

From single neurons to populations and back

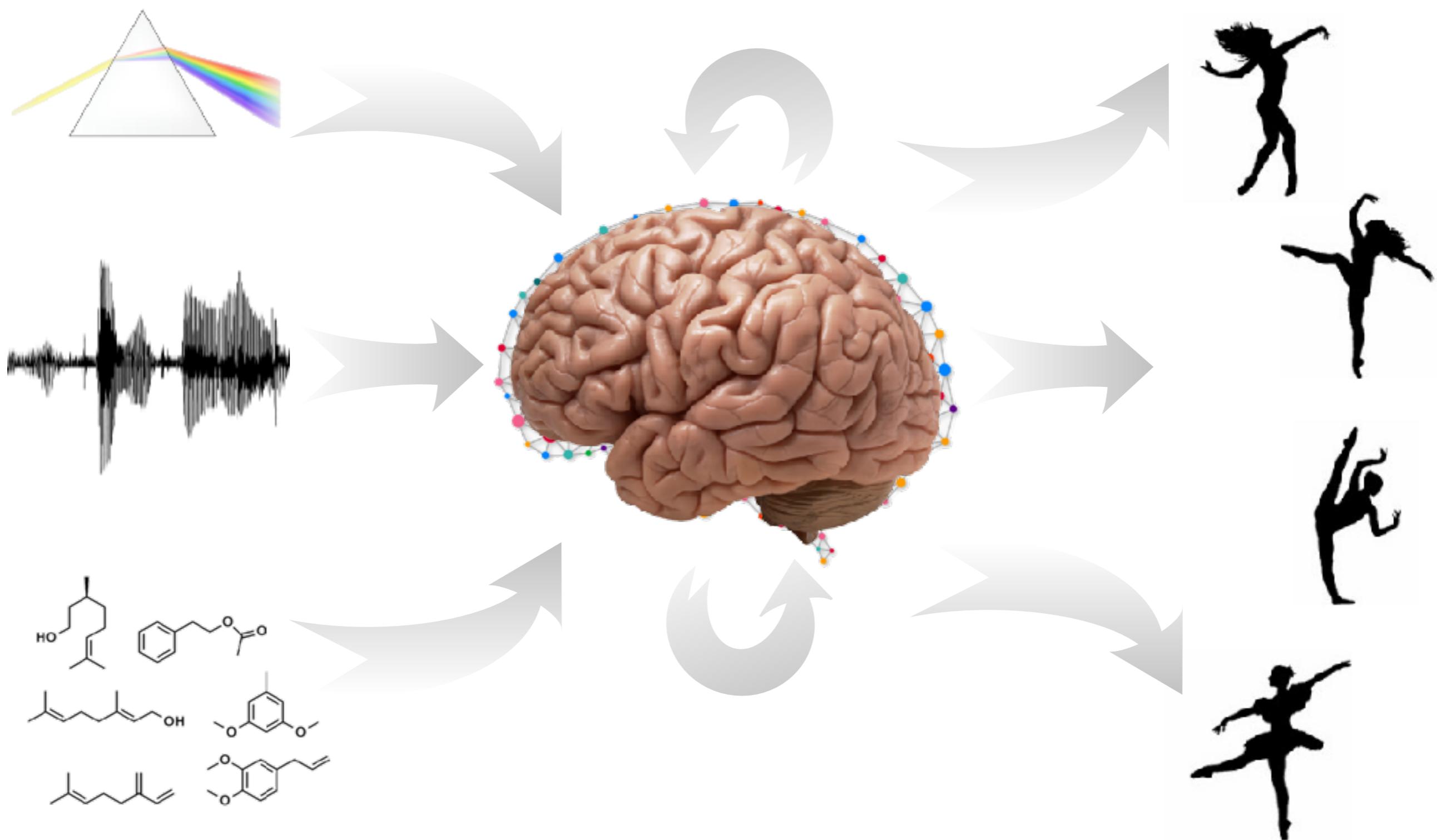
Tatiana Engel

Cold Spring Harbor Laboratory

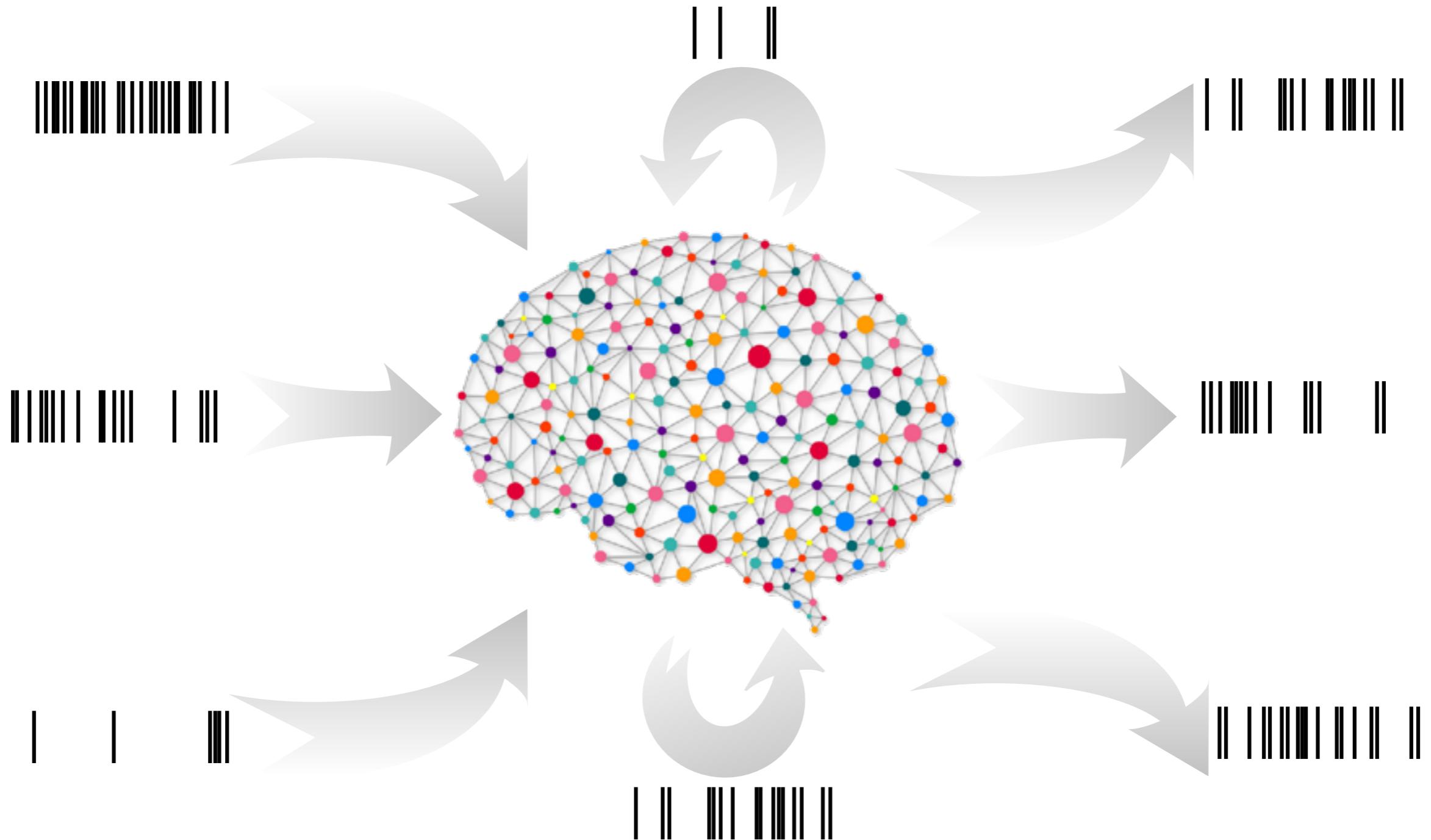
Outline

1. Tuning curves of single neurons
2. Neural variability and correlations
3. Neural population dynamics
4. Spatiotemporal population dynamics in the primate visual cortex
5. Learning interpretable models of neural dynamics from spikes

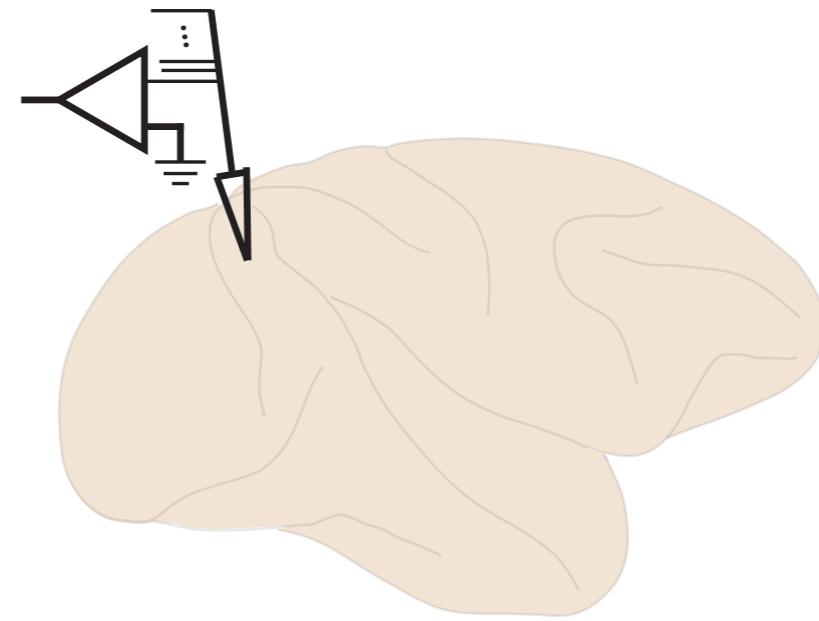
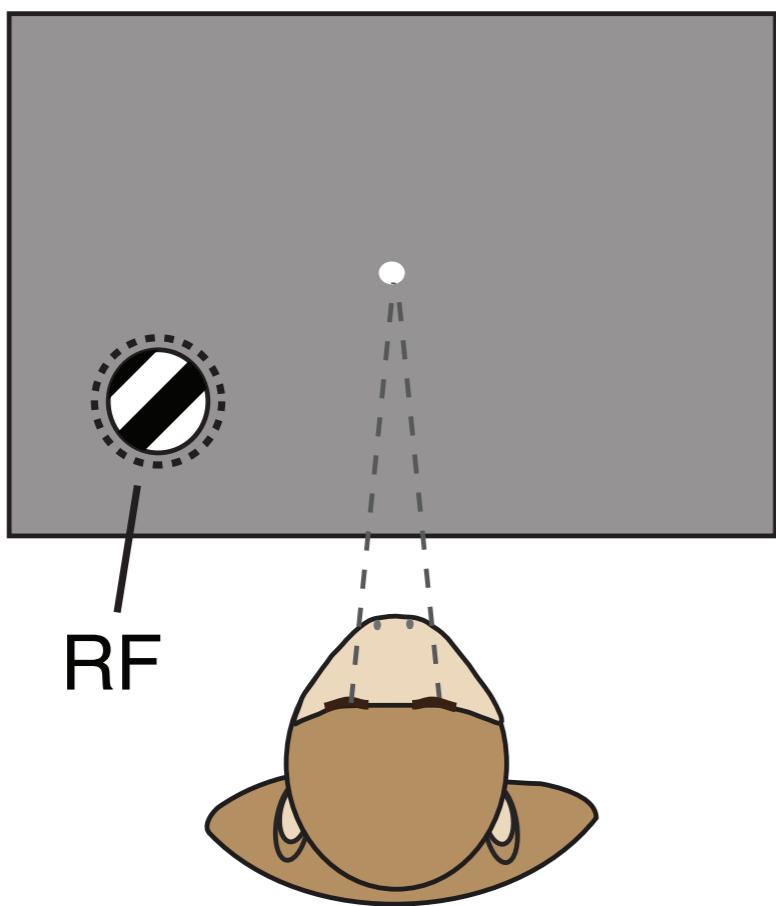
Dynamic brain activity



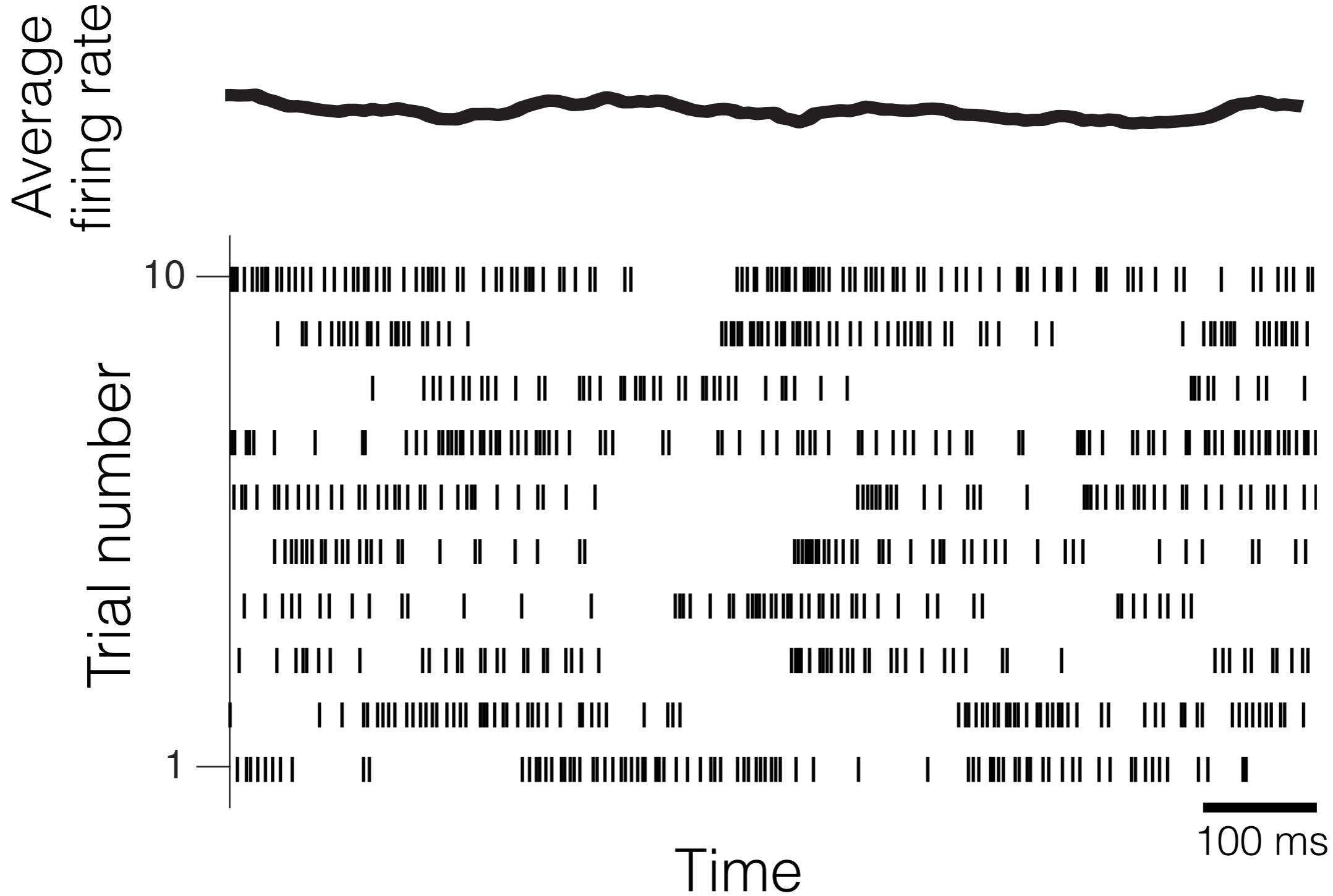
Dynamic brain activity



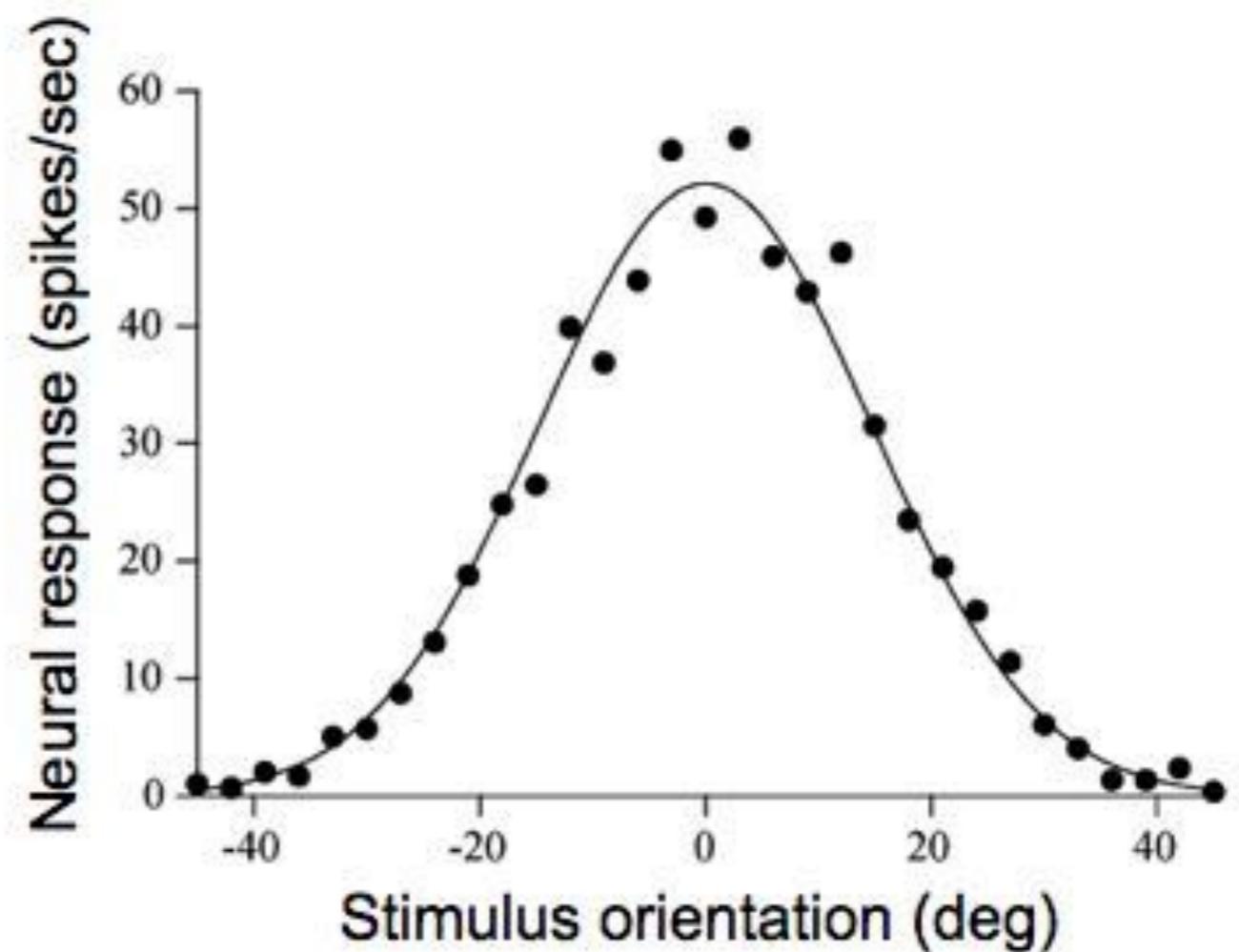
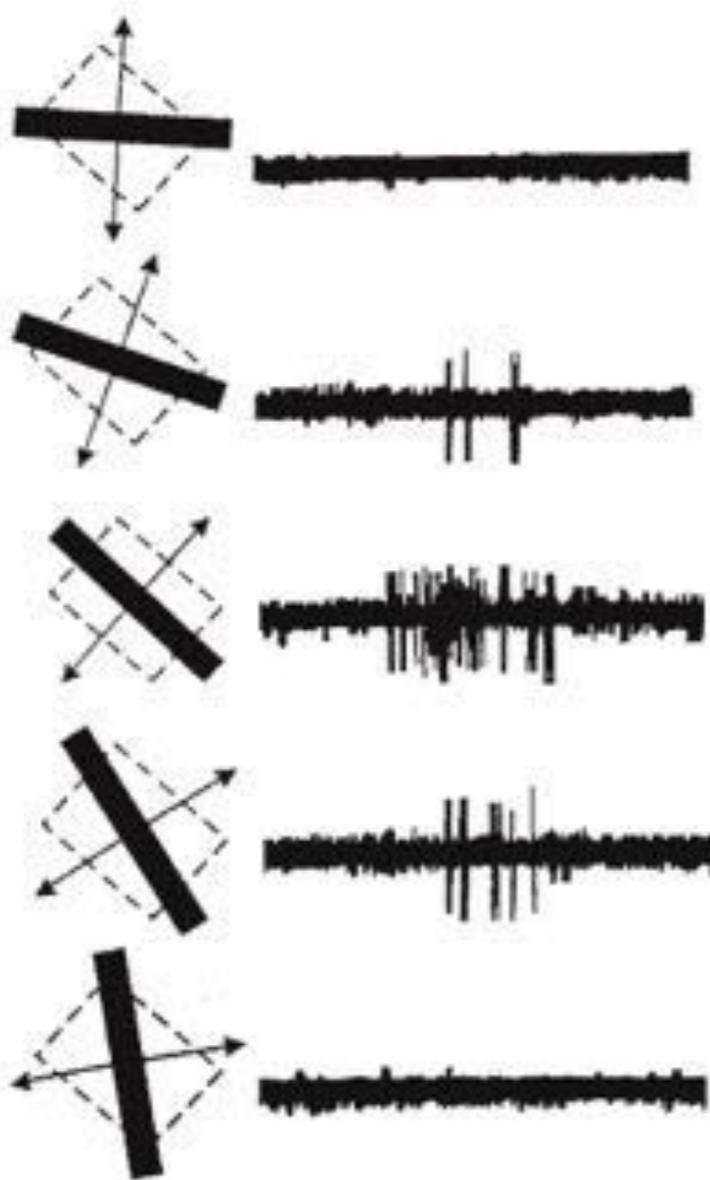
Single-neuron recordings



Single-neuron recordings

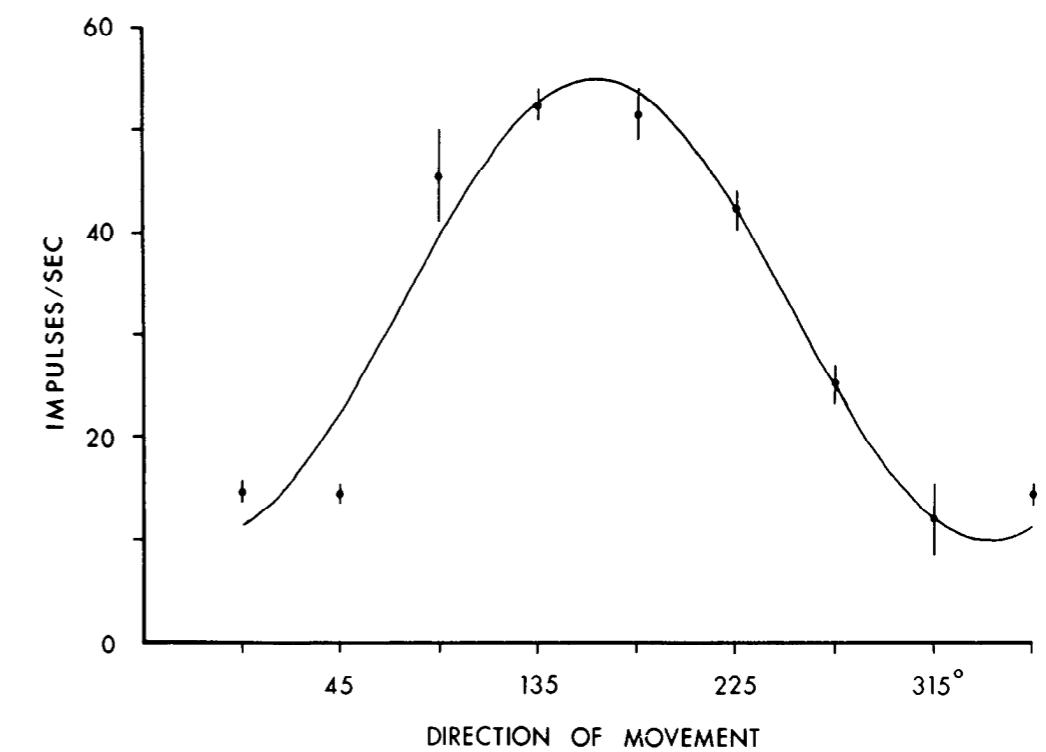
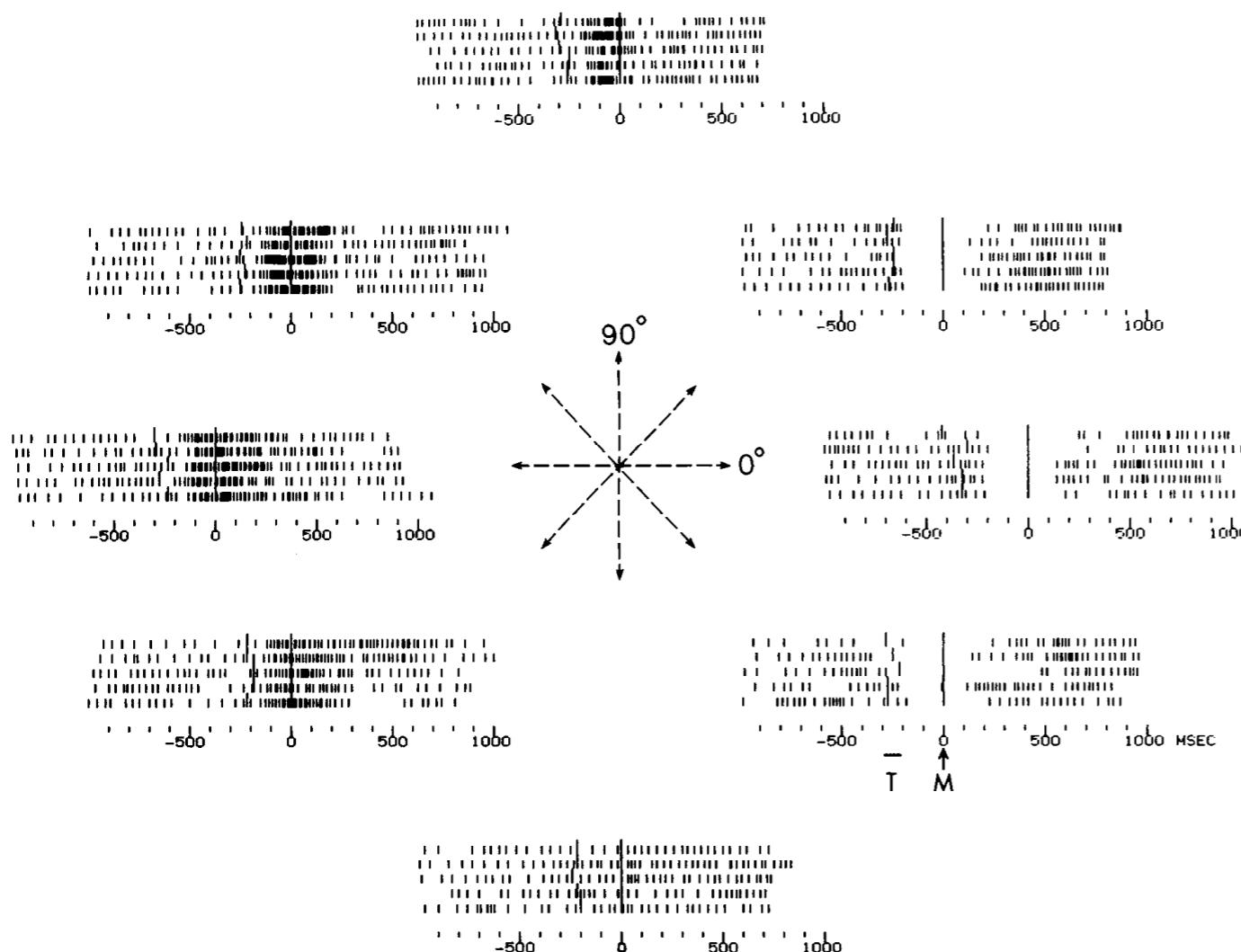


Tuning curves in the visual cortex



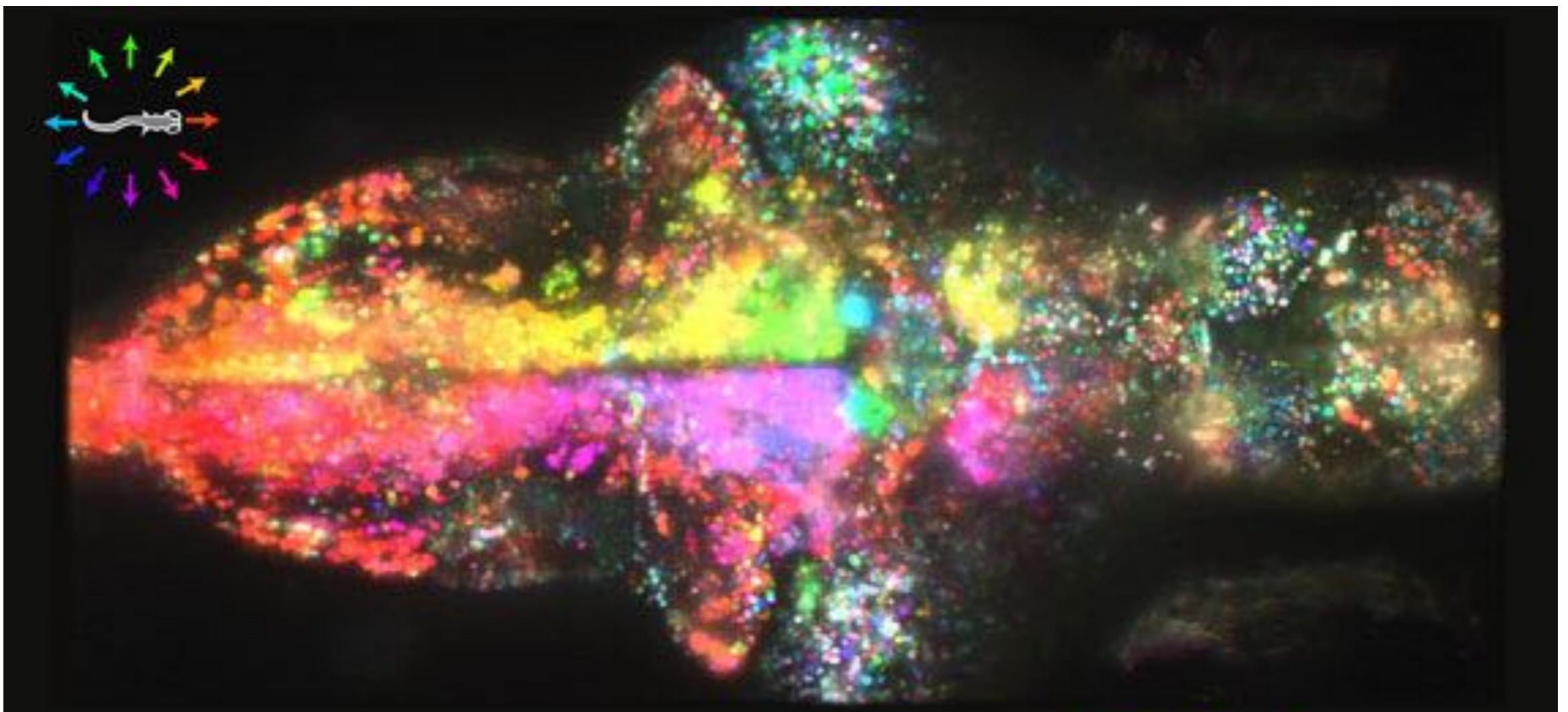
Hubel & Wiesel, *J Neurosci*, 1968

Tuning curves in the motor cortex



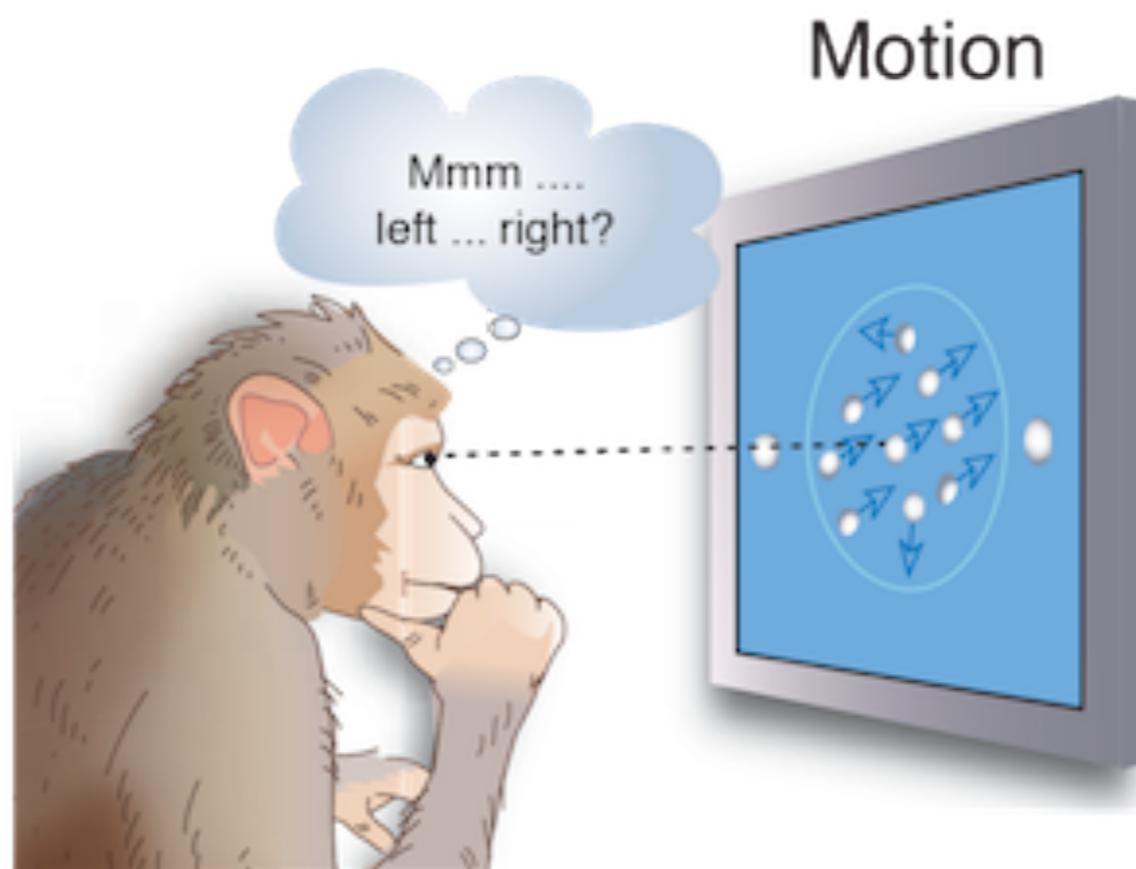
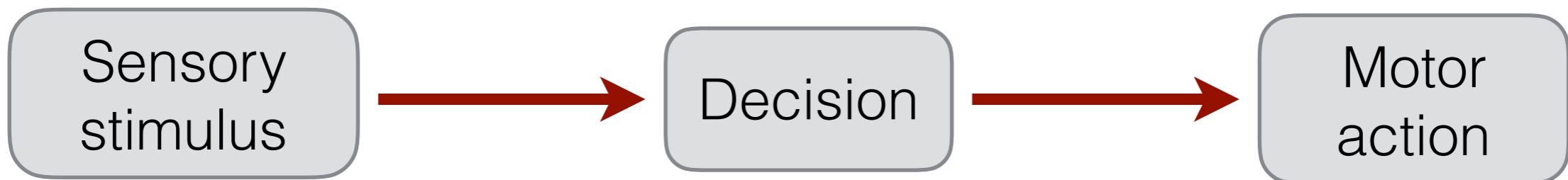
Georgopoulos et al, *J Neurosci*, 1982

