Lecture 5: Firing Rates and Spike Statistics

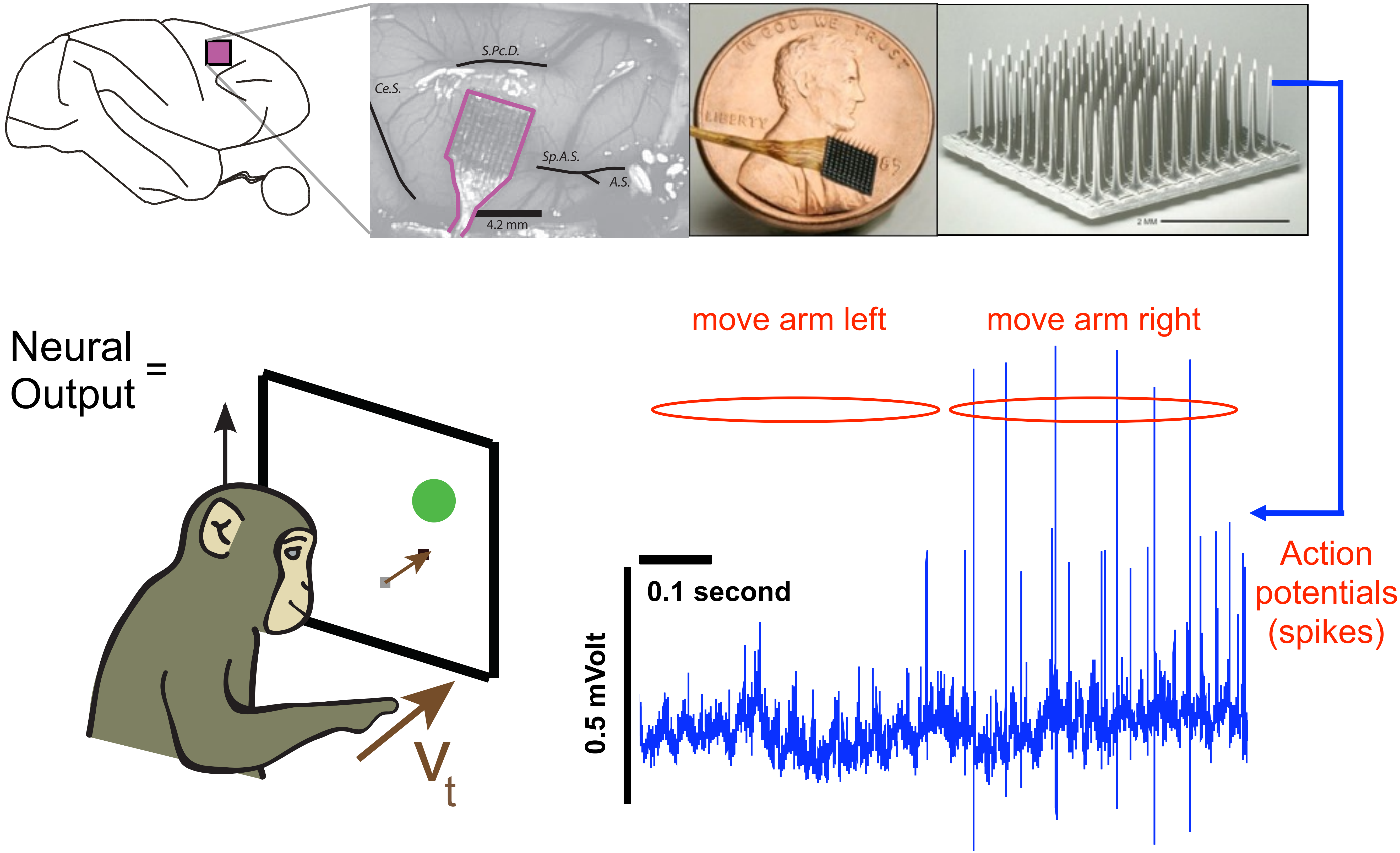
- Reading assignment from Dayan & Abbott:
  - Chapter 1 – Neural Encoding I: Firing Rates and Spike Statistics
  - p. 12-28 of PRML.

- We now know quite a bit about the electrical properties of neurons, including a first-principles understanding of:
  - Ion channels
  - Membrane potential
  - Action potential generation
  - Action potential propagation

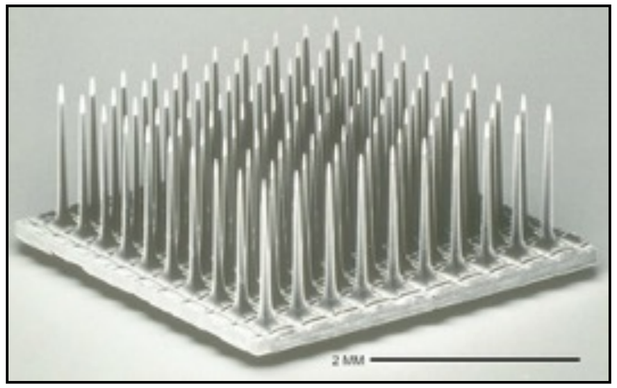
- As discussed in class, we could continue learning about various fundamental neuroscience topics including neurotransmitters, synapses, development, genetics, etc…

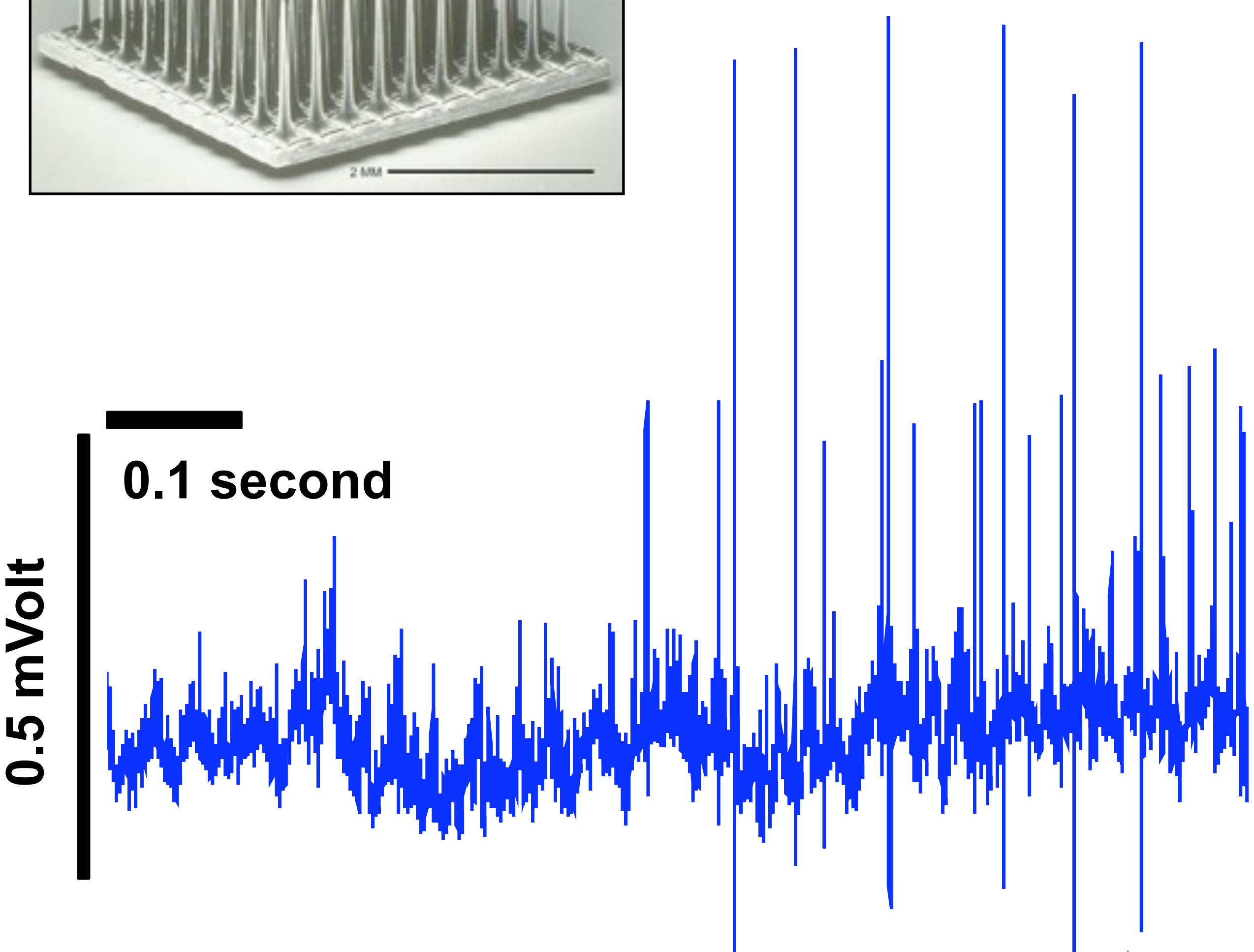
- Though this would (hopefully!) be interesting and fun, it would constitute a course in neuroscience – not a course in “NeuroEngineering”.

Neural Recordings Encode Arm Movements



Spike & LFP Processing

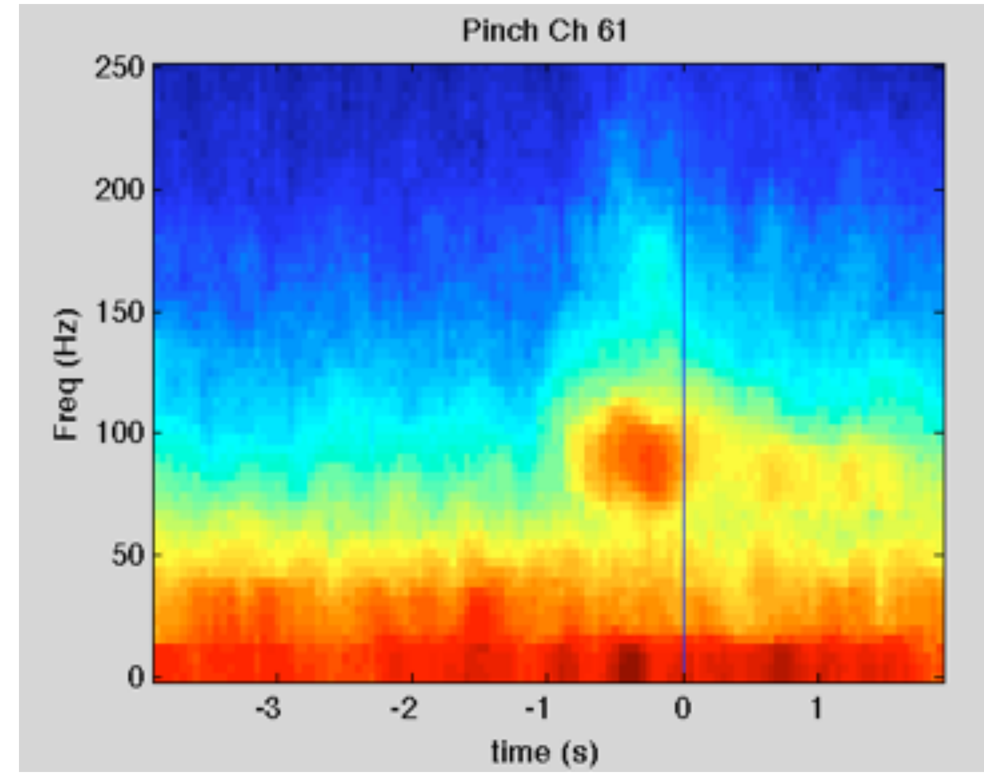


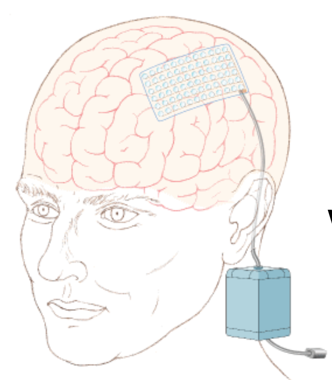


Sampled ~30 kHz
with 7.5 kHz low-pass
(anti-aliasing) filter

< ~200 Hz

Local Field Potential (LFP)



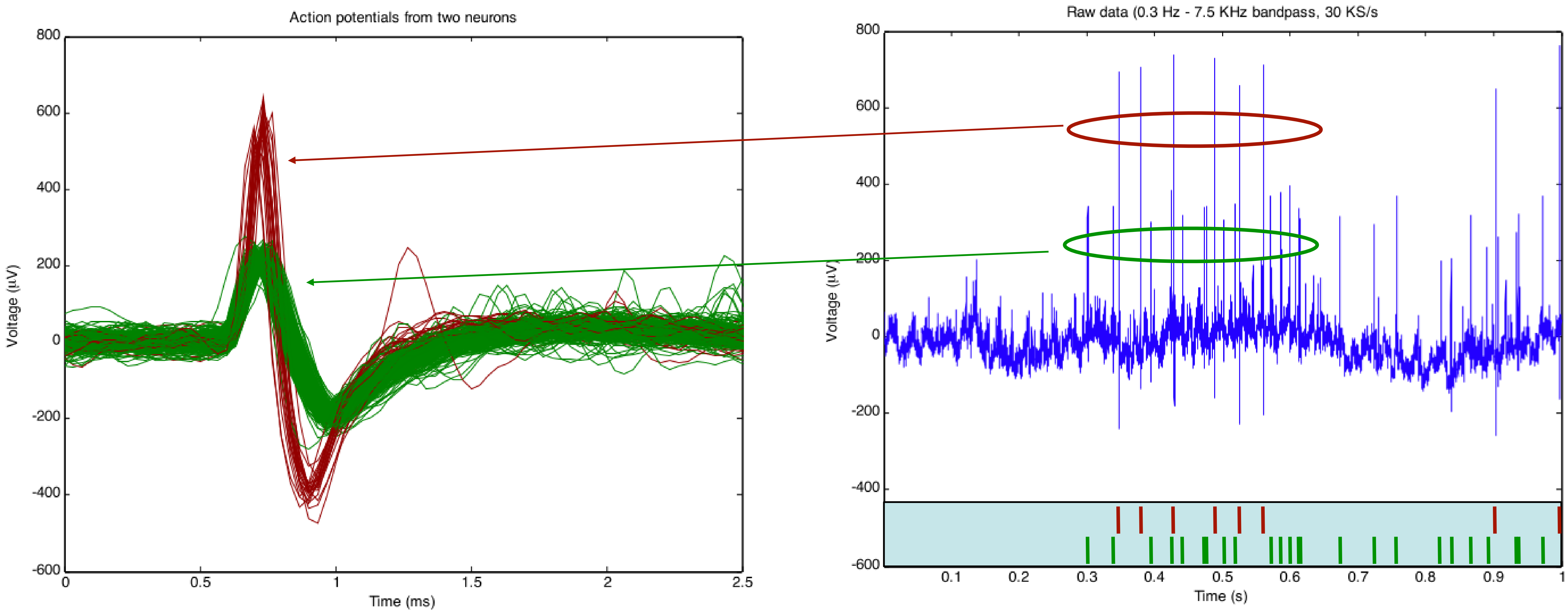


LFP
w/EEG & ECoG

> ~600 Hz

Action Potential (Spike) Times

Spike Processing

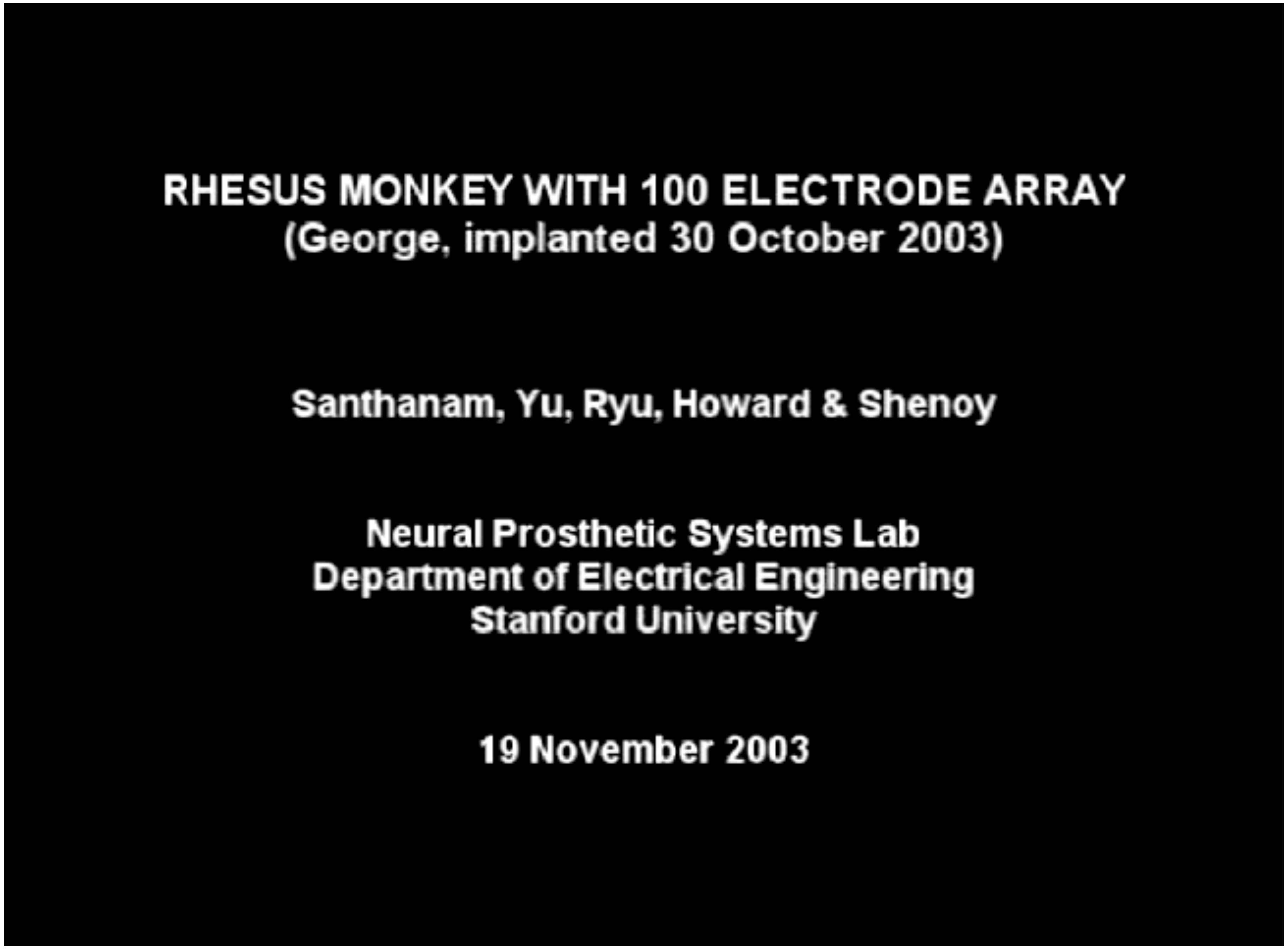


Can sort shapes to identify individual neurons

Virtual lab tour

• We will be looking at various representations of spikes (full AP waveform, rasters, histograms, etc.) but it is useful have a “look and feel” in mind.

• Thus, a virtual lab tour including listening to action potentials stream in:



Neural Encoding and Decoding

- Neurons represent and transit information by firing sequences of spikes.
- Spikes are fired in various temporal patterns.

- The study of neural coding involves measuring and characterizing how stimulus attributes (light, sound intensity, or motor actions) are represented by spikes.

