

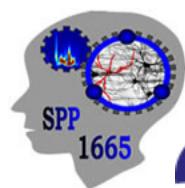
Spike Train Analysis I: spike train, stochastic process, and rate analysis

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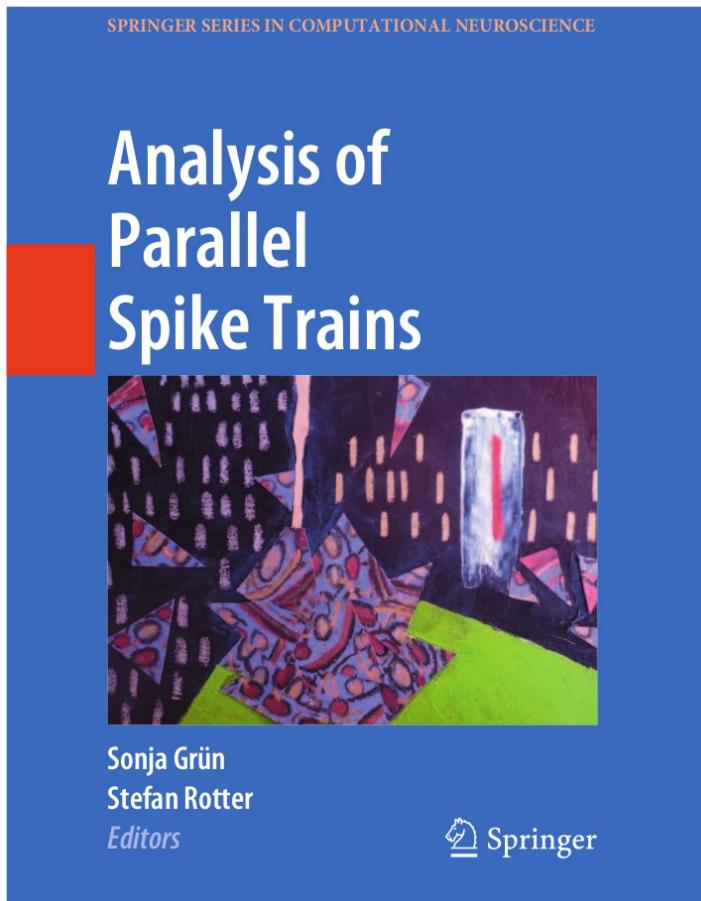
9th Latin American School on Computational Neuroscience (LASCON 2024)
NeuroMat, University of Sao Paulo, Sao Paulo, Brazil | January 22, 2024

Acknowledgements



Human Brain Project

Reference



Analysis of Parallel Spike Trains
Eds: Sonja Grün and Stefan Rotter
Springer Series in Computational
Neuroscience, 2010

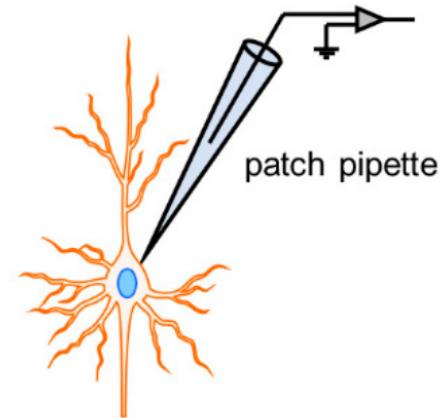
Outline

- **Obtaining spike train data**
 - Recording of spikes
 - Extraction of spikes
 - spike sorting, single unit activity / multi unit activity
- **Analysis of single spike trains**
 - Stochastic characterization
 - Poisson process, gamma process
 - inter-spike interval (ISI), rate
 - Neuronal response
 - peri-stimulus time histogram (PSTH)
 - Example applications

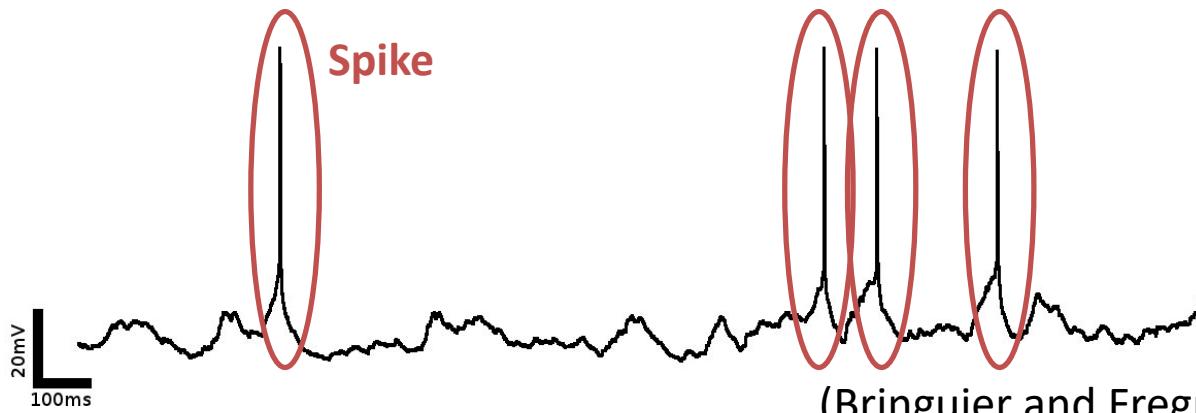
Recording of spikes | recording techniques

- **Intracellular recording**

- Electrode inserted (intracellular) or attached (patch, juxtacellular) to a cell
- Membrane potential of a single cell



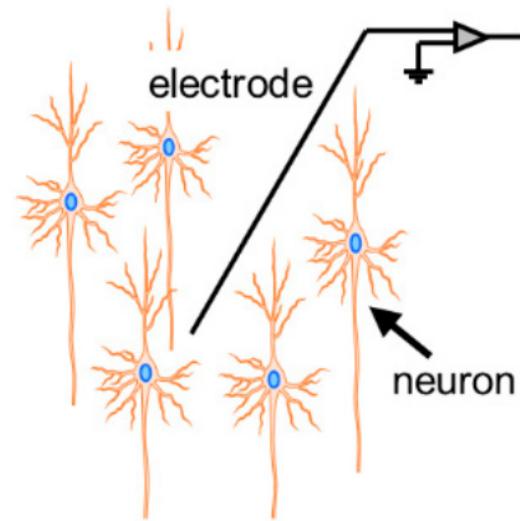
(Noguchi et al., *Sensors* 2021)



(Bringuier and Fregnac, 1997)

Recording of spikes | recording techniques

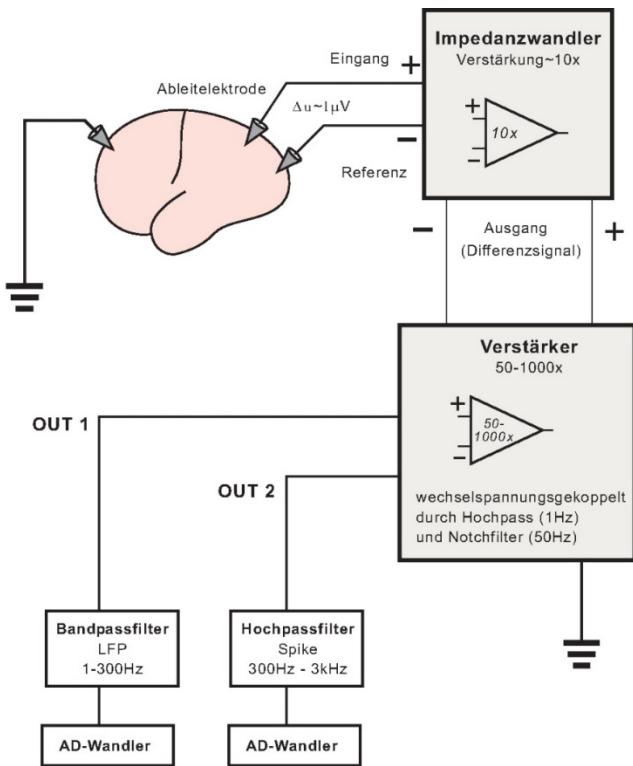
- **Extracellular recording**
 - Electrode in the extracellular medium
 - Mixture of various signals
 - Action potentials generated by nearby cells
 - Local field potential (LFP): slow fluctuations of the electric potential in the extracellular medium



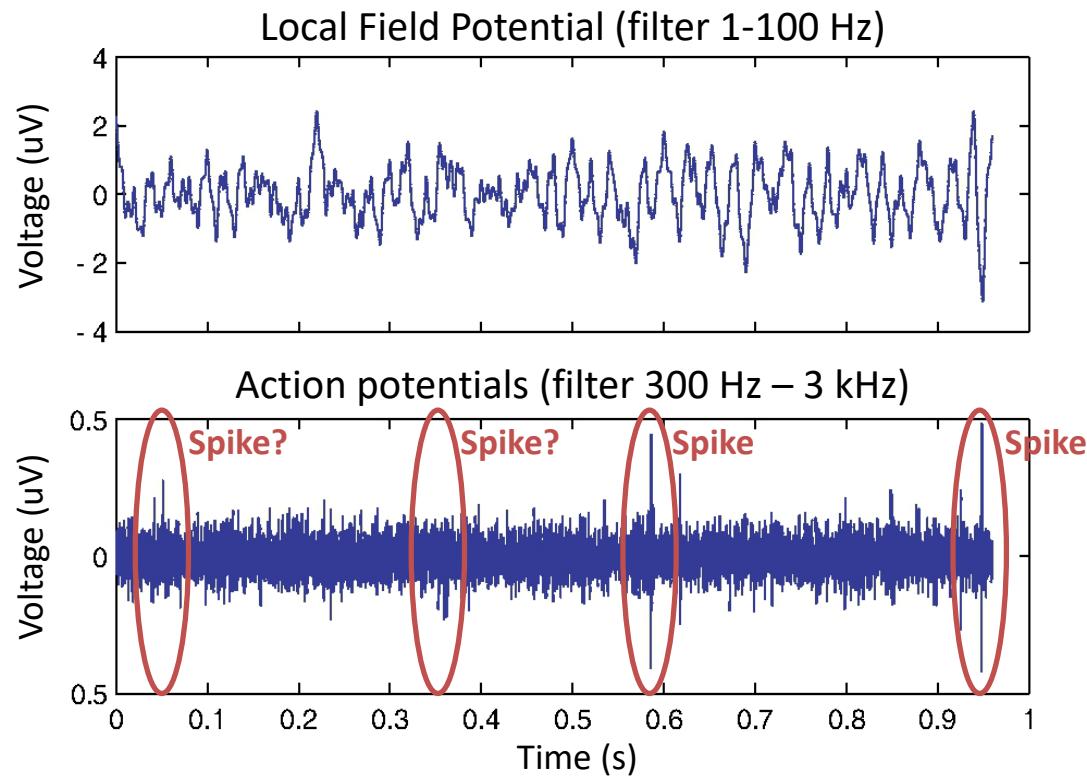
(Noguchi et al., Sensors 2021)