Tuning curves across the whole brain



Freeman et al, *Nat Methods*, 2014

Brain's internal processing: Decision making

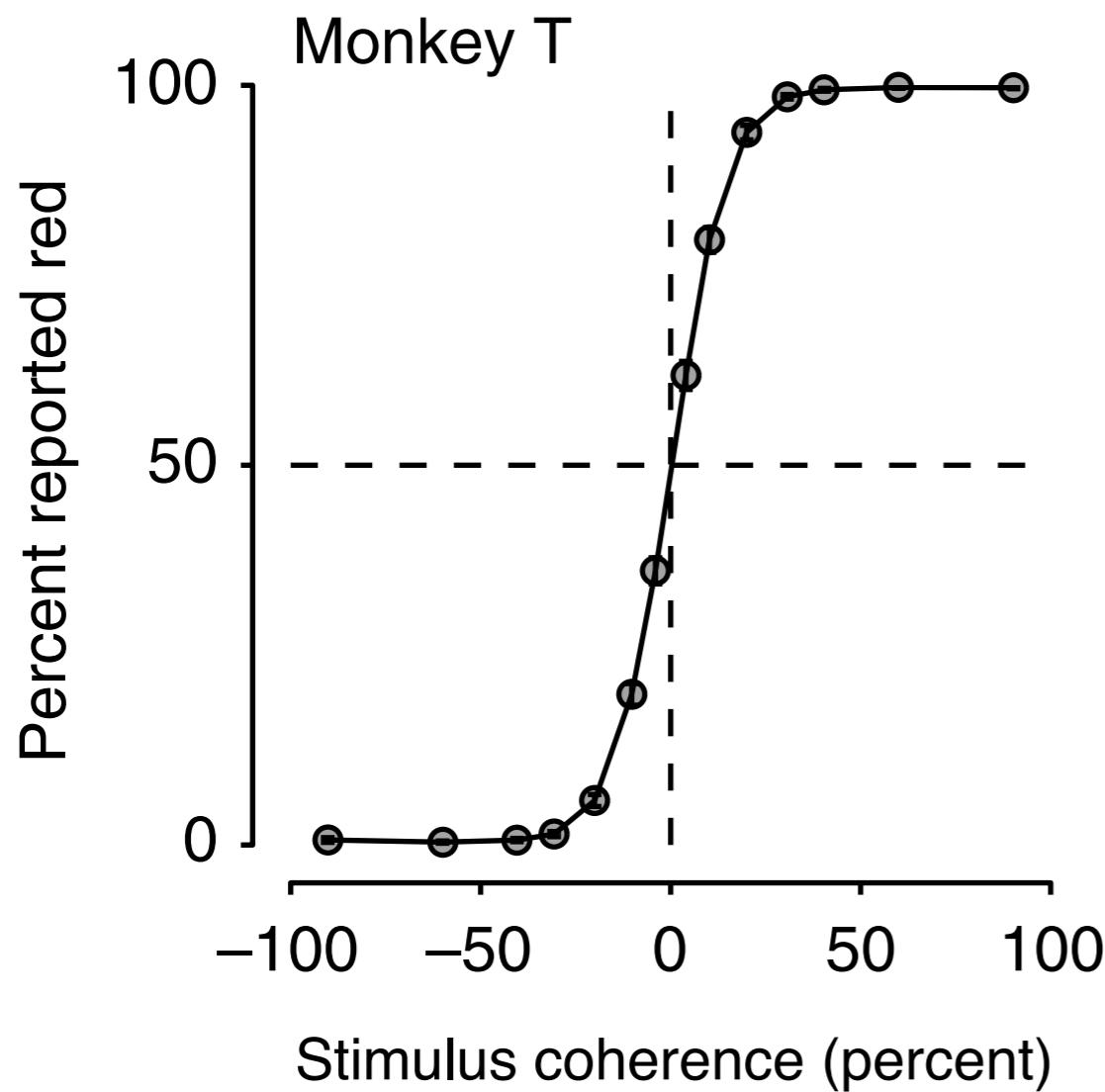


Varying decision difficulty

Removed large video showing random dot stereograms with various coherence. Decreased coherence increases difficulty of assessing direction of motion.

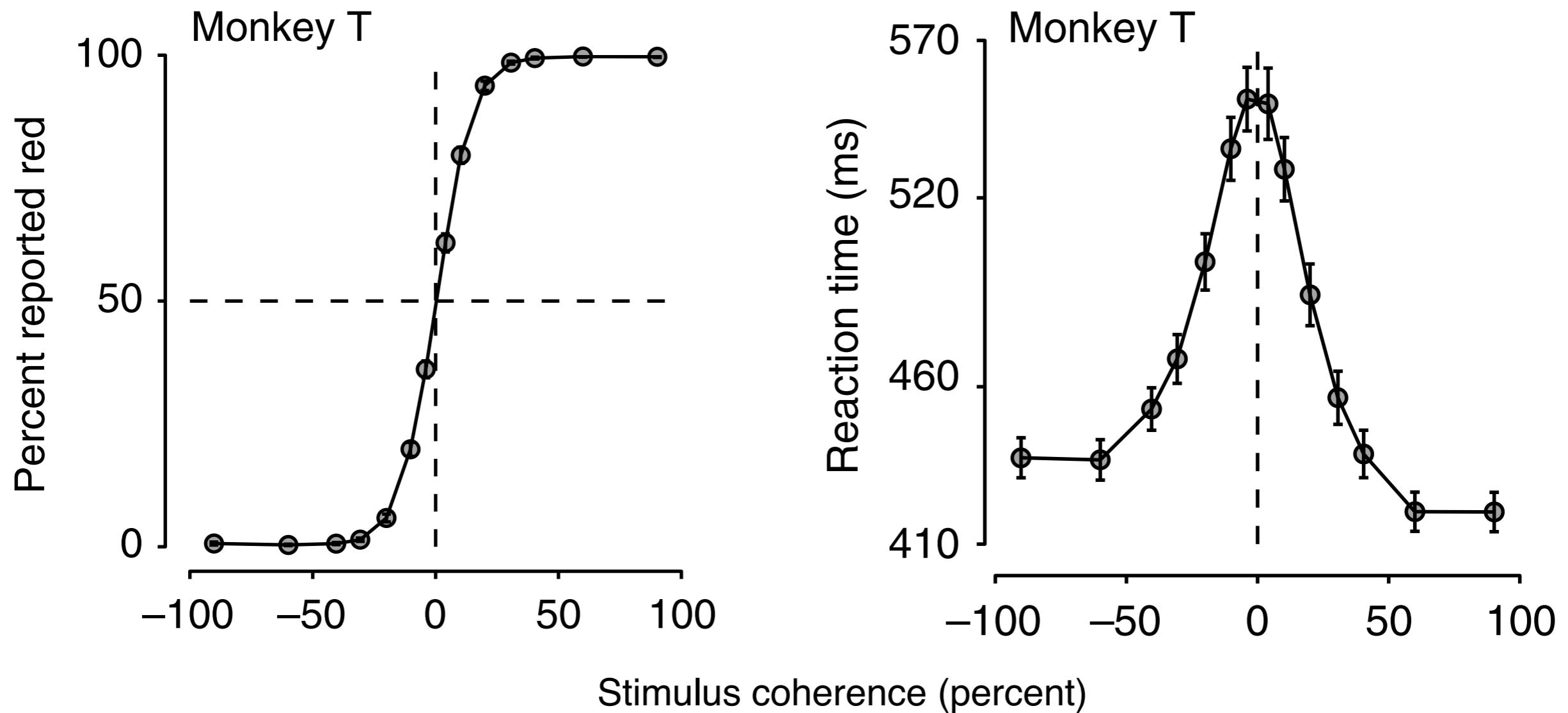
Stimulus coherence

Behavioral variability of decision making



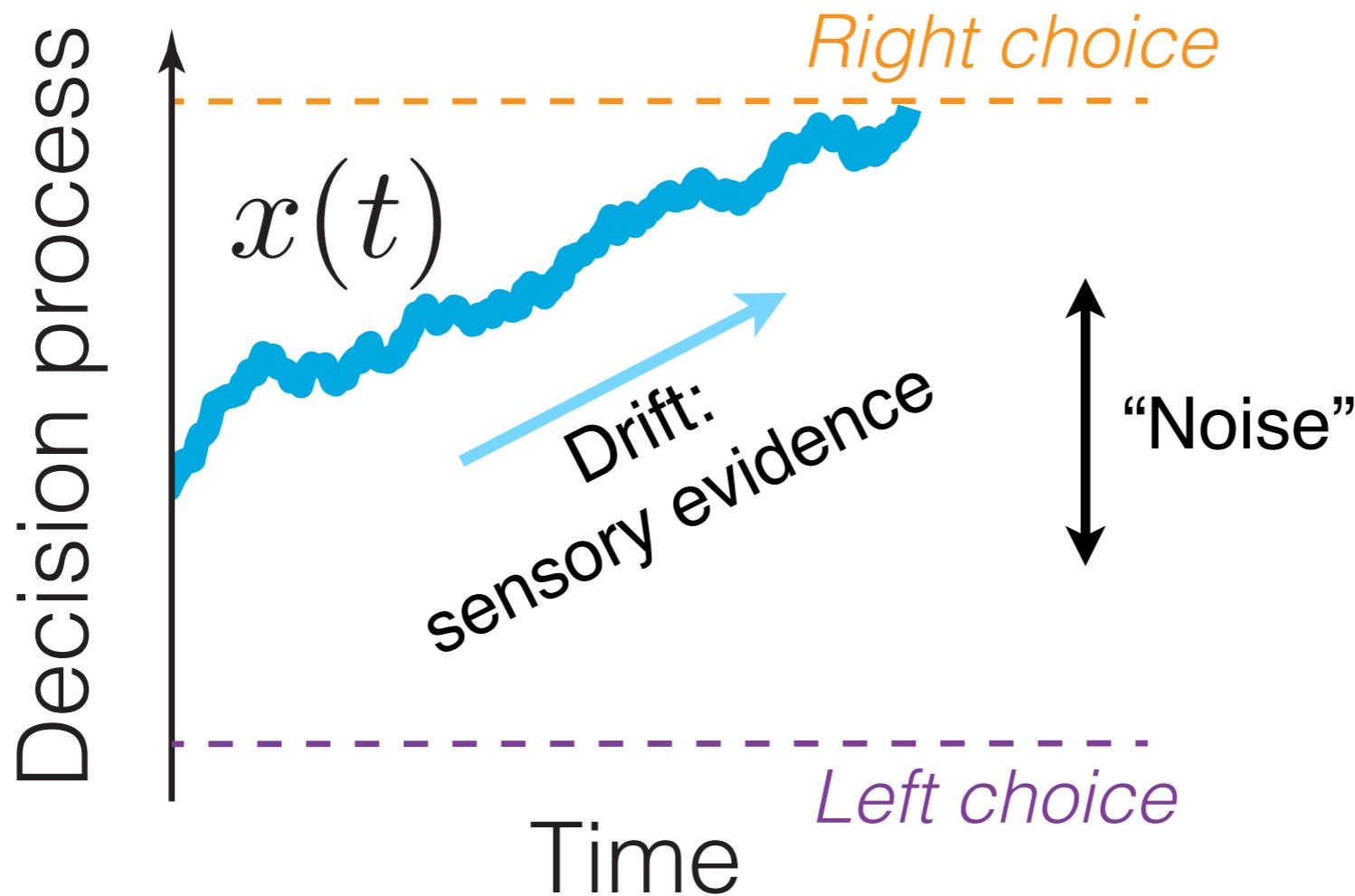
Chandrasekaran et al, *Nat Commun*, 2017

Behavioral variability of decision making



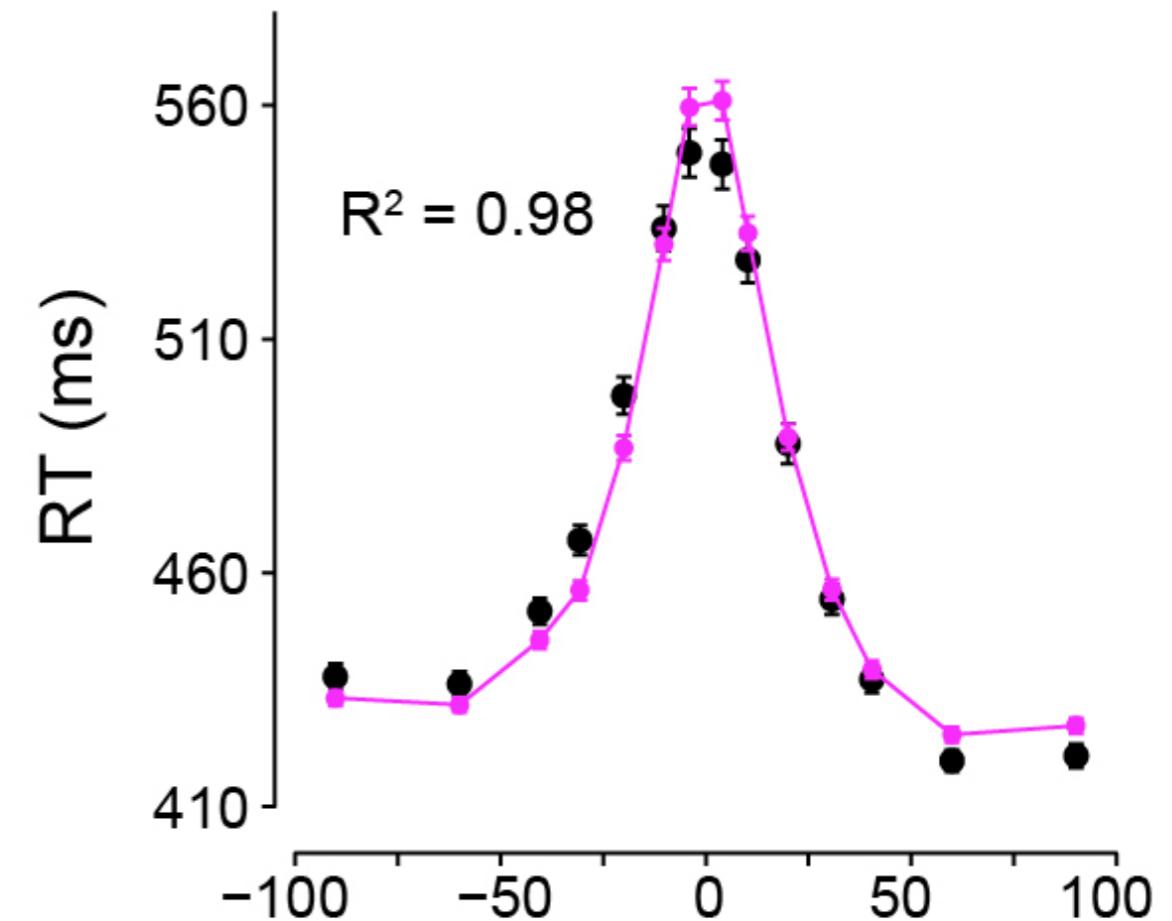
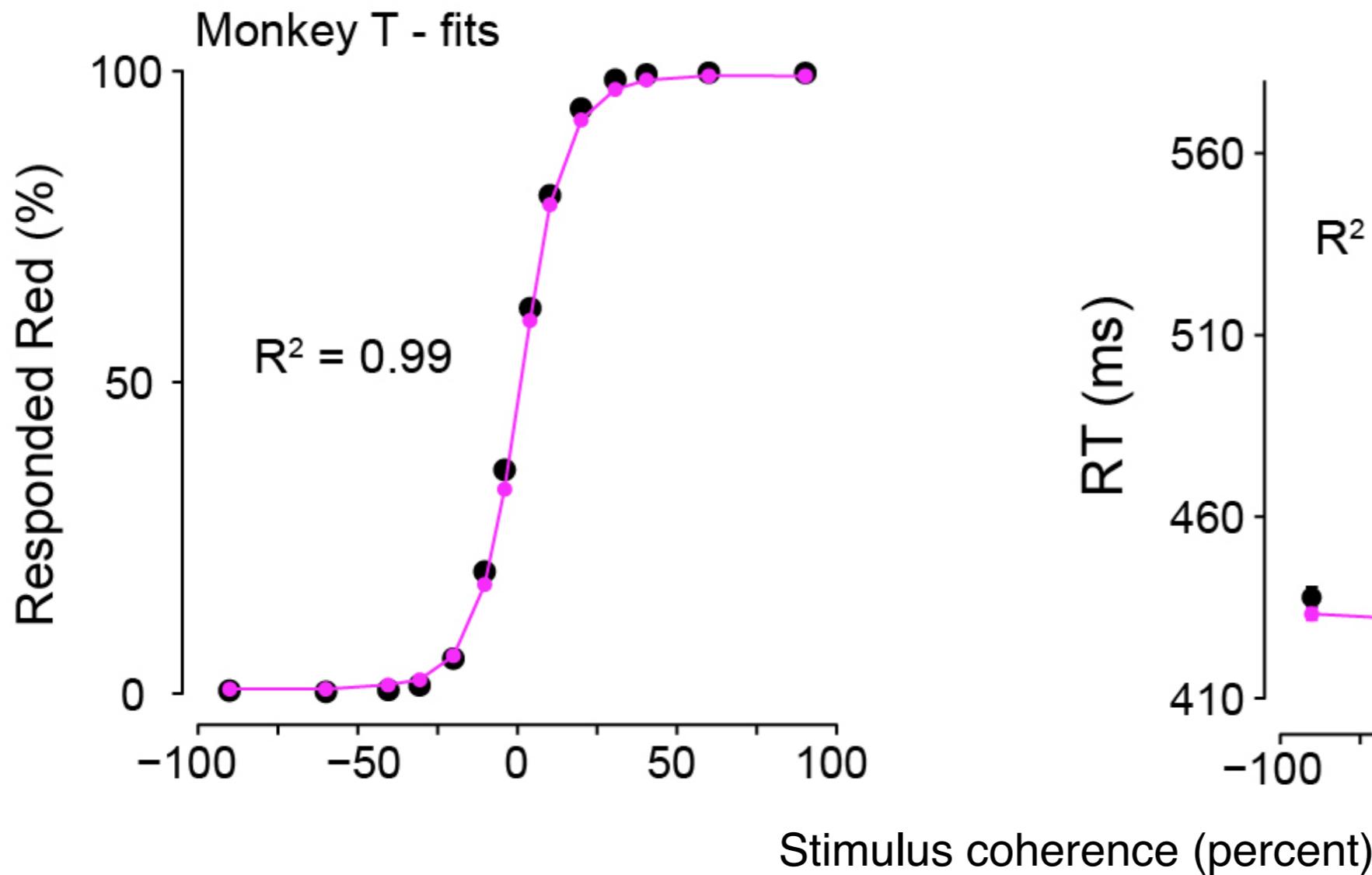
Chandrasekaran et al, *Nat Commun*, 2017

Behavioral model of decision making



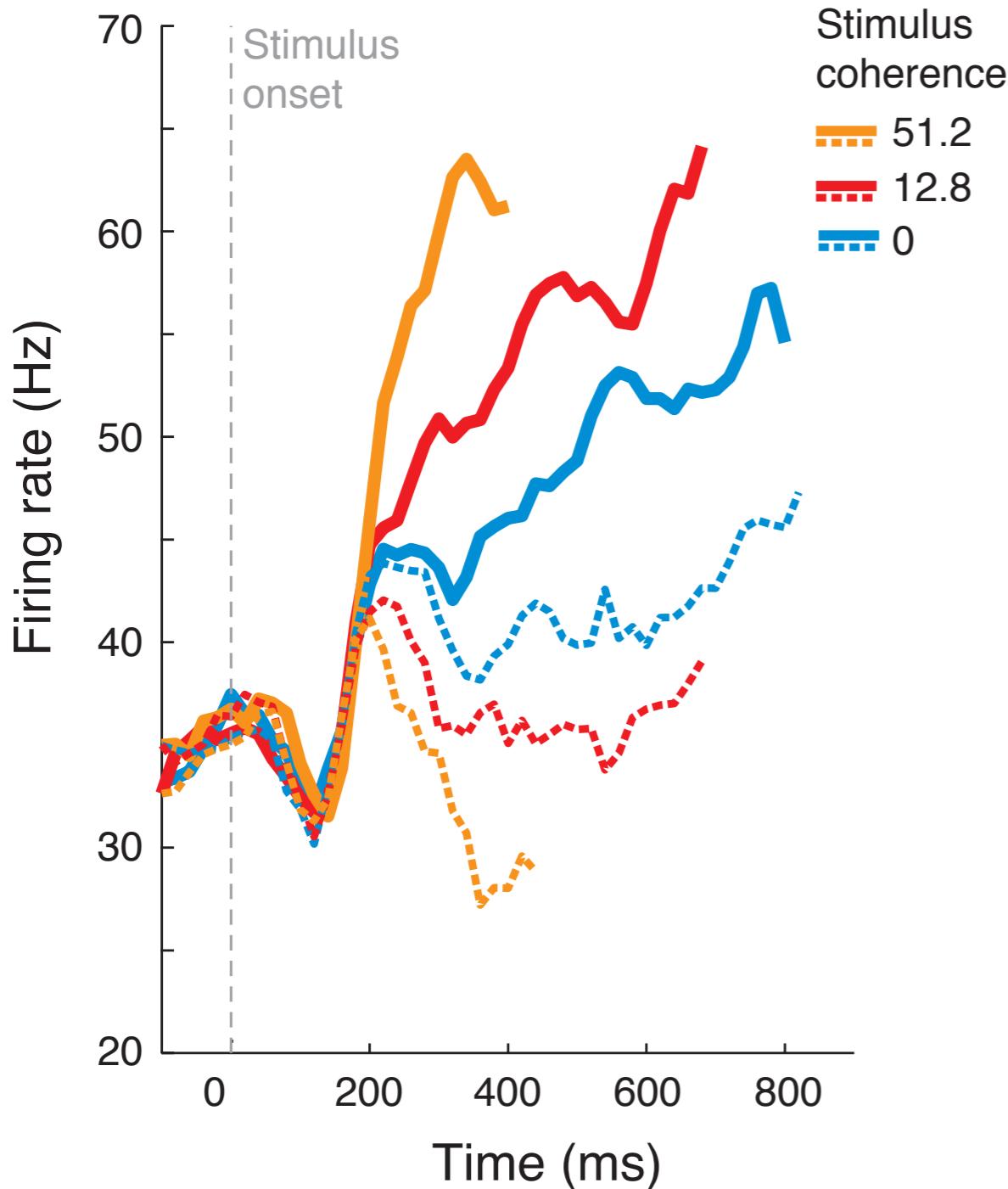
“Noisy” accumulation of sensory evidence

Drift-diffusion model captures behavior



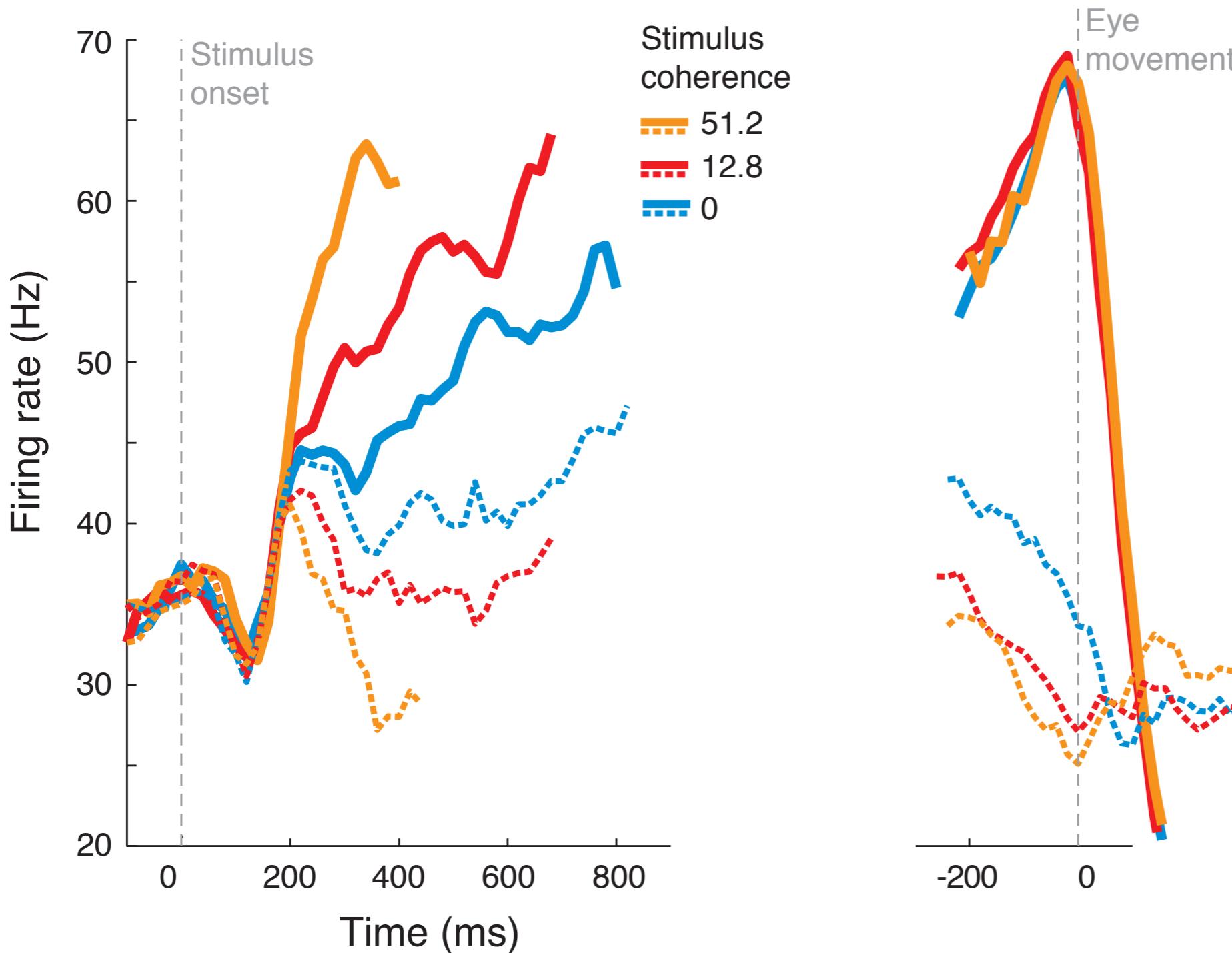
Chandrasekaran et al, *Nat Commun*, 2017