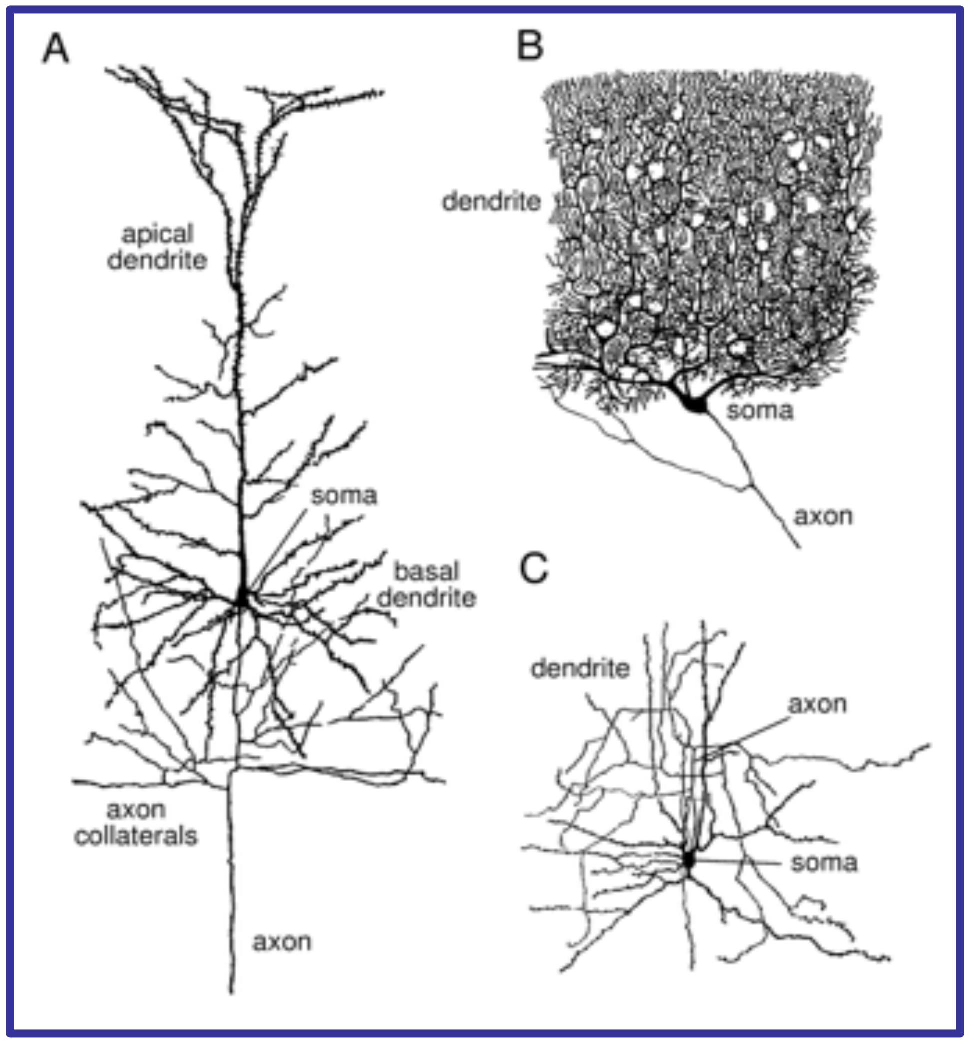
- **Neural encoding** – the map from stimulus to neural response.
  - Can measure how neurons respond to a wide variety of stimuli.
  - Then construct models; attempt to predict responses to other stimuli.
  - We will discuss encoding in this lecture.

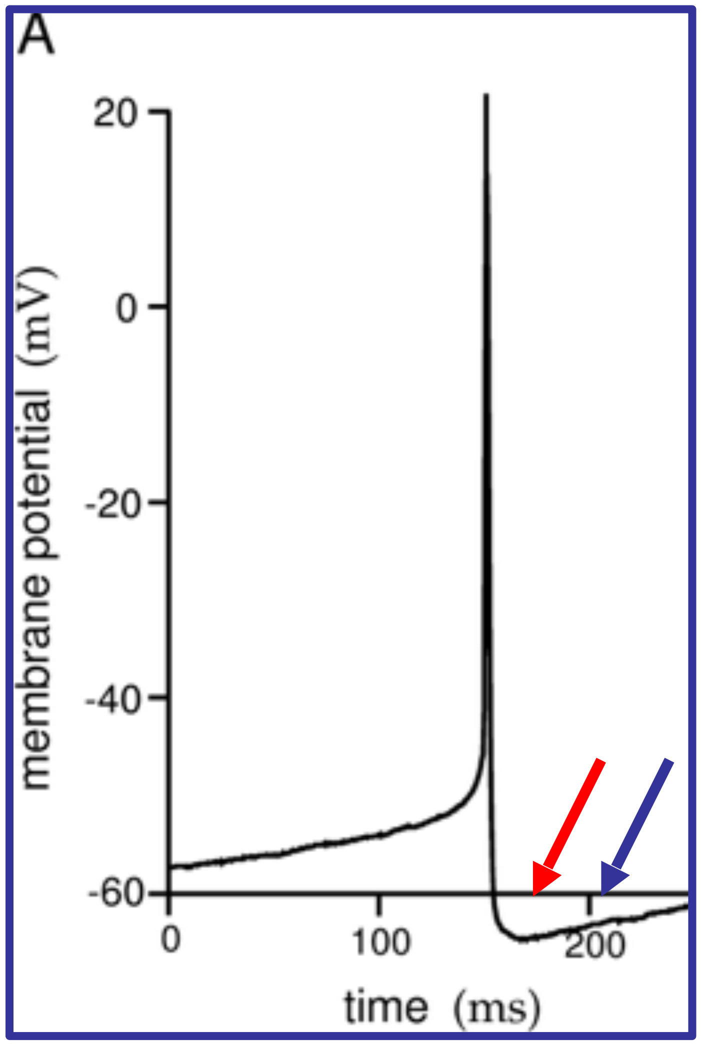
- **Neural decoding** – the map from response to stimulus.
  - Attempt to reconstruct a stimulus, or certain aspects of that stimulus, from the spike sequence it evokes.
  - We will discuss decoding extensively in the rest of this course.

Neurons and Action Potentials

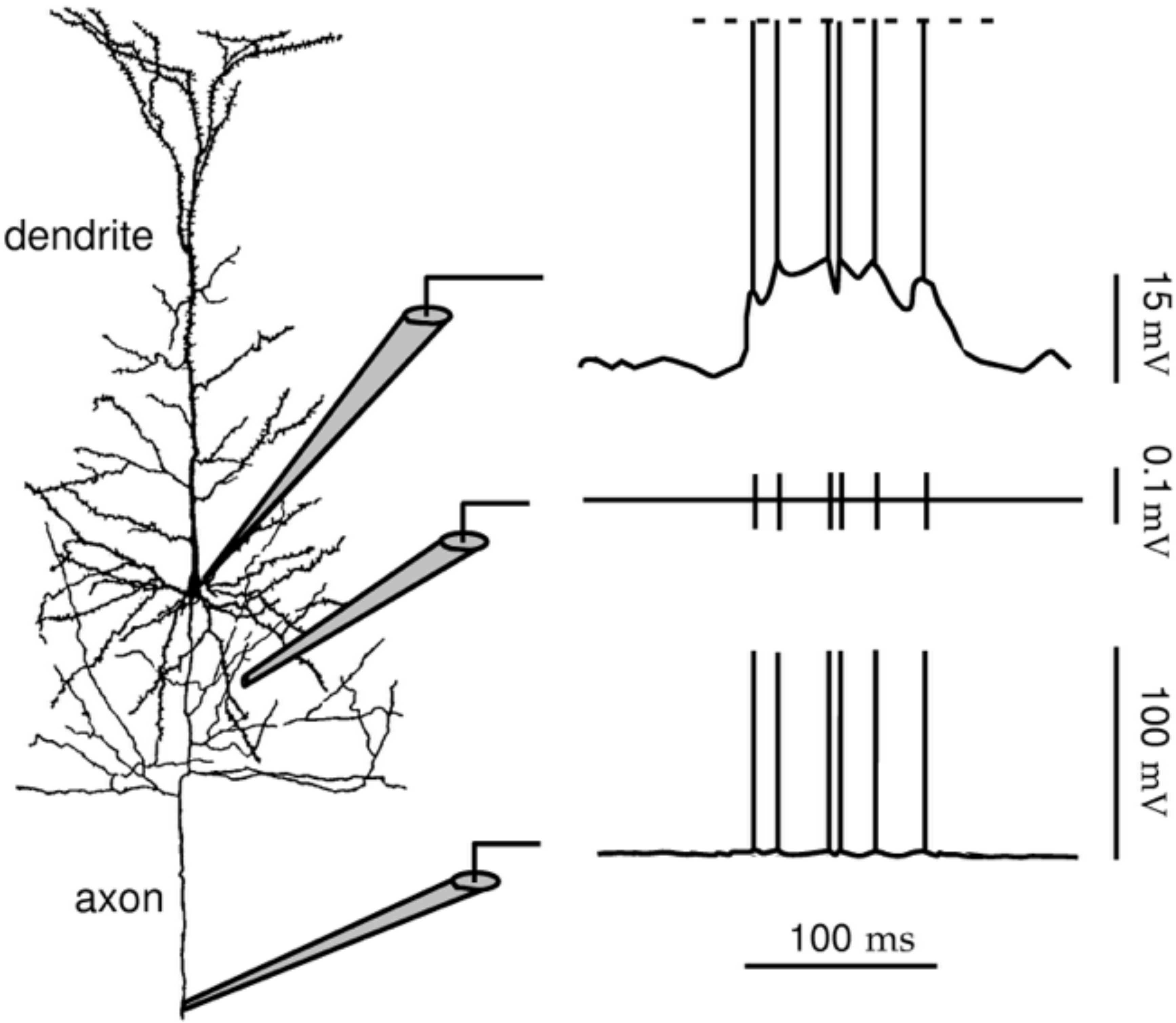
As discussed in previous lectures:

- Neuron morphology varies considerably, and influences function.
- Action potential are V_m deflections (~100 mV, ~1ms).
- Absolute refractory period lasts a few ms.
- Relative refractory period lasts a few 10’s of ms.





Intra- & Extra-Cellular Recordings



Intra-cellular recording at soma (APs and subthreshold potentials).

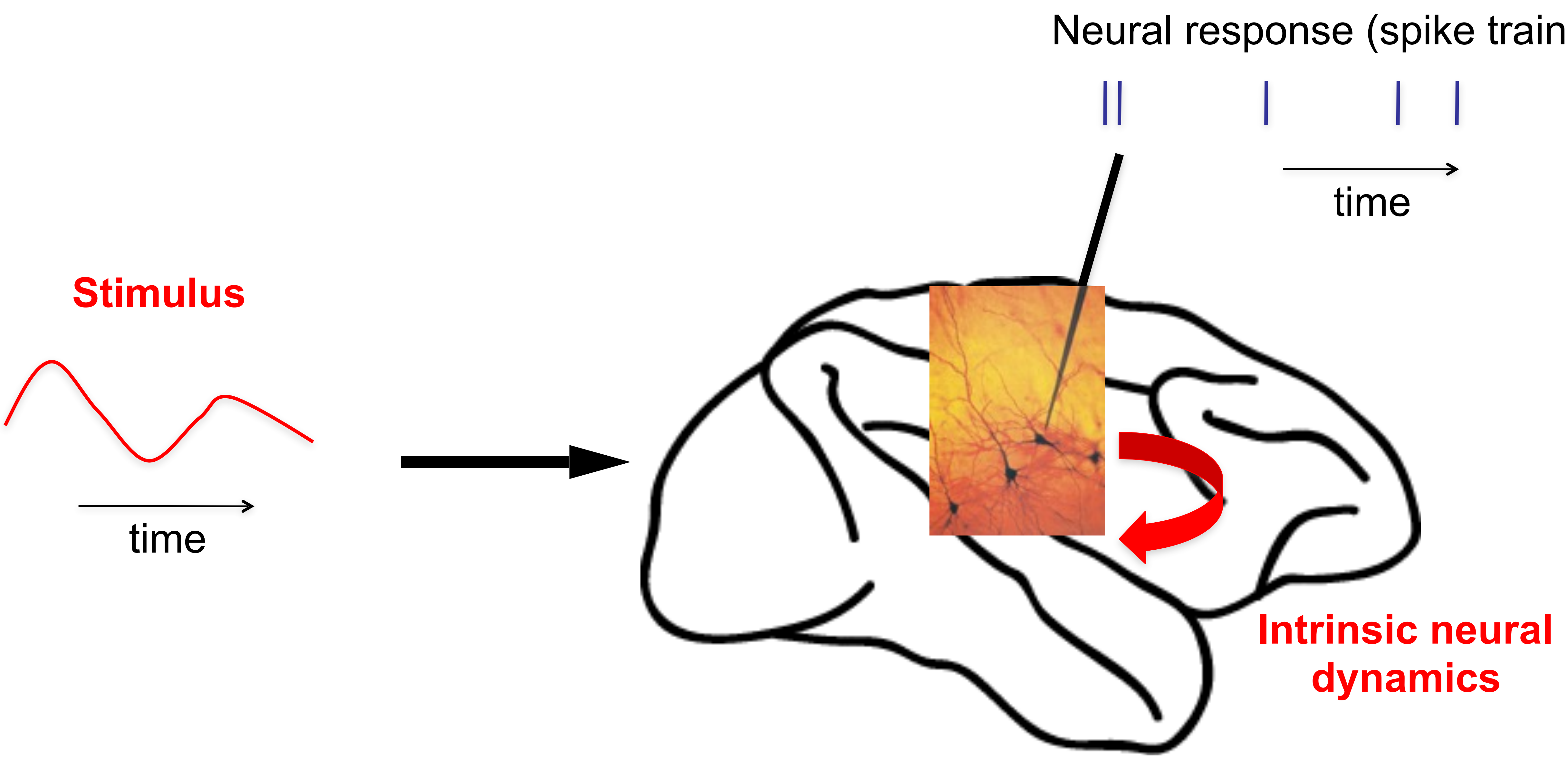
Extra-cellular recording near soma (APs, no subthreshold potentials).

Intra-cellular recording in axon (APs, no subthreshold potentials).

From Stimulus to Response

Characterizing the stimulus → response relationship is difficult because neural responses are "complex" and variable. In particular,

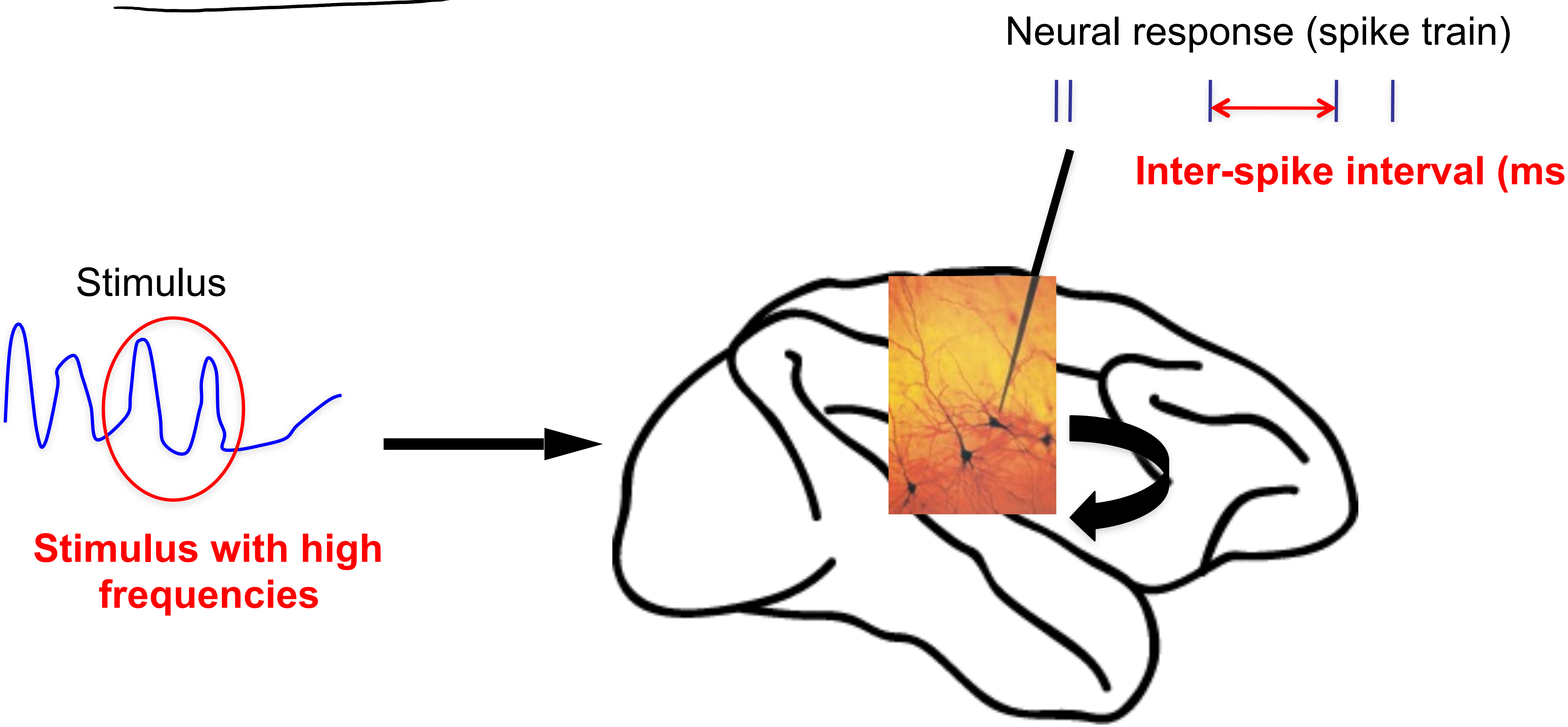
1) Spike sequences reflect both <u>intrinsic neural dynamics</u> and <u>temporal characteristics of stimulus</u>.



From Stimulus to Response

Characterizing the stimulus → response relationship is difficult because neural responses are "complex" and variable. In particular,

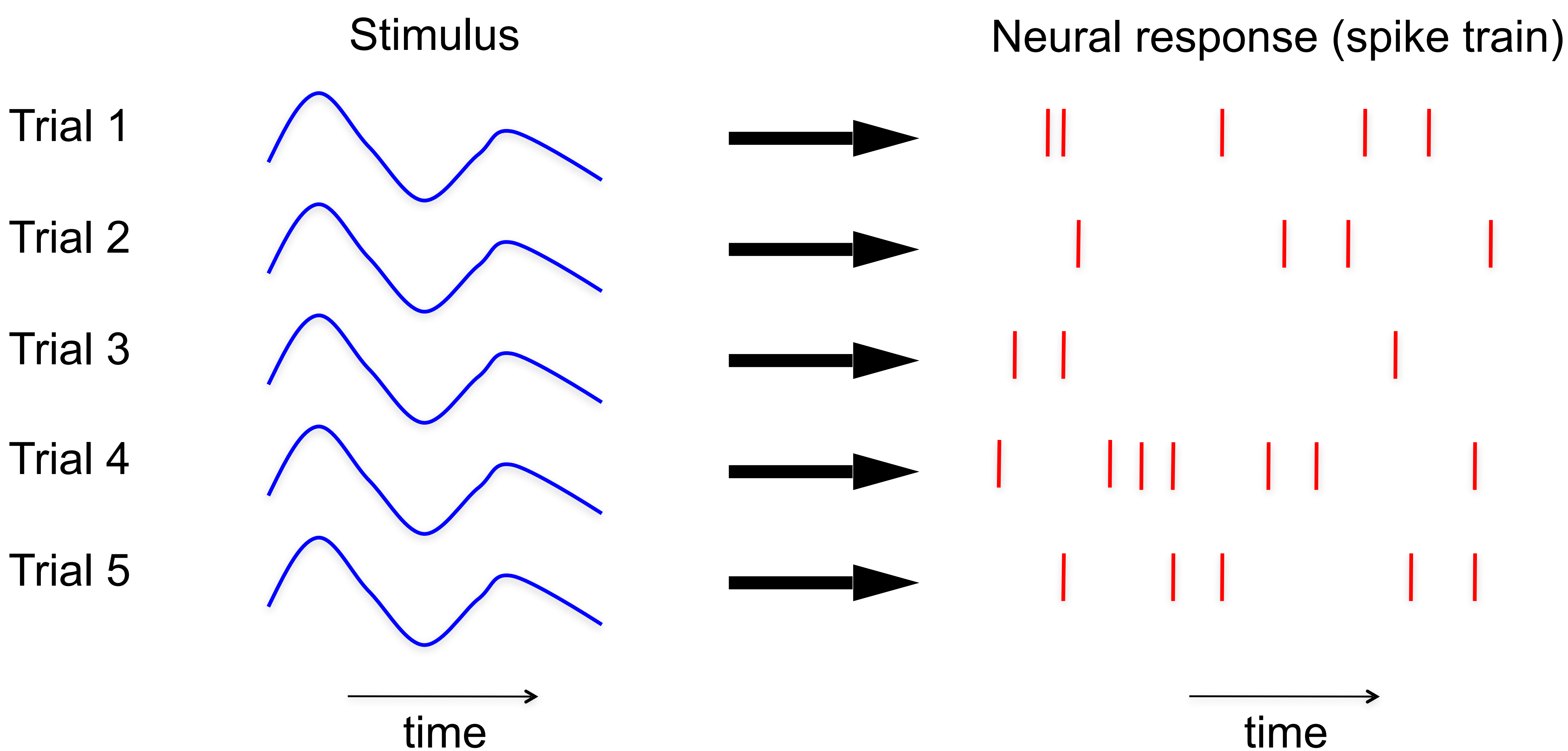
2) Identifying features of response that encode changes in stimulus is difficult, especially if stimulus changes on times scale of inter-spike interval.



