Welcome!

#pod-031

(Reviewed by: Keerthana and Deepak)

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Agenda

- **Day-#1**
  - Tutorial part 1 (What models)
    - 2 Exercises
  - Tutorial part 2 (How models)
    - 2 Exercises
  - Tutorial part 3 (Why models)
    - 2 Exercises

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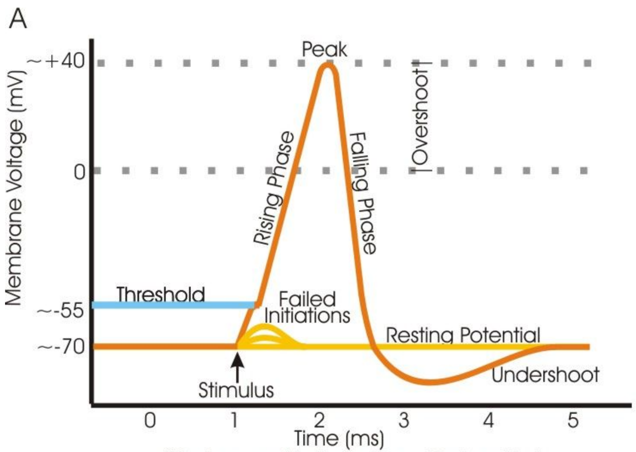
Brain and Spikes

Neurons compute and communicate by transforming synaptic input patterns into output spike trains. The nature of this transformation depends crucially on the properties of voltage-gated conductances* in neuronal membranes. These intrinsic membrane conductances can enable neurons to generate different spike patterns including brief, high-frequency bursts that are commonly observed in a variety of brain regions.

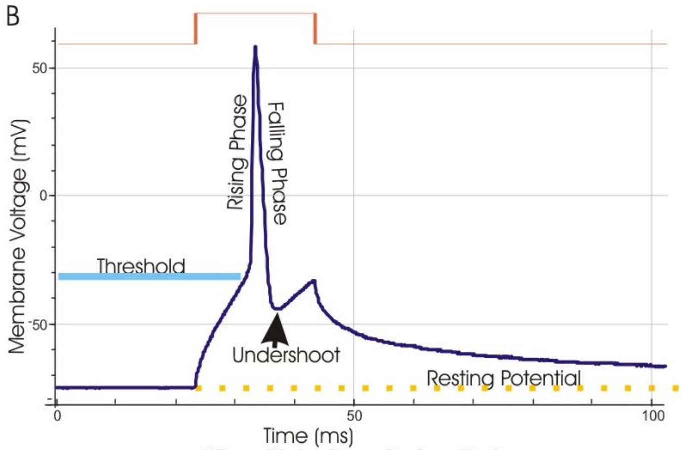
Voltage differences cause action potentials/spikes (also called Nerve Impulses).

*Conductance due to **Voltage-gated** ion channels. **Voltage-gated** ion channels are a class of transmembrane proteins that form ion channels that are activated by changes in the electrical membrane potential near the channel.

Ref: http://kepecslab.cshl.edu/papers/kepecs_lisman03_Information_encoding_and_computation_with_spikes.pdf