Single-neuron responses during decision making

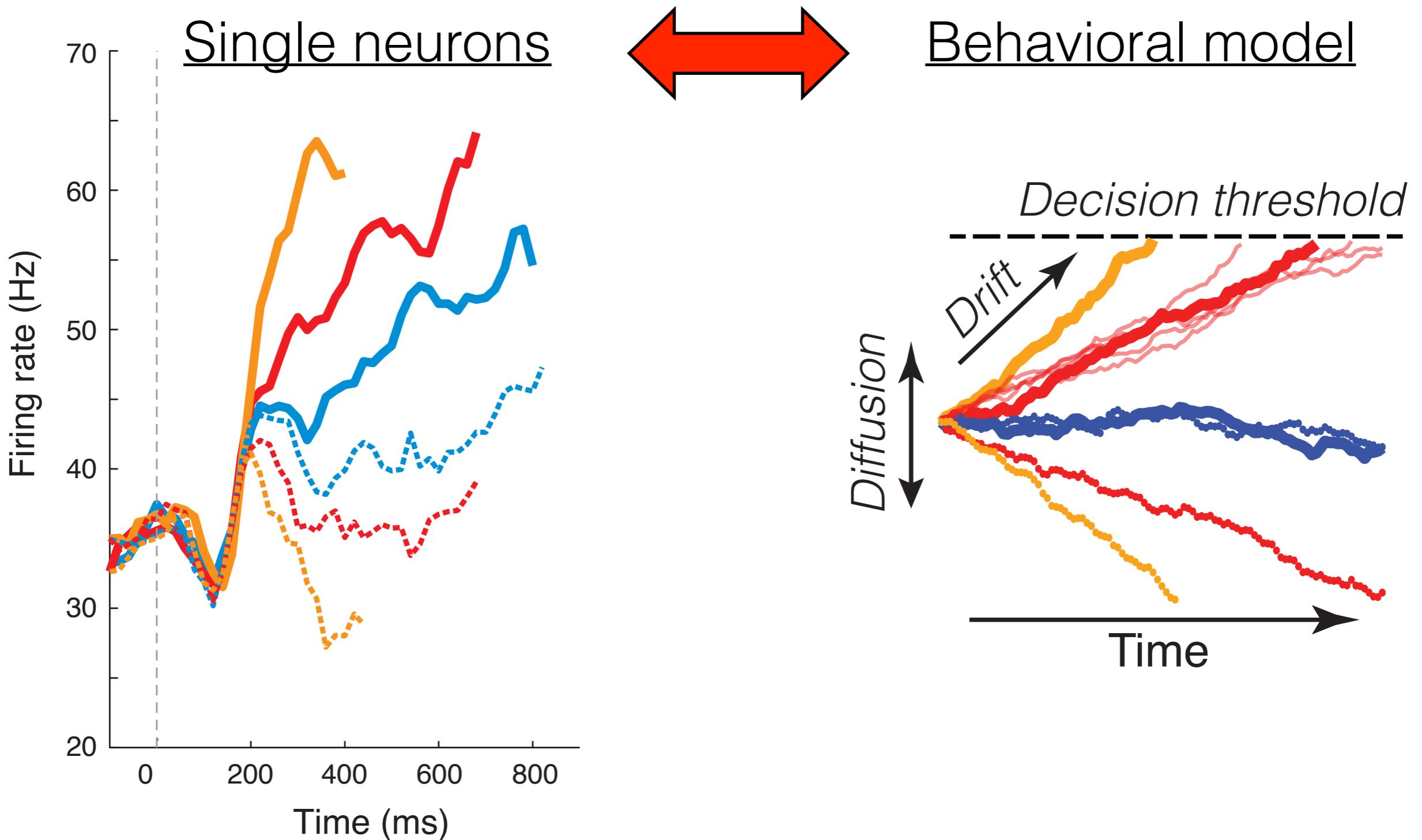


Gold & Shadlen, *Annu Rev Neurosci*, 2007

Single-neuron responses during decision making

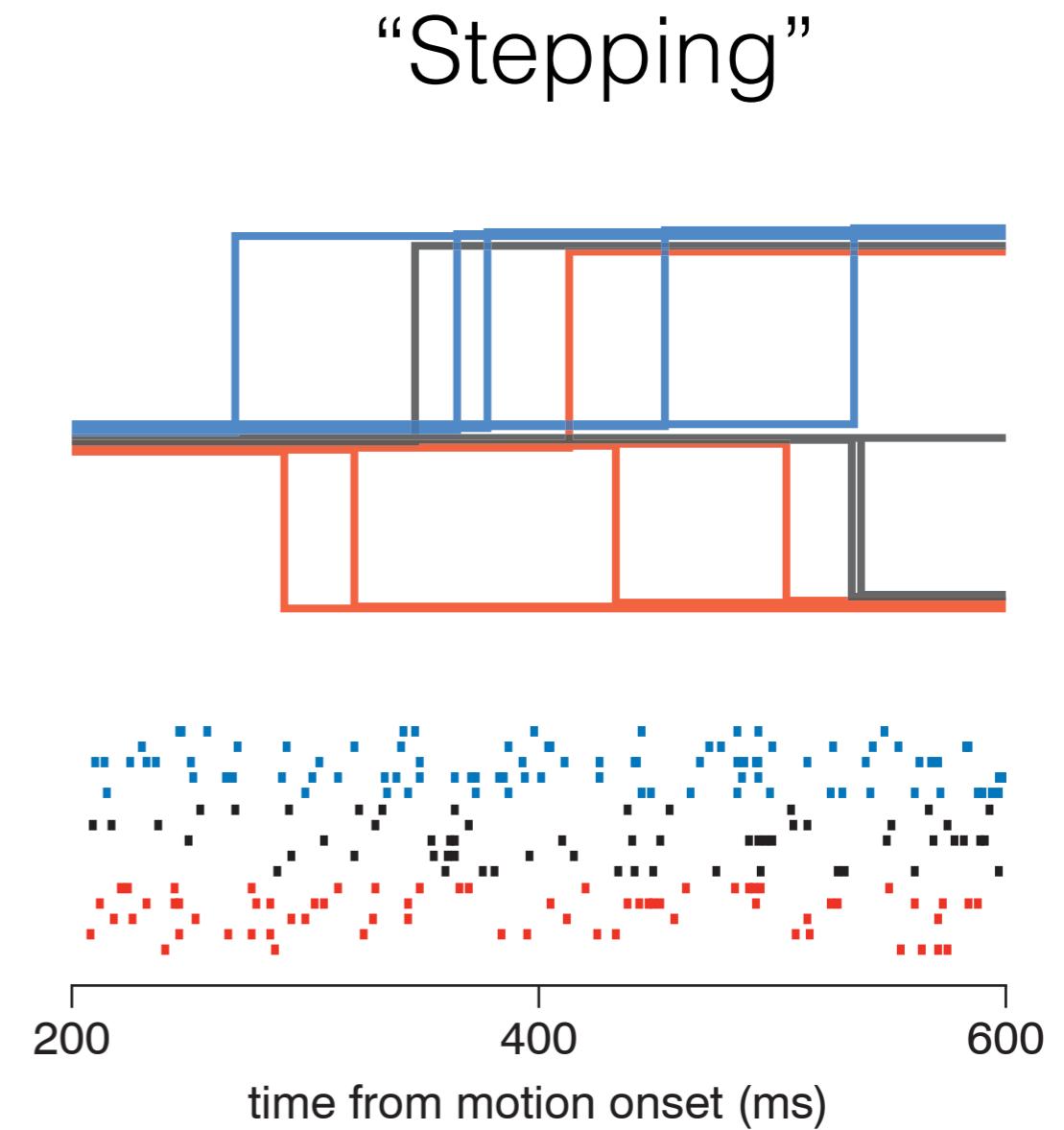
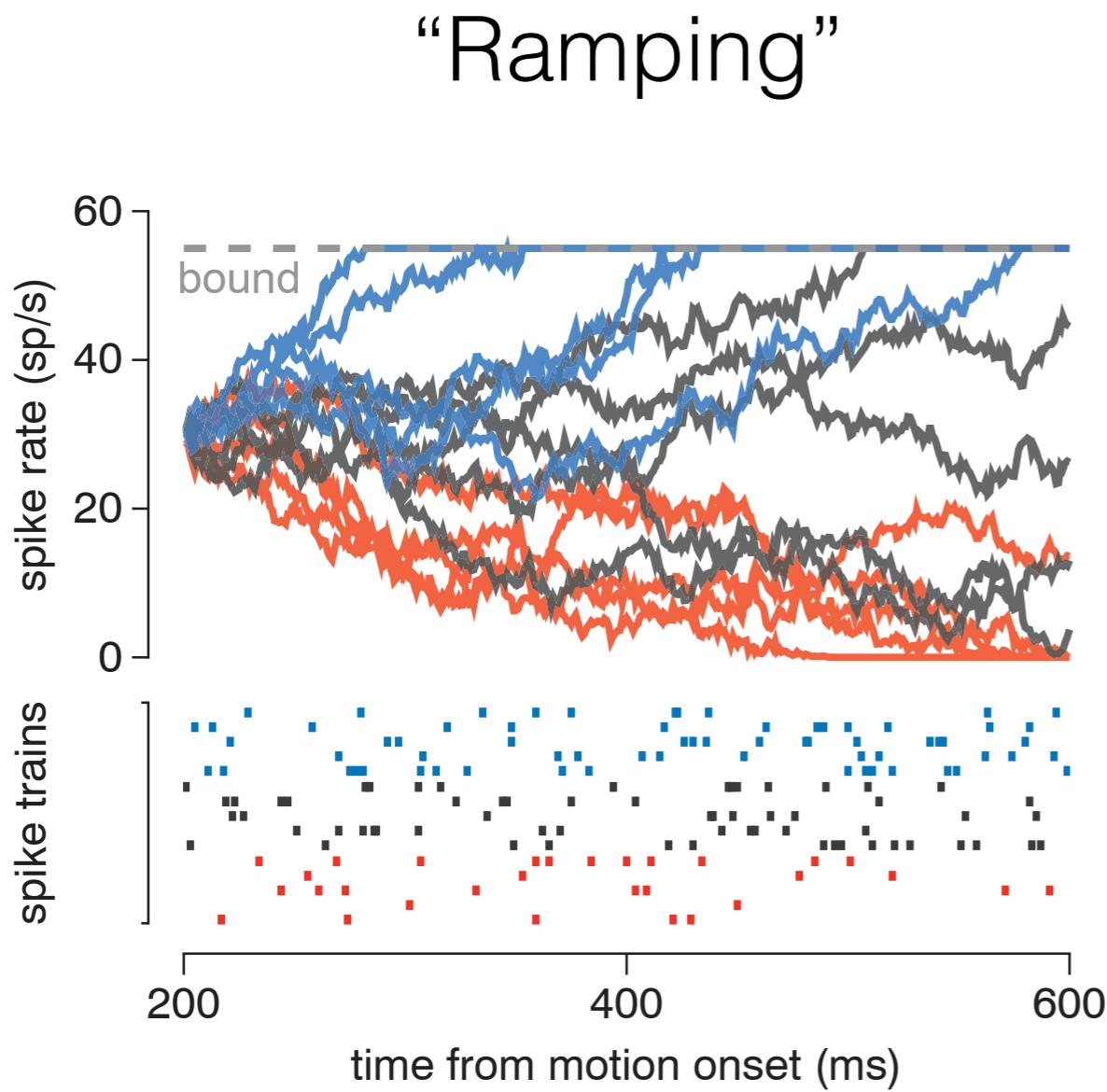


Single-neuron responses during decision making

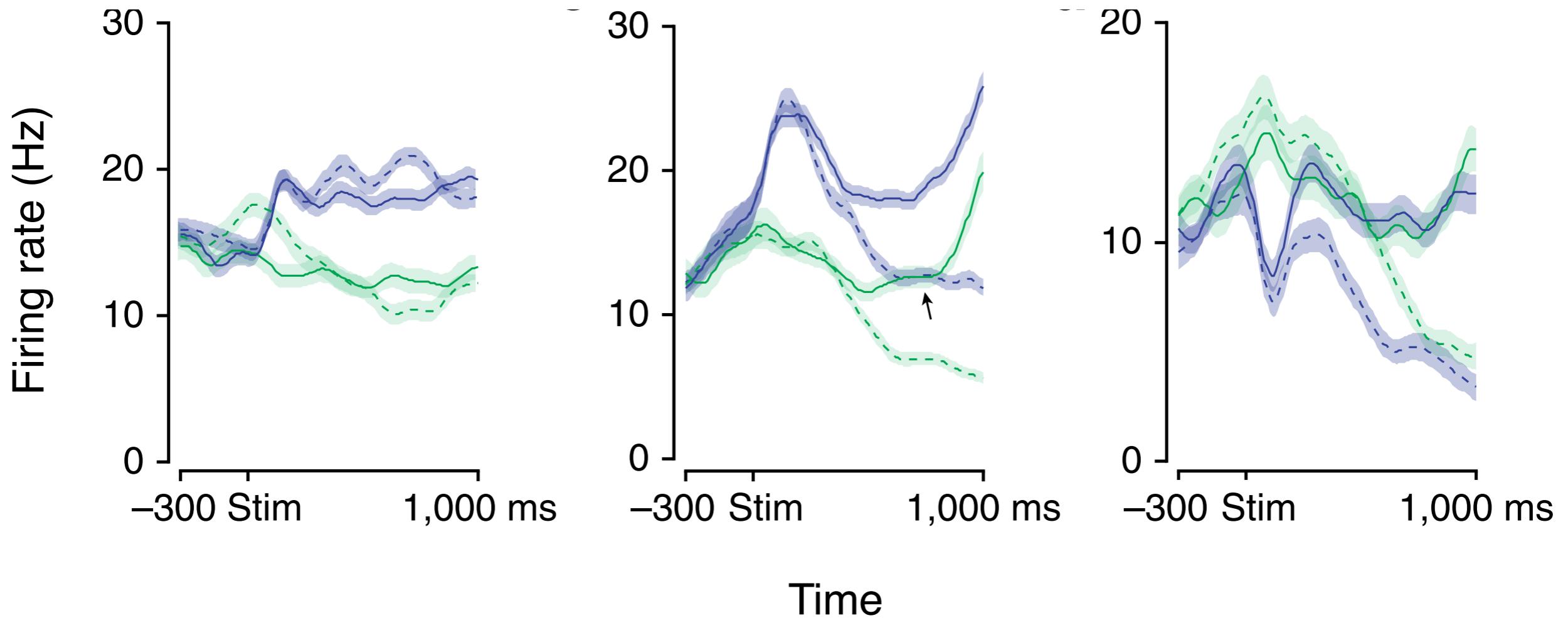


Gold & Shadlen, *Annu Rev Neurosci*, 2007

Hypothetical decision-related responses on single trials



Heterogeneity of single-neuron responses



Raposo et al, *Nat Neurosci*, 2014

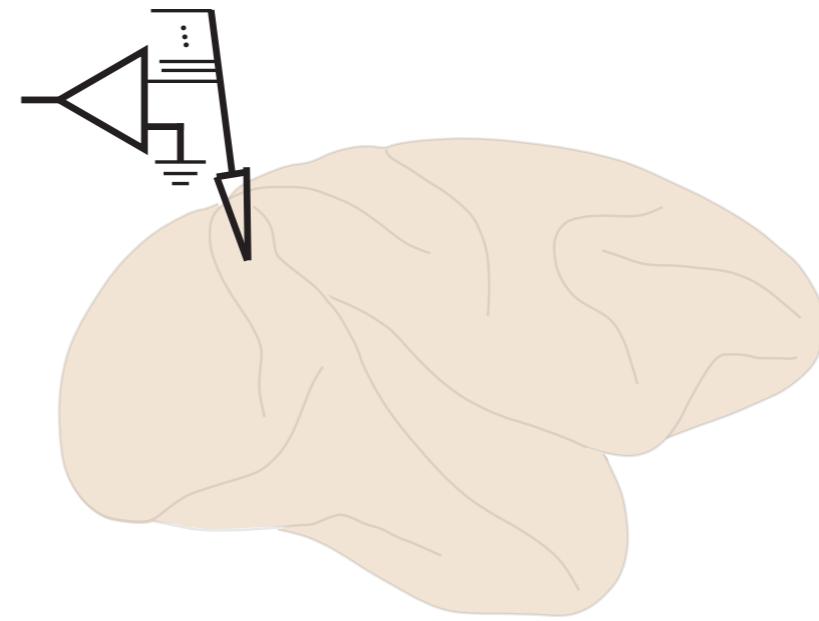
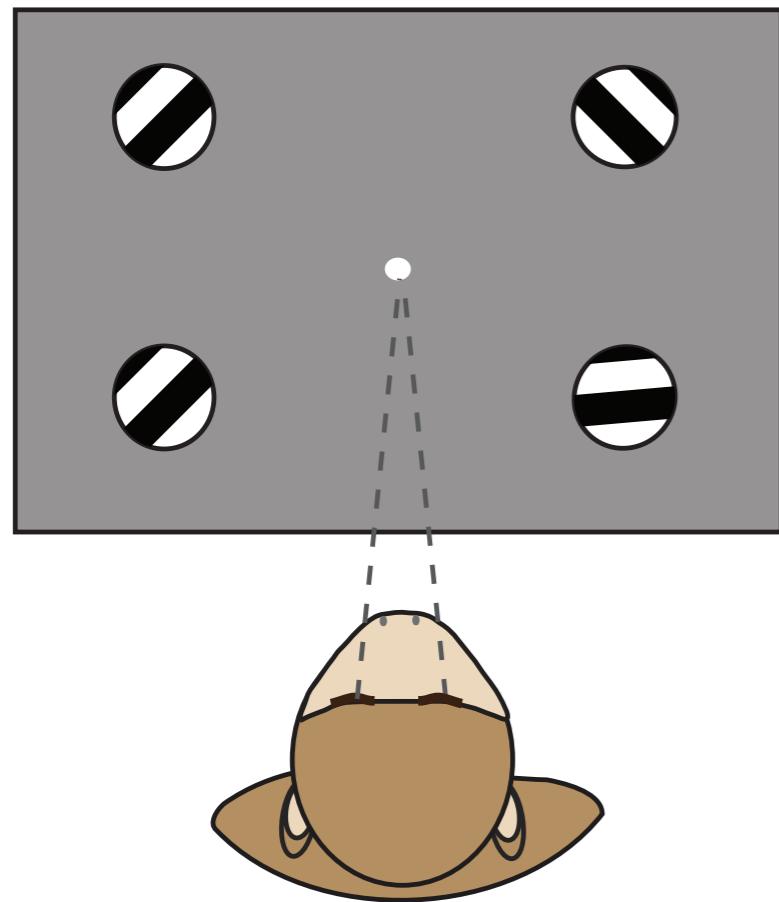
Challenges to the classical single-neuron view

- neural dynamics on single trials
- heterogeneity of single neuron responses
- sources of “noise” in neural responses and behavior

Outline

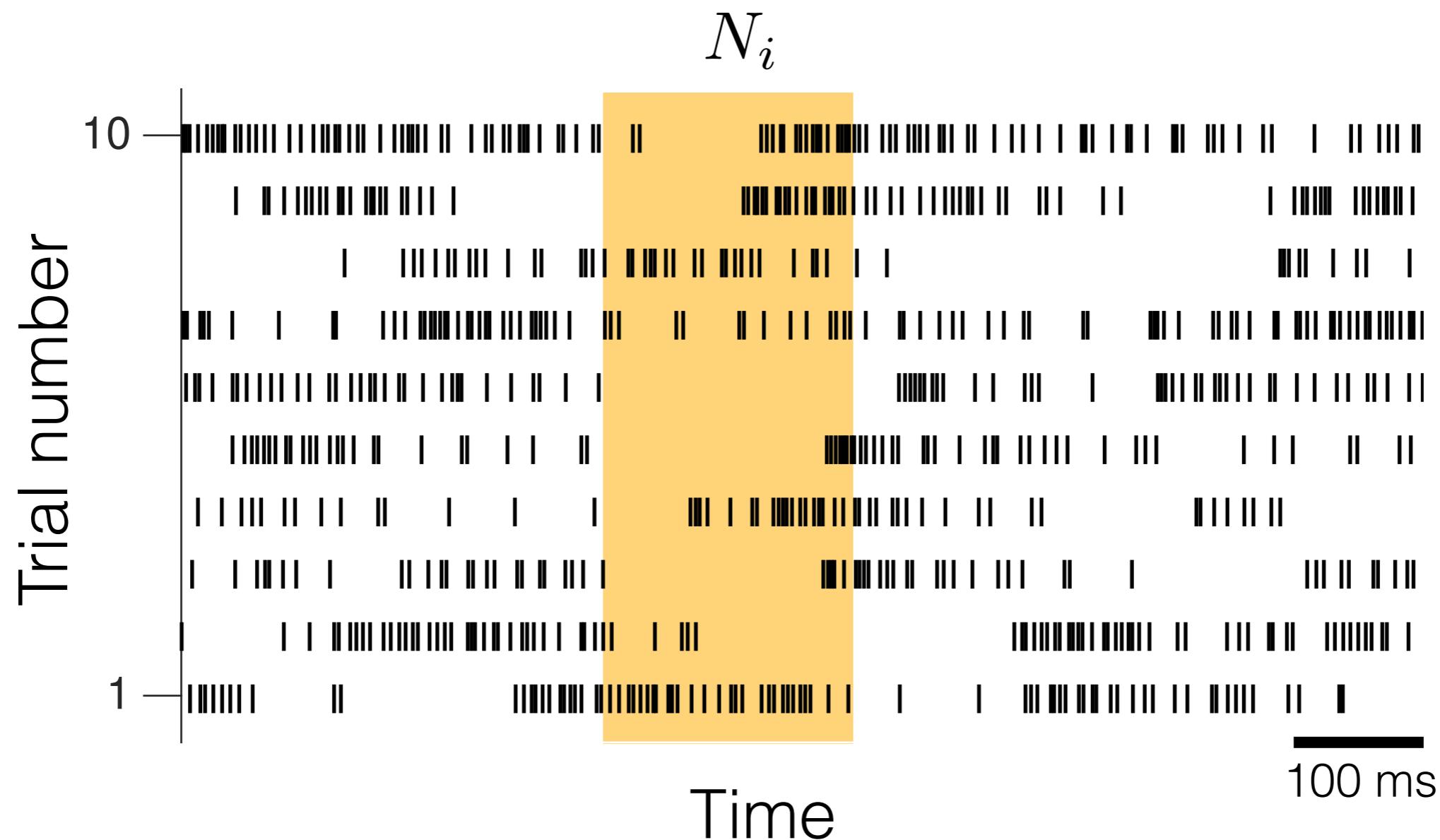
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Neural variability during behavior



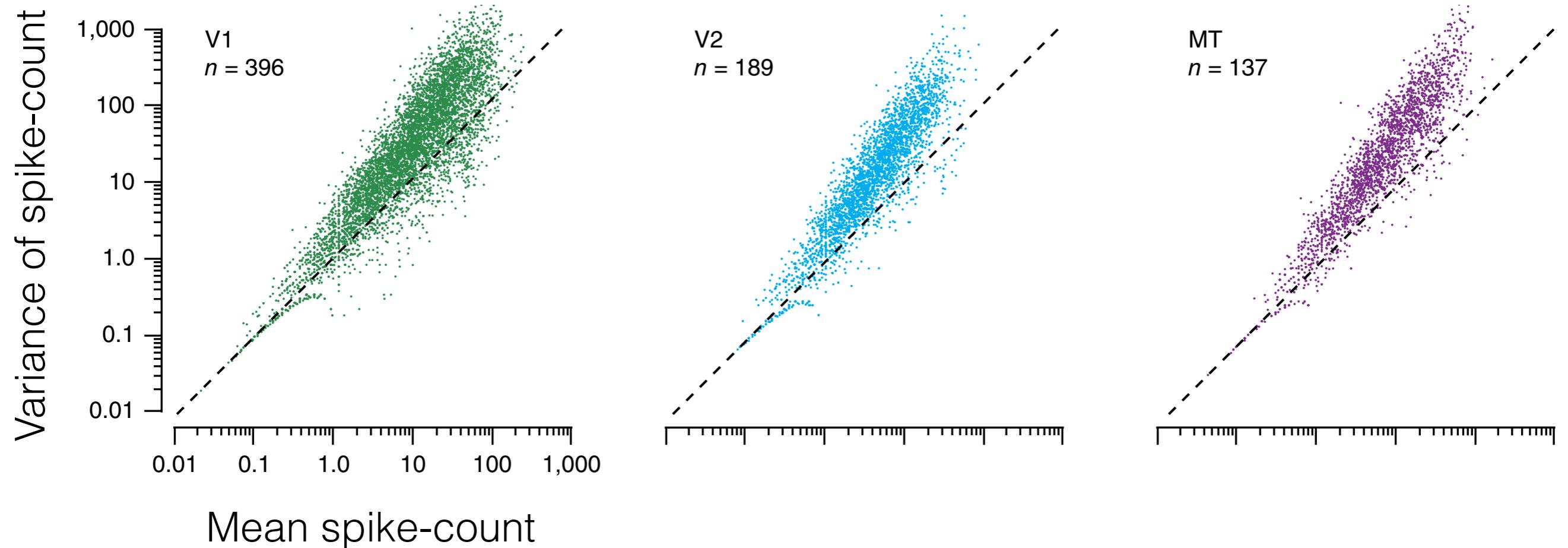
Neural variability during behavior

Fano factor: $FF = \frac{\text{Var}[N]}{\text{E}[N]}$



Super-Poisson spike-count variability

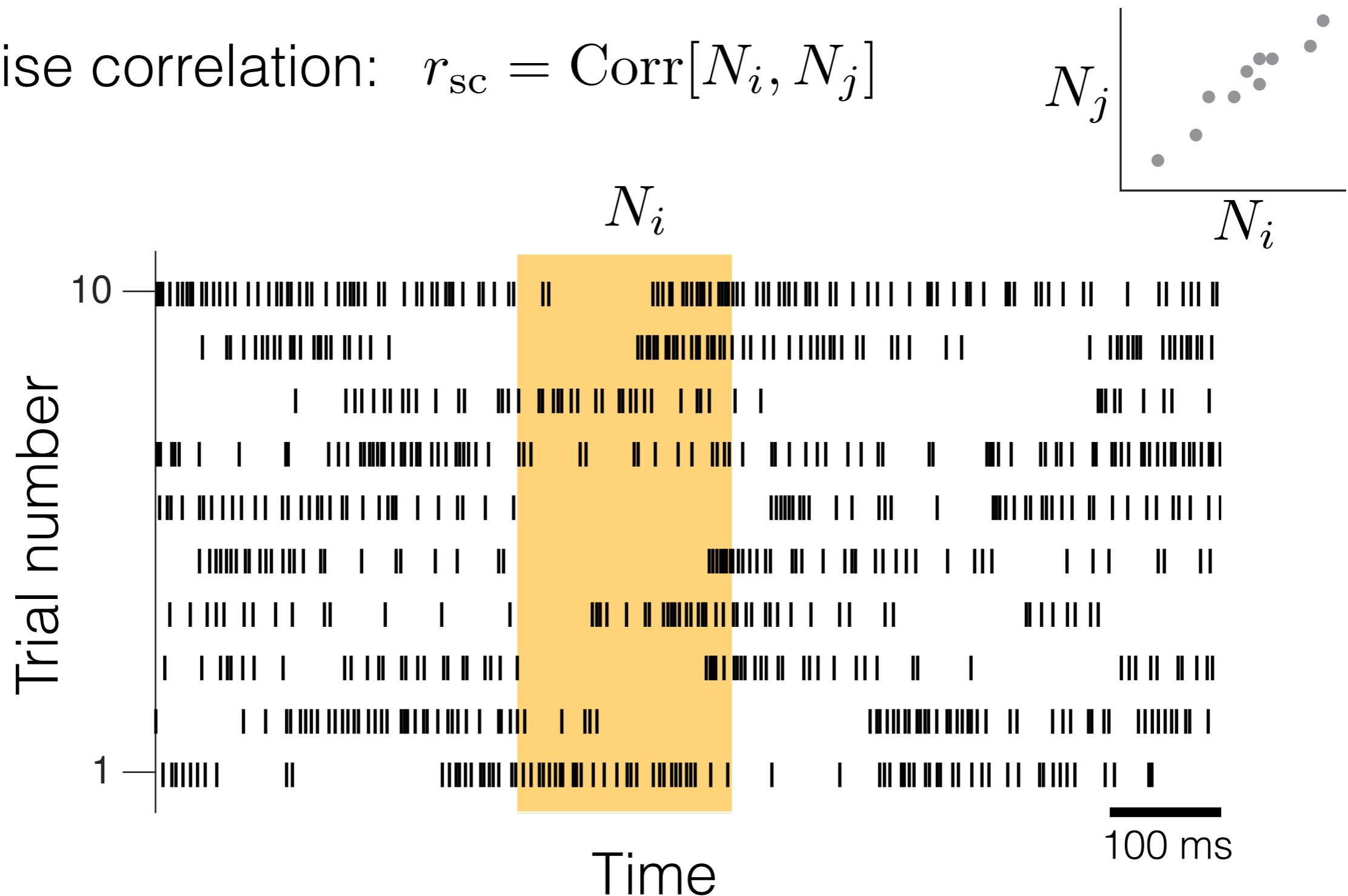
$$FF > 1$$



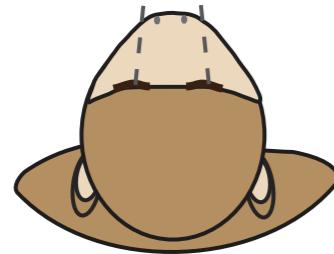
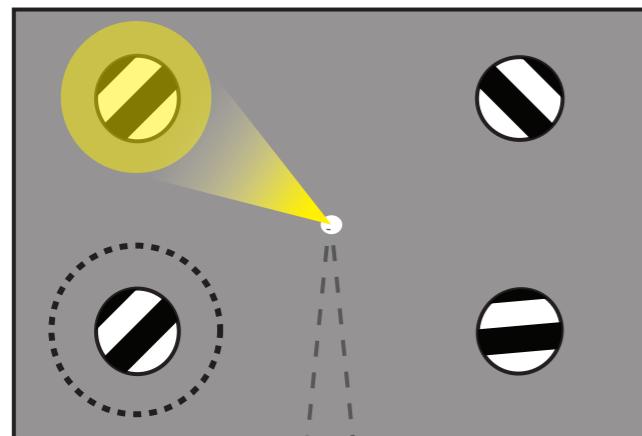
Goris et al, Nat Neurosci, 2014
Rabinowitz et al., eLife, 2015

Neural variability during behavior

Noise correlation: $r_{sc} = \text{Corr}[N_i, N_j]$



Noise correlations are modulated during attention

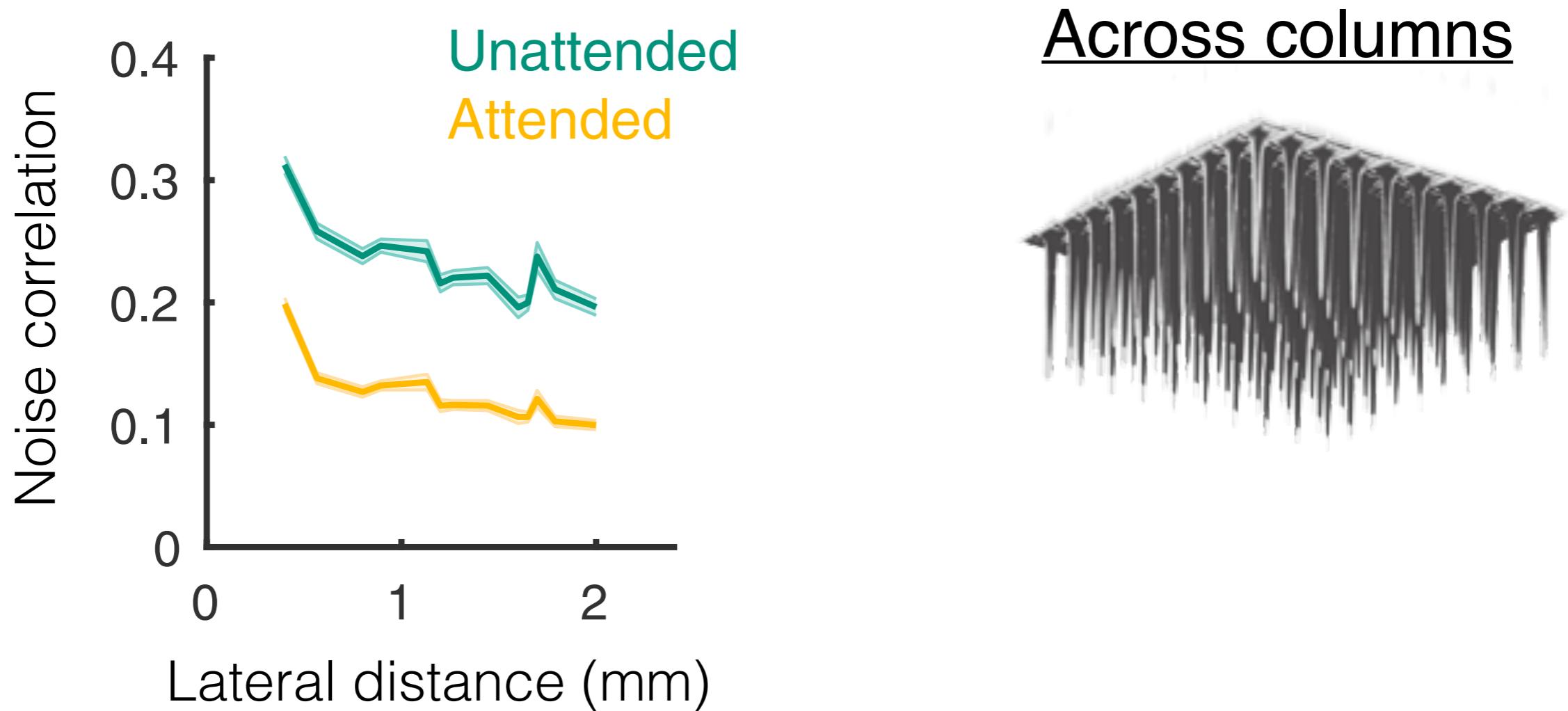


$$FF_{\text{Attention}} < FF_{\text{Control}}$$

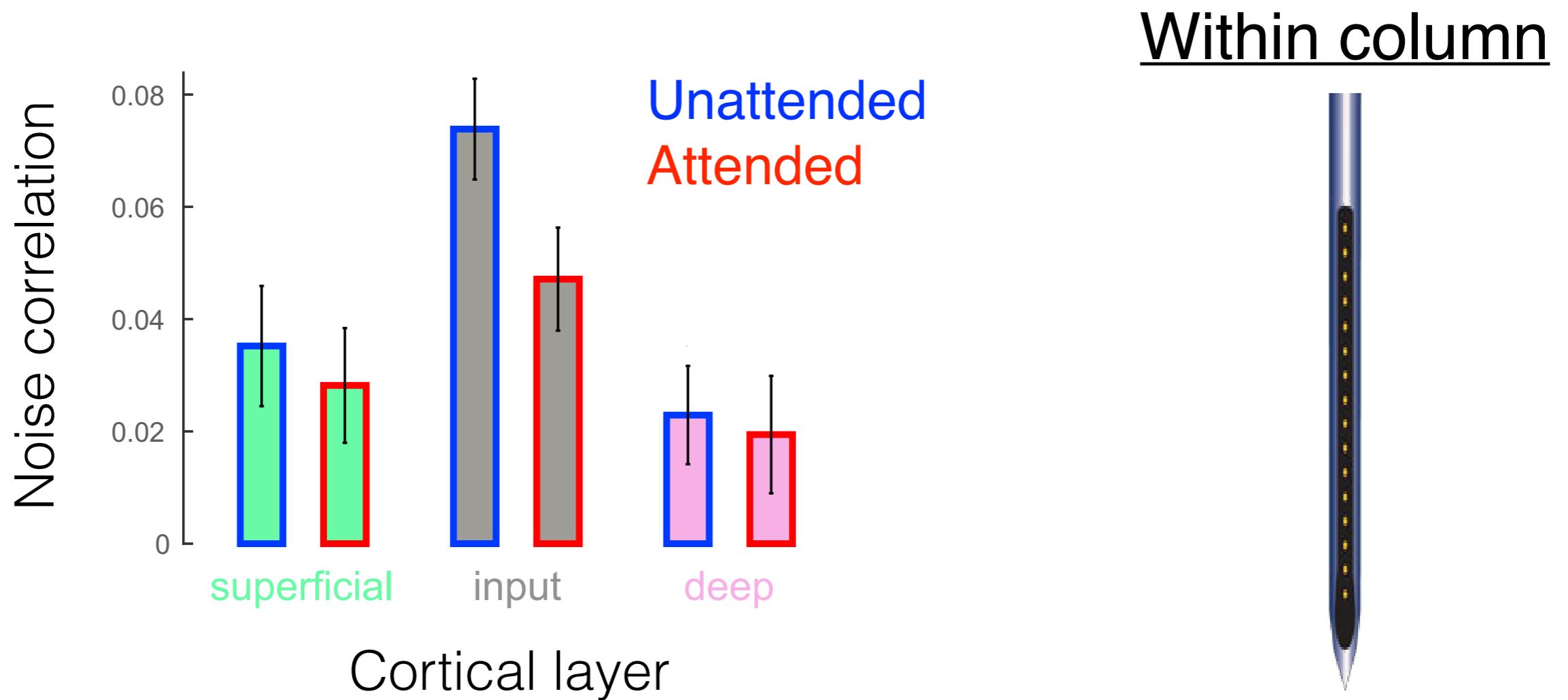
$$r_{\text{sc, Attention}} < r_{\text{sc, Control}}$$