Recording of spikes | extracellular recording

Typical setup



Recording



(From: Diploma thesis Gordon Pipa)

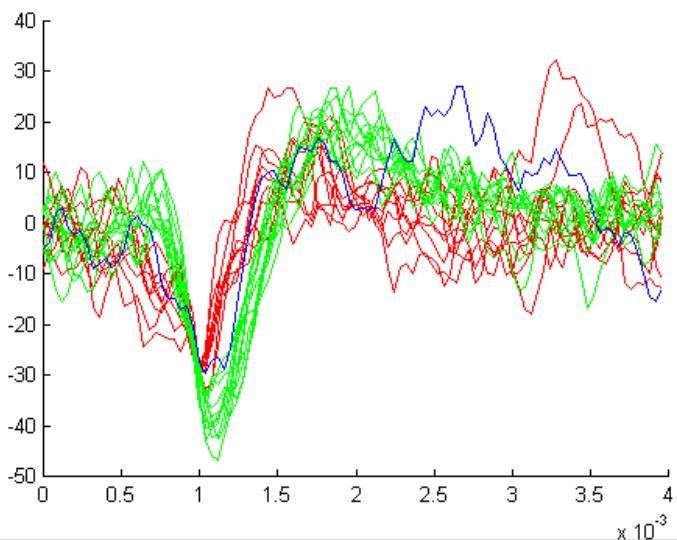
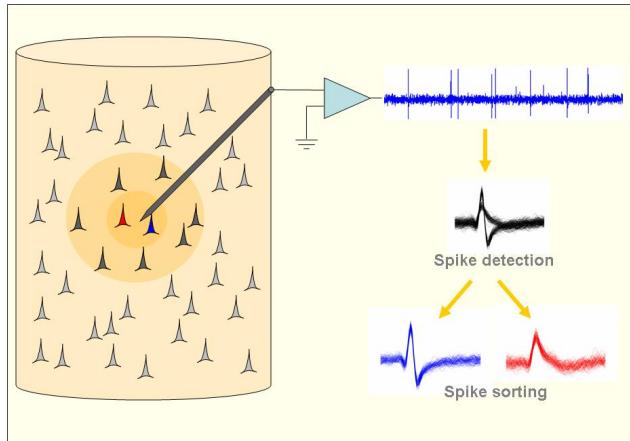
Recording of spikes | summary

- Neuronal action potentials are recorded as **spikes** in voltage traces.
 - Intracellular recording: **single cell**, well defined spikes
 - Extracellular recording: **multiple cells**, candidate spikes on top of noise
- spikes need to be **extracted from the raw signal**

Outline

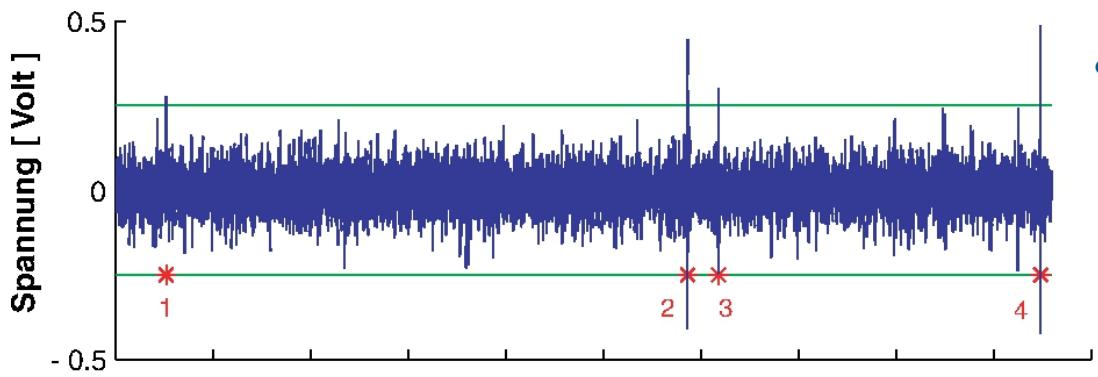
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Spike shapes

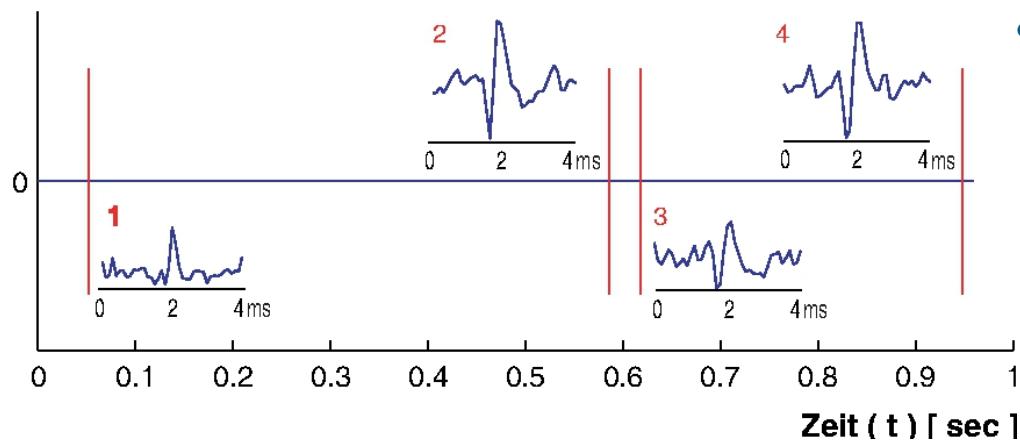


- Action potentials of a single neuron do have a unique shape
 - Very similar even across different neurons
- Extracellular spikes of different neurons have **different shapes and amplitudes**
 - The larger **the distance from the electrode**, the smaller the spikes
 - Due to different positions of the electrode tip in relation to **the cell morphology**

Extraction of spikes | multi-unit activity



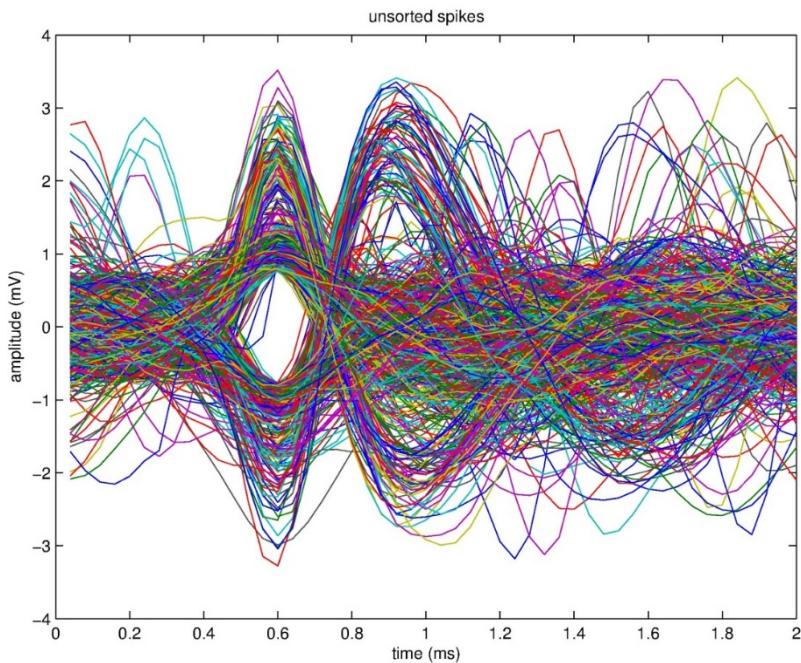
- The high-pass filtered signal contains the spiking activities of a number of nearby neurons



- Peaks exceeding a certain threshold are picked up as spikes
→ multi-unit activity (MUA)

Extraction of spikes | spike waveforms

- Extracted spikes have different waveforms
- A group of spikes with similar waveforms
→ spikes of a single neuron
- To study the activity of single neurons separately, spikes need to be sorted based on their waveforms:
spike sorting

