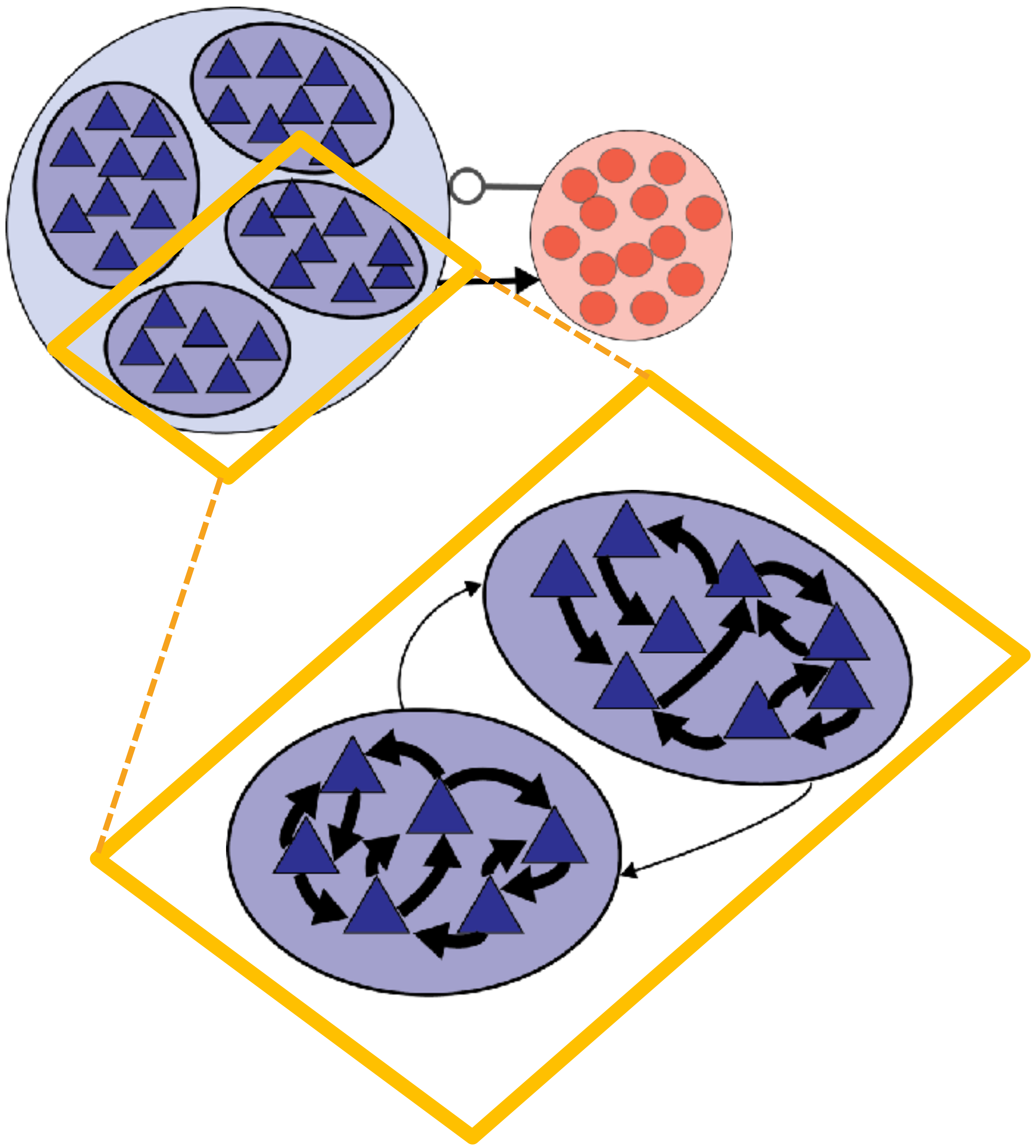
→ spike

→ reset

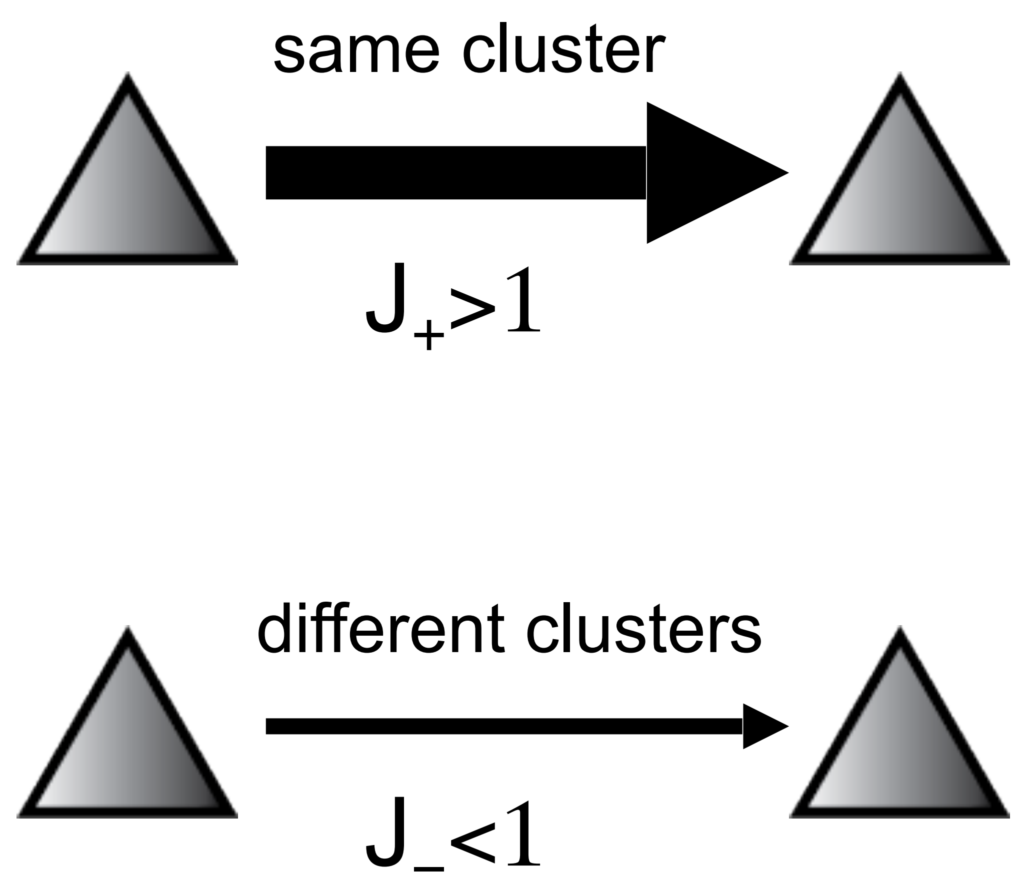



[van Vreeswijk & Sompolinsky, 1996] [Haider et al., 2006]
[Amit & Brunel, 1997] [Renart et al., 2007]

# Clustered network



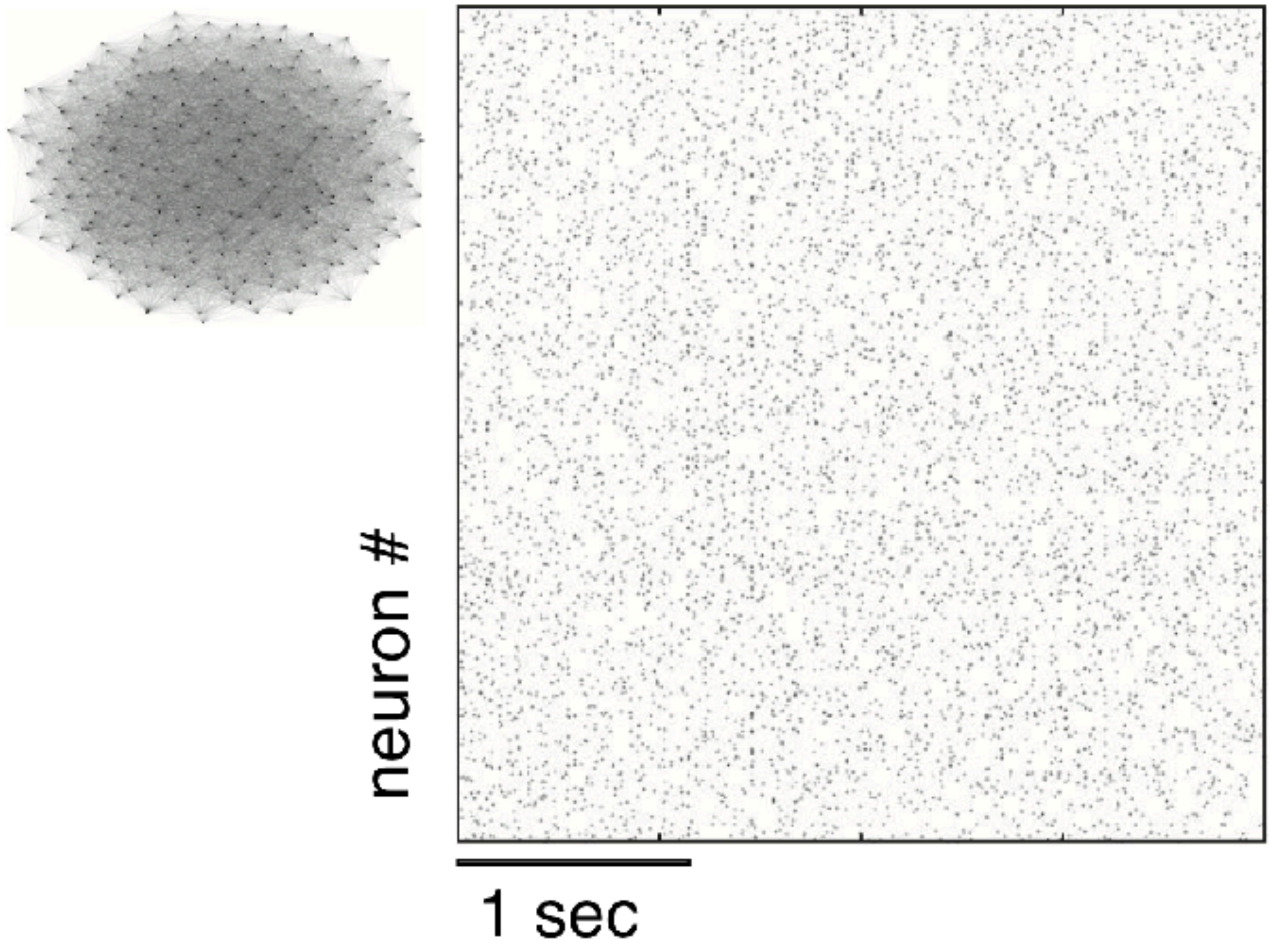
Recurrent E → E synaptic weights:

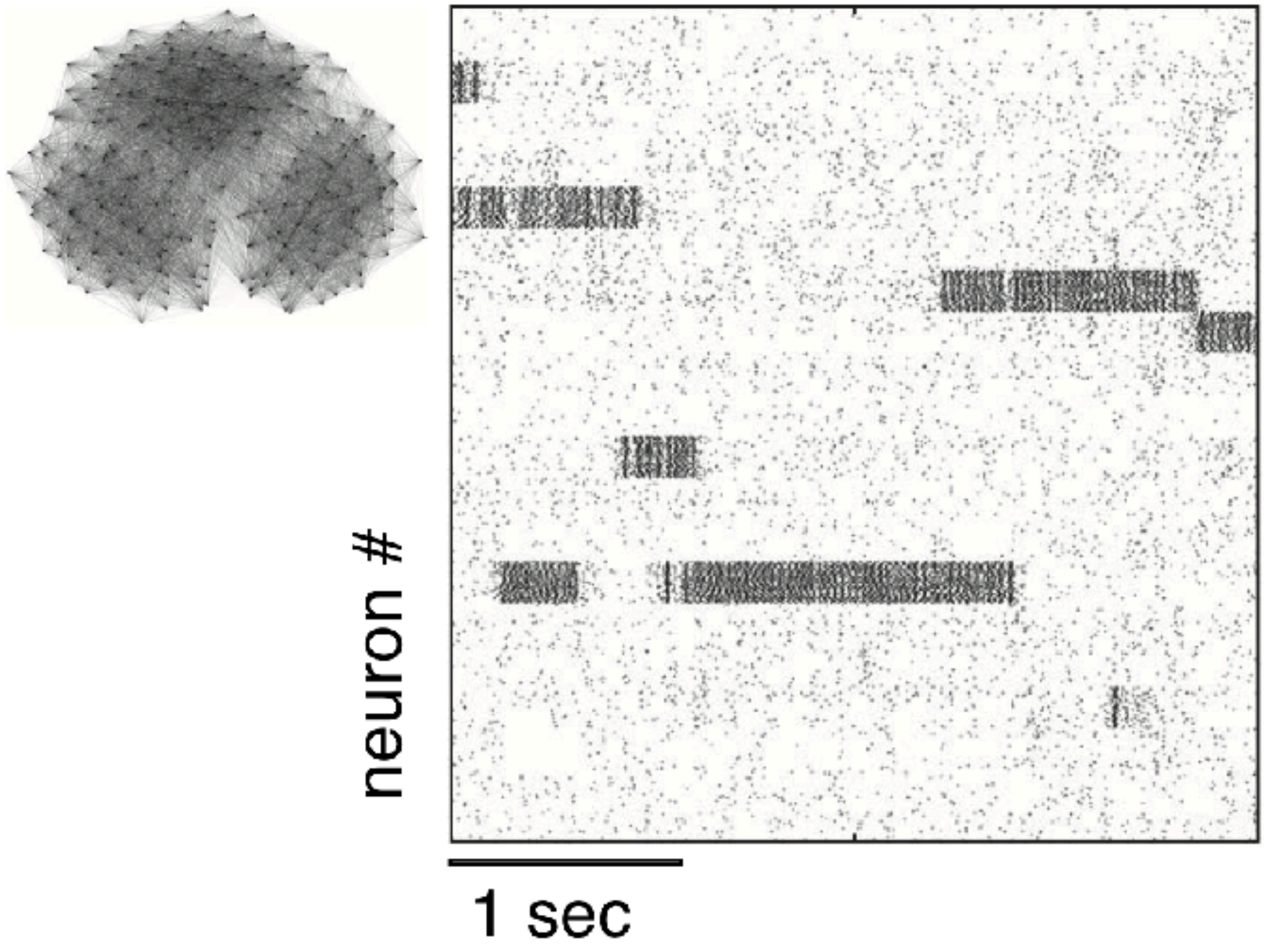




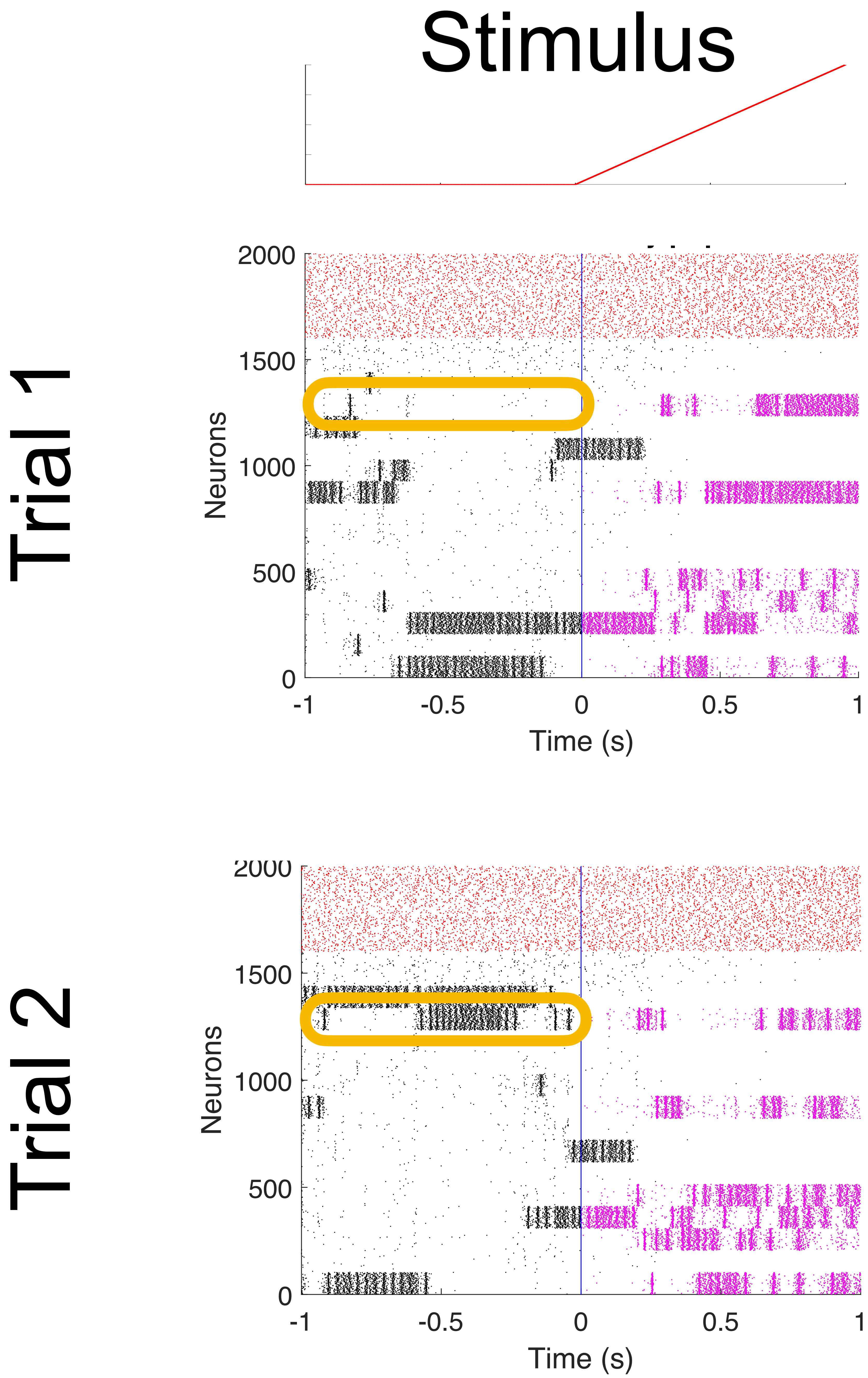
[Amit & Brunel, 1997]
[Deco & Hugues, 2012]
[Litwin–Kumar & Doiron, 2012]
[Mazzucato et al., 2015]

# Clustered network




[Litwin-Kumar & Doiron, 2012]

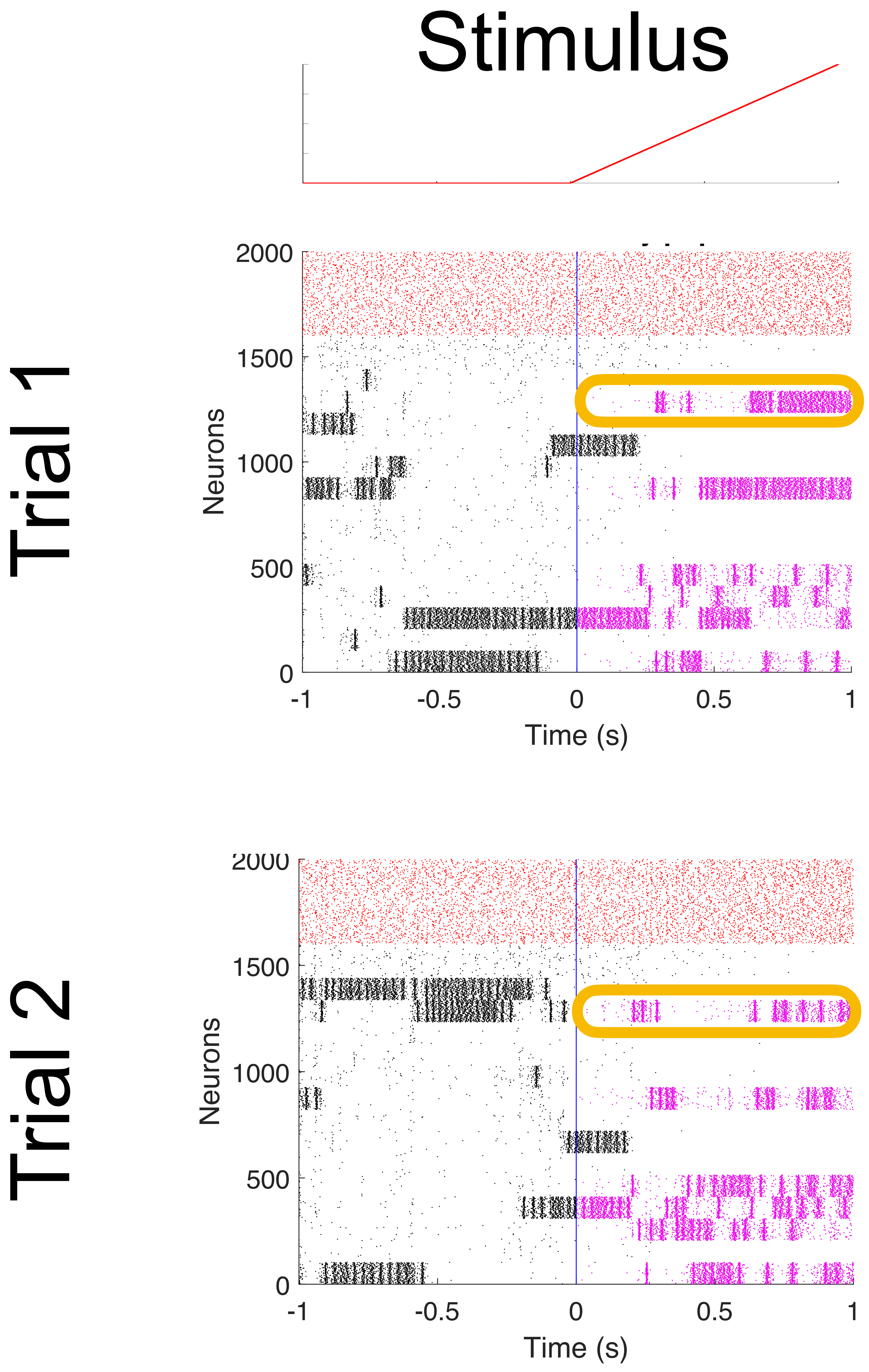



Trial-to-trial variability:

Fano factor = Var(rate) / Mean(rate)

Fano(spont) > Fano(evoked)

[Deco & Hugues, 2012]
[Litwin-Kumar & Doiron, 2012]
[Mazzucato et al, 2015]




Trial-to-trial variability:

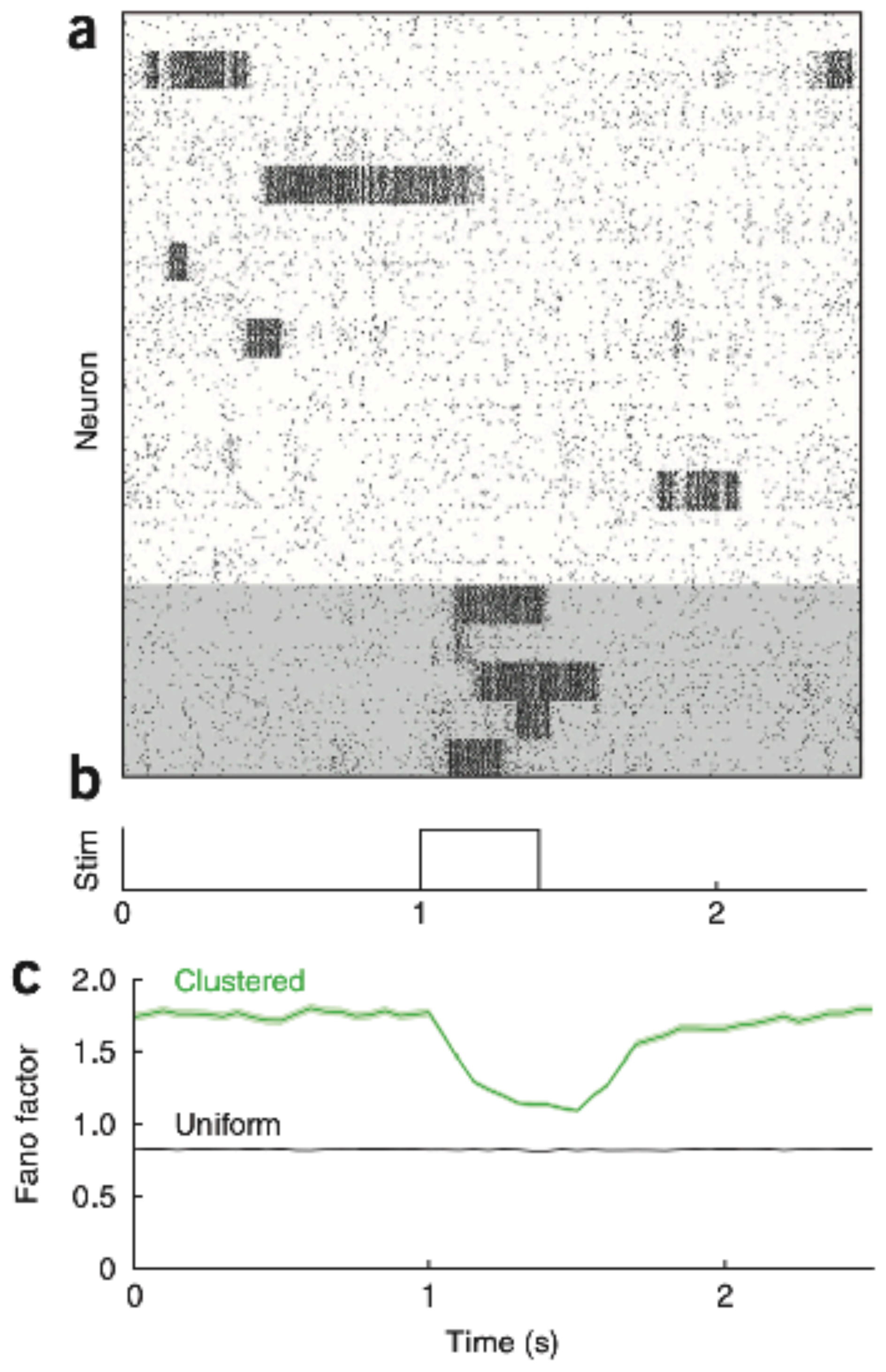
Fano factor = Var(rate) / Mean(rate)

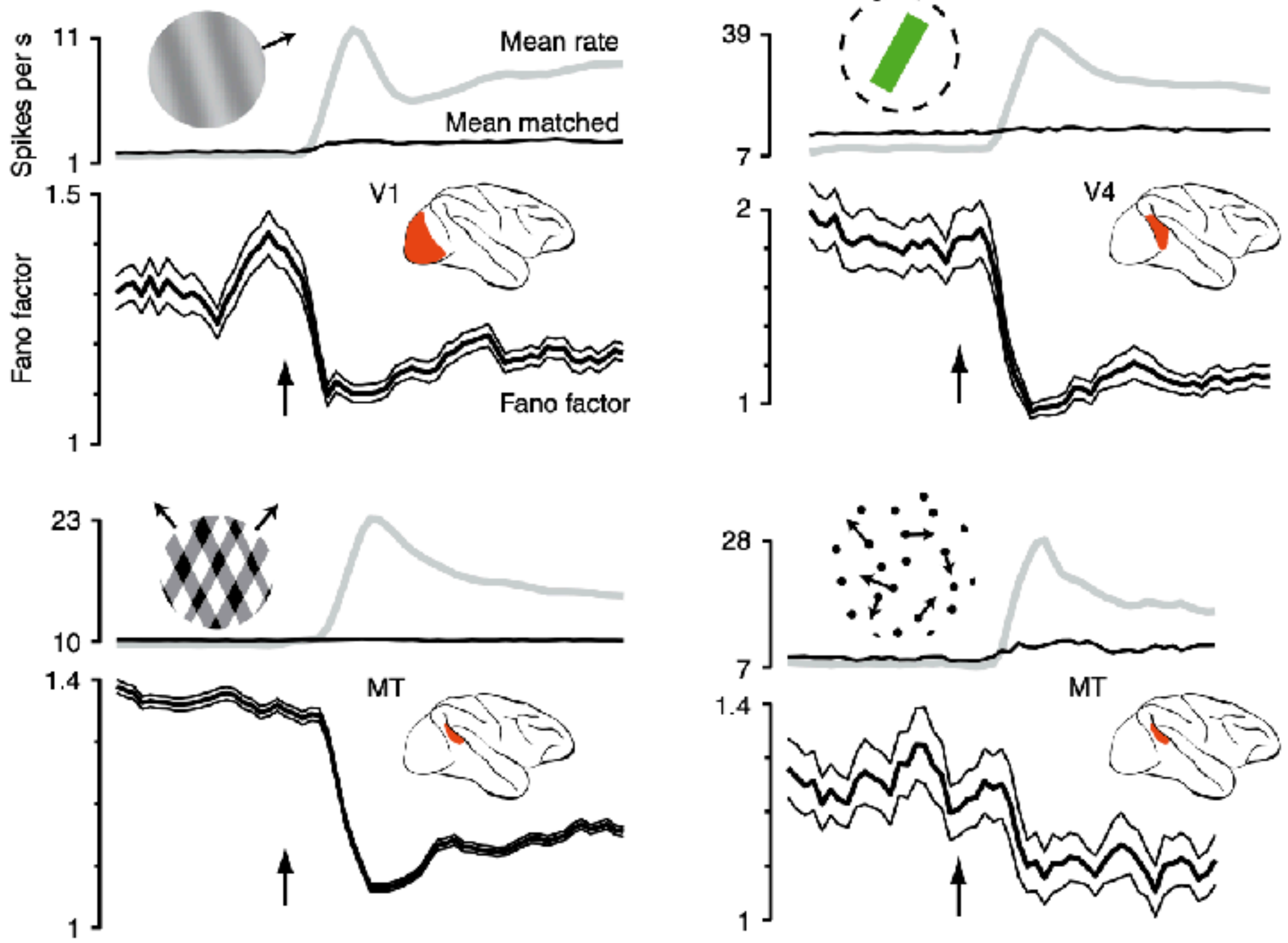
Fano(spont) > Fano(evoked)