Mitchel et al, Neuron, 2009
Cohen & Maunsell, Nat Neurosci, 2009

Noise correlations depend on anatomical dimensions



Noise correlations depend on anatomical dimensions



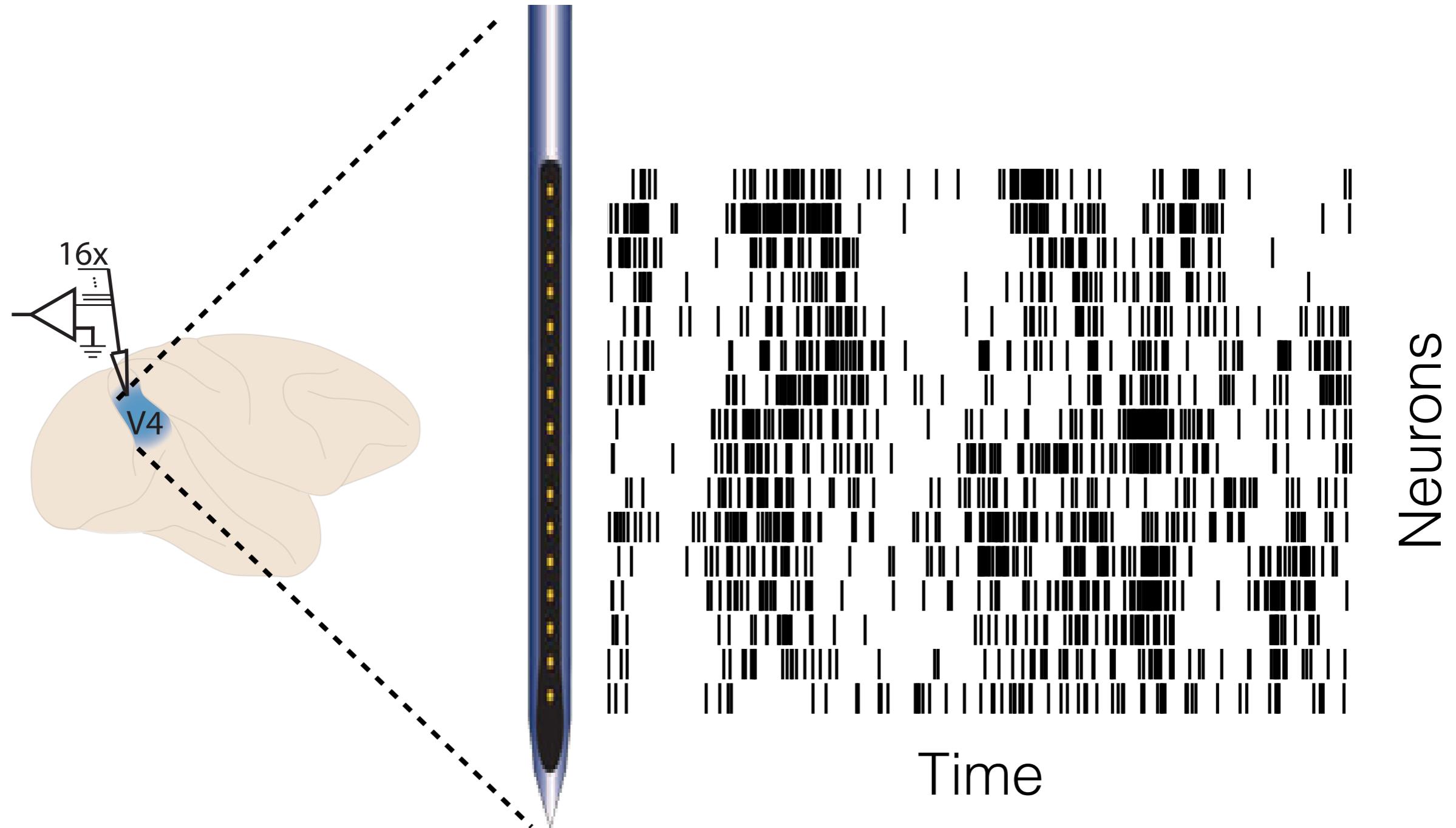
Neural variability and correlations

- super-Poisson fluctuations ($FF > 1$)
- correlated fluctuations ($r_{sc} > 0$)
- fluctuations structure depends on anatomical dimensions
- fluctuations are modulated during changes of behavioral states

Outline

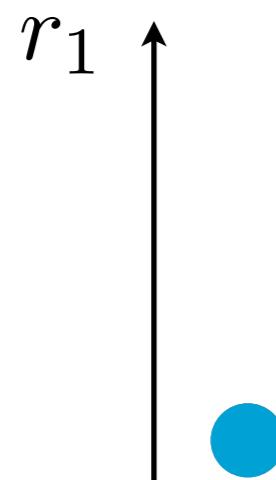
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Large-scale neural activity recordings

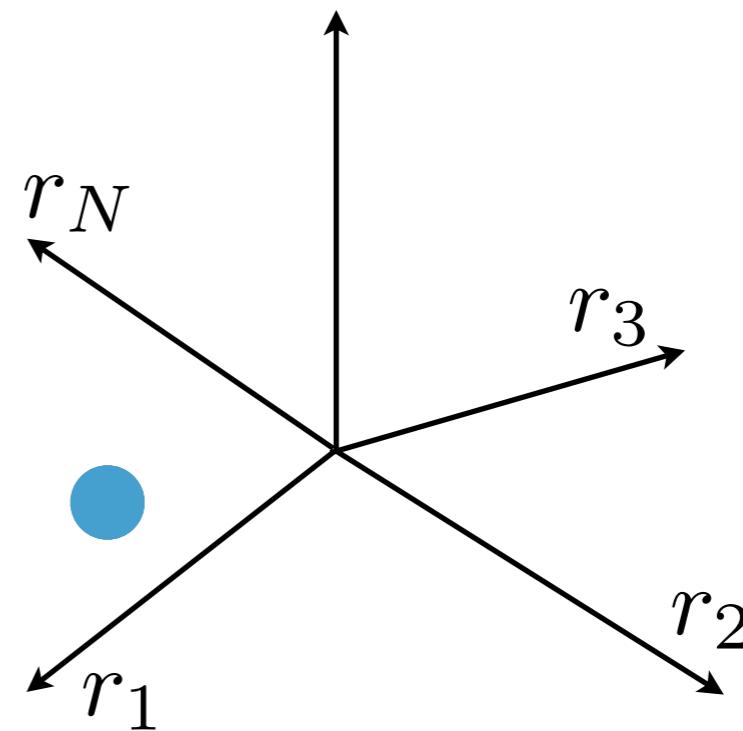


Neural population dynamics

Single neuron

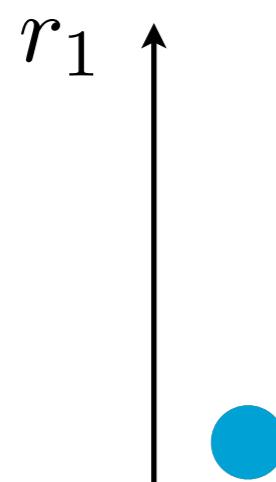


Neural population state

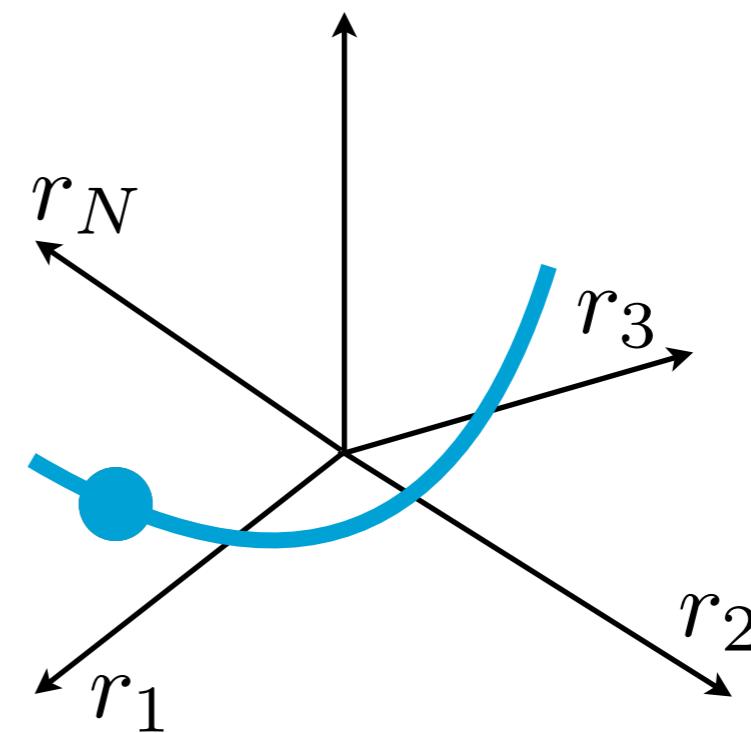


Neural population dynamics

Single neuron

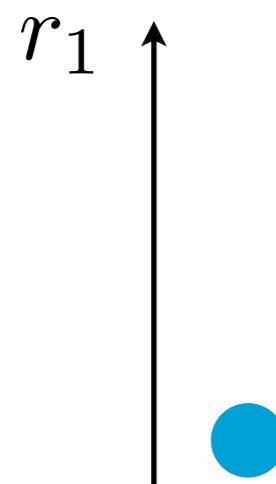


Neural population dynamics

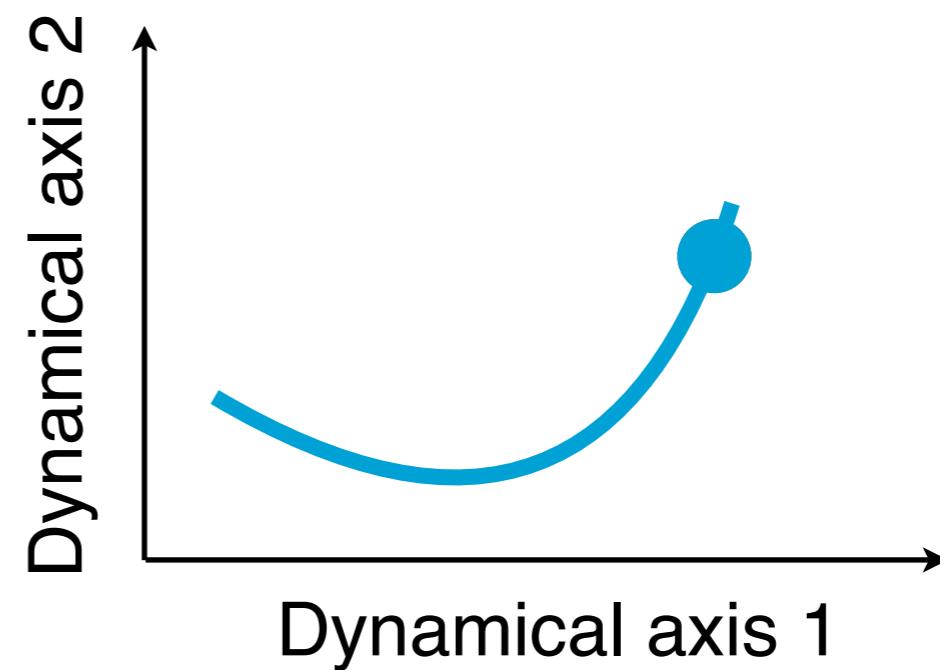


Neural population dynamics

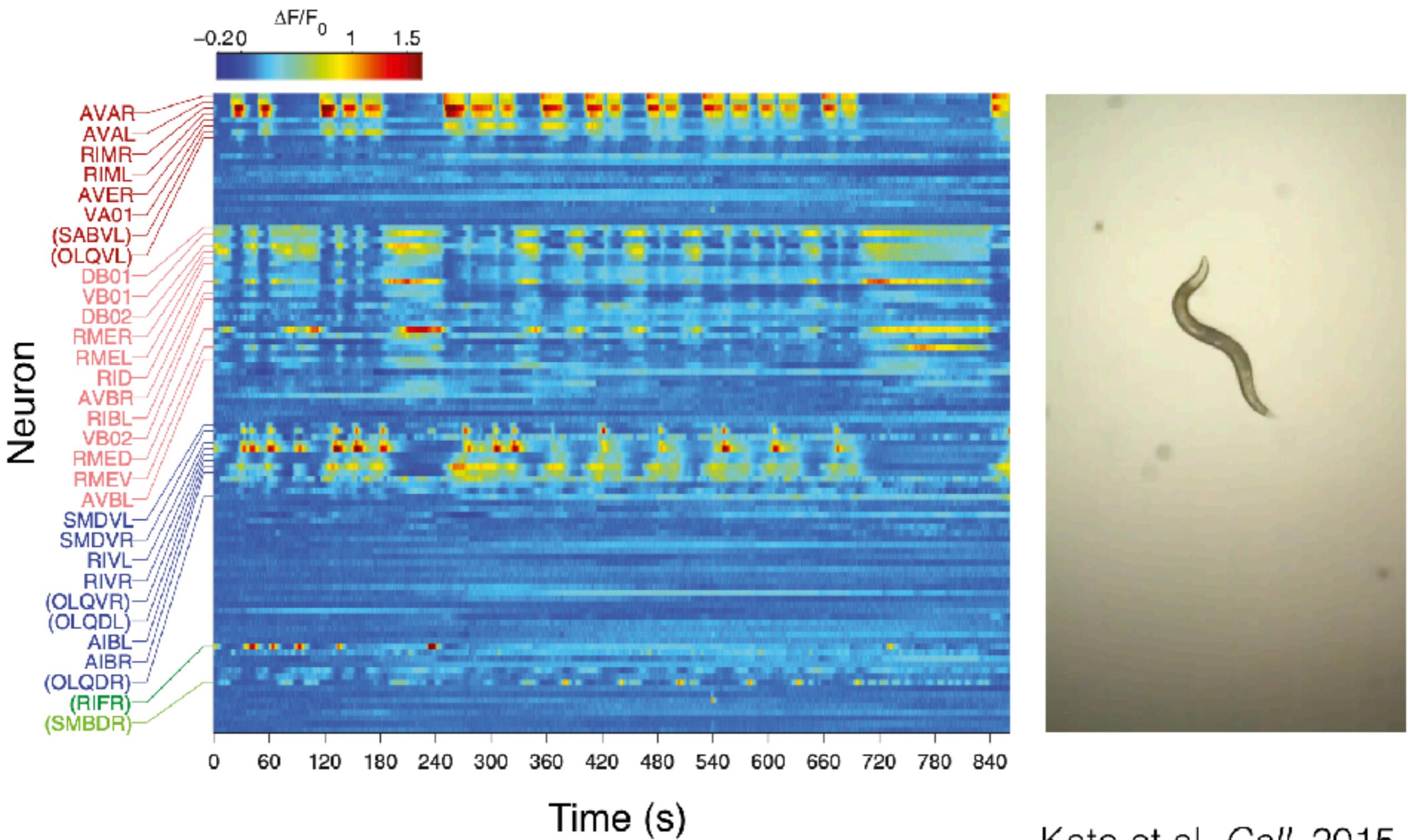
Single neuron



Neural population dynamics

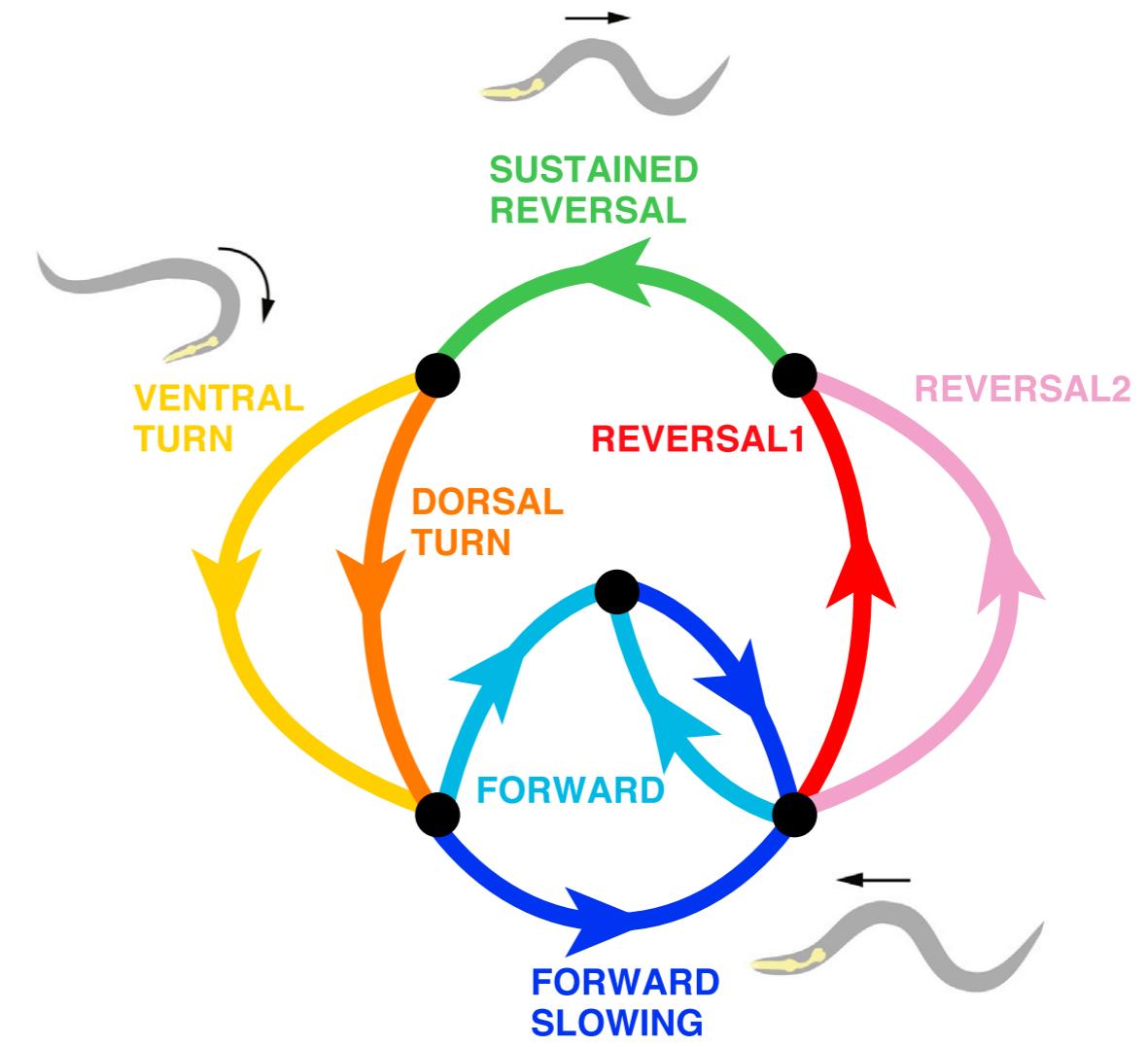
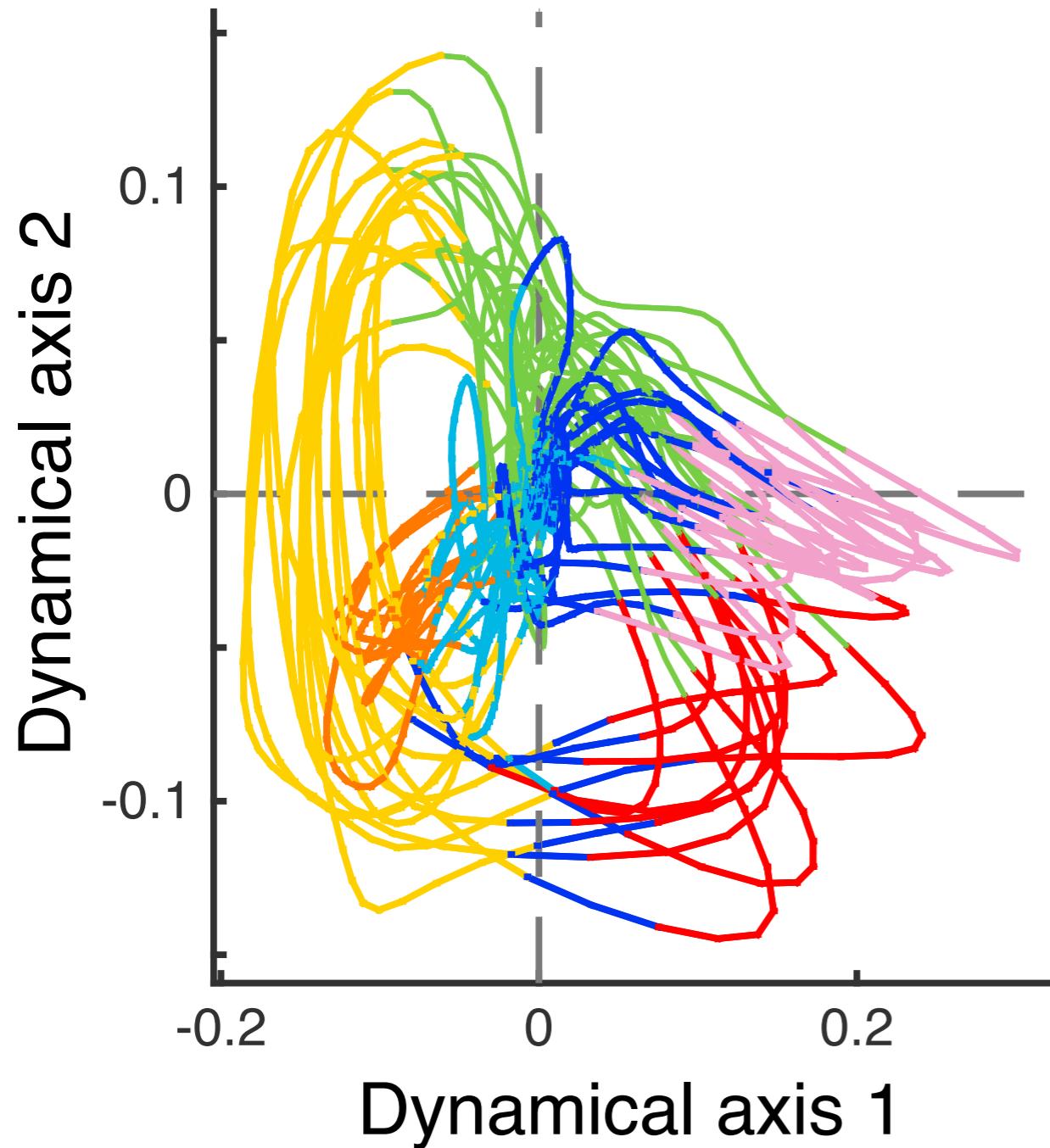


Brain-wide dynamics in *C. elegans*



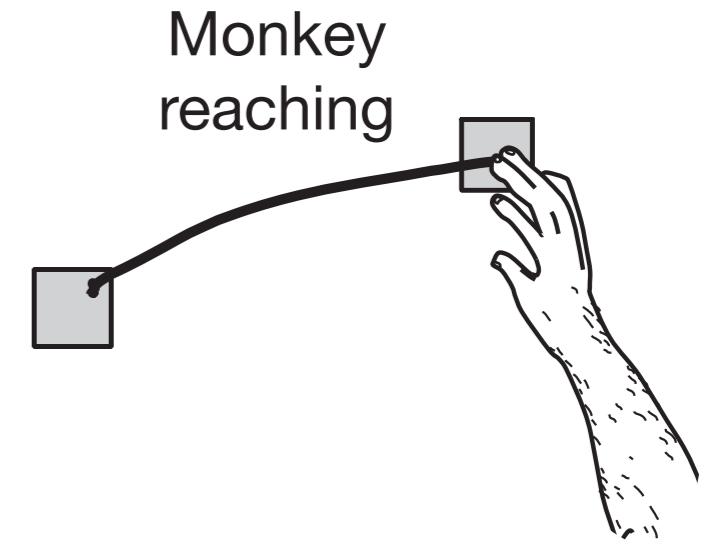
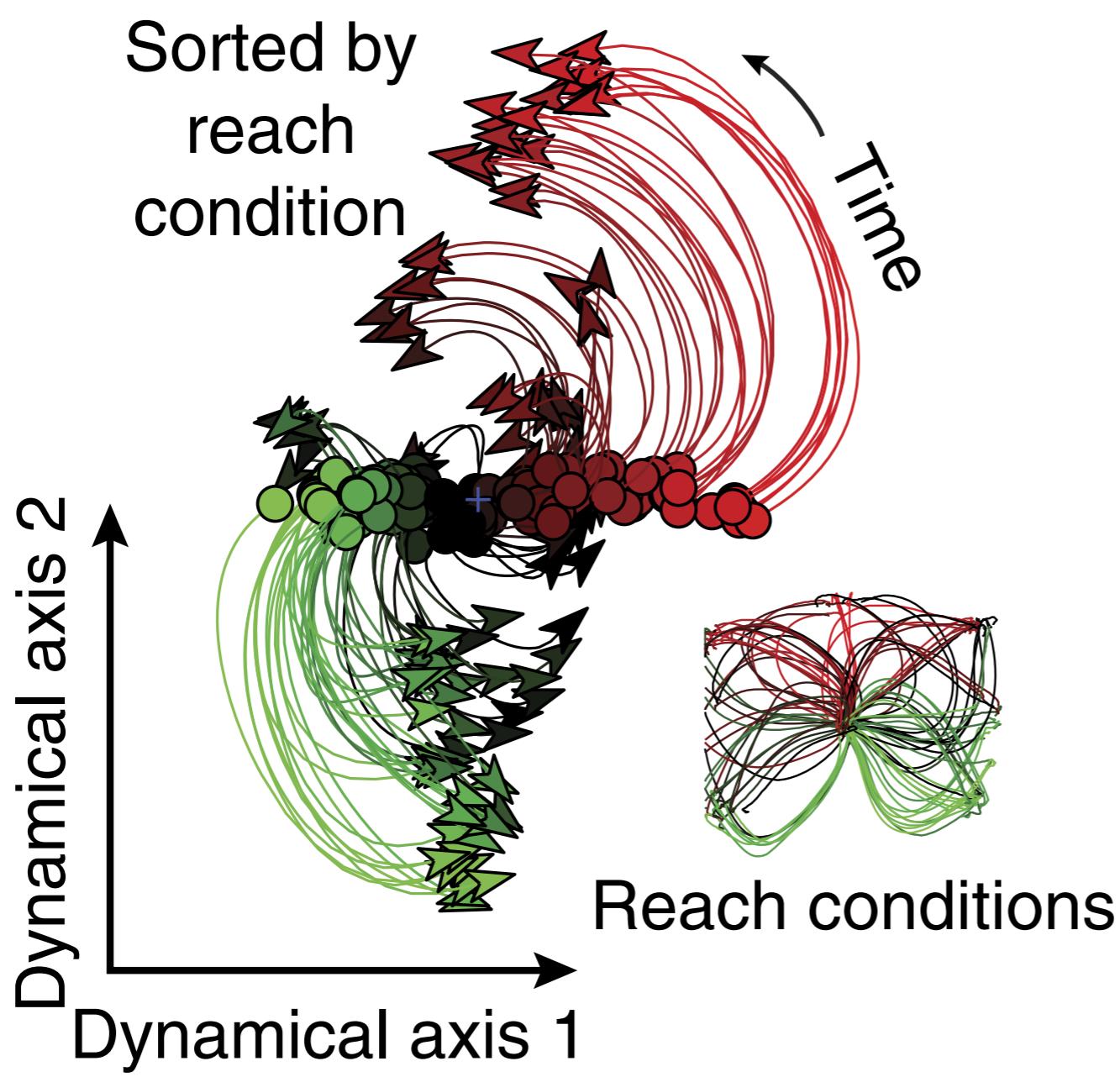
Kato et al, *Cell*, 2015

Brain-wide dynamics in *C. elegans*



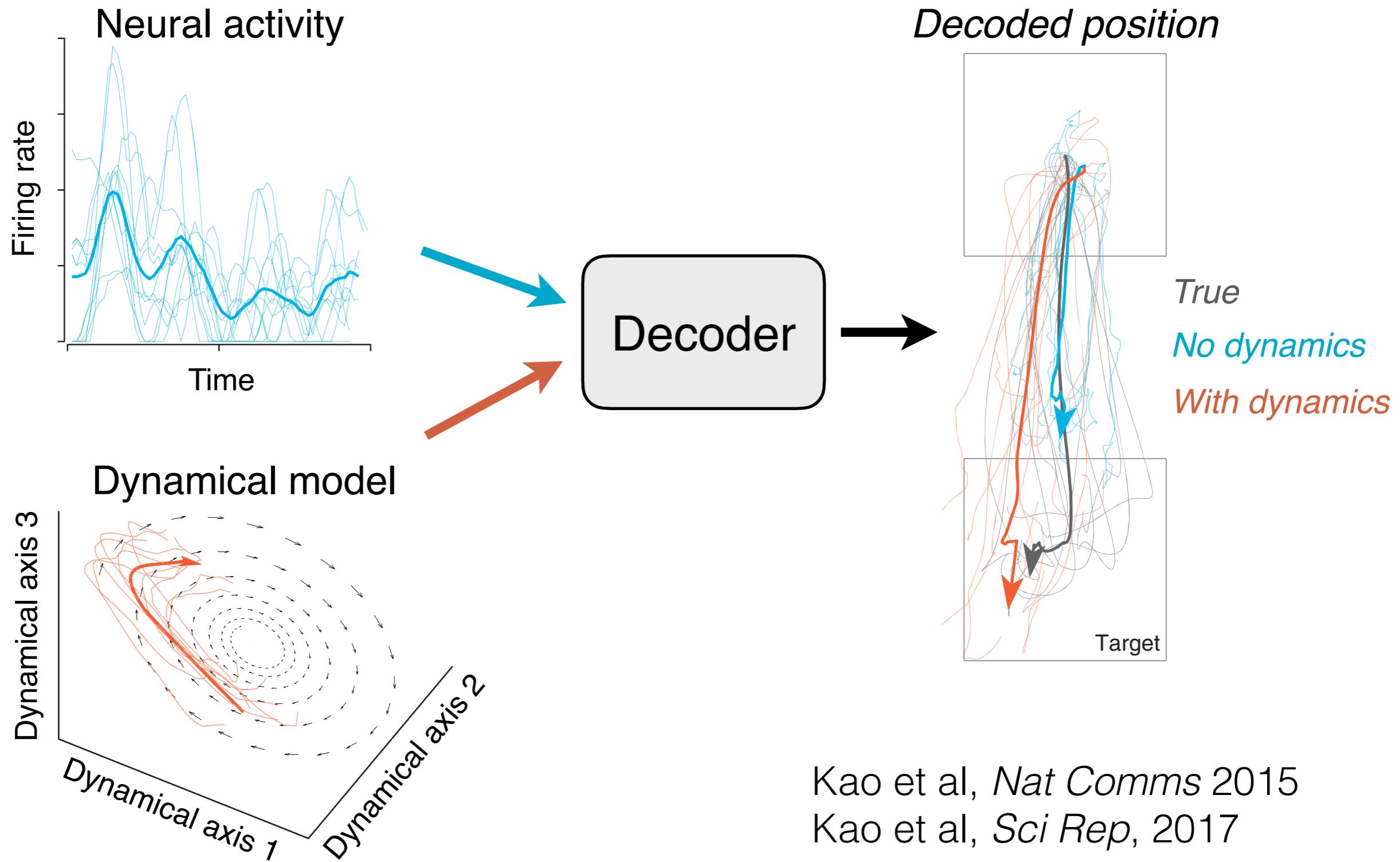
Kato et al, *Cell*, 2015

Neural population dynamics in the primate motor system



Churchland et al, *Nature*, 2012

Brain-machine interface enhanced by neural dynamics



Spontaneous activity in the brain

Video from Sofroniew et al, eLife 2016

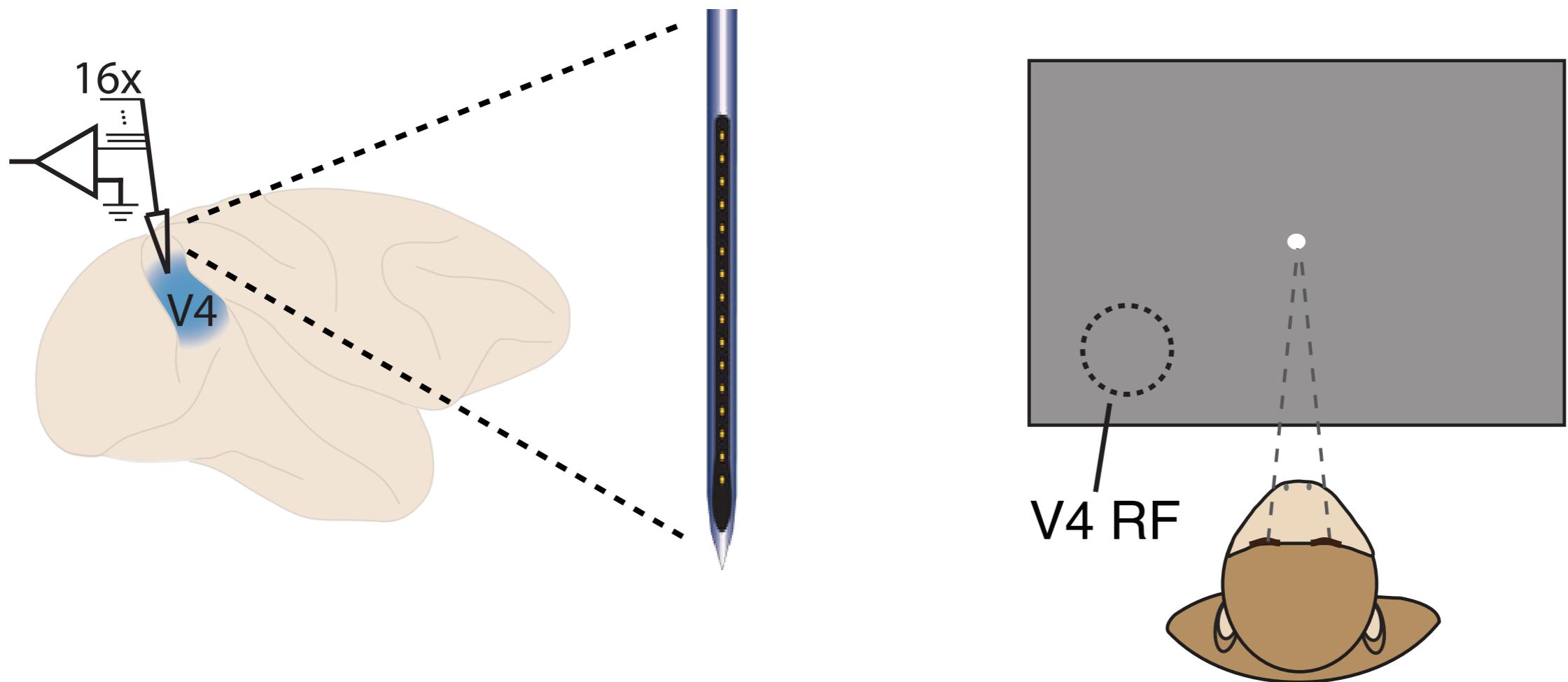
Neural population dynamics

- linked to sensorimotor computations
- related to behavior on single trials
- stable over time
- invariant to the number of recorded neurons
- could potentially account for correlated variability