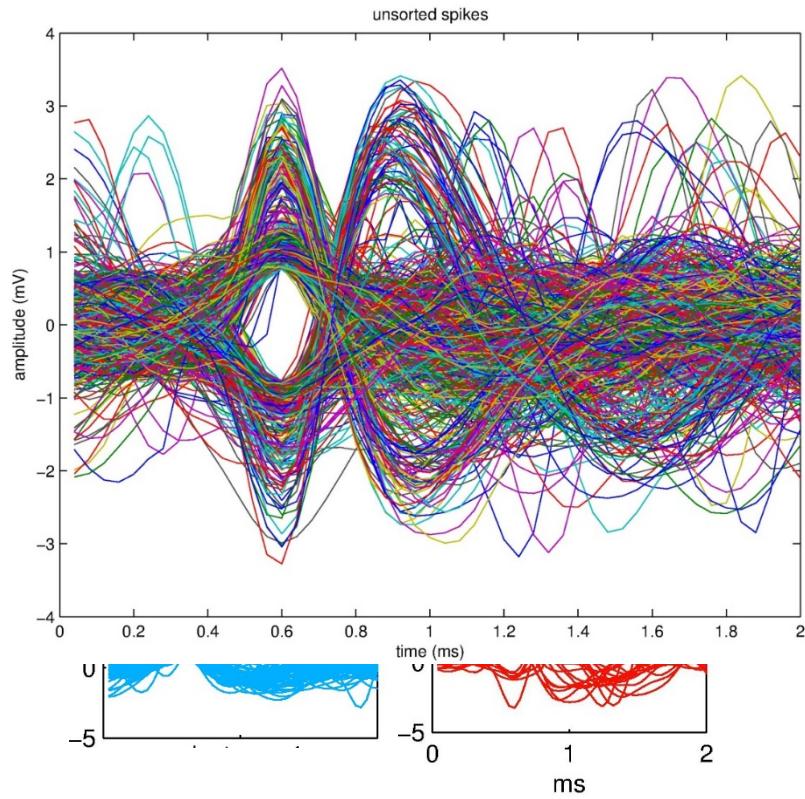
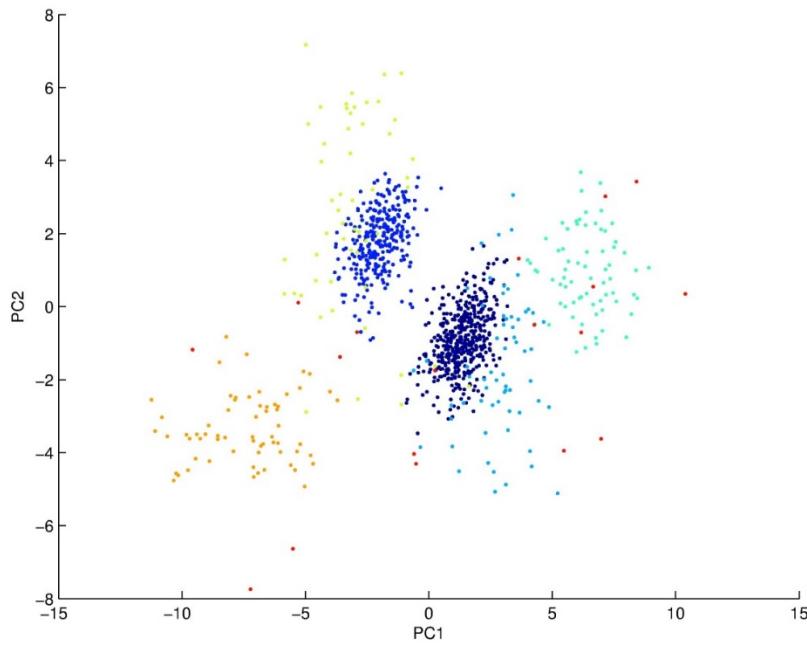


Difficult task - many algorithms available

Author/Year	Number of Features/Description	Classification Method/Algorithm
Gibson et al. ^{17,18}	2 Areas under the positive (integral I_P) and negative (integral I_N) phases of the action potential—that is, the Integral Transform (IT).	Fuzzy C-means clustering.
Jahanmiri-Nezhad et al. ⁴	2 Peak-to-valley amplitude of the action potential, and the area under the curve (sum of absolute values).	K-means clustering + Gaussian mixture model estimation.
Kamboh & Mason ³ , Saeed & Kamboh ²¹	2 Zero-Crossing Features (ZCF) of the spike. ZC1 (the sum of all the values before zero-crossing) and ZC2 (the sum of values after zero-crossing).	K-means clustering + Mahalanobis distance.
Zviagintsev et al. ¹⁵	2 Integral Transform (IT). Discrete and normalized spike integrals I_P and I_N .	Segmented Principal Component algorithm + Principal Component Analysis (PCA).
Lewicki ¹³	3 Positive peak amplitude of the spike, peak-to-valley amplitude, and the waveform duration.	K-means clustering + Euclidean distance and Scaled Principal Component score.
Yang et al. ¹⁶	3 Positive peak amplitude of the spike, and the positive [F_{14}] and negative peaks of the spike first derivative (FD).	Spike derivative-based feature extraction algorithm. Spike height + Peaks of spike derivatives.
Paraskevopoulou et al. ^{19,20}	3 Positive peak [F_{14}] of the spike FD, and the positive [F_{18}] and negative [F_{19}] peaks of the spike second derivative (SD).	10-iteration K-means clustering + Squared Euclidean metric.
Yang et al. ²³	3 Integral of repolarization (IR) of the spike, and the positive [F_{14}] and negative peaks of the spike FD.	20-iteration K-means clustering + Euclidean metric.
Balasubramanian & Obeid ¹	5 Spike power, spike amplitude range, negative and positive deflections, and the spike gradient slope.	Fuzzy logic-based feature extraction system.
Sonoo & Stalberg ¹²	5 Peak-to-valley amplitude of the spike, waveform duration, negative Integral Transform (nIT), ratio (nIT/maximum peak), and the logarithm of the maximum rise of the spike.	Nearest-neighbor Methods + Discriminant Analysis (DA).
Su et al. ²²	6 Spike peak amplitude, peak roundness (i.e., the spike peak [F_{19}] of the SD), the root-mean-square of pre-spike amplitude, the highest repolarization rate, the afterhyperpolarization (i.e., afterspike minimum), and the correlation coefficient between the spike and the reference waveform.	K-means clustering + Principal Component Analysis (PCA).
Bestel ¹²	7 Positive and negative peaks of the action potential, left and right spike angles, negative and positive signal energy of a continuous-time signal, and the core spike duration.	Expectation maximization (EM) method + Gaussian basis functions.
Stewart et al. ¹⁴	7 Peak-to-valley amplitude of the spike, waveform duration, trailing waveform duration, leading waveform aspect ratio, trailing waveform aspect ratio, waveform transition slope, and event duration.	Nearest-neighbor Methods + Discriminant Analysis (DA).

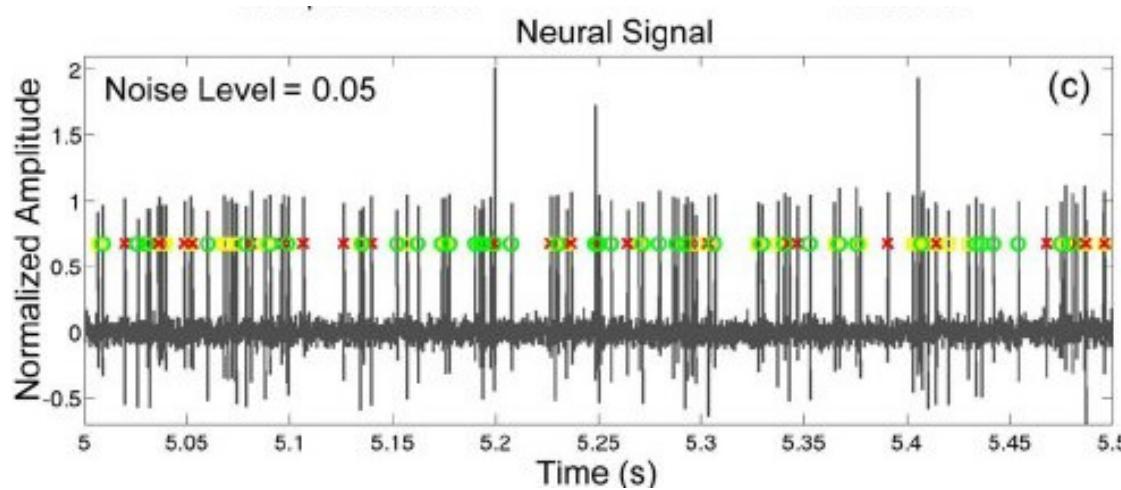
Extraction of spikes | spike sorting

- Standard approach:
feature extraction (e.g., PCA) + clustering (e.g., k-means)



Extraction of spikes | single unit activity

- Each group of sorted spikes is considered as a **single-unit activity** (SUA)
- Thus, an MUA recorded on a single electrode is sorted into multiple SUAs (given multiple clusters)
- Each SUA is reduced to a **series of spike times**: **spike train**



http://www.scholarpedia.org/article/Spike_sorting

Extraction of spikes | summary

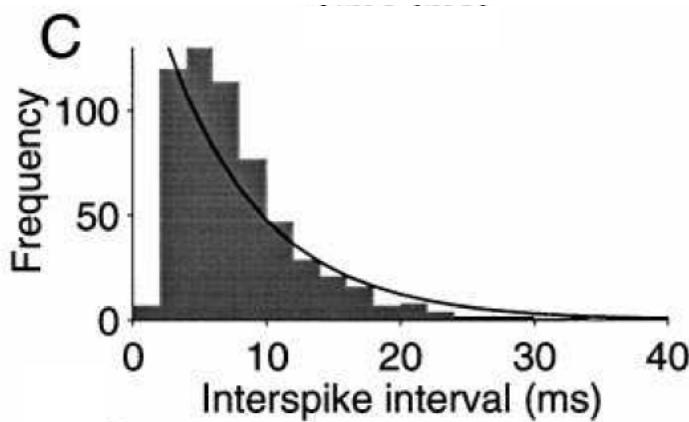
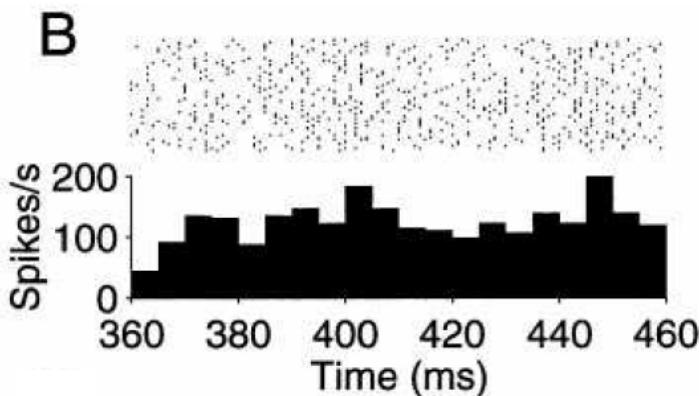
- Extracellular recording contains spikes from multiple neurons.
- Spikes extracted by thresholding: **multi-unit activity (MUA)**
- MUA is sorted according to the shapes of individual spikes:
spike sorting
- Spikes after the sorting are supposed to originate from an identical neuron, called **single unit activity (SUA)**.

