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Spike Train Analysis I:

spike train, stochastic process, and rate analysis

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Brain Science Institute
RIKEN

Helmholtz Portfolio Theme
SMHB
Supercomputing and
Modeling for the
Human Brain

HBP
Human Brain Project

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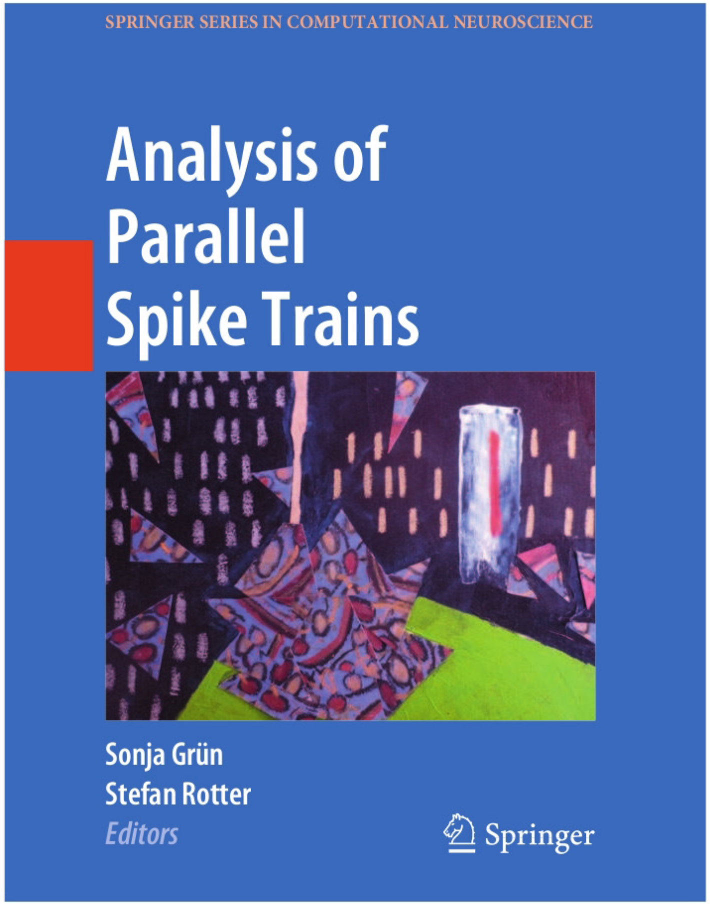
Reference



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

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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

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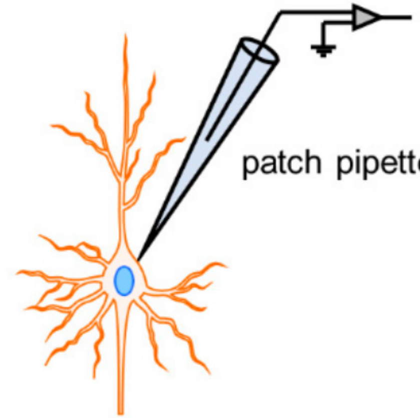
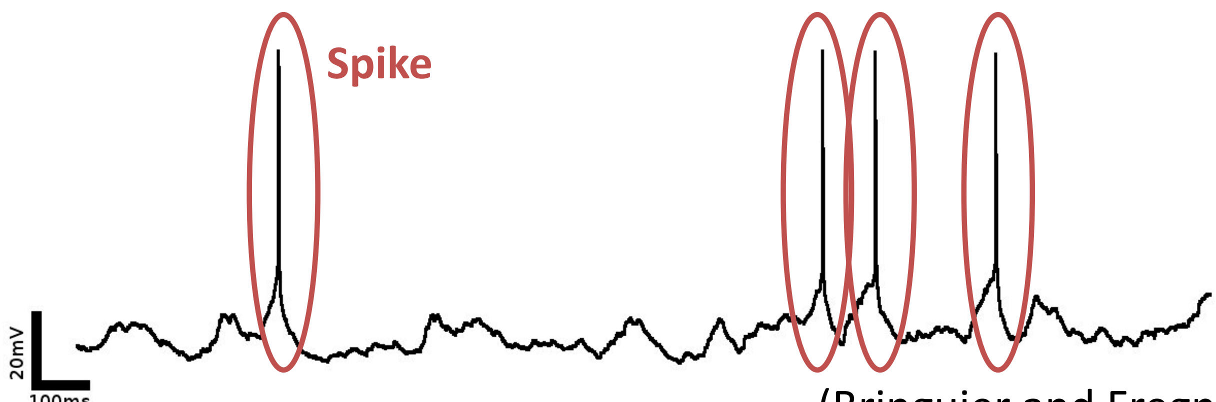
Recording of spikes | recording techniques

- **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)

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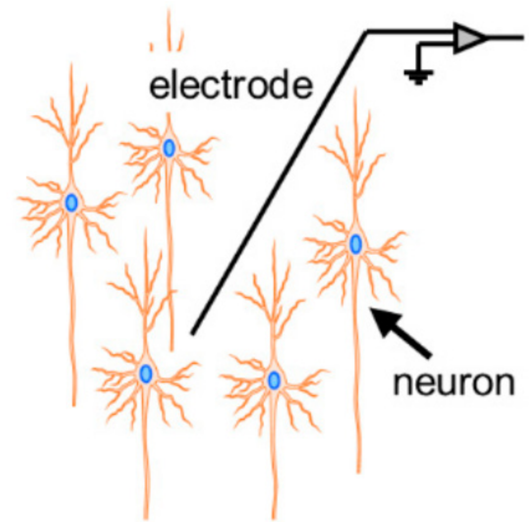
Recording of spikes | recording techniques

- **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)

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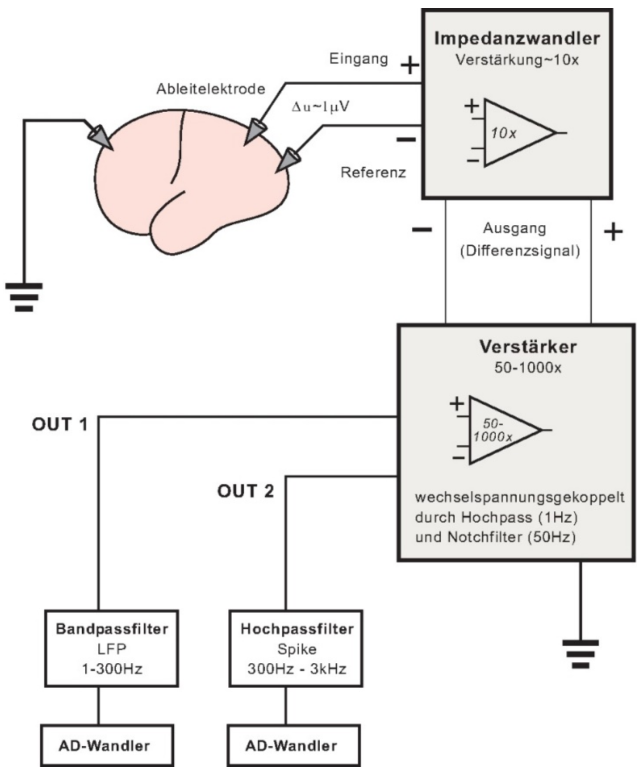
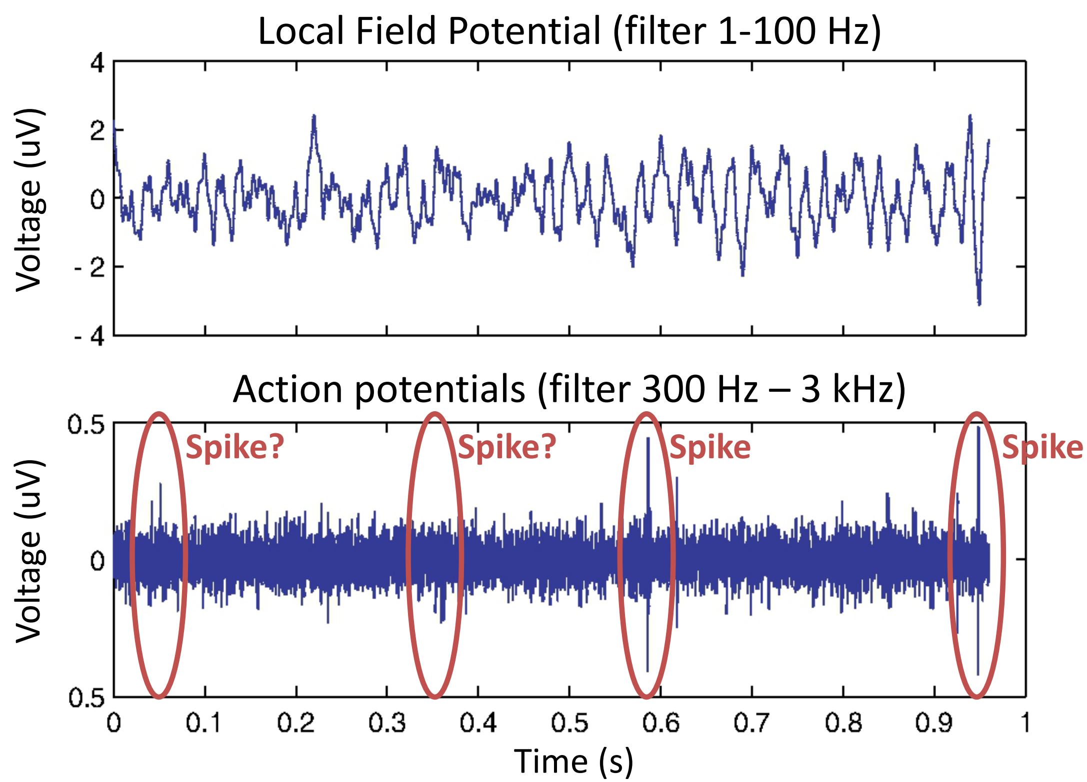
Recording of spikes | extracellular recording