From Stimulus to Response

Characterizing the stimulus → response relationship is difficult because neural responses are "complex" and variable. In particular,

3) Neural responses vary from trial-to-trial even when the same stimulus is presented repeatedly.

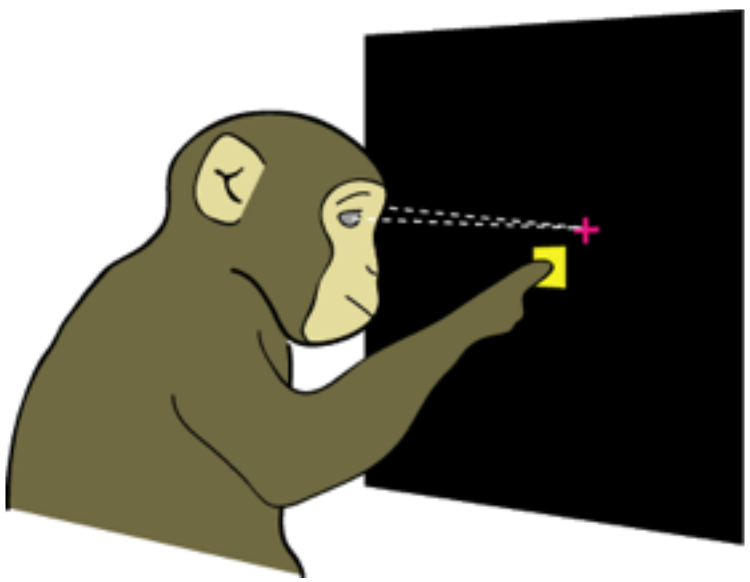


Why are neural responses variable?

- Randomness associated with biophysical processes involved in spike generation and transmission (e.g., neurotransmitter release at presynaptic terminal, opening / closing of ion channels)

- Variable levels of arousal and attention

- Effects of other cognitive processes:



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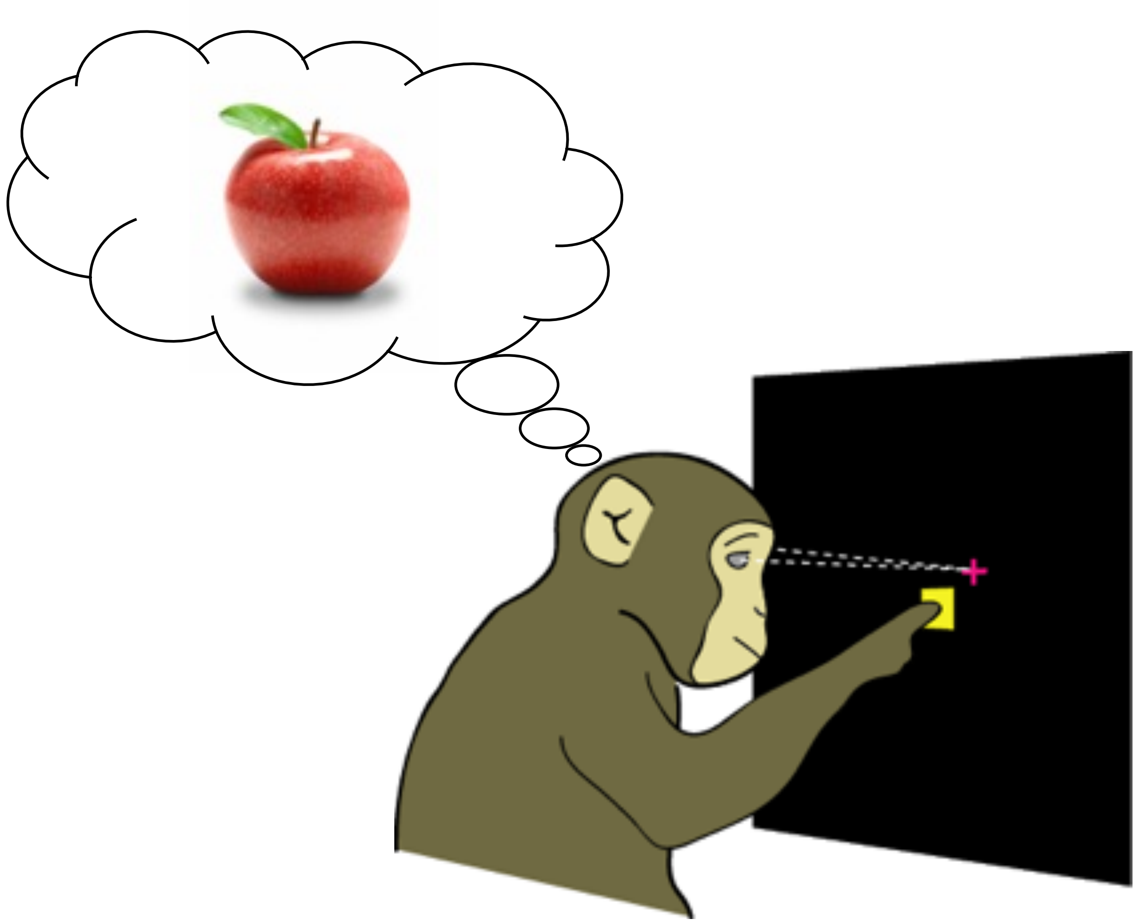

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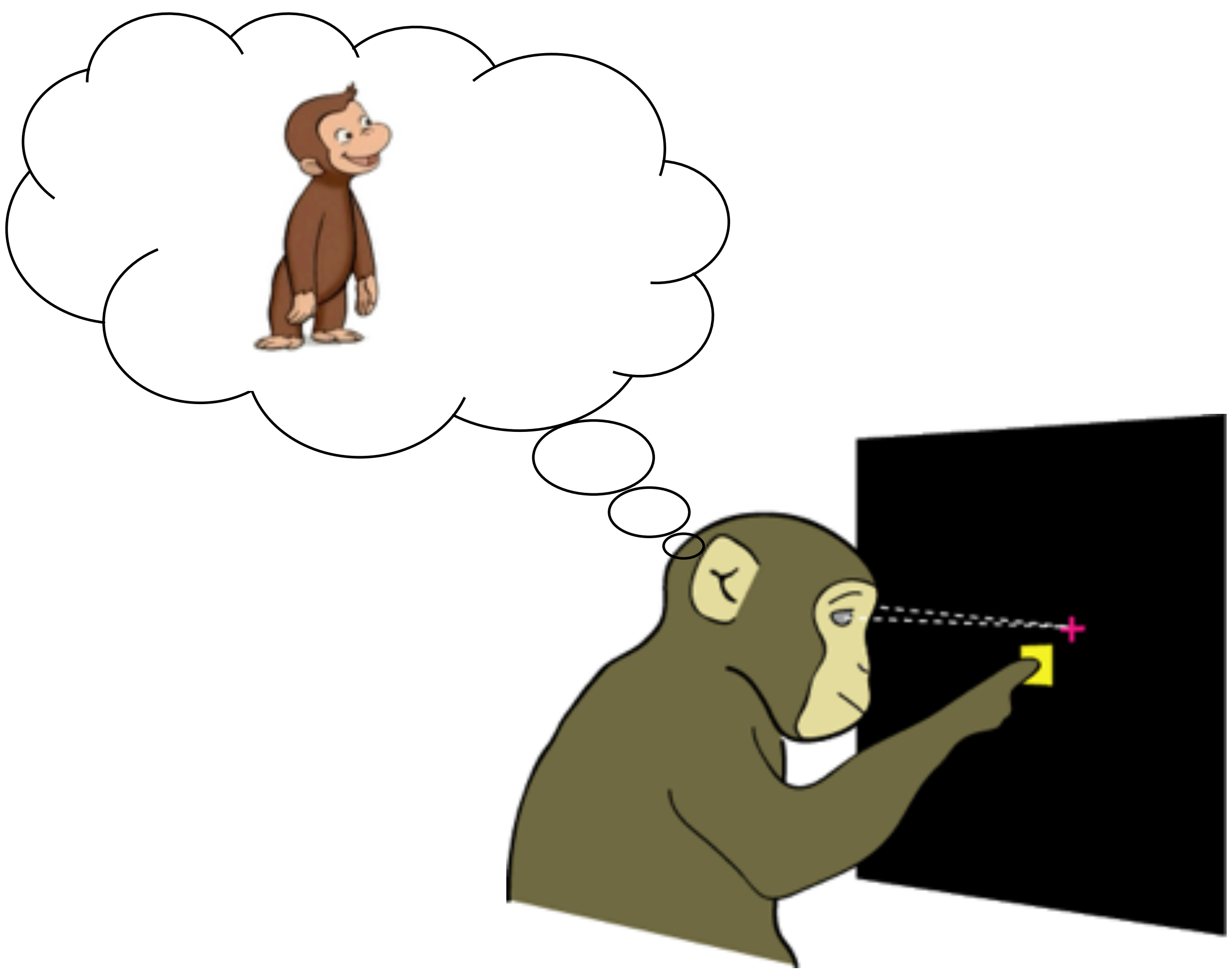

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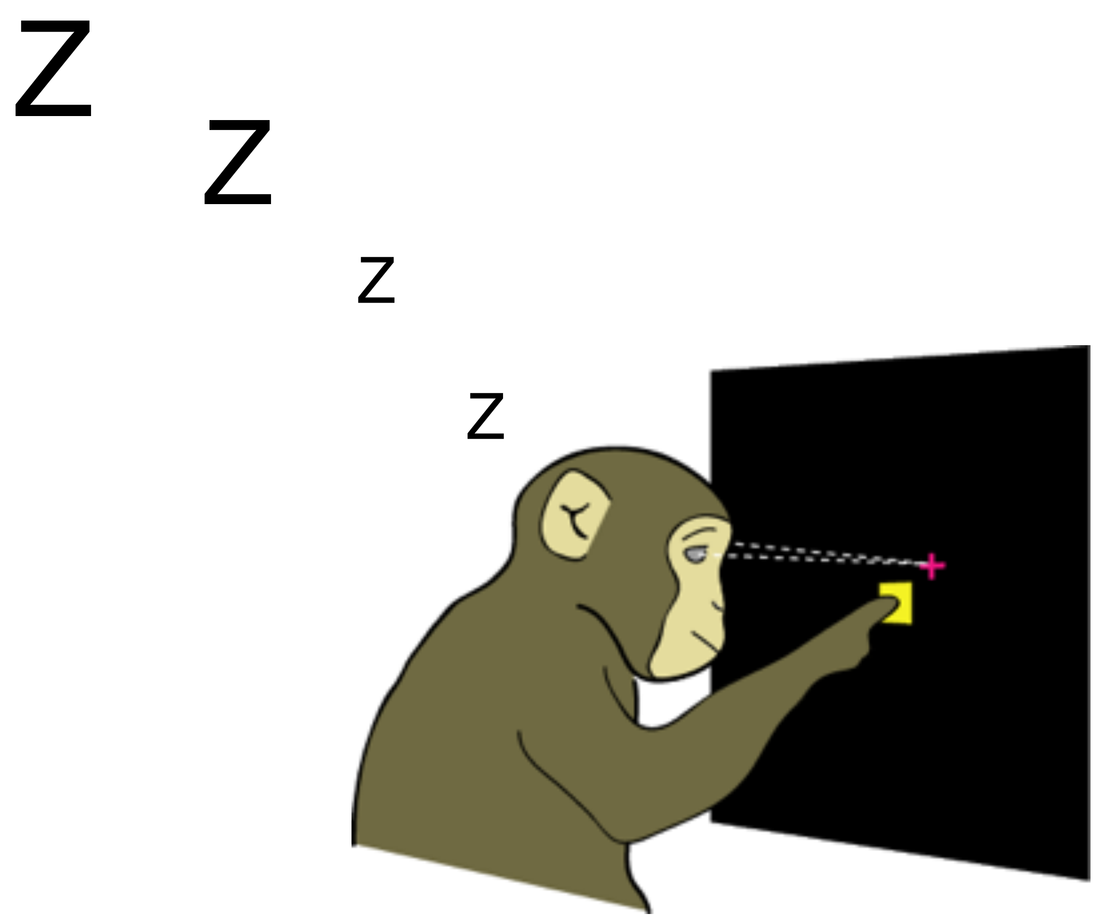


From Stimulus to Response

Characterizing the stimulus → response relationship is difficult because neural responses are "complex" and variable.

Thus, we cannot predict the exact timing of every spike.

Our goal is to find a model for the **probability** that different spike sequences are evoked by a specific stimulus.

Population Codes

- Many neurons respond to a given stimulus.

- Stimulus features are, therefore, encoded by the activities of large neural populations (e.g., millions).

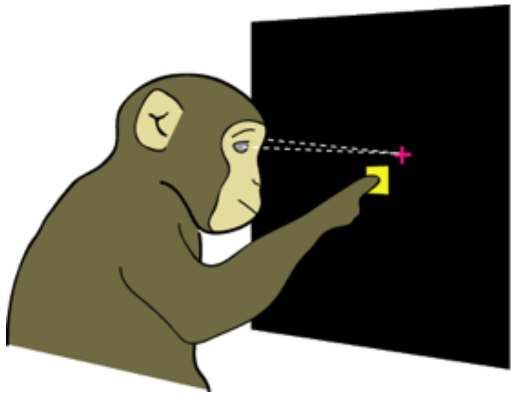
- To study population codes we must do more than just study the firing patterns of single neurons.

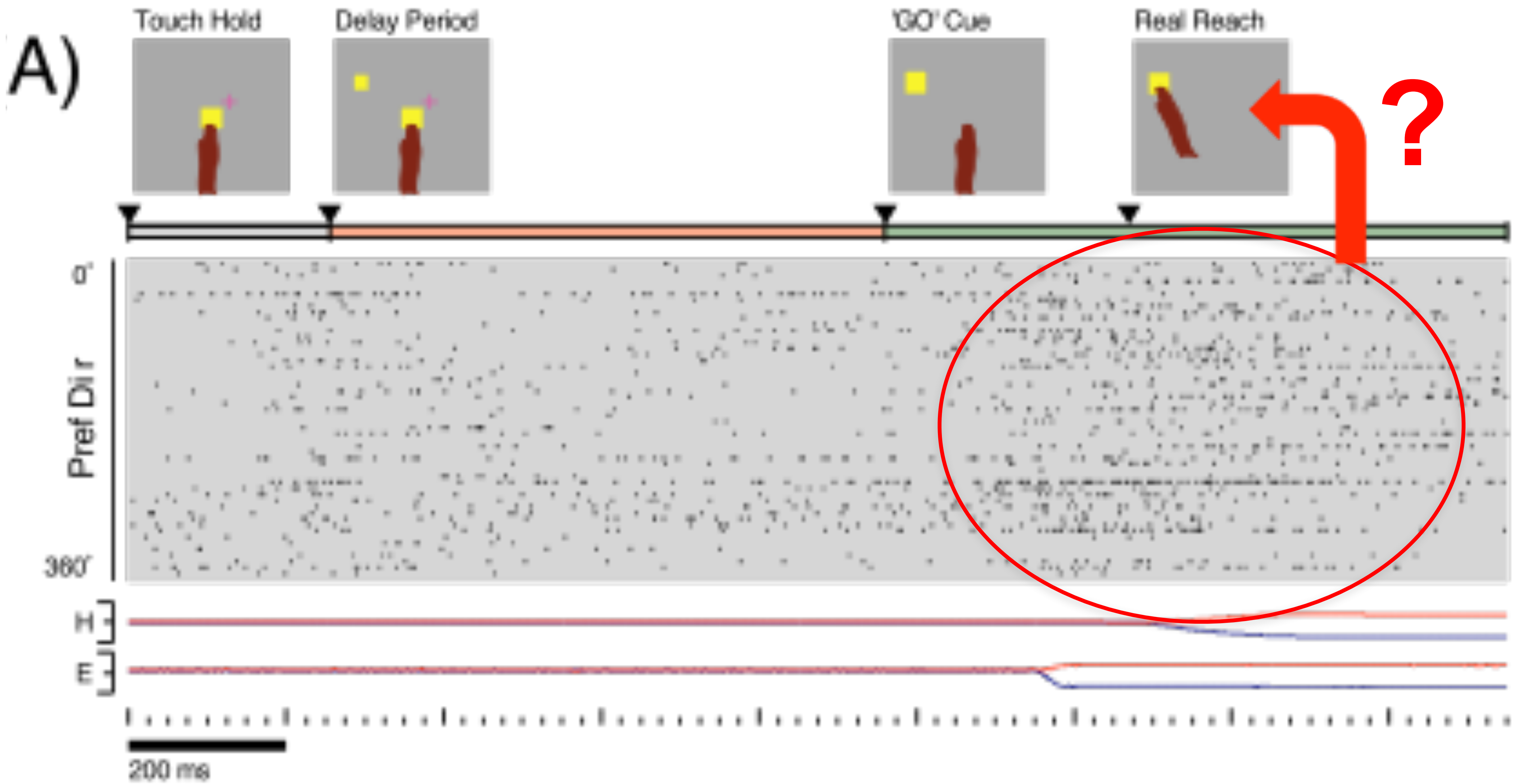
- Must also study the relationship of firing patterns to each other across the population of responding neurons.

- BIG PICTURE – if we wish to understand how information is encoded in neurons and populations of neurons, we must acquaint ourselves with some of the appropriate mathematical measures.

Example to Clarify the Challenge of Encoding/Decoding

- How does a population of neurons (in motor cortex) encode, with spike times, where the arm will move next?
- How is the actual arm movement encoded?

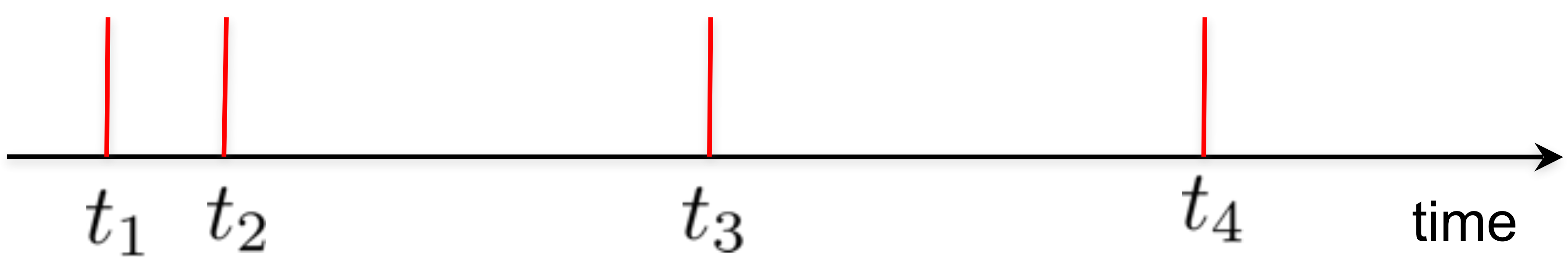




Spike Trains

- APs encode and convey information through their timing.
- AP duration, amplitude and shape are highly stereotyped (don't encode).
- Neglecting the brief duration of the actual AP (~1 ms), we can characterize an AP sequence with a list of spike times, t_i.

$$\rho(t) = \sum_{i=1}^{n} \delta(t - t_i)$$



Firing Rates

- Recall that the sequence of APs generated by a given stimulus varies from trial to trial.