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Variability of spike trains

- Spiking activity of a neuron is often highly variable with respect to...
 - timings of single spikes
 - number of spikes in a certain time interval
 - intervals between consecutive spikes: **inter-spike intervals (ISIs)**



(Shadlen and Newsome, 1998)

Stochastic characterization | Poisson process

- Consider a spike train as a realization of a stochastic point process (i.e., randomly generated series of increasing numbers, representing spike times)
- **Poisson process**
 - probability distribution of ISI: $P(\text{ISI} = \tau) = \lambda e^{-\lambda\tau}$
 - parameter λ : the **rate** of the process
 - probability distribution of spike count per unit time:
 $P(\text{count} = n) = \lambda^n e^{-\lambda} / n!$ (Poisson distribution)
 - mean: λ , standard deviation: $\sqrt{\lambda}$
 - at any infinitesimal time interval Δt , the probability of spike generation is $\lambda \Delta t$ (irrespective of spiking history)

Stochastic characterization | gamma process

- ISI distribution of a Poisson process has the highest probability at 0, which is not realistic.
- **Gamma process**

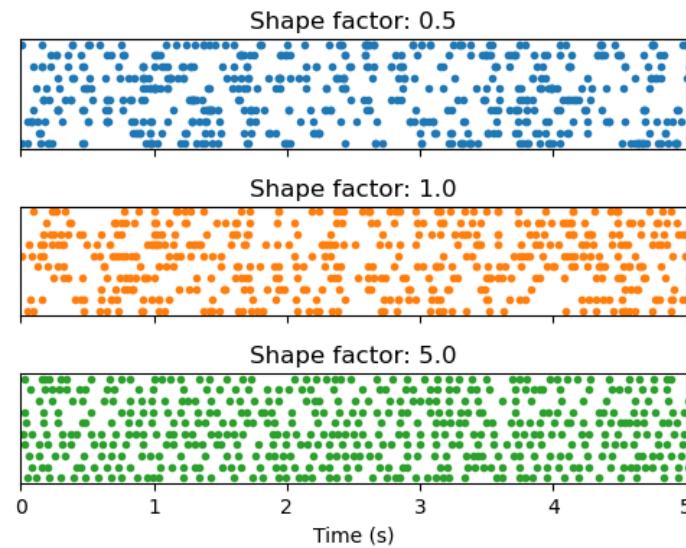
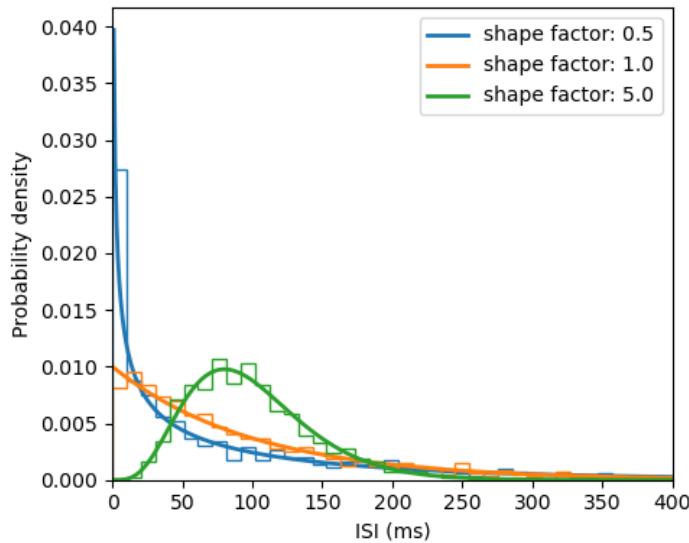
- probability distribution of ISI:

$$P(\text{ISI} = \tau) = \frac{\lambda^k}{\Gamma(k)} \tau^{k-1} e^{-\lambda\tau} \text{ (gamma distribution)}$$

- parameter λ : the “rate” of the process
 - CAUTION: λ is *not* the firing rate of the generated spike train, which is λ/k .
 - parameter k : **shape** parameter ($k = 1 \rightarrow$ Poisson)
 - when k is an integer, this is the distribution of the sum of k ISIs of a Poisson process of rate λ .

Stochastic characterization | example data

- Gamma process with $k = 1$ is equivalent to Poisson process
- Gamma process with $k > 1$ generates more **regular** spike trains than Poisson process.
- Gamma process with $k < 1$ generates more **bursty** spike trains than Poisson process



Stochastic characterization | summary

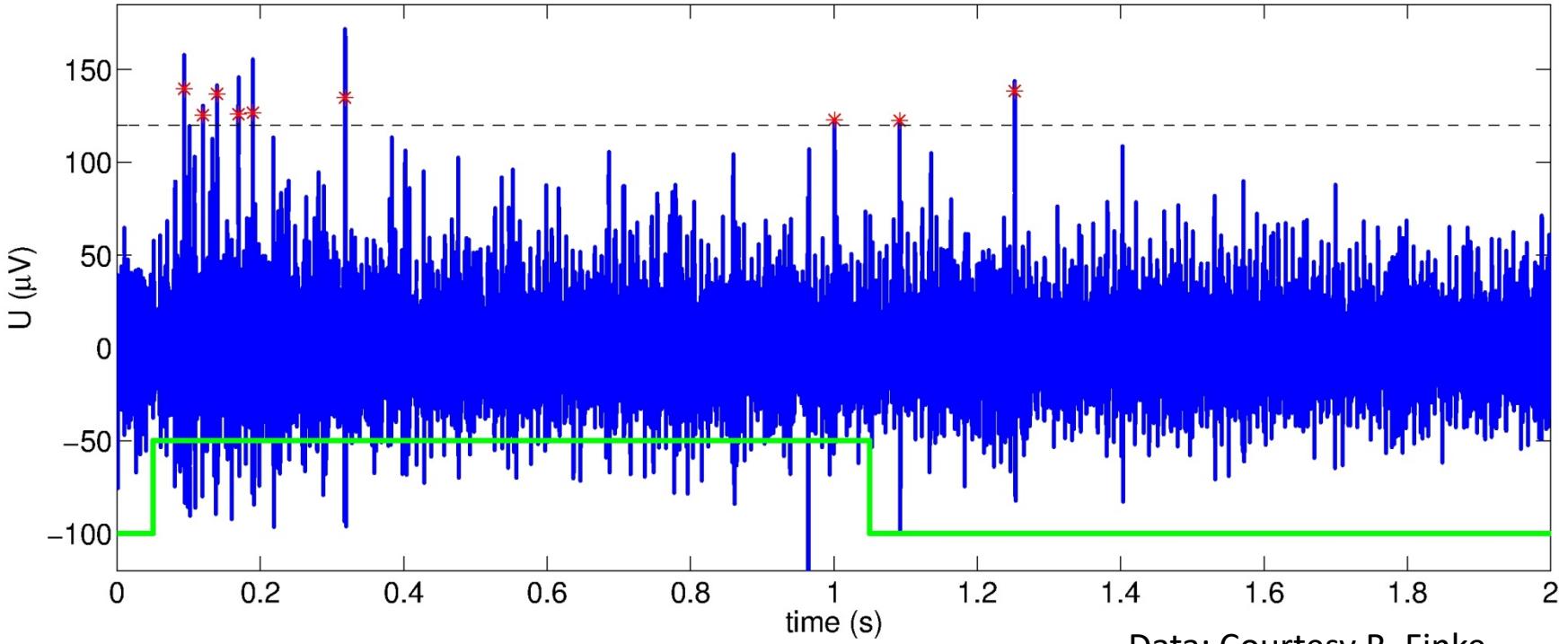
- Spiking activity is often highly variable.
 - **ISI distribution** is a convenient way of illustrating the variability
- Stochastic point processes are widely used to characterize the variability of spike trains
 - **Poisson process**: rate λ
 - **Gamma process**: rate λ , shape k (regularity / burstiness)
- Spike trains of an identical firing rate can be variable in many different ways
 - If you characterize a spike train only by the rate, you are discarding all the information contained in the variability.

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Neuronal response | example

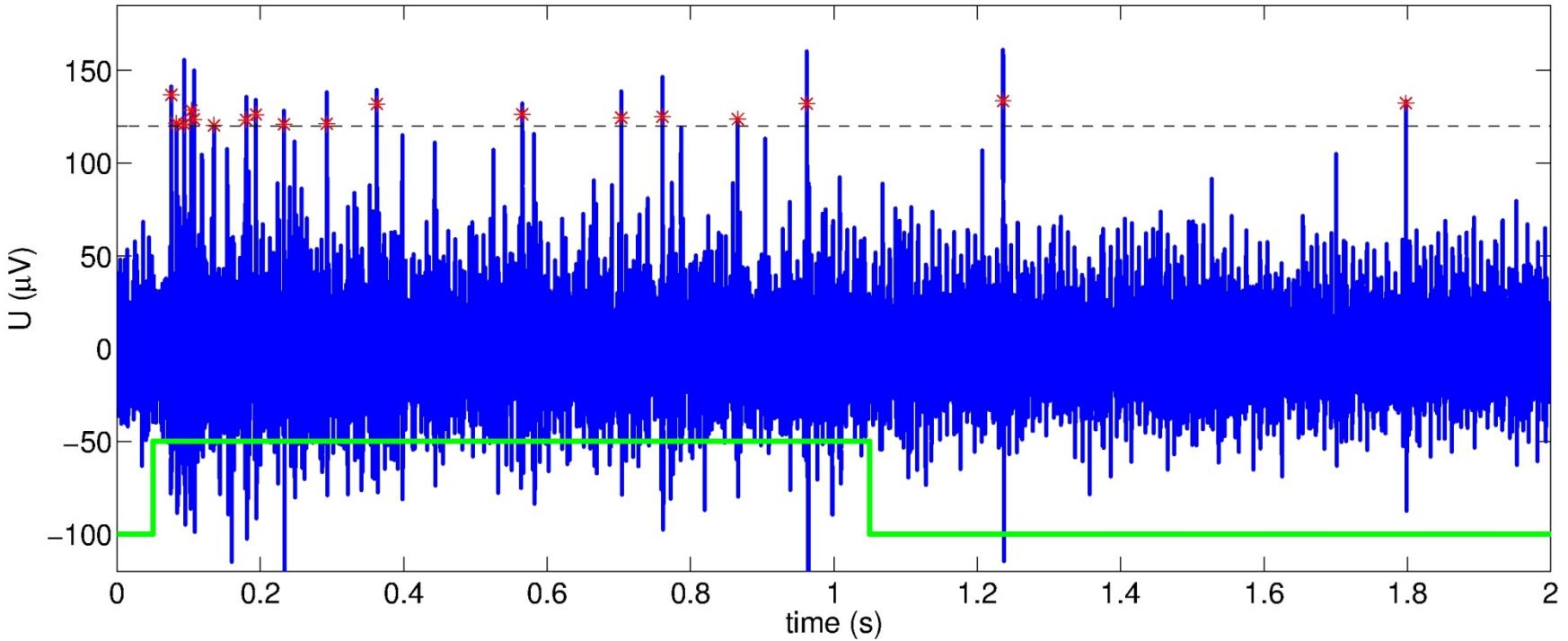
- Spiking activity modulated by odor presentation