“Schematic” Action Potential



“Real” Action Potential

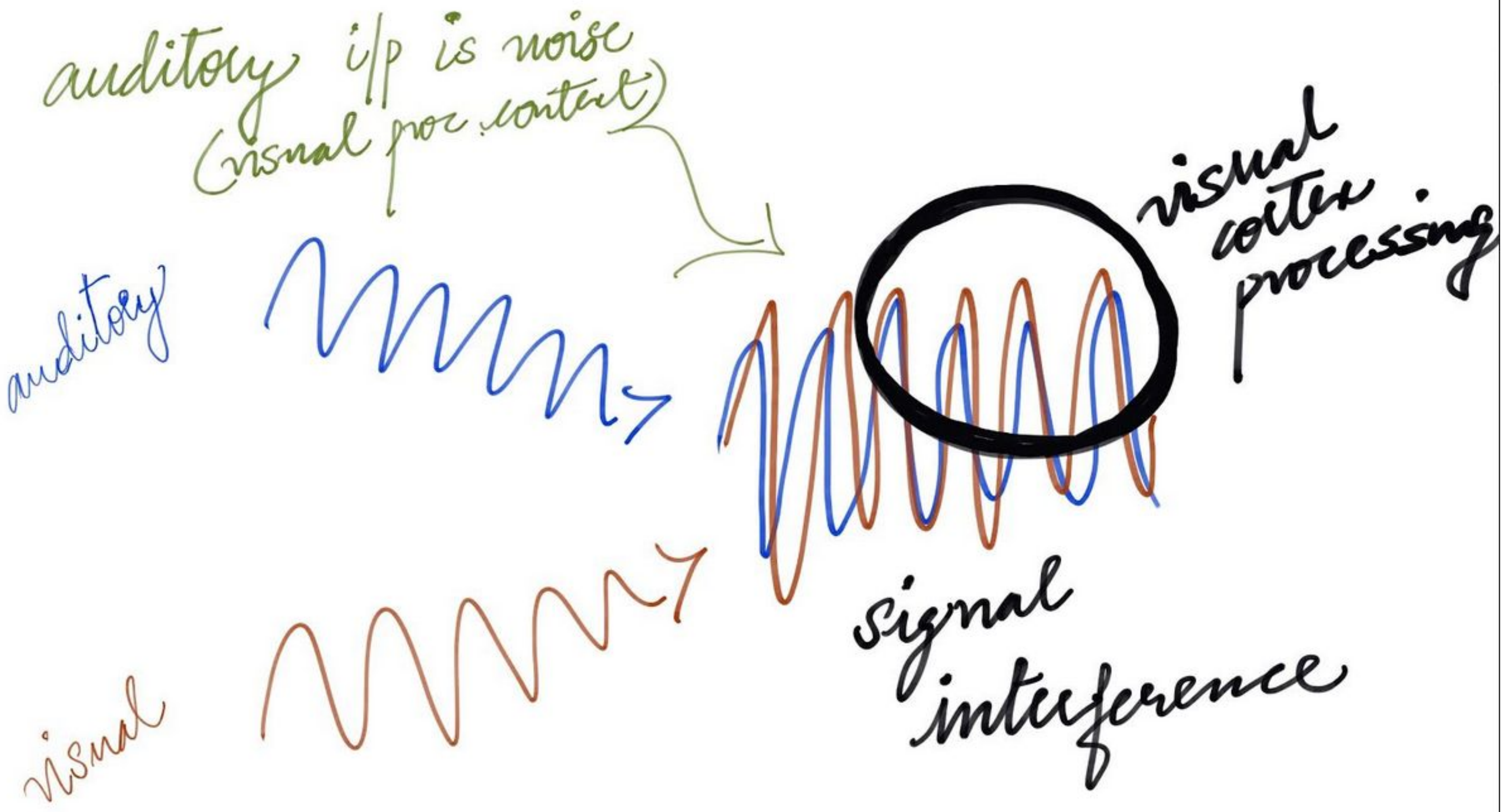
Spiking and Information Transfer

Spiking in the brain is the inherent mechanism for information encoding-decoding and transfer.

How does noise come into the neural picture?

External sensory stimuli are intrinsically noisy because they are either thermodynamic or quantum mechanical in nature. And hence, all forms of chemical sensing are affected by thermodynamic noise. Subsequent transduction processes amplify the sensory signal and convert it into an electrical one.

Ref: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2631351/


auditory i/p is noise
(visual proc. context)
auditory
visual
visual
cortex
processing
signal
interference

Spiking and Information Transfer

Why does shannon entropy come into play?

If you think of the nerve as a communication channel where there are signals and noise:

In information theory, the Shannon–Hartley theorem tells the maximum rate at which information can be transmitted over a communications channel of a specified bandwidth in the presence of noise. It is an application of the noisy-channel coding theorem to the archetypal case of a continuous-time analog communications channel subject to Gaussian noise.

Summary - How spiking affects Information Transfer (encoding-decoding)

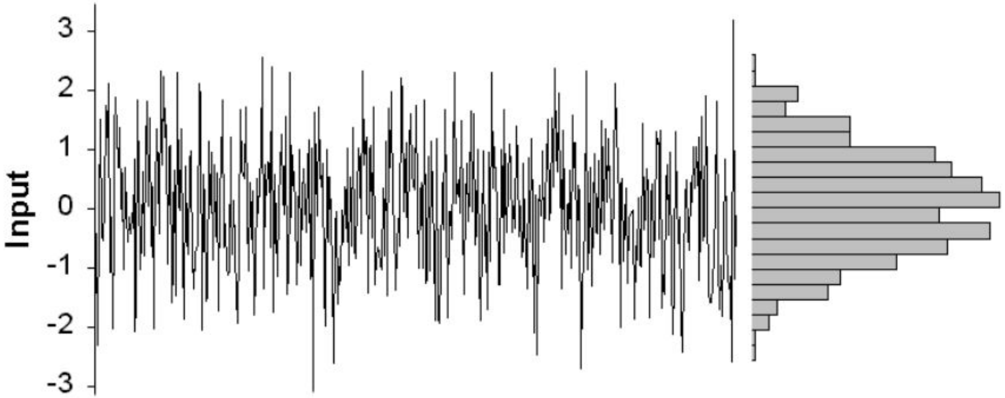
The link between stimulus and response can be studied from two opposite points of view. Neural encoding refers to the map from stimulus to response. The main focus is to understand how neurons respond to a wide variety of stimuli, and to construct models that attempt to predict responses to other stimuli. Neural decoding refers to the reverse map, from response to stimulus, and the challenge is to reconstruct a stimulus, or certain aspects of that stimulus, from the spike sequences it evokes.

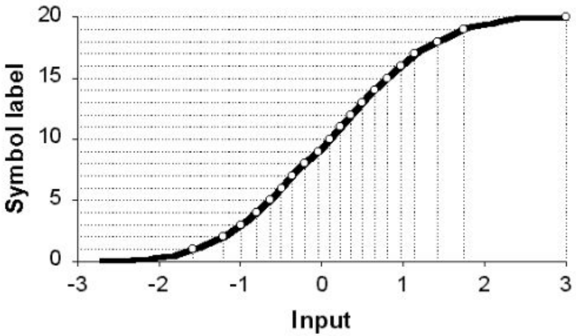
A sequence, or 'train', of spikes may contain information based on different coding schemes. In motor neurons, for example, the strength at which an innervated muscle is contracted depends solely on the 'firing rate', the average number of spikes per unit time (a 'rate code'). At the other end, a complex 'temporal code' is based on the precise timing of single spikes. They may be locked to an external stimulus such as in the visual and auditory system or be generated intrinsically by the neural circuitry.

Ref: https://courses.cs.washington.edu/courses/cse528/13sp/lecture-slides/Lecture6.pdf
https://en.wikipedia.org/wiki/Neural_coding

Efficient coding

In order to encode stimuli effectively, an encoder should match its outputs to the statistical distribution of the inputs





Shape of the I/O function should be determined by the distribution of natural inputs