[Deco & Hugues, 2012]
[Litwin-Kumar & Doiron, 2012]
[Mazzucato et al, 2015]

MODEL

DATA




Fano(spont) > Fano(evoked)

[Deco & Hugues, 2012]
[Litwin-Kumar & Doiron, 2012]
[Mazzucato et al, 2015]

[Churchland et al, 2010]

# Goals

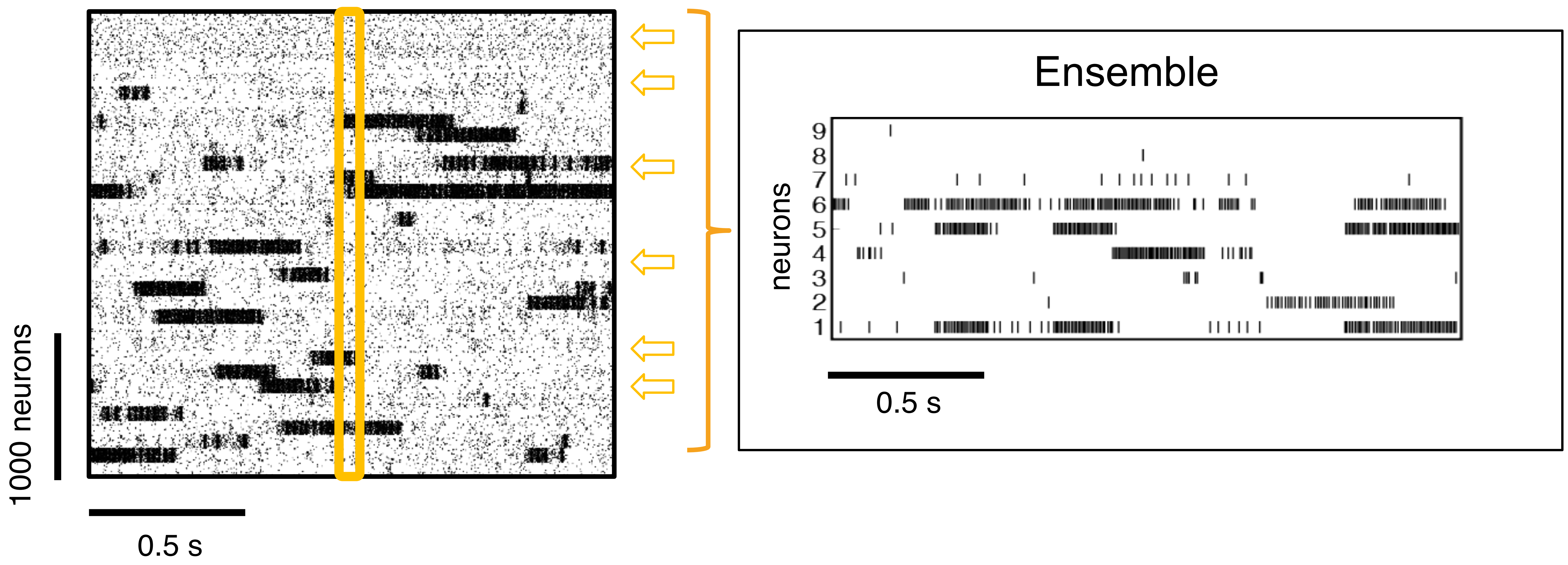
**Part I - Theory**

- **Metastable activity in cortical circuits**
- **Hidden Markov Models fit to metastable activity**
- **Modeling metastable activity with attractor networks**

**Part II - Exercise**

- **HMM: model selection with gaussian emissions**
- **Fit Poisson-HMM to spike trains**
- **Challenge: A model of arousal in attractor networks**

# Clustered network

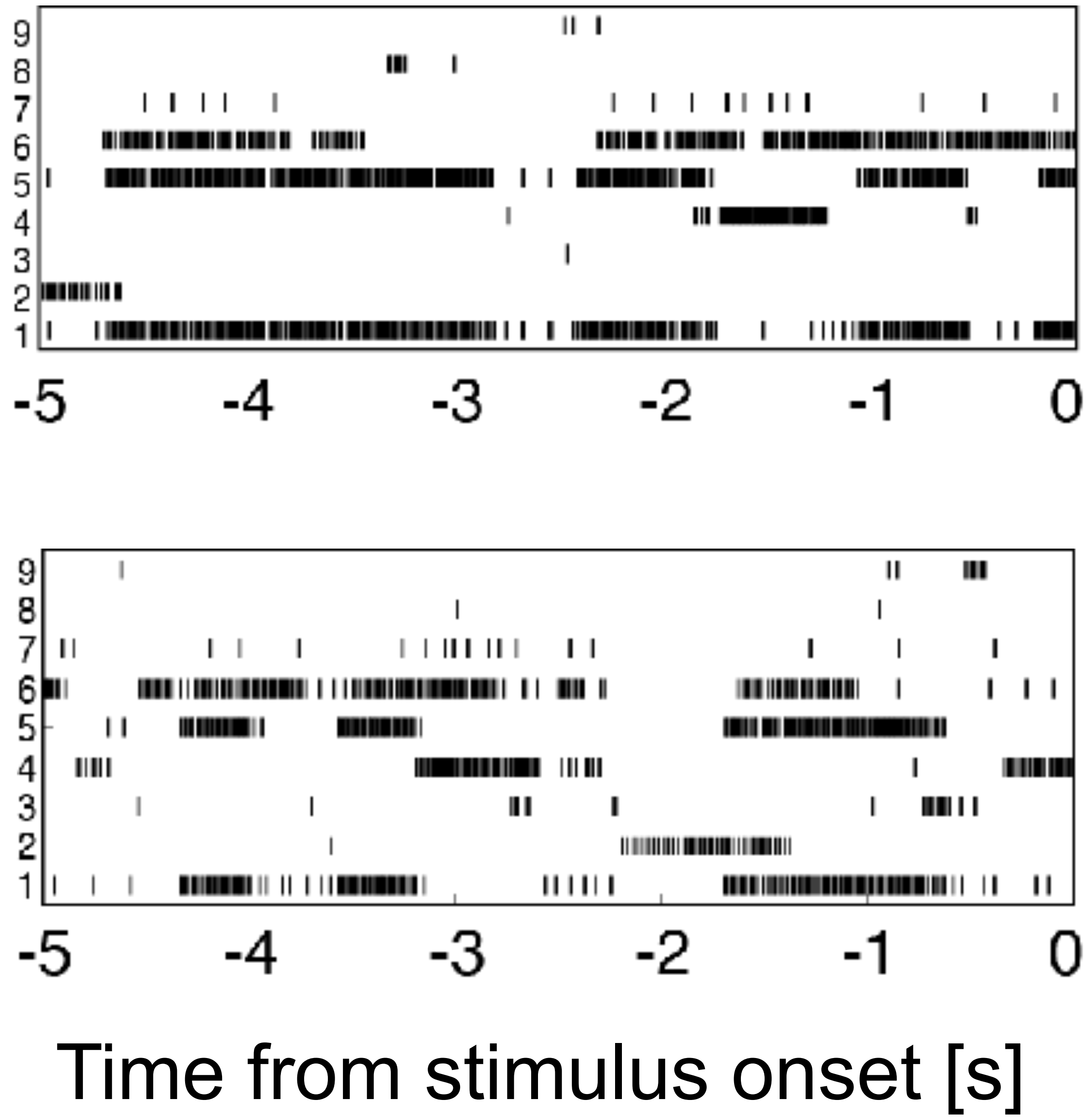



[Mazzucato et al., 2015, 2016]

# Clustered network

DATA

MODEL

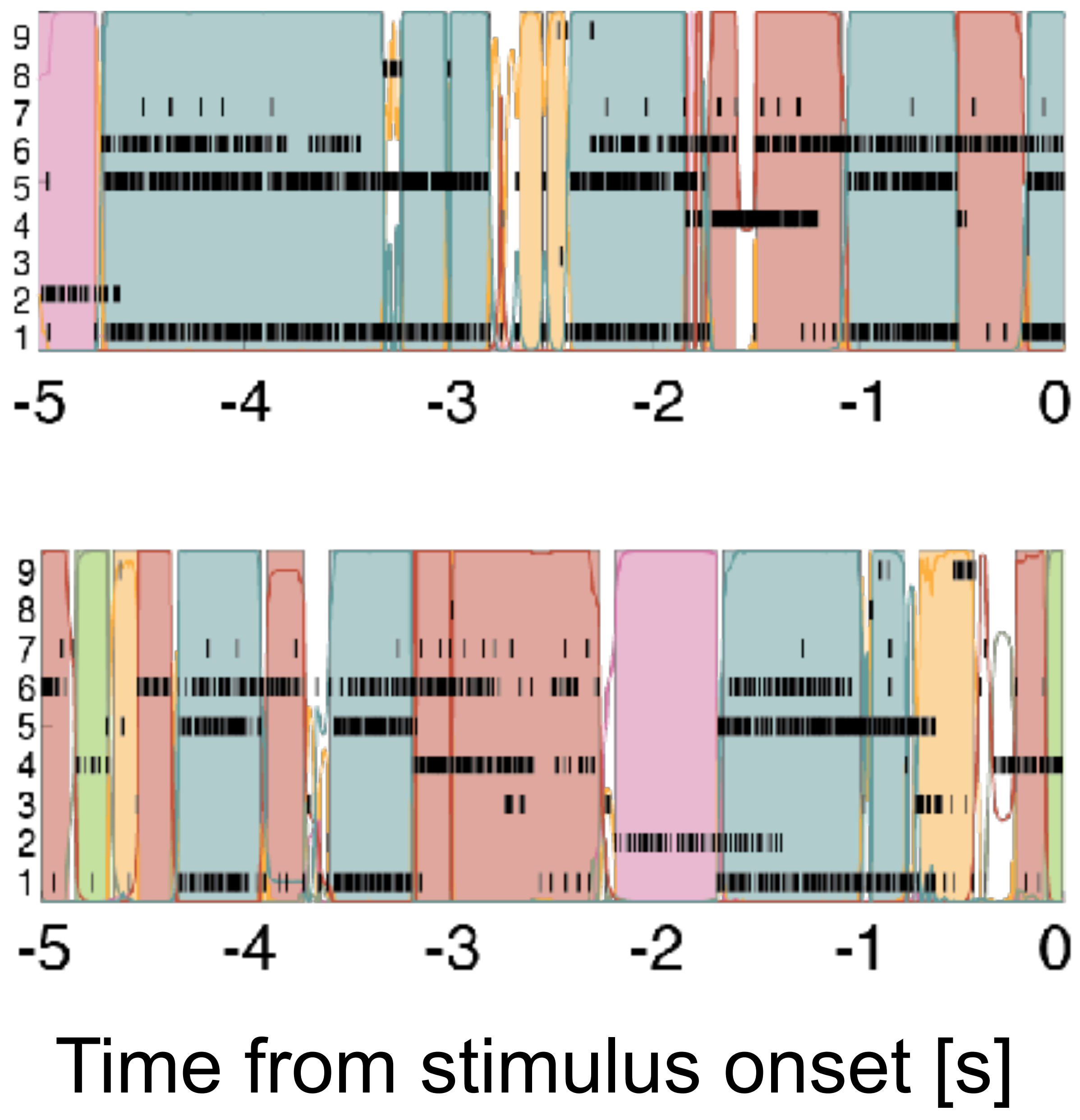



[Mazzucato et al., 2015]

# Clustered network

DATA

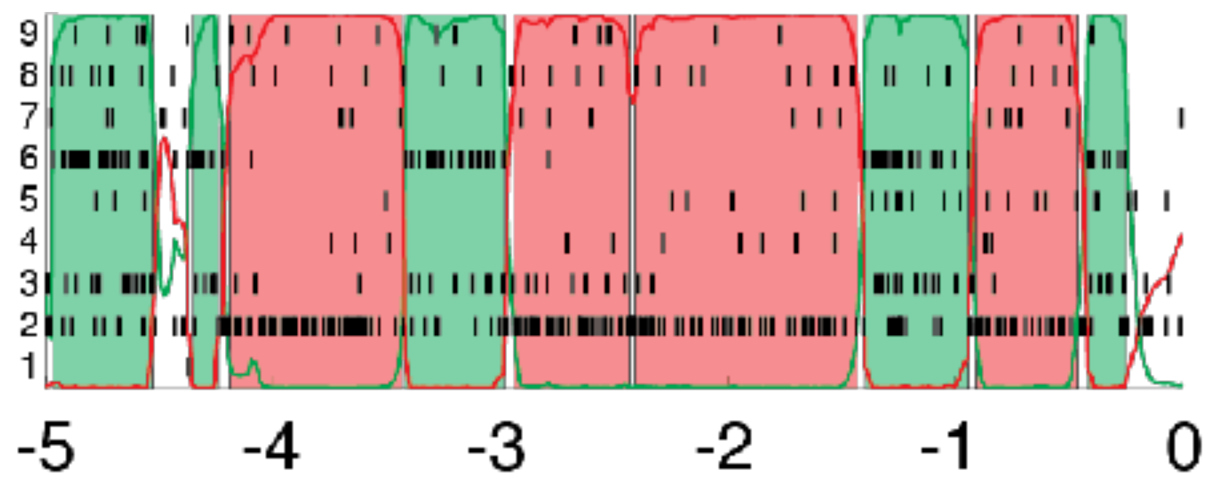
MODEL

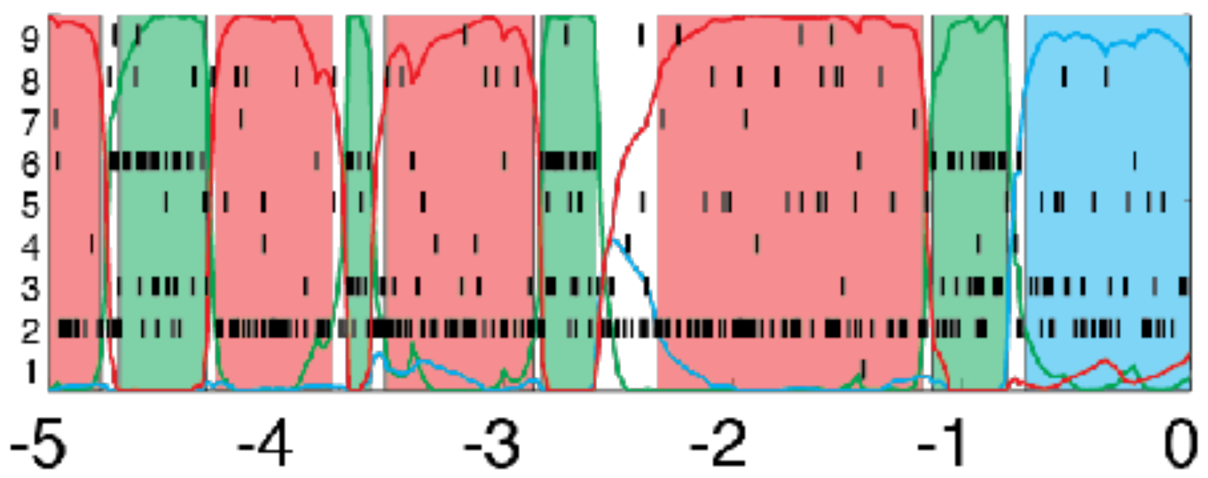



[Mazzucato et al., 2015]

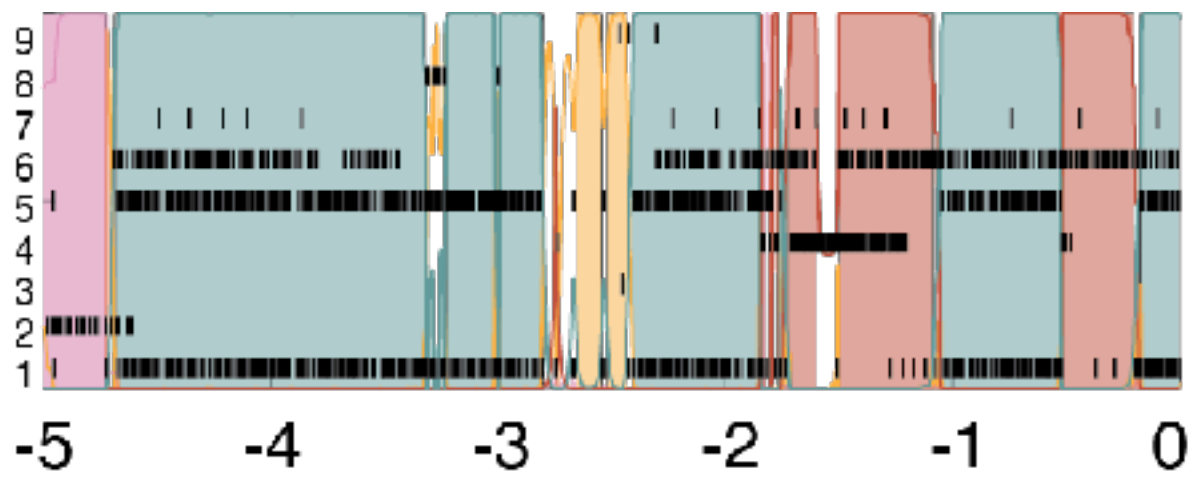
# Clustered network

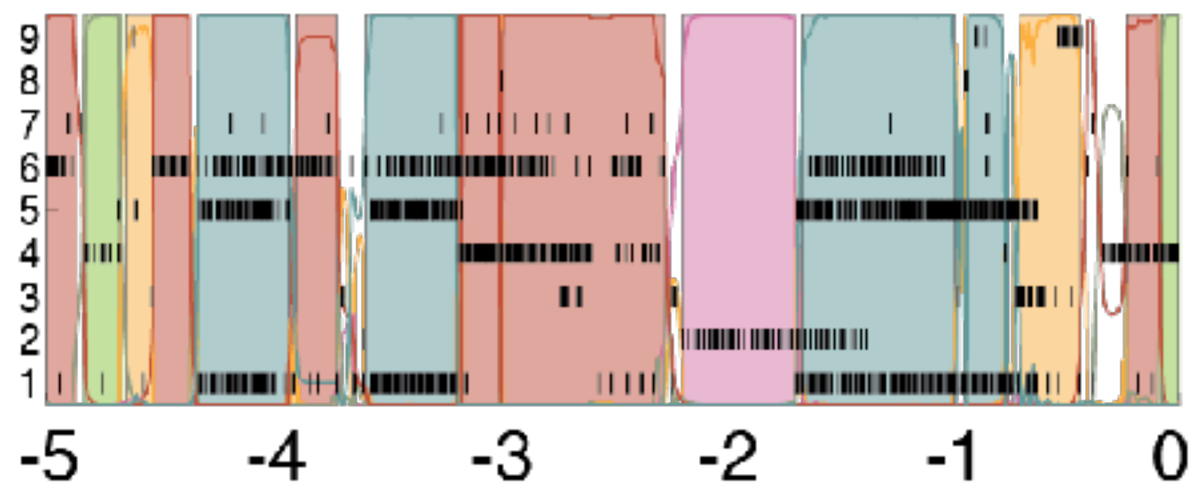
| DATA | MODEL |
|---|---|




Time from stimulus onset [s]




Time from stimulus onset [s]

[Mazzucato et al., 2015]

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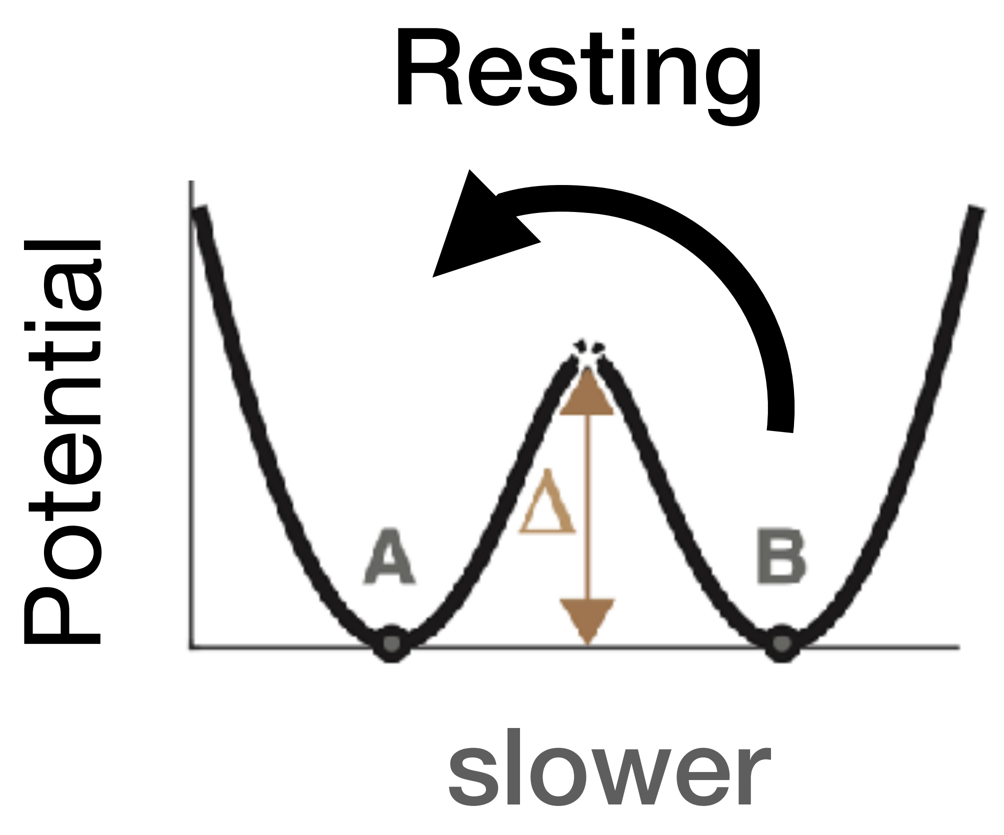
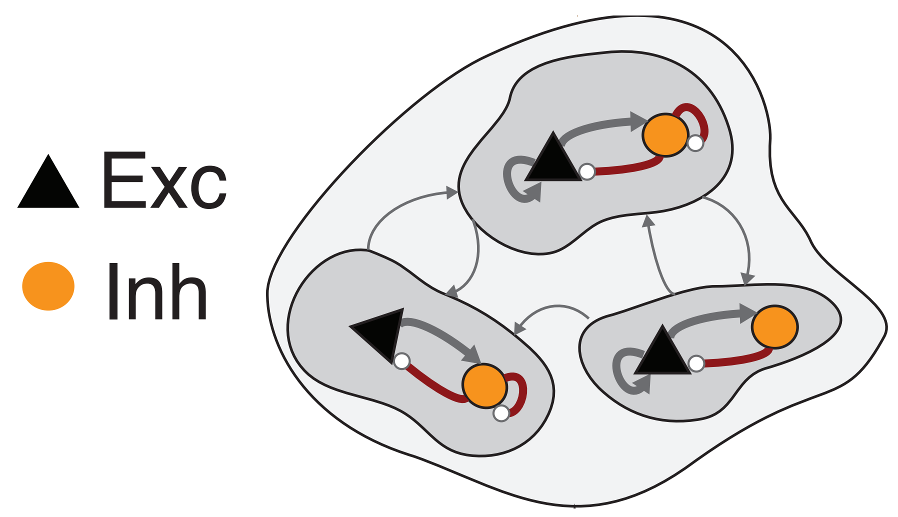
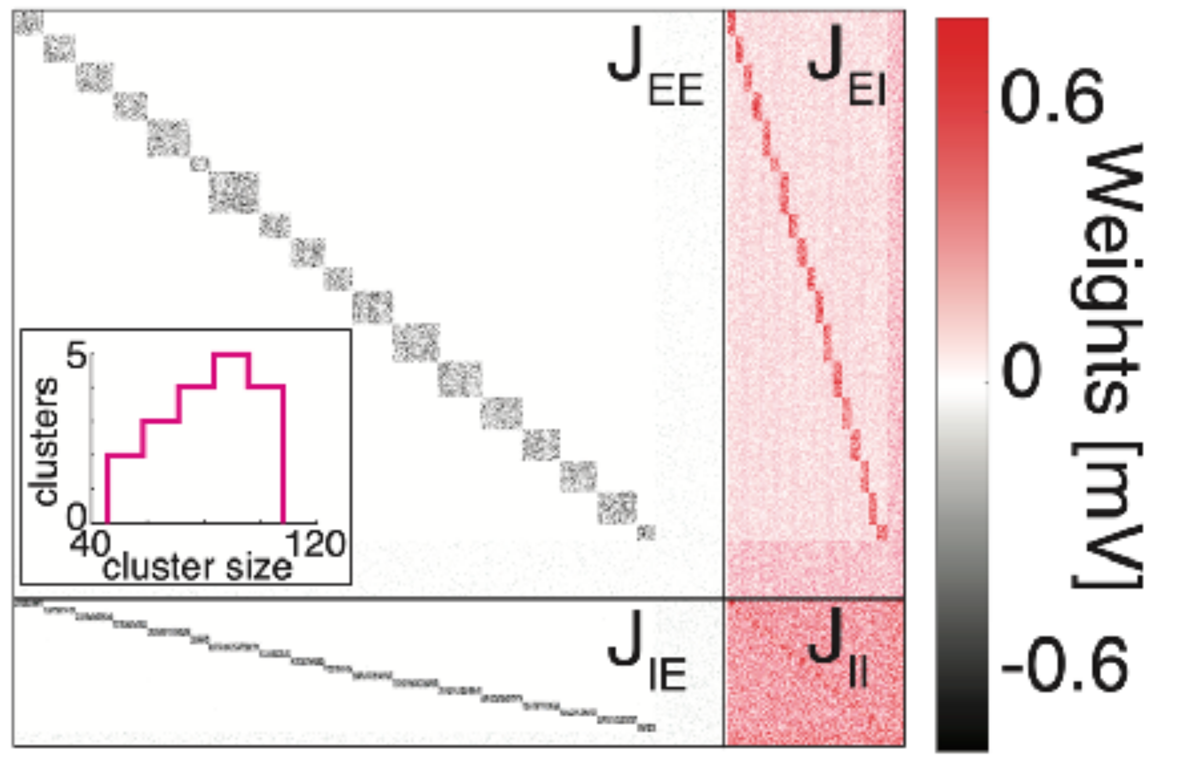
# Ongoing activity