Typical setup



Recording



(From: Diploma thesis Gordon Pipa)

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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

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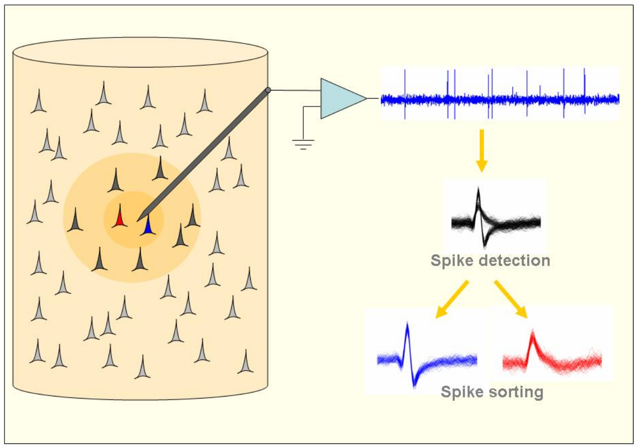
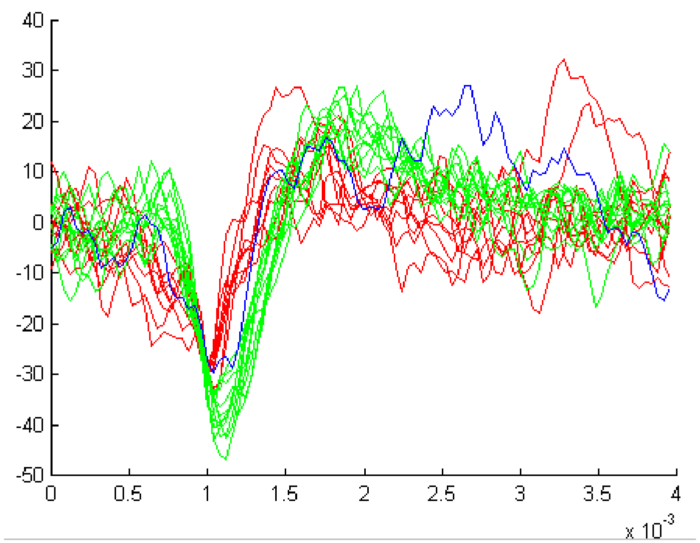
Spike shapes





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

- 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

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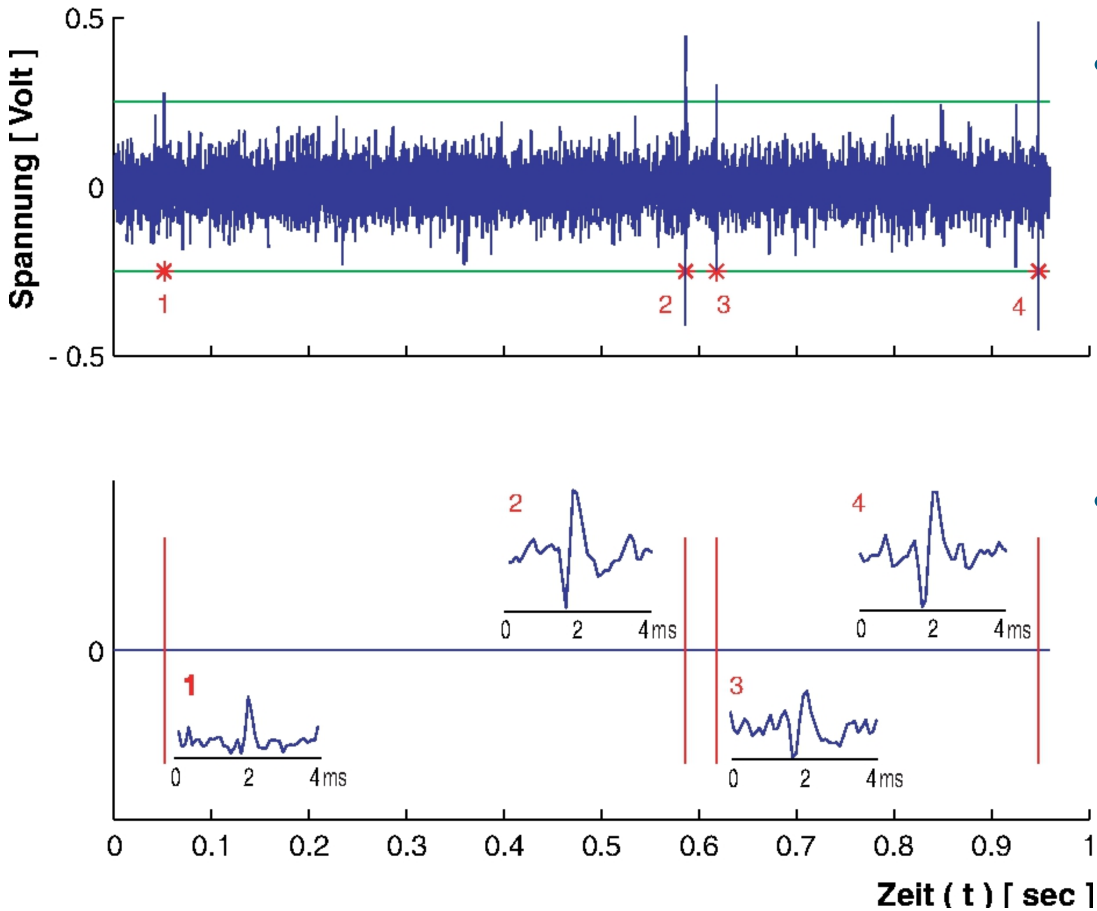
Extraction of spikes | multi-unit activity



- 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)

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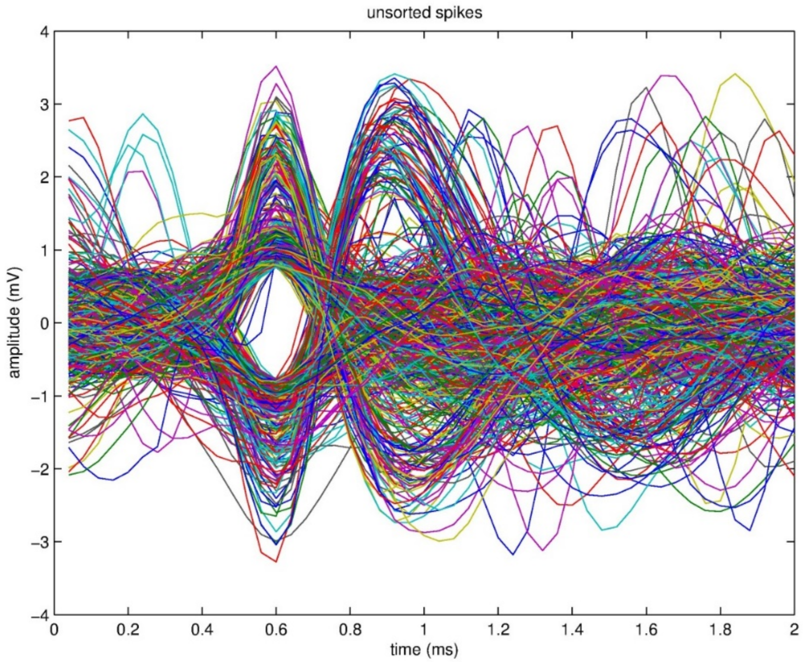
Extraction of spikes | spike waveforms

- 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



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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[2]	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).