Optimizes information between output and input

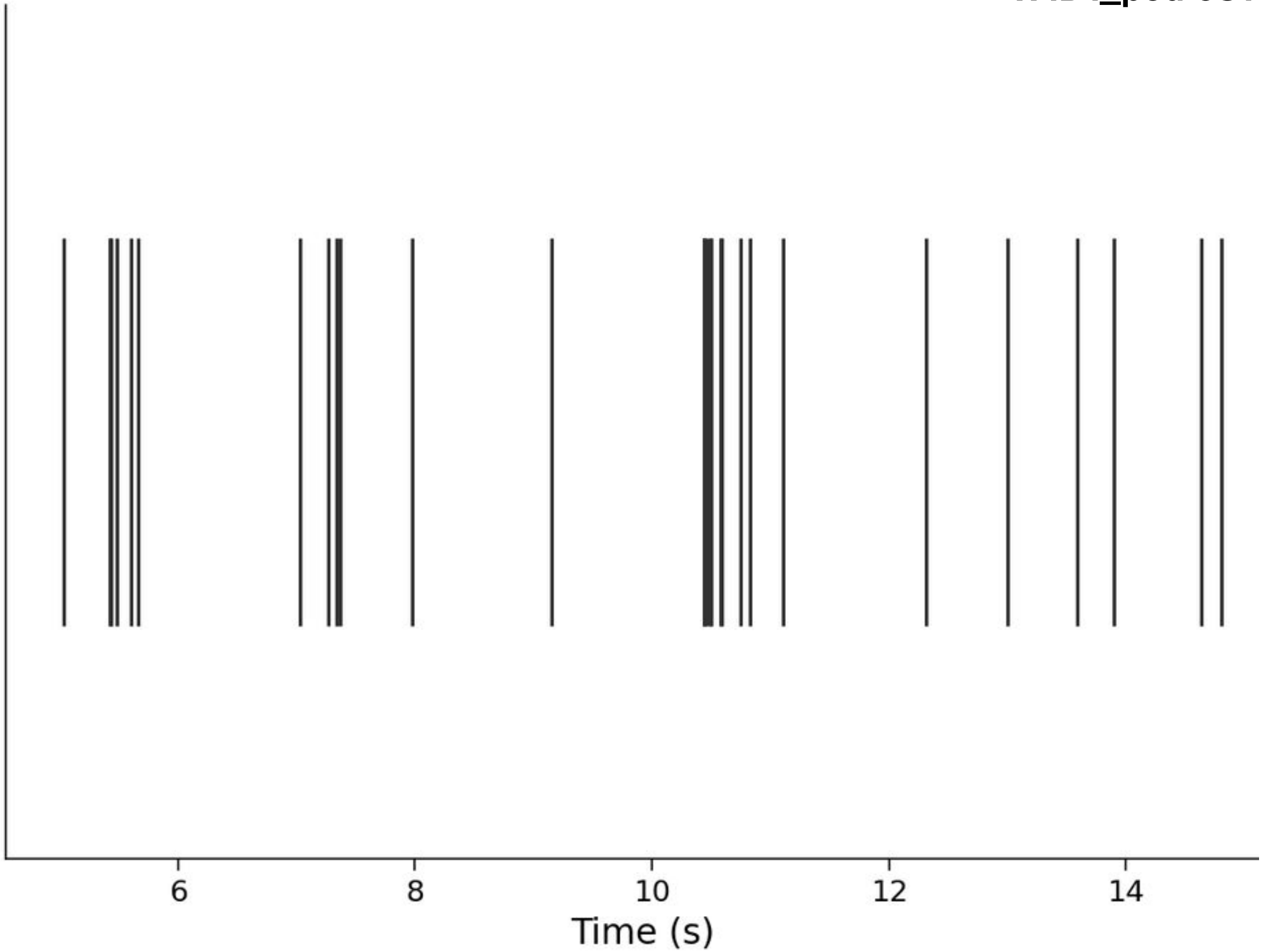
Tutorial #1 Explanations

Structure of Steinmetz data

[No. of neurons, [. . . .]]

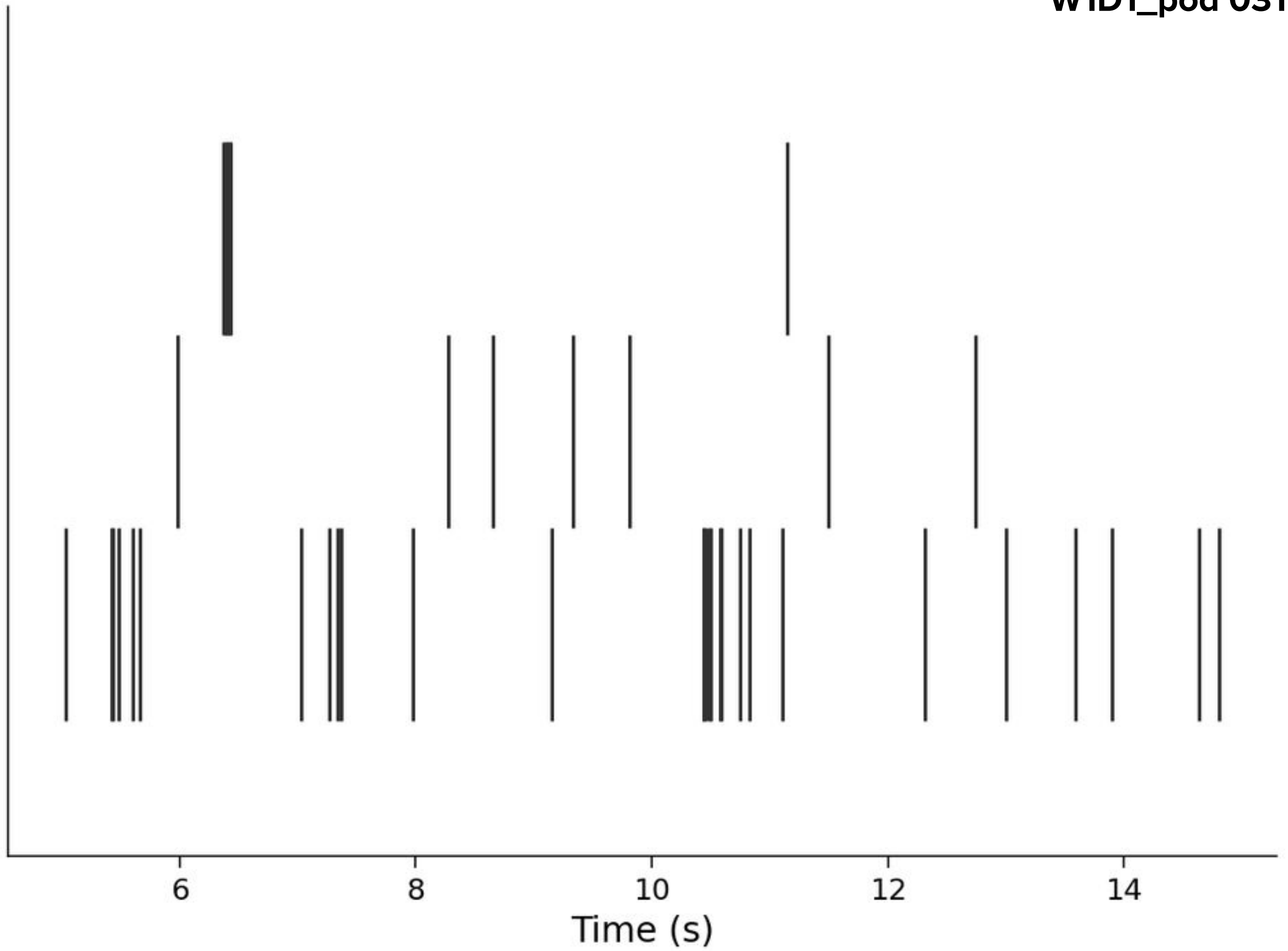
array of spike times!