Data: Courtesy R. Finke

Neuronal response | example

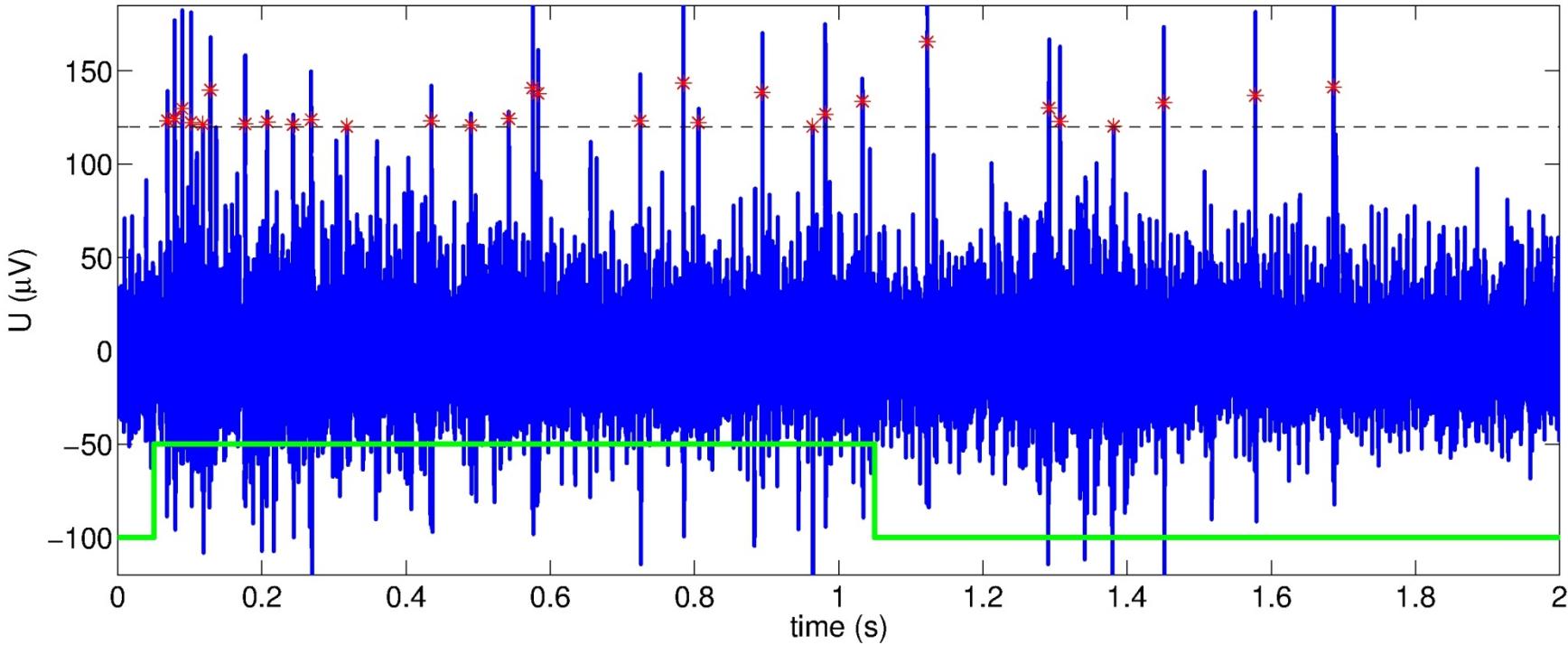
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Data: Courtesy R. Finke

Neuronal response | example

- Spiking activity modulated by odor presentation



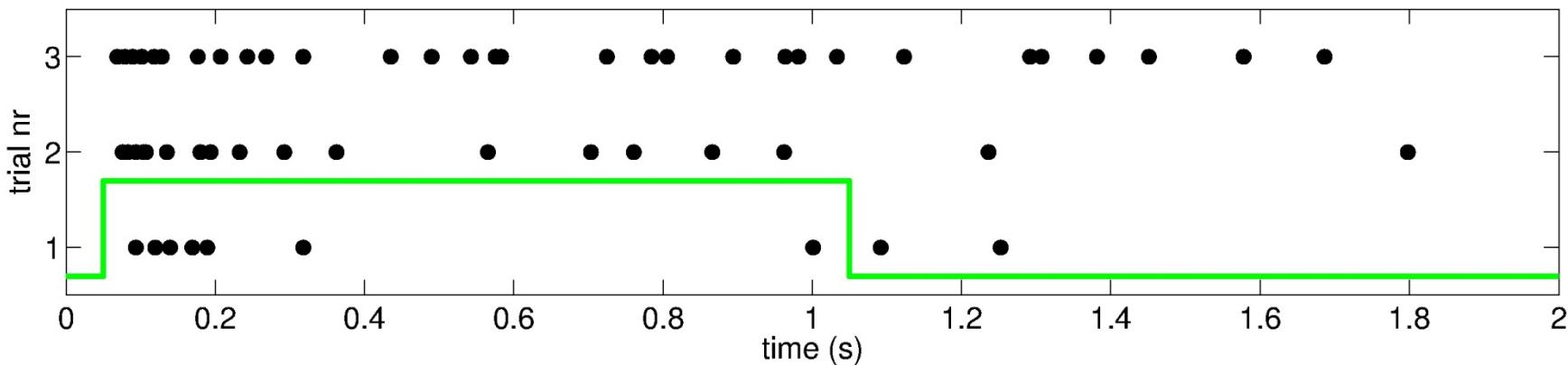
Data: Courtesy R. Finke

Neuronal response | observations

- Spike count changes in relation to stimulus presentation.
→ '**response**'
- Spike timing varies across presentations.
- Spike count varies across presentations
→ responses appear **stochastic**
- Assuming Poisson process as the underlying stochastic process, the response can be considered as **a stimulus dependent modulation of the rate parameter**.
→ need for estimation of time-varying firing rate

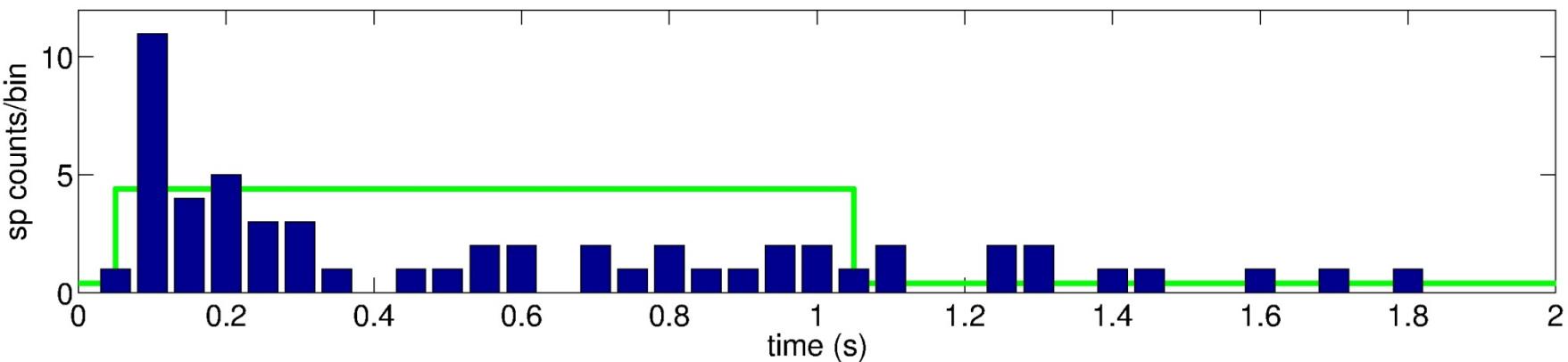
Neuronal response | dot display

- **Dot display (or raster plot)**
 - Each dot represents a spike
 - Each row represents a spike train of one trial
 - Spike trains from multiple trials aligned to a specific experimental/behavioral event

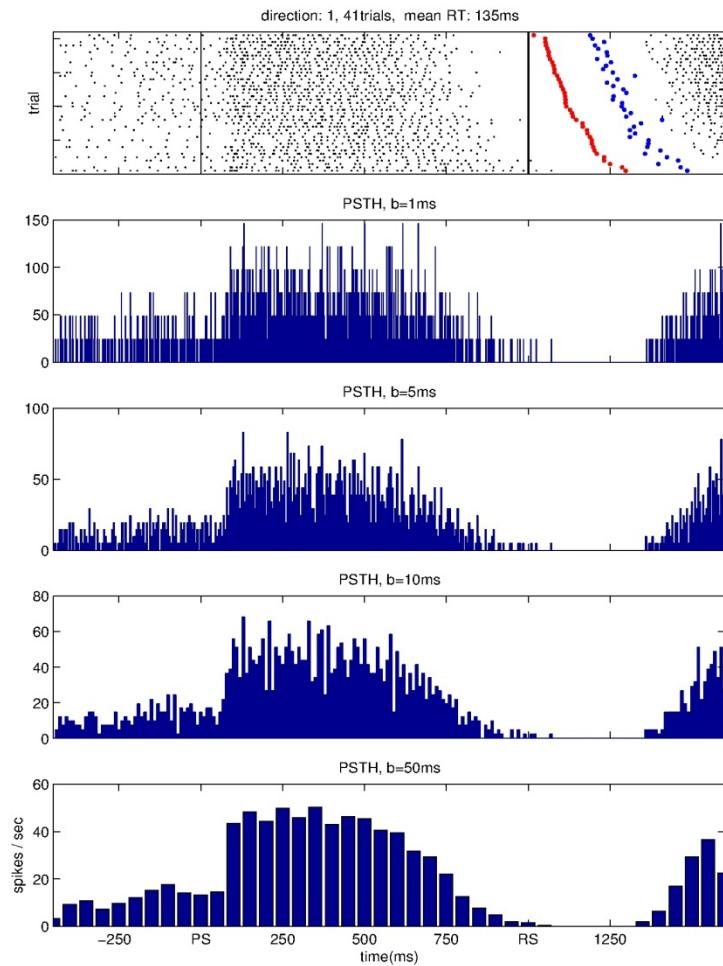


Neuronal response | PSTH

- **Peri-stimulus time histogram (PSTH)**
 - Histogram of counts of spike occurrences across trials within pre-defined **bins**
 - Goal: **estimate underlying firing rate profile**, assumed to be common across all trials