Table 1 in Caro-Martín et al., Scientific Reports (2018) 8(1):17796. doi: 10.1038/s41598-018-35491-4

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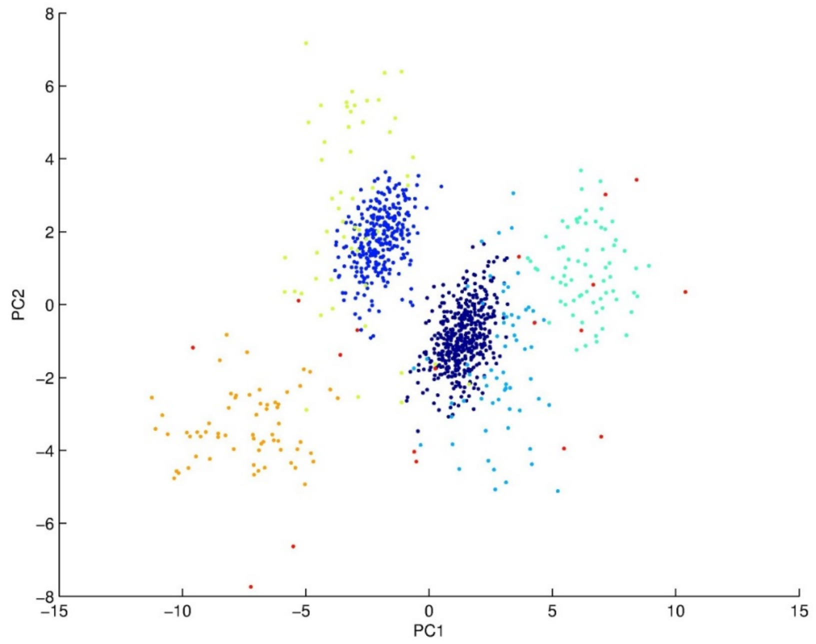
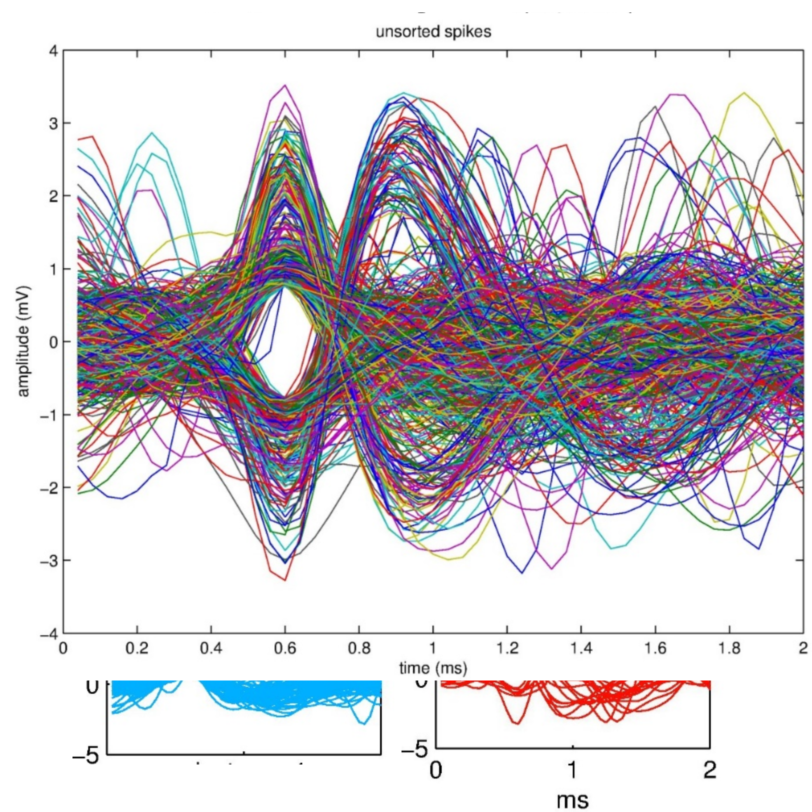
Extraction of spikes | spike sorting

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





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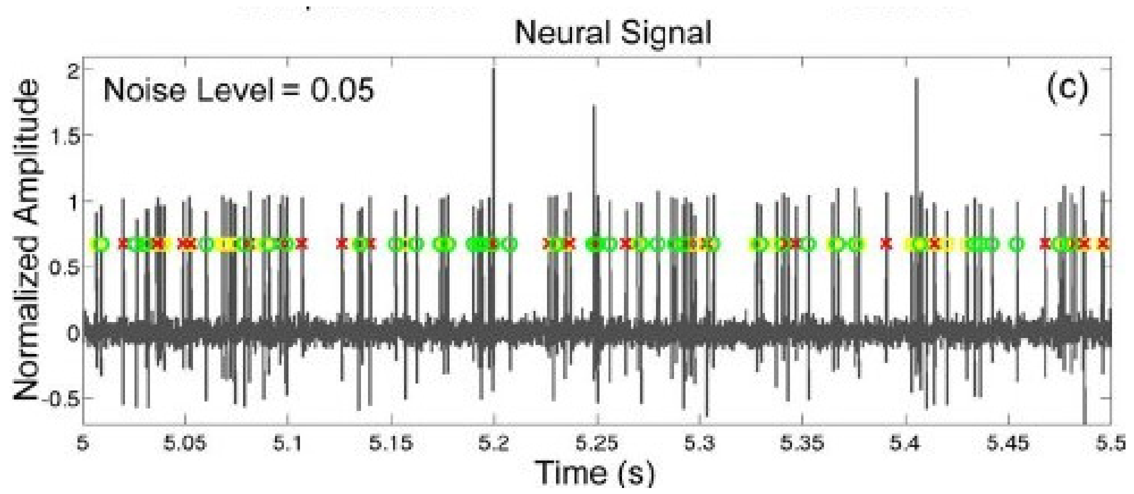
Extraction of spikes | single unit activity

- 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

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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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  - Example applications

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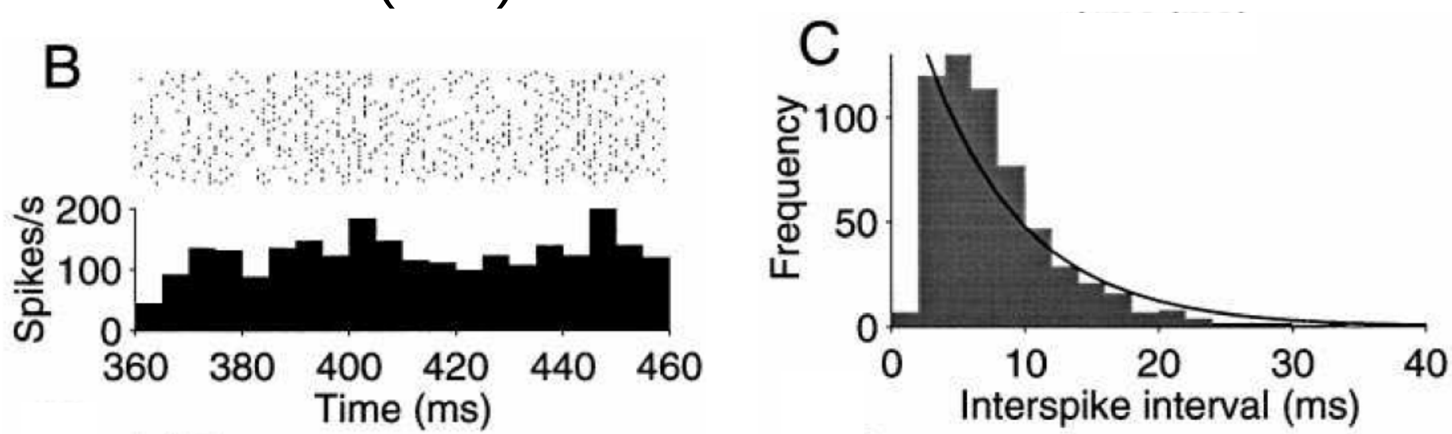
Variability of spike trains

- 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)

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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: $P(\mathrm{ISI} = \tau) \ = \lambda e^{-\lambda\tau}$
    - parameter λ: the **rate** of the process
  - probability distribution of spike count per unit time: $P(\mathrm{count} = n) = \lambda^n e^{-\lambda}/n!$ (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)

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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:

    $P(\mathrm{ISI} = \tau) = \frac{\lambda^k}{\Gamma(k)} \tau^{k-1} e^{-\lambda\tau}$ (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 ($k = 1$ → Poisson)
    - when k is an integer, this is the distribution of the sum of k ISIs of a Poisson process of rate λ.

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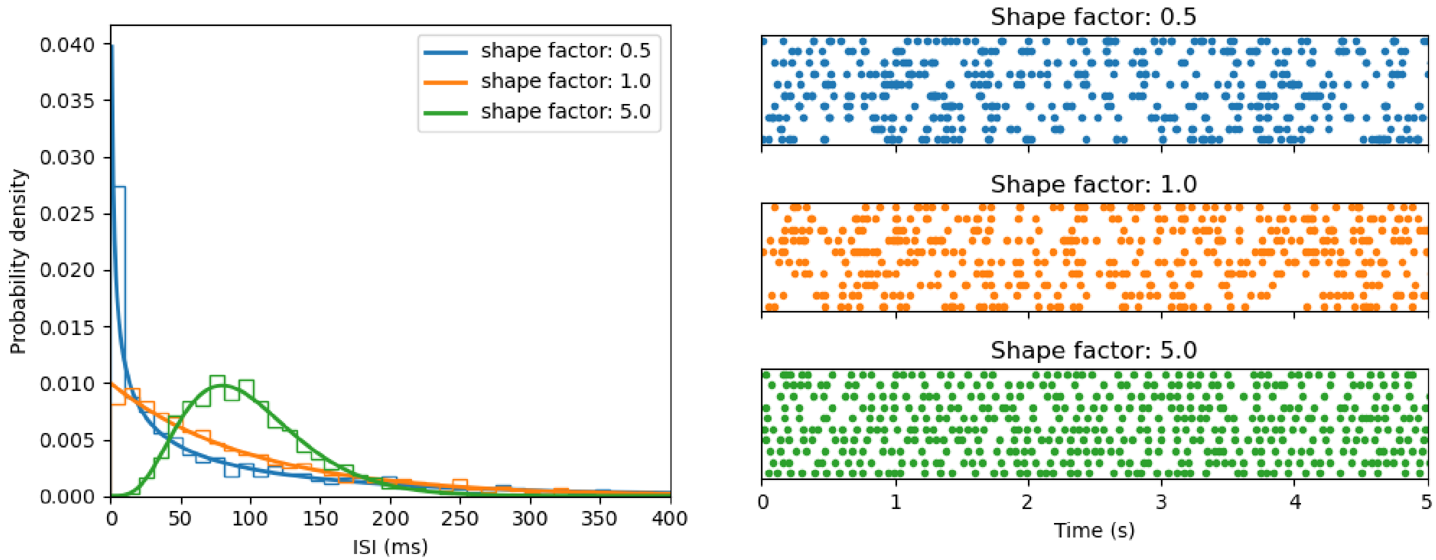
Stochastic characterization | example data