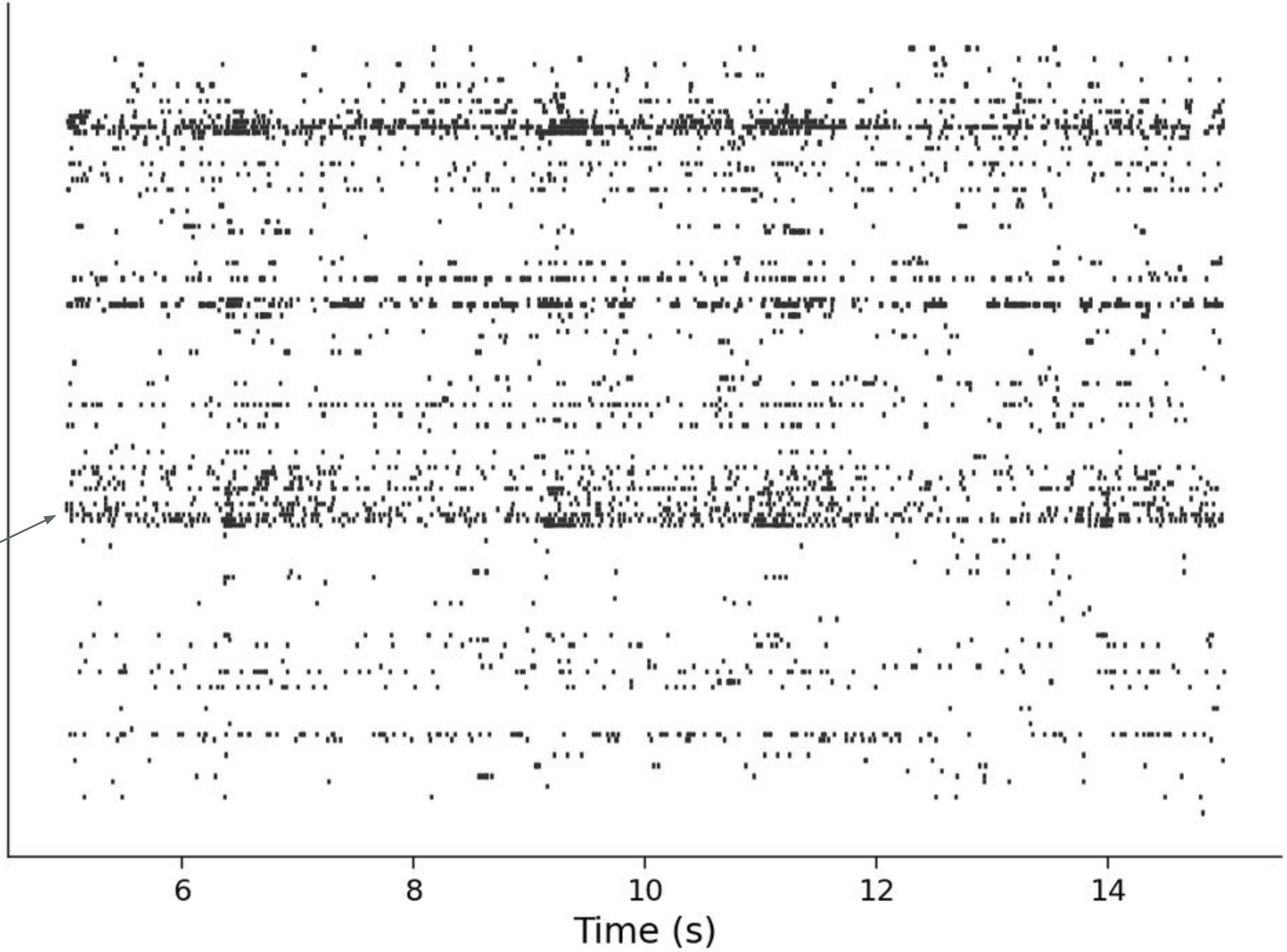
Spike times Of single neuron



Spike times Of multiple Neurons

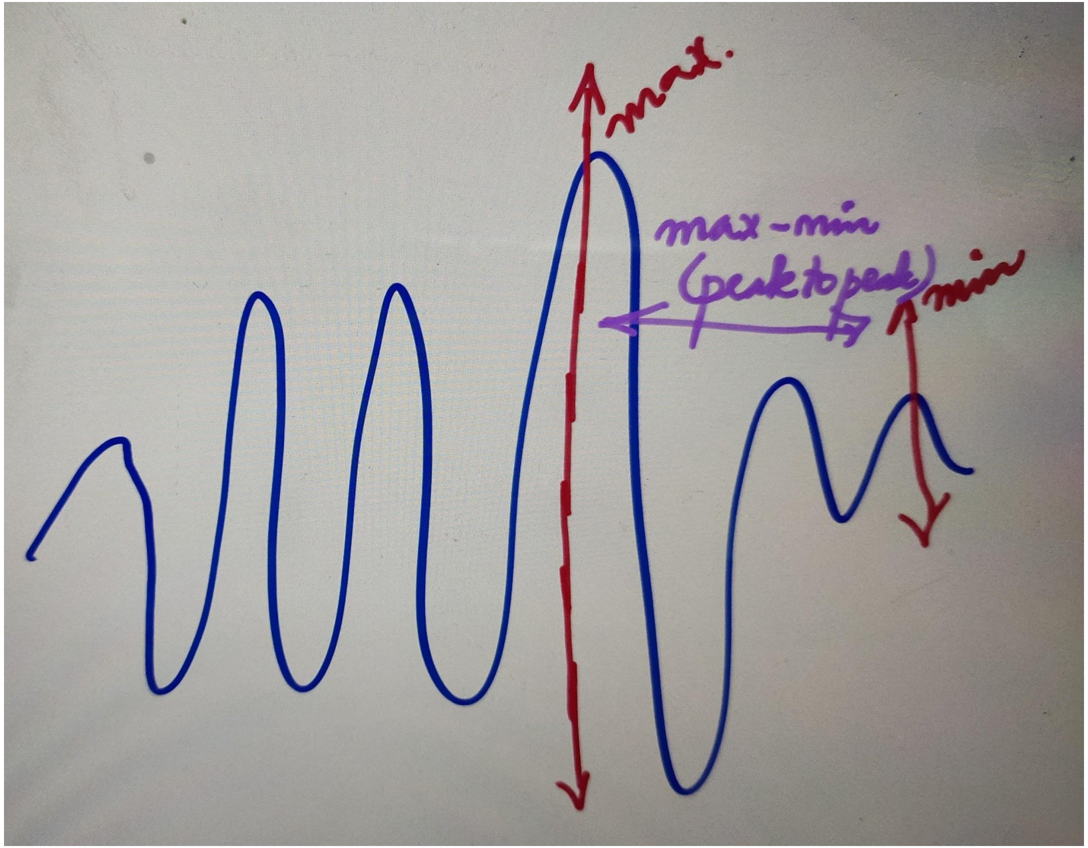
Raster Plot





Spike recording of every 5th neuron.