Neuronal response | rate estimation



Data: Courtesy A. Riehle

joe153-1; compl. info; 11-May-2004

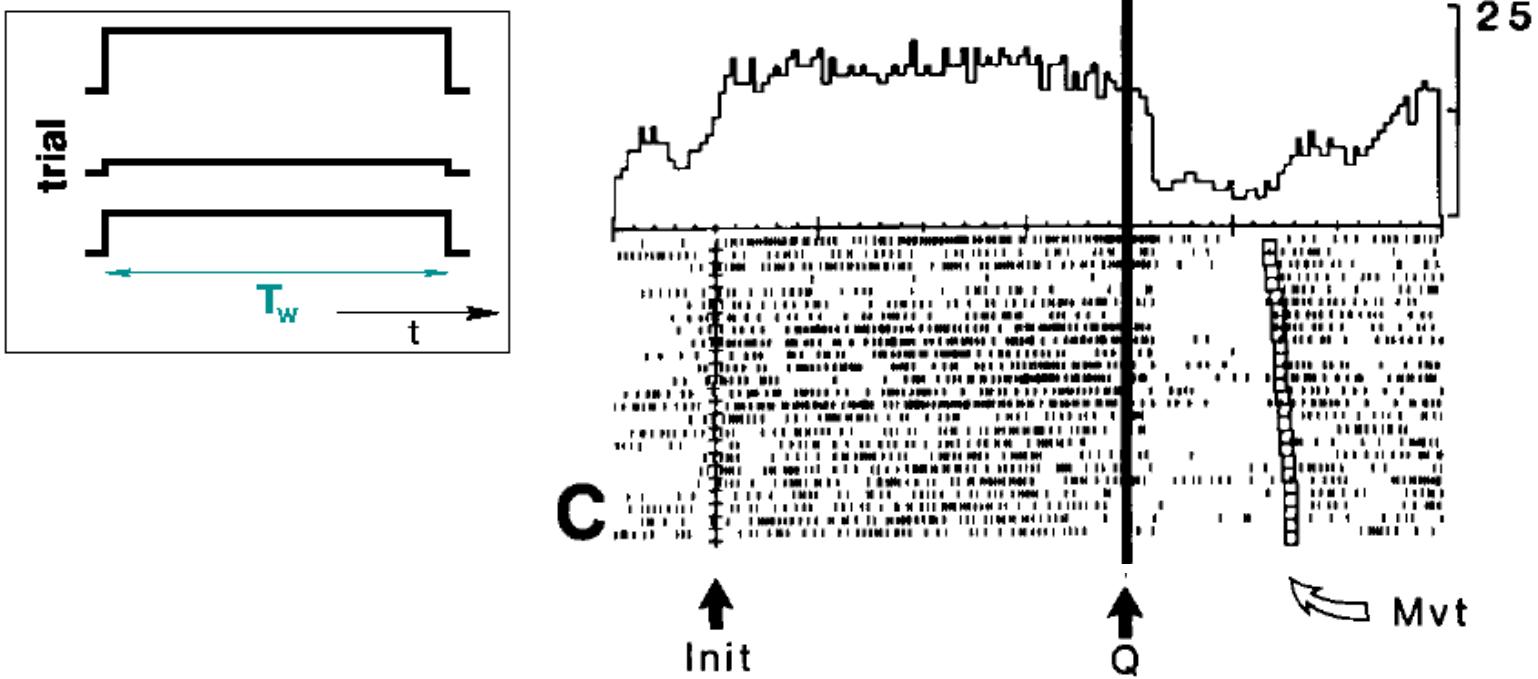
- PSTH: estimate of firing rate (# spikes/sec)
 - The more trials, the better the estimate
 - Bin size: parameter to choose

Neuronal response | rate estimation

- Following **assumptions** need to be met for characterization of neuronal response using PSTH
 - Underlying stochastic point process: **Poisson process**
 - No history dependence
 - Parameterized only by (time-varying) firing probability
 - Stationarity across trials: **system reacts to the same manipulation in the same way** (same rate, same time course, etc.)
- But, in reality...

Neuronal response | violation of assumptions

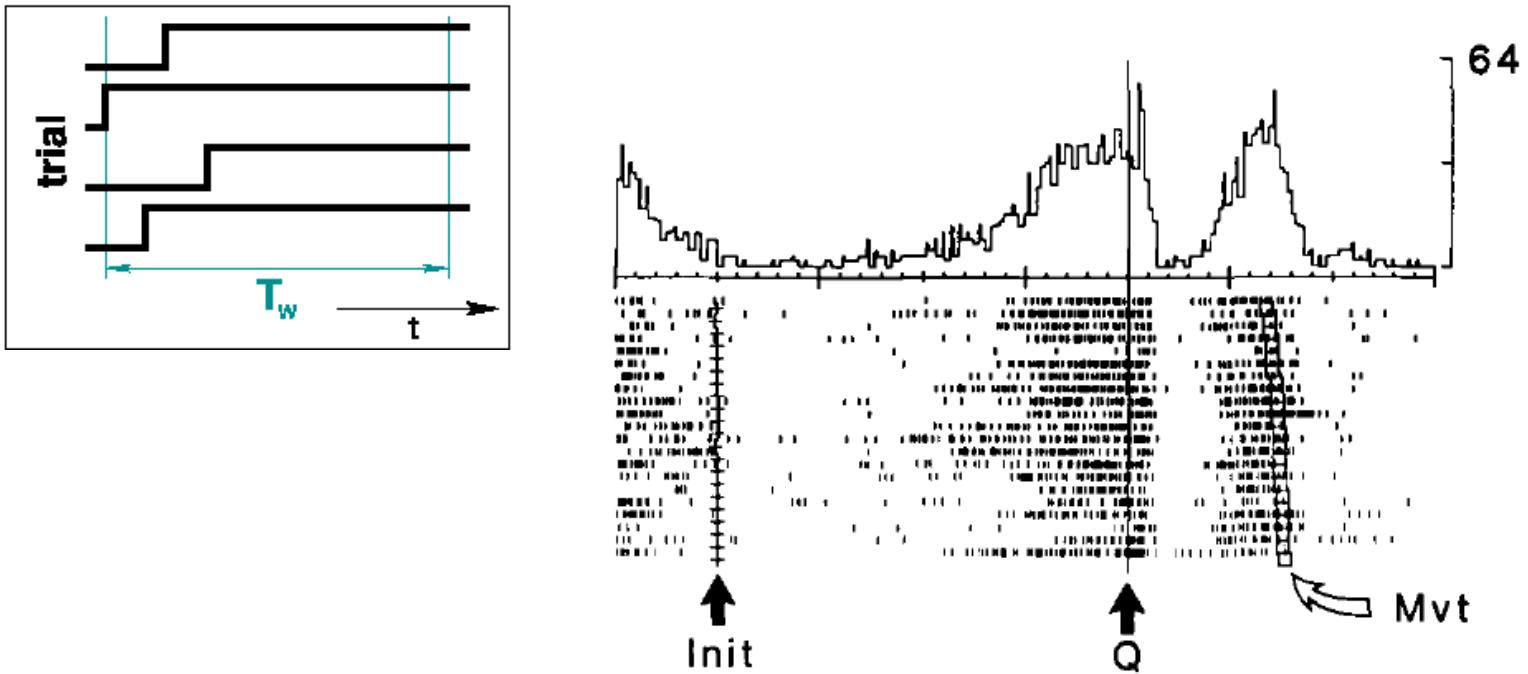
- Large variability of rate across trials



From: Vaadia et al. (1988)

Neuronal response | violation of assumptions

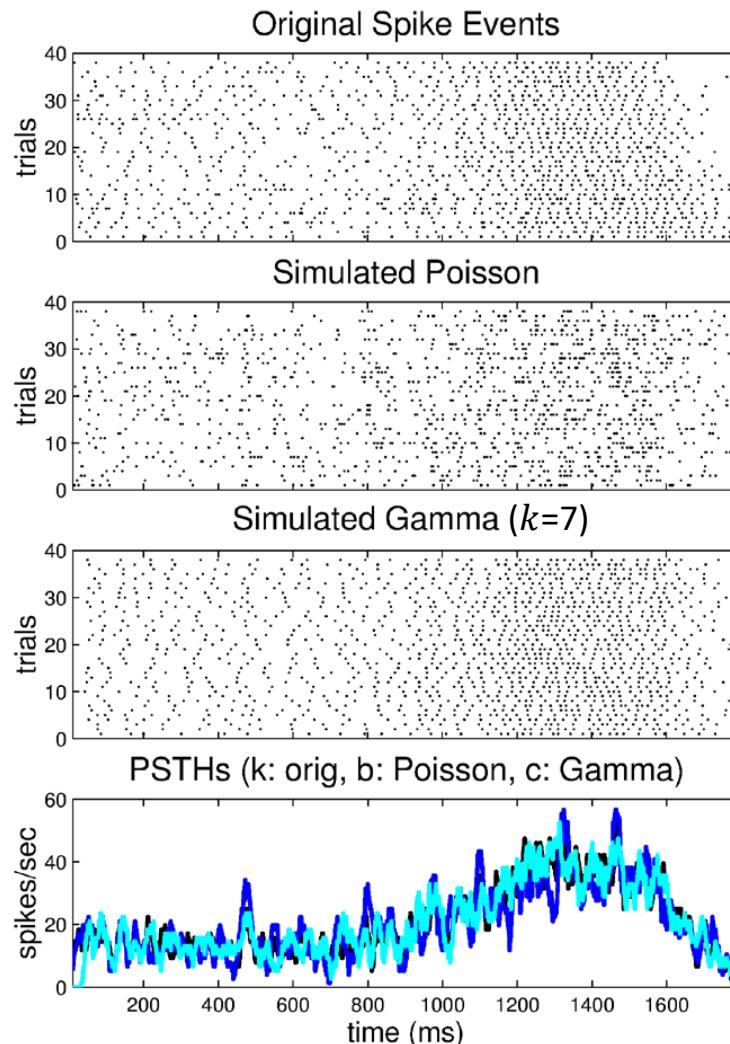
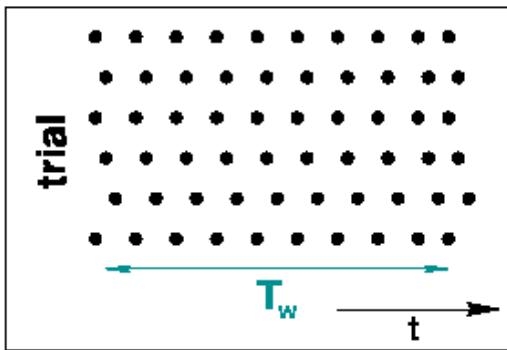
- Large variability of latency across trials