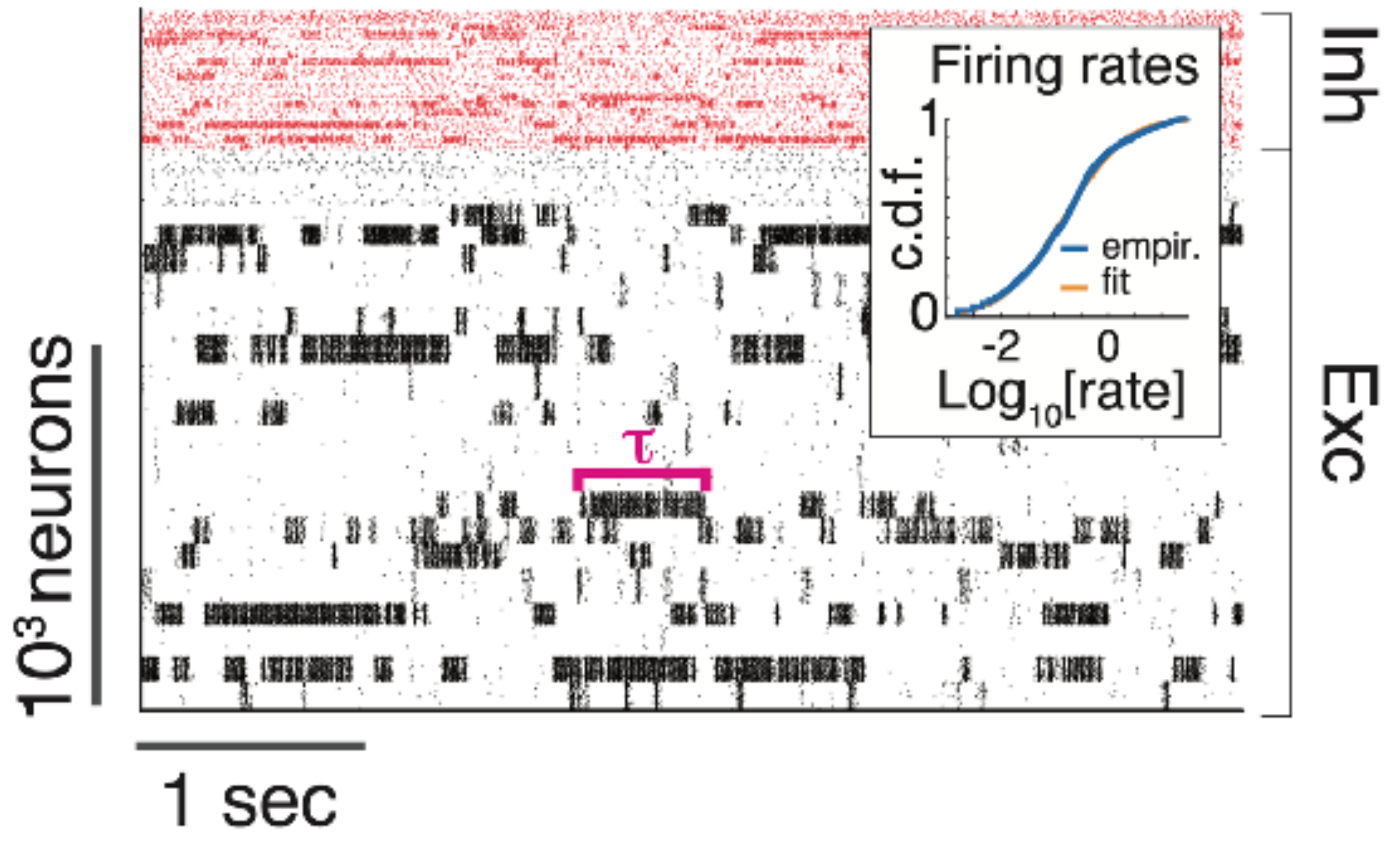


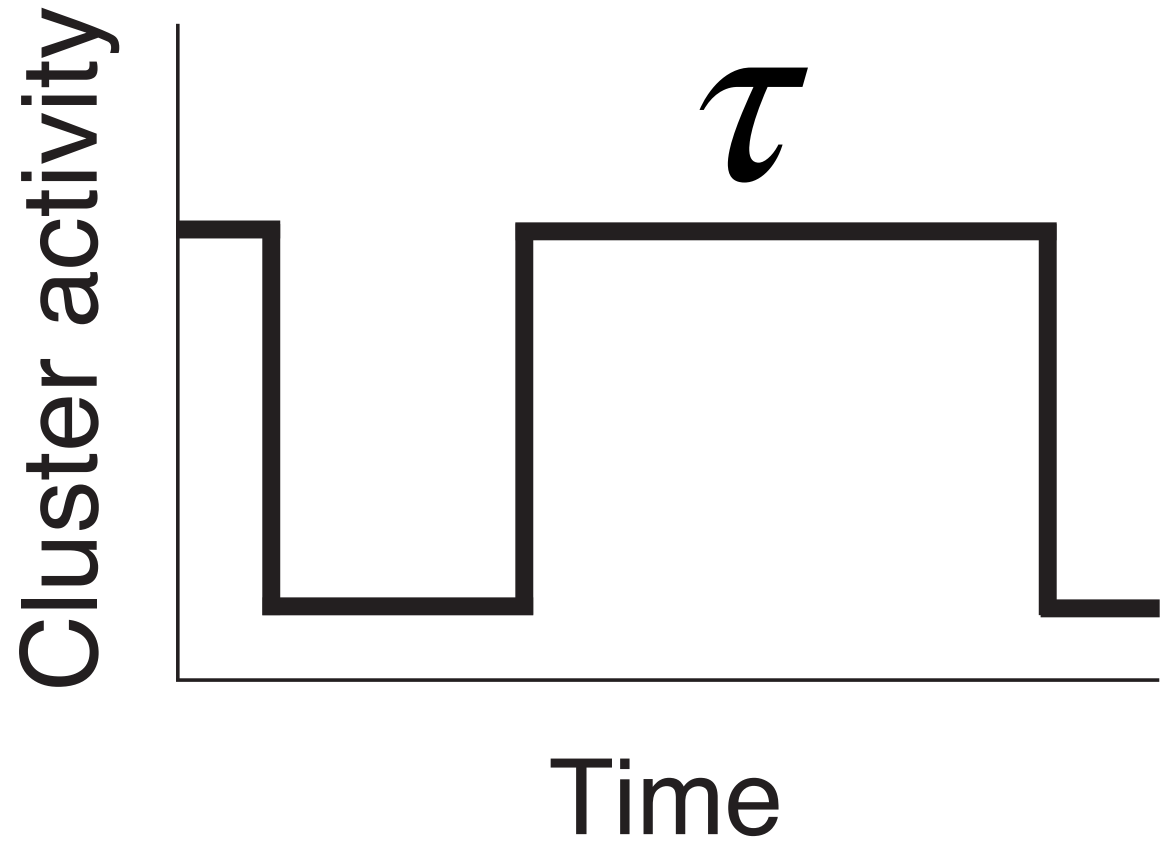




## Synaptic weights




## Ongoing activity

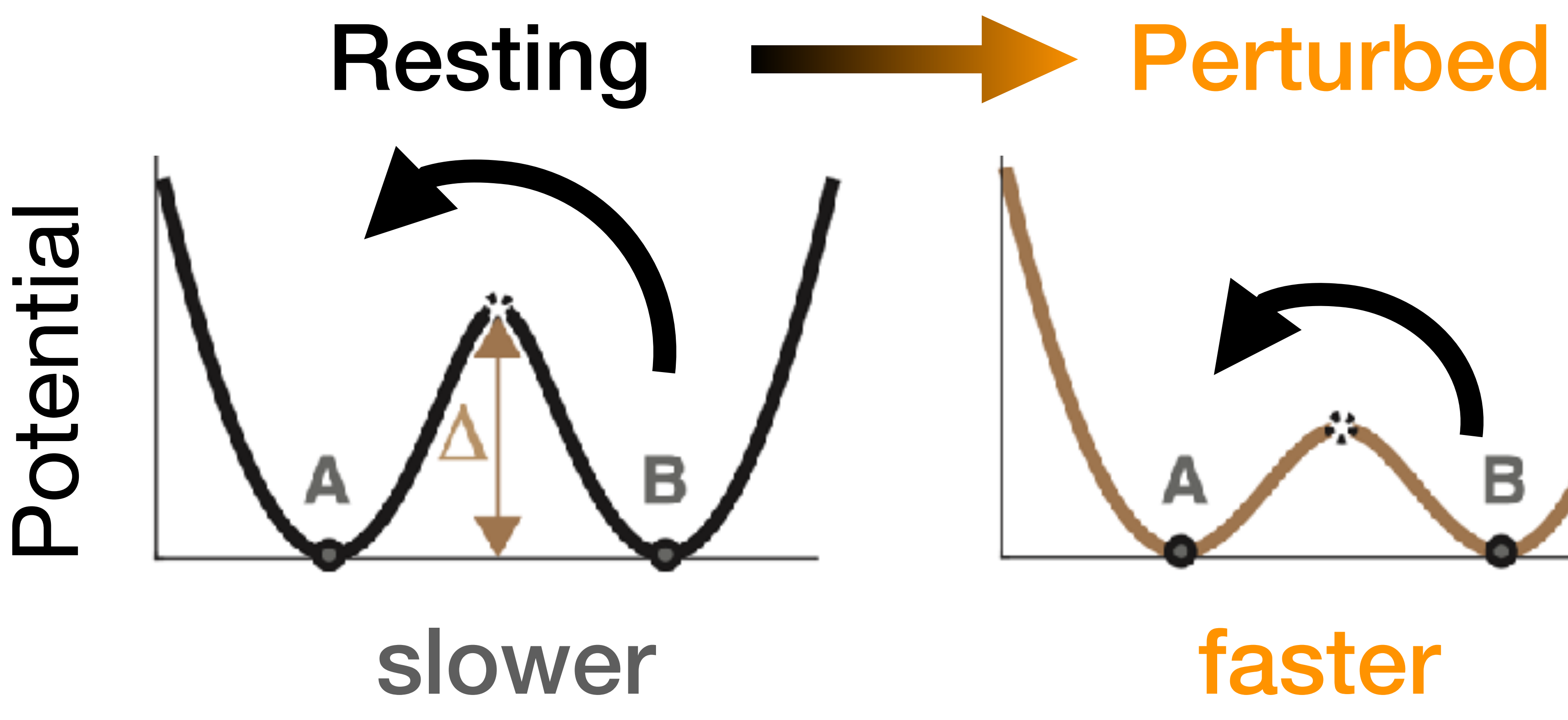


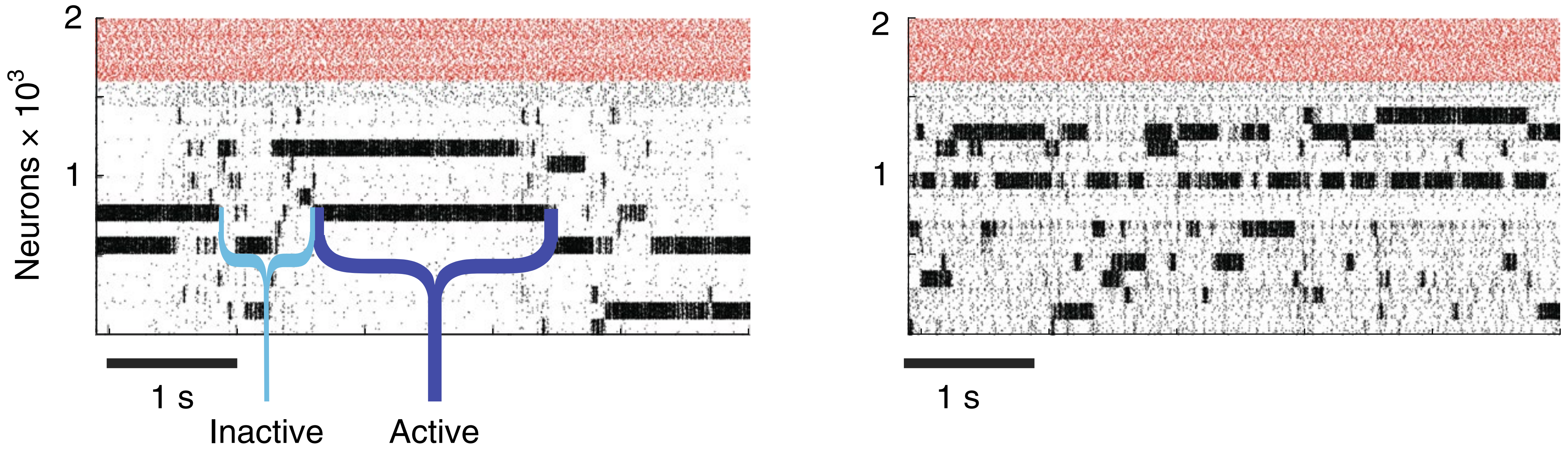



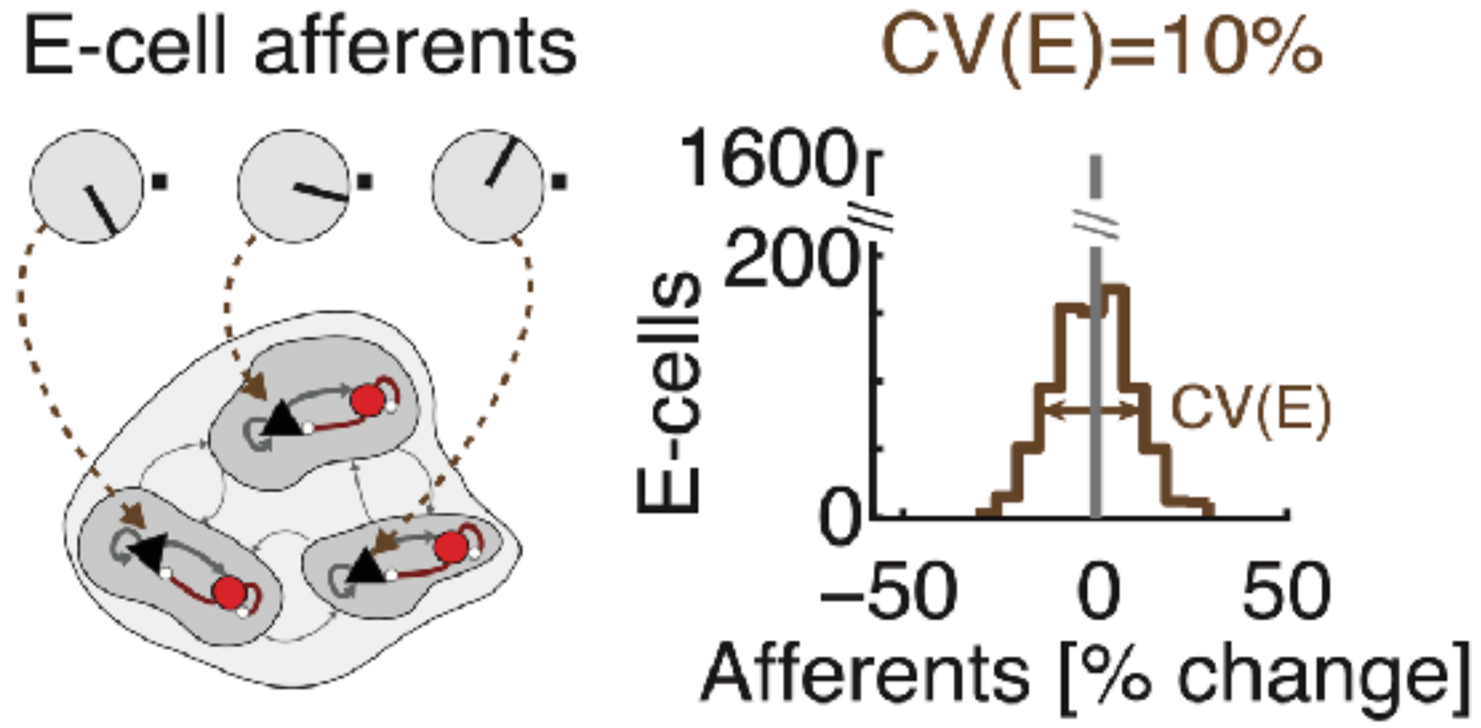

**Barrier height —> Transition time**

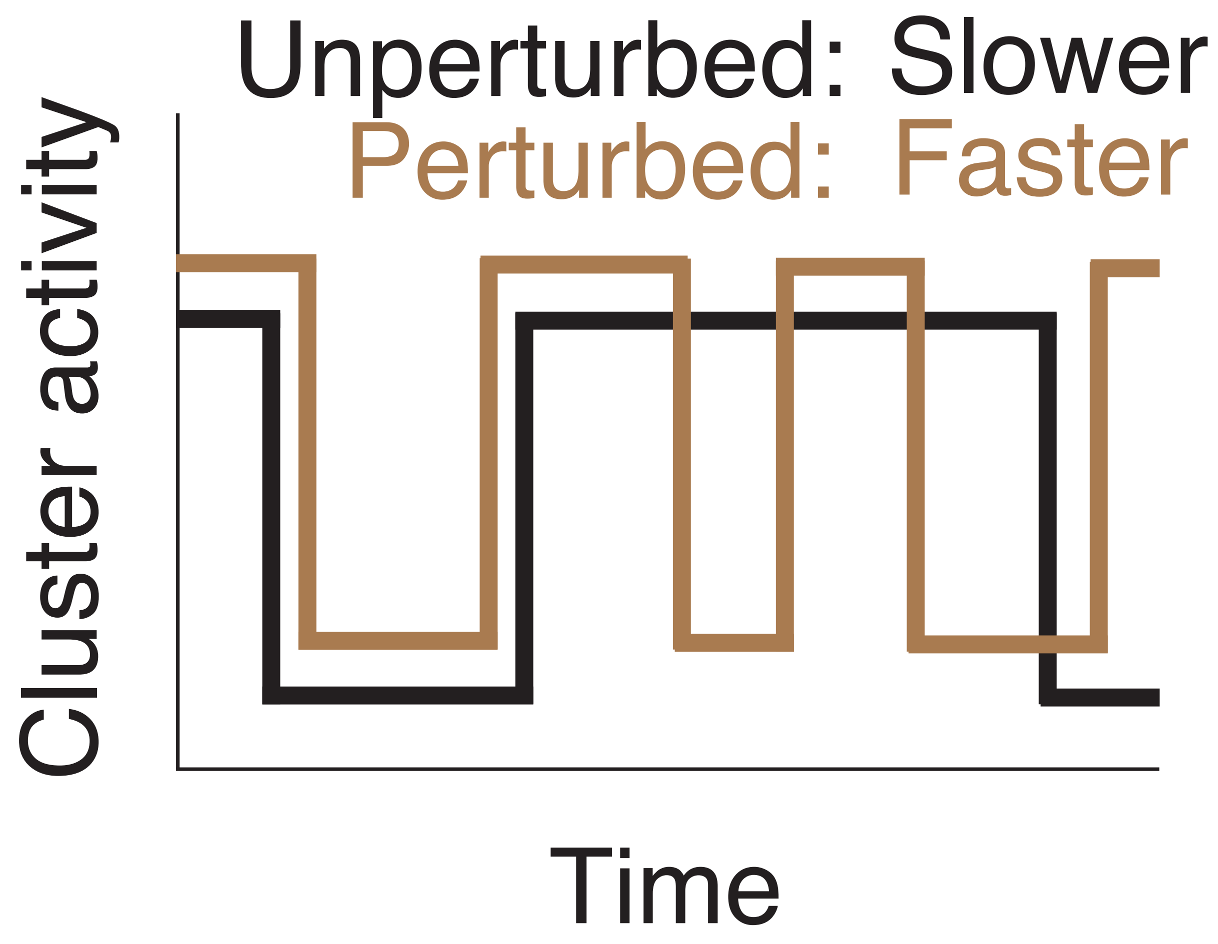
[LM et al, 2019]
[Wyrick & LM, 2021]

# Ongoing activity



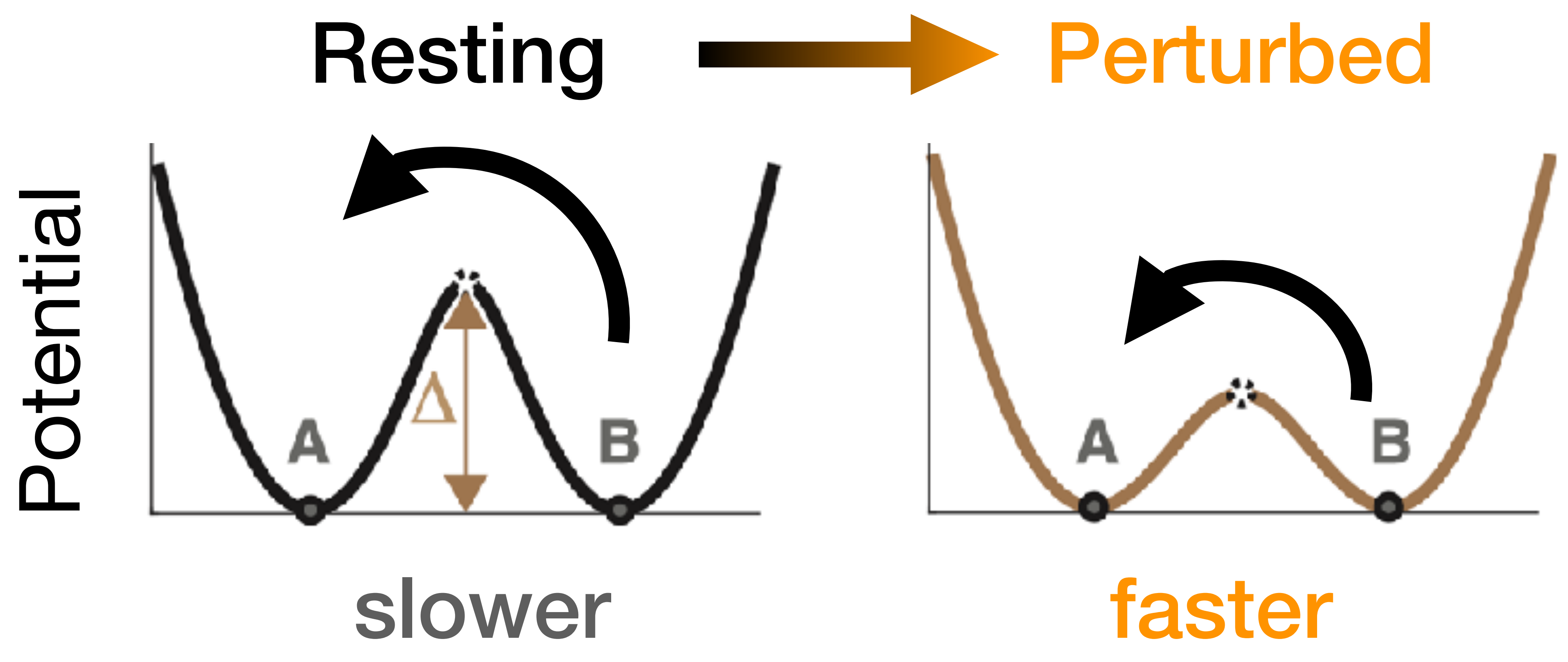



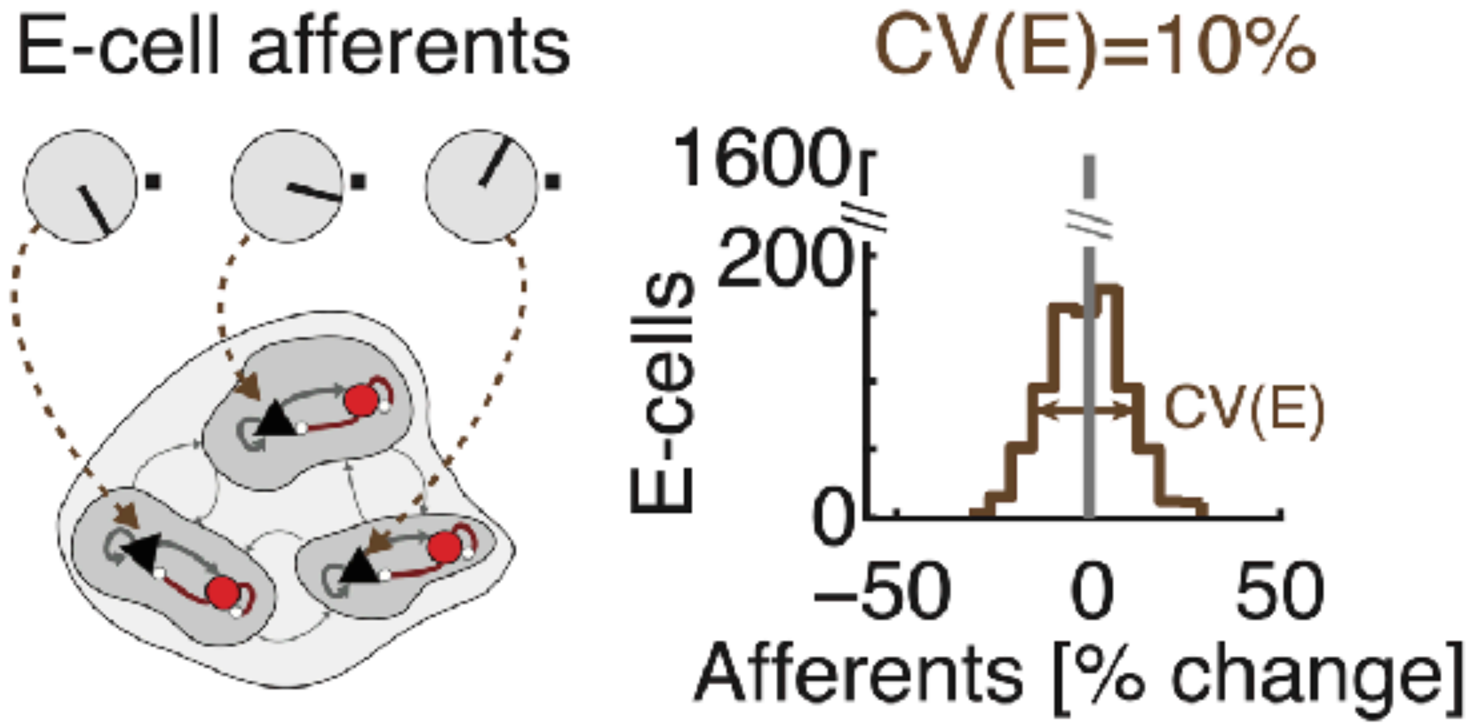



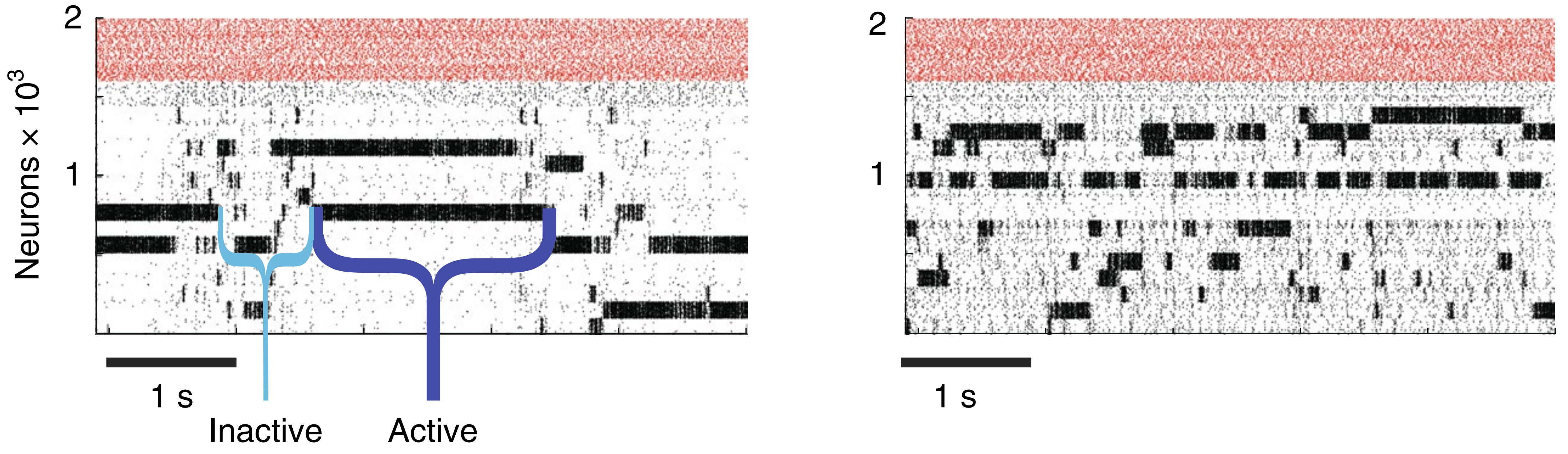

**Lower barrier —> Faster transition time**

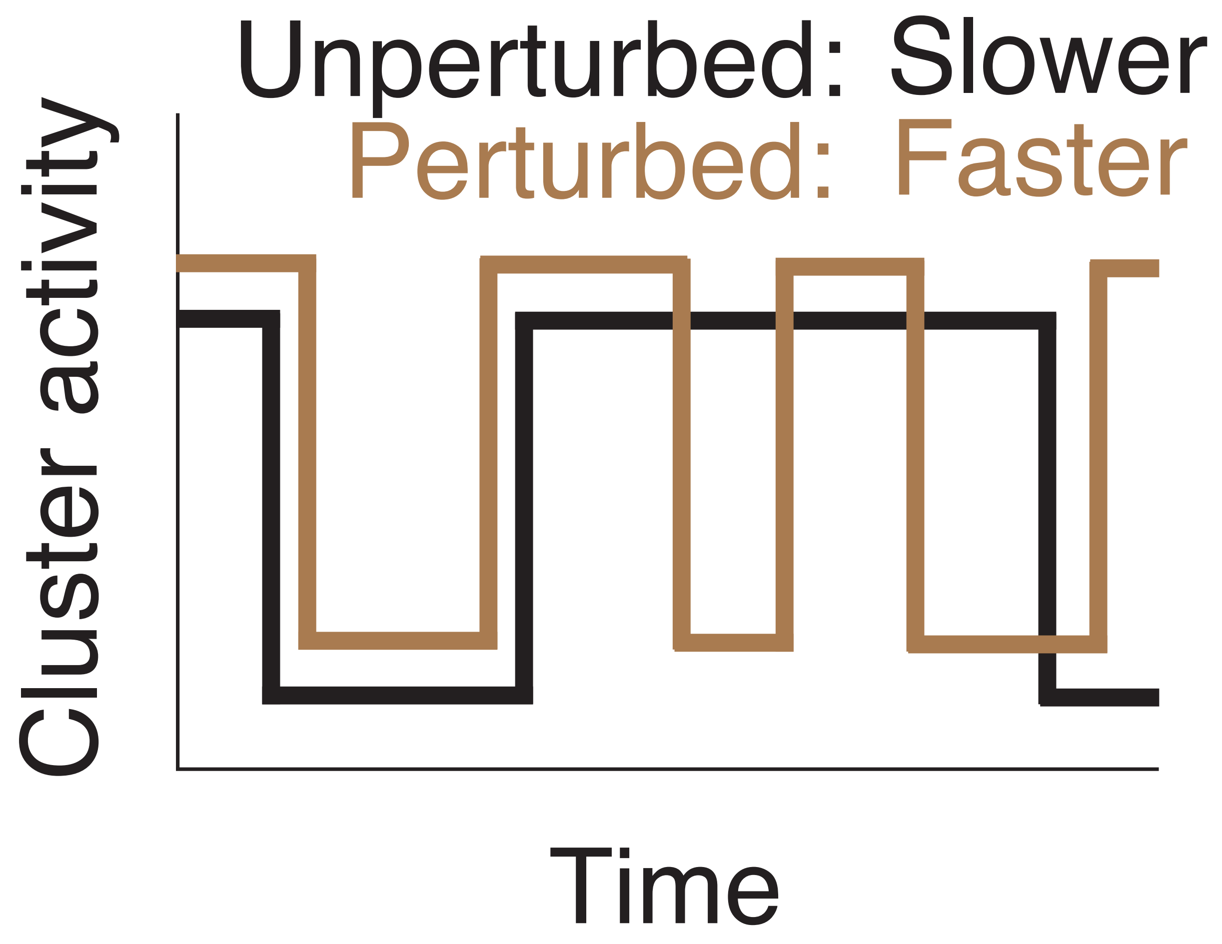
[LM et al, 2019]
[Wyrick & LM, 2021]