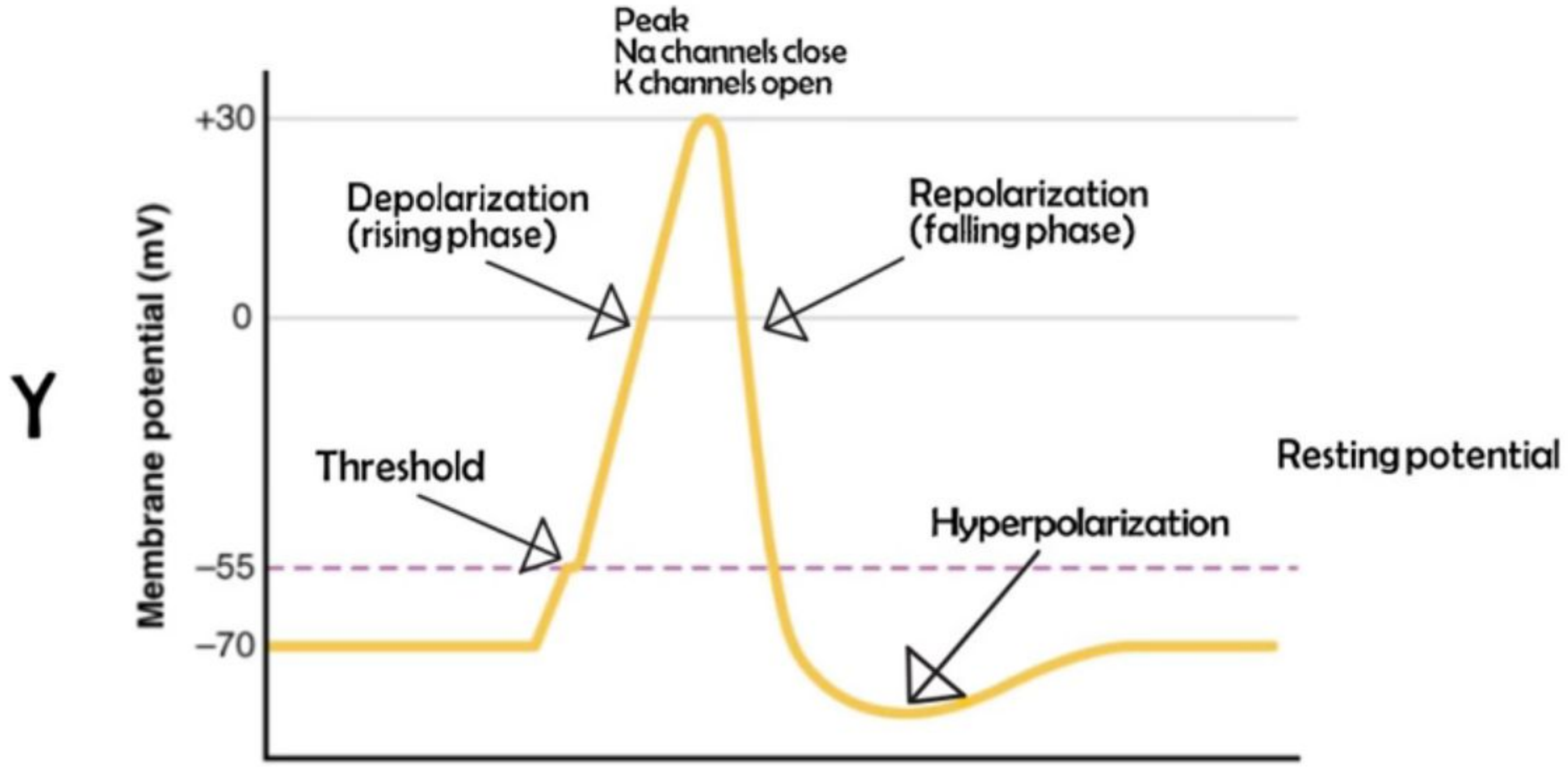
Visualizing neuronal spiking activity



Refractory periods

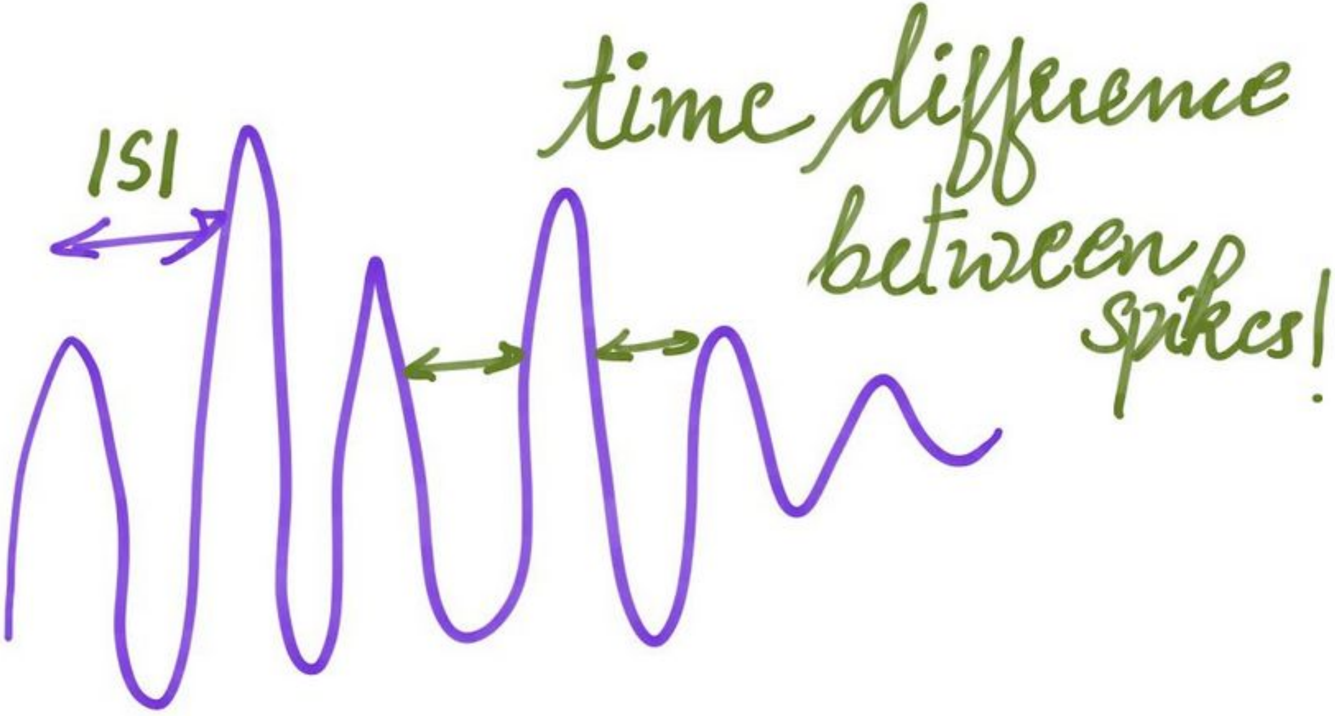
Refractory period is a period of time during which an organ or cell is incapable of repeating a particular action, or (more precisely) the amount of time it takes for an excitable membrane to be ready for a second stimulus once it returns to its resting state following an excitation.

In neurons they can only fire as quickly as their metabolic processes can support, and there is a minimum delay between consecutive spikes of the same neuron.



Ref: https://www.youtube.com/watch?v=W2hHt_PXe5o

Inter-spike intervals (ISI)



Inter-spike intervals (ISI)

Shorter ISIs are predominant, with counts decreasing rapidly (and smoothly, more or less) with increasing ISI. However, counts also rapidly decrease to zero with *decreasing* ISI, below the maximum of the distribution (8-11 ms). The absence of these very low ISIs agrees with the refractory period hypothesis: the neuron cannot fire quickly enough to populate this region of the ISI distribution.

<u>Inference:</u> The ISI histograms seem to follow continuous, monotonically decreasing functions above their maxima.

Why Inter-spike intervals (ISI)?

The spike itself is an all-or-none phenomenon, so information is coded not in the amplitude of a spike but in the timing of spikes. Accordingly, electrophysiologists, who study the electrical behaviour of neurons, are interested in the patterning of spikes in particular neurons, which they typically analyze by way of an interspike interval histogram.

Ref: https://www.tau.ac.il/~tsirel/dump/Static/knowino.org/wiki/Interspike_interval.html

Tutorial #2
Explanations

Food for thought

Why do we have entropy? Are neuron firings random?

Neural responses can vary from trial to trial even when the same stimulus is presented repeatedly. There are many potential sources of this variability including variable levels of arousal and attention, randomness associated with various biophysical processes that affect neuronal firing, and the effects of other cognitive processes taking place during a trial. In response to a long sample of time varying stimuli, the spike train of a single neuron varies, and we can quantify this variability by the entropy per unit time of the spike train.

We are basing the probability density with information theory theoretically using the Shannon equation.