From: Vaadia et al. (1988)

Neuronal response | violation of assumptions

- Deviation from Poisson



Neuronal response | summary

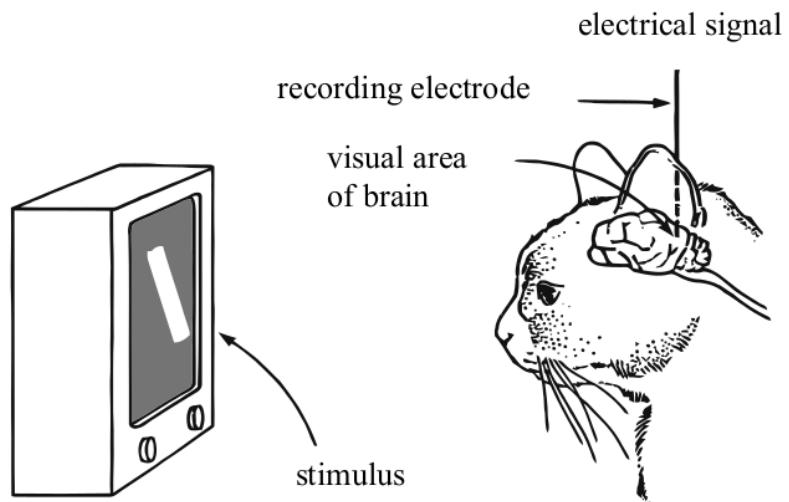
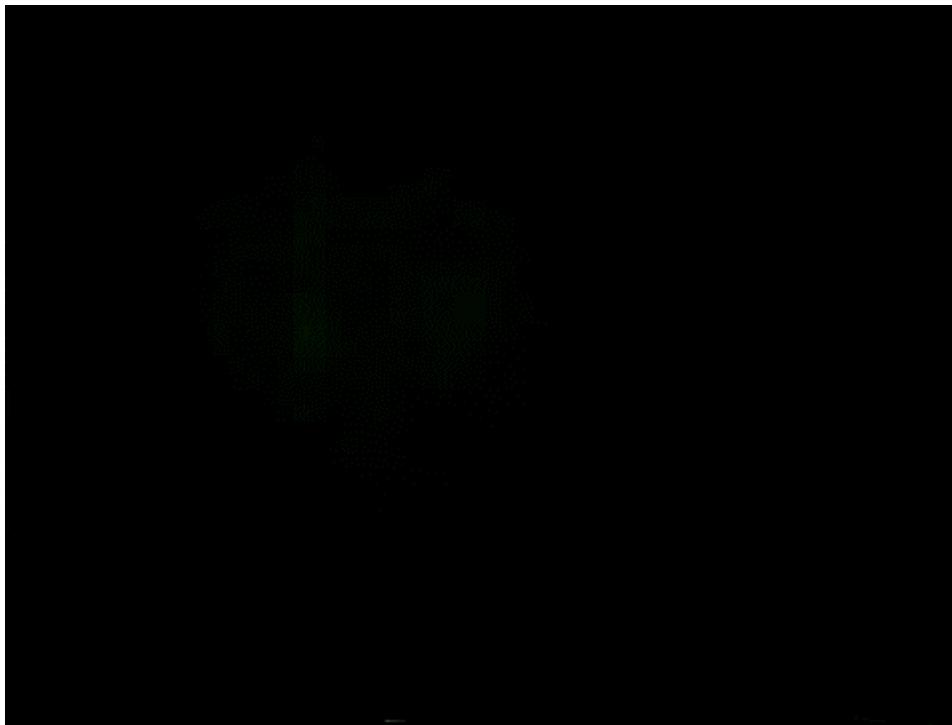
- Peri-stimulus time histogram (PSTH):
the standard method to characterize neuronal responses
- Neuronal firing rate can be directly estimated from the PSTH
- There are underlying assumptions for characterization by the PSTH
 - Poisson process
 - stationarity across trials

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Application | receptive field of V1 cells

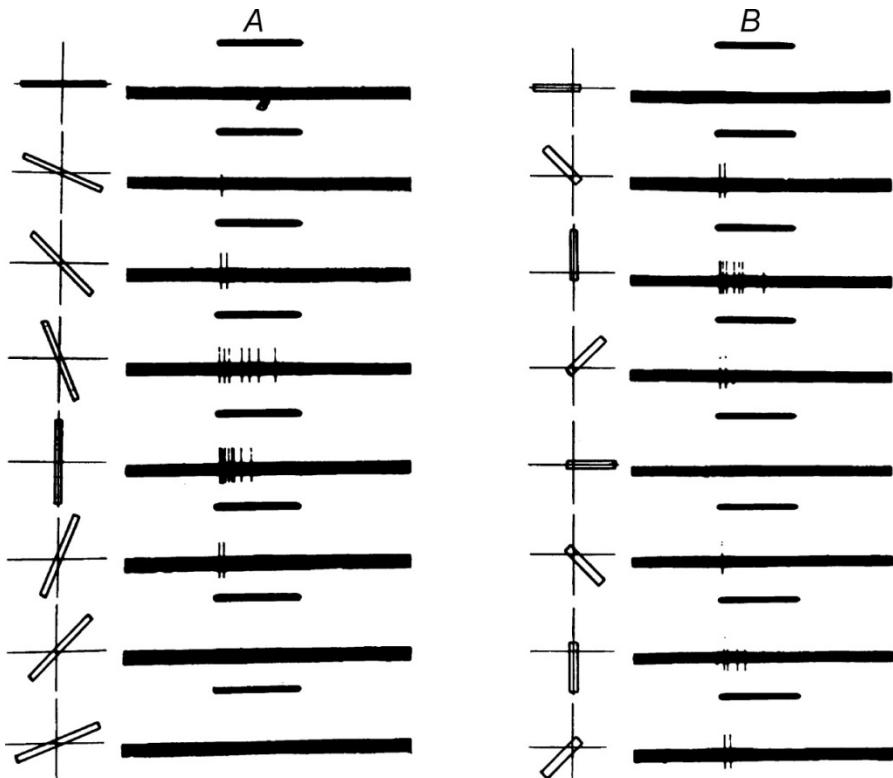
- Hubel and Wiesel (1959), recording from cat visual cortex



Nguyen et al., in *Explainable AI* (2019)

Movie available at: <http://www.science.smith.edu/departments/neurosci/courses/bio330/h%26w.html>

Application | orientation selectivity in V1

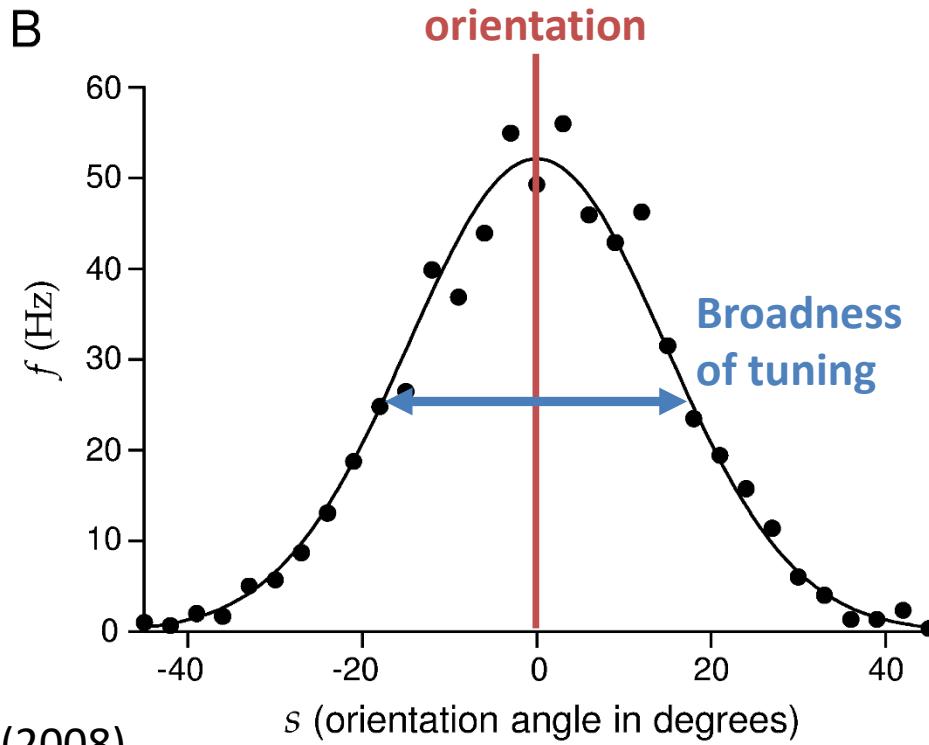
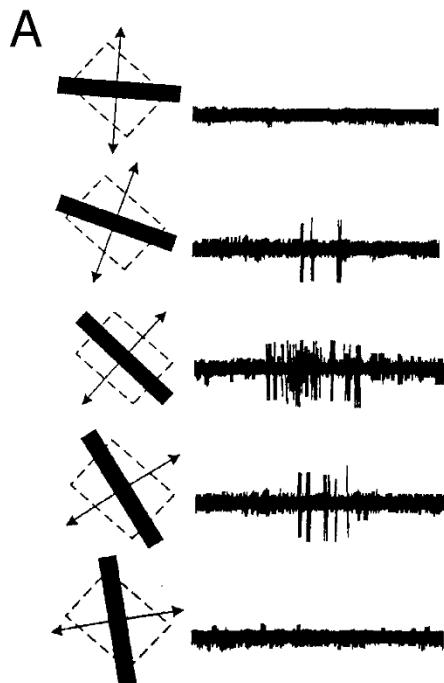


From: Hubel and Wiesel (1959)

- Each V1 neuron has a particular region in the visual field, in which a stimulus triggers the firing of that neuron
→ receptive field
- A large part of V1 neurons respond strongly to bar stimuli in a particular orientation
→ orientation selectivity