Outline

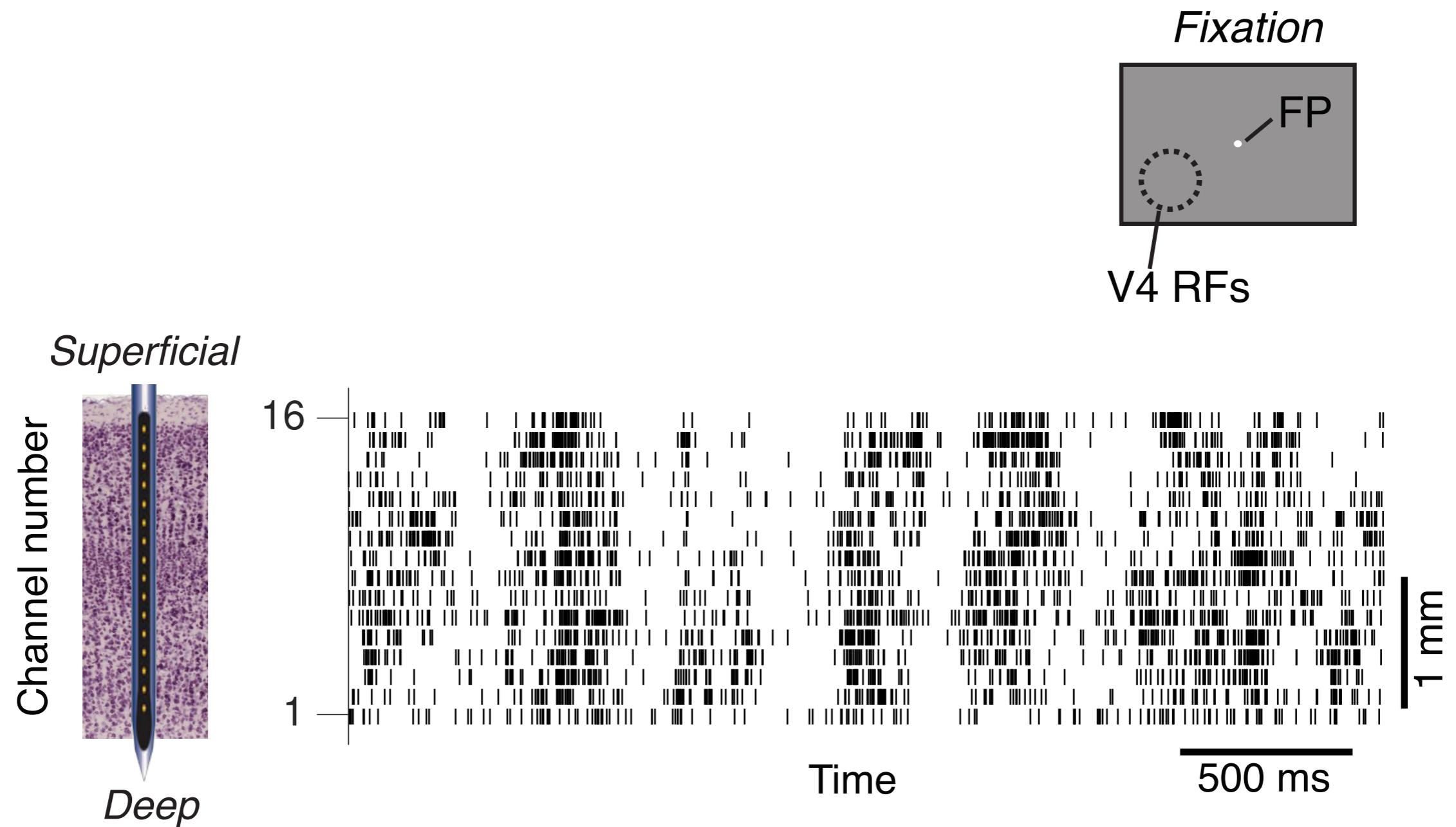
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Laminar recordings from single cortical columns



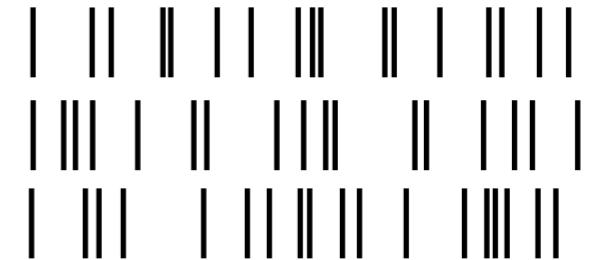
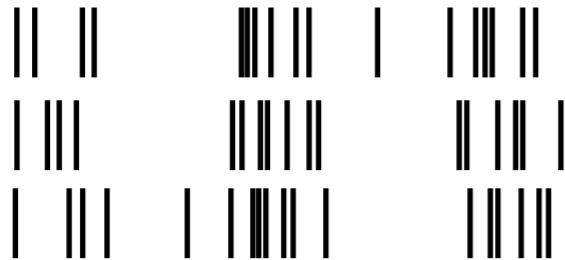
Nick Steinmetz, Tirin Moore

Spontaneous On-Off transitions in spiking activity of single columns



Engel et al, Science, 2016

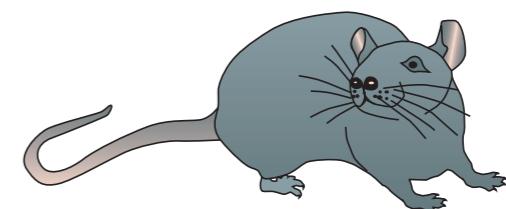
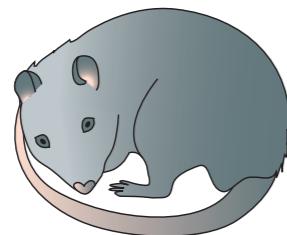
Cortical state dynamics



Global arousal

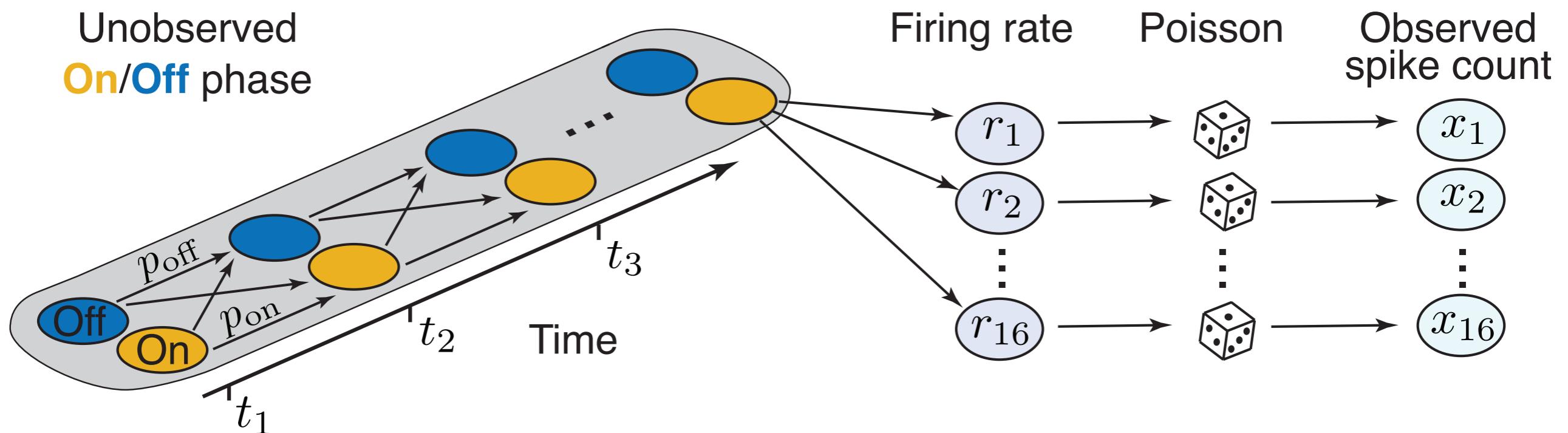
Slow-wave sleep
Anesthesia

Awake

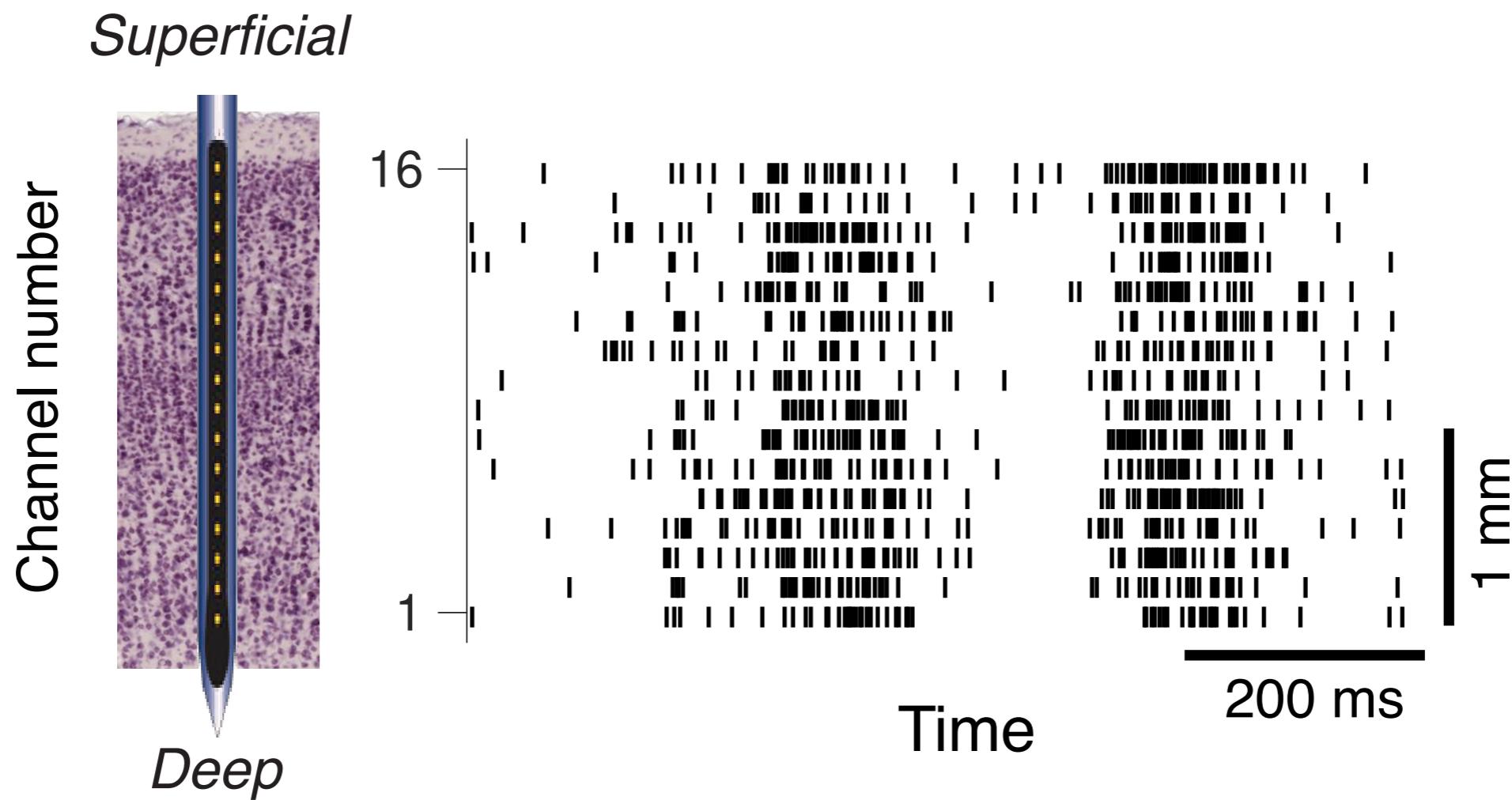


How are the On-Off dynamics related to changes in global arousal?

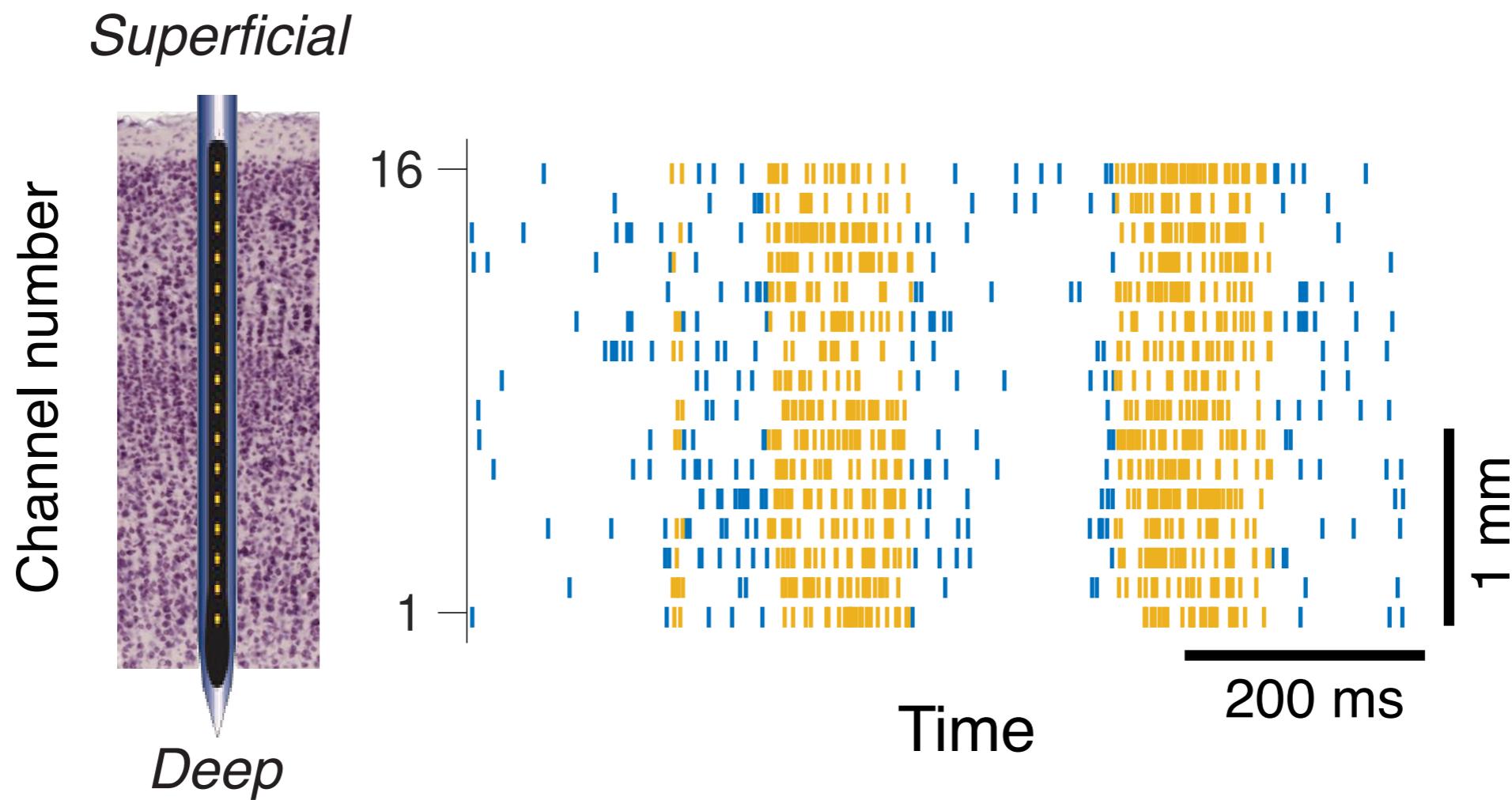
Hidden Markov Model of On-Off dynamics



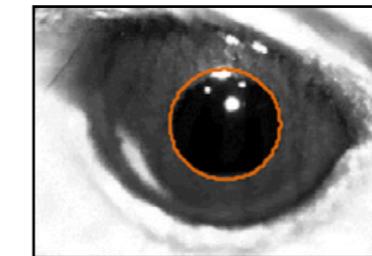
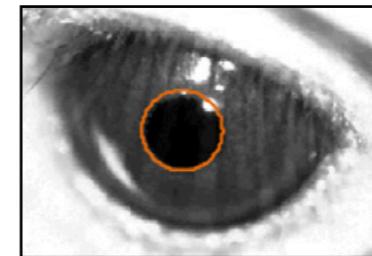
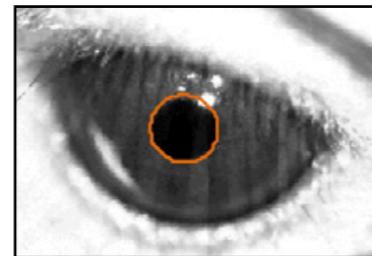
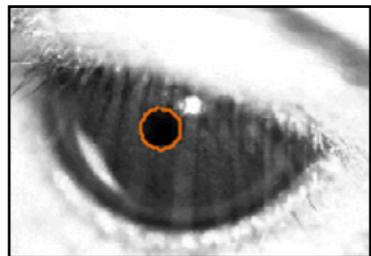
HMM decodes transition times on single trials



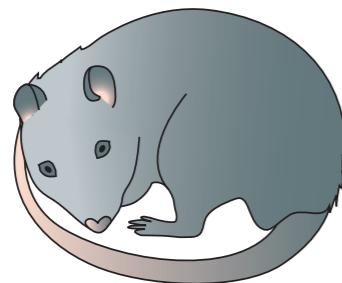
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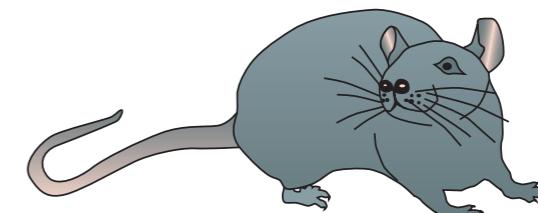
Continuum of arousal states is reflected in pupil size



Global arousal



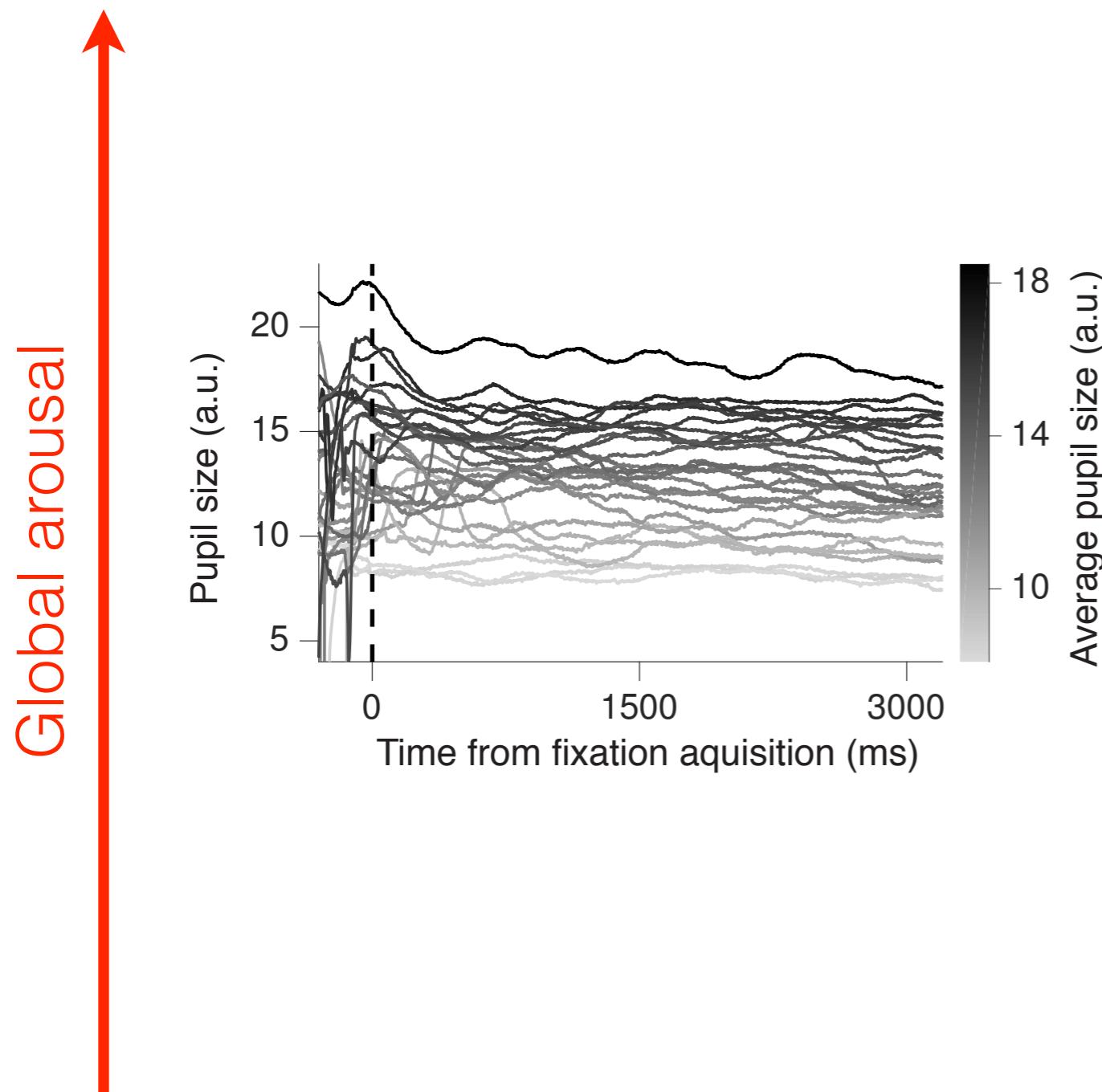
Slow-wave sleep
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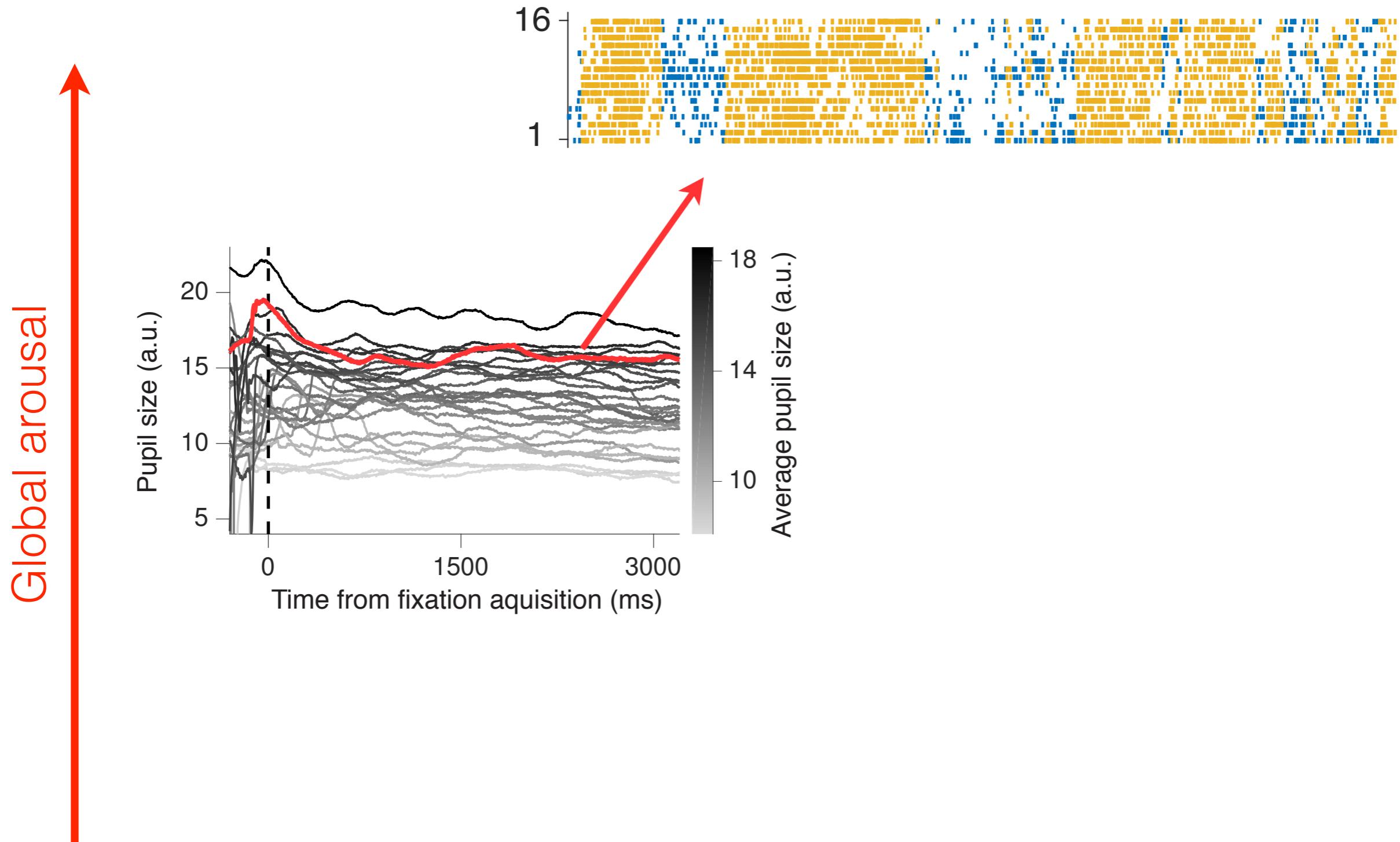
Alert
Actively behaving

Reimer et al, Neuron, 2014
Vinck et al., Neuron, 2015

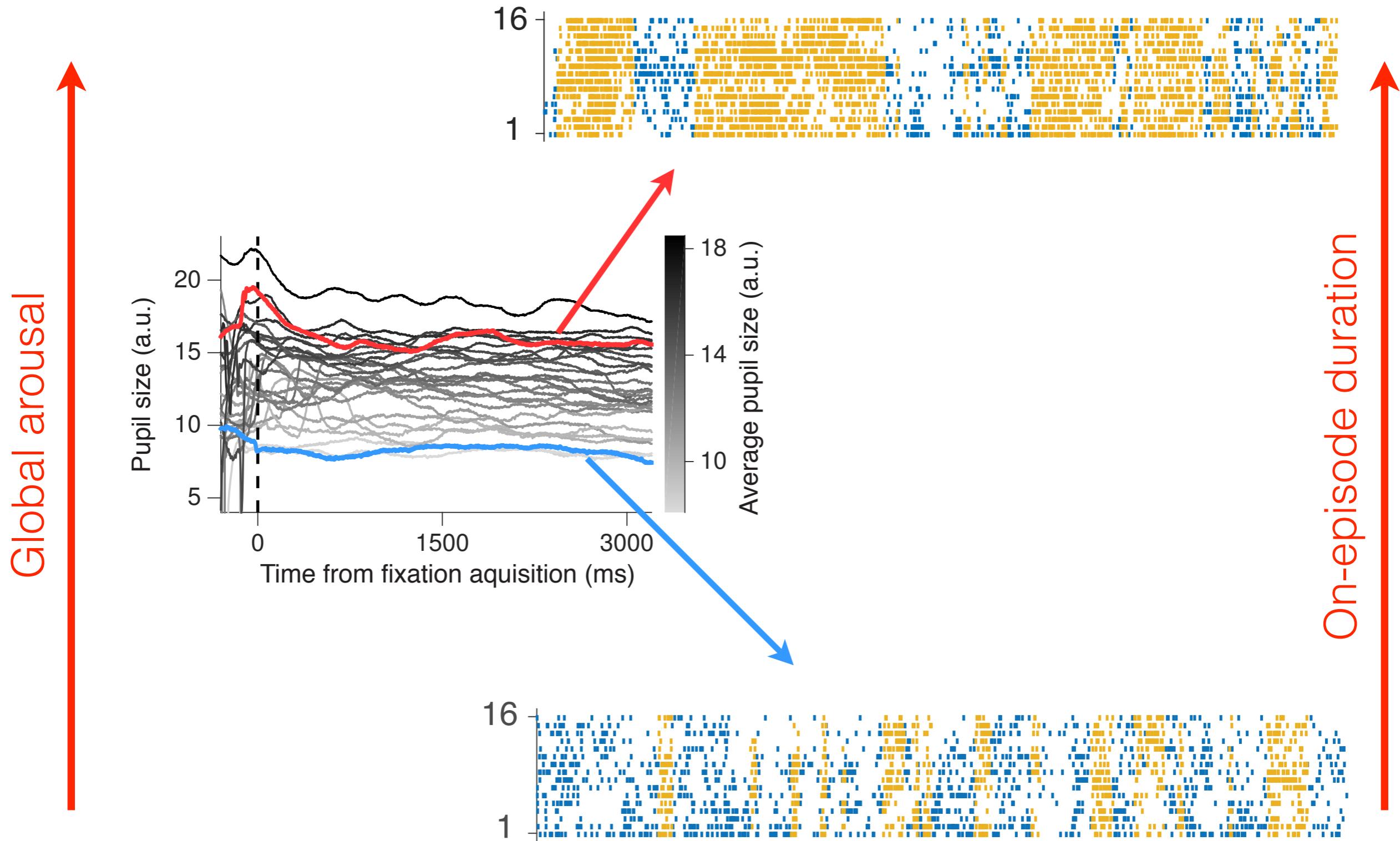
On-Off dynamics reflect global arousal



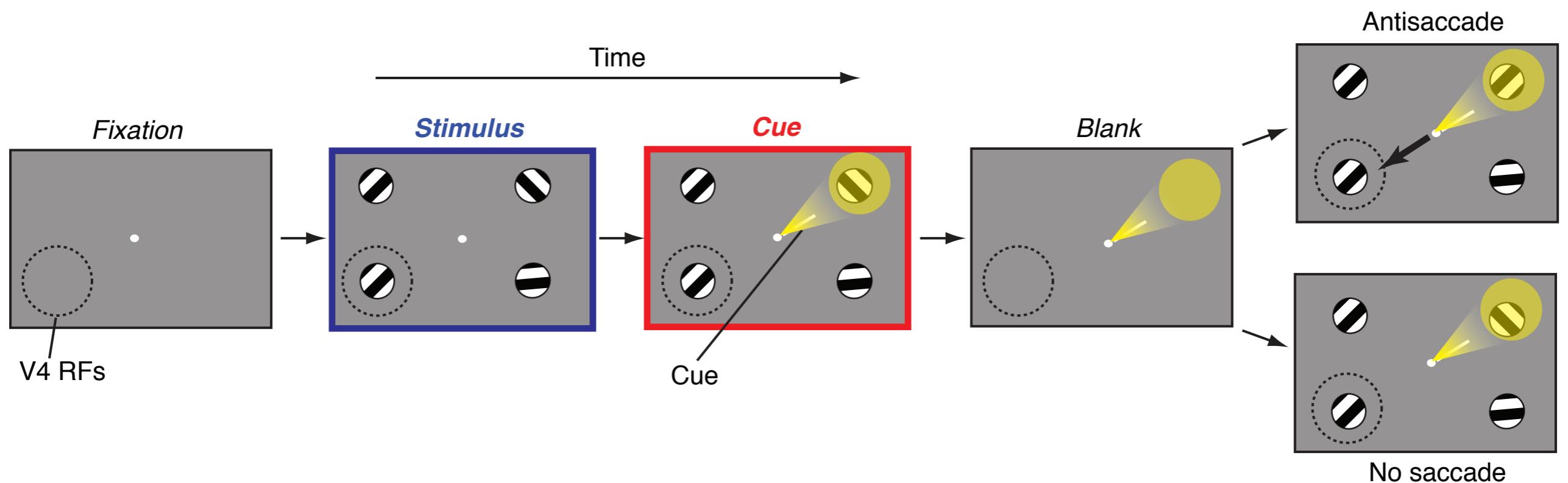
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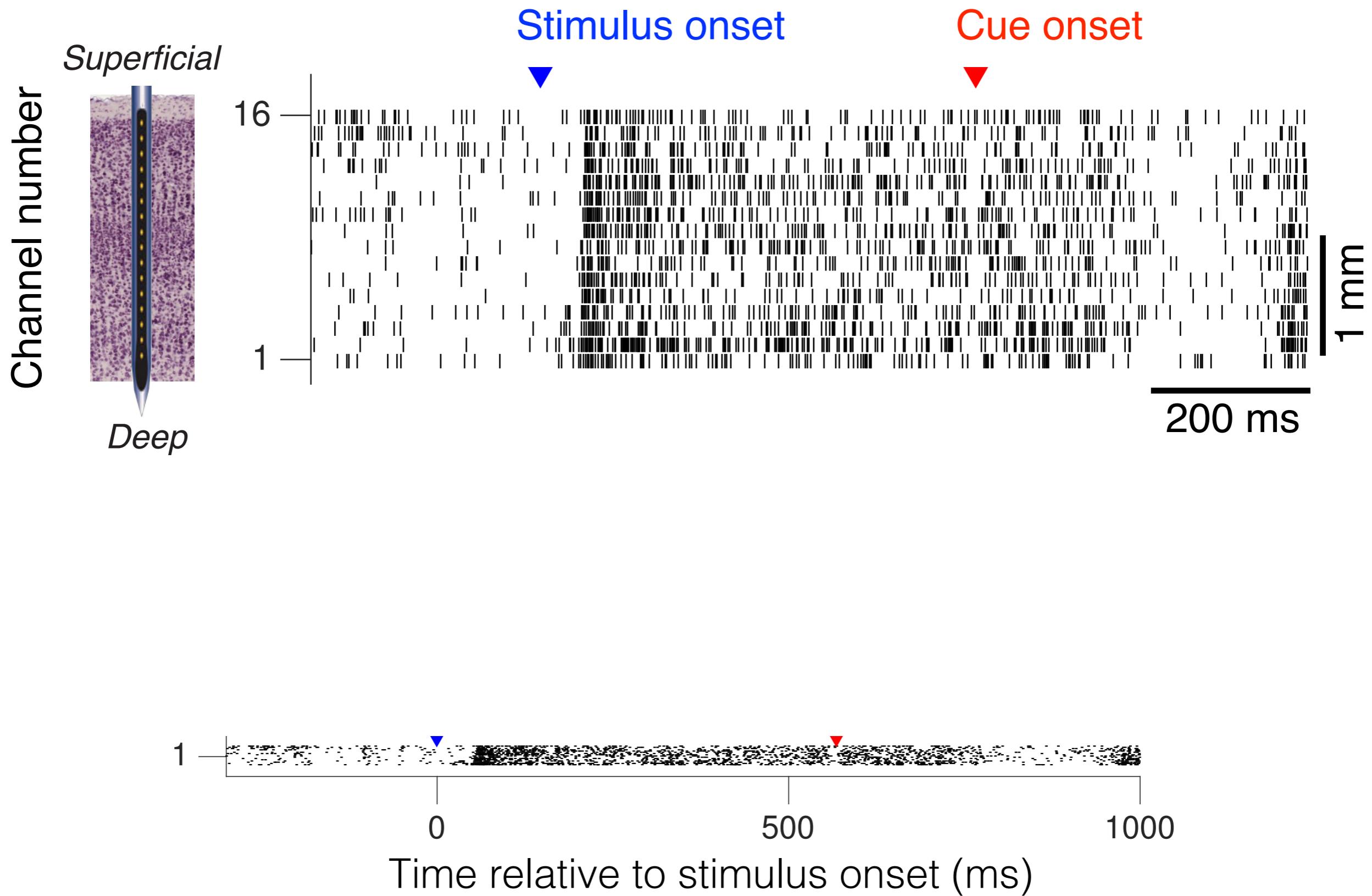
On-Off dynamics reflect global arousal