Ref: https://www.mdpi.com/1099-4300/16/11/5721/htm
http://www.stat.columbia.edu/~liam/teaching/neurostat-spr12/papers/bialek-et-al/strong+al_98a.pdf
https://www.dam.brown.edu/people/elie/NEUR_1680_2012/Abbott%20Dayan%20Chapter%201.PDF

Shannon Entropy

probability mass function!

$$H_b(X) = -\sum_{x \in X} p(x) \log_b p(x)$$

Entropy

mass ⇒ distribution contained in that value!

Case 1 : Excitatory Neuron behavior

Only way membrane potential decrease is upon spike event

Case 2 : Inhibitory neuron behavior

membrane potential decrease due to steady state etc.

$$dV_m = -\beta V_m + \alpha I$$

current membrane potential

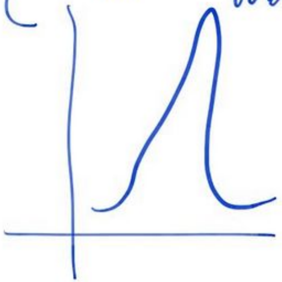
leakage potential

Tutorial #3
Explanations

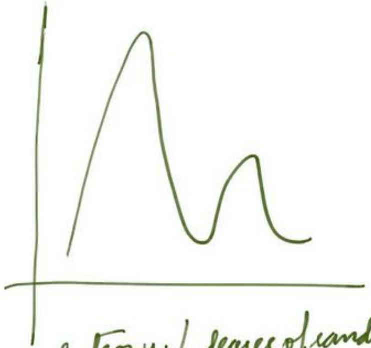
Entropy of distributions

Task: computing entropy of a discrete probability dist. given mass function.

location of peak doesn't affect entropy.

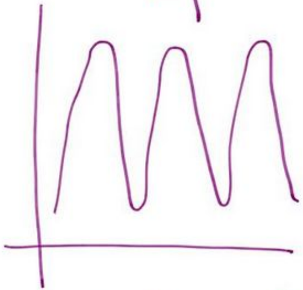


all mass is conc. on a single event.



entropy / degree of randomness decreases (increased certainty of falling on 1 peak)

N peaks



Uniform dist. highest entropy $= \log_b N$

What? Models!
(Descriptive!)

Goal of What models

- Load a dataset (Steinmetz here) with spiking activity from hundreds of neurons and understand how it is organized
- Make plots to visualize characteristics of the spiking activity across the population
- Compute the distribution of "inter-spike intervals" (ISIs) for a single neuron
- Consider several formal models of this distribution's shape and fit them to the data "by hand"

What models

Helps look at what the data looks like for any particular model. (Exploratory Data Analysis); may help apply transformations or "pre-processing" to create a working representation of the data of interest

Descriptive modeling is a mathematical process that describes real-world events and the relationships between factors responsible for them.

Eg: Clustering by behavior/statistics etc. (Variable based segmentation)

What models

“presents the main features of the data”
“a summary of the data”

Data randomly generated from a “good” descriptive model will have the same characteristics as the real data

Ref: http://www.stat.columbia.edu/~madigan/DM08/descriptive.ppt.pdf

How? Models!

(Mechanistic!)

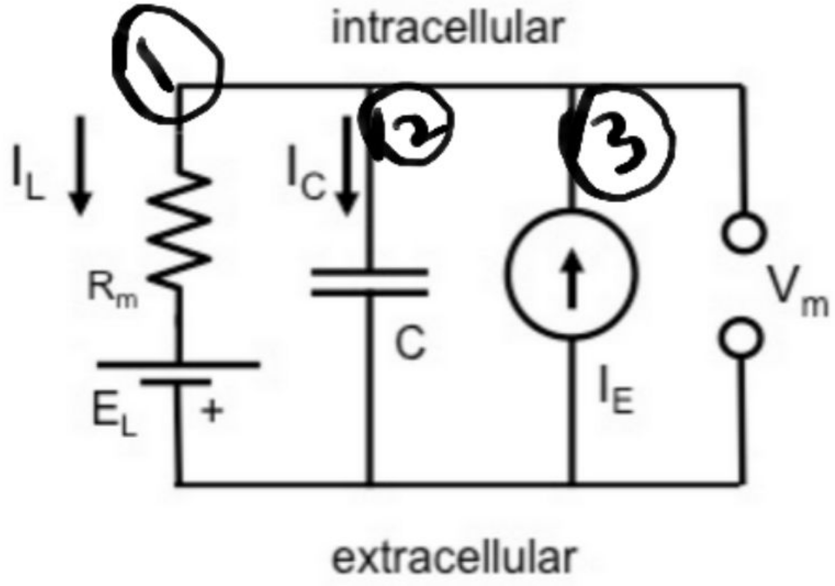
How models

Mechanistic models specify assumptions and attempt to incorporate known factors about the systems surrounding the data into the model, while describing the available data. Mechanistic models are based on an understanding of the behavior of a system's components

Model parameters have an actual physical meaning, which facilitates the scientific interpretation of the results while explaining how complex functions are performed.

Eg: Model predicting when tides will occur! (use laws of physics)

LIF Neuron Equation



Current(2) = Current(3) + Current(1)

$$C_m \frac{dV_m}{dt} = -(V_m - V_{rest})/R_m + I$$

Ref:
https://ocw.mit.edu/resources/res-9-003-brains-minds-and-machines-summer-course-summer-2015/tutorials/tutorial-2.-matlab-programming/MITRES_9_003SUM15_fire.pdf

Why? Models!
(Bayesian!)

Why models

A statistical **model** can be seen as a procedure/story describing how some data came to be. A **Bayesian model** is a statistical **model** where you use probability to represent all uncertainty within the **model**, both the uncertainty regarding the output but also the uncertainty regarding the input (aka parameters) to the **model**.

Ref: http://mlg.eng.cam.ac.uk/zoubin/talks/lect1bayes.pdf

Why Shannon Entropy?