Application | tuning curve of V1 cells

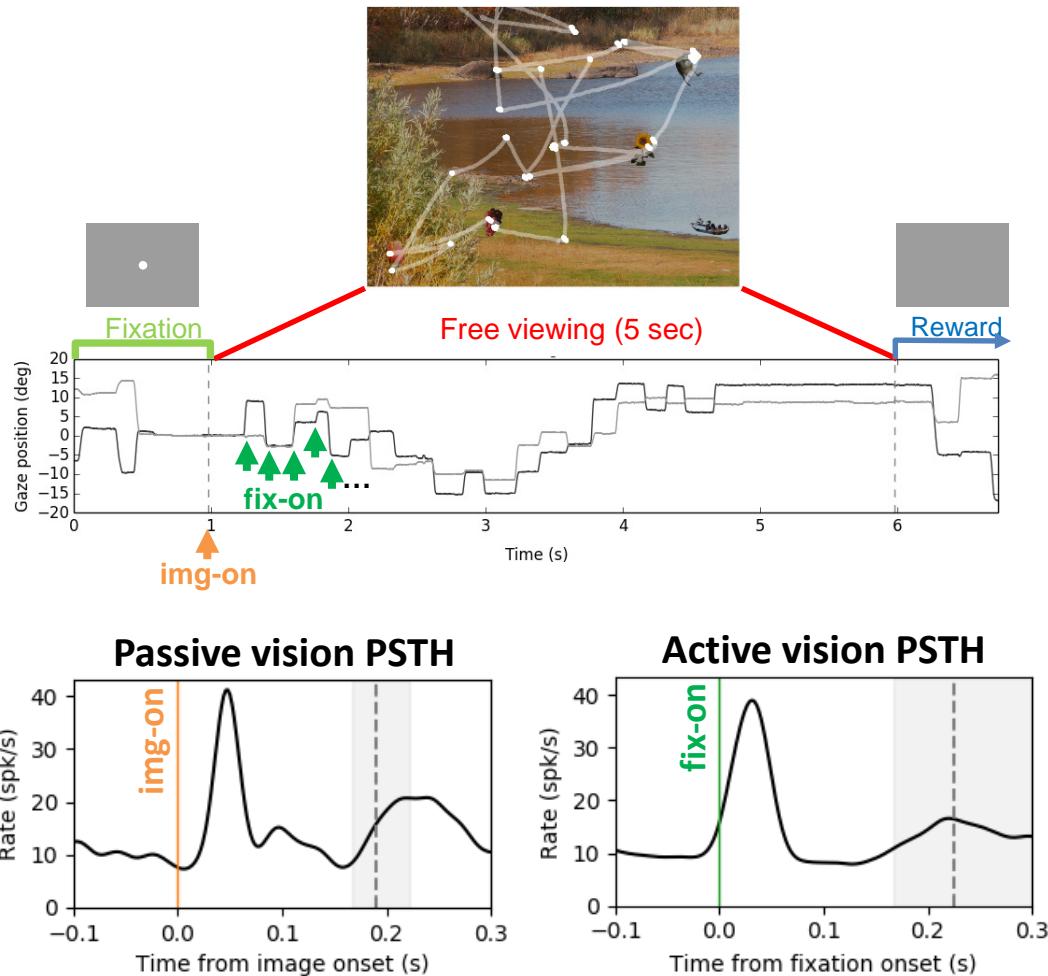
- Orientation tuning curve



From: Dayan and Abbott (2008)

Application | V1 response to fixated images

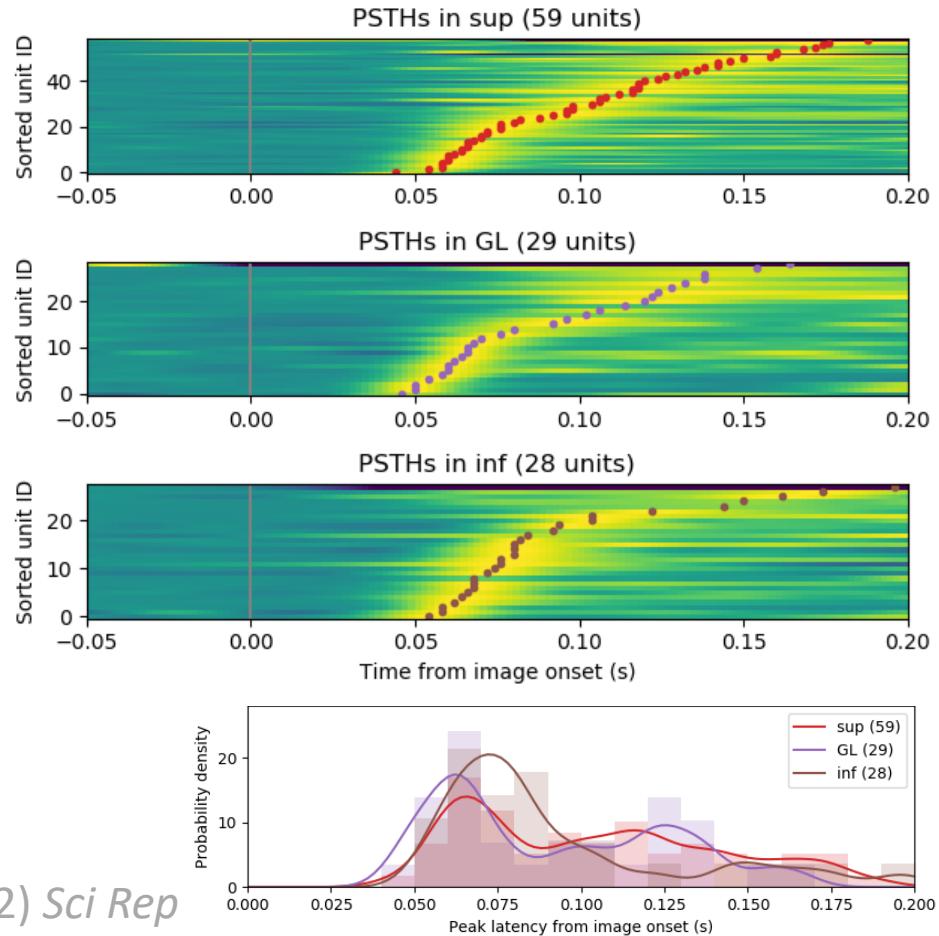
- V1 neurons of freely-viewing macaques
- Two PSTHs per neuron: triggered by **img-on** or **fix-on**
- Response to **img-on** → **passive vision**
- Response to **fix-on** → **active vision**



Application | V1 response to fixated images

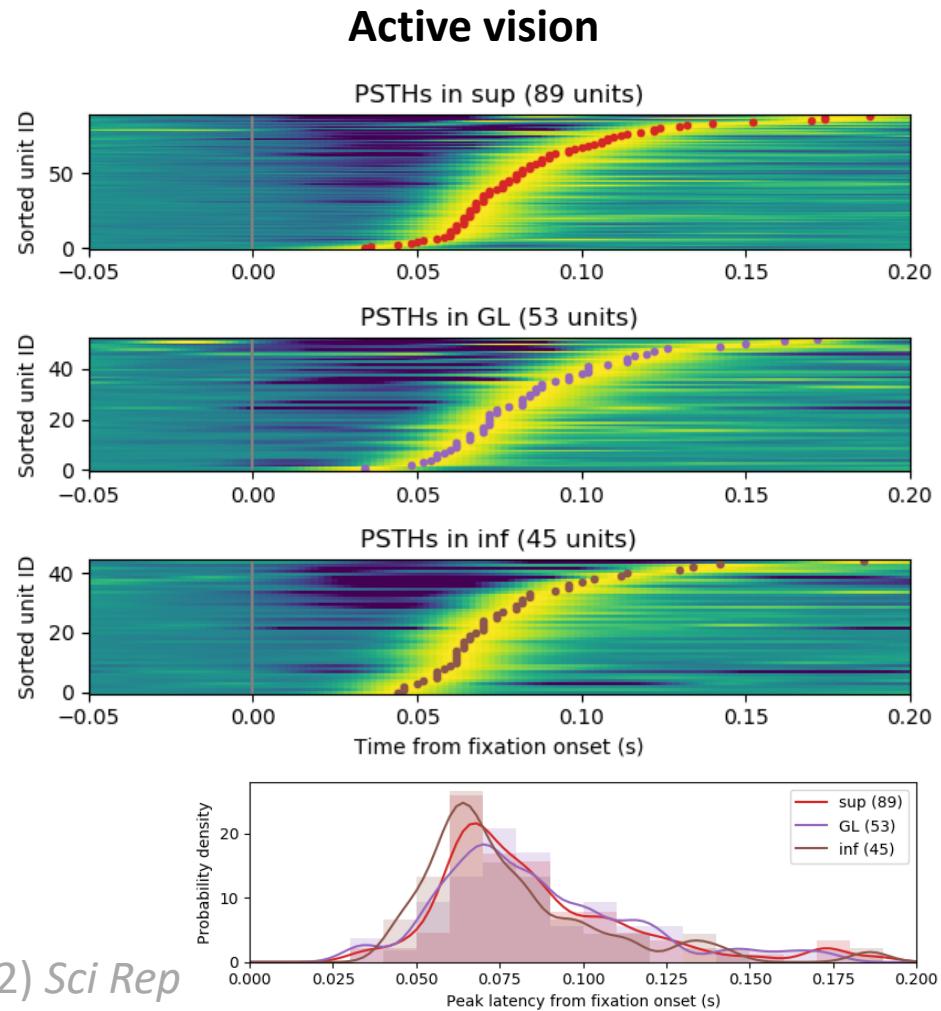
- Units recorded in different cortical layers: supra-granular (**sup**), glanular (**GL**), and infra-granular (**inf**)

Passive vision



Application | V1 response to fixated images

- Units recorded in different cortical layers: supra-granular (**sup**), granular (**GL**), and infra-granular (**inf**)
- In active vision, **PSTH peak latency becomes shorter** than in passive vision, especially in **sup** and **inf**



Example applications | summary

- Neurons in the primary visual cortex (V1) have...
 - **receptive field**: a particular region of the visual field in which a stimulus triggers the firing of that neuron.
 - **orientation preference**: a particular orientation of stimulus to which that neuron respond strongly; quantified by a **tuning curve** in terms of firing rate
- During active vision, **V1 neurons shorten their rate response latency**, especially in supra- and infra-granular layer.
 - These are the layers that receive **top-down projections** (i.e., cortico-cortical projections from higher-level visual cortices)
→ enhanced top-down influence during active vision?