# Ongoing activity




**Challenge:**

- **Fit HMM to resting and perturbed conditions**
- **Compare state dwell times**

[LM et al, 2019]
[Wyrick & LM, 2021]

Metastable activity:

- is observed in many cortical areas and tasks
- is involved in sensory and cognitive processes
- can emerge spontaneously in clustered spiking networks

www.mazzulab.com

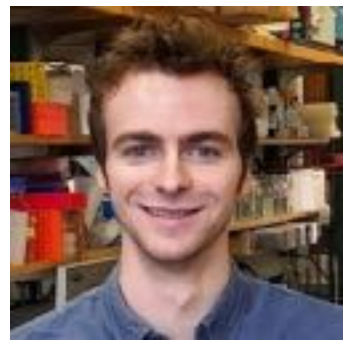

Stefano Recanatesi


Lia Papadopoulos


David Wyrick


Audra McNamee


Nicu Istrate


Peregrine Painter


Merav Stern
(Hebrew U.)


Alireza Tavanfar
(Champalimaud)


# Funding

NIH National Institute on Deafness and Other Communication Disorders

BRAIN INITIATIVE

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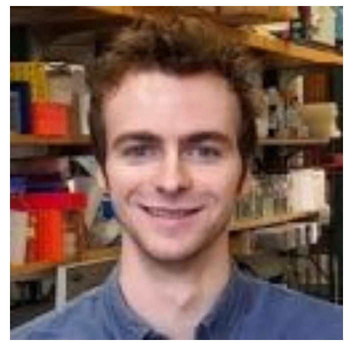

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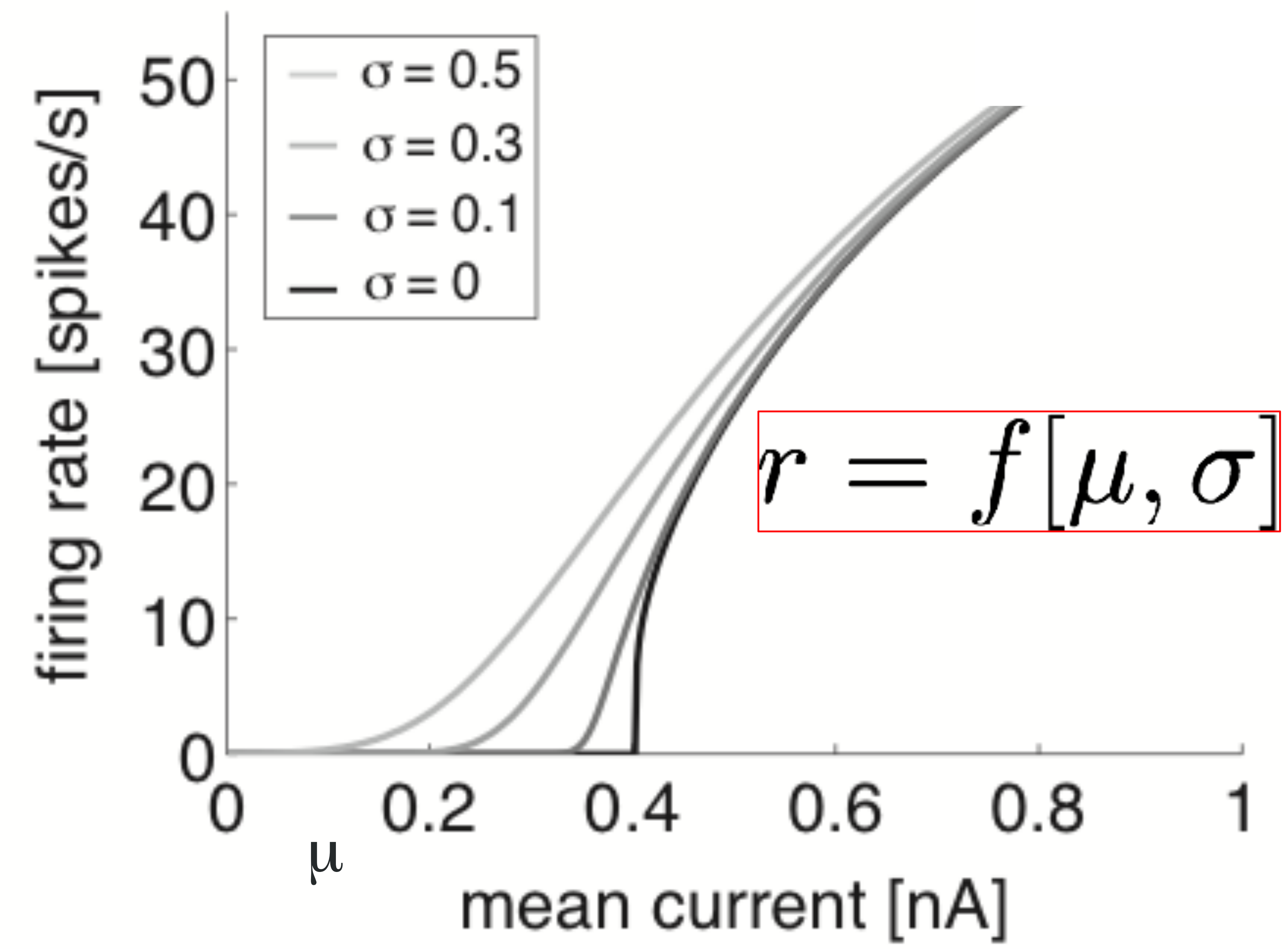
BRAIN INITIATIVE


# Supplementary details

# Transfer function




$$r = f[\mu, \sigma]$$

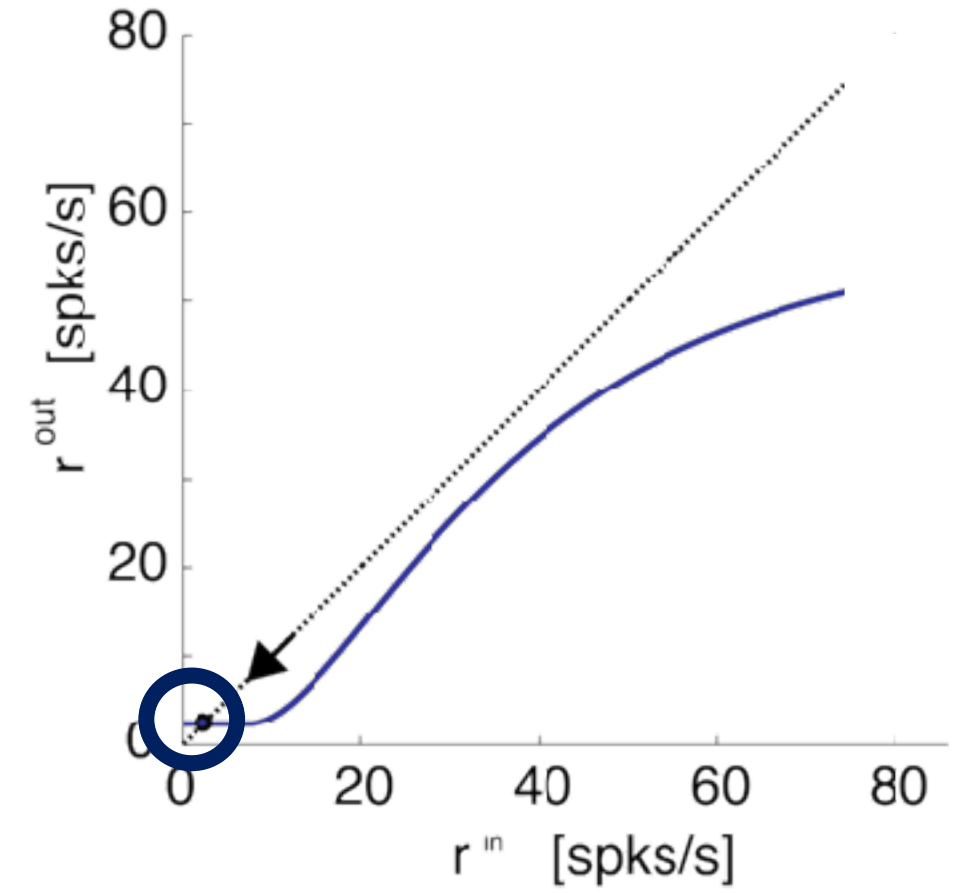
$$\mu = \mu(r)$$
$$\sigma = \sigma(r)$$

[Amit & Brunel, 1997]

# Model – Attractors

$$r^{out} = f\left[\mu(r^{in}), \sigma(r^{in})\right]$$

$$r^{out} = r^{in}$$ fixed point

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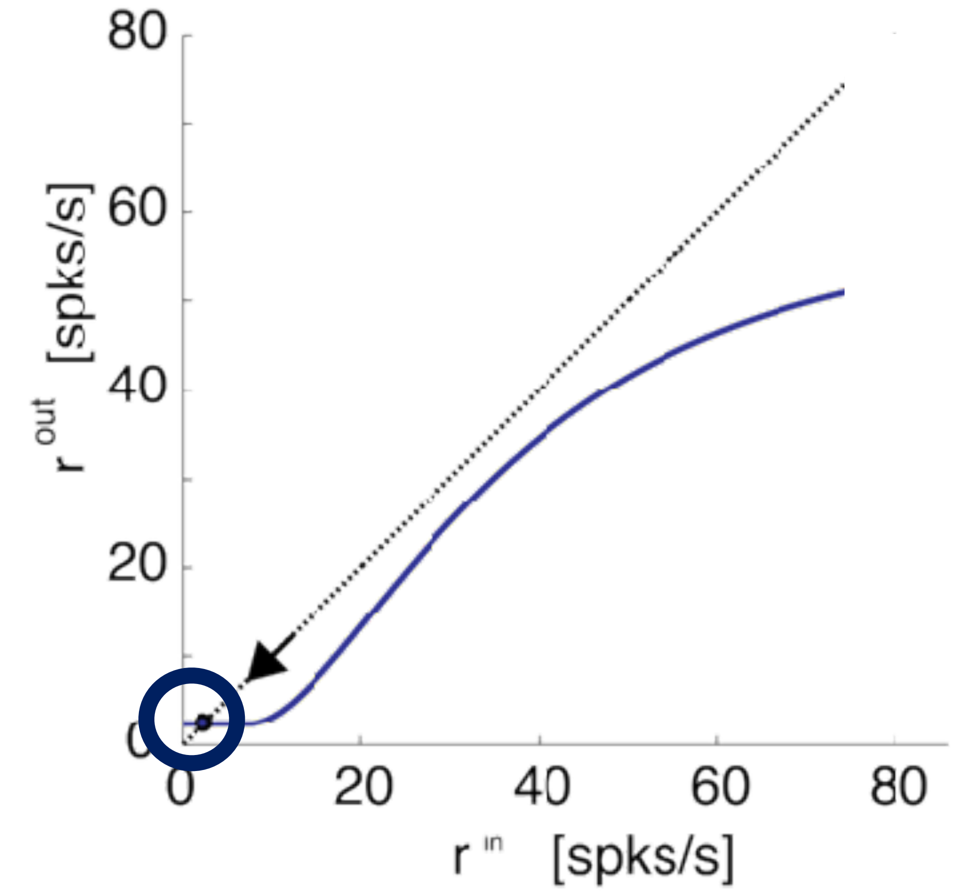
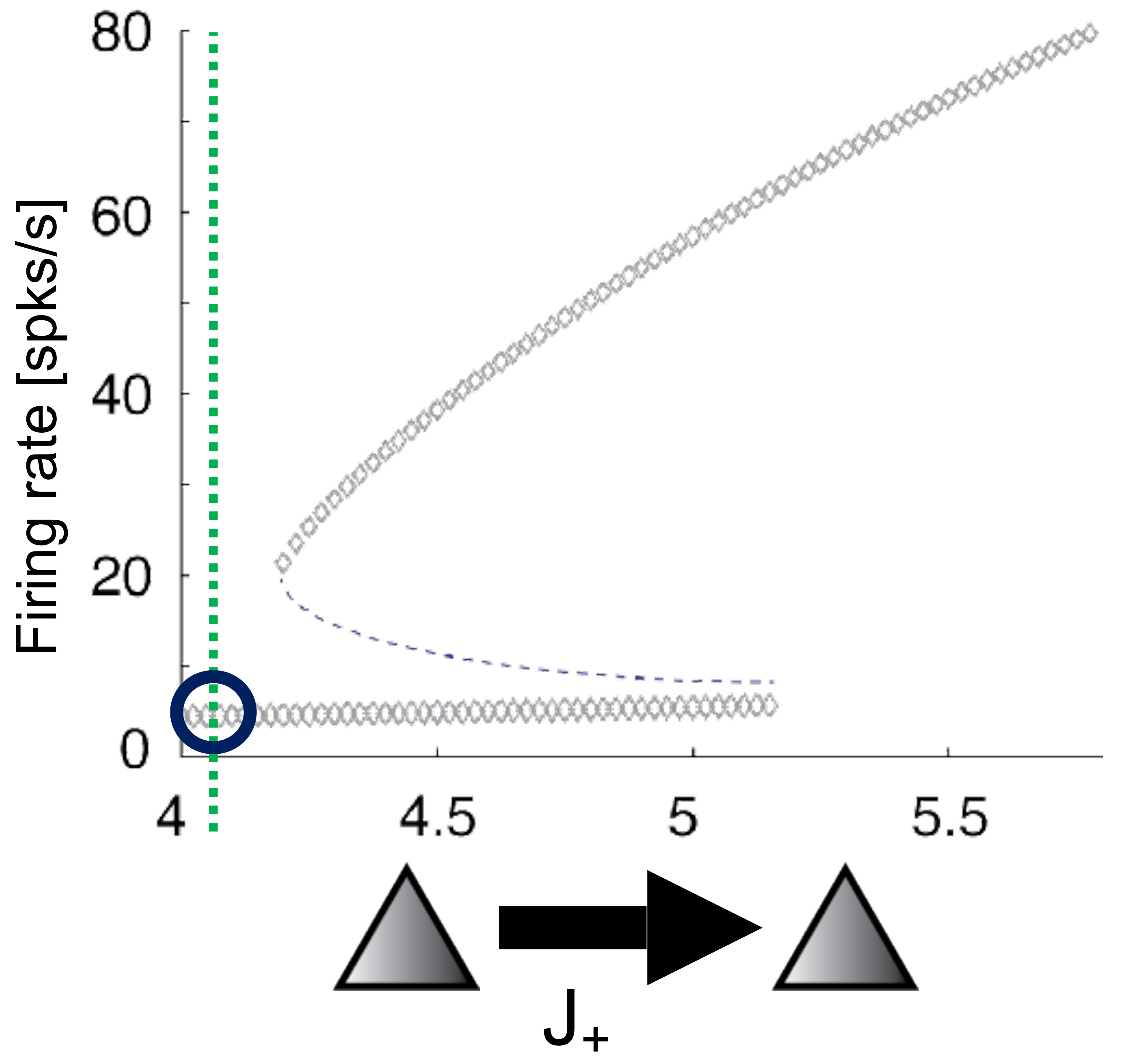



Network attractors (stable states)

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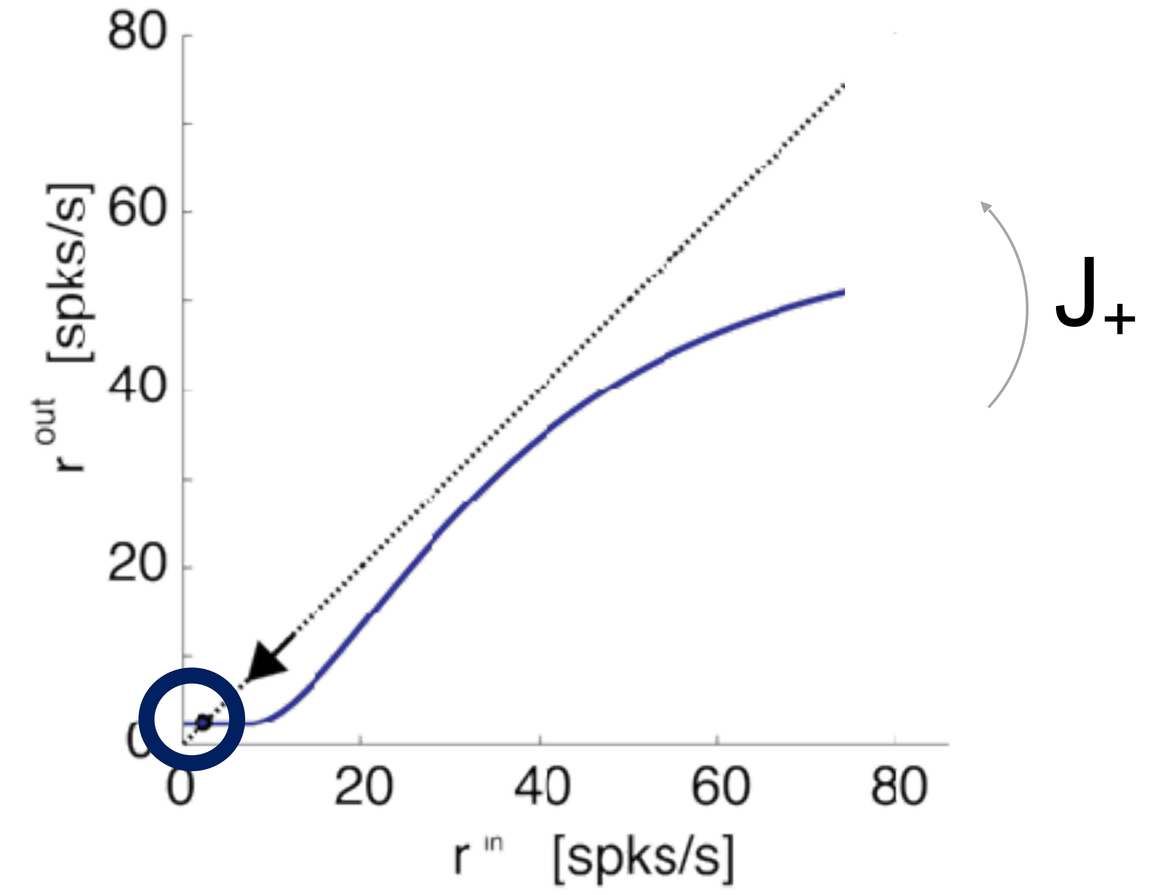


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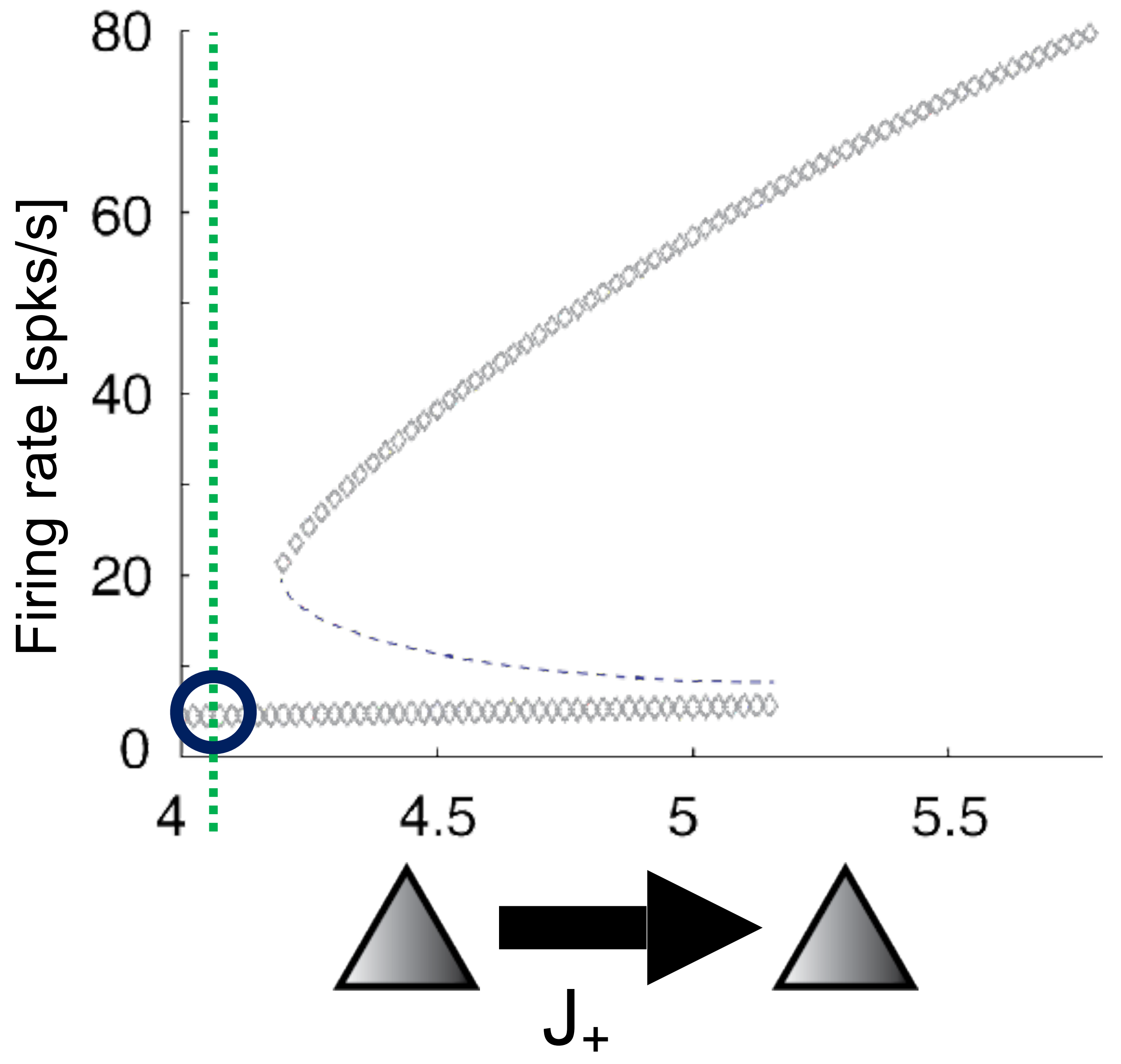


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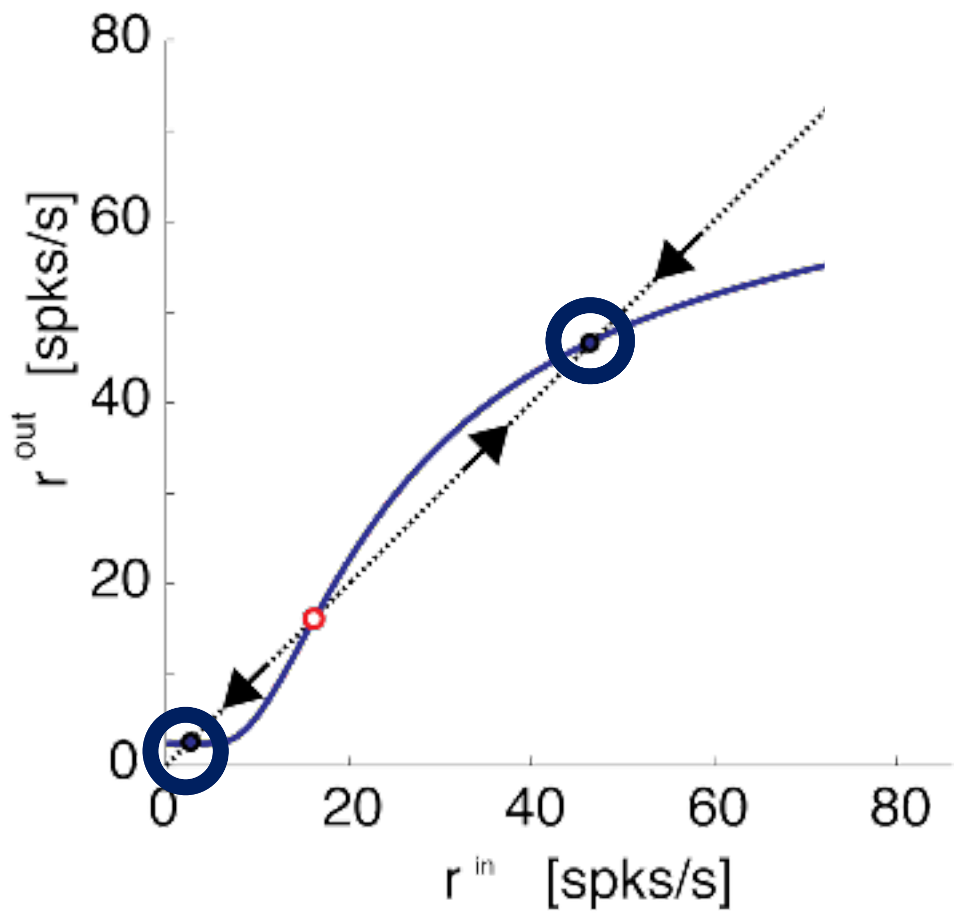