- 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



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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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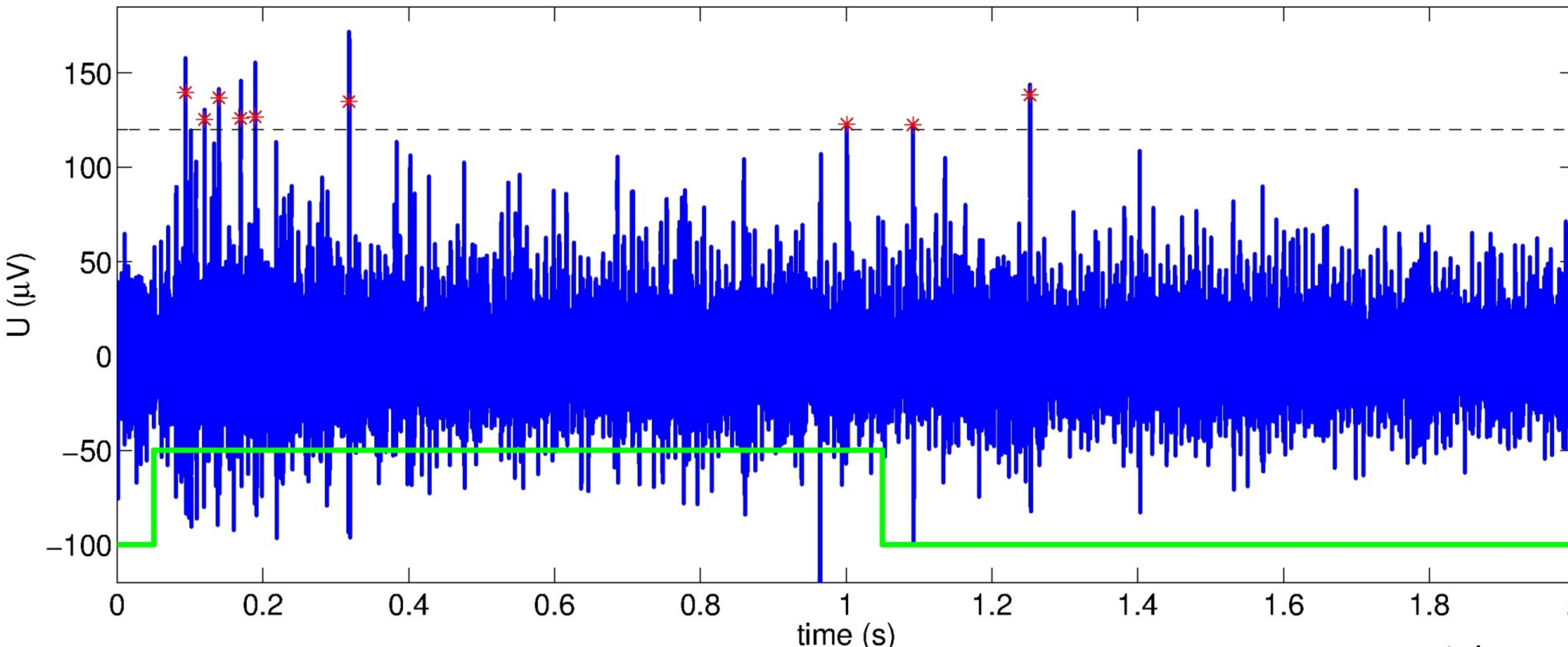
Neuronal response | example

- Spiking activity modulated by odor presentation



Data: Courtesy R. Finke

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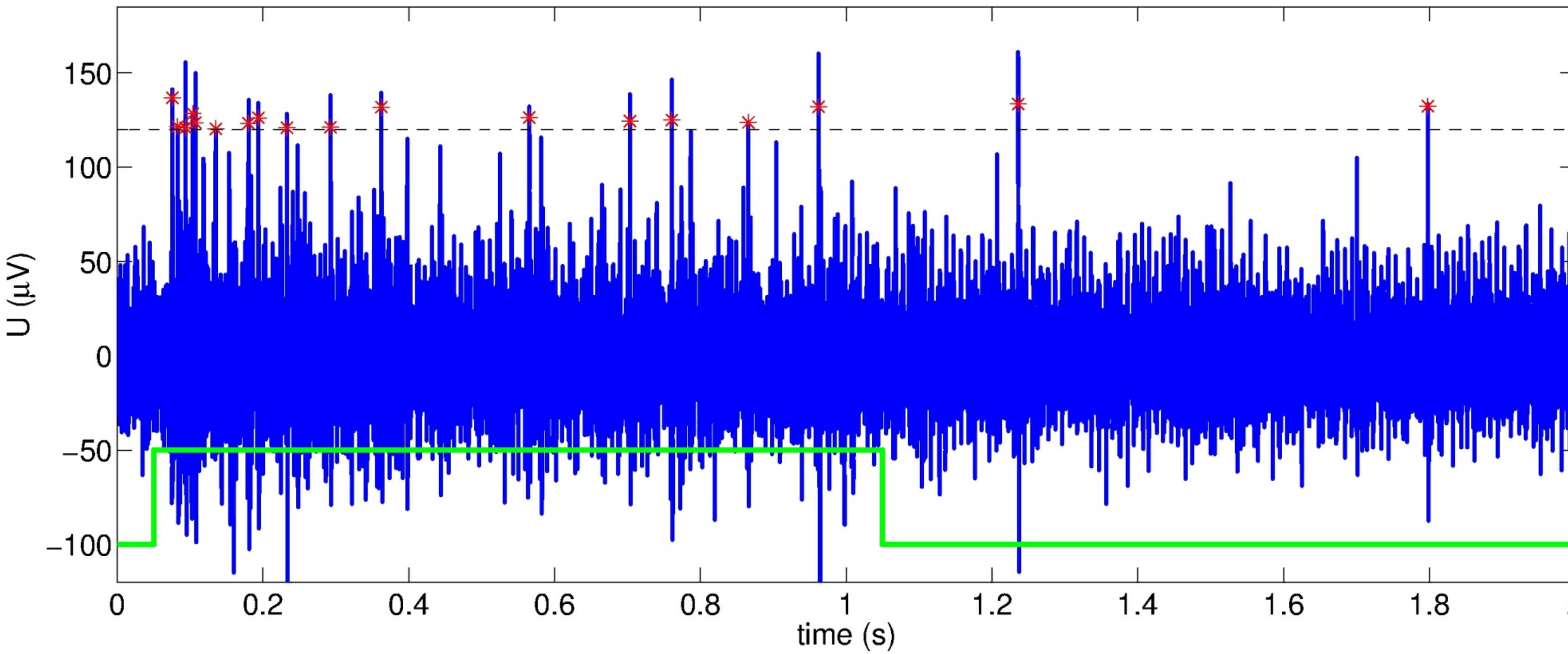
Neuronal response | example

