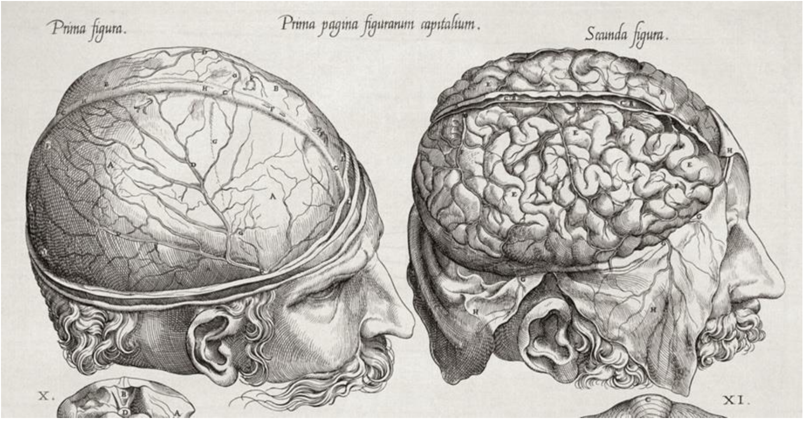
What is real?

How do you define ‘real’?

“ If you're talking about what you can feel, what you can smell, what you can taste and see, then ‘real’ is simply electrical signals interpreted by your brain. This is the world that you know.”

Morpheus, in *the Matrix*.



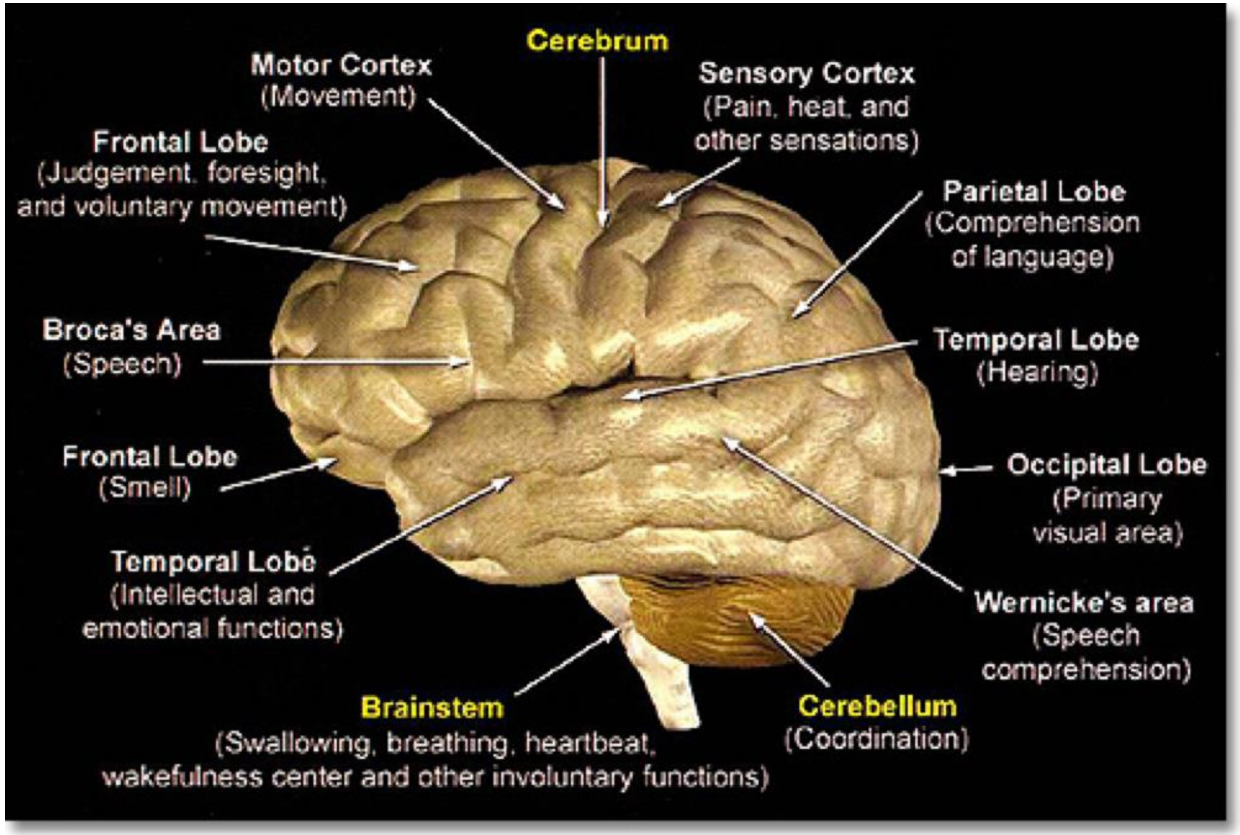
Foundations of Computational Neuroscience (1):

Basics of Neuroscience
& How is information encoded in the brain?