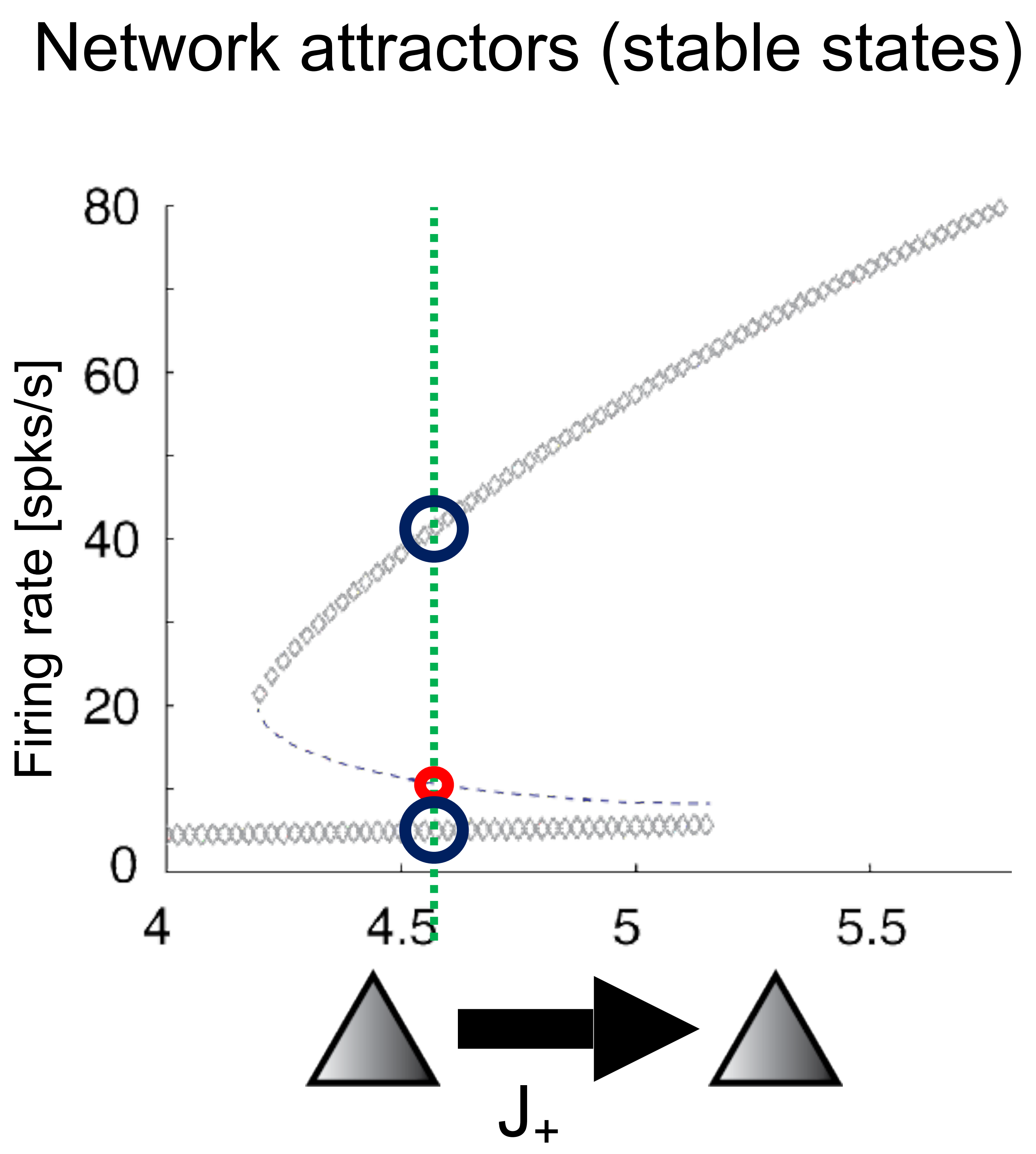


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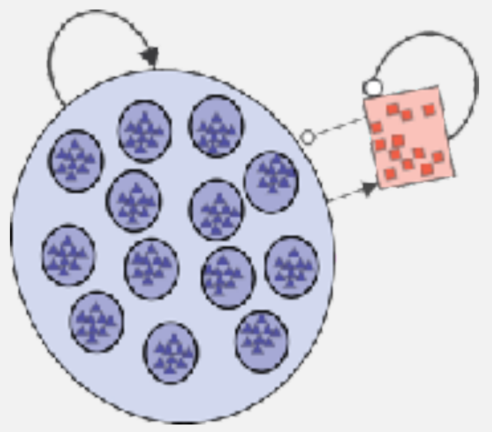
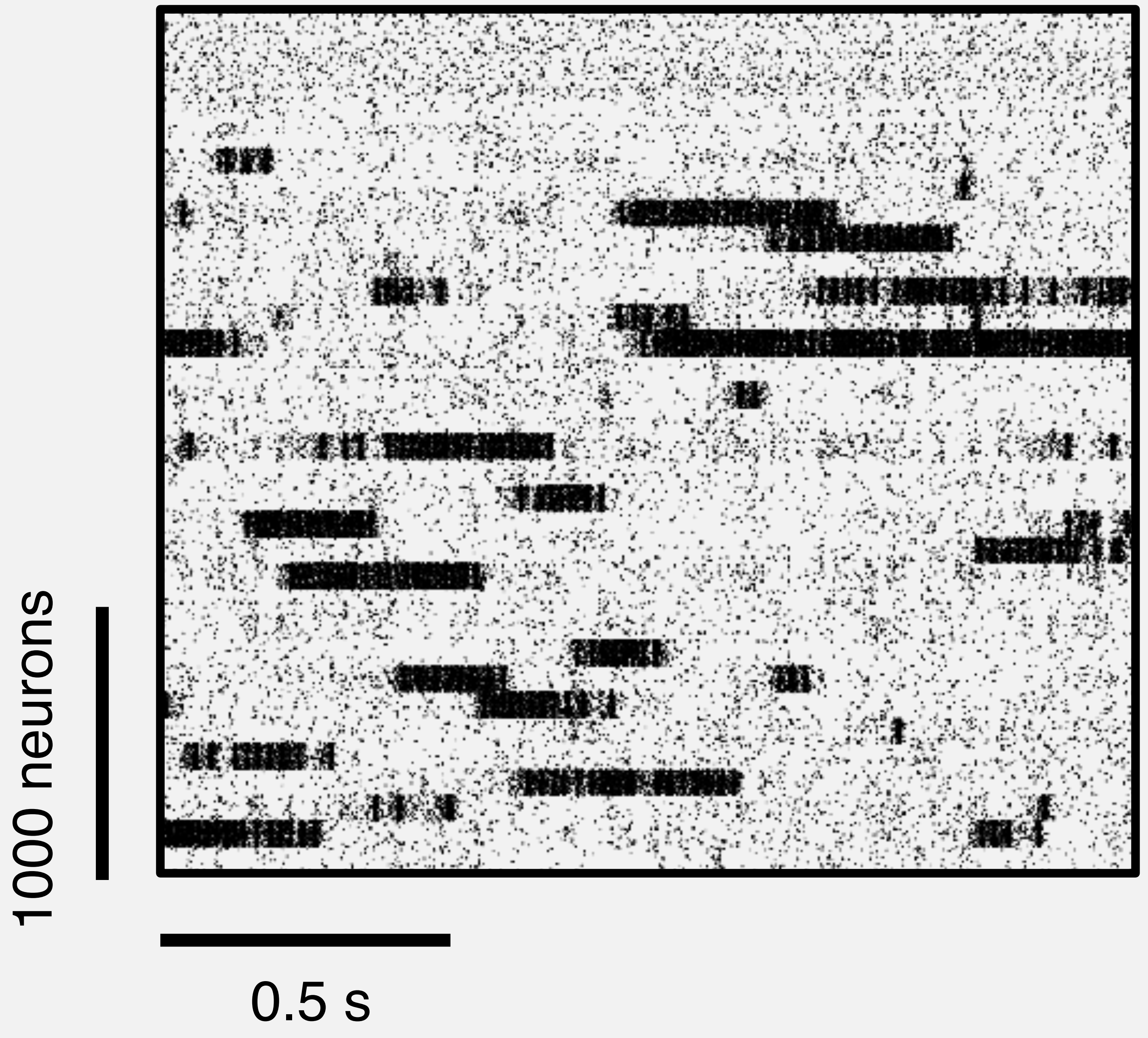
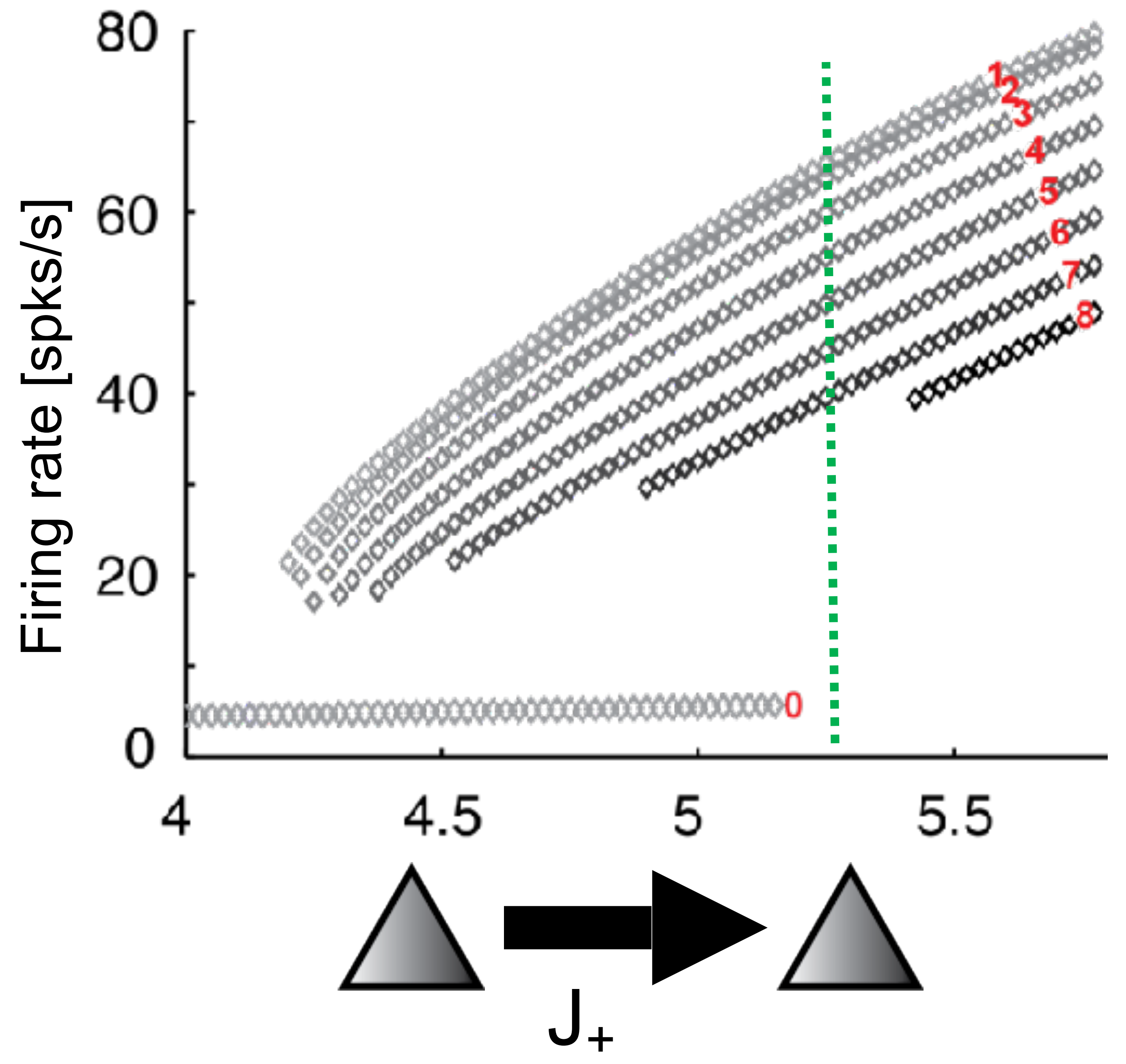
# Model – Spontaneous activity






$$r_i = f\left[\mu_i(\overrightarrow{r}), \sigma_i(\overrightarrow{r})\right]$$

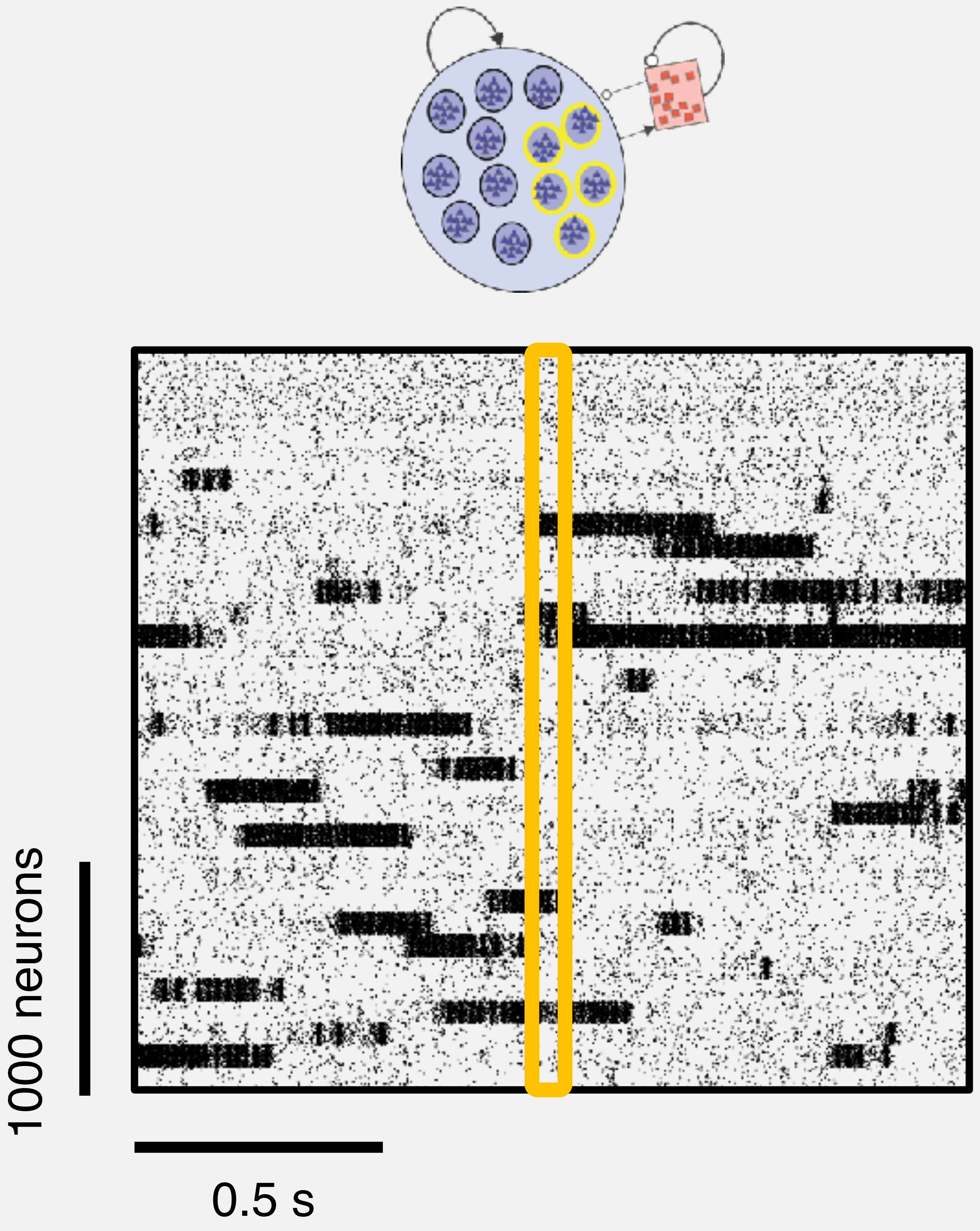
Attractor landscape




MFT details ▶

[Mazzucato et al., 2015, 2016]

# Model – Spontaneous activity

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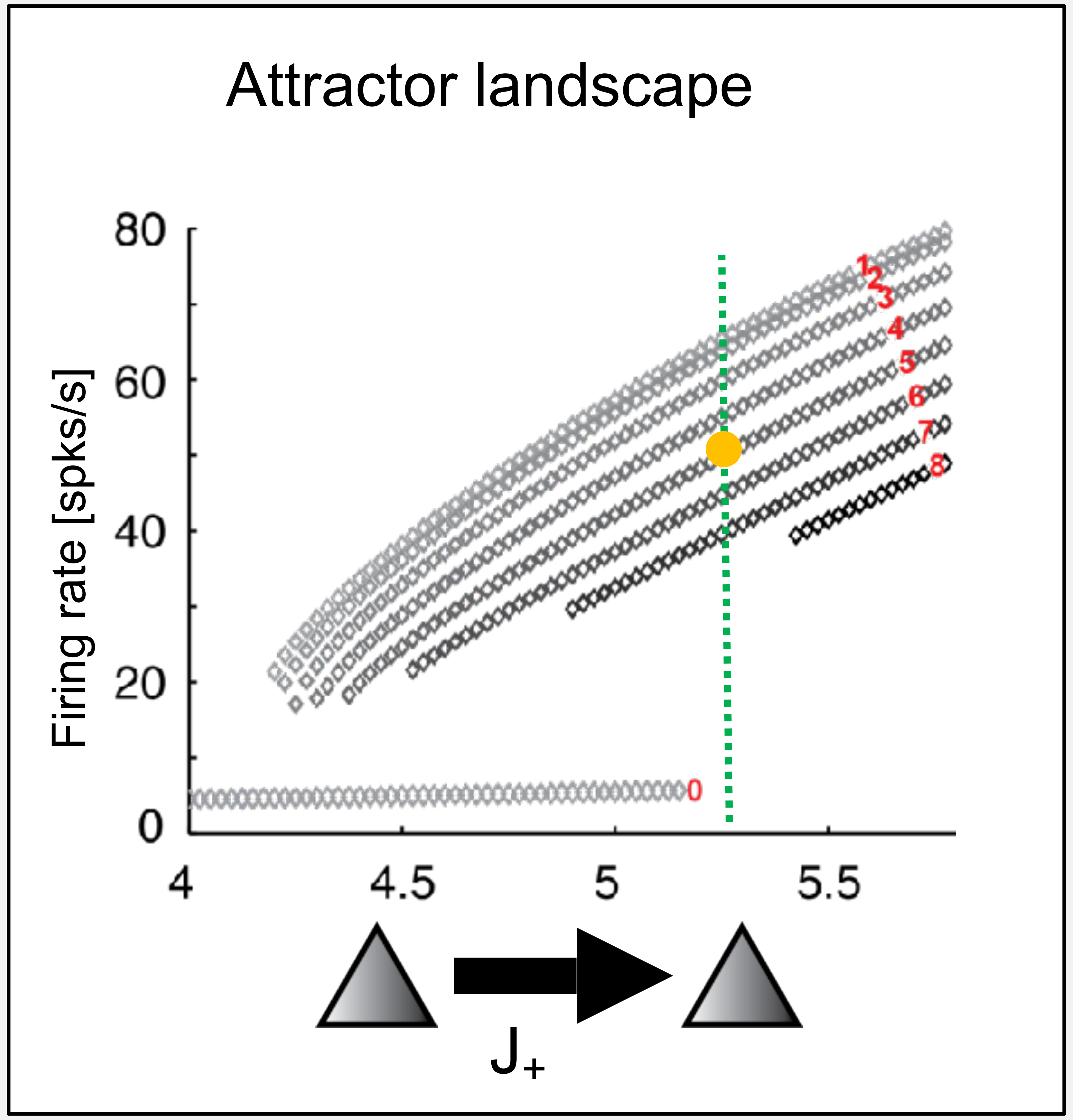


MFT details

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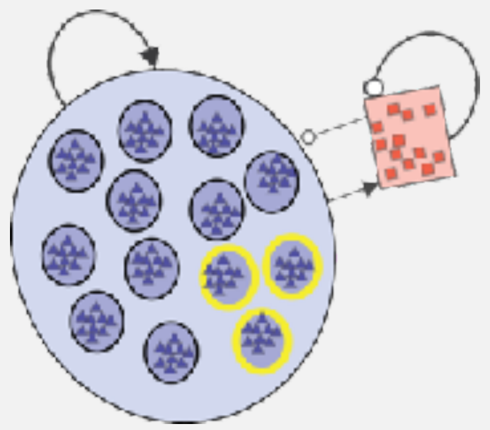

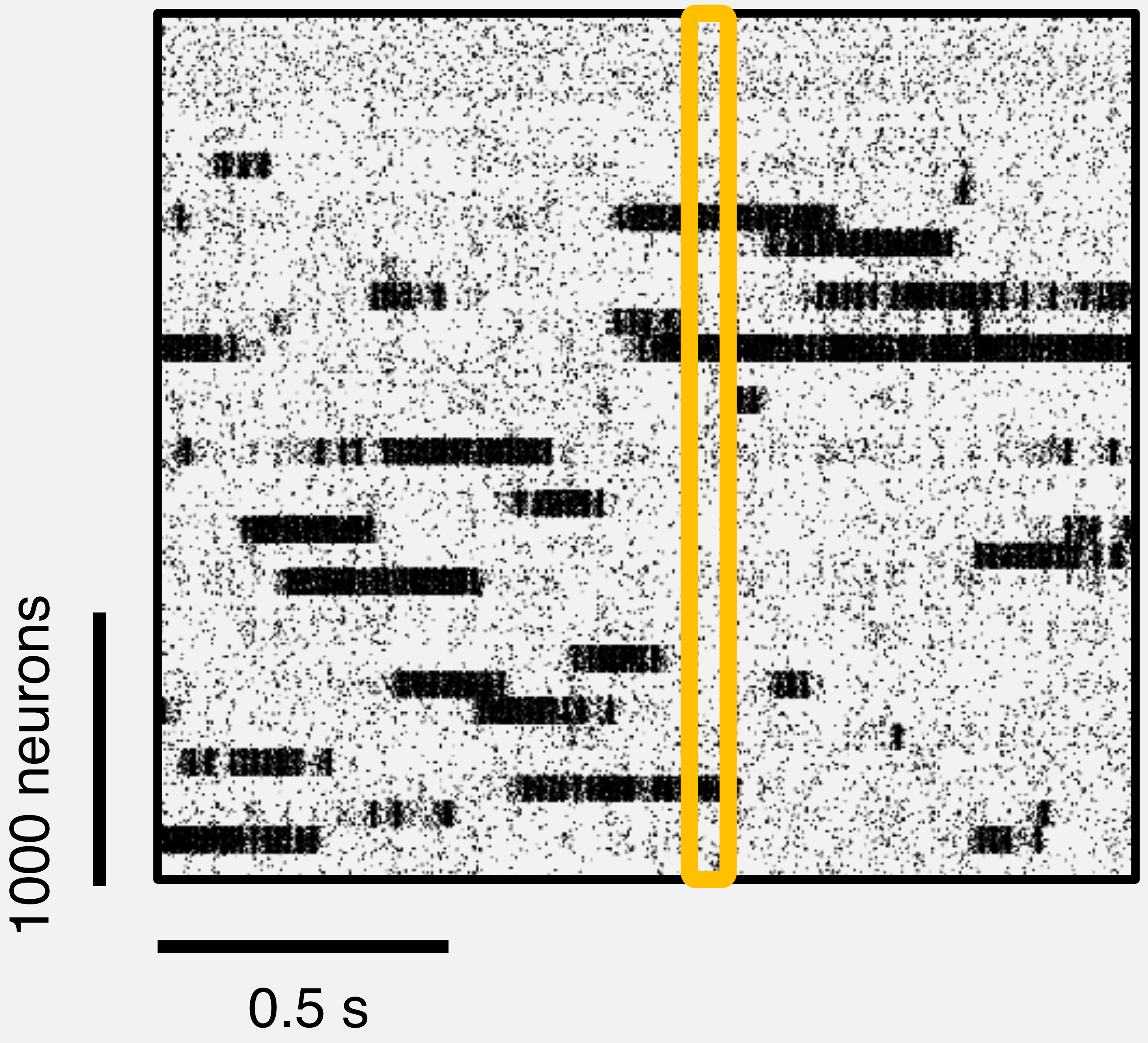


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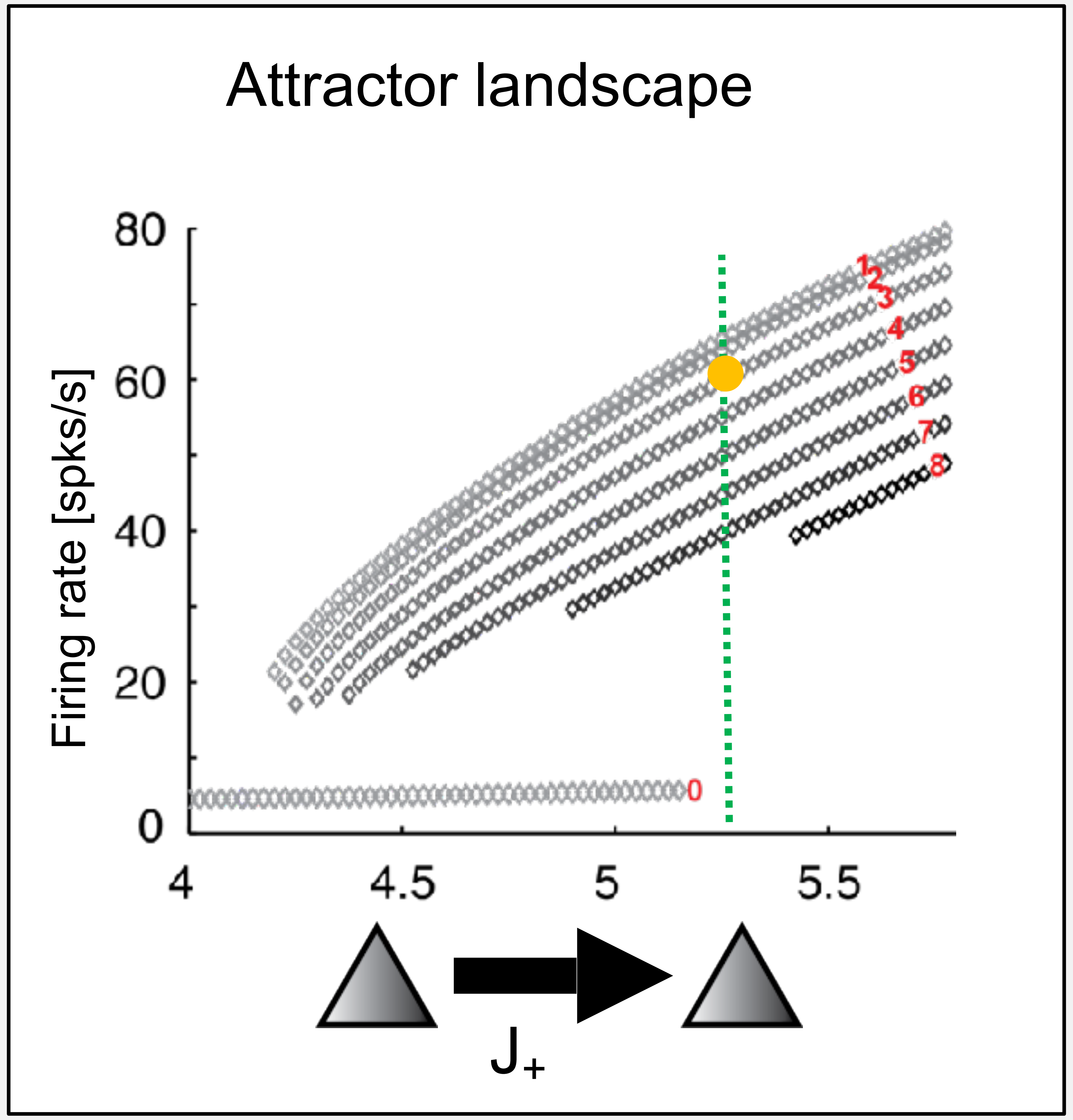
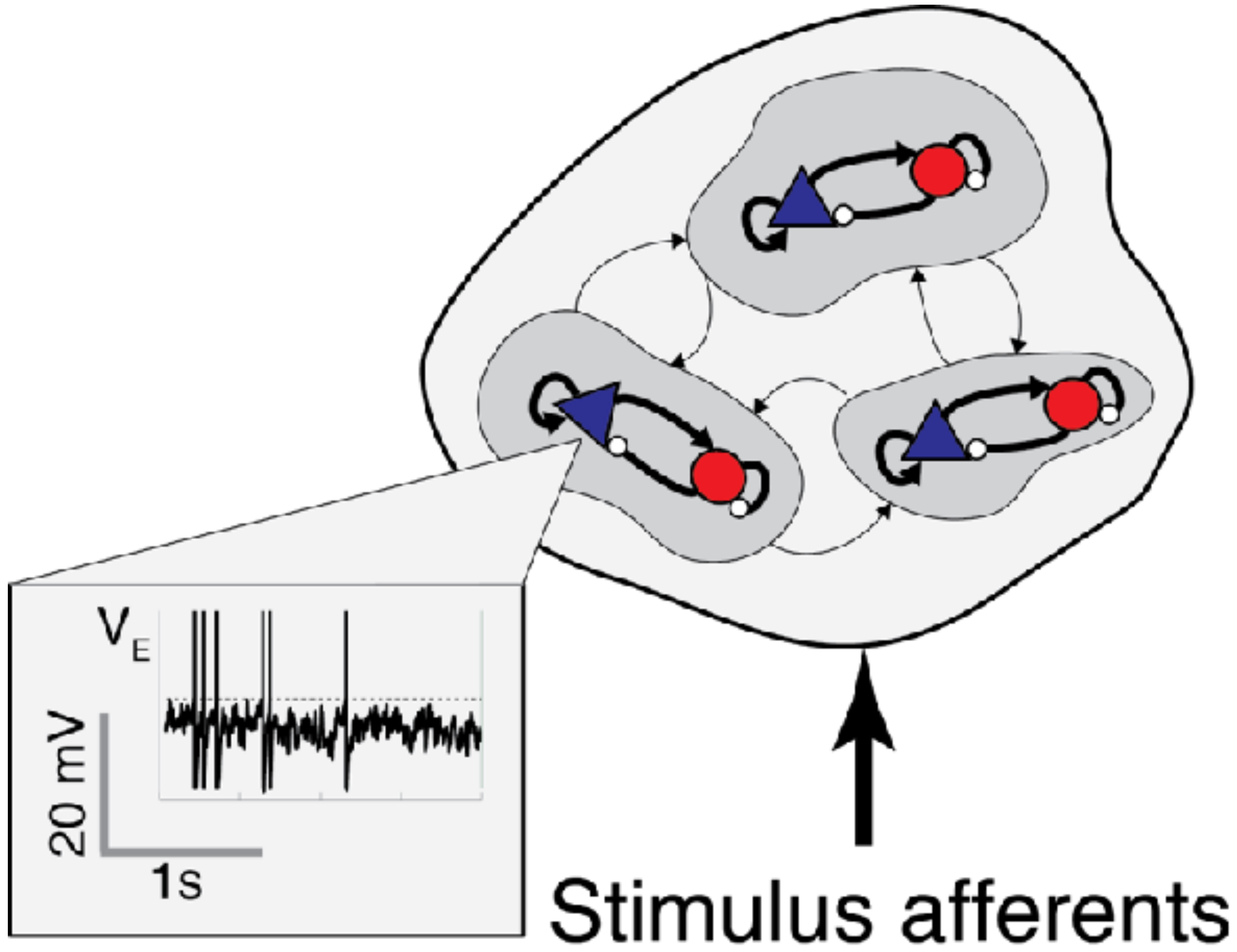