- Spiking activity modulated by odor presentation



Data: Courtesy R. Finke

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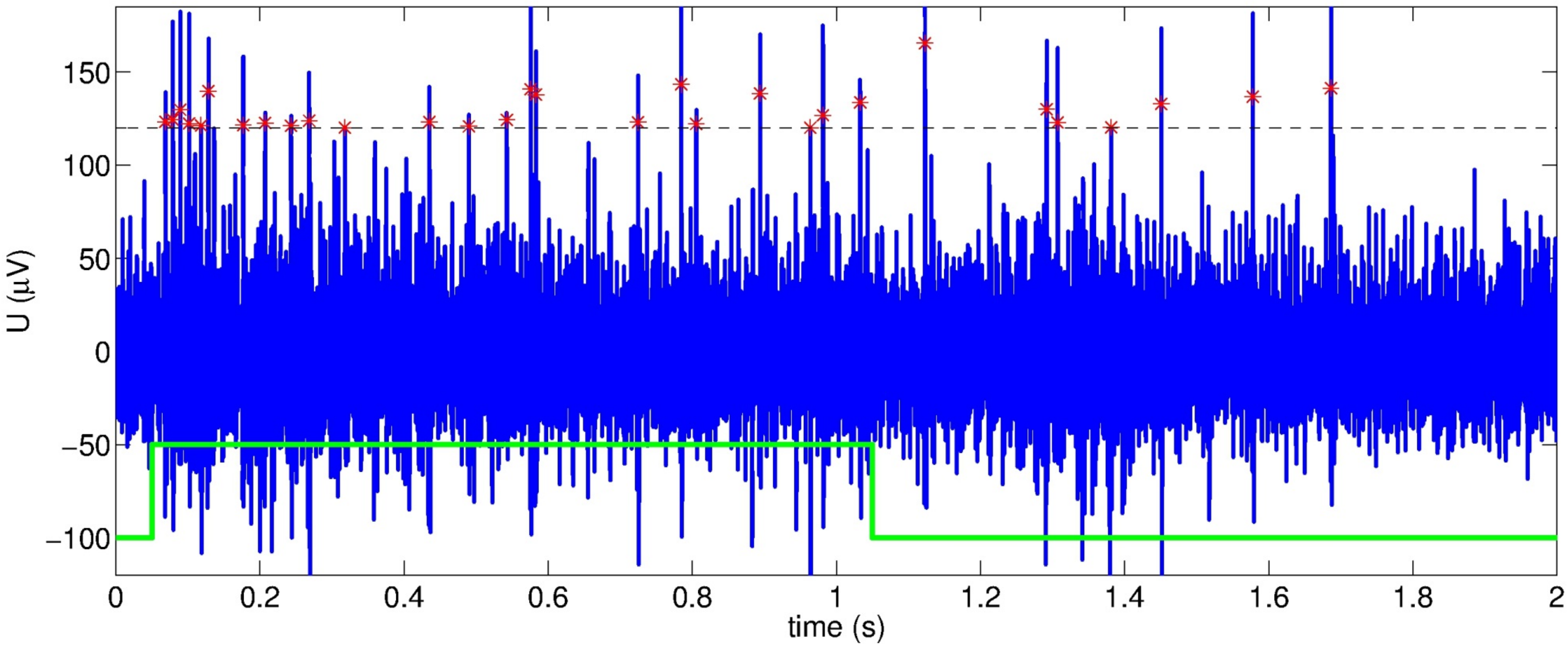
Neuronal response | example

- Spiking activity modulated by odor presentation



Data: Courtesy R. Finke

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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

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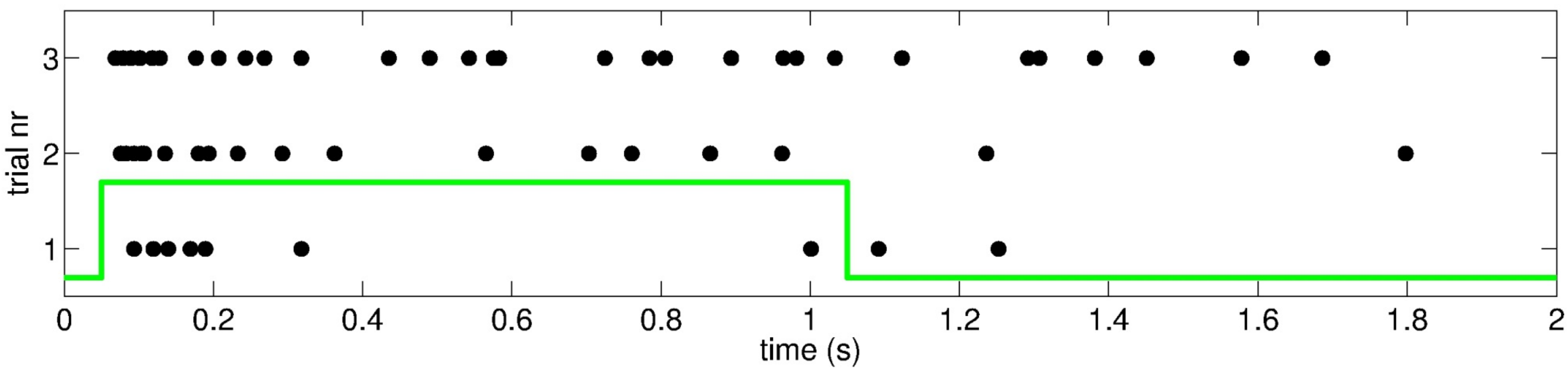
Neuronal response | dot display

- **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



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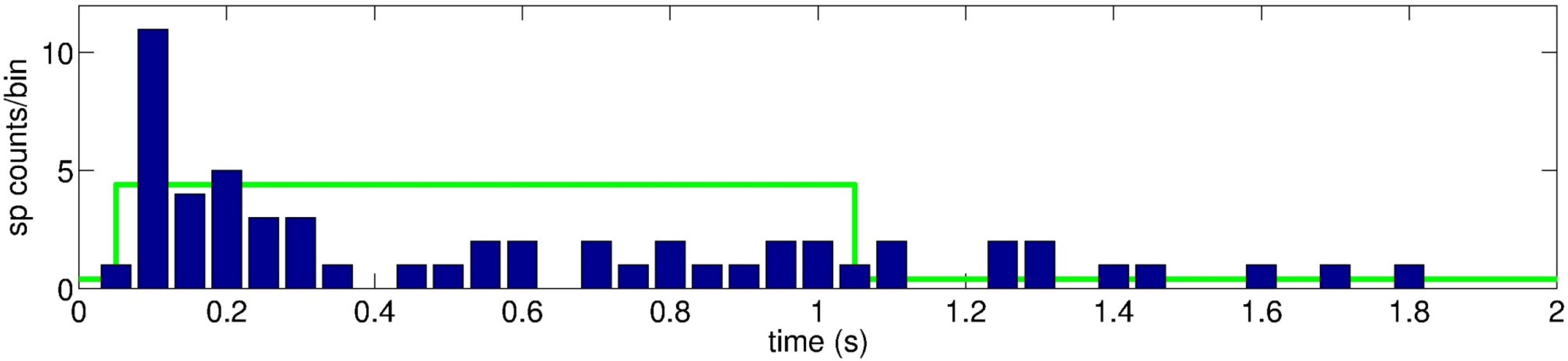
Neuronal response | PSTH

- **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



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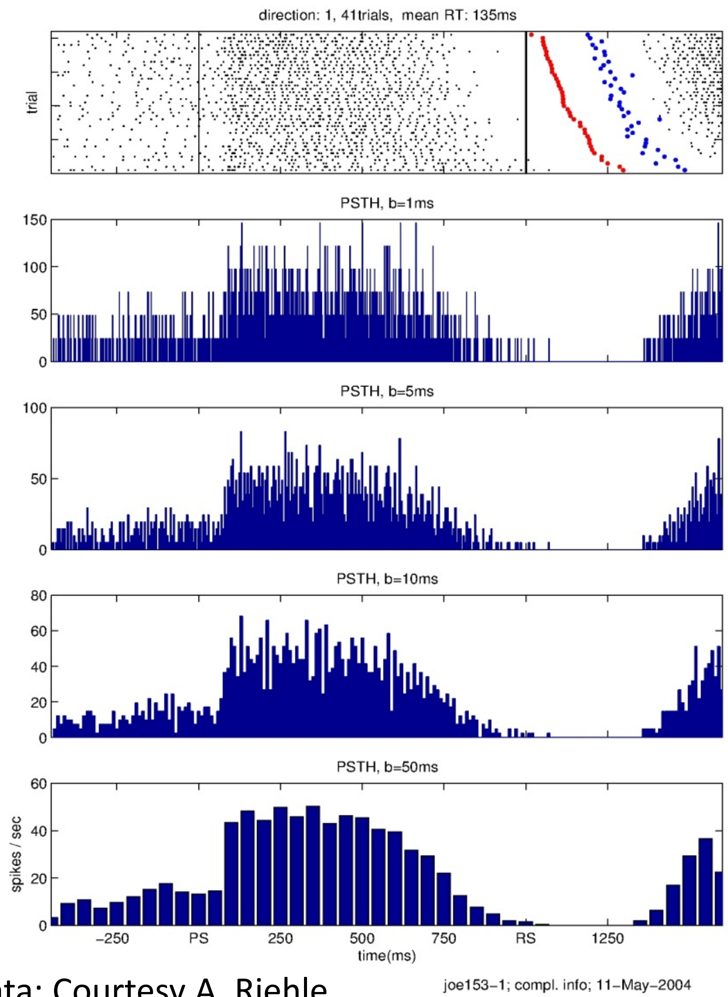
Neuronal response | rate estimation



Data: Courtesy A. Riehle

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

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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...