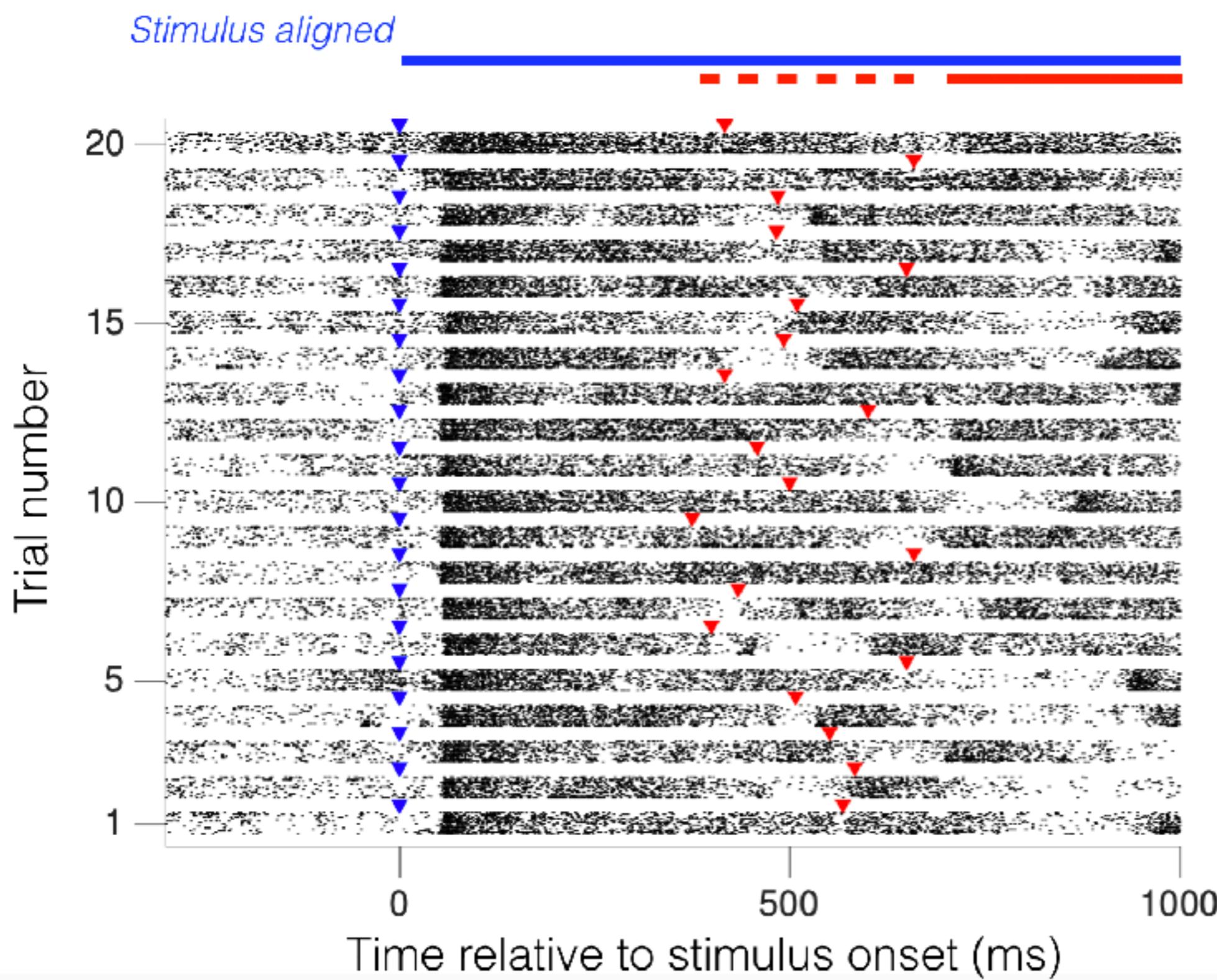
Attention task



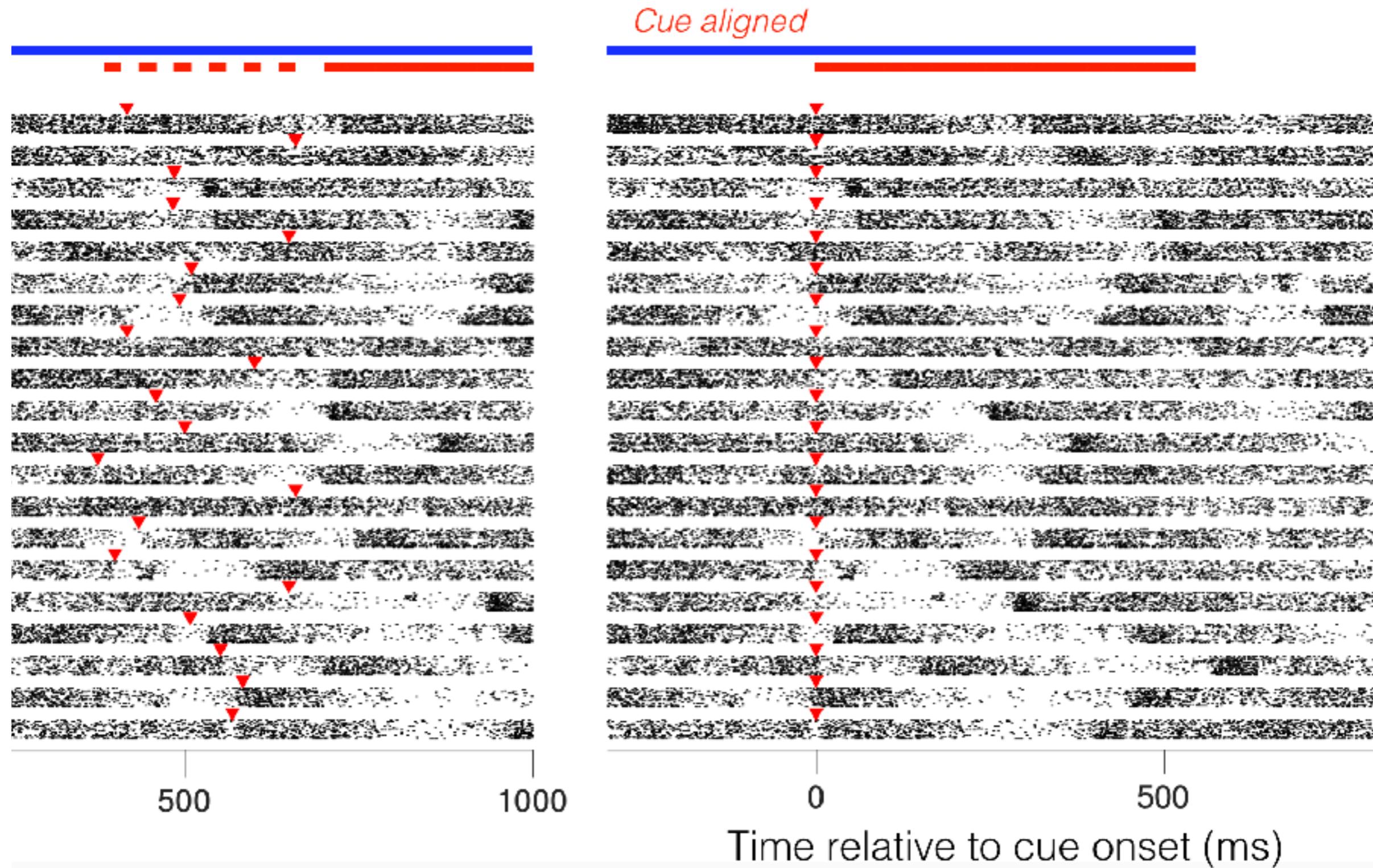
On-Off transitions during attention task



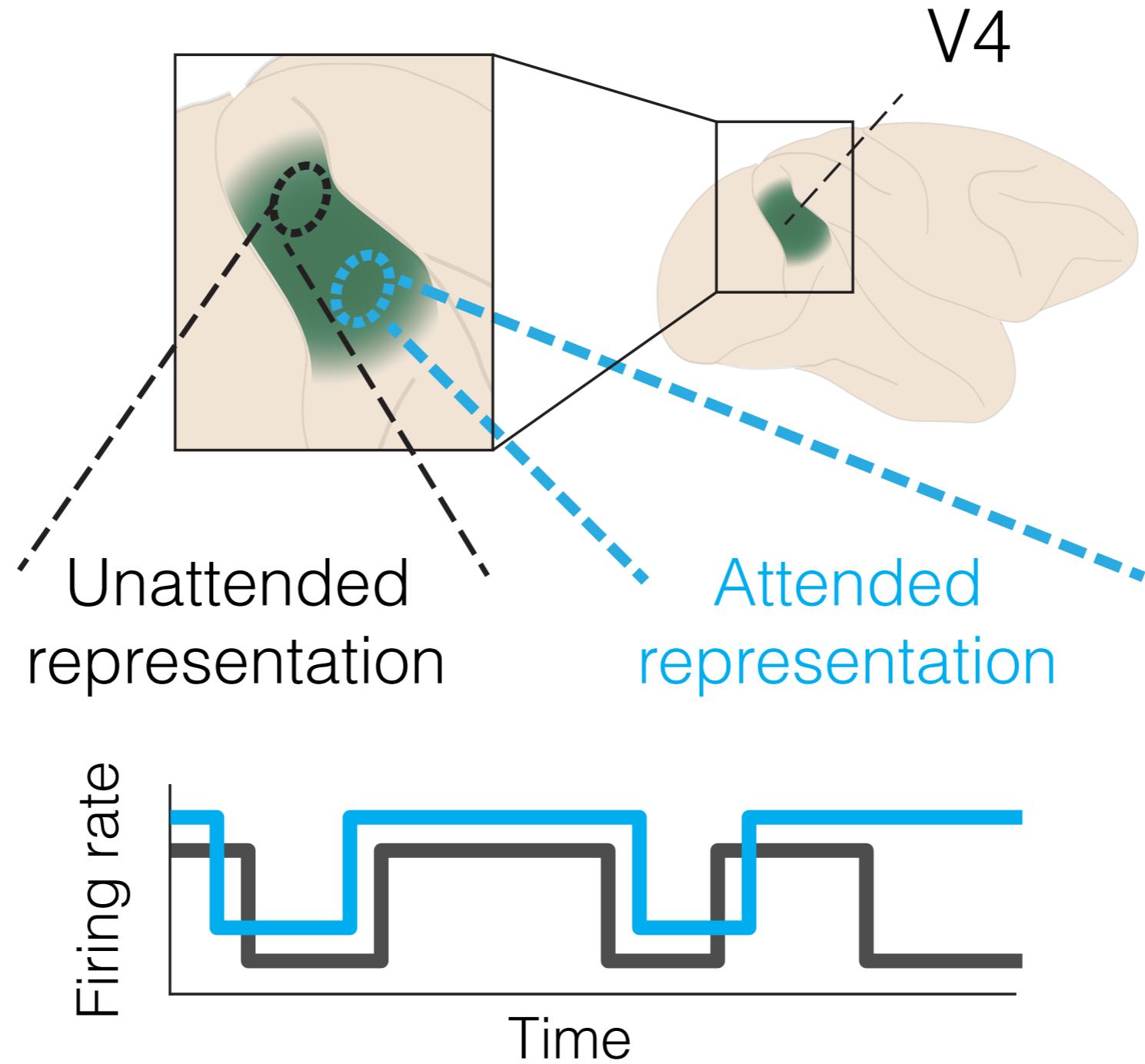
On-Off transitions during attention task



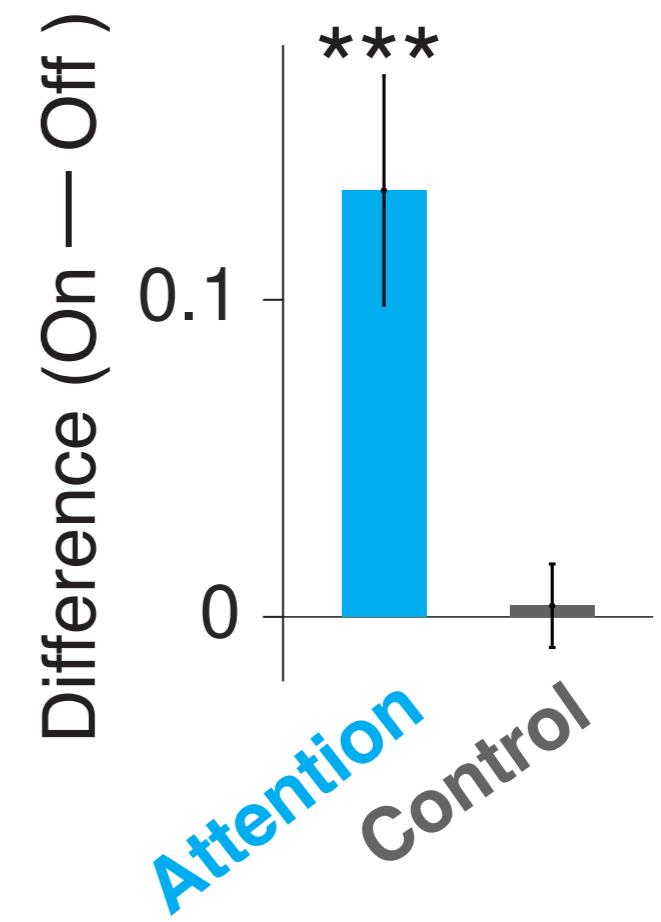
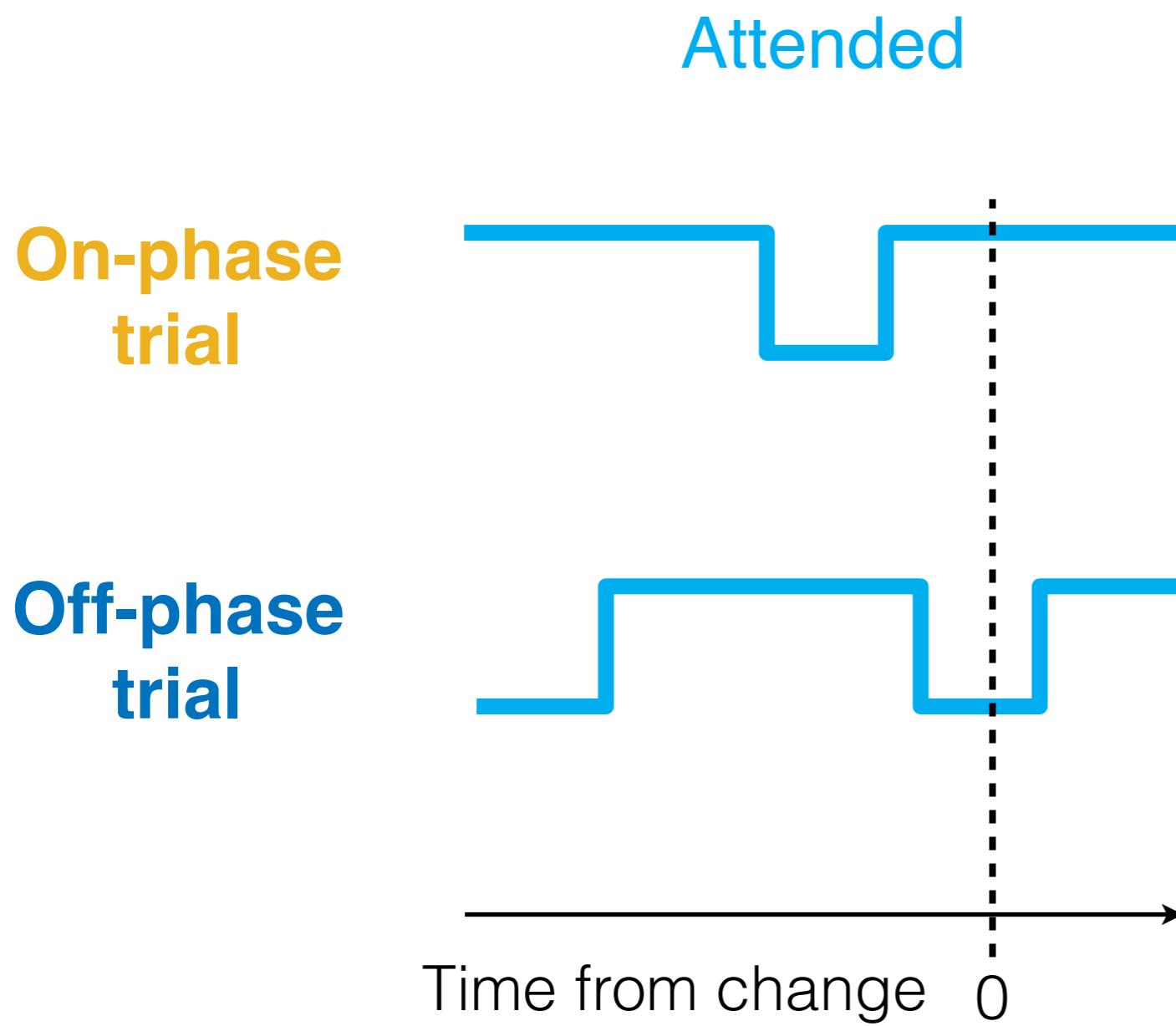
On-Off transitions during attention task



Local modulation of cortical state

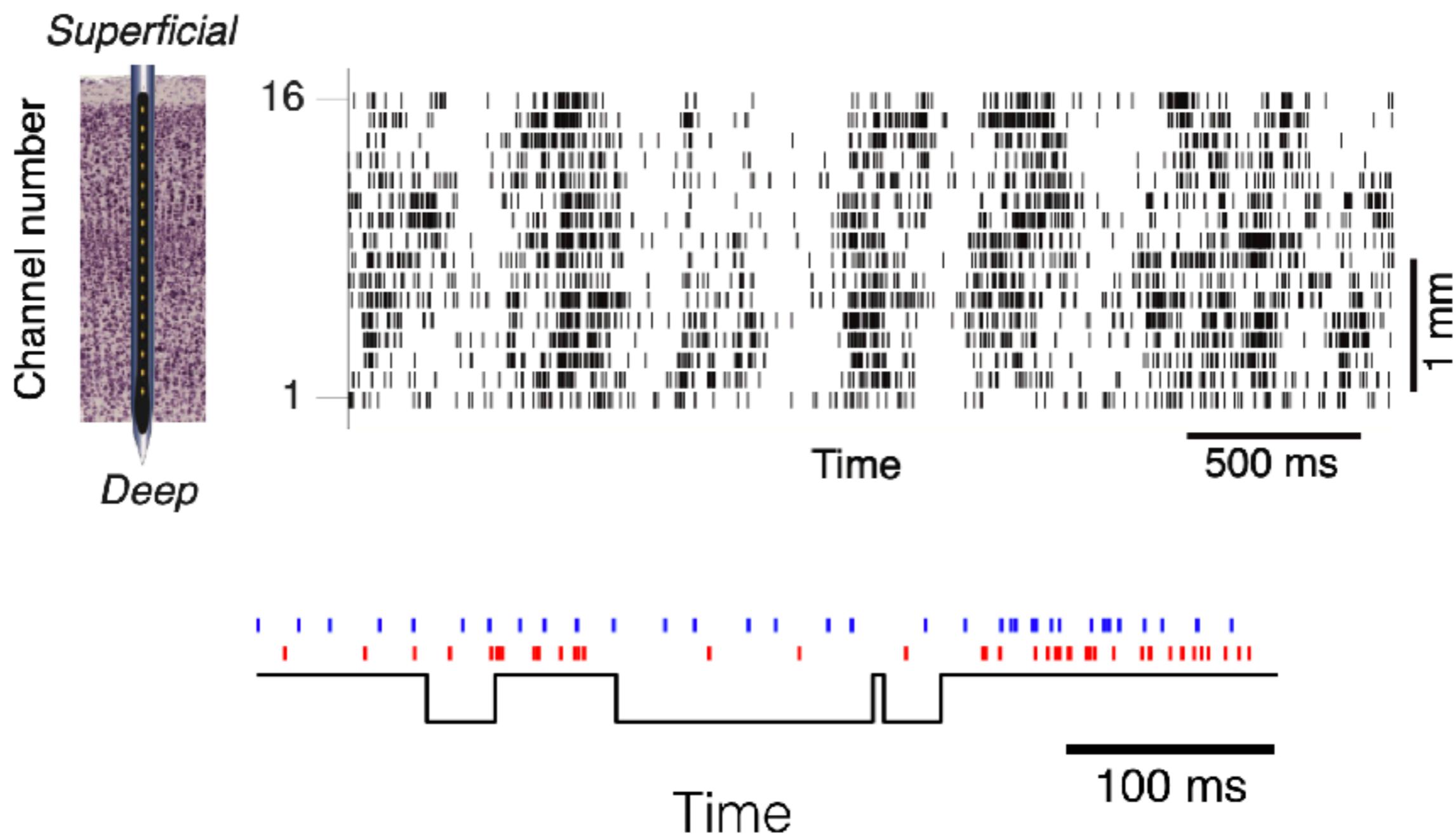


Instantaneous On-Off phase predicts behavioral performance

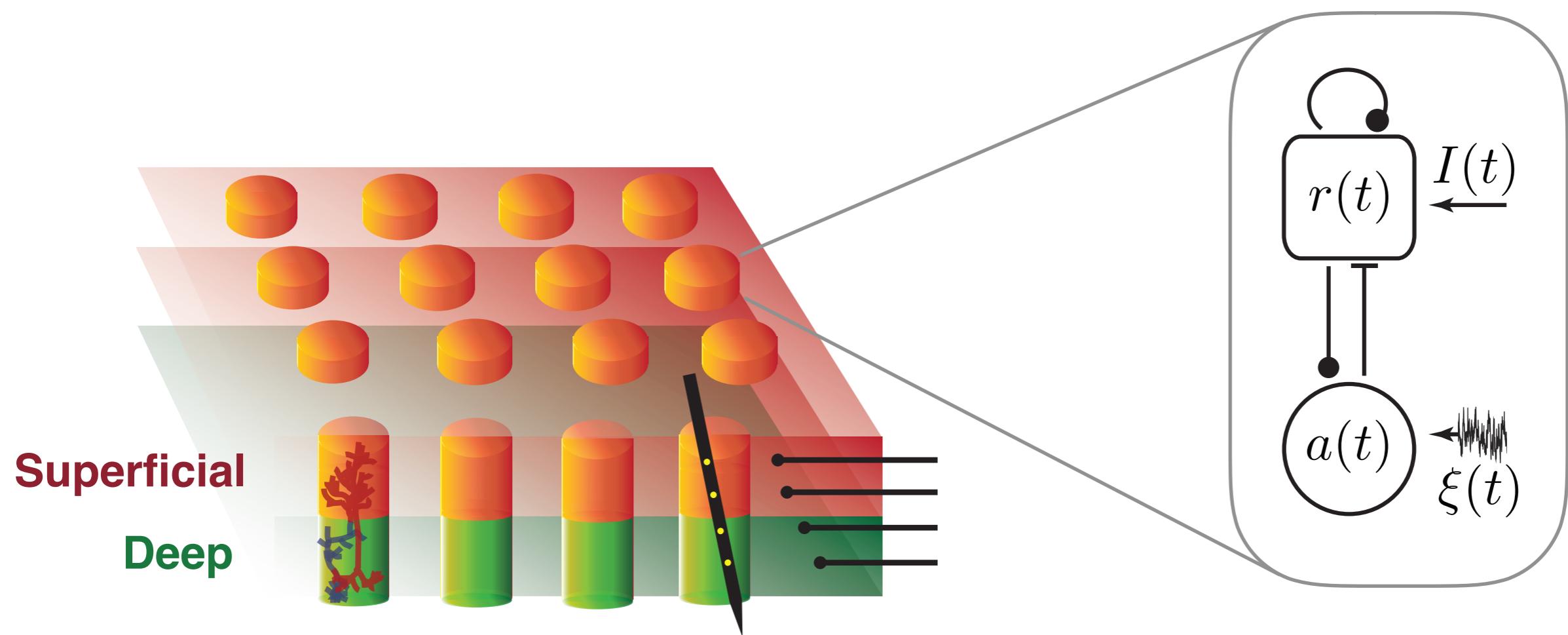


Engel et al, Science, 2016

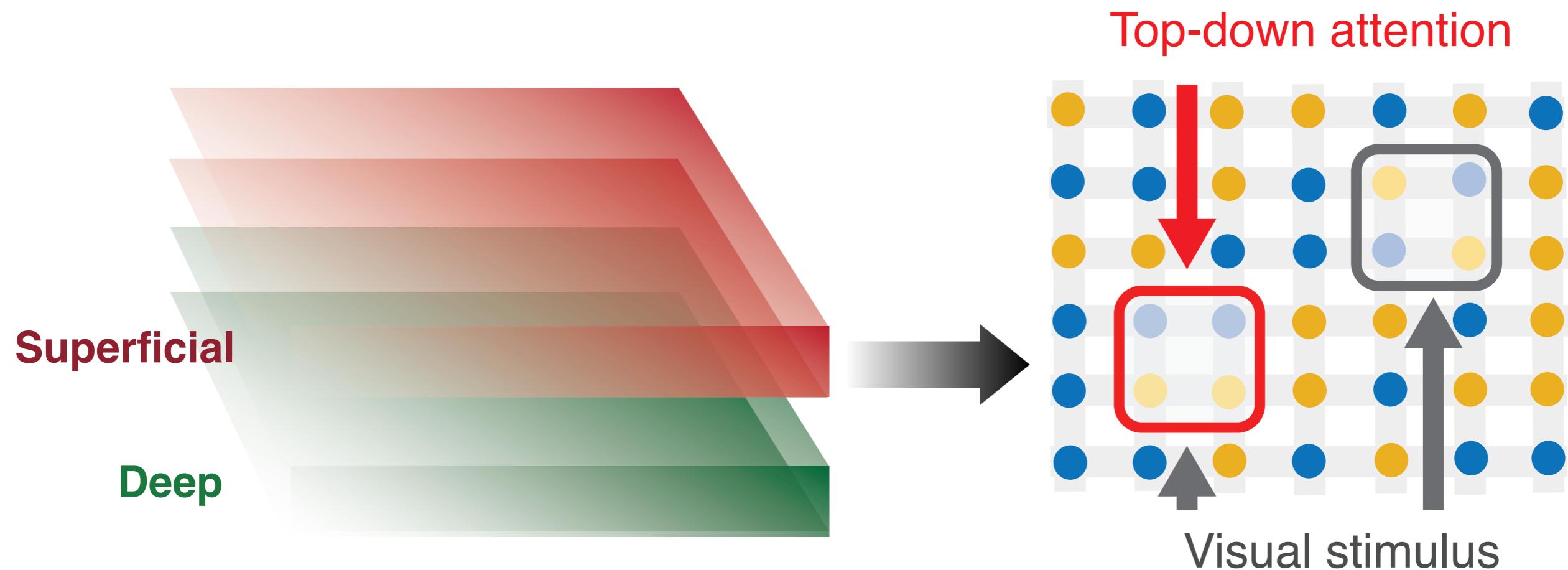
Linking noise correlations and spatiotemporal On-Off dynamics



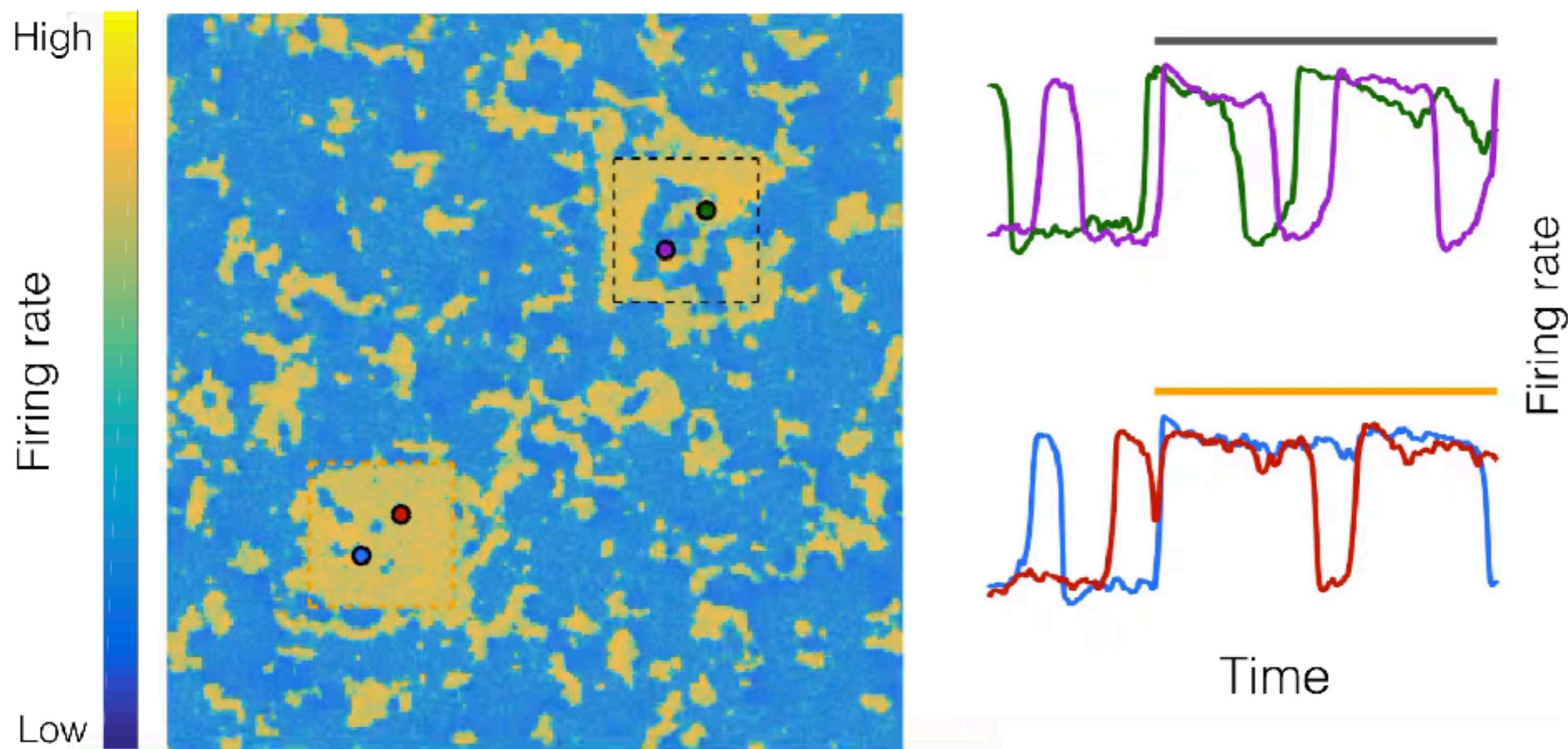
Network model of interacting columns



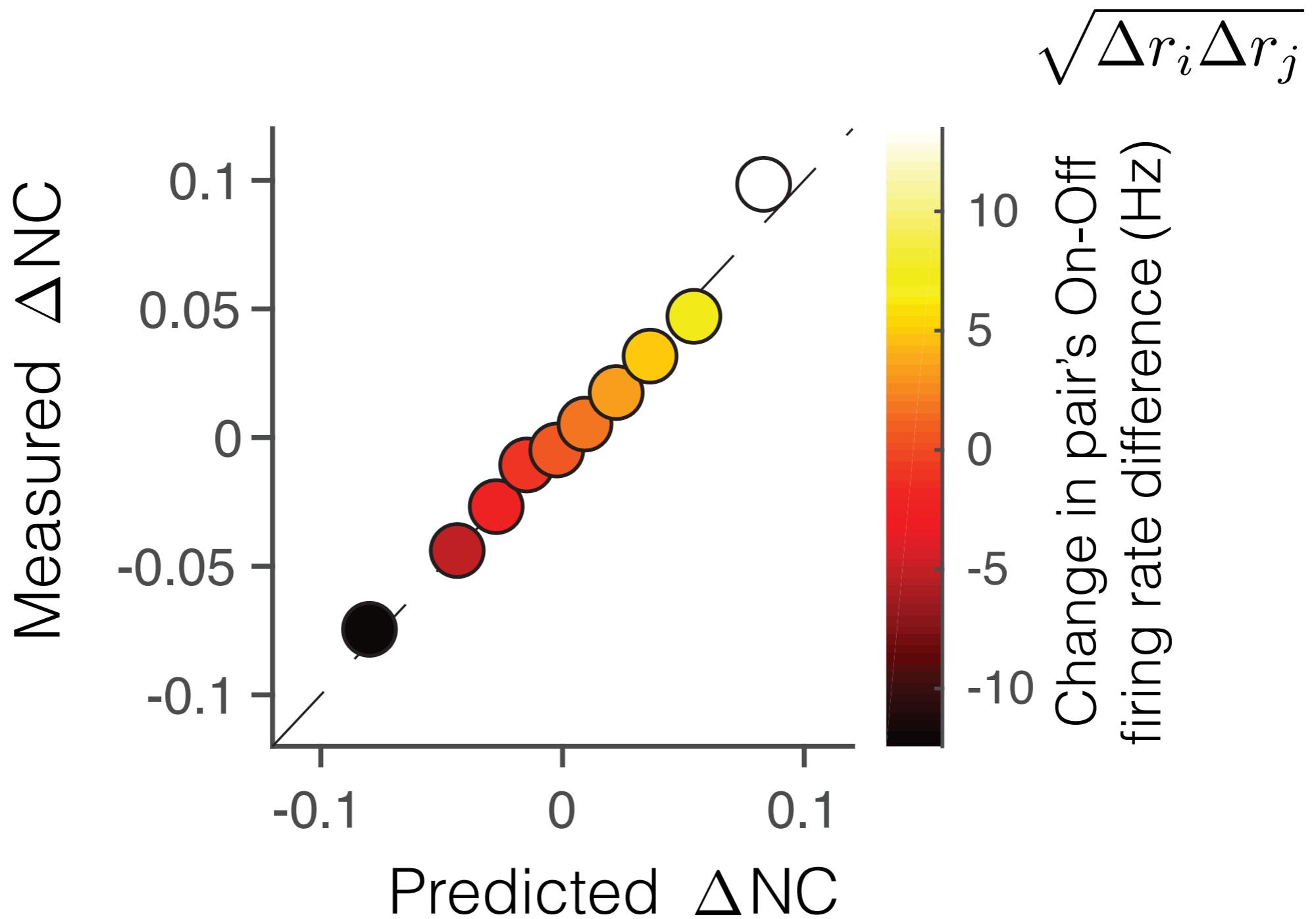
Network model of interacting columns



Spatiotemporal On-Off dynamics in the network model



On-Off dynamics account for noise correlations within column



Spatiotemporal dynamics in the visual cortex

- On-Off dynamics synchronous across layers
- modulated globally by arousal and locally during selective attention
- account for correlated variability