MFT details ▶

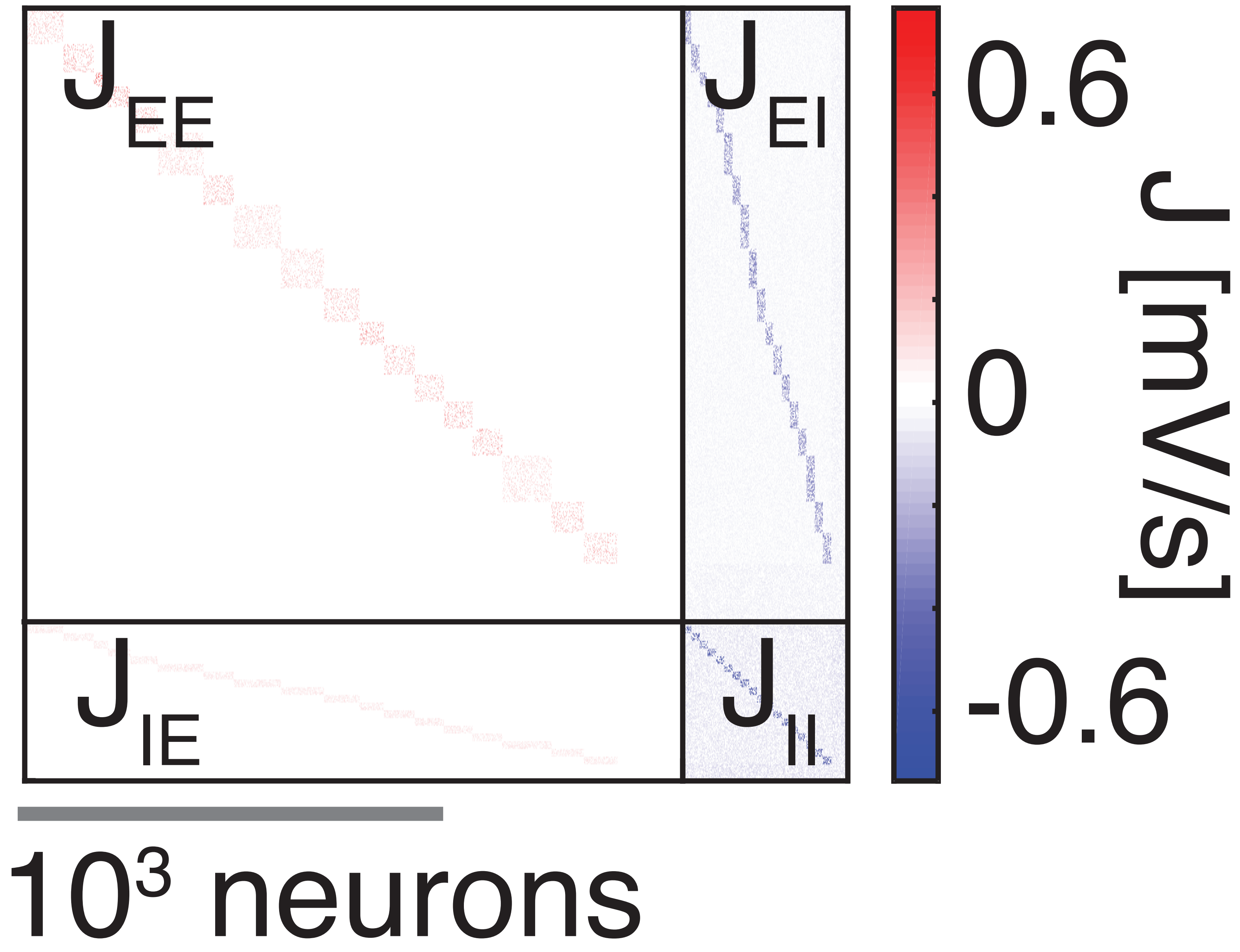
[Mazzucato et al., 2015, 2016]

# Attractor networks

E & I clusters

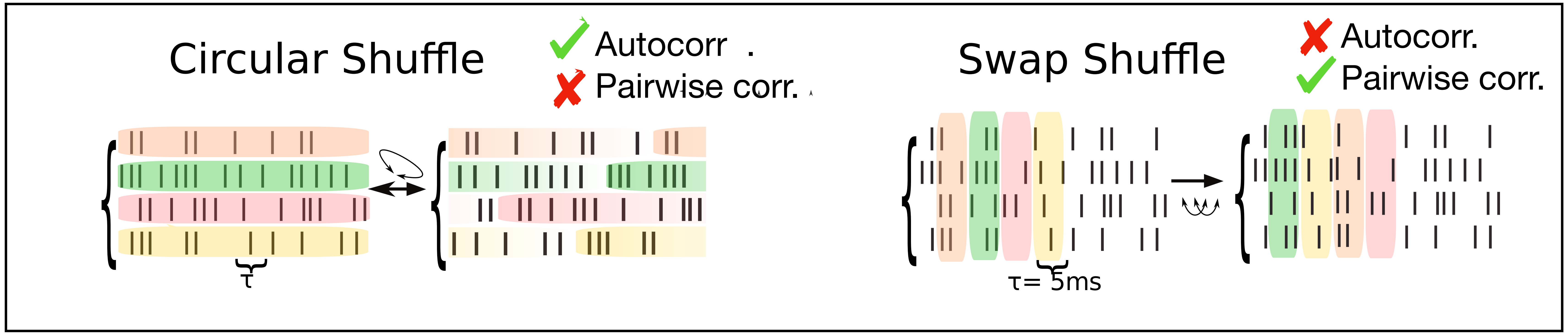



Synaptic weights J




[Deco & Hugues, 2012]
[Litwin-Kumar & Doiron, 2012]
[Mazzucato et al, 2019]
[Wyrick et al, 2021]

## Pattern sequences capture dynamics beyond auto- and pairwise




K-fold cross-validation: train HMM on K-1 folds

test on hold-out fold

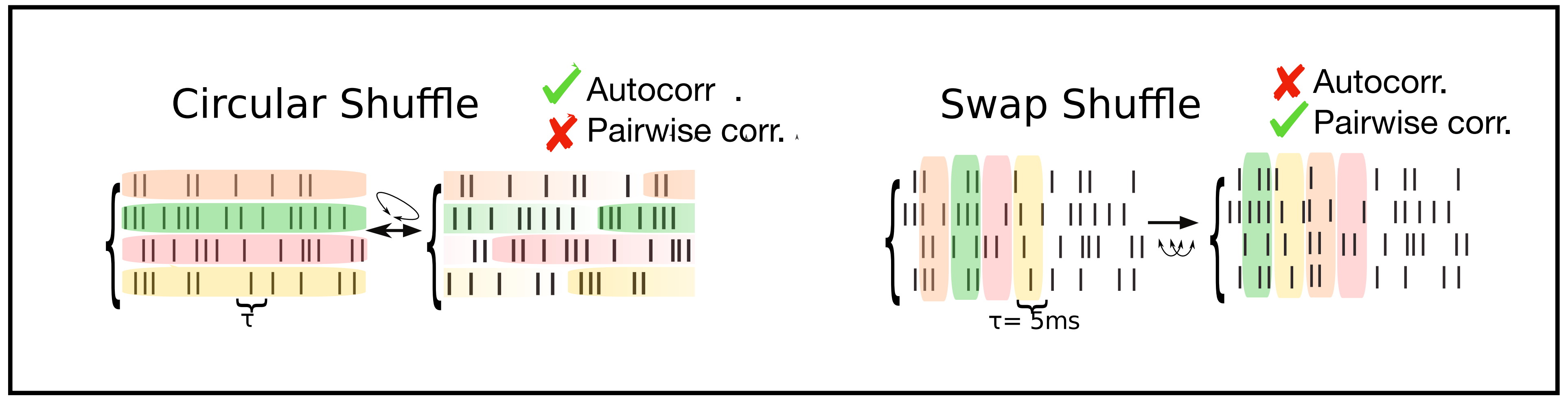
Data

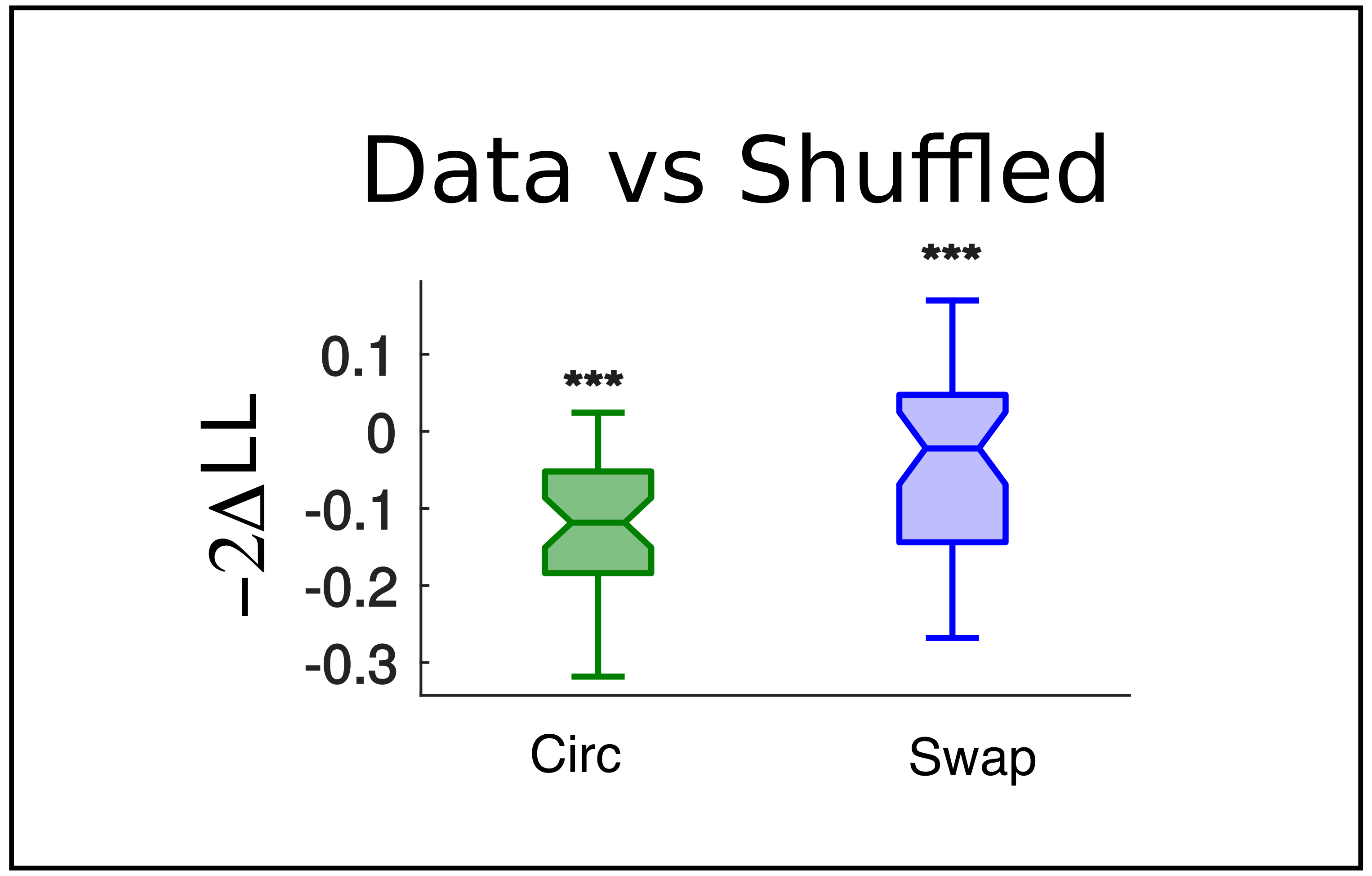
‘Circular’ shuffle

‘Swap’ shuffle

[Maboudi et al., 2018]

# Pattern sequences capture dynamics beyond auto- and pairwise



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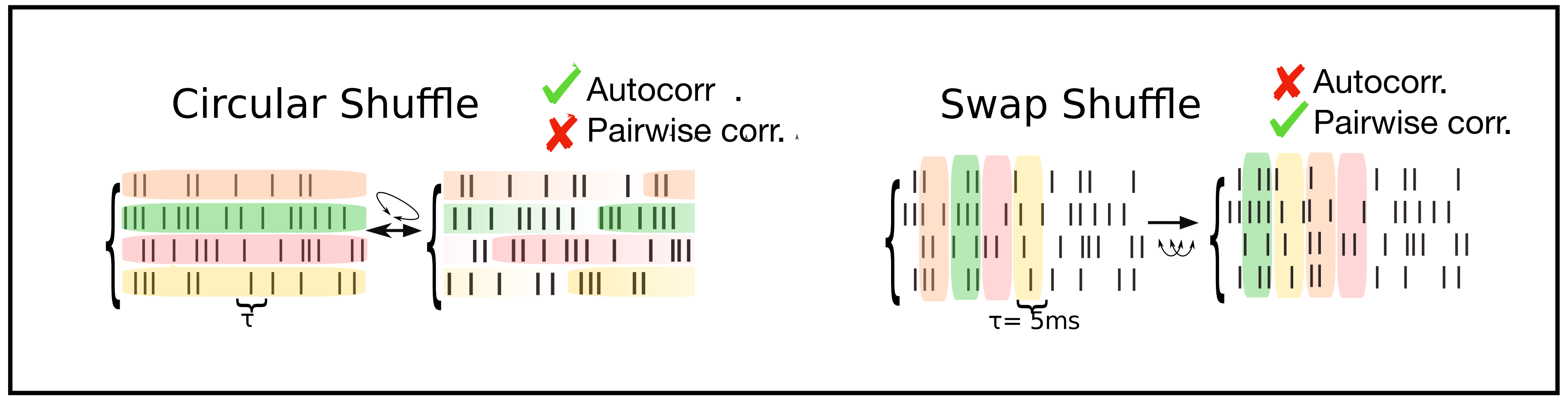


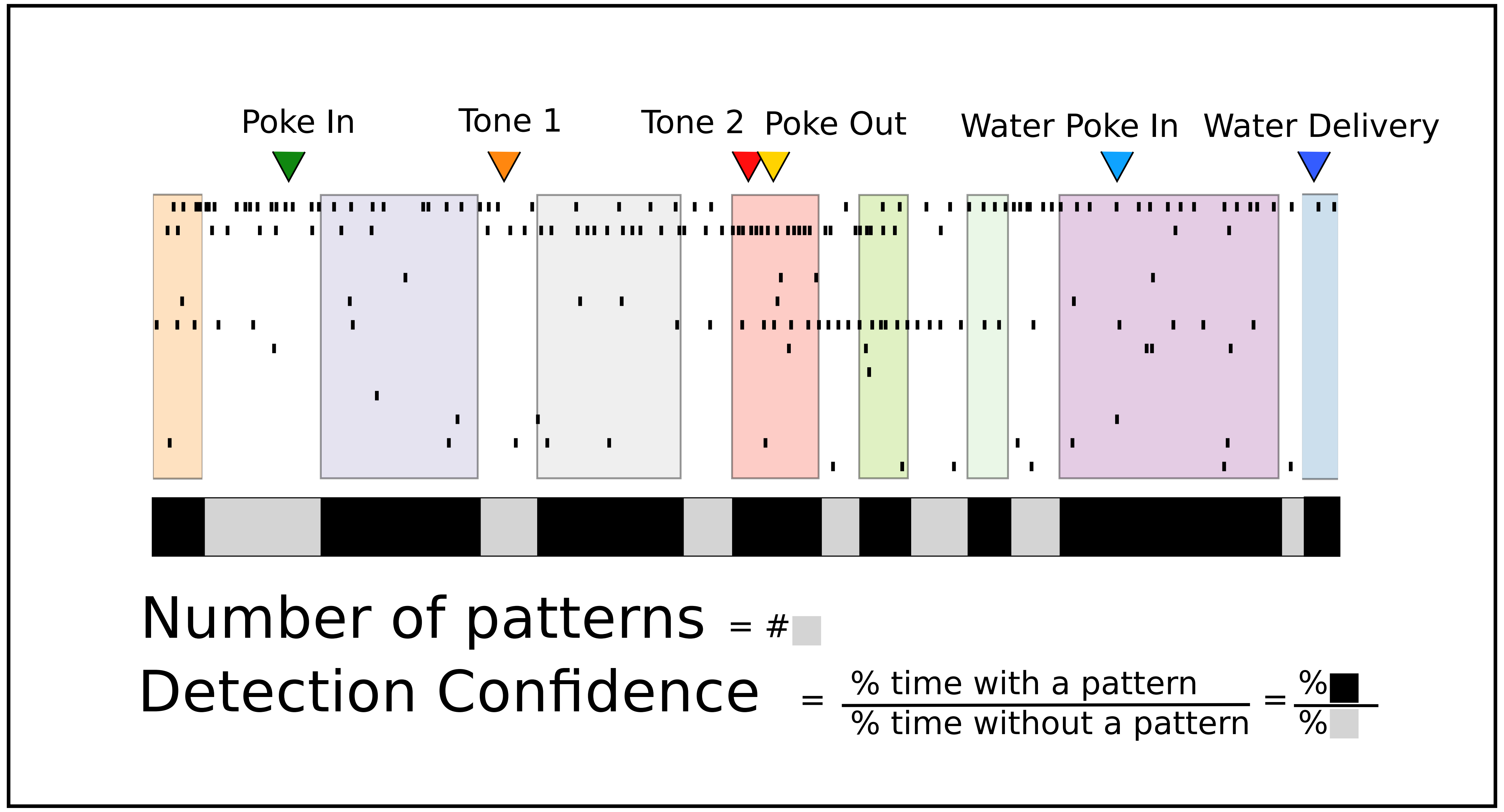

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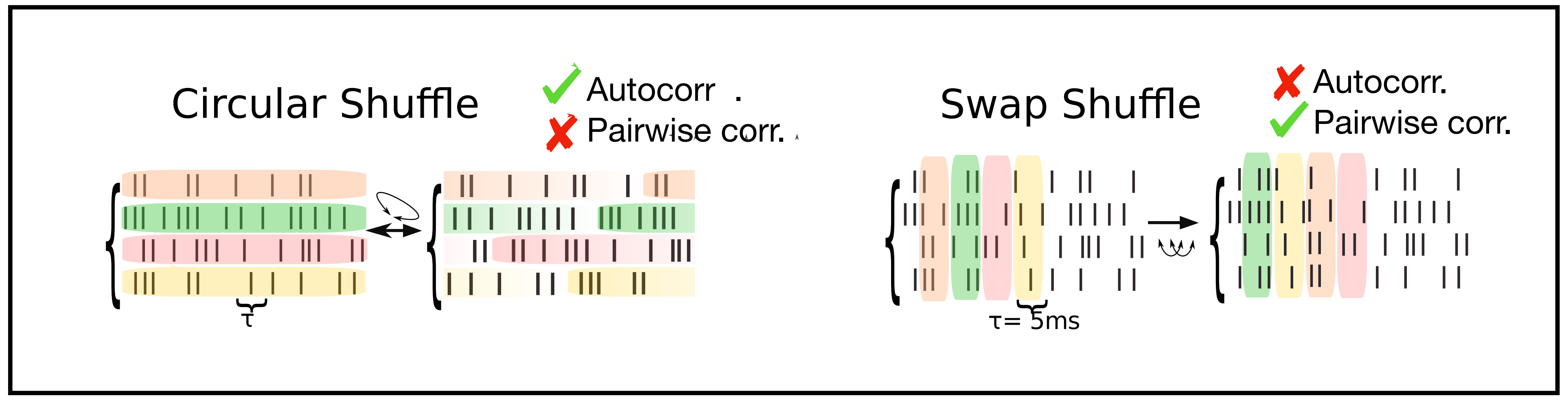
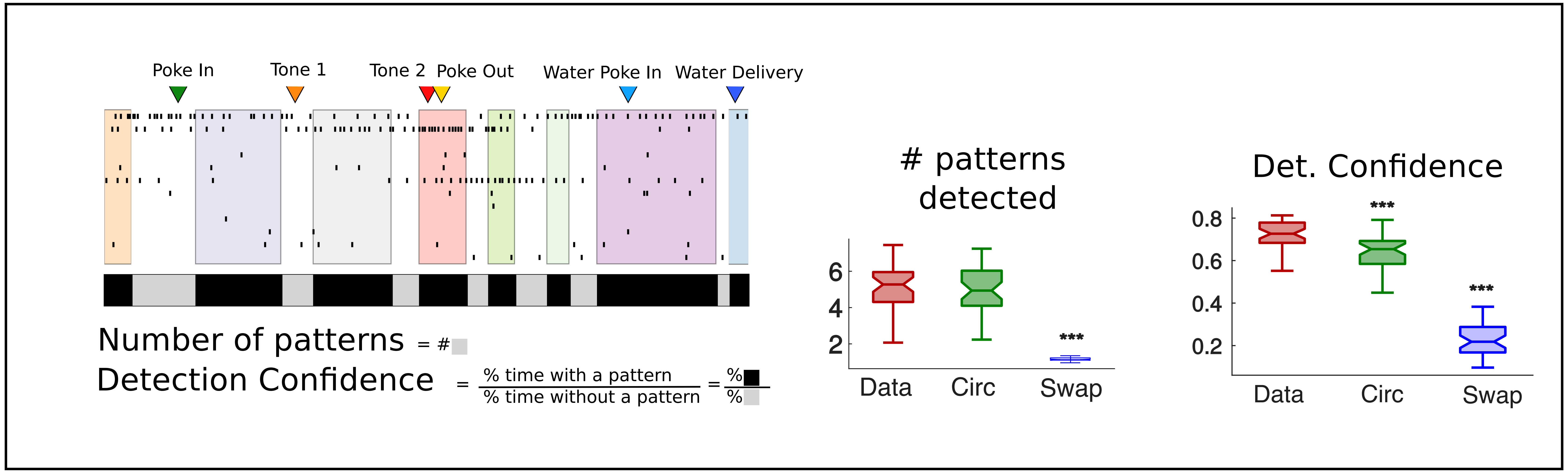
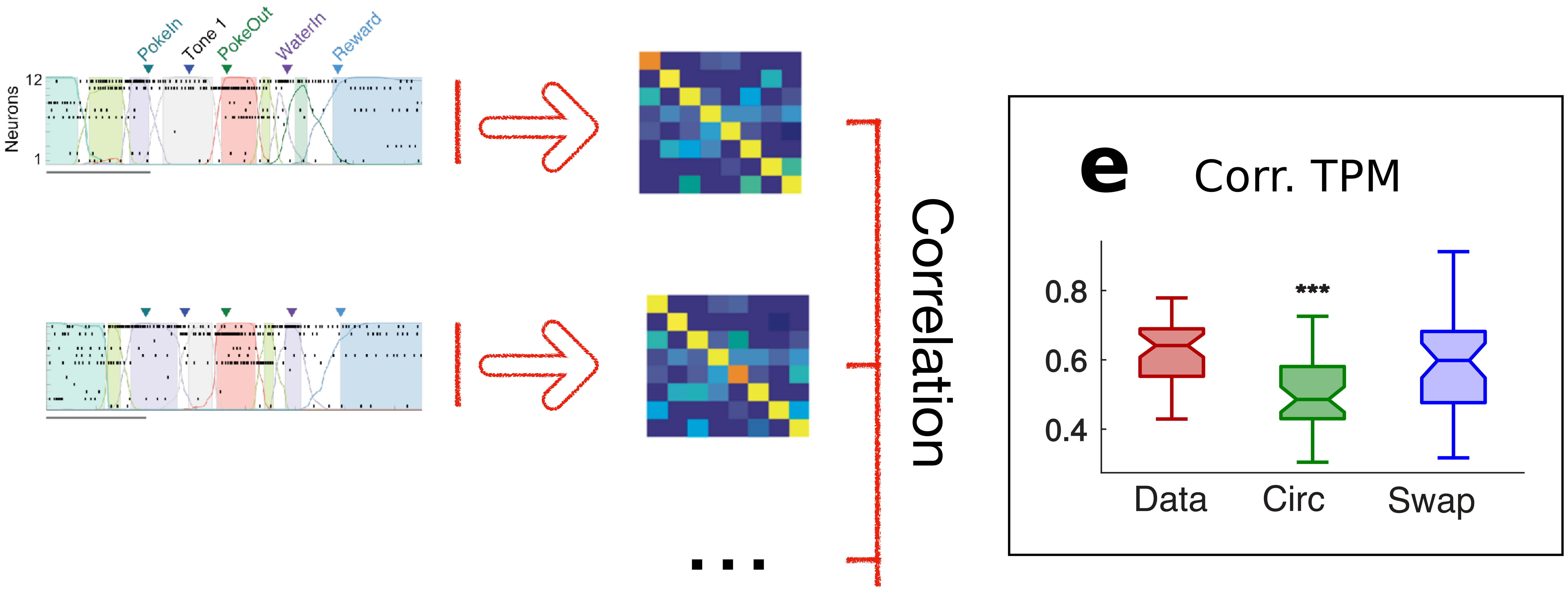