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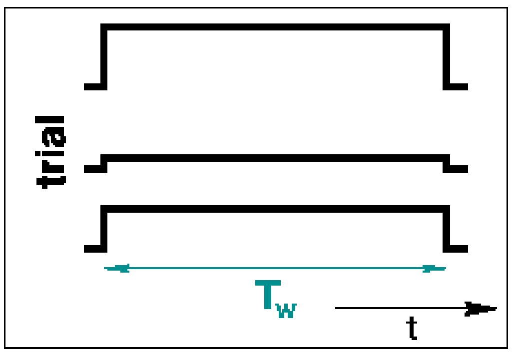
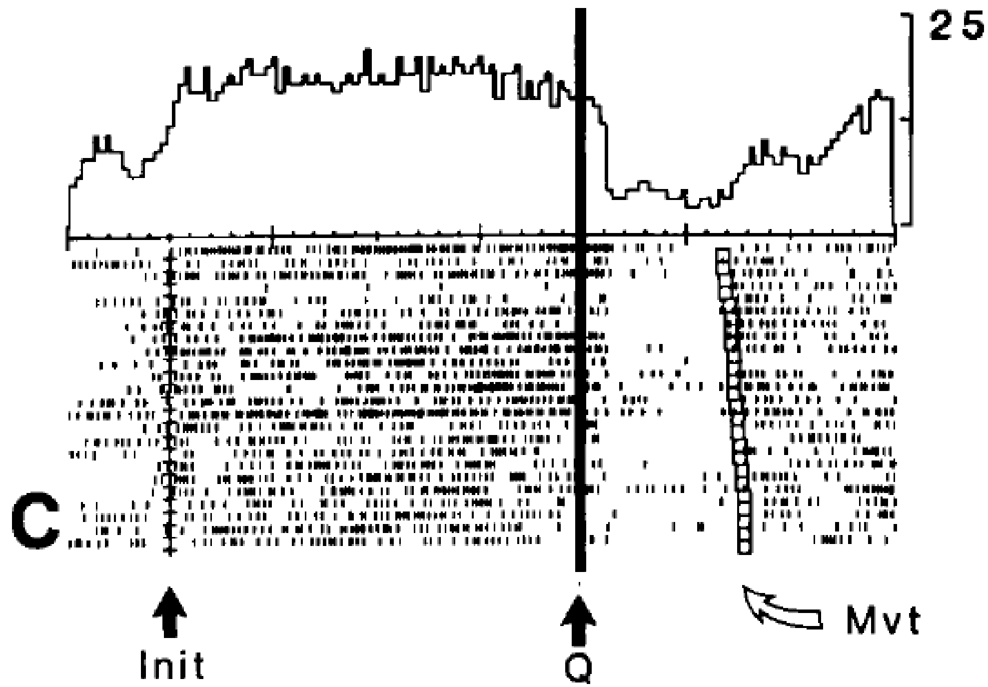
Neuronal response | violation of assumptions

- Large variability of rate across trials





From: Vaadia et al. (1988)

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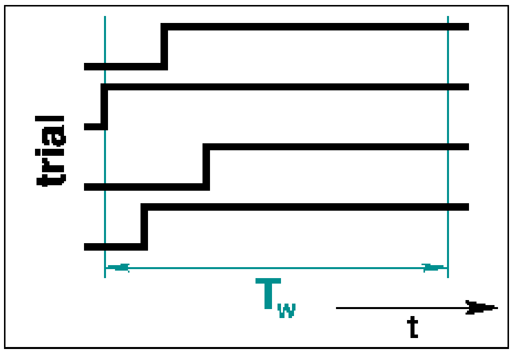
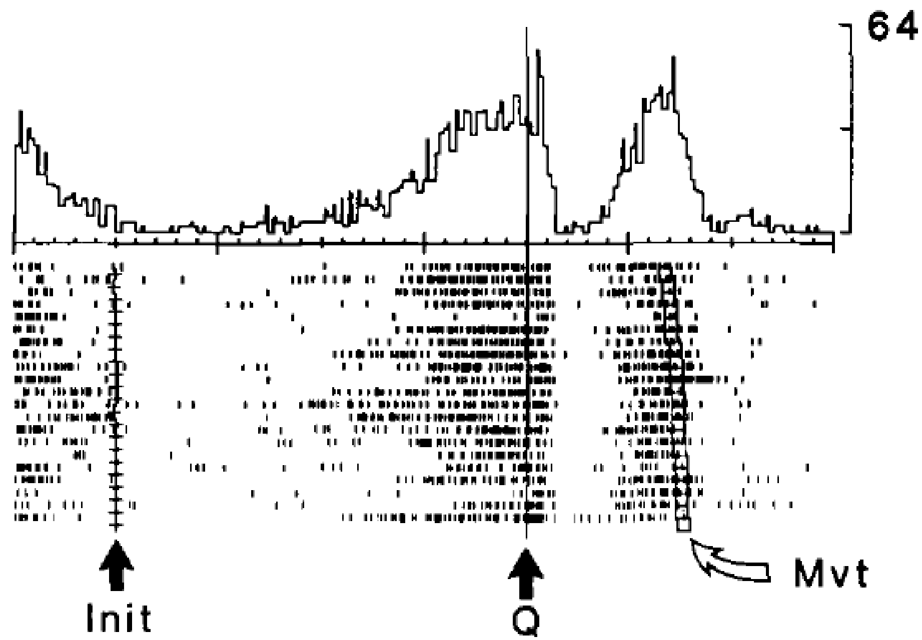
Neuronal response | violation of assumptions

- Large variability of latency across trials





From: Vaadia et al. (1988)

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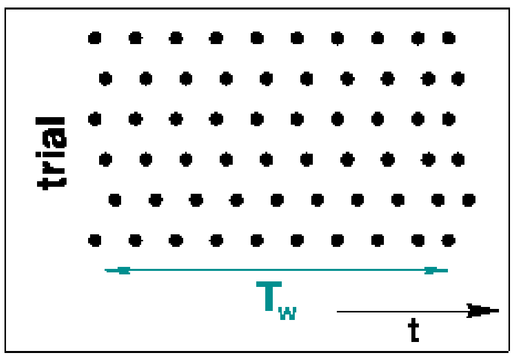
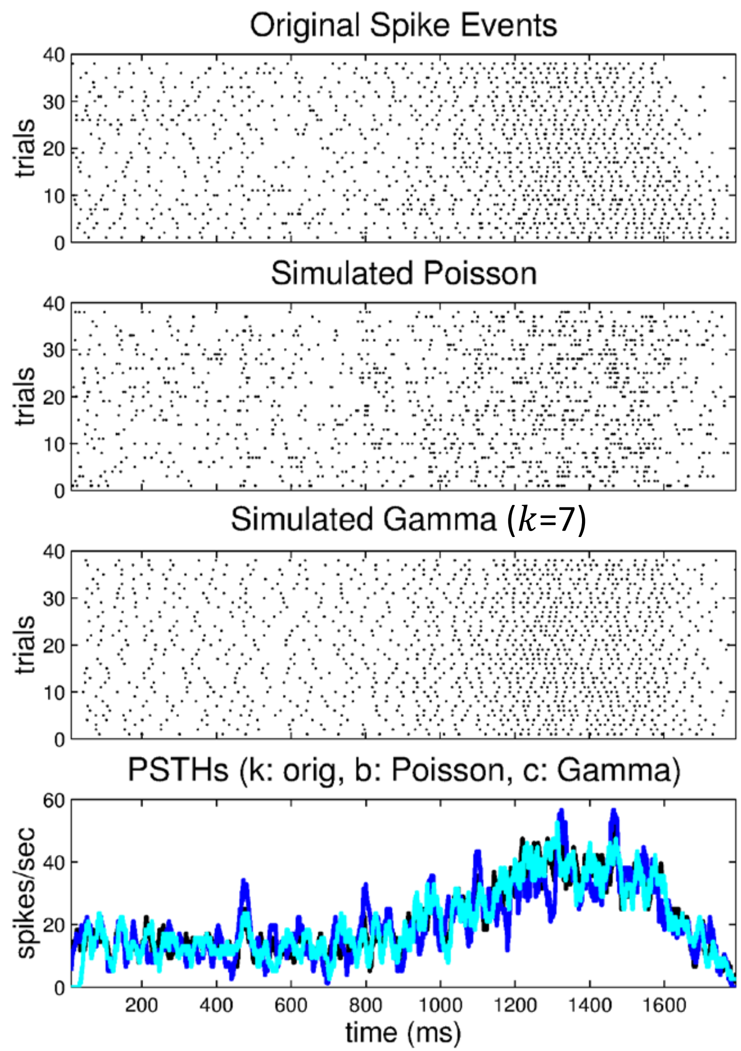
Neuronal response | violation of assumptions