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Limitations of existing methods for neural population dynamics

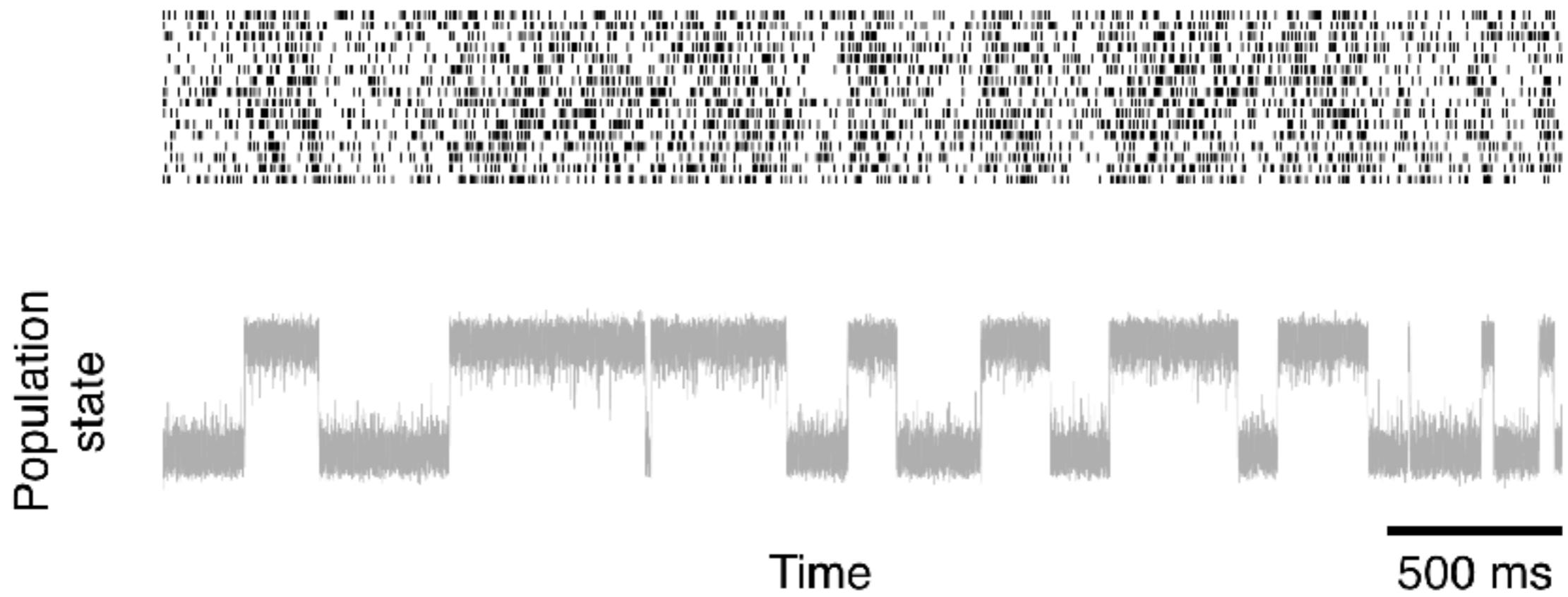
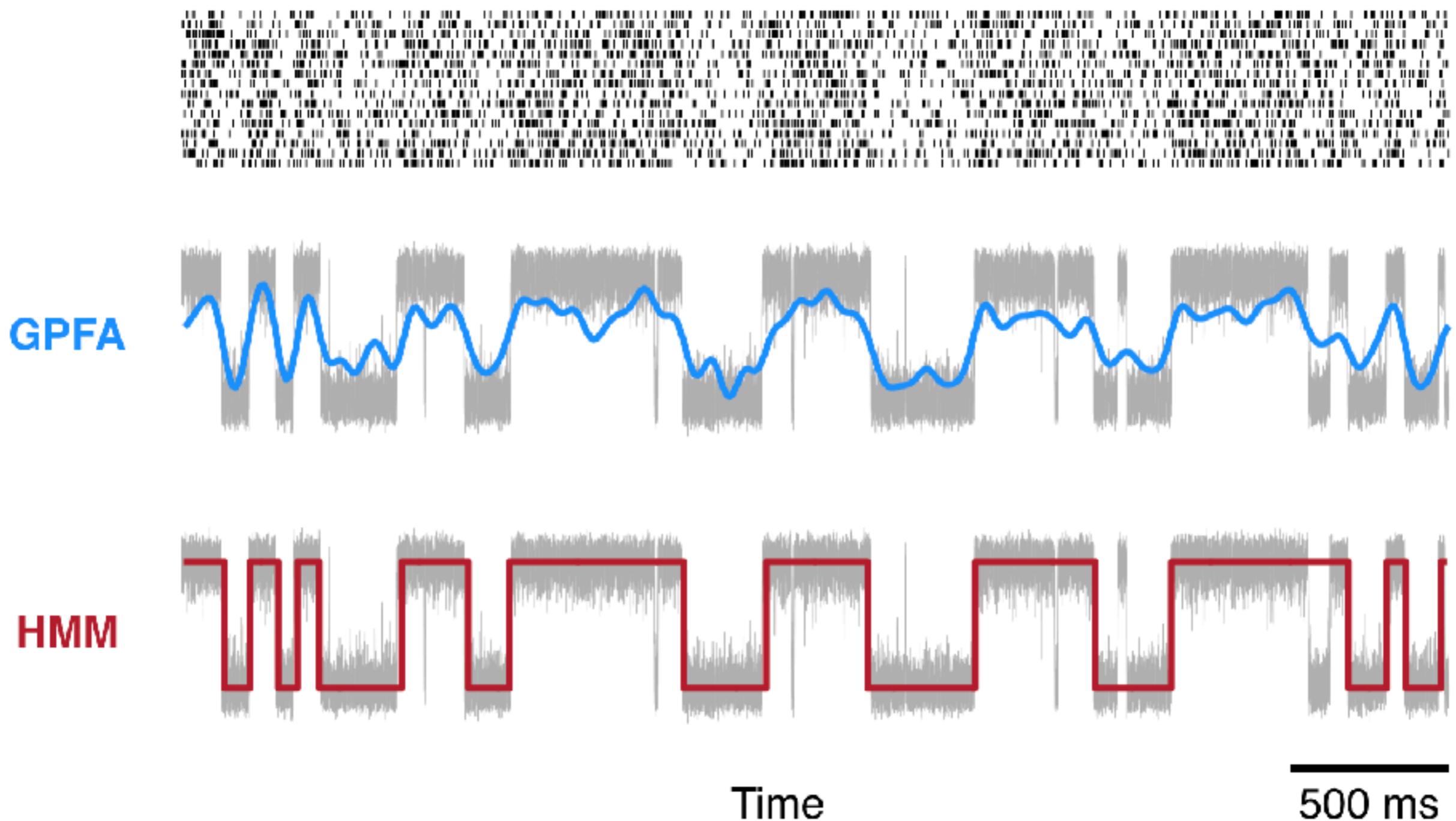
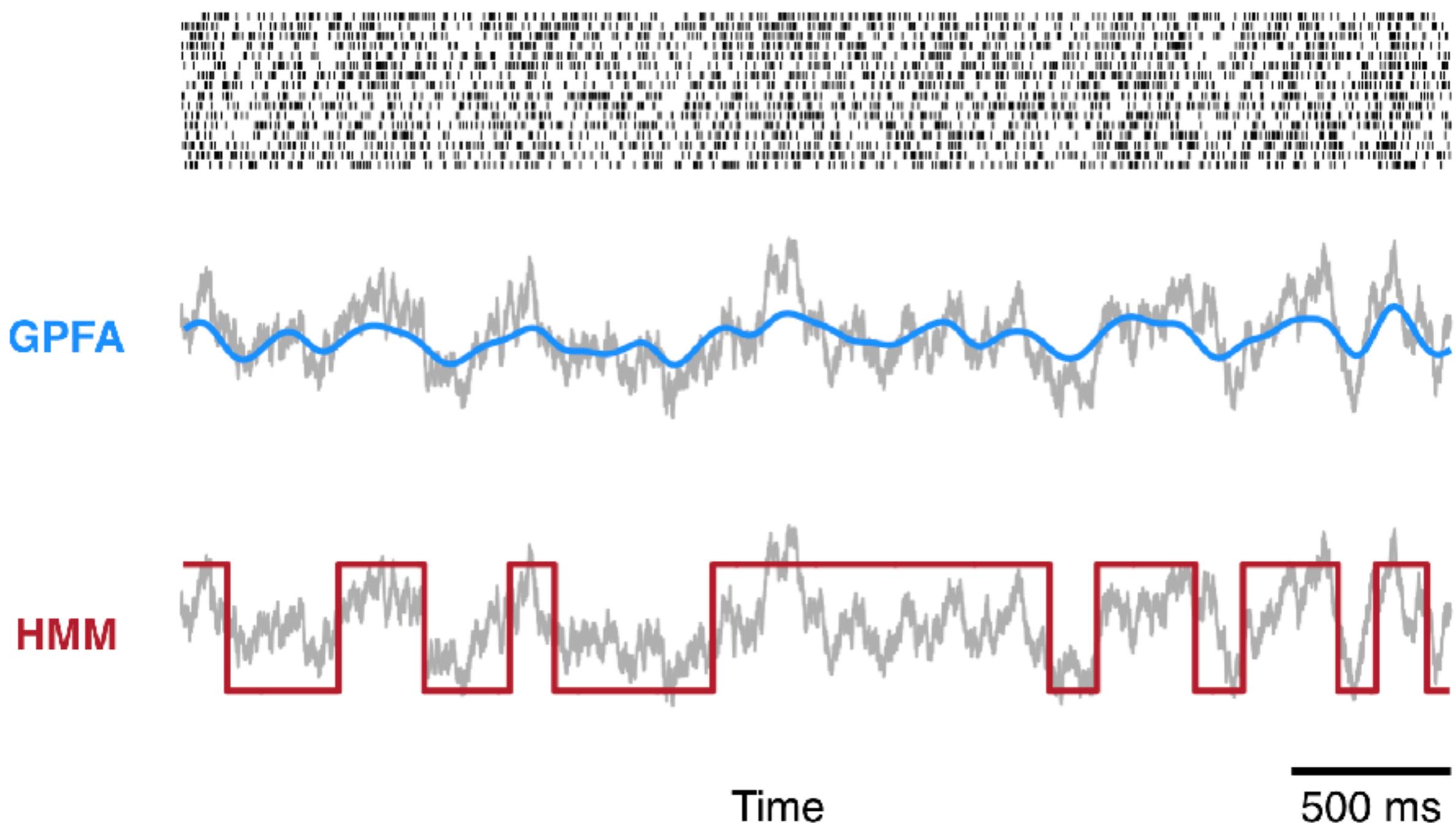


Illustration with synthetic data

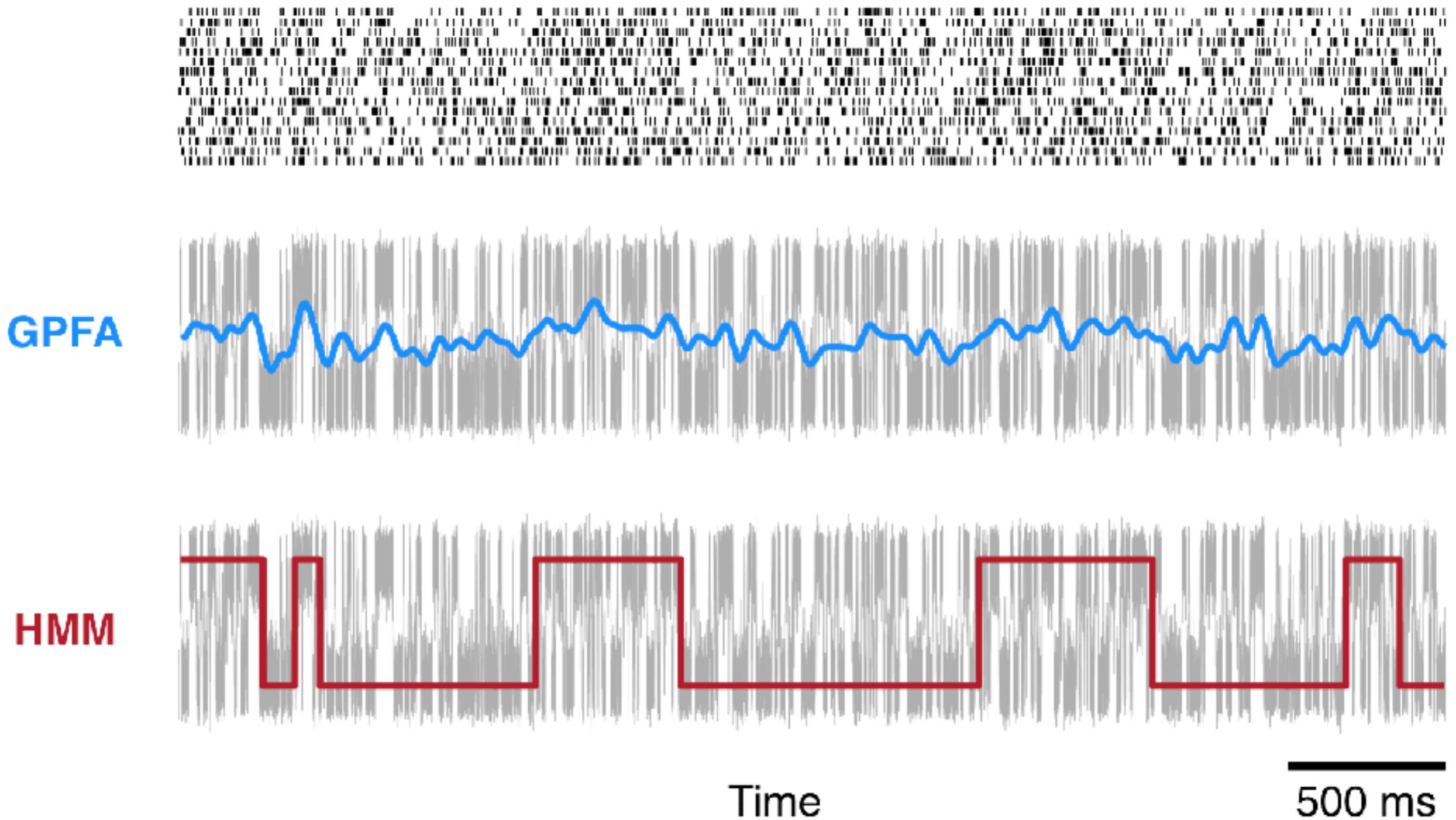
Existing methods fit data with
ad hoc dynamical models



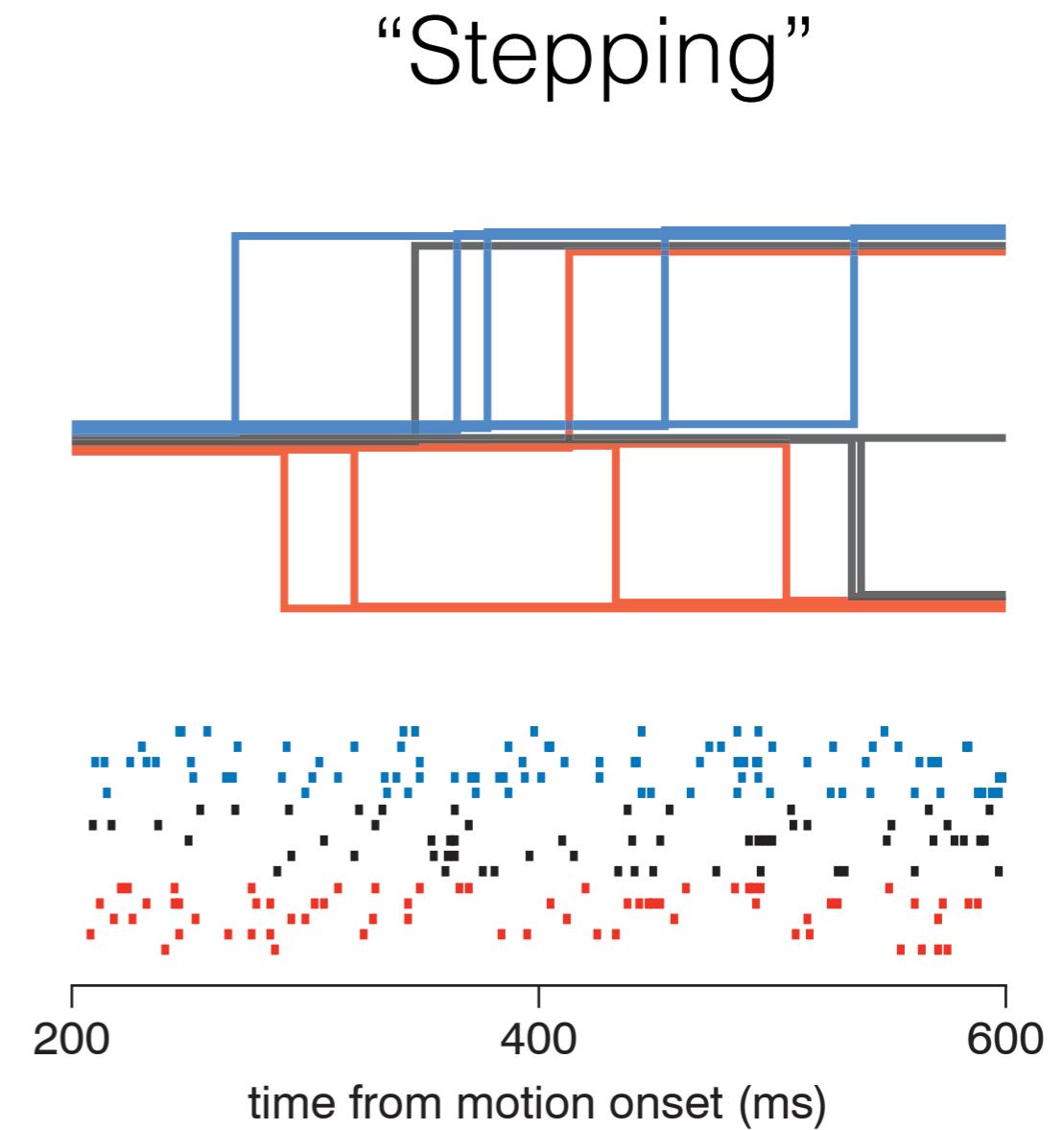
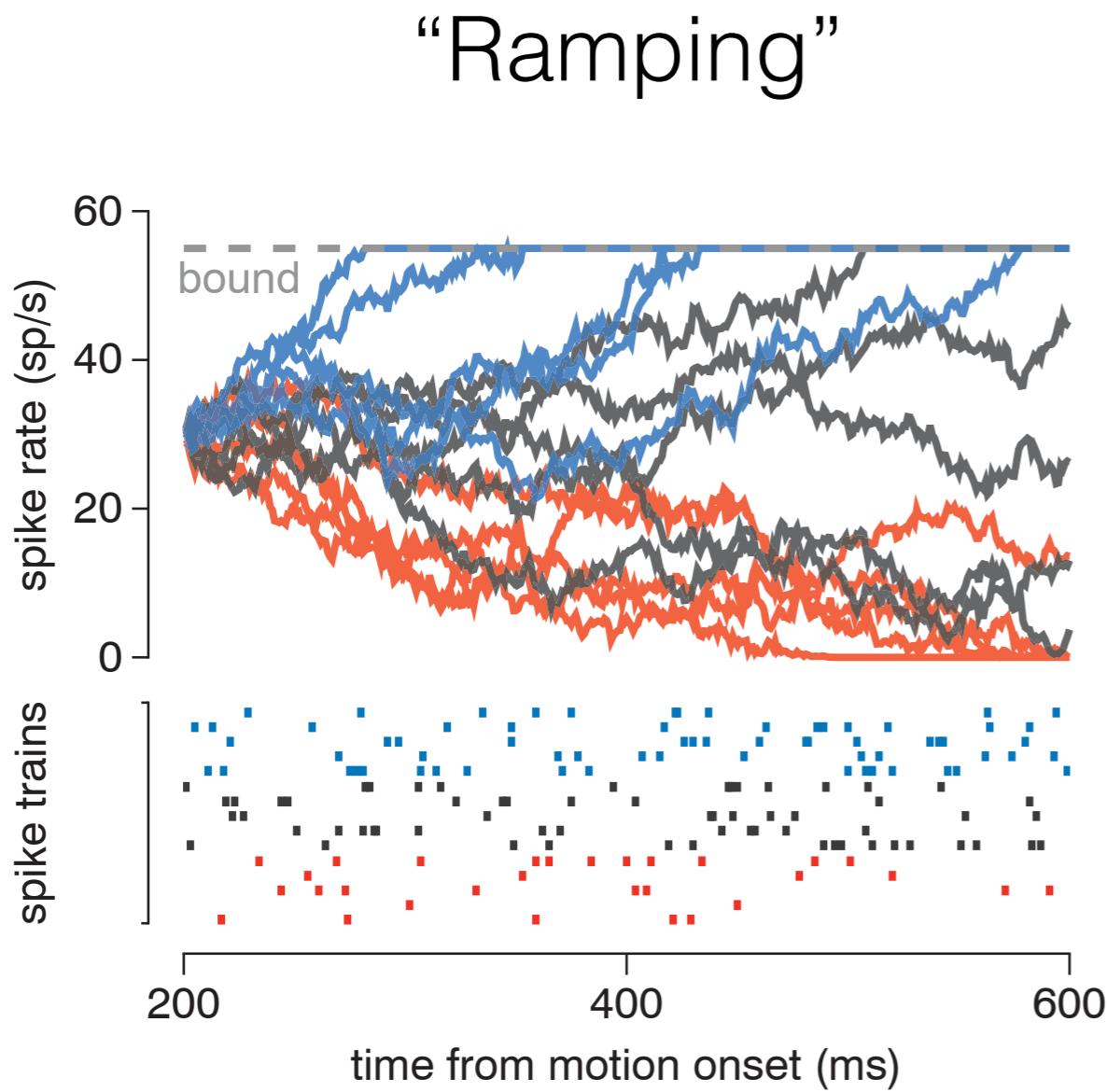
Ad hoc models can fit any data



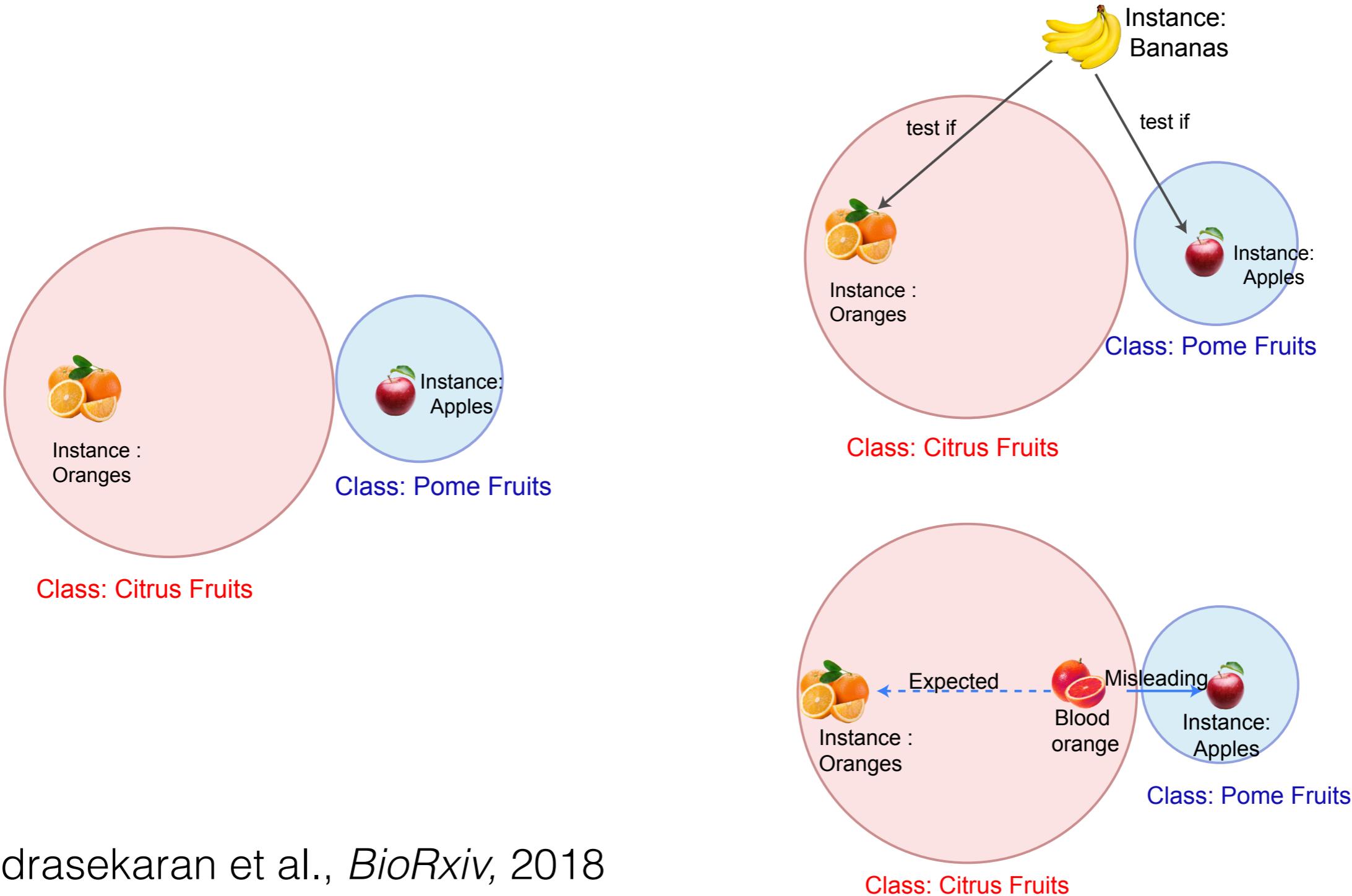
Models fail to capture fast dynamics due to spike binning



Hypothetical decision-related responses on single trials

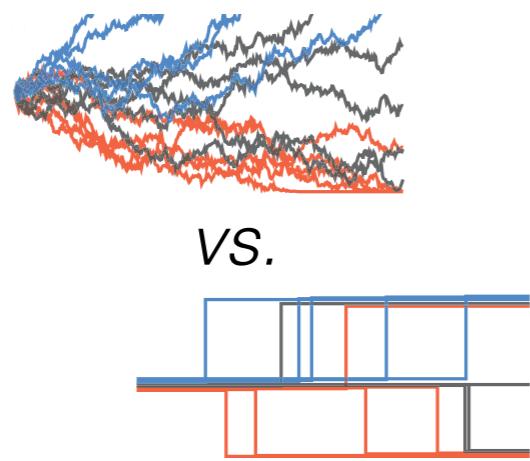


Brittleness of model selection

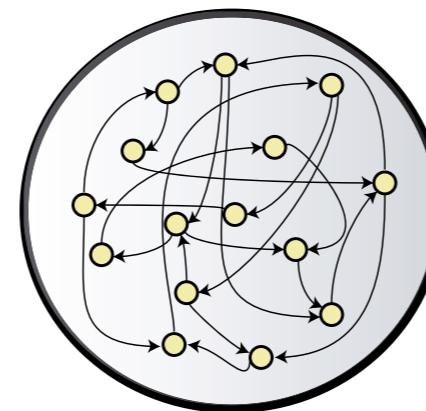


Approaches for inferring neural dynamics

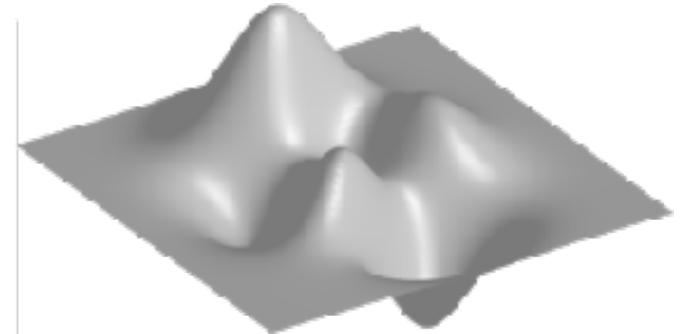
Parametric



Overparametrized



Non-parametric



Capacity

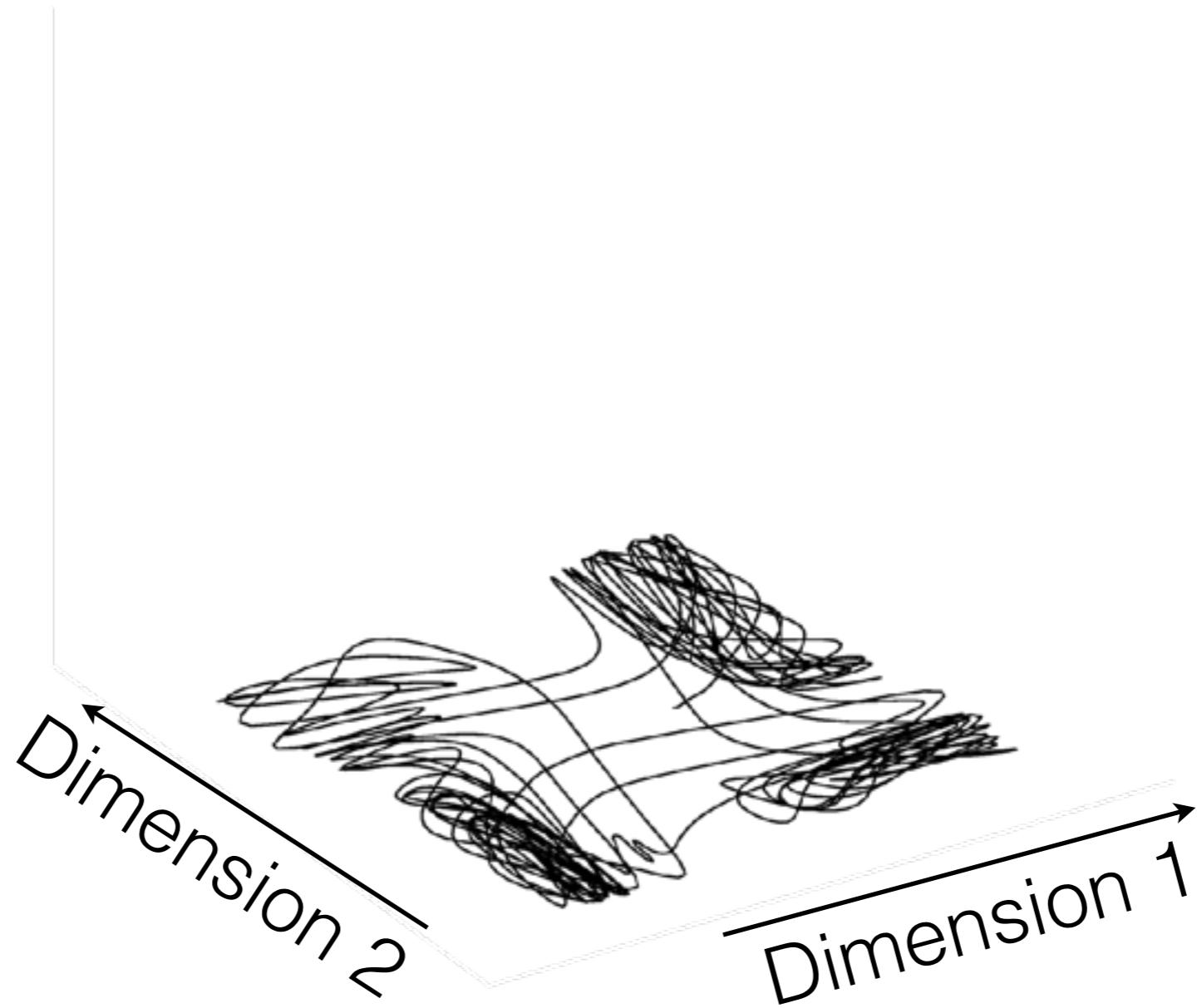


Interpretability



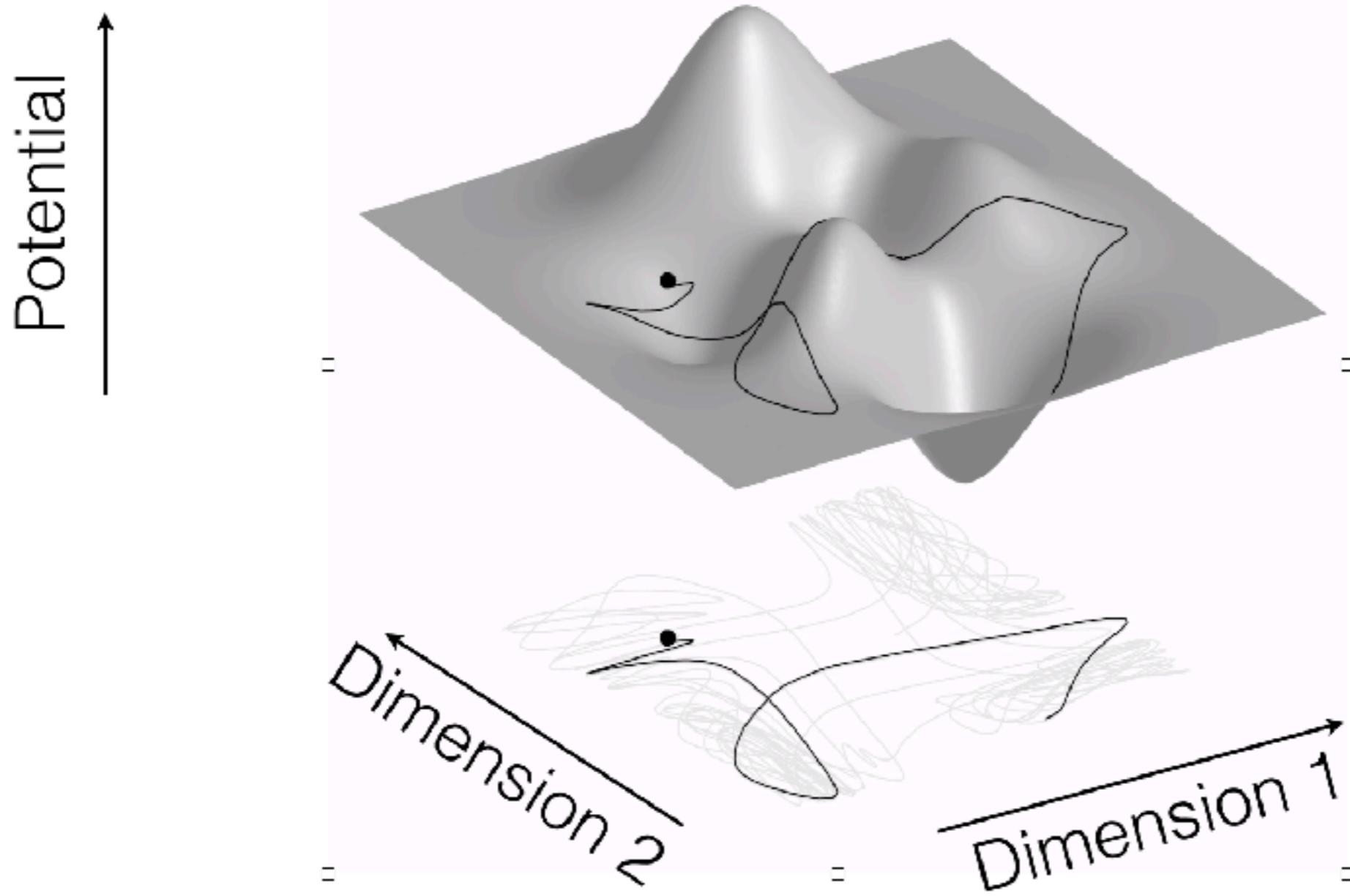
Model discovery: searching the entire space of possible dynamics