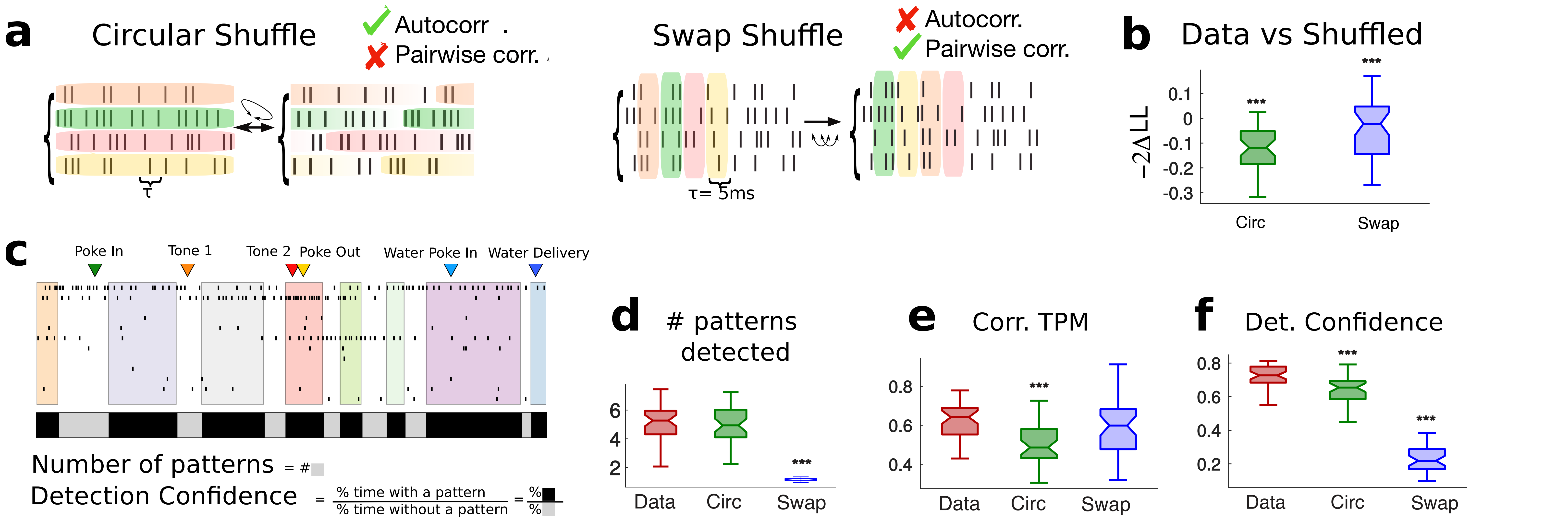
# Pattern sequences capture dynamics beyond auto- and pairwise

## Highly reliable sequences



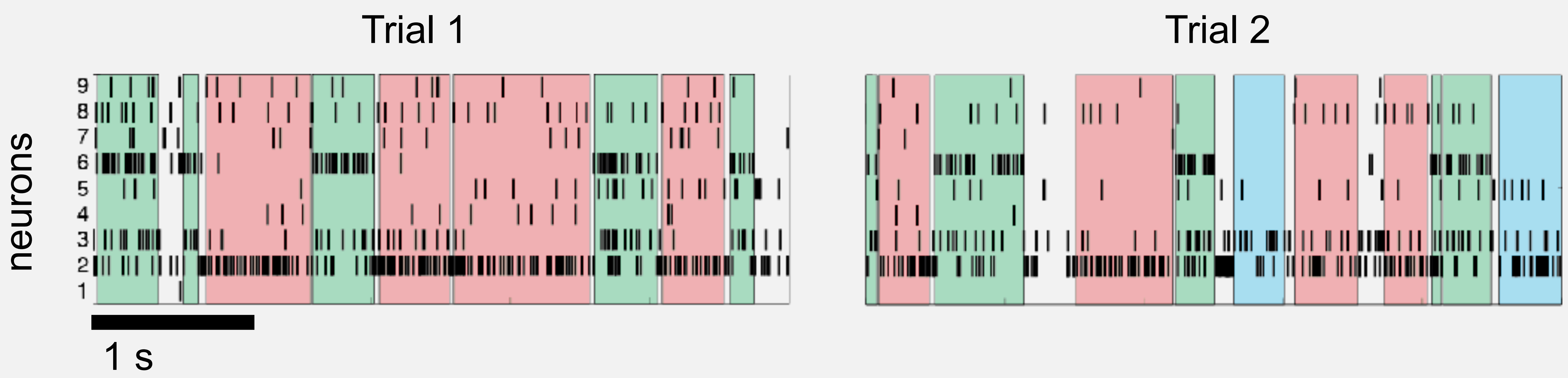
# Pattern sequences capture dynamics beyond auto- and pairwise

41 sessions - 7 animals

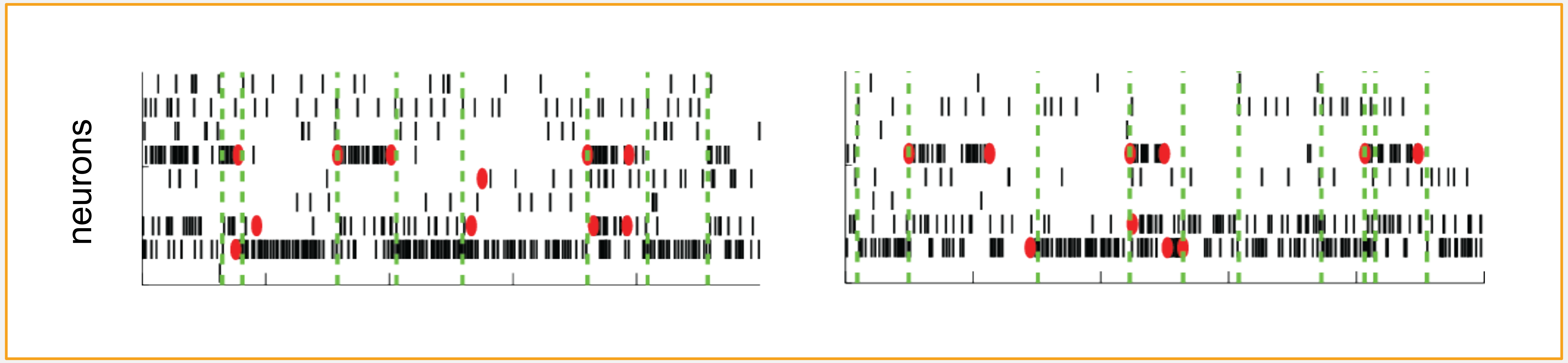


# Data – Spontaneous activity

- Post hoc sanity check tests



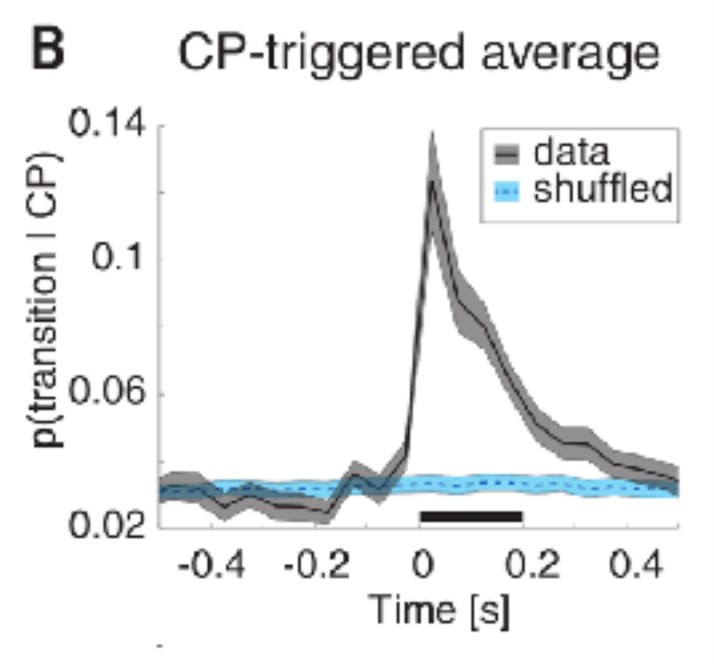

Compare single units Change-Points with HMM state transitions

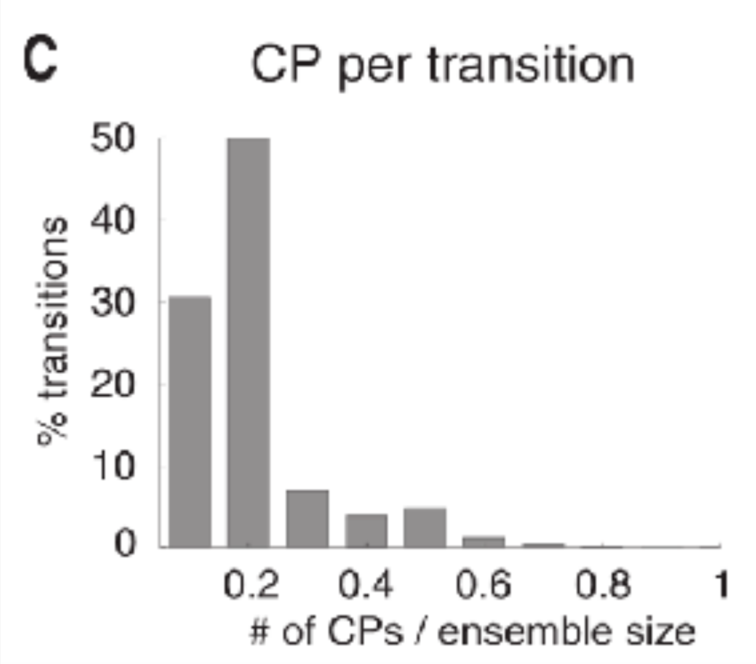



[Mazzucato et al., 2015]

# Data – Spontaneous activity

- Post hoc sanity check tests

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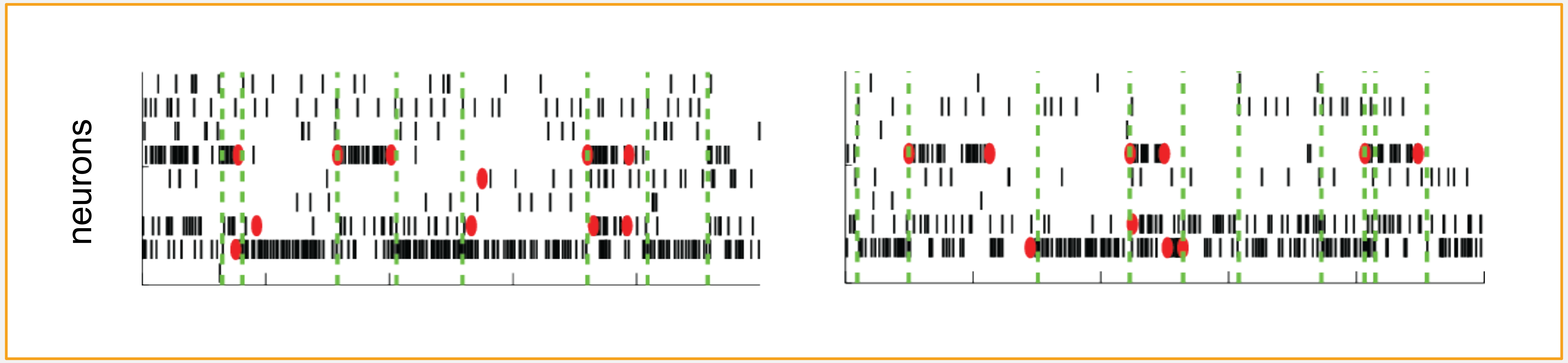



[Mazzucato et al., 2015]

# Data – Spontaneous activity

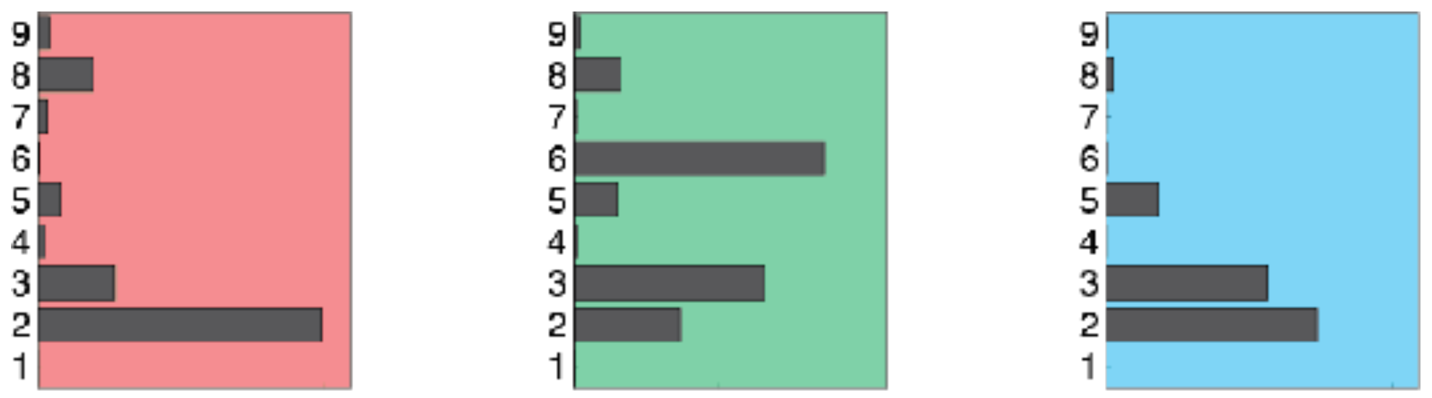
- Firing rate across states


1. Firing rate estimate *r* for neuron *i* in state *q* in single trial: *M-step of EM fit*

observations

$$r_i(q) = -\frac{1}{\Delta t} \ln \left( 1 - \frac{\sum_{t=1}^{T} p(S_t = q) y_i(t)}{\sum_{t=1}^{T} p(S_t = q)} \right)$$

posterior prob. of state q



[Mazzucato et al., 2015]

# Data – Spontaneous activity

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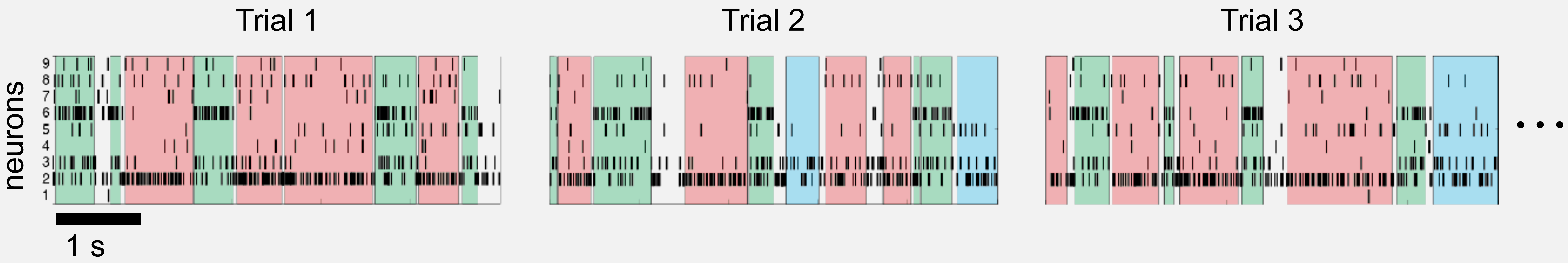
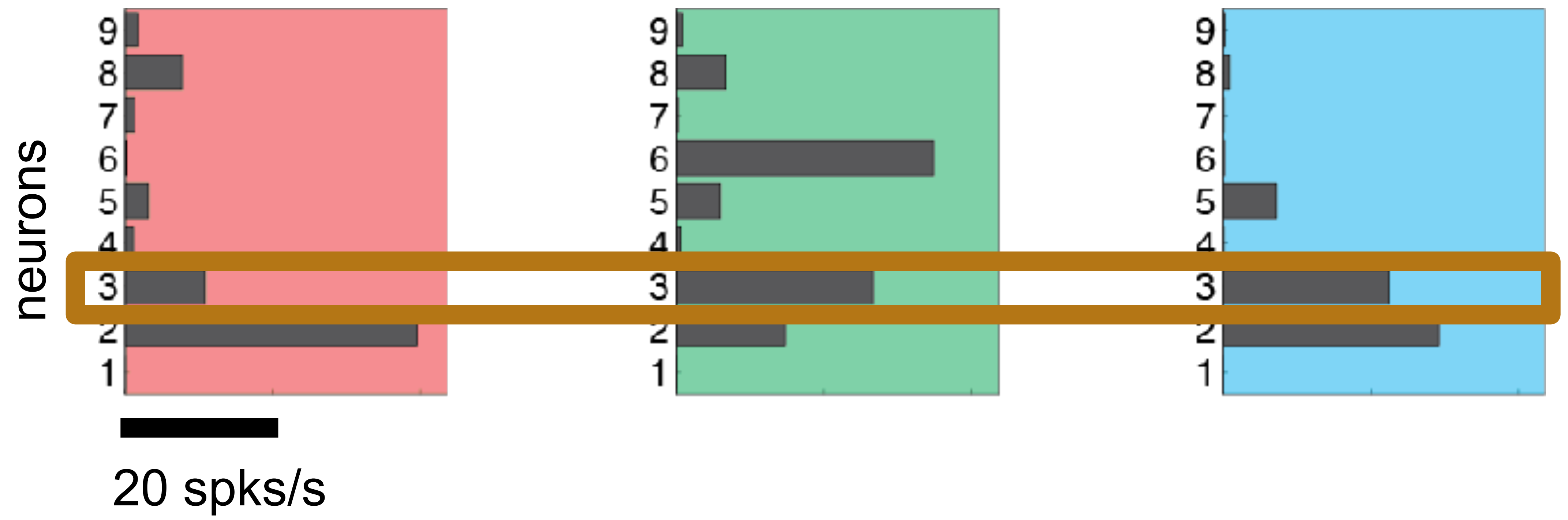



Neuron #3: two rates across states→ **“bistable”**

[Mazzucato et al., 2015]

# Data – Spontaneous activity

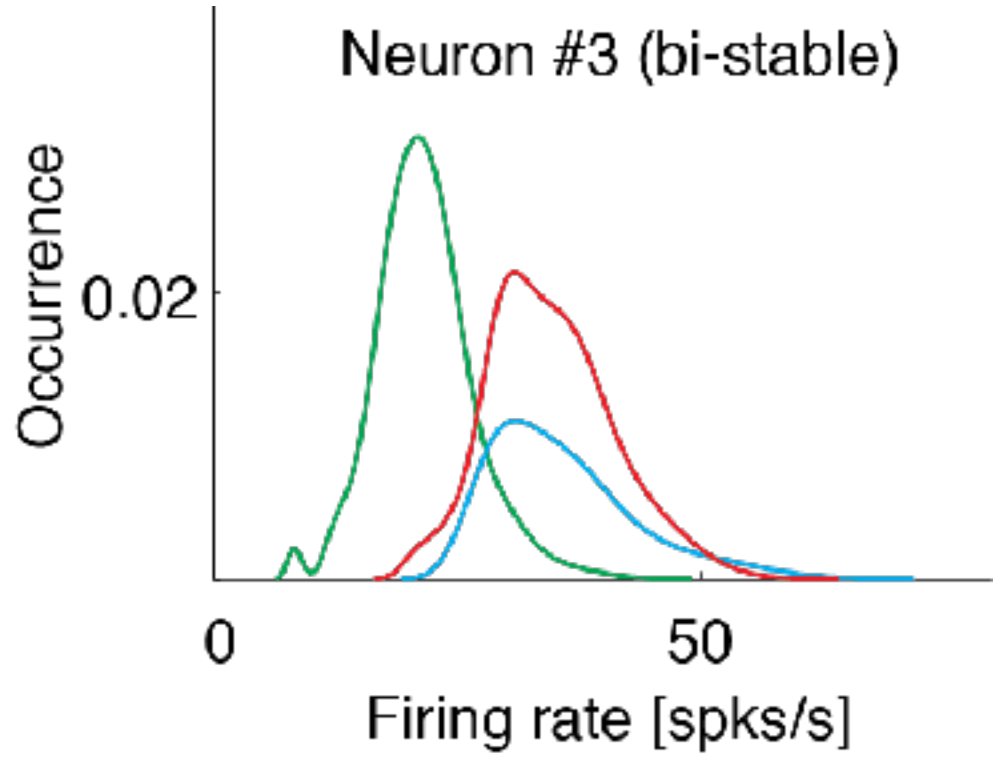
- Firing rate across states


1. Firing rate estimate *r* for neuron *i* in state *q* in single trial: *M-step of EM fit*

observations

$$r_i(q) = -\frac{1}{\Delta t} \ln \left( 1 - \frac{\sum_{t=1}^{T} p(S_t = q) y_i(t)}{\sum_{t=1}^{T} p(S_t = q)} \right)$$

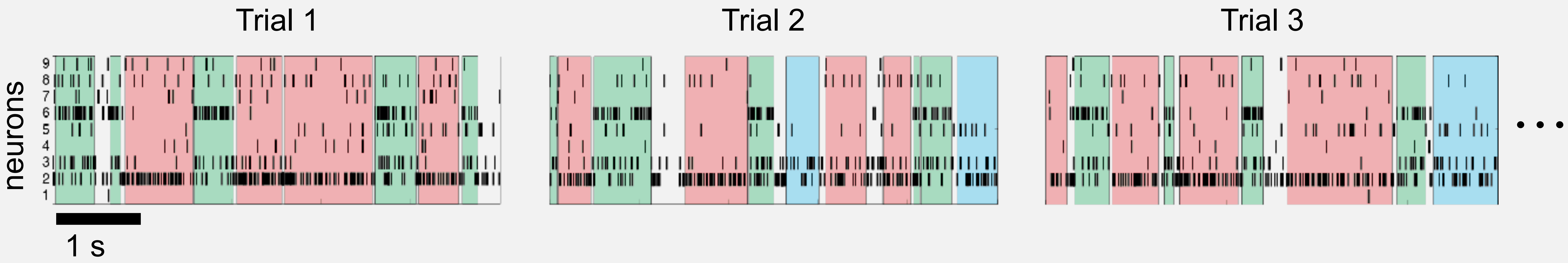
posterior prob. of state q

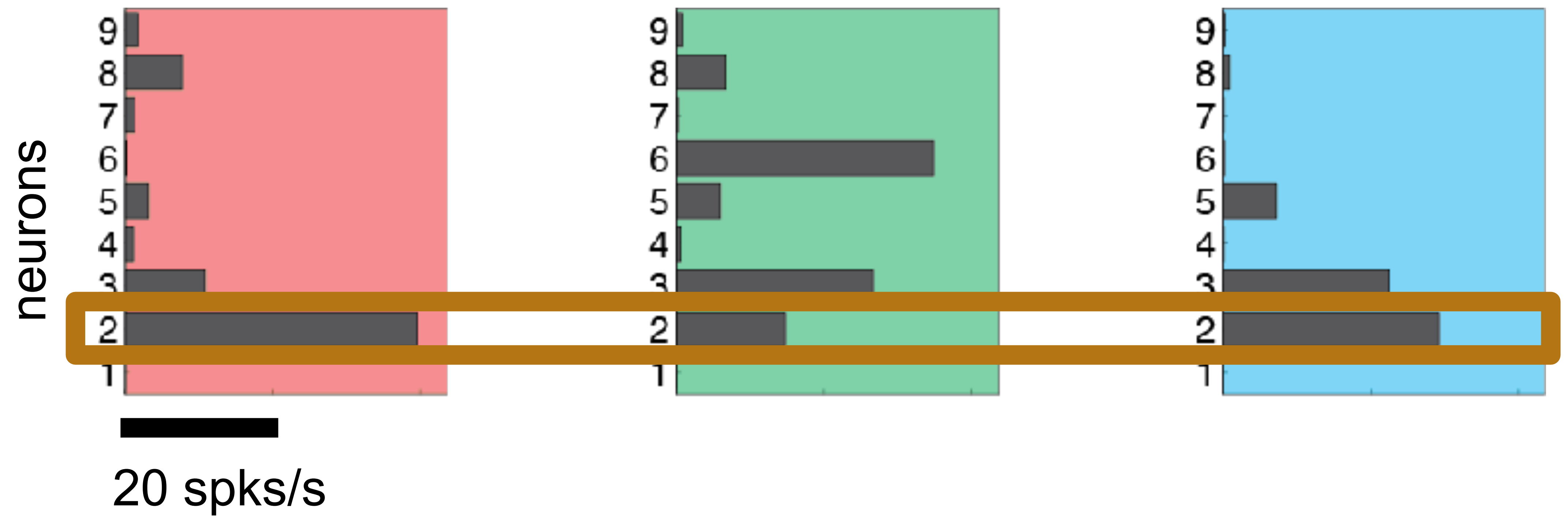



[Mazzucato et al., 2015]

# Data – Spontaneous activity

- Firing rate across states



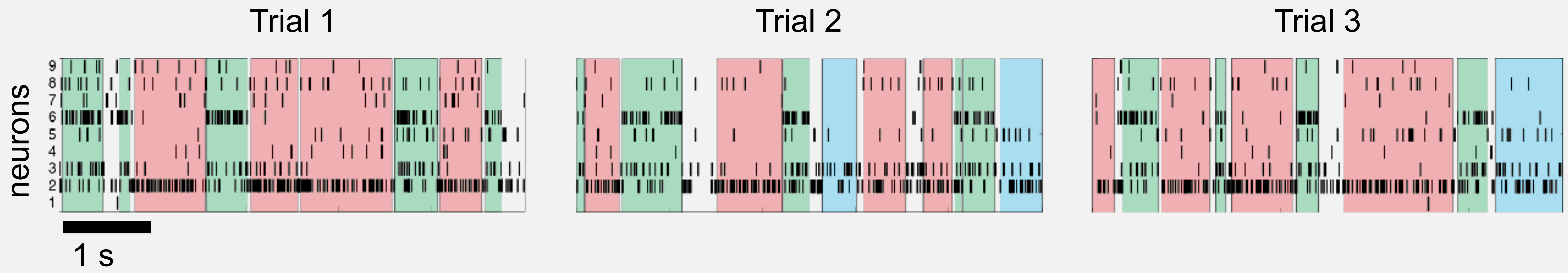




Neuron #2: three rates across states→ **“multistable”**

[Mazzucato et al., 2015]