- Deviation from Poisson





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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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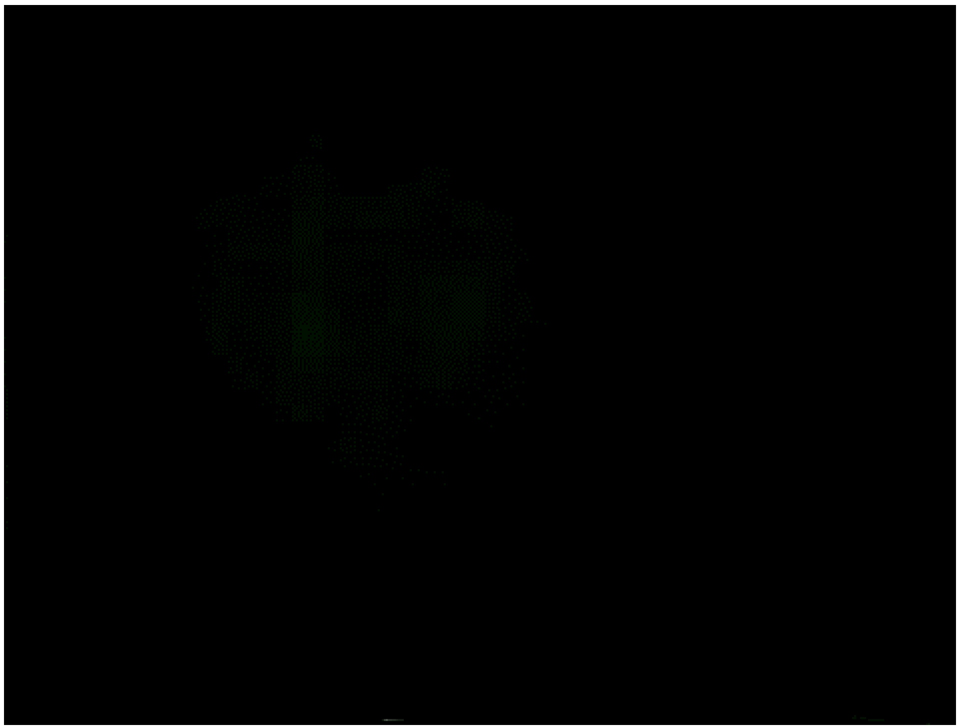
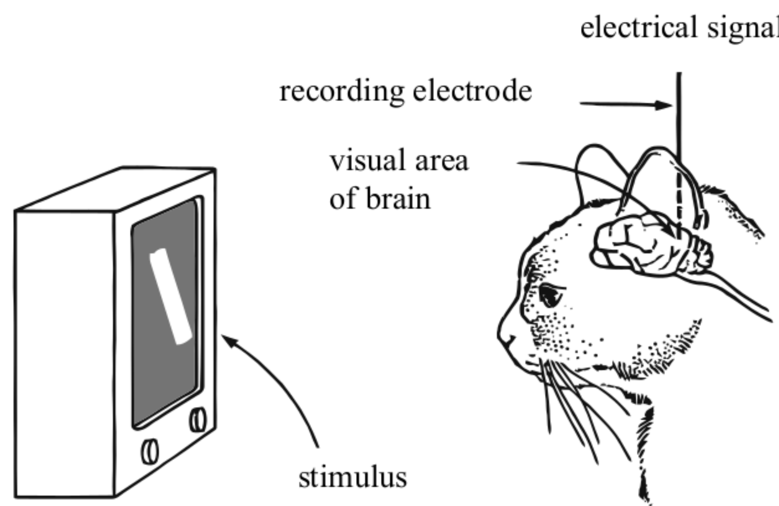
Application | receptive field of V1 cells

- 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

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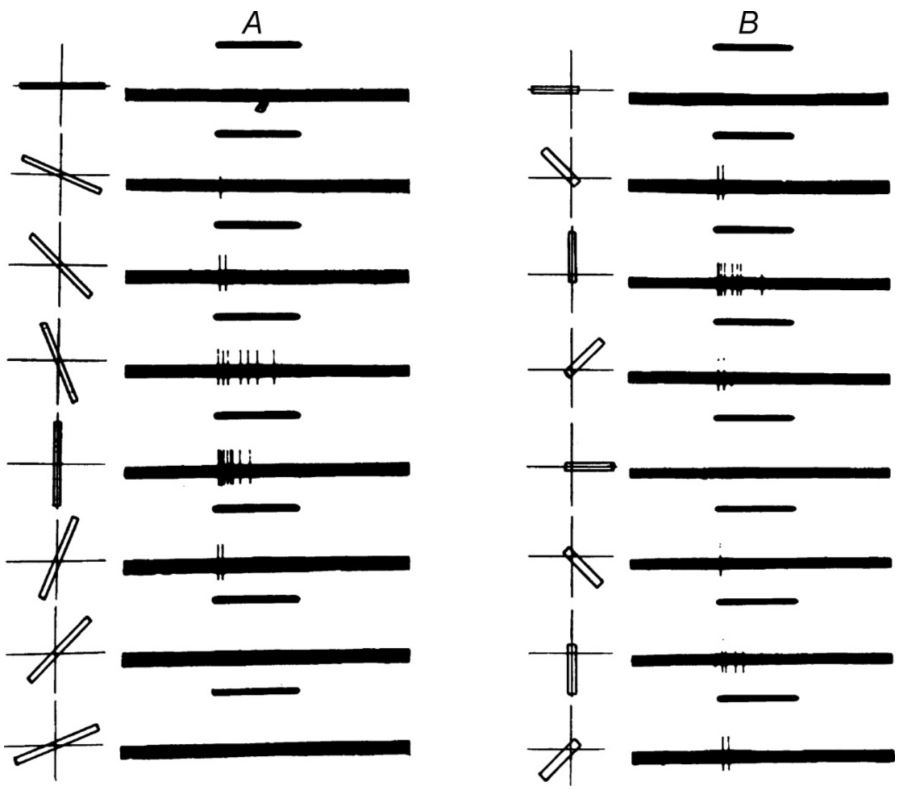
Application | orientation selectivity in V1



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

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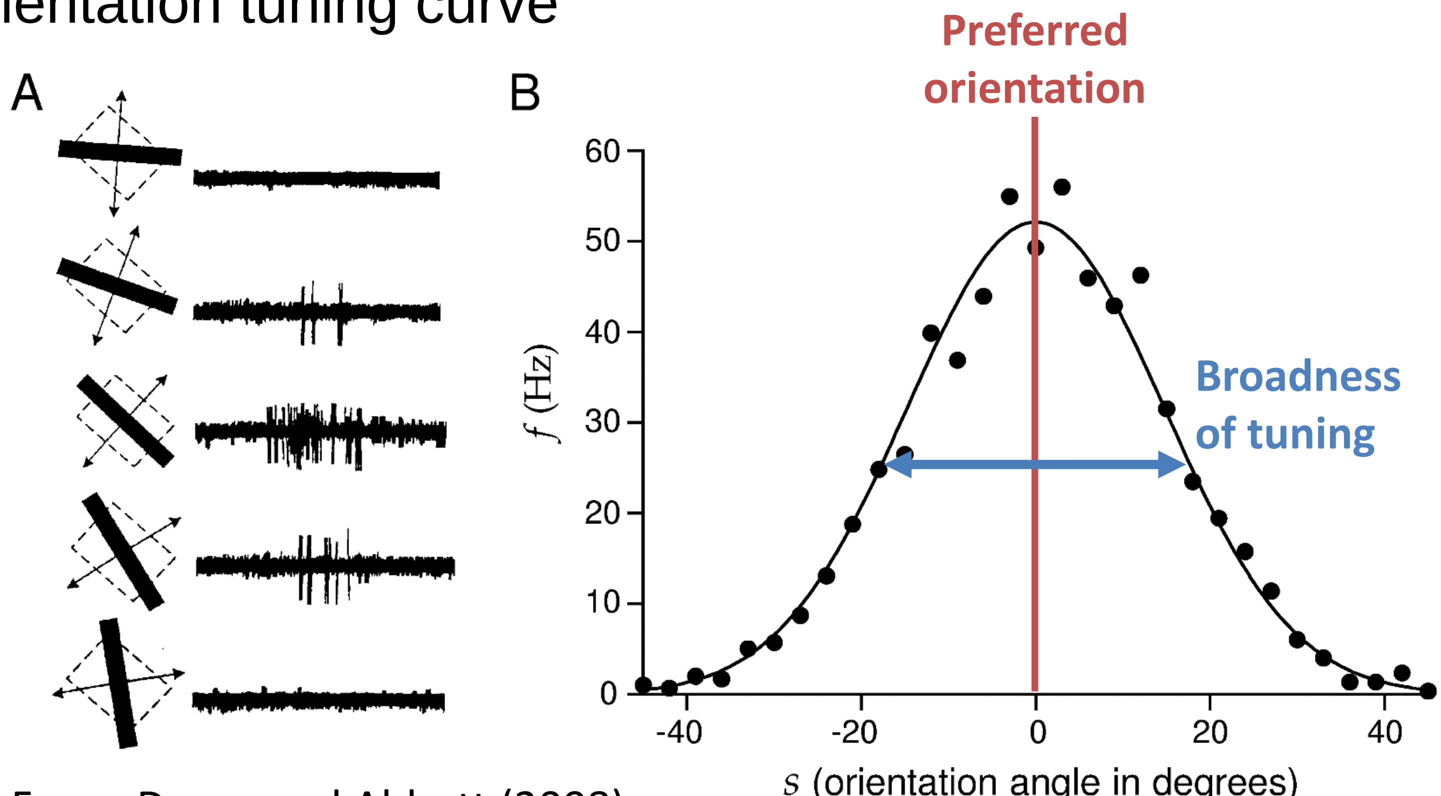
Application | tuning curve of V1 cells