$$\dot{X} = F(X) + \xi(t)$$



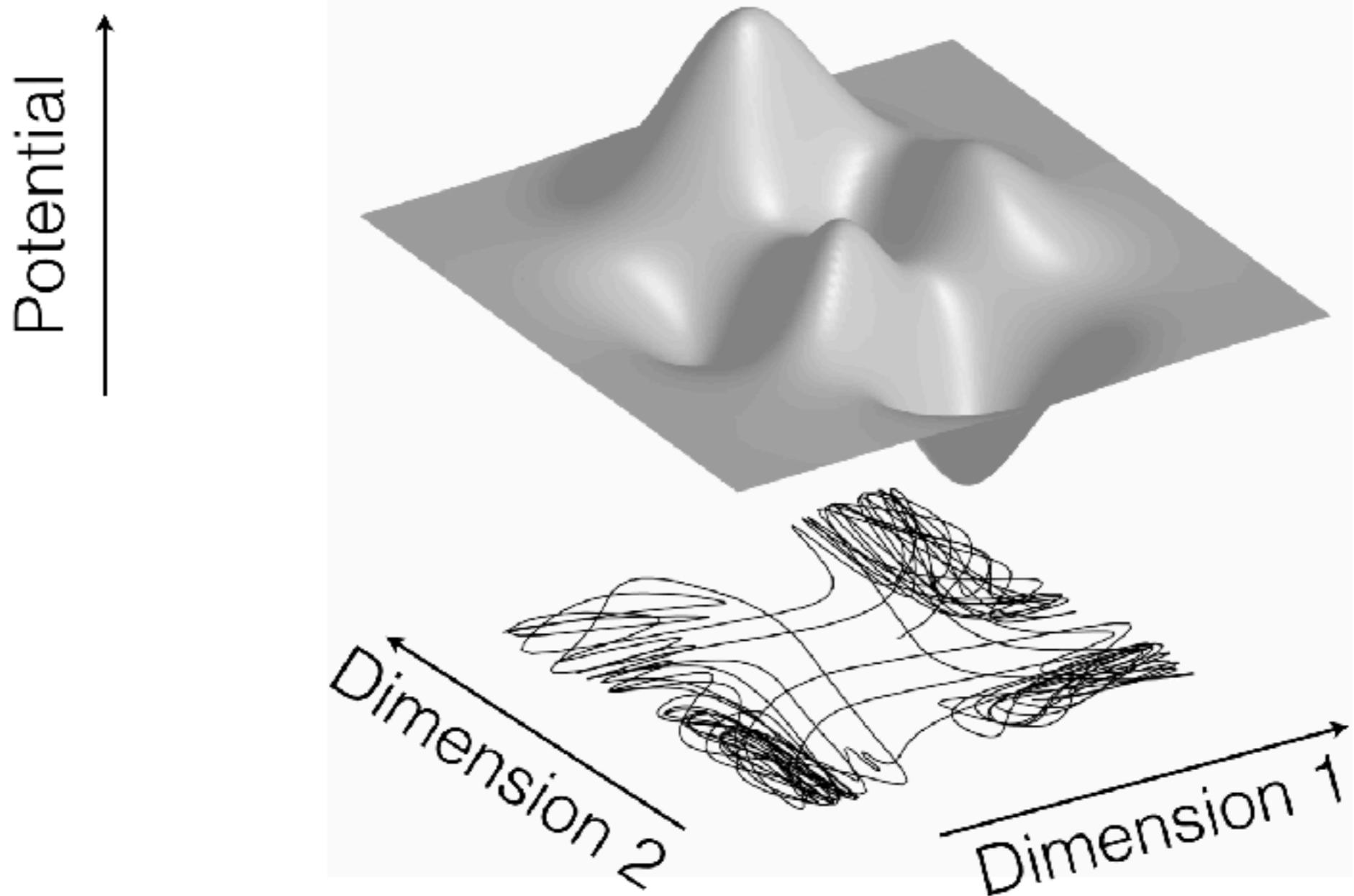
Model discovery: searching the entire space of possible dynamics

$$\dot{X} = F(X) + \xi(t)$$



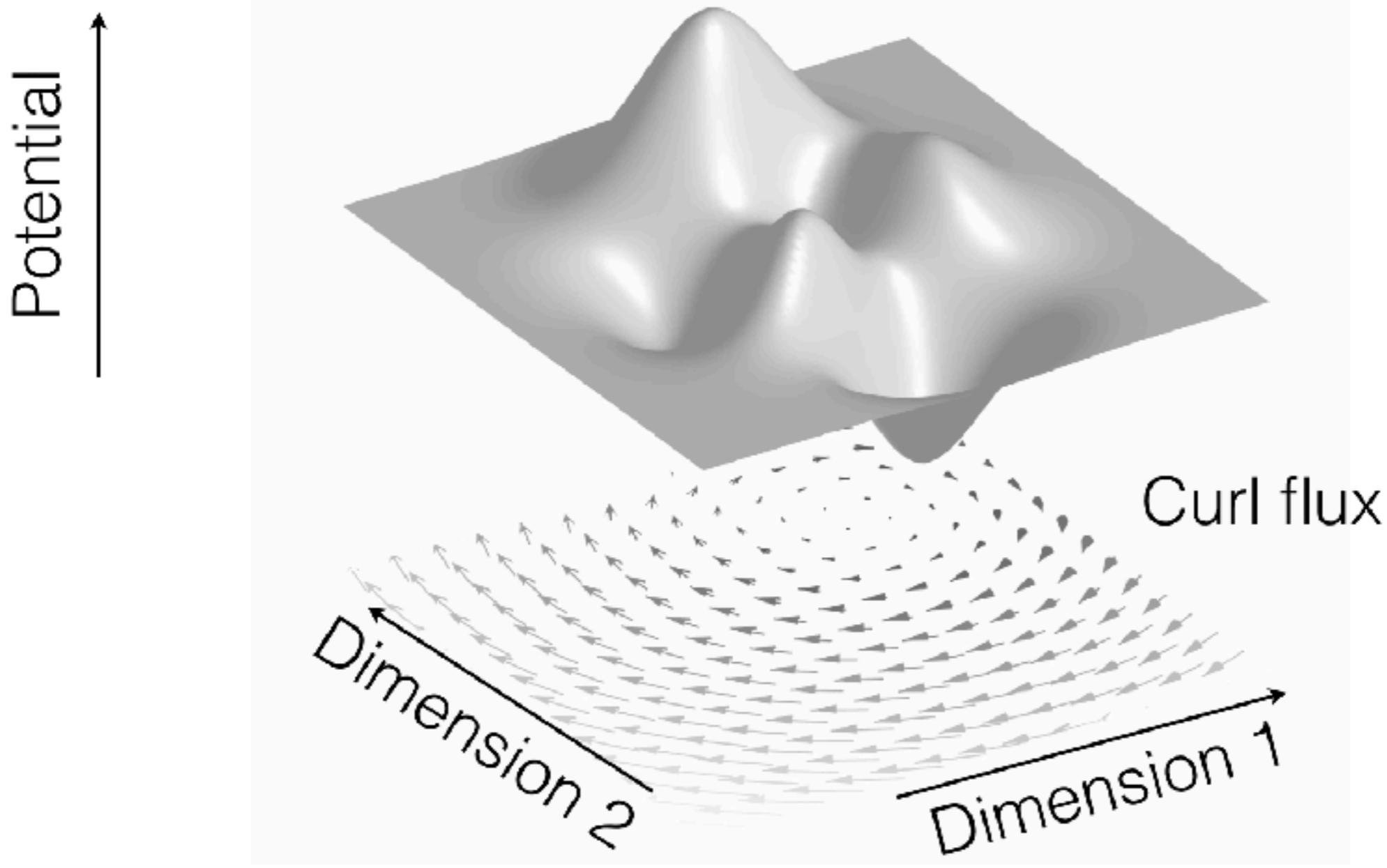
Model discovery: searching the entire space of possible dynamics

$$\dot{X} = F(X) + \xi(t)$$

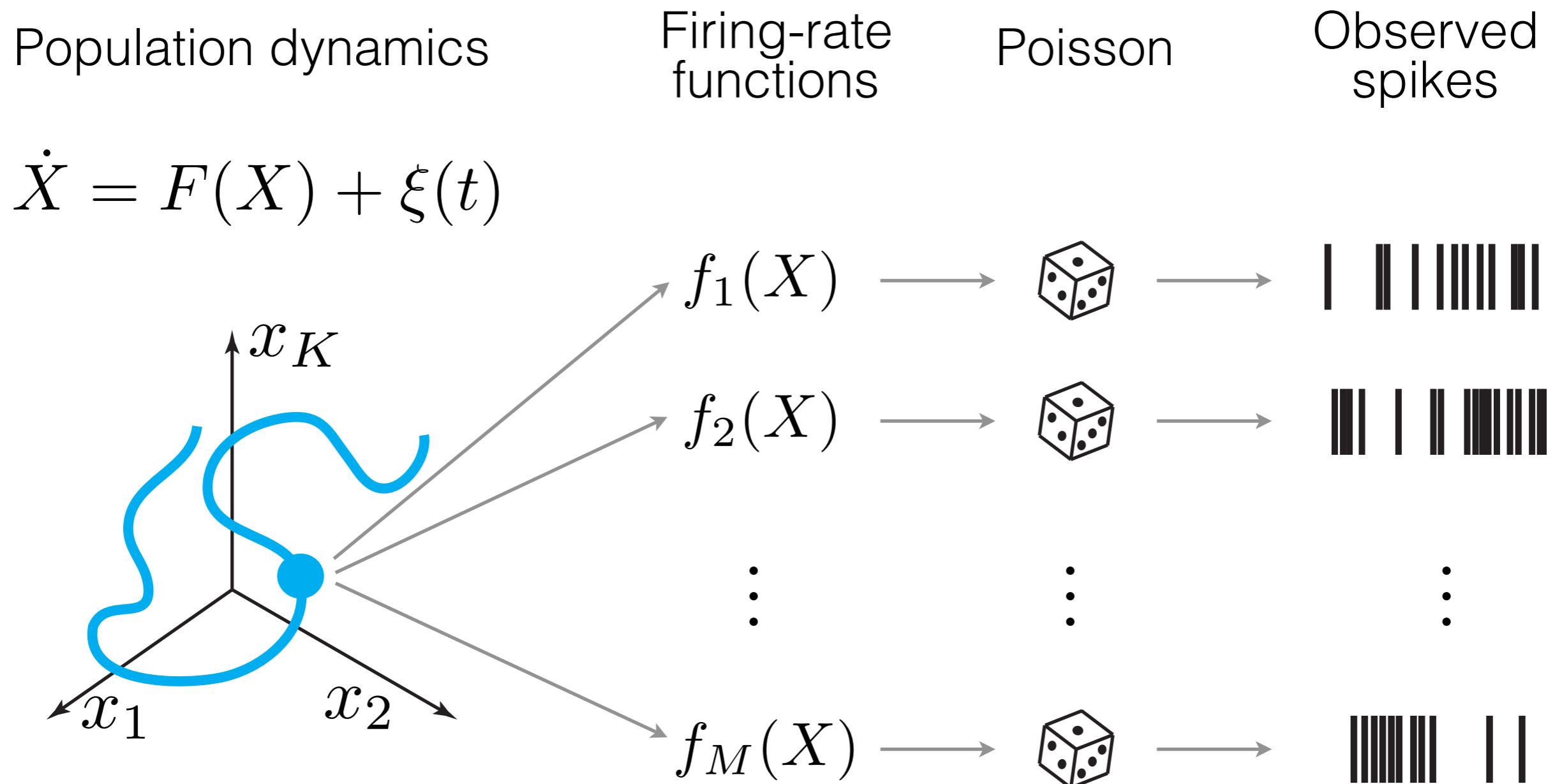


Model discovery: searching the entire space of possible dynamics

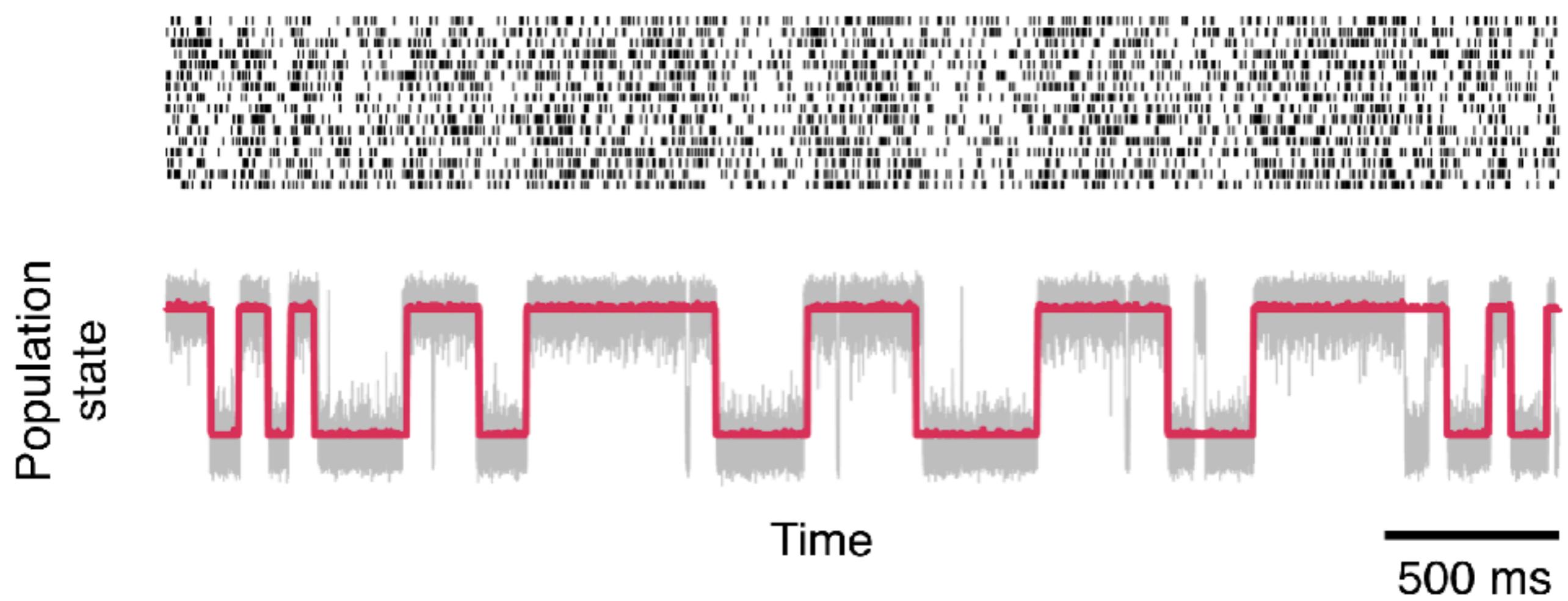
$$\dot{X} = F(X) + \xi(t)$$



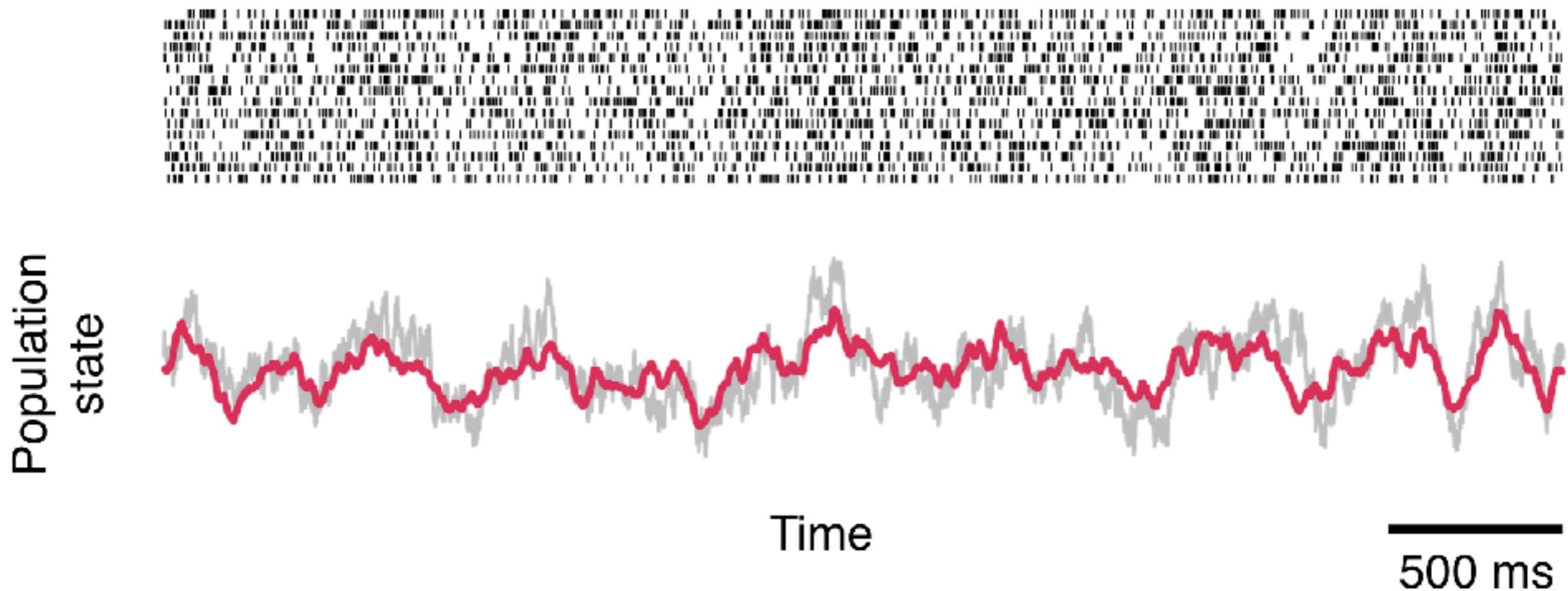
Nonparametric inference framework



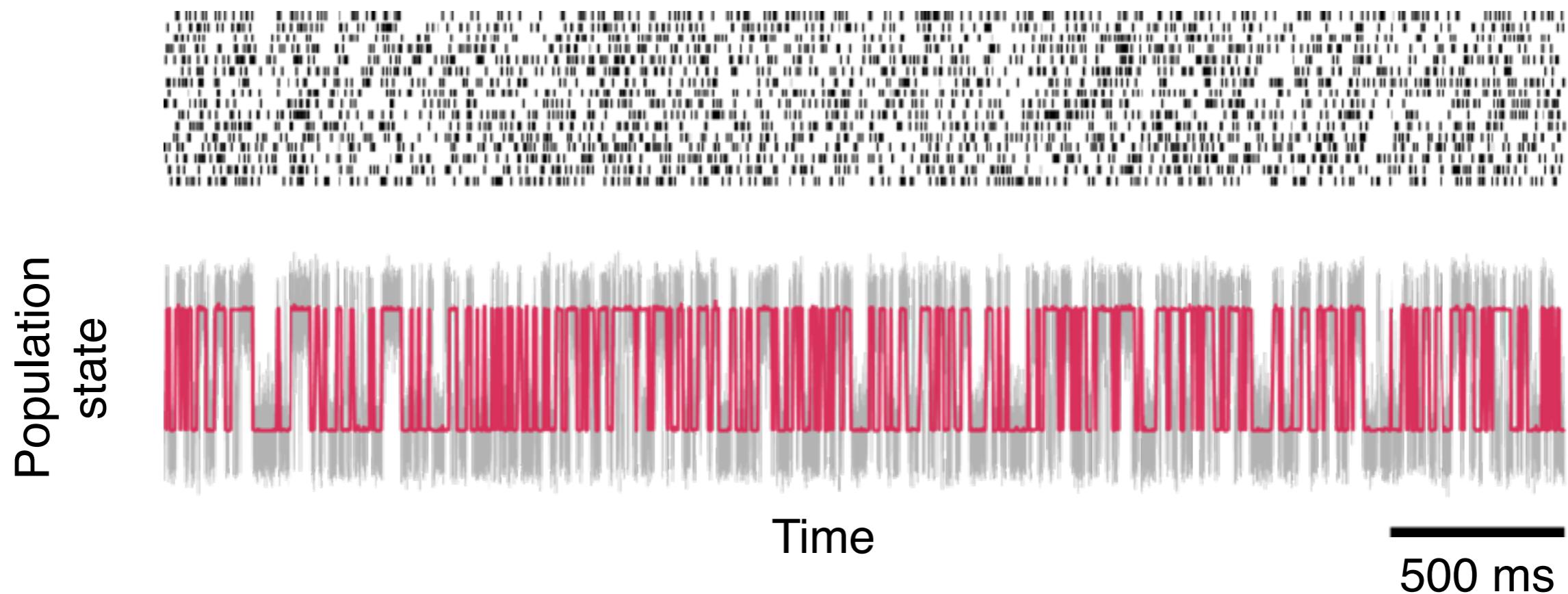
Dynamics underlying spiking are
accurately recovered



Different dynamics are recovered
within the same framework



Even fast dynamics are recovered
accurately

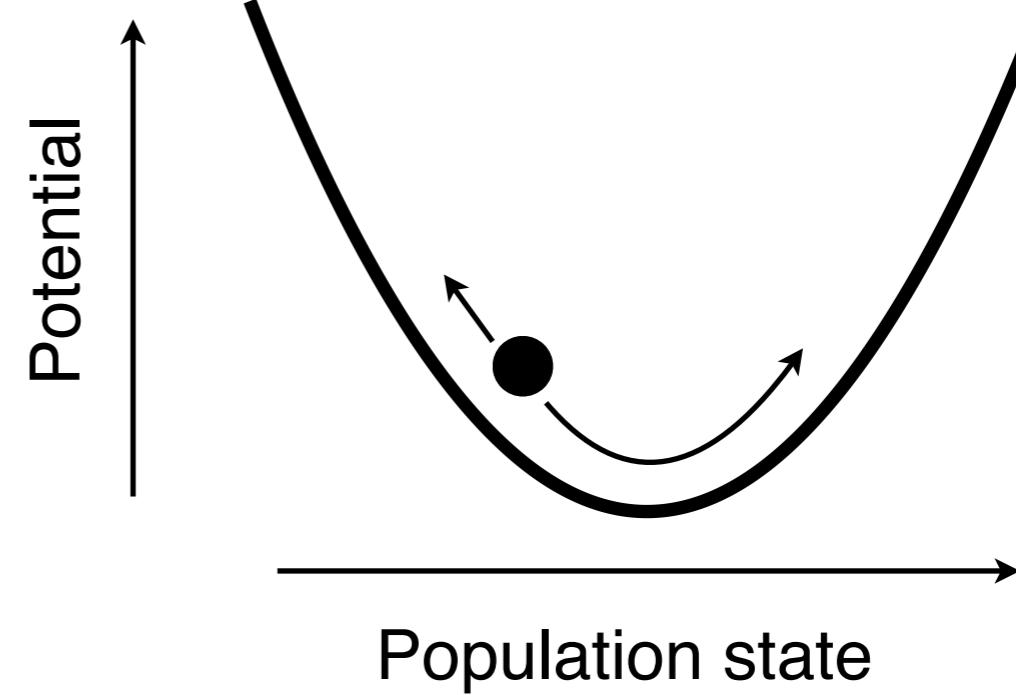
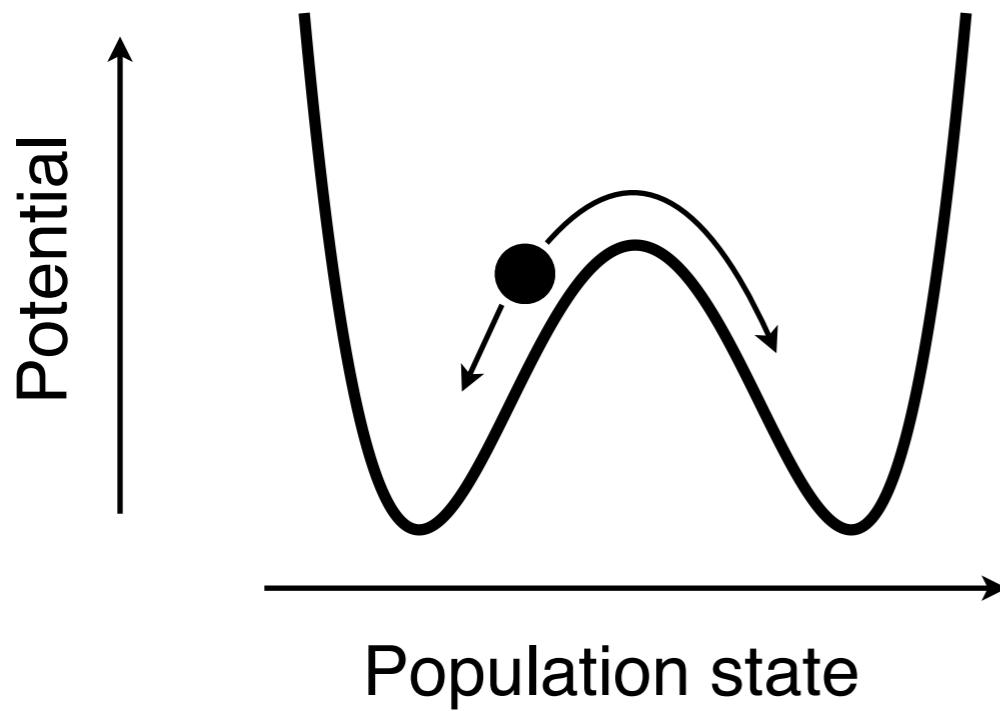


Landscape of dynamical forces

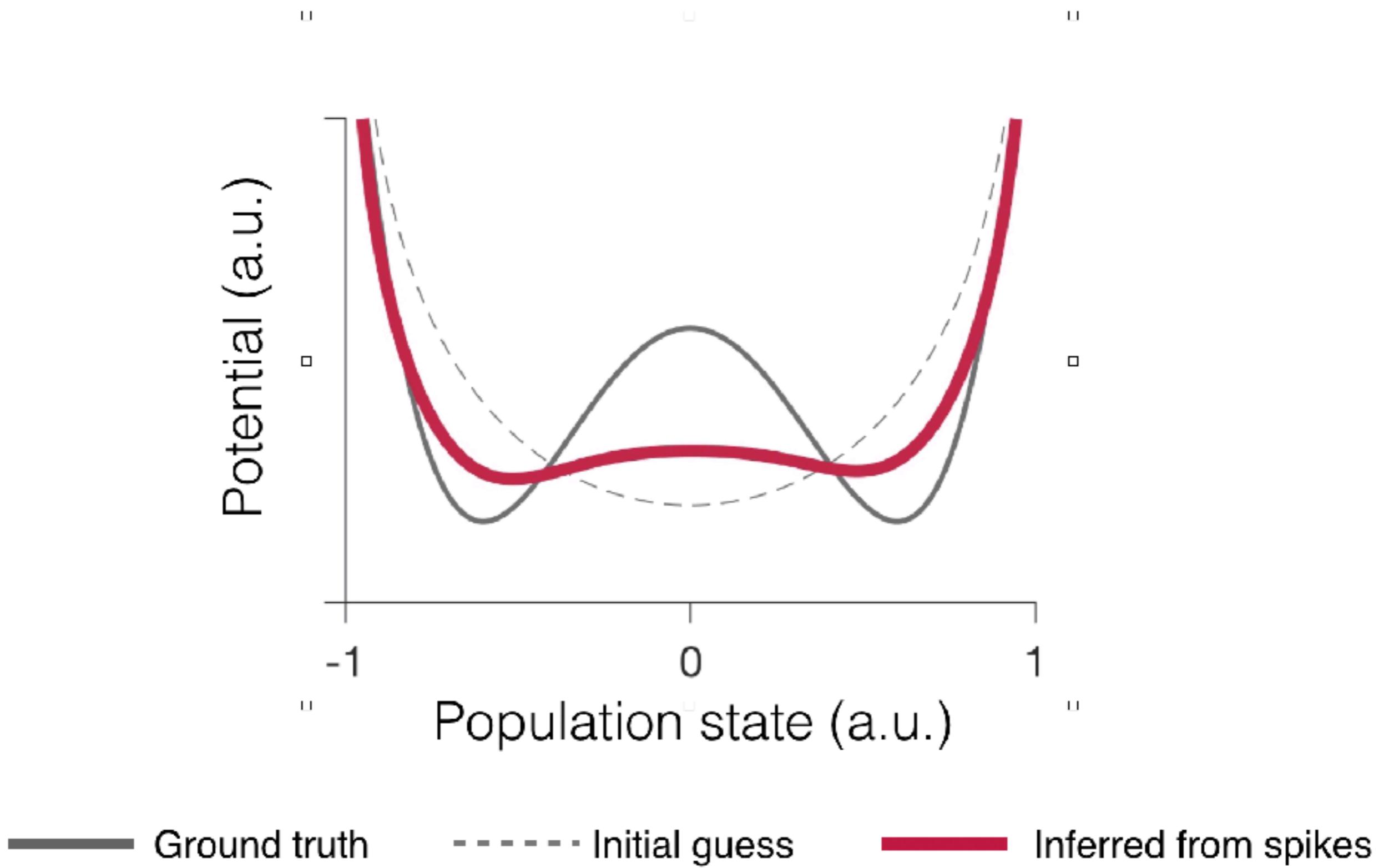
Switching



Continuous



Dynamics are uncovered from spikes



Learning interpretable models of neural dynamics from spikes

- non-parametric framework for model discovery
- generalization and interpretability are different optimization objectives
- universal tradeoff between generalization and complexity identifies interpretable models

Outline

1. Tuning curves of single neurons
2. Neural variability and correlations
3. Neural population dynamics
4. Spatiotemporal population dynamics in the primate visual cortex
5. Learning interpretable models of neural dynamics from spikes

Acknowledgements

Engel Lab @CSHL

Mikhail Genkin

Yanliang Shi

James Roach

Cina Aghamohammadi

Robert Kwapich

Collaborators

Nick Steinmetz

Tirin Moore

Kwabena Boahen

Alexander Thiele

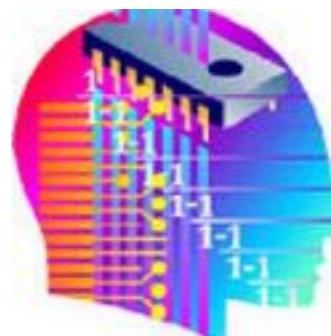
Alwin Gieselman



Cold Spring Harbor
Laboratory



NIH BRAIN
Initiative



The Swartz
Foundation



Pershing Square
Foundation