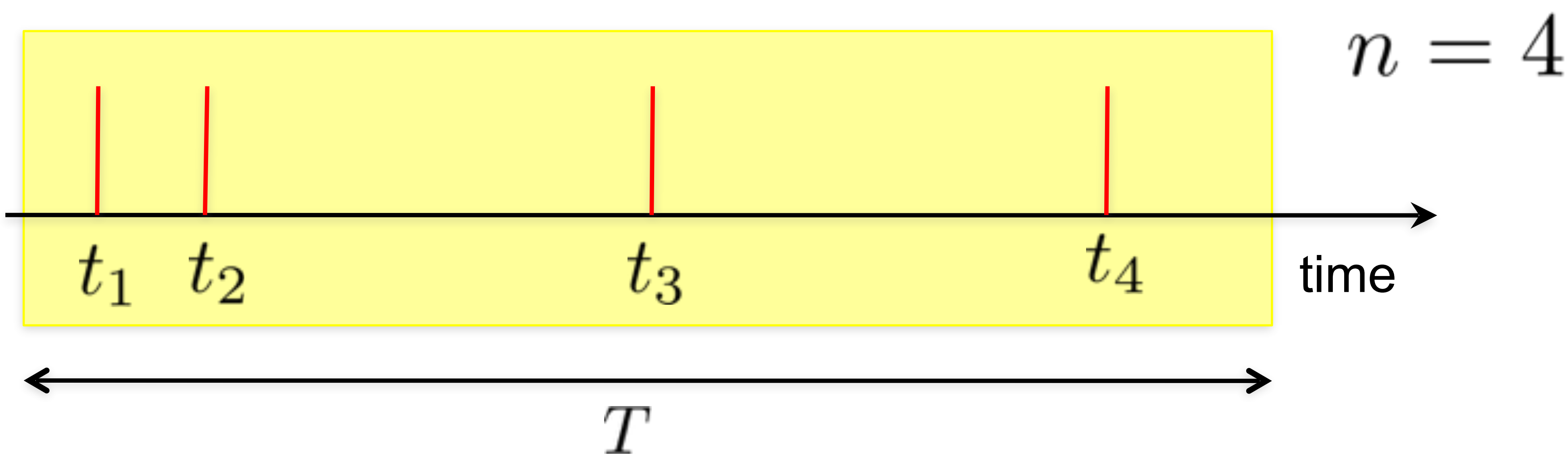
- Thus neural responses are typically treated statistically / probabilistically.

- Neural responses can be characterized by **firing rates**, rather than by specific spike sequences.

Firing Rates

In its simplest form, the firing rate is obtained by counting the number of spikes in a time window.

Thus, firing rate has units of *spikes per second*, or *Hz*.



Firing rate

Spike count in window

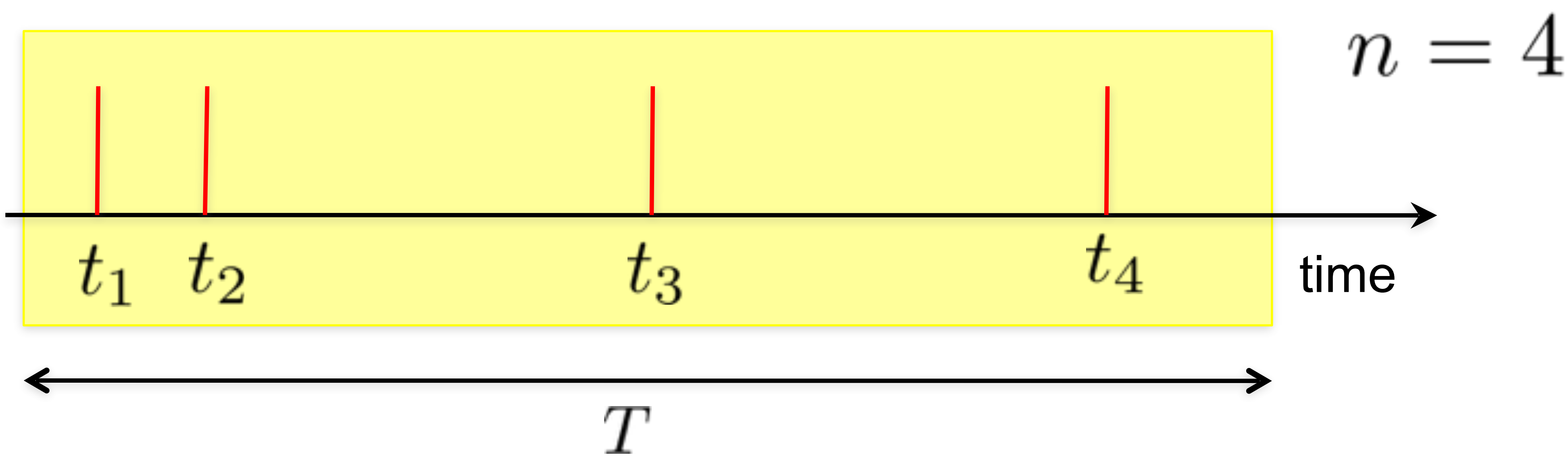
$$\lambda = \frac{n}{T}$$

where $n = \int_0^T \rho(\tau) d\tau$

Firing Rates

With this definition of firing rate, what are we missing?

Time-varying properties of the neural response.



Firing rate

Spike count in window

$$\lambda = \frac{n}{T}$$

where $n = \int_0^T \rho(\tau)d\tau$

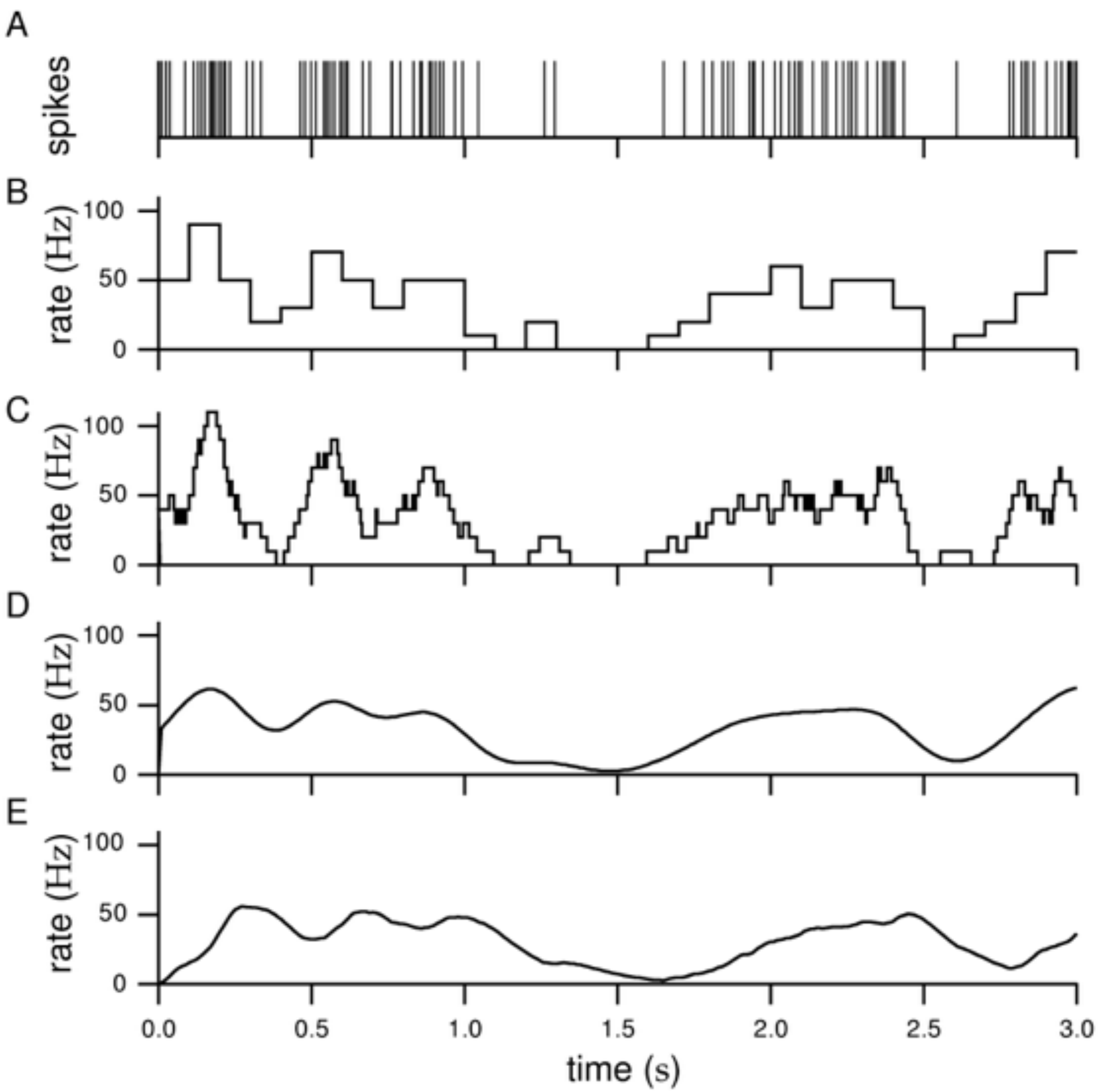
Motivation for Estimating Time-Varying Firing Rates

A neuron's firing rate typically varies over time, so we're likely to lose information by collapsing across the entire trial.

It's like averaging all the frames of a movie into a single frame. That averaged frame is not likely to tell you much about what happened during the movie.

Estimating Time-Varying Firing Rates

There are many ways to approximate a time-varying firing rate from a spike train:



Raw spike train

Counts in 100 ms windows (non-overlapping)

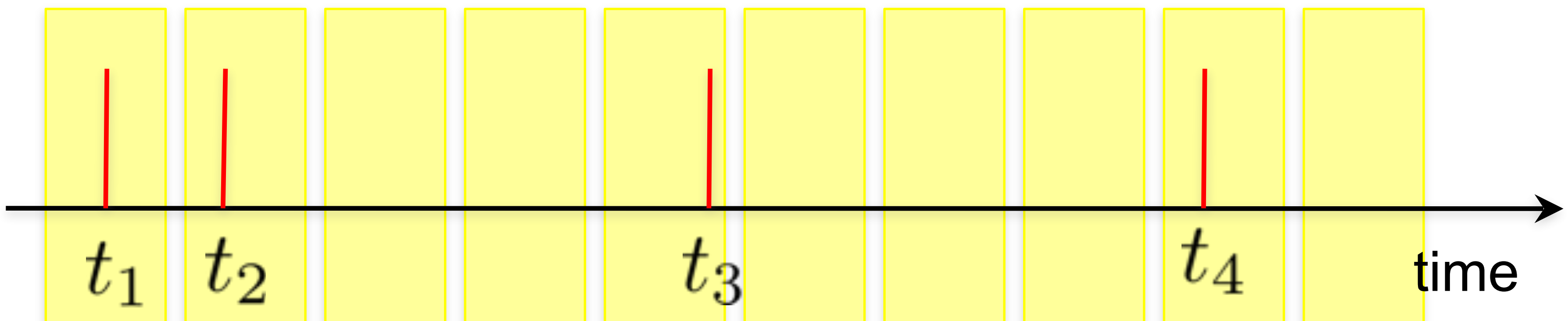
Counts in 100 ms windows (sliding)

Convolution with Gaussian

Convolution with one-sided exponential

Challenges of Estimating a Time-Varying Firing Rate from a Single Spike Train

1) If we want high temporal resolution, bins must be made small. But counts are then primarily zero or one.



2) Firing rate estimate is sensitive to randomness ("noise") in spike generation. We would like to discard this random component.

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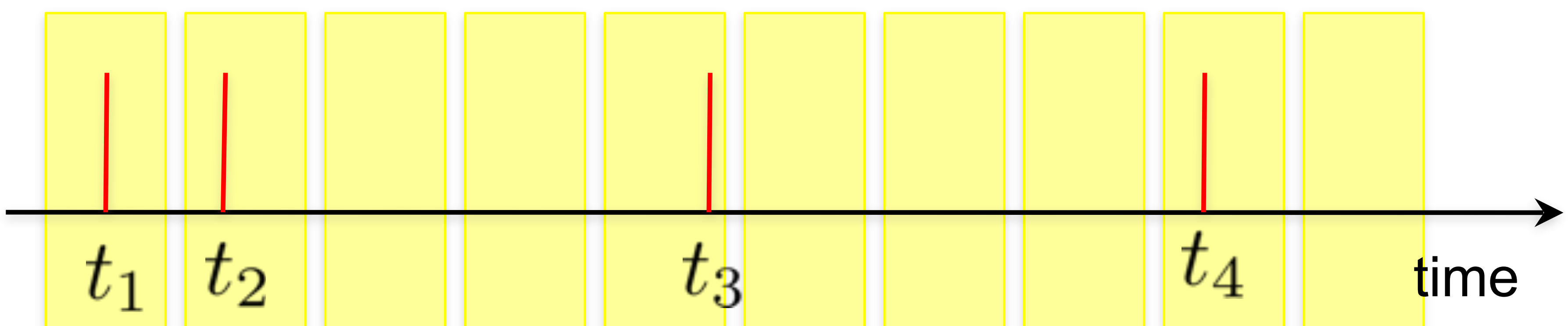
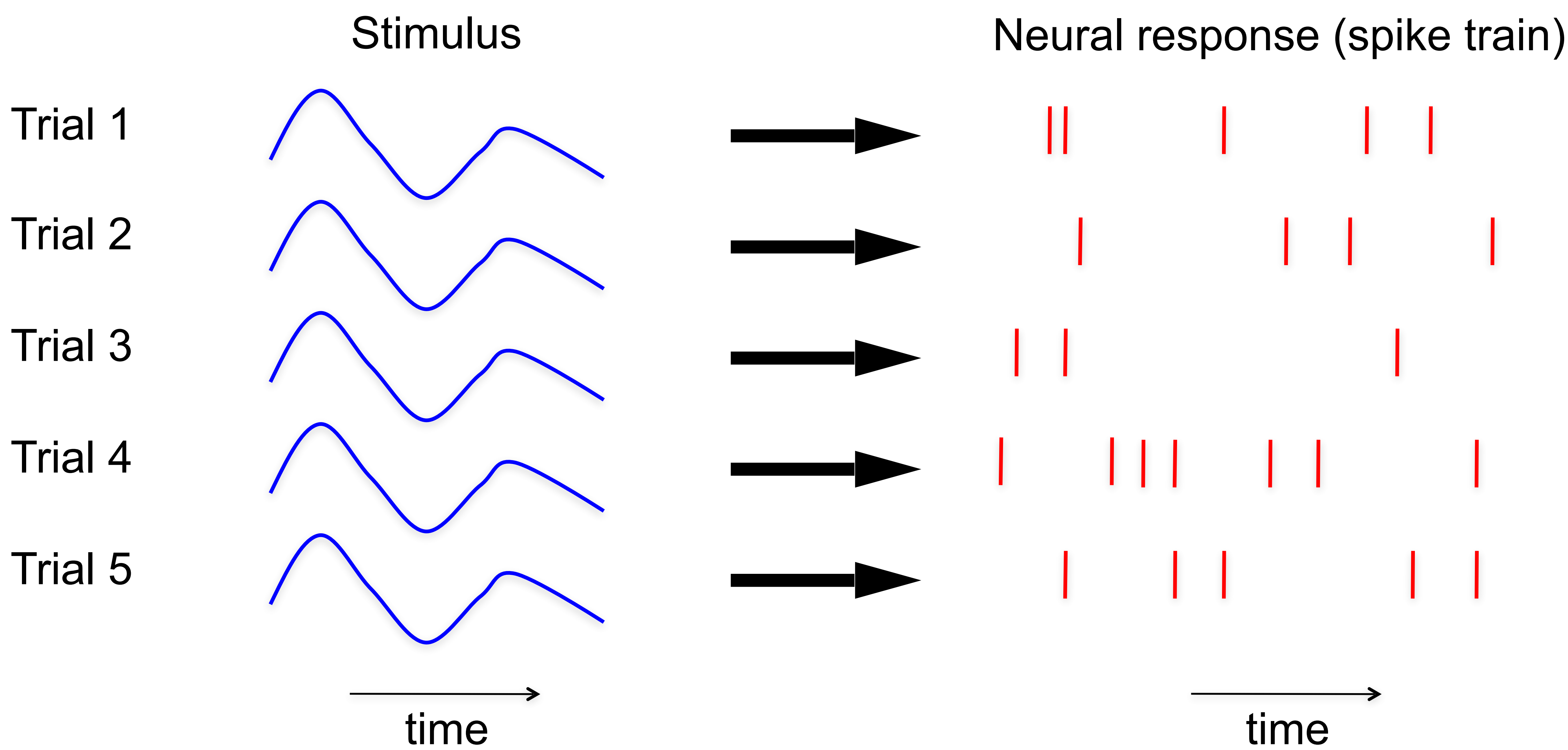


2) Firing rate estimate is sensitive to randomness ("noise") in spike generation. We would like to discard this random component.

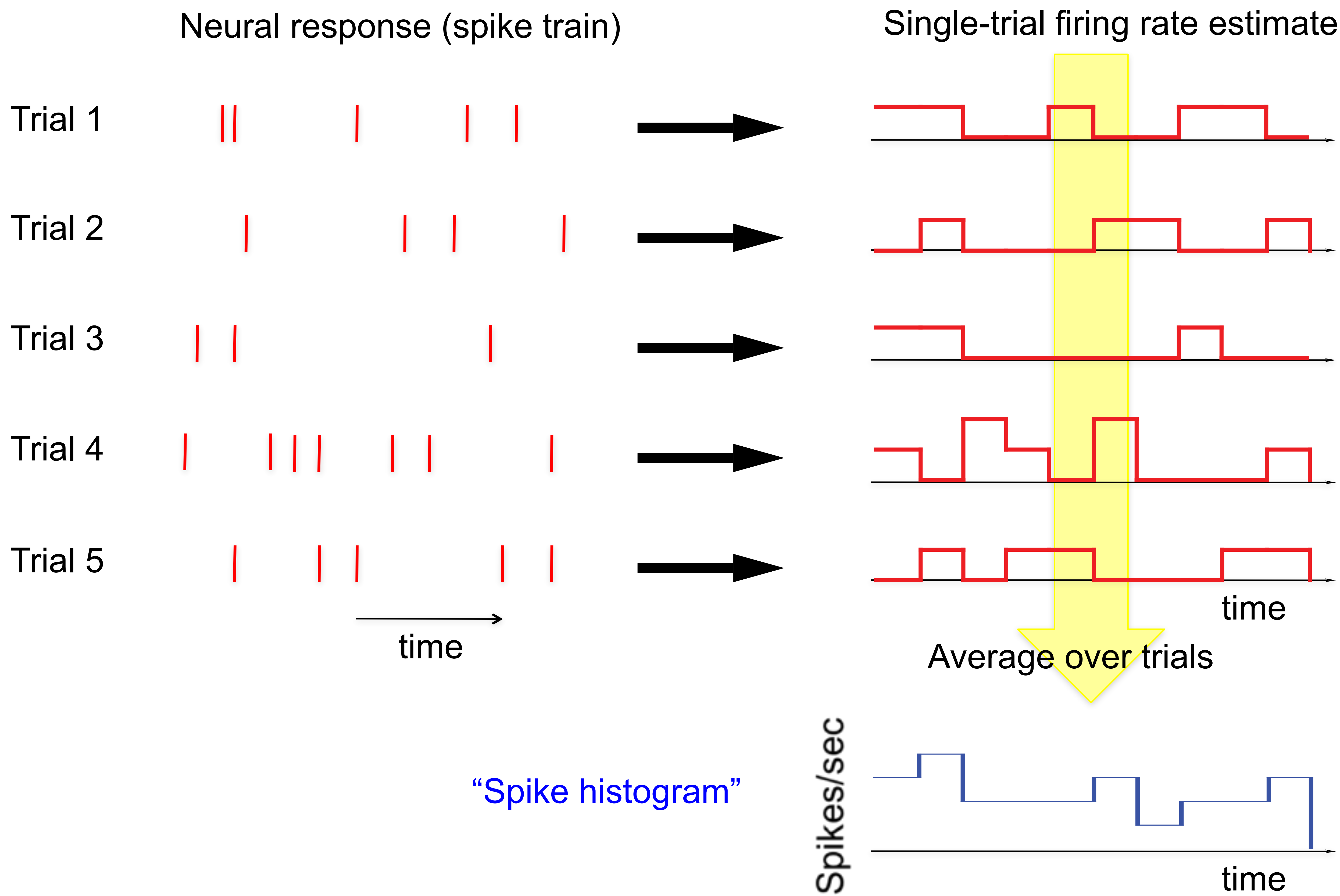
How can we get both high temporal resolution and beat down the noise when estimating firing rates?