Peggy Seriès, IML
Informatics, University of Edinburgh, UK
pseries@inf.ed.ac.uk

CCN 2026 - lecture 2

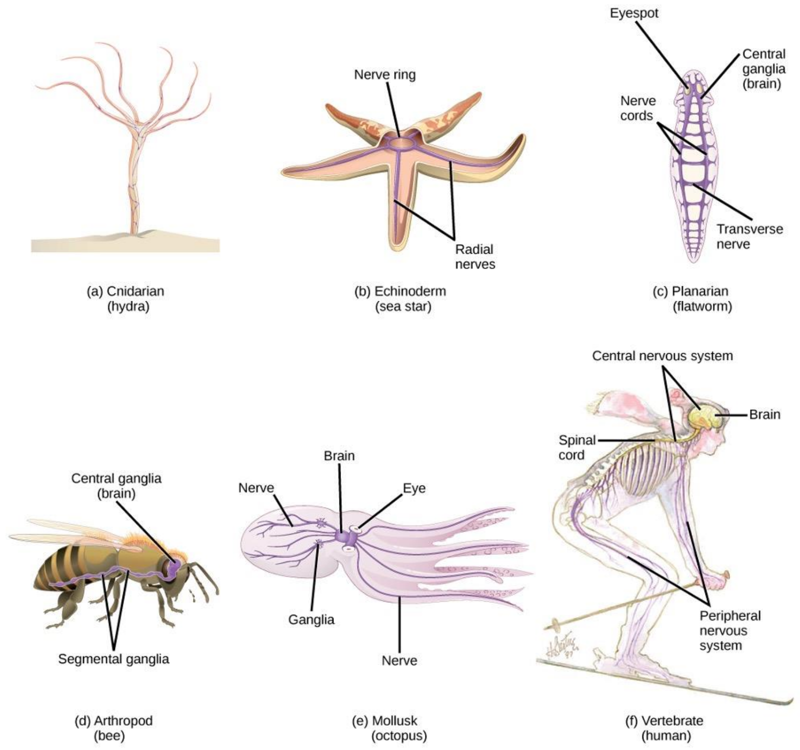
The Brain

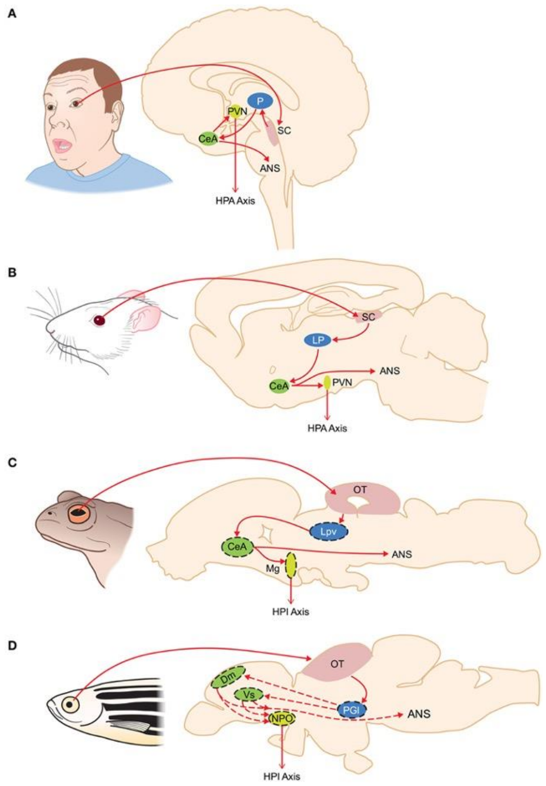


- **Neurons and Glial cells (insulating, supporting, nourishing neurons).**
- **10^11 neurons** in human brain, each link to up to 10,000 other neurons
- consumes 20% of the total body energy budget