# Data – Spontaneous activity

- Firing rate across states

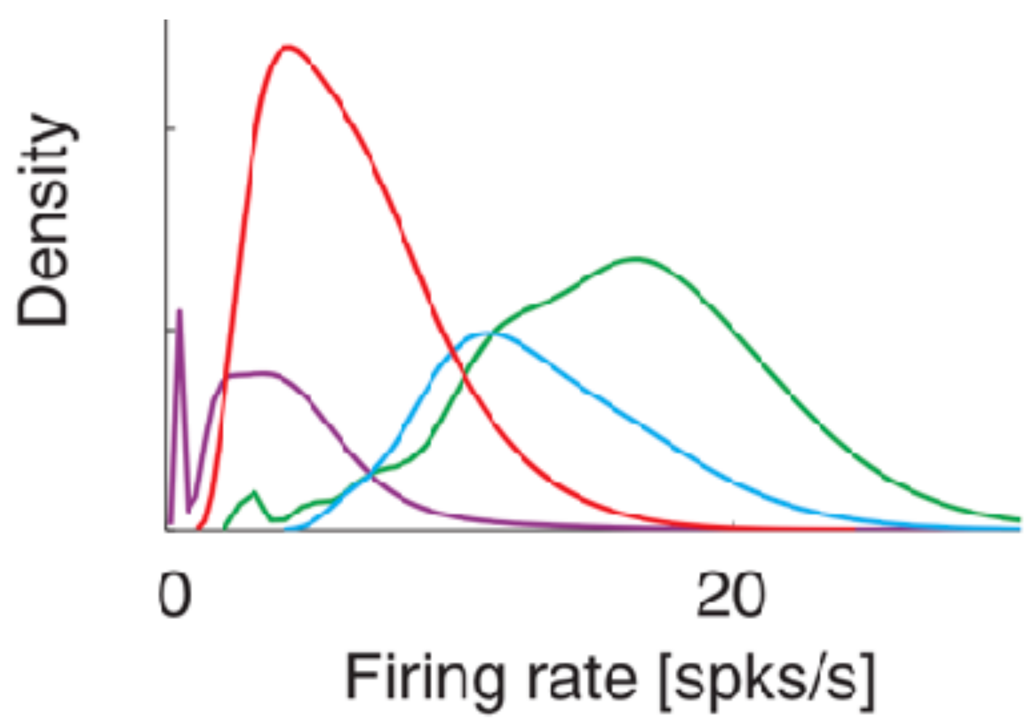



1. Firing rate estimate *r* for neuron *i* in state *q* in single trial: *M-step of EM fit*

observations

$$r_i(q) = -\frac{1}{\Delta t}\ln\left(1 - \frac{\sum_{t=1}^{T} p(S_t = q)\, y_i(t)}{\sum_{t=1}^{T} p(S_t = q)}\right)$$

posterior prob.
of state q

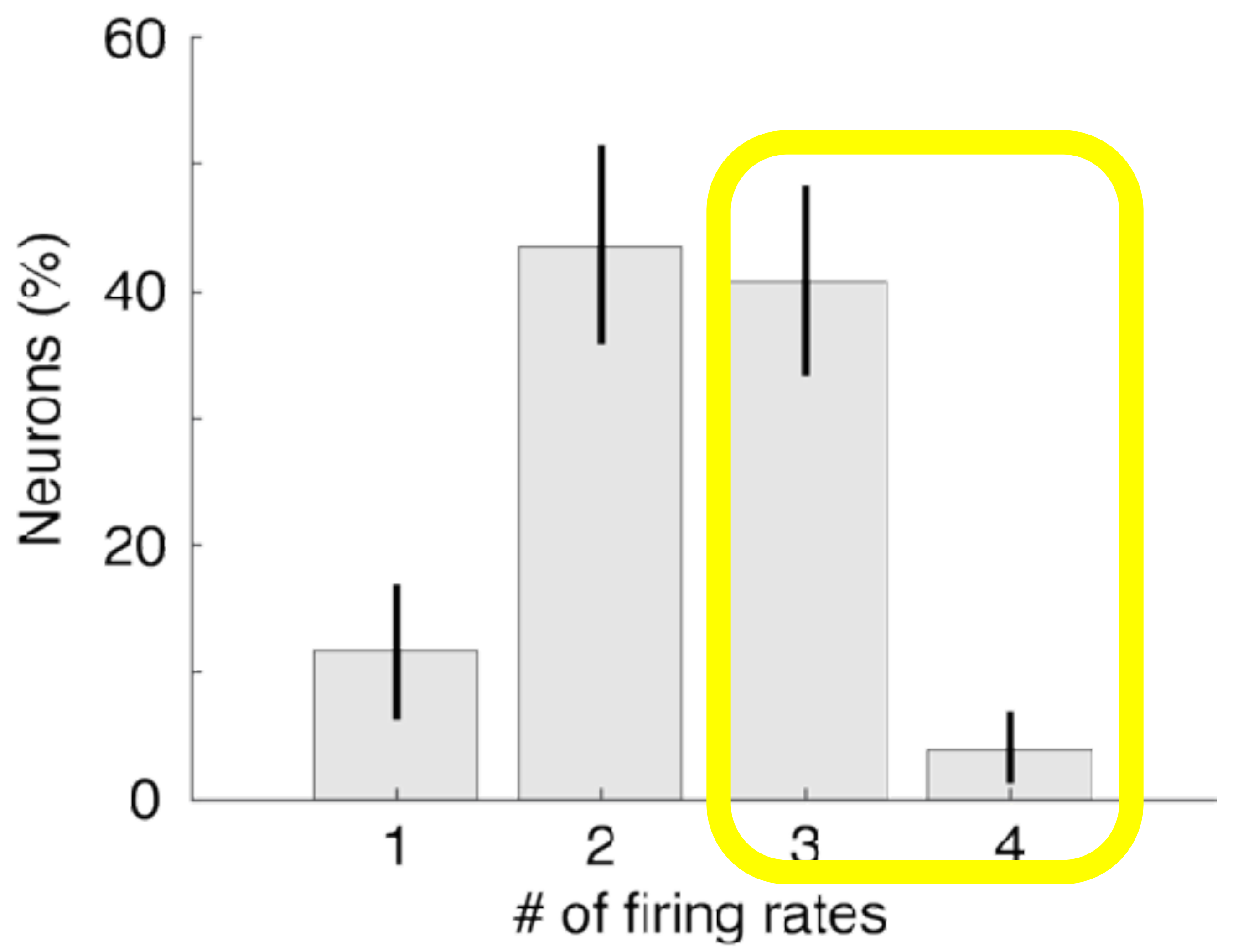



[Mazzucato et al., 2015]

# Data – Spontaneous activity

## Multistability

42% of neurons have 3 or more firing rates across states:

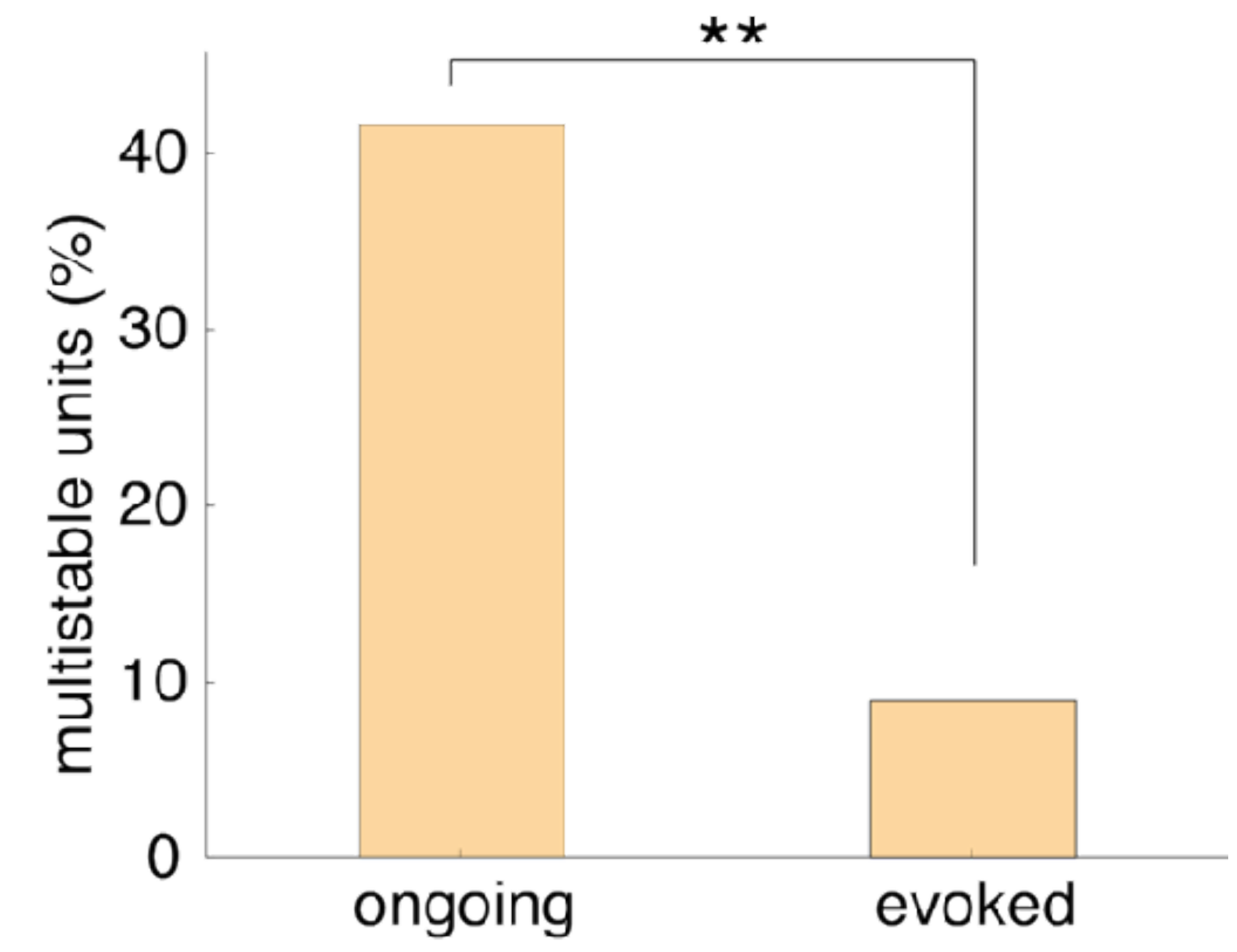



[Mazzucato et al., 2015]

# Stimuli reduce multistability

- Only **bistable** neurons are observed in response to stimulation

DATA




[Mazzucato et al., 2015]

# Circuit models of attractor dynamics

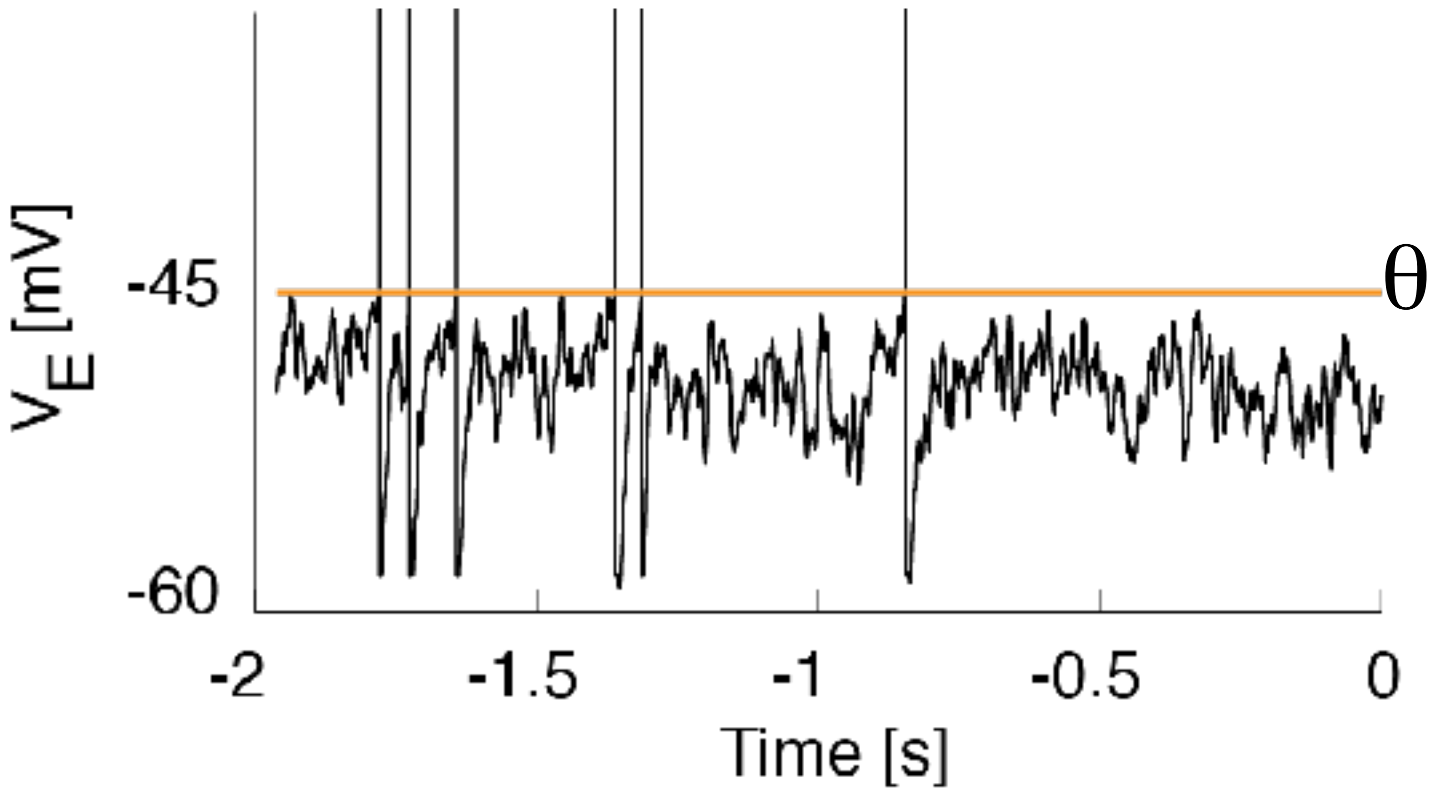
# Model – Neuron

PSC: $$\tau_s \frac{dI_i}{dt} = -I_i + I_{ext}(t) + \sum_j^{pre} J_{ij} \sum_n^{spikes} \delta(t - t_j^{(n)})$$

Potential: $$\tau_m \frac{dV_i}{dt} = V_L - V_i + I_i(t)$$

b.c.: $V(t^*) = \theta$

→ spike




[van Vreeswijk & Sompolinsky, 1996]
[Amit & Brunel, 1997]
[Haider et al., 2006]
[Renart et al., 2007]

# Model – Neuron

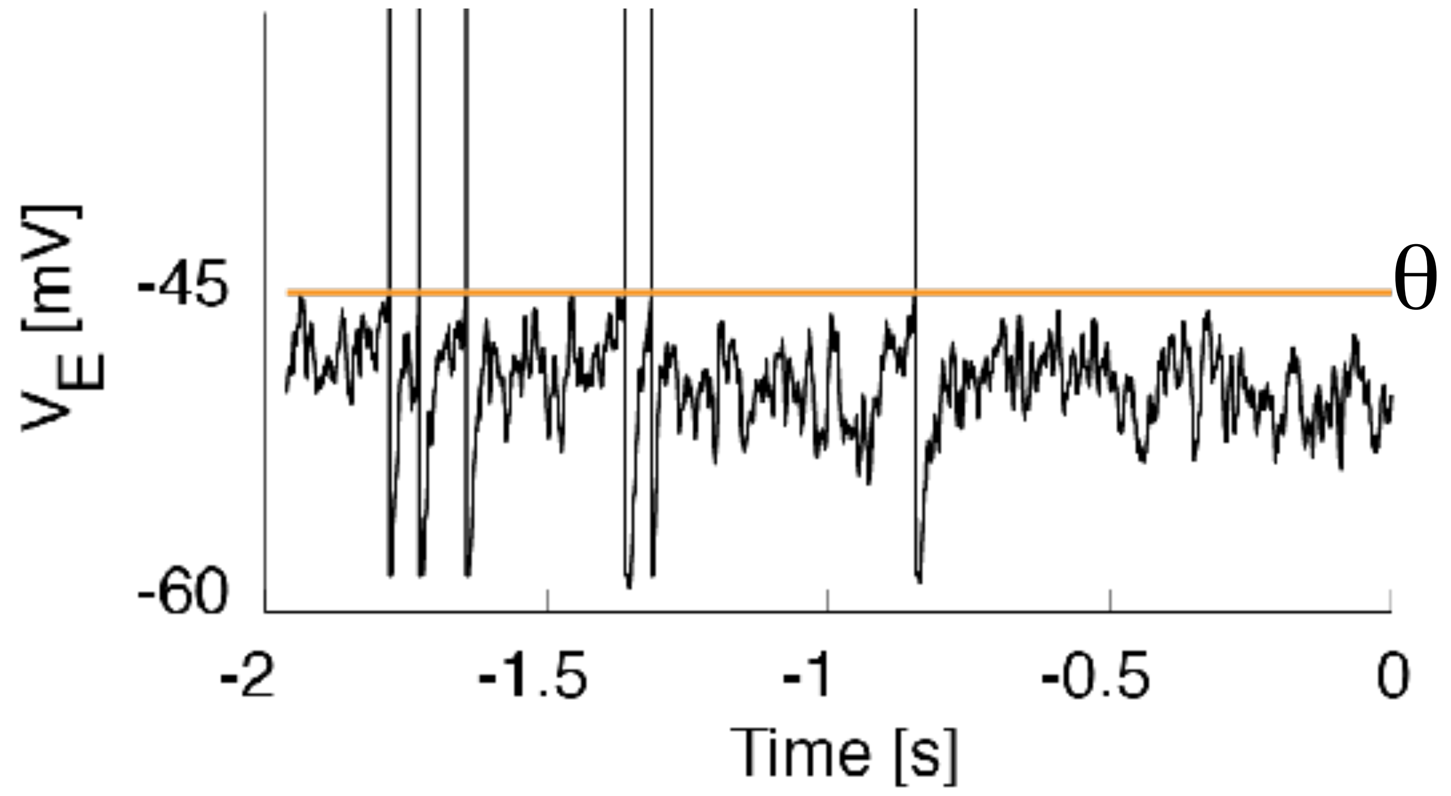
Ornstein–Uhlenbeck process

PSC: $$\tau_s \frac{dI_i}{dt} = -I_i + I_{ext}(t) + \boxed{\sum_j^{pre} J_{ij} \sum_n^{spikes} \delta(t - t_j^{(n)})}$$

Potential: $$\tau_m \frac{dV_i}{dt} = V_L - V_i + I_i(t)$$

b.c.: $V(t^*) = \theta$

→ spike




[Amit & Brunel, 1997]

# Model – Neuron

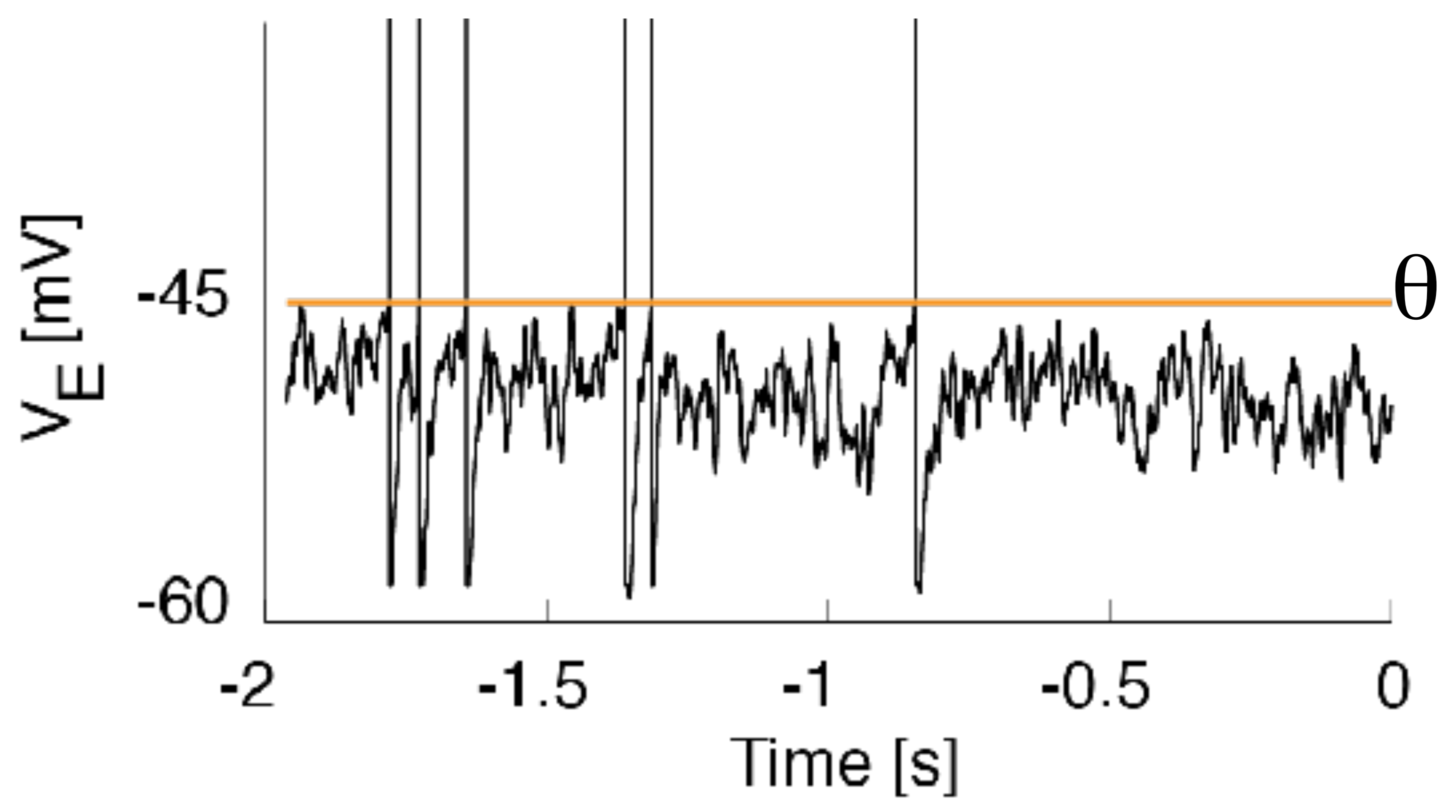
Ornstein–Uhlenbeck process

PSC: $$\tau_s \frac{dI_i}{dt} = -I_i + I_{ext}(t) + \boxed{\mu + \sigma\eta(t)}$$

Potential: $$\tau_m \frac{dV_i}{dt} = V_L - V_i + I_i(t)$$

b.c.: $V(t^*) = \theta$

→ spike



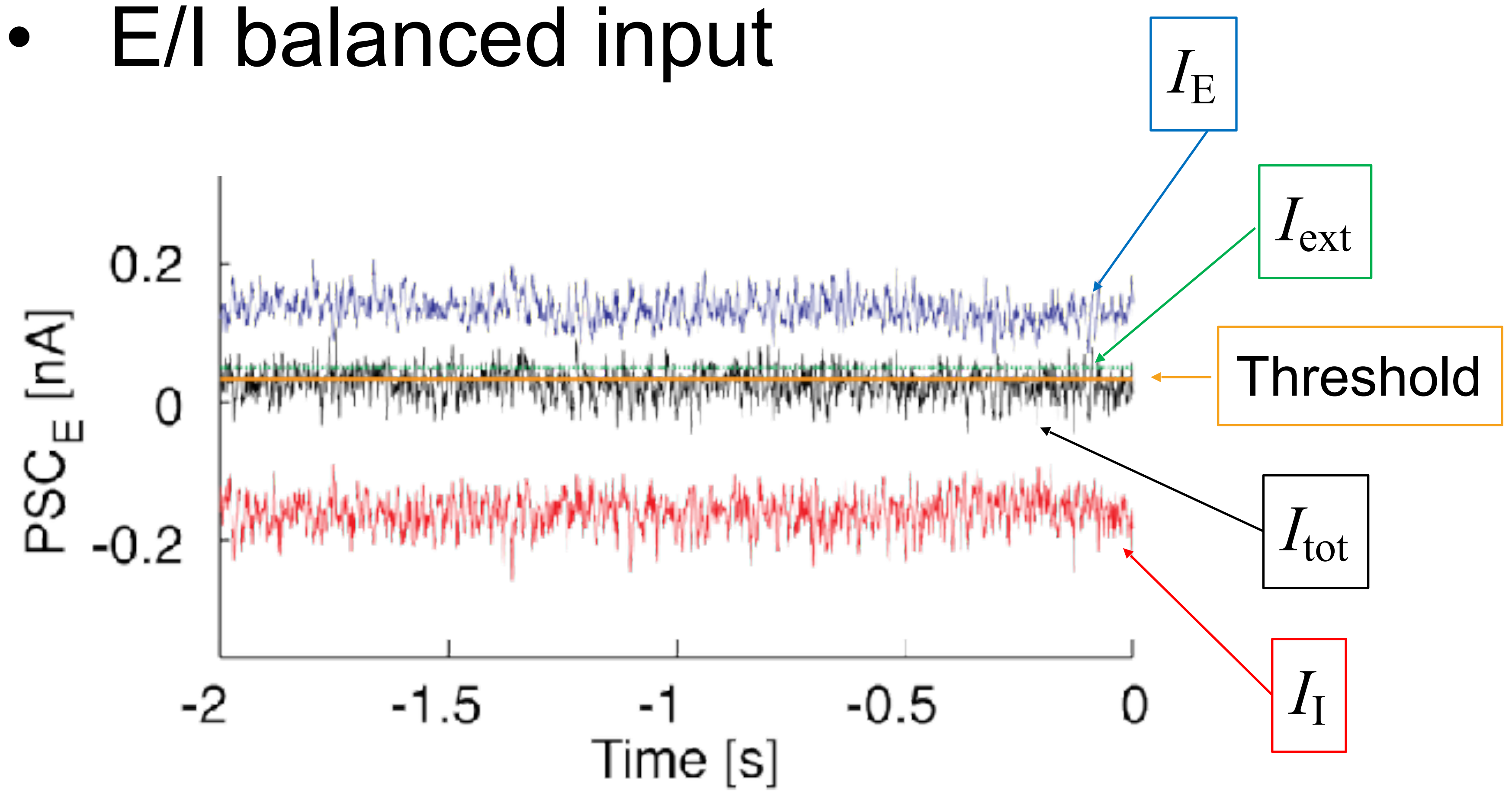

[Amit & Brunel, 1997]

# Model – Spontaneous activity

## Leaky Integrate–and–Fire neuron

$$\tau_m \frac{dV}{dt} = V_L - V + (I_E + I_I + I_{ext})$$

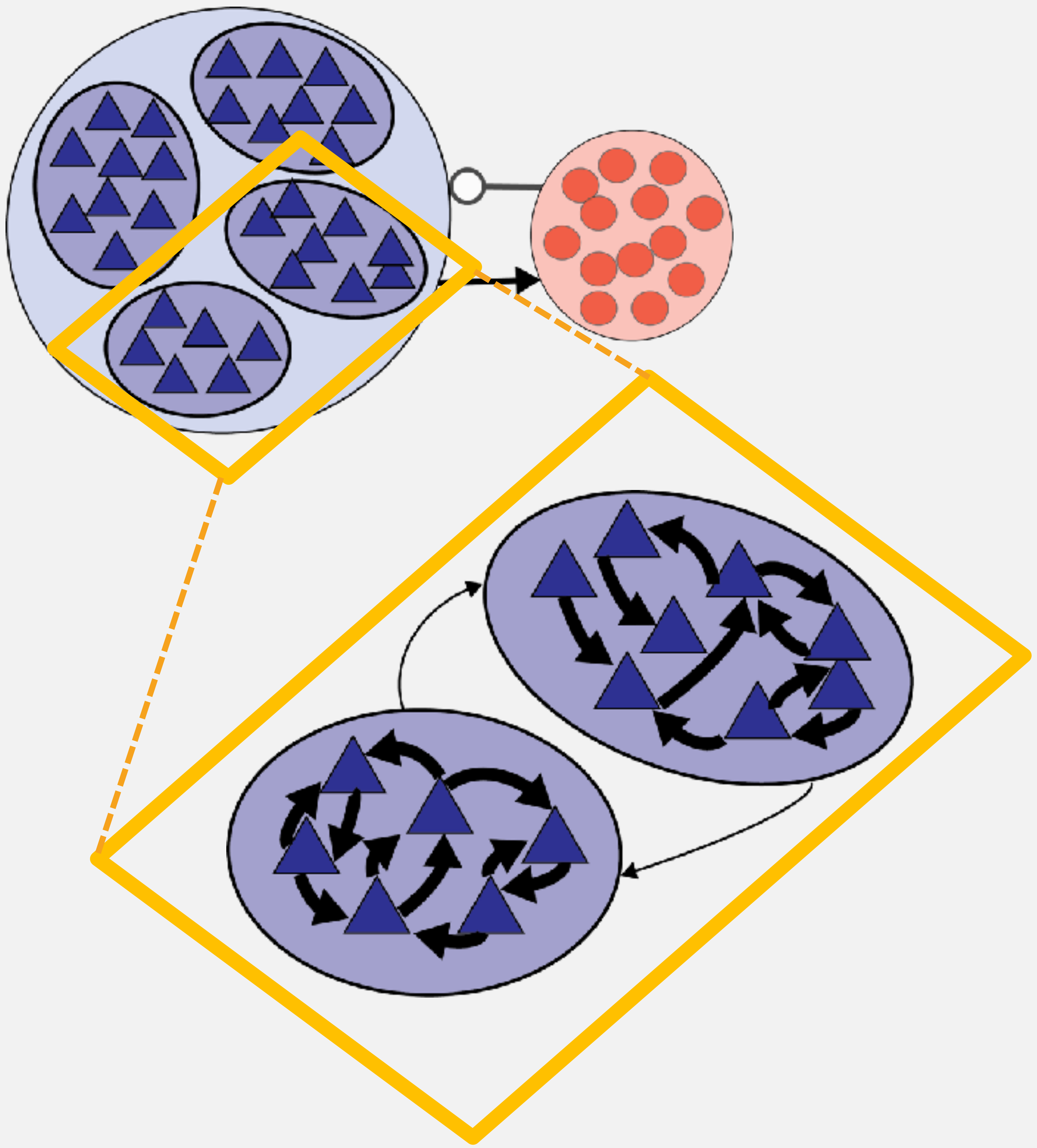
- E/I balanced input





[Haider et al., 2006]
[van Vreeswijk & Sompolinsky, 1996]
[Renart et al., 2007]

# Model – Network architecture



Recurrent E → E synaptic weights:

same cluster

$J_+ > 1$

different clusters

$J_- < 1$

[Amit & Brunel, 1997]
[Deco & Hugues, 2012]
[Litwin–Kumar & Doiron, 2012]
[Mazzucato et al., 2015]