One common way: Average across many trials.

Trial-Averaged Firing Rates



Trial-Averaged Firing Rates

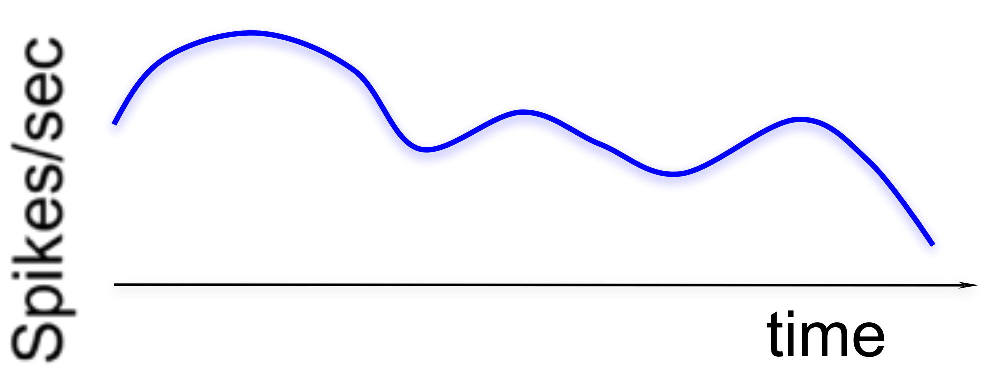


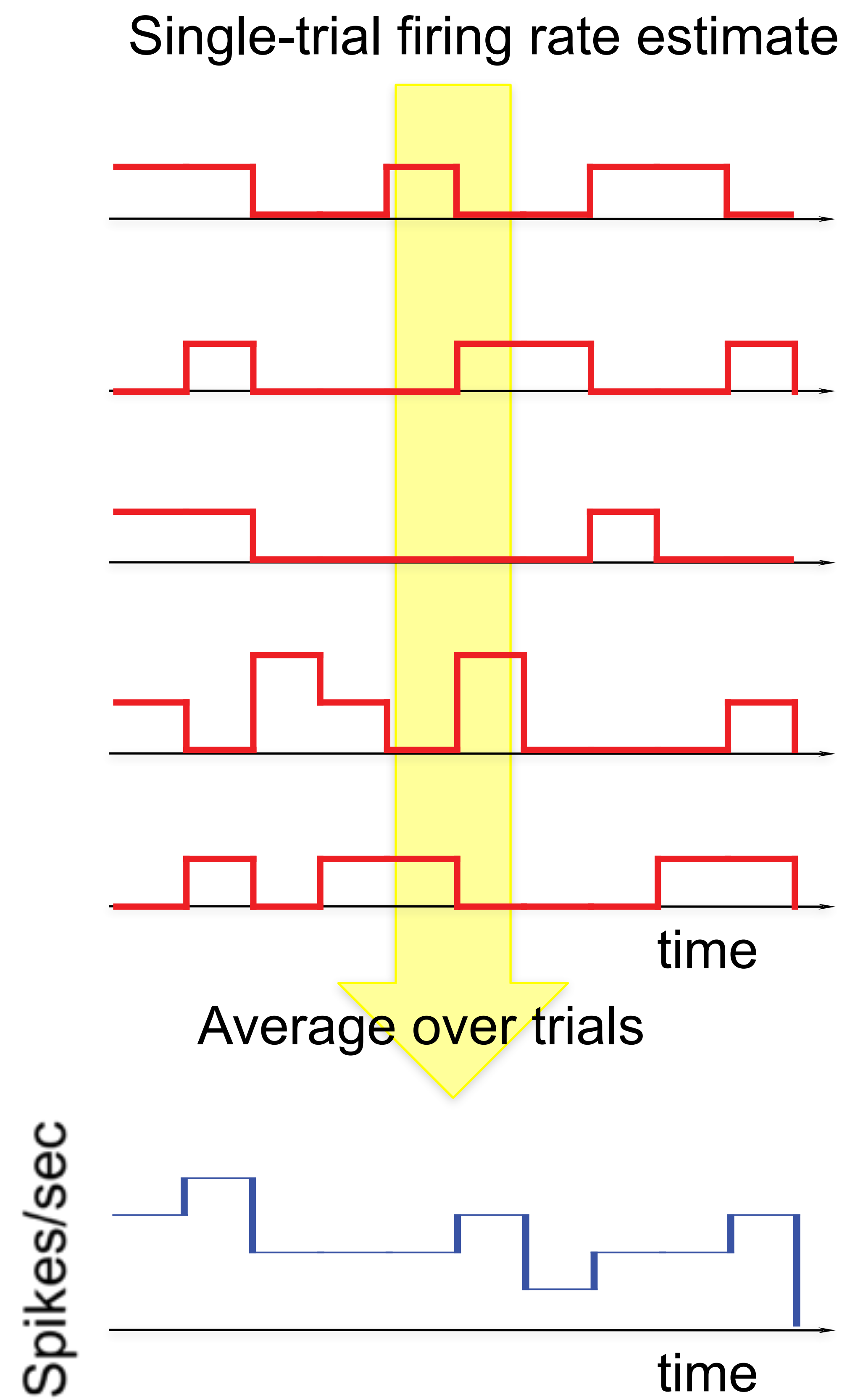
Trial-Averaged Firing Rates

To make a spike histogram look nice,

- use small spike count windows
- average over a large number of trials

In the limit, this will produce a smoothly-varying firing rate.





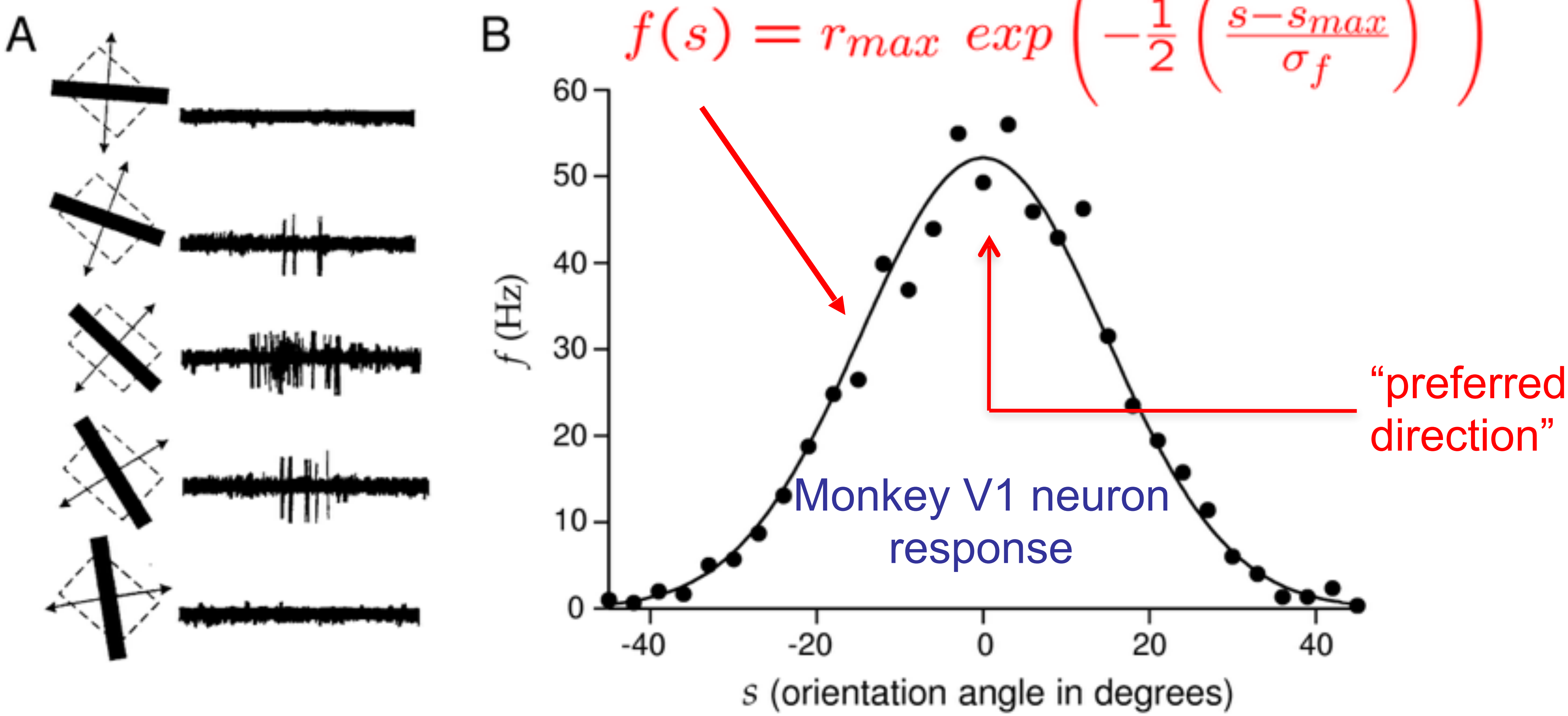
How are neural responses related to sensory stimulus or motor action?

To keep things simple for now, we will take spike counts across a large window, thus ignoring the time-varying structure that may be present in the spike trains.

Tuning Curves

- Neural responses typically depend on many different stimulus properties.
- Here we consider the dependence on just one stimulus attribute.
- Simple approach:
  - Count the number of spikes fired during the presentation of a stimulus.
  - Repeat stimulus presentation many times to better estimate the mean count.
  - Vary the stimulus attribute of interest, *s*.
  - Plot result and (optionally) fit parameterized function to data.

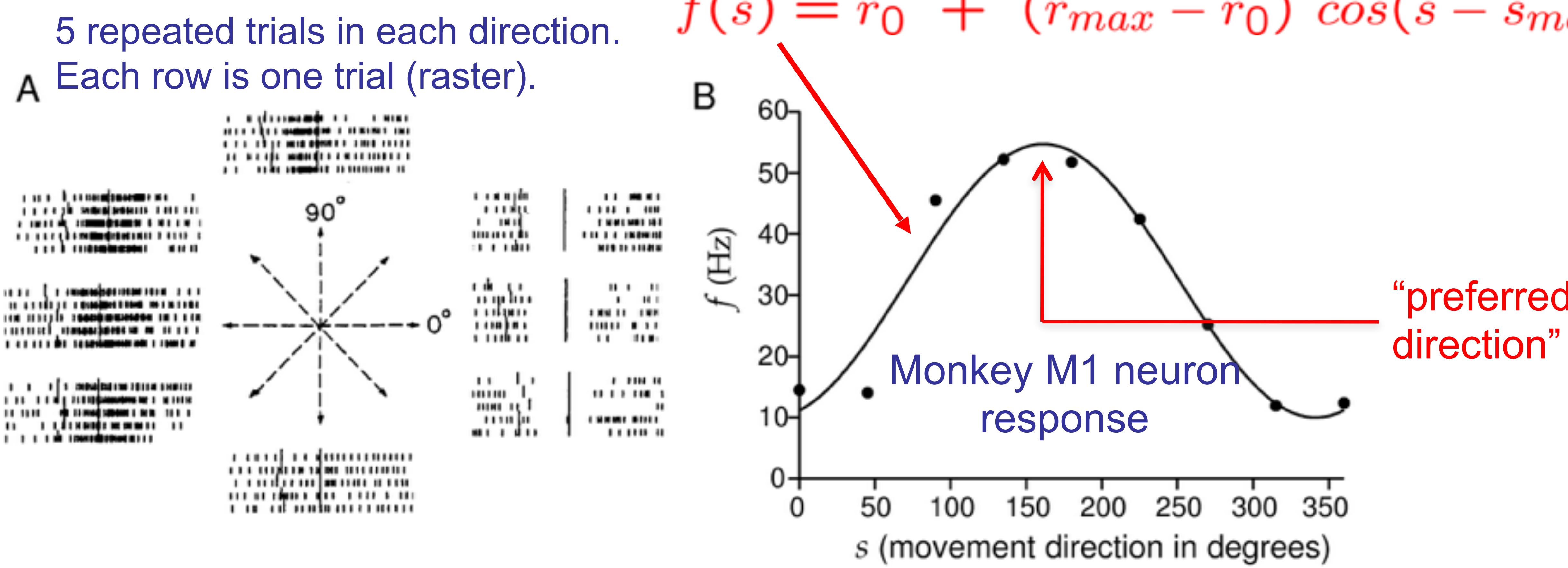
$$f(s) = r_{max}\ exp\left(-\frac{1}{2}\left(\frac{s-s_{max}}{\sigma_f}\right)^2\right)$$



Tuning Curves

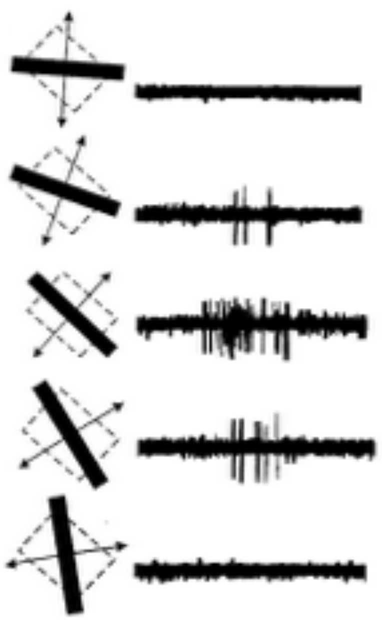
- Tuning curves also characterize responses from neurons in motor areas.
- In this example, a monkey is trained to reach in different directions, *s*.
- Count number of spikes firing during arm movement.
- Repeat movement many times to better estimate the mean count.

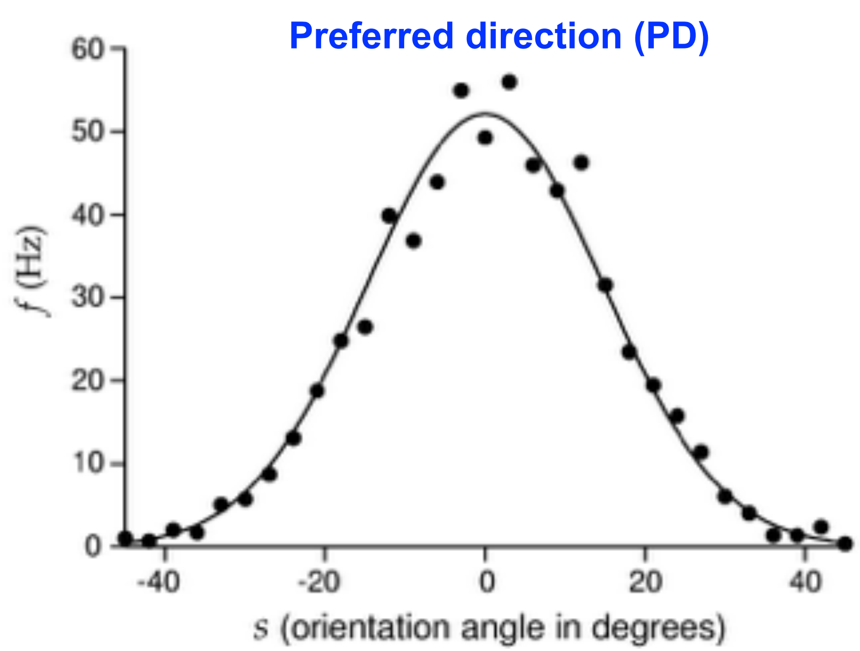
$$f(s) = r_0 + (r_{max} - r_0)\ cos(s - s_{max})$$



Food for thought: Should we think of visual and motor systems in the exact same way (i.e., tuning curves)?

Visual system: Hubel & Wiesel and colleagues



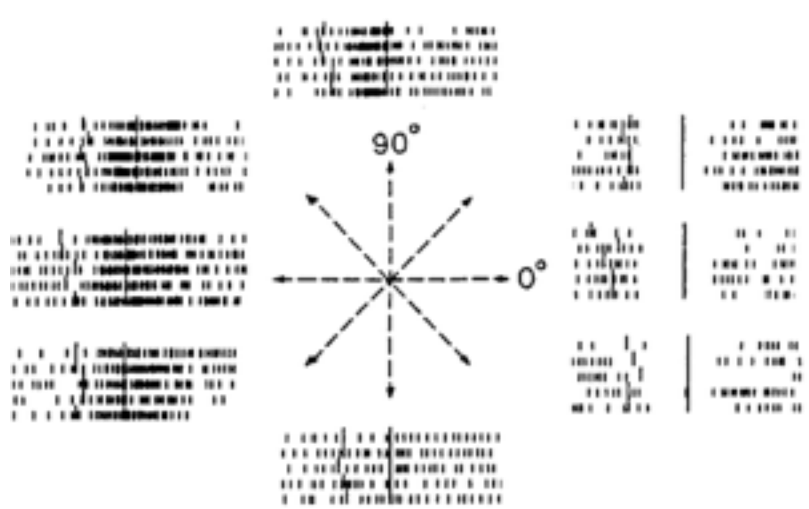


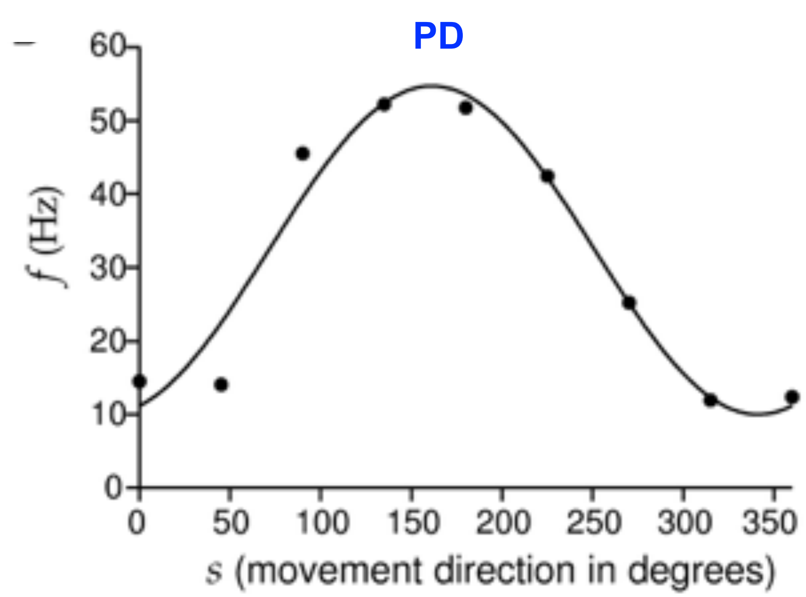
Role of visual system presumably to internally represent the outside world

Neurons extract key visual features, summarized by largely static tuning curves

Thus PDs are largely invariant to contrast and speed of moving edges (i.e., neurons encode movement direction)

Motor system: Georgopoulos & Schwartz and colleagues





Role of **motor system** presumably to **generate time-varying signals** to drive muscles, **not to represent movement**

Neurons **generate (cause)** time-varying signals, and most are **not well captured by static tuning curves with simple functions**

PDs are **not invariant** in time, to movement speed, or to movement extent (i.e., tuning curves are time varying, complex & heterogeneous)

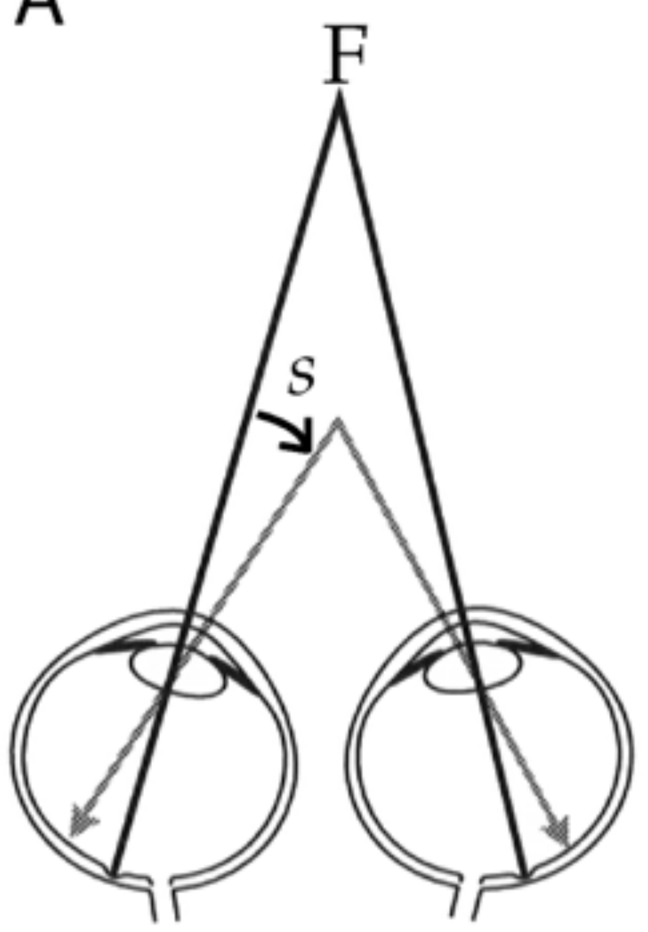
Shenoy, Churchland, Sahani (2013) *Ann. Rev. Neurosci.*
Churchland & Shenoy (2007b) *J Neurophysiol.*
Also: Fetz, Todorov, Cisek, Scott, Kalaska, Graziano, …

Tuning Curves

- One last example of tuning (disparity, or stereoscopic depth).