Assumption is that every neuron’s firing state is binary (All or none principle)

Probability that a neuron will fire an action potential is influenced by many different unknown factors (such as the neuron's firing threshold, degree of connectivity with presynaptic inputs, and so forth), the distinction between a firing state and a resting state can be studied as a binary random variable in Shannon's theory of communication.

Ref: https://www.frontiersin.org/articles/10.3389/fncom.2020.00037/full

Why Shannon Entropy?

Neurons can only fire so often in a fixed period of time, as the act of emitting a spike consumes energy that is depleted and must eventually be replenished. To communicate effectively for downstream computation, the neuron would need to make good use of its limited spiking capability.

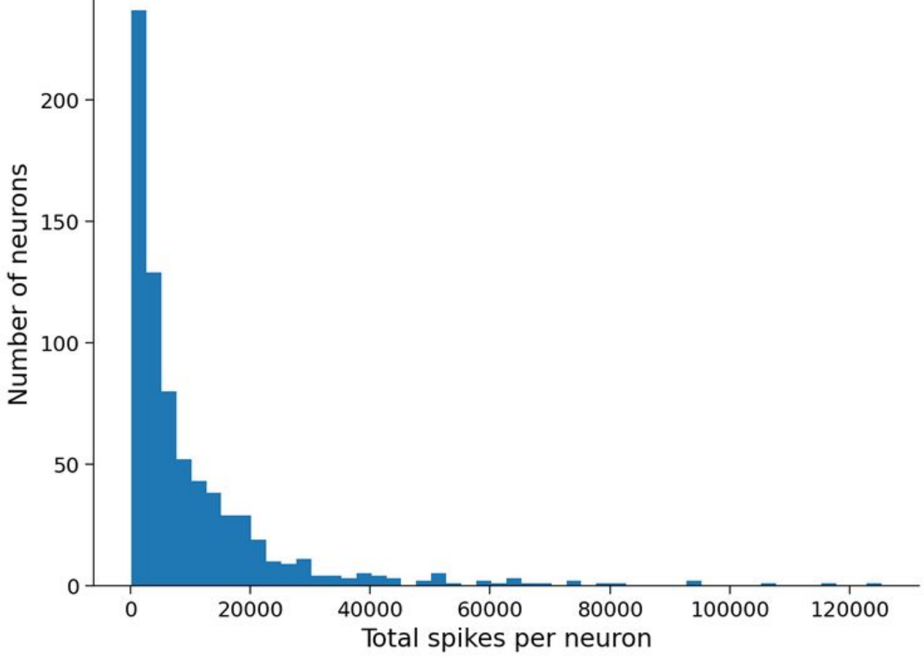
Framing as an optimisation problem will help find maximum ability of a neuron to communicate information.

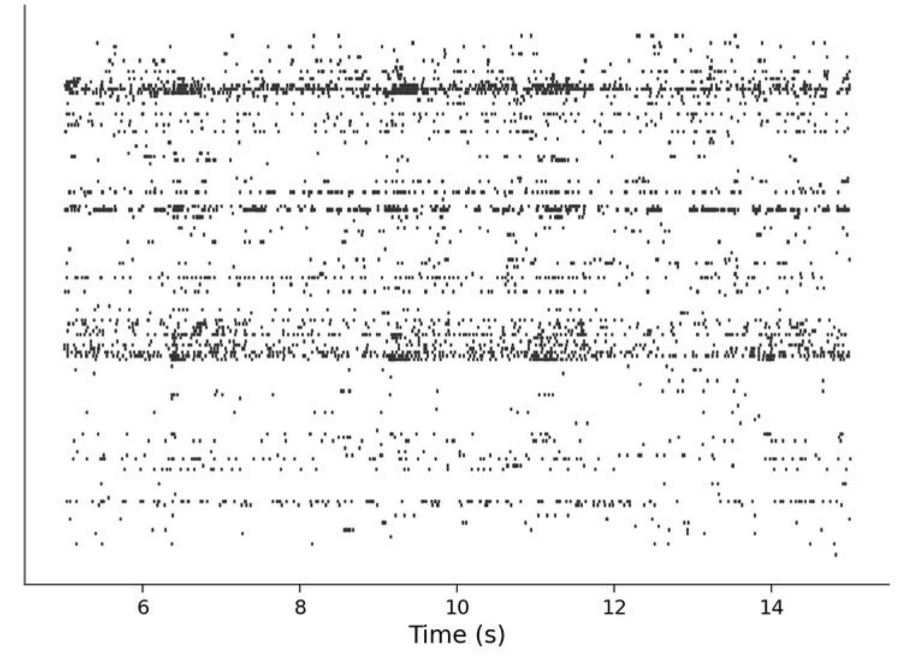
Fixing the mean of the ISI distribution is equivalent to fixing its inverse: the neuron's mean firing rate. If a neuron has a fixed energy budget and each of its spikes has the same energy cost, then by fixing the mean firing rate, we are normalizing for energy expenditure. This provides a basis for comparing the entropy of different ISI distributions.

Summary

- We used "what" models to discover that the ISI distribution of real neurons is closest to an exponential distribution
- We used "how" models to discover that balanced excitatory and inhibitory inputs, coupled with a leaky membrane, can give rise to neuronal spiking with exhibiting such an exponential ISI distribution
- We used "why" models to discover that exponential ISI distributions contain the most information when the mean spiking is constrained

How does info on the right relate to one on the left?





Interpretation

Image on the right shows firing of neurons in real time where each dot is an action potential/spike!

On the left is a summation of the spikes (Quantification)

Intuition behind modelling neuronal Self-information

When an unlikely outcome of an event (random variable) is observed, we associate it with a high amount of information. Contrarily, when a more likely outcome is observed, we associate it with a smaller amount of information. It is very helpful to think of self-information as the surprise associated with an event.

The surprisal event is associated with neuronal firing as the outcome is least predictable.

The smaller the probability of an event, the higher its self-information, and the more surprising the event would be to observe.
NOTE: self information is associated with the distribution of ISI's and not the neuron itself.

Ref: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5582596/