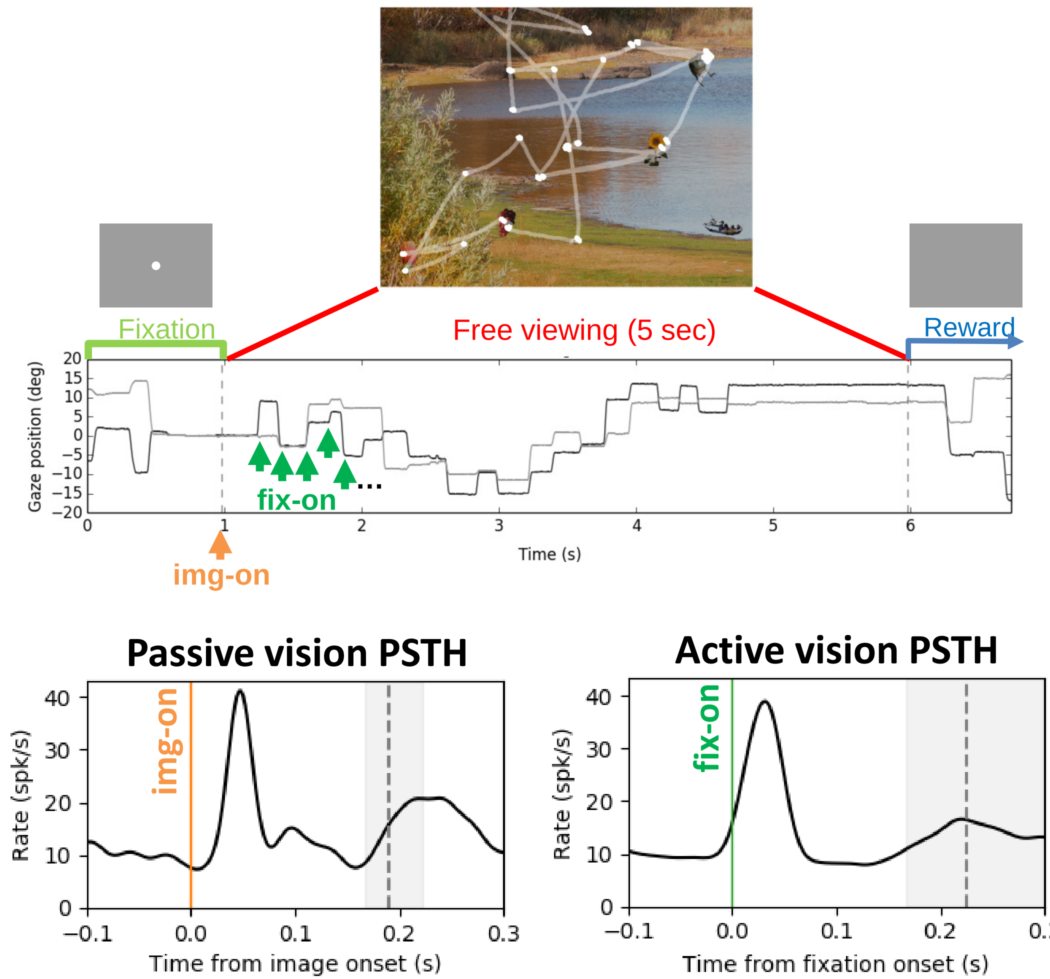
- Orientation tuning curve



From: Dayan and Abbott (2008)

Application | V1 response to fixated images

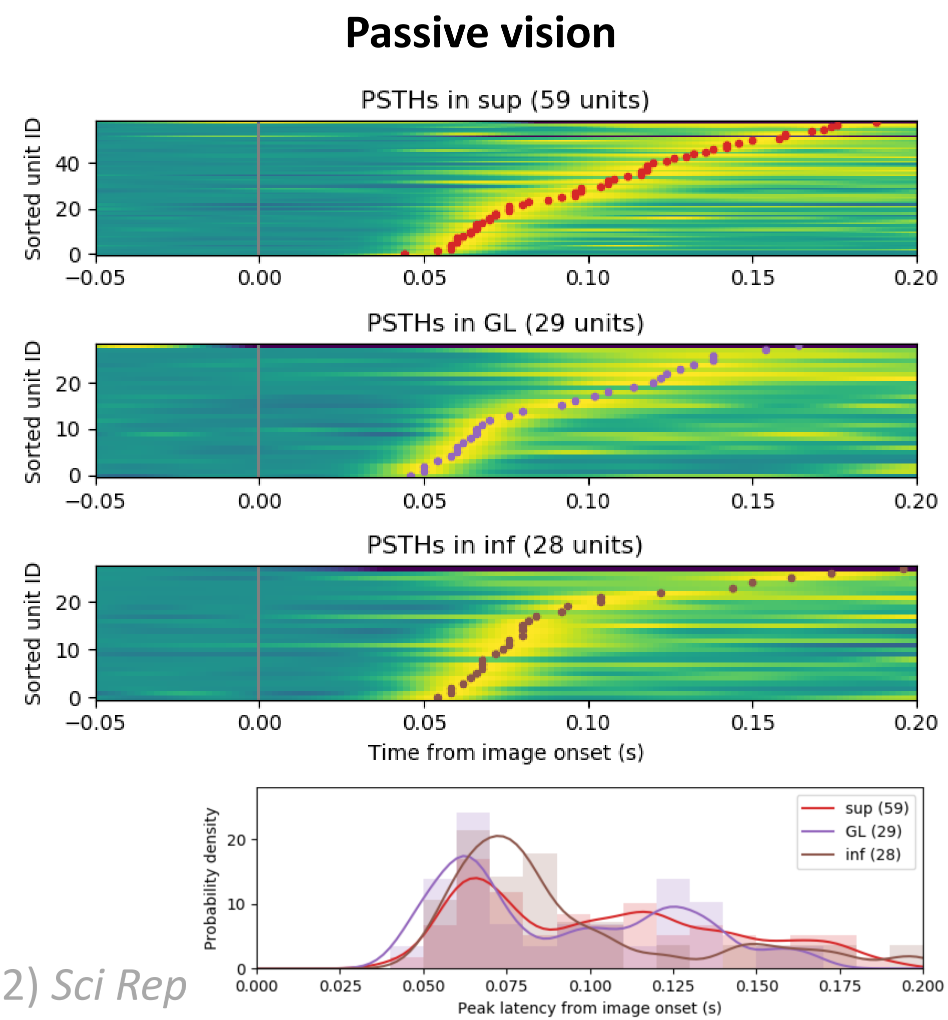
- V1 neurons of freely-viewing macaques
- Two PSTHs per neuron: triggered by **img-on** or **fix-on**
- Response to **img-on**
  → **passive vision**
- Response to **fix-on**
  → **active vision**



Ito et al. (2022) *Sci Rep*

Application | V1 response to fixated images

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



Ito et al. (2022) *Sci Rep*

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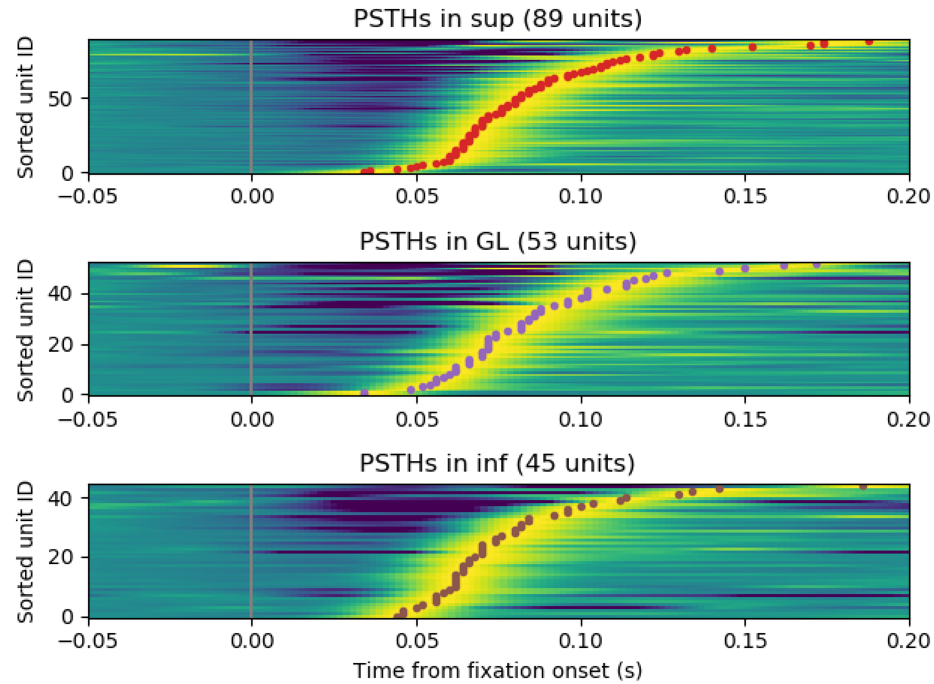
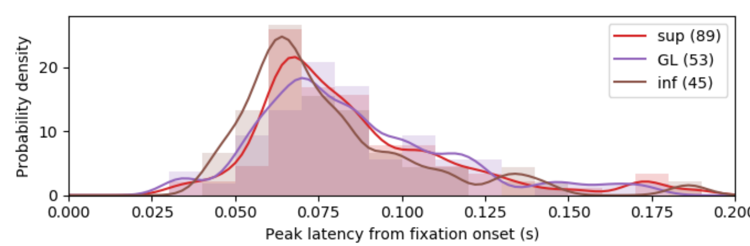
Application | V1 response to fixated images

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

Active vision





Ito et al. (2022) *Sci Rep*

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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?

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