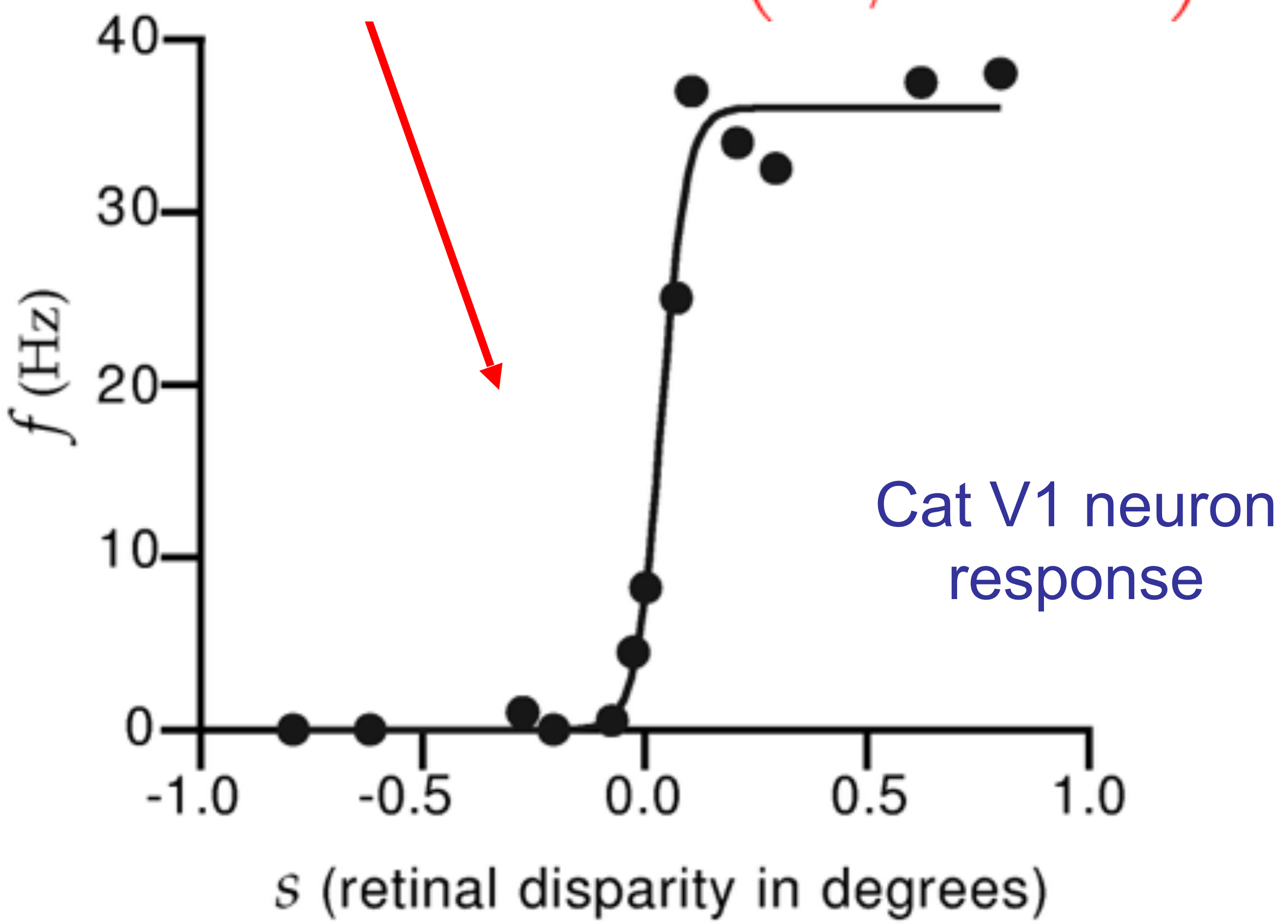
- This example illustrates the last tuning-curve functional form that is commonly observed in cortex: sigmoidal.

A



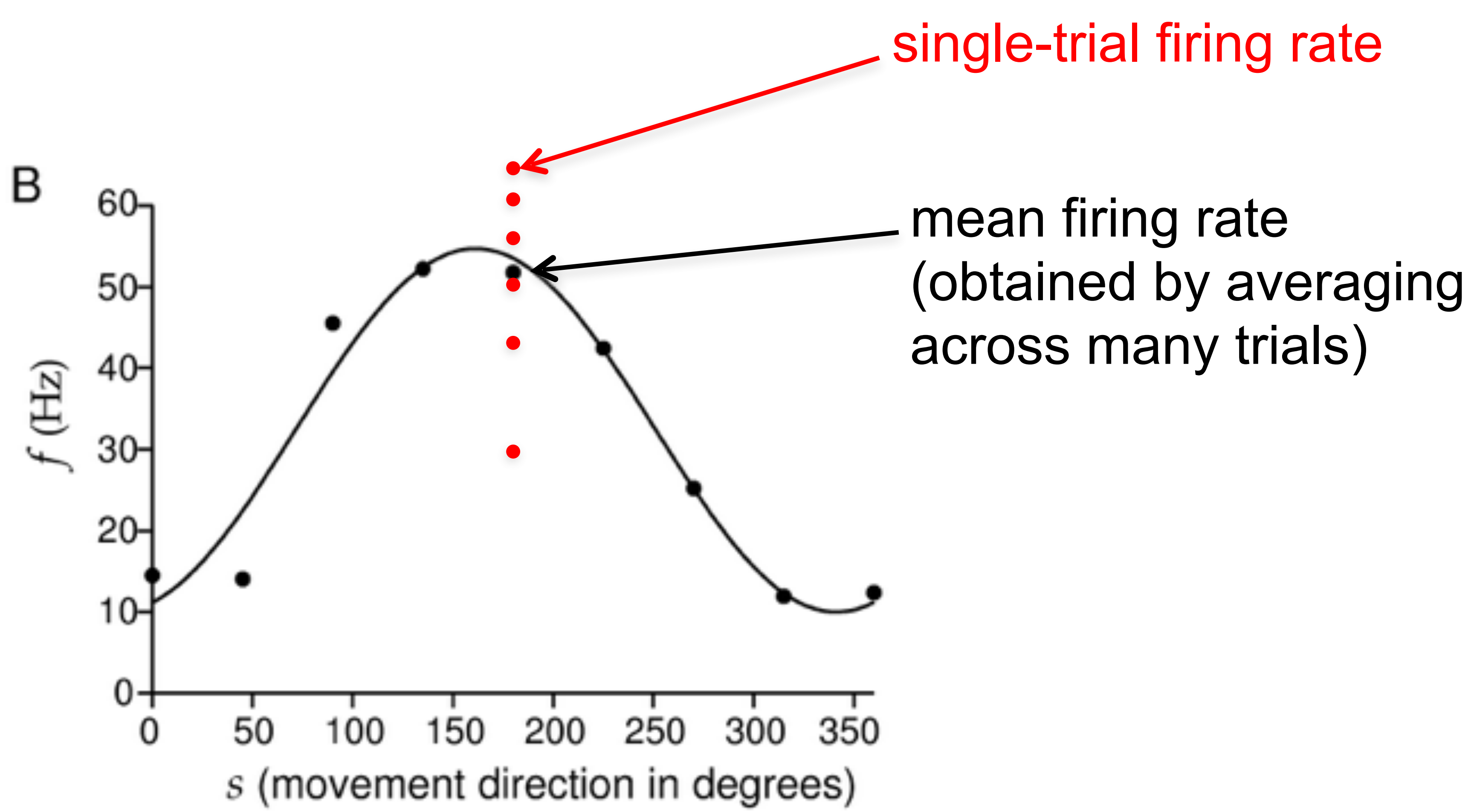
B

$$f(s) = \frac{r_{max}}{1+exp\left((s_{1/2}-s)/\Delta_s\right)}$$



Noise

- Tuning curves allow us to predict the mean firing rate, given a stimulus.
- They do not describe how firing rate varies from trial to trial.



Noise

- Single-trial responses are probabilistic, not deterministic.

- Noise models describe the probability distribution, representing the firing rate on any given trial, about the mean $f(s)$.

- The standard deviation for the noise distribution can be:

    - Independent of the mean $f(s)$ → additive noise.

    - Dependent on the mean $f(s)$ → e.g., Poisson noise

- We will soon discuss a stochastic spike-generator model (Poisson) that will allow us to examine noise in finer detail.

What Makes a Neuron Fire?

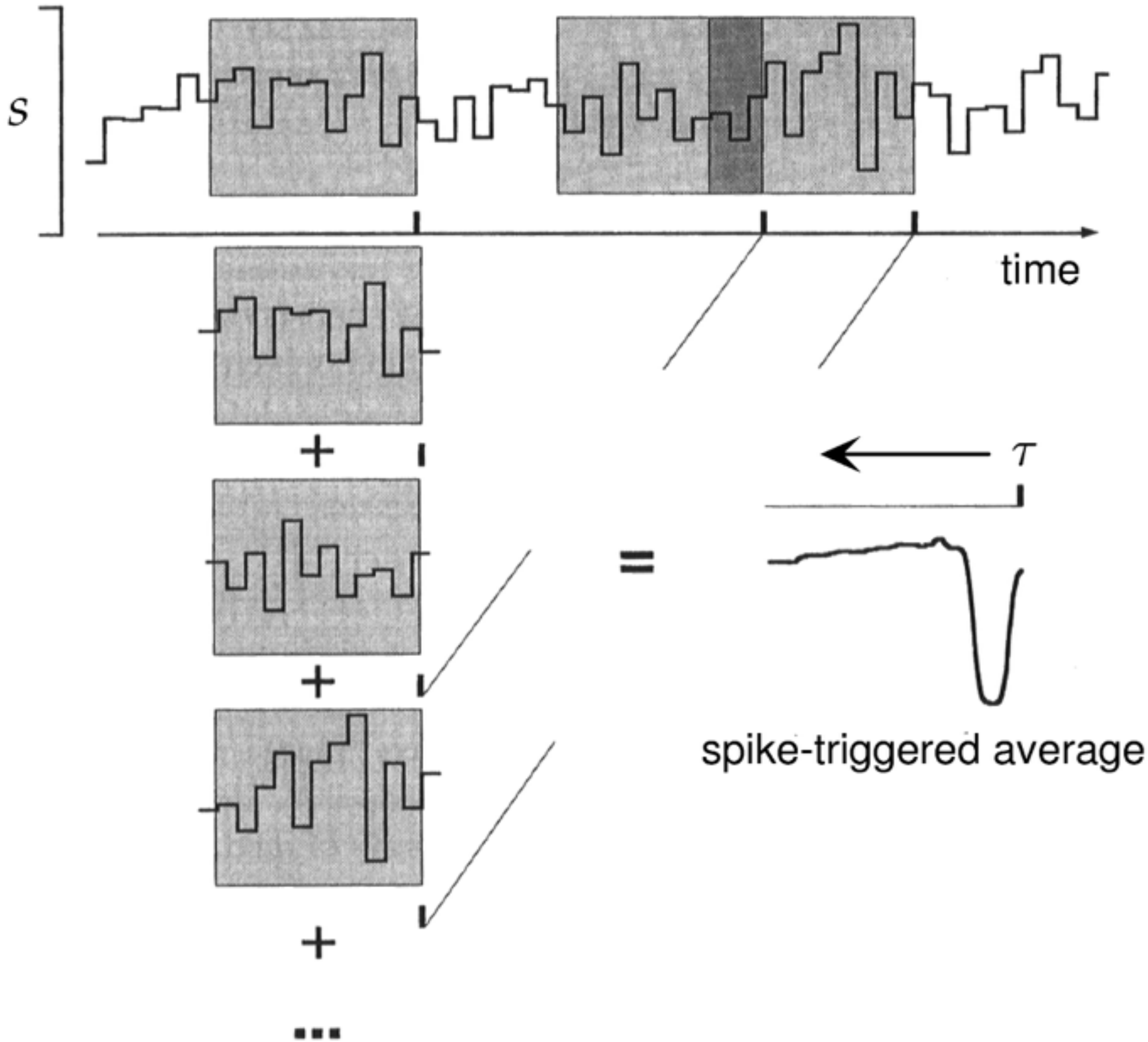
- Response tuning curves characterize the average response of a neuron to a given stimulus.

- What about averaging the stimuli that produce a given response? Yes, can do this too.

- Can trigger on action potential and ask, “What, on average, did the stimulus do before an action potential was fired?”

- Called “spike-triggered average”.

Spike-Triggered Average



The Spike-Triggered Average

• Spike-triggered average stimulus, $C(\tau)$, is average value of stimulus, *s*, over a time interval τ before spike is fired:

$$C(\tau) = \left\langle \frac{1}{n} \sum_{i=1}^{n} s(t_i - \tau) \right\rangle$$

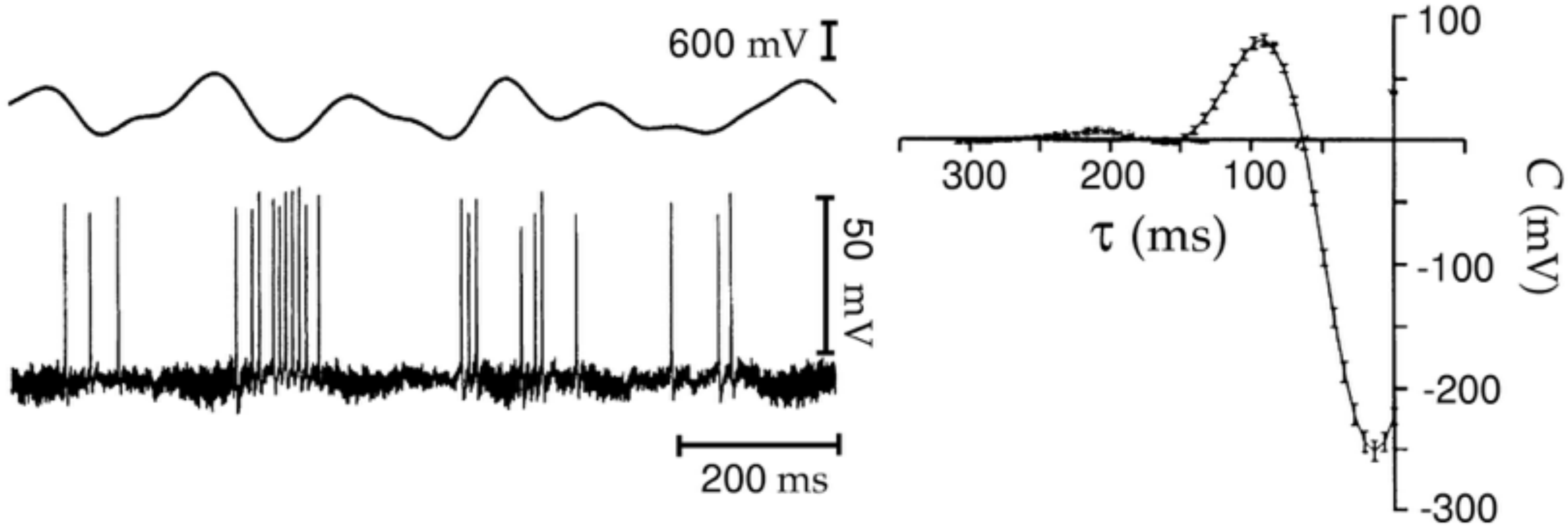
ith spike time

average over all trials

• We expect $C(\tau)$ to approach 0 for τ > correlation time between stimulus and response.

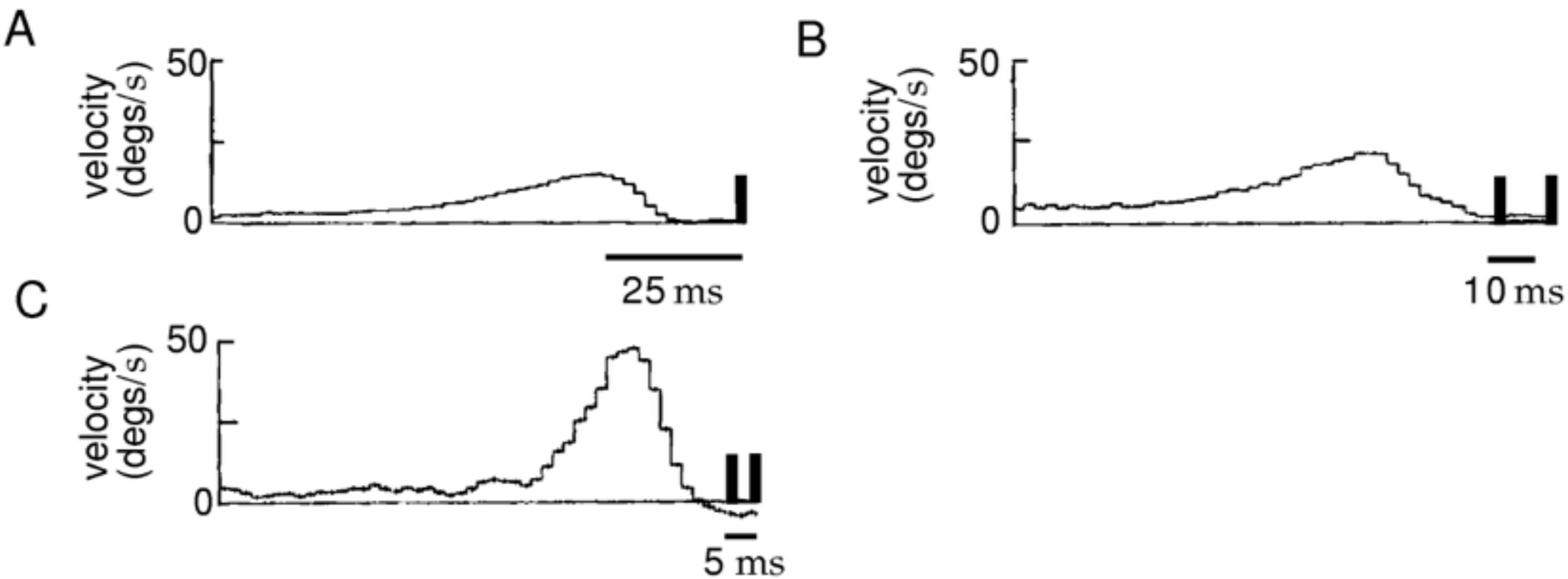
• We expect $C(\tau) = 0$ for $\tau < 0$ since response cannot depend on future stimuli.

Spike-Triggered Average: Example



- Weakly electric fish generate oscillating electric fields (top trace).
- Distortions in electric field (nearby objects) are detected by skin sensors.
- Spike-triggered average (right panel) shows that a spike is generated, on average, following a small positive and then larger negative E field.

Multiple-Spike Triggered Average: Example



Blowfly H1 neuron responding to moving visual stimuli.

A) Average stimulus velocity triggered on single spike.
B) Average stimulus velocity triggered on spike pair (separated by 10 ms).
C) Average stimulus velocity triggered on spike pair (separated by 5 ms).

Spike-Train Statistics

• A complete description of the stochastic relationship between a stimulus and a response would require us to know the probabilities corresponding to *every* sequence of spikes that can be evoked by the stimulus.

• However, the number of possible spike sequences is typically so large that determining or even roughly estimating all of their probabilities of occurrence is impossible.

• Instead, we must rely on some statistical model that allows us to estimate the probability of an arbitrary spike sequence.

Spike-Train Statistics

- *Point process* – stochastic process that generates a sequence of events, such as APs.

- *Renewal process* – point process where the probability of an event depends only on the immediately preceding event (intervals between successive events are independent).

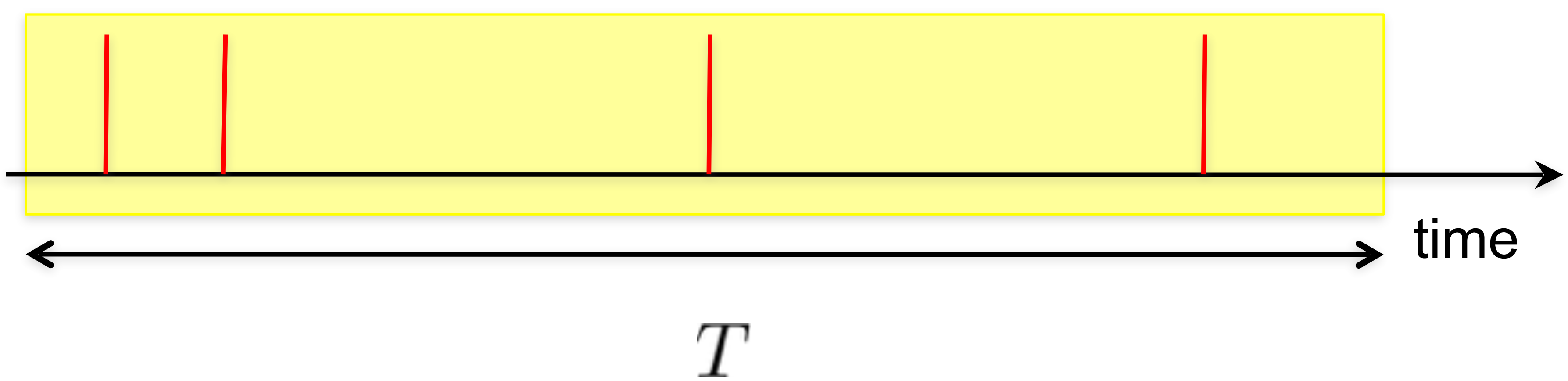
- *Poisson process* – point process where no dependence at all on preceding events (events are statistically independent).

- The Poisson process is an extremely useful, and widely used, approximation of stochastic neuronal firing.

Comparison with Data

- Poisson process is simple and useful, but does it match data variability?
- Let X be the spike count in a bin of duration T.

$$X \sim \text{Poisson}(\lambda T)$$



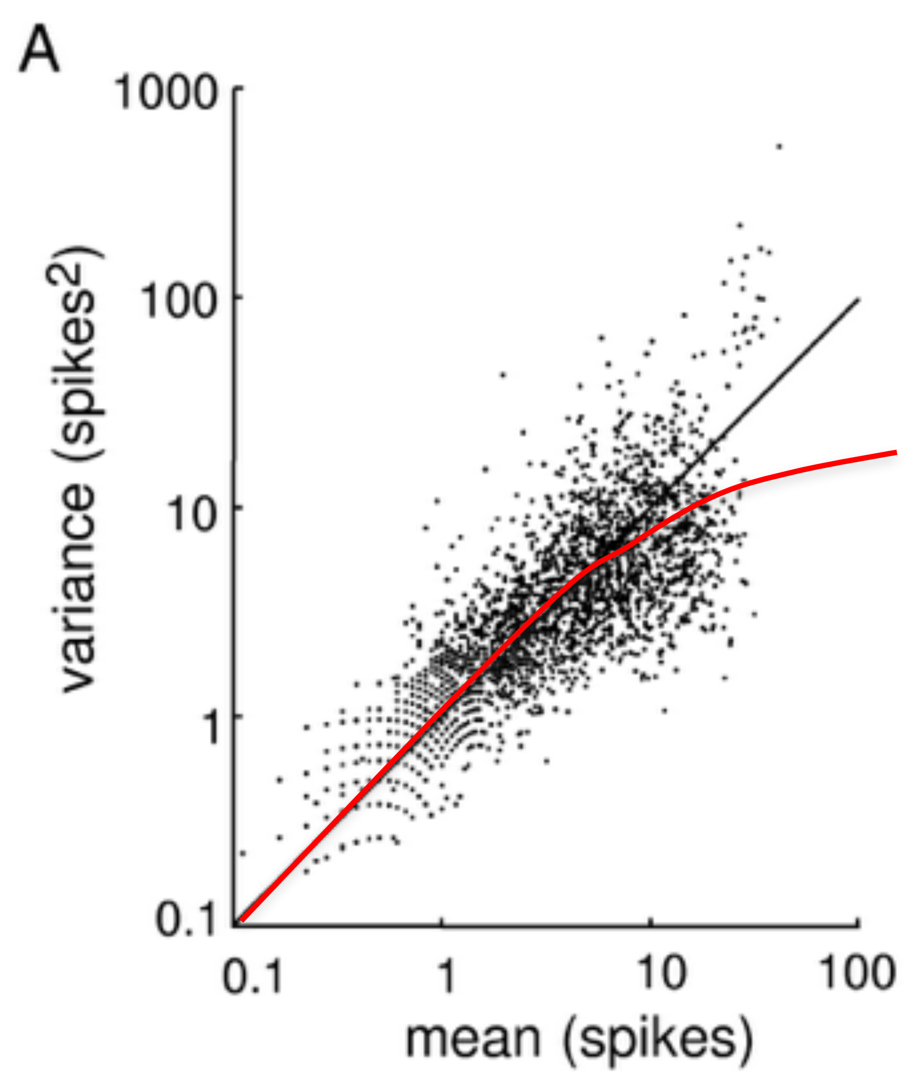
$$E[X] = \lambda T$$

$$\text{var}(X) = \lambda T$$

$$\text{Fano factor} = \frac{\text{var}(X)}{E[X]} = 1$$

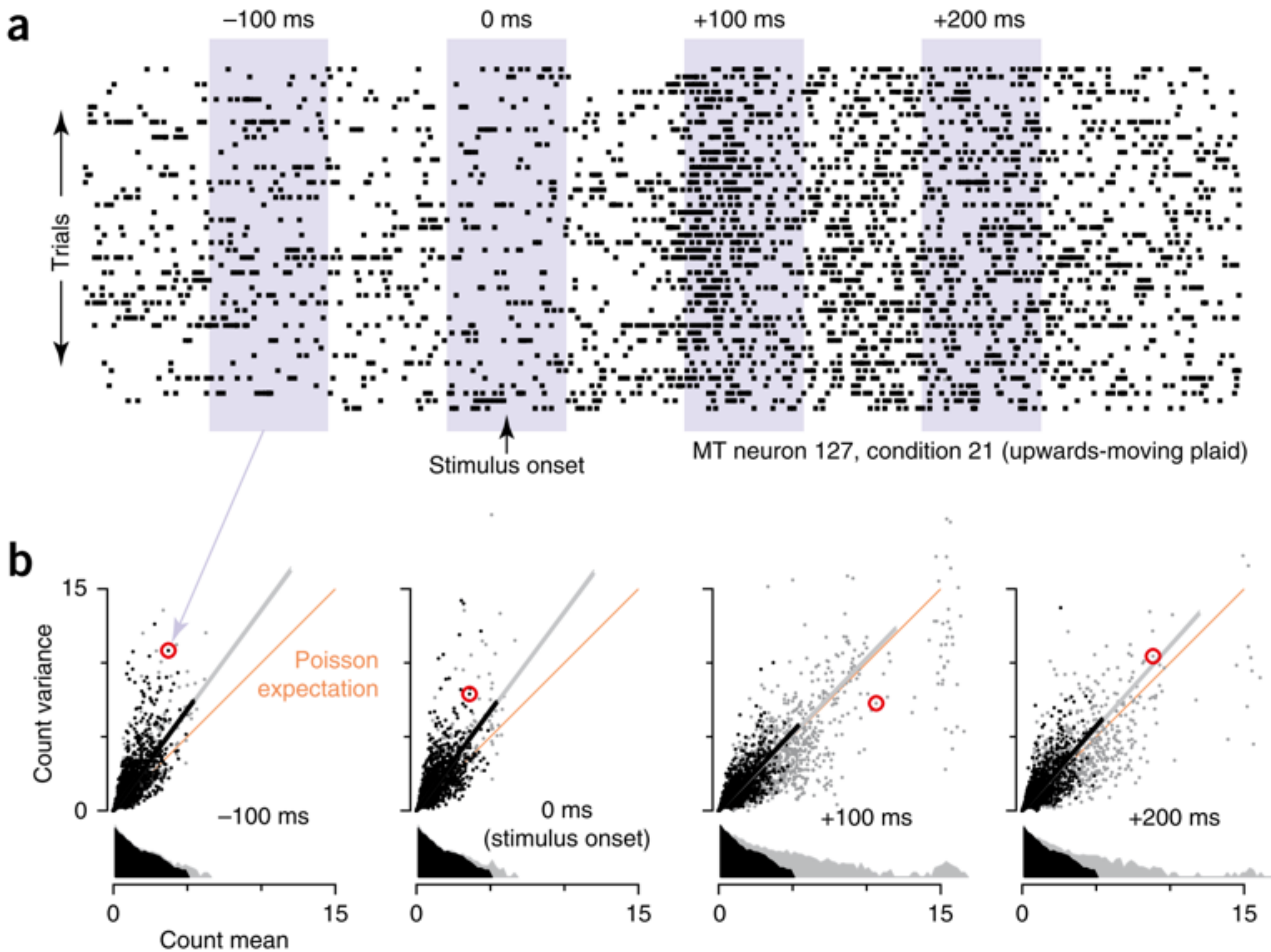
Example from Primate Medial Temporal (MT) Area

• This is an example where a Poisson distribution models the counts well.



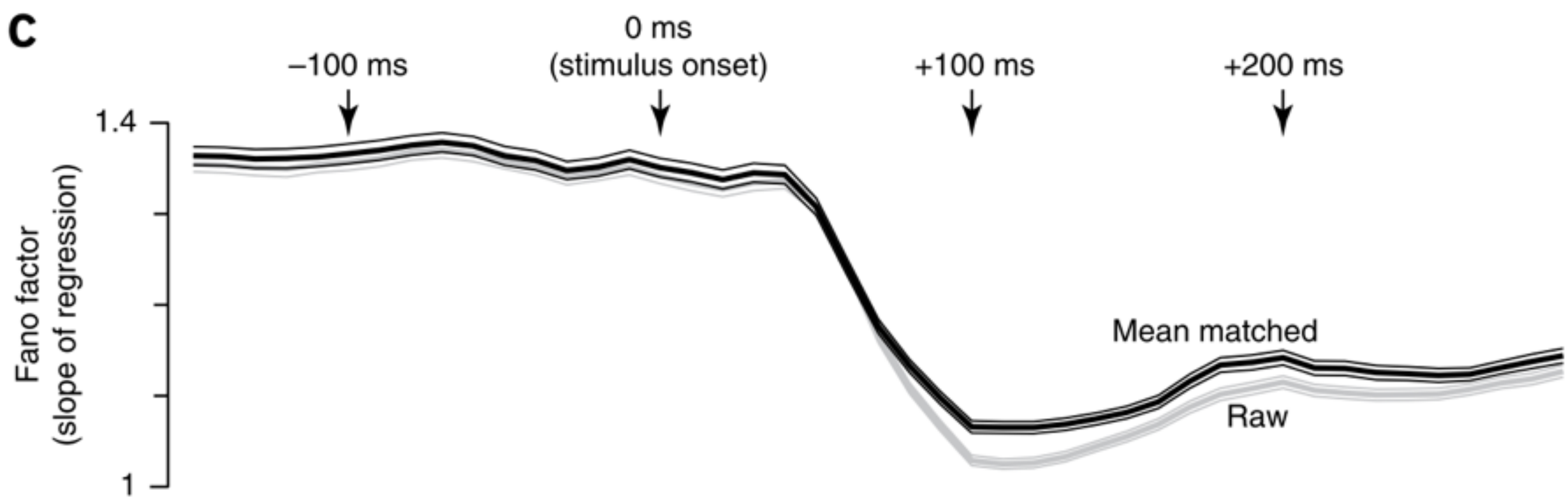
• Typically, fits aren't this good with real data.
• Refractory period can lead to more regular spiking (i.e. lower variance) at higher firing rates than would be predicted by Poisson.

Example from recent data



Churchland*, Yu*, et al, Nature Neuroscience 2010.

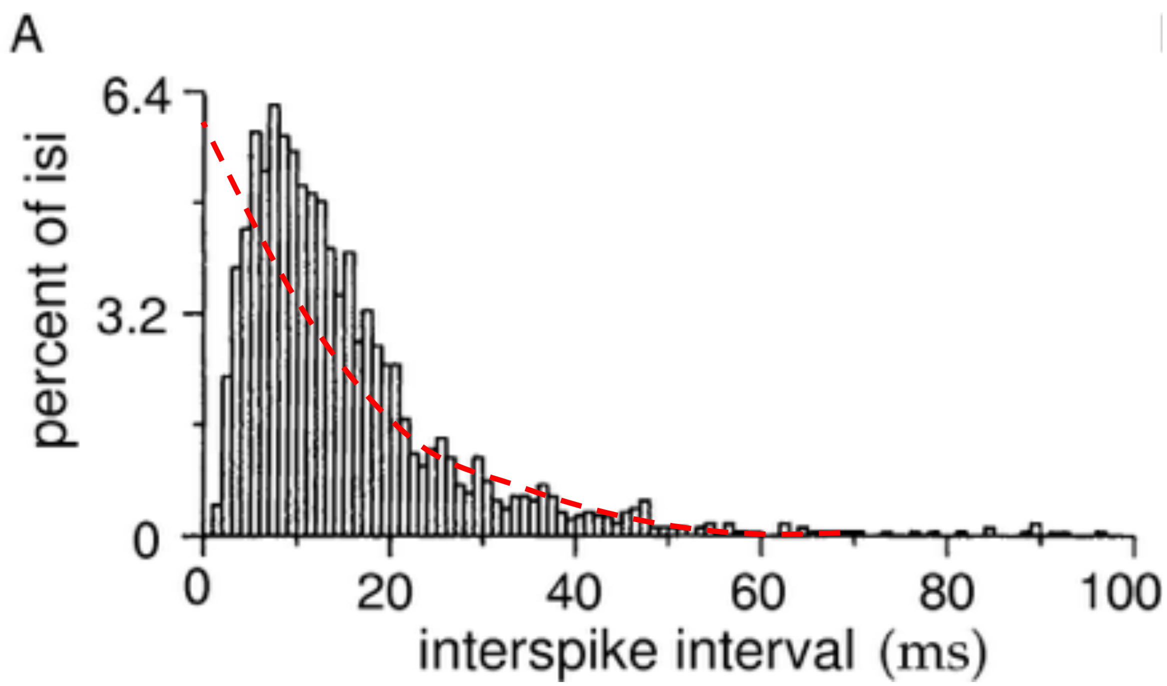
Example from recent data



Churchland*, Yu*, et al, Nature Neuroscience 2010.

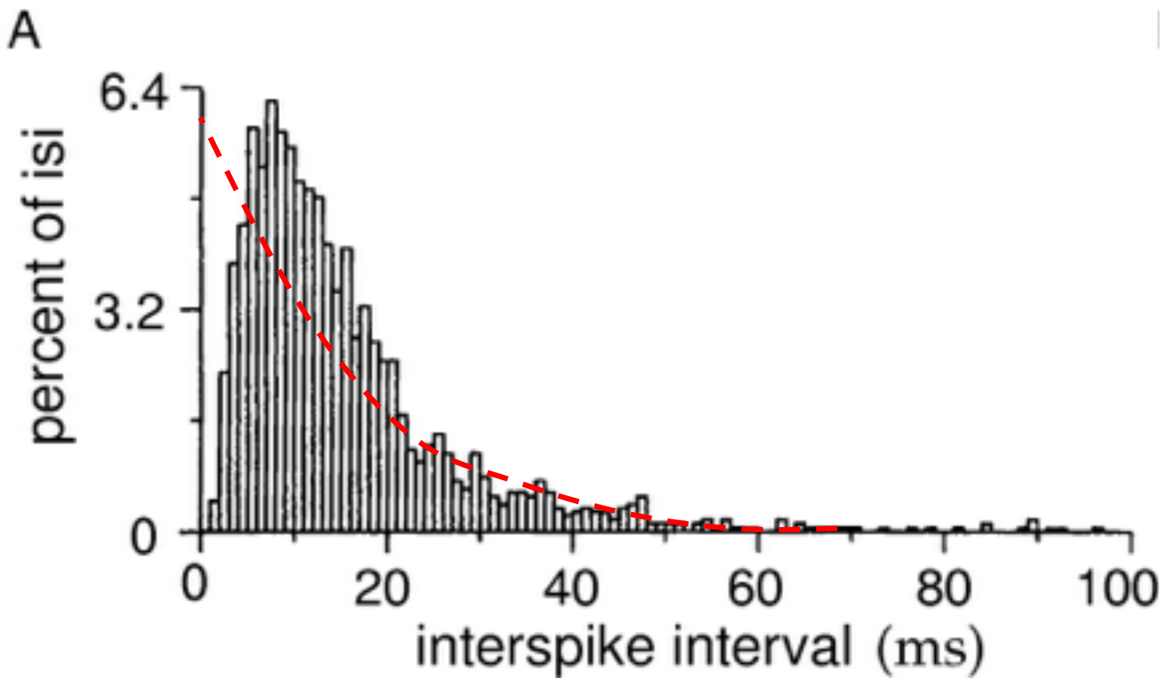
Inter-spike Interval (ISI) Distribution

- Poisson process predicts exponentially-distributed ISI’s (red curve).
- Example from primate MT area:



- This ISI distribution is very typical of real neural data.
- Why are ISI’s not exponentially distributed for real neural data?

Why are ISI's not exponentially distributed?

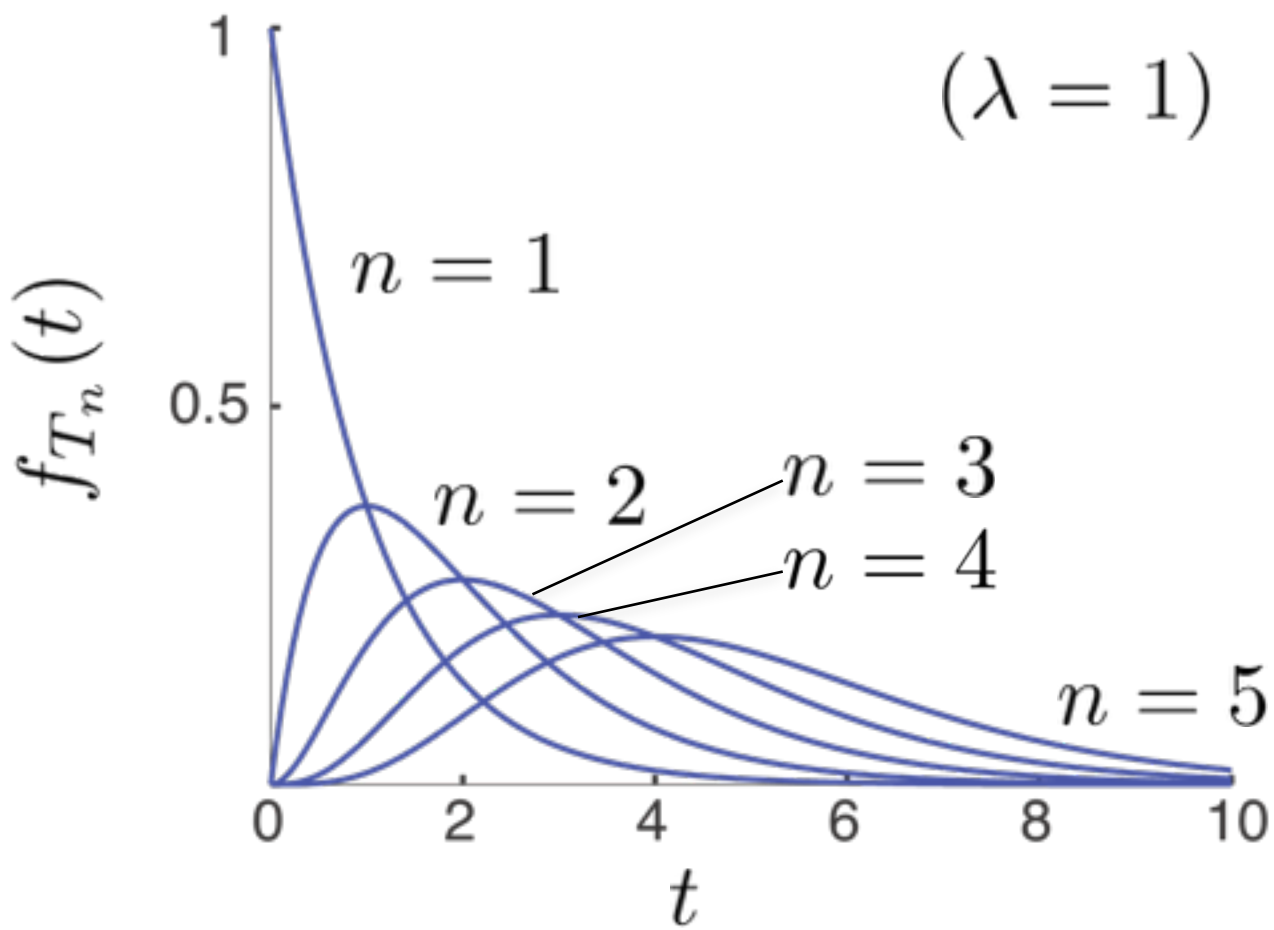


1) Real data have few or no short ISI's due to refractory period.

2) Firing rates typically vary over time.

What is a better model for ISI's?

Gamma Distribution



n is the order of the Gamma distribution

$n = 1$ is the exponential distribution

ISI's are better modeled using Gamma distribution with $n > 1$

Gamma Distribution

Let $T_n = t_1 + \ldots + t_n$, where $t_1, \ldots, t_n \sim \exp(\lambda)$ i.i.d.

T_n is an nth order Gamma random variable

$$f_{T_n}(t) = \lambda e^{-\lambda t} \frac{(\lambda t)^{n-1}}{(n-1)!} \qquad \text{for } \lambda > 0 \text{ and } t > 0.$$

Intuition: The larger the order n (i.e., the more exponentially-distributed random variables are added together), the fewer small ISI's will appear in the Gamma distribution.

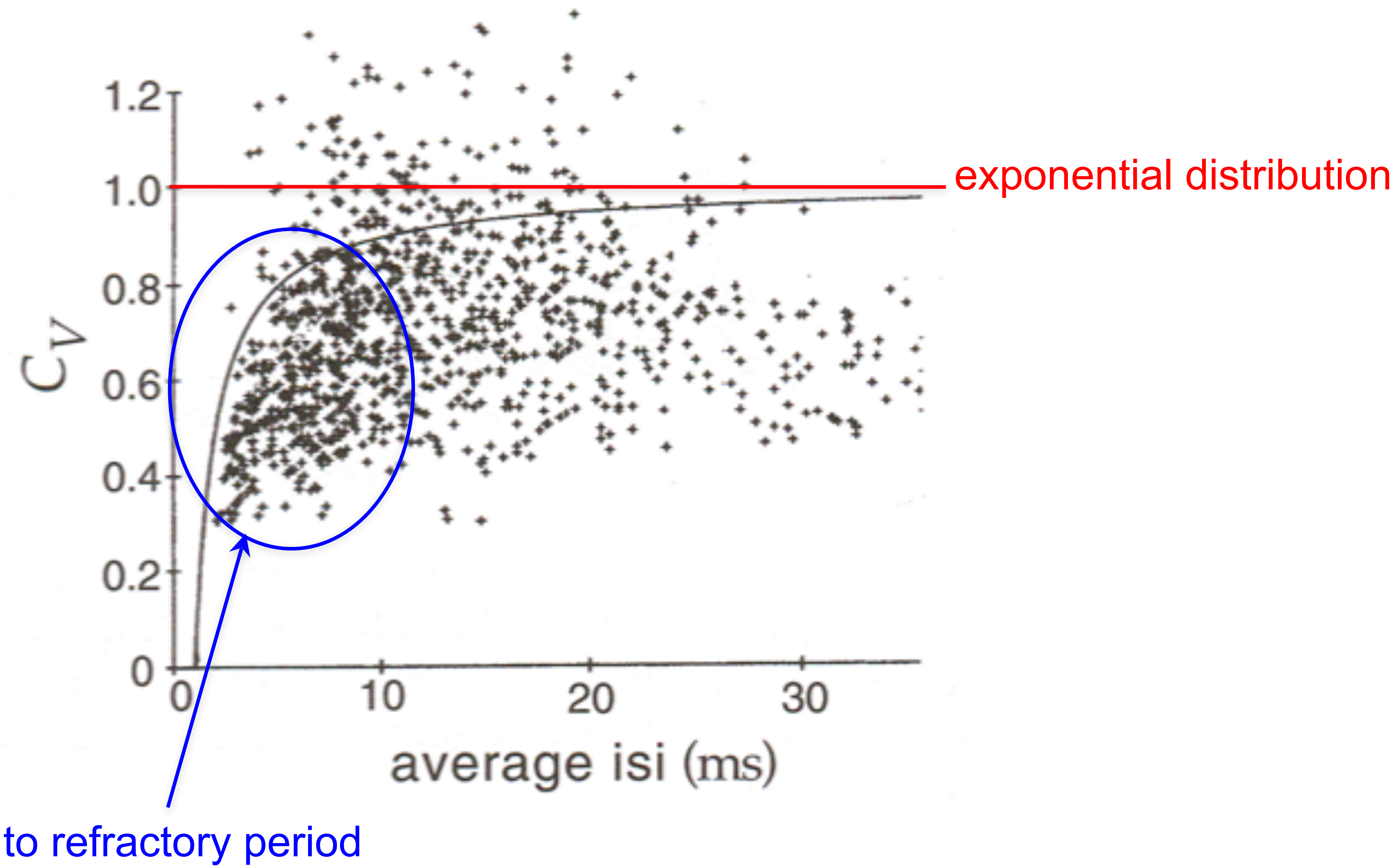
Coefficient of Variation (C_V) of ISI's

$$\text{Let } t \sim \exp(\lambda),$$

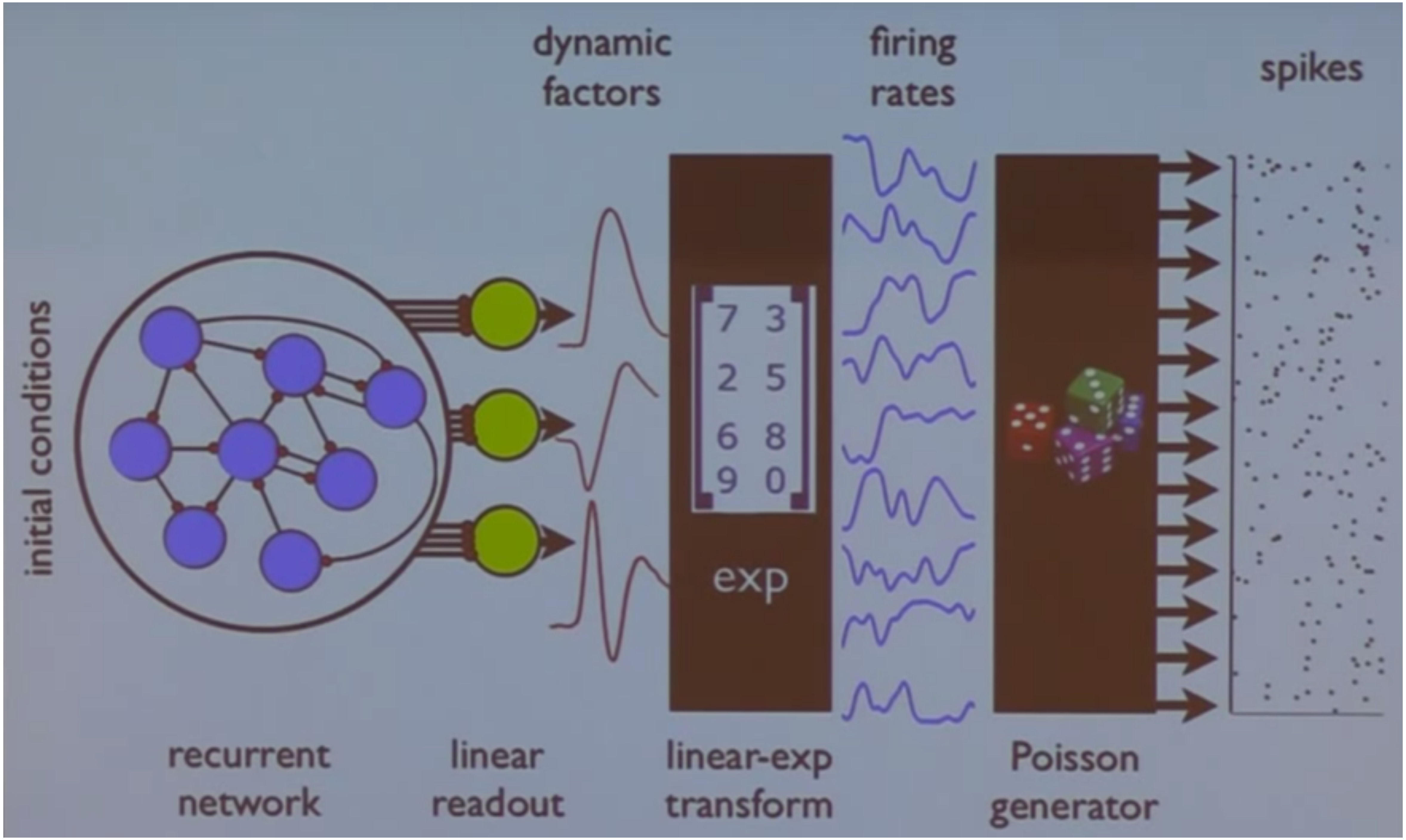
$$E[t] = \frac{1}{\lambda} \qquad \text{var}(t) = \frac{1}{\lambda^2}$$

$$C_v = \frac{\sqrt{\text{var}(t)}}{E[t]} = 1$$

Coefficient of Variation (C_V) of ISI's

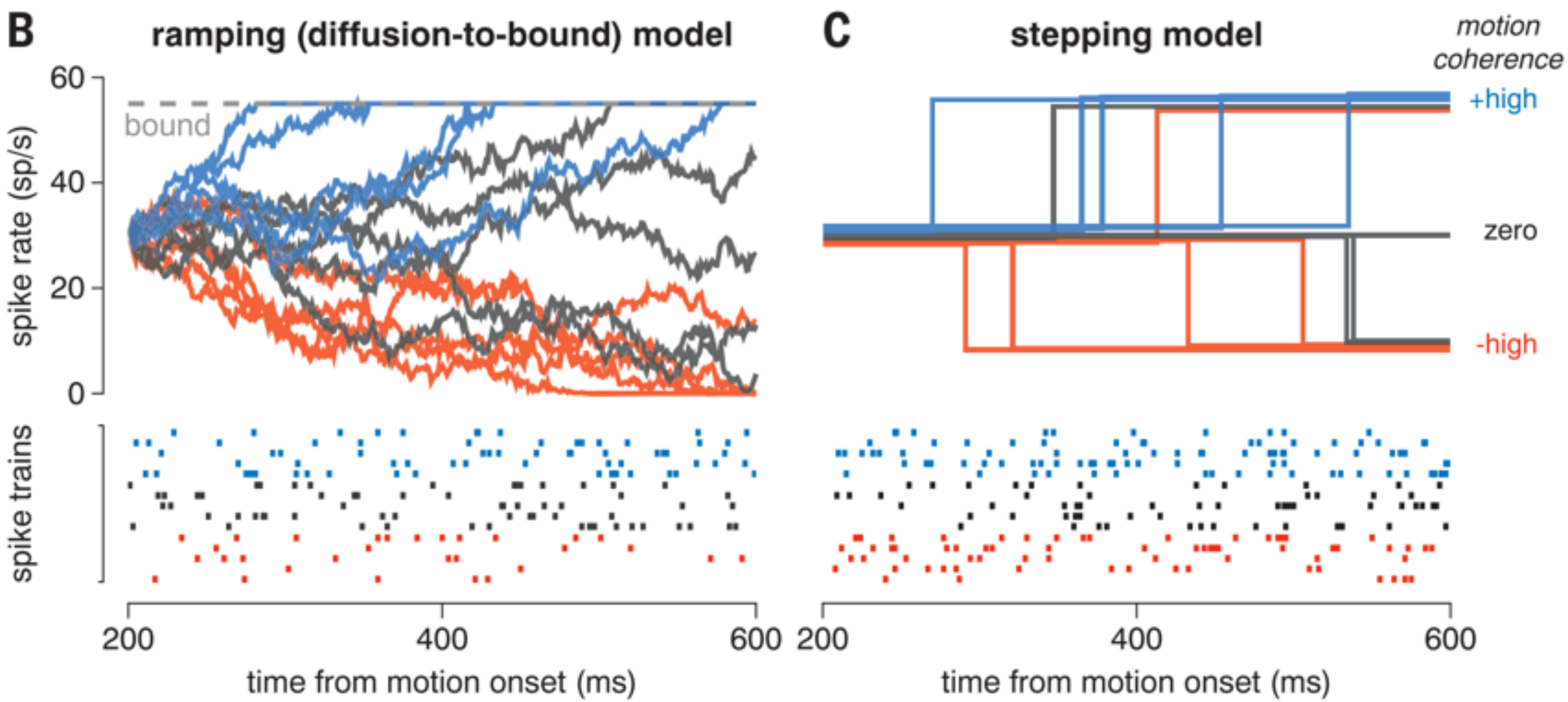


Where might Poisson processes come up?



Pandarinath et al., COSYNE 2017

Where might Poisson processes come up?



Latimer et al., Science 2015

Where might Poisson processes come up?

Ramping model:

$$x_{j,1} = x_0 + \epsilon_{j,0} \quad (2)$$

$$x_{j,t+1} = x_{j,t} + \beta_{c(j)} + \epsilon_{j,t} \quad (3)$$

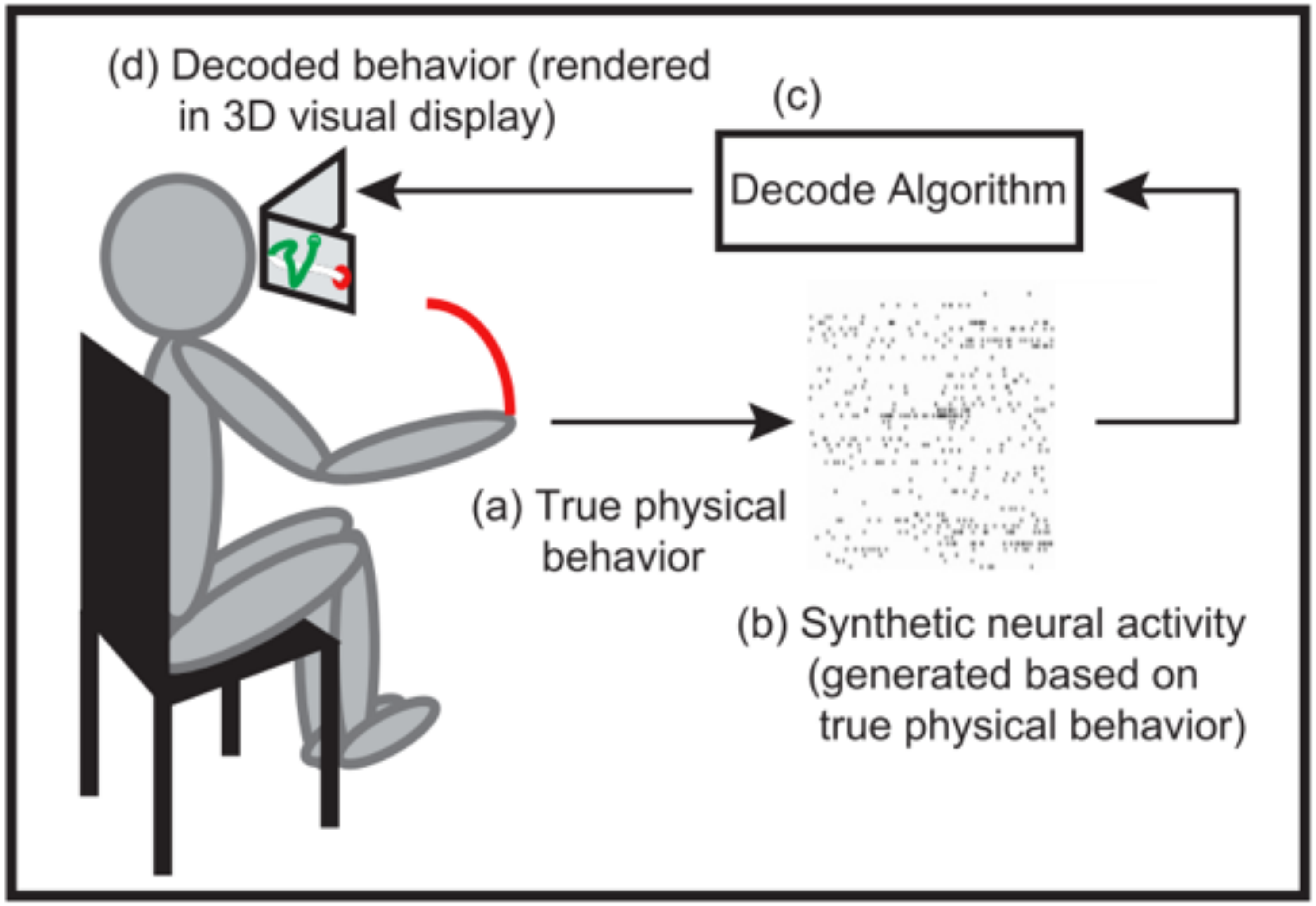
$$\epsilon_{j,t} \sim \mathcal{N}(0, \omega^2) \quad (4)$$

$$\tau_j = \begin{cases} \inf_t x_{j,t} \geq 1 & : \text{ if there exists } x_{j,1:T_j} \geq 1 \\ \infty & : \text{ otherwise} \end{cases} \quad (5)$$

$$\boxed{\begin{aligned} y_{j,t} | t < \tau_j &\sim \text{Poisson}\left(\log(1 + \exp(\gamma x_t))\Delta_t\right) \quad (6) \\ y_{j,t} | t \geq \tau_j &\sim \text{Poisson}\left(\log(1 + \exp(\gamma))\Delta_t\right) \quad (7) \end{aligned}}$$

Latimer et al., Science 2015

Where might Poisson processes come up?



$$\lambda_t^{(k)} = (\lambda_{max}^{(k)} - \lambda_{min}^{(k)}) c^{(k)} \cdot x_t + \lambda_{min}^{(k)}$$

$$y_t \,\big|\, \lambda_t \sim \mathrm{Poisson}\big[h(\lambda_t)\big]$$

Cunningham et al., J Neurophys 2011