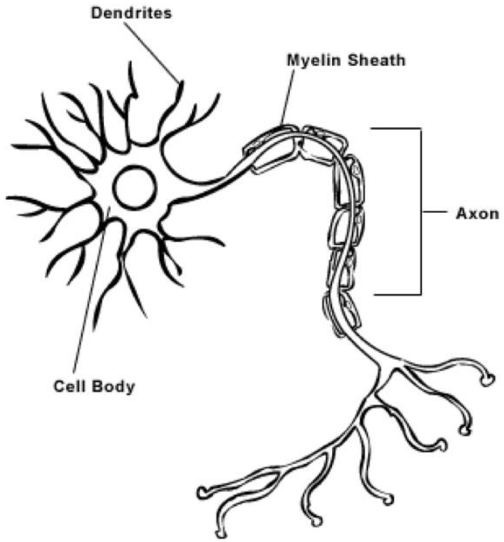
Evolution of the Brain

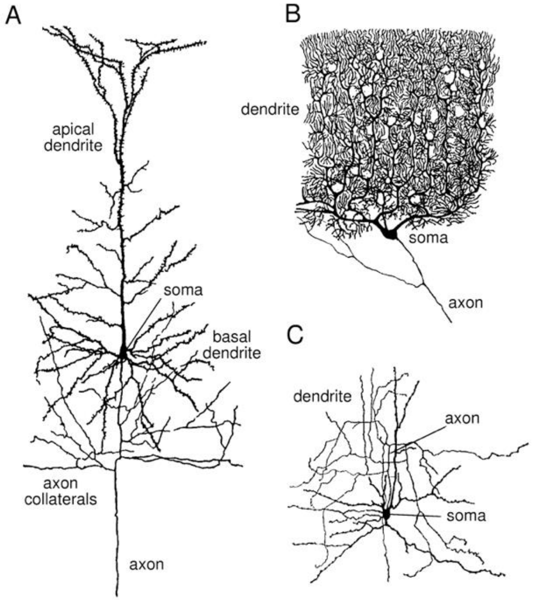
- Nervous systems vary in structure and complexity. A structure that has evolved but main principles are conserved: signal detection, motor control
- Subcortex is evolutionarily ancient, controls reflexive stimulus-response behaviours. Cortex evolved later for learning flexible/complex behaviours





Neurons





Neuron = cell, diverse morphologies

Dendrites: receive inputs from other cells, mediated via synapses.

Soma (cell body): integrates signals from dendrites. 4-100 micrometers.
Action potential: All-or-nothing event generated if signals in soma exceed threshold.

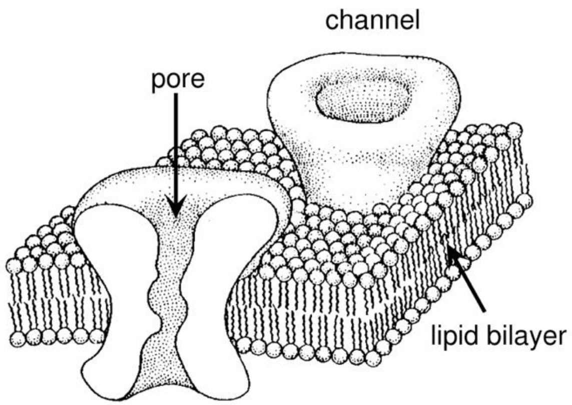
Axon: transfers signal to other neurons.

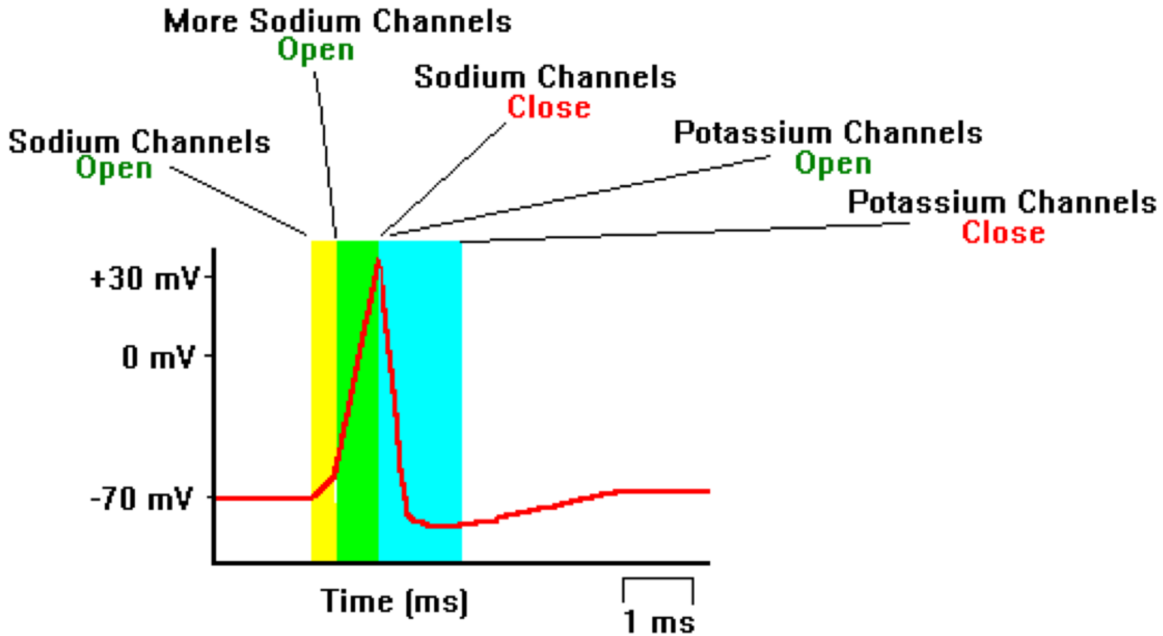
Synapse: contact between pre- and postsynaptic cell.
- Efficacy of transmission can vary over time.
- Excitatory or inhibitory.
- Chemical or electrical.

10^16 synapses in young children (decreasing with age --1-5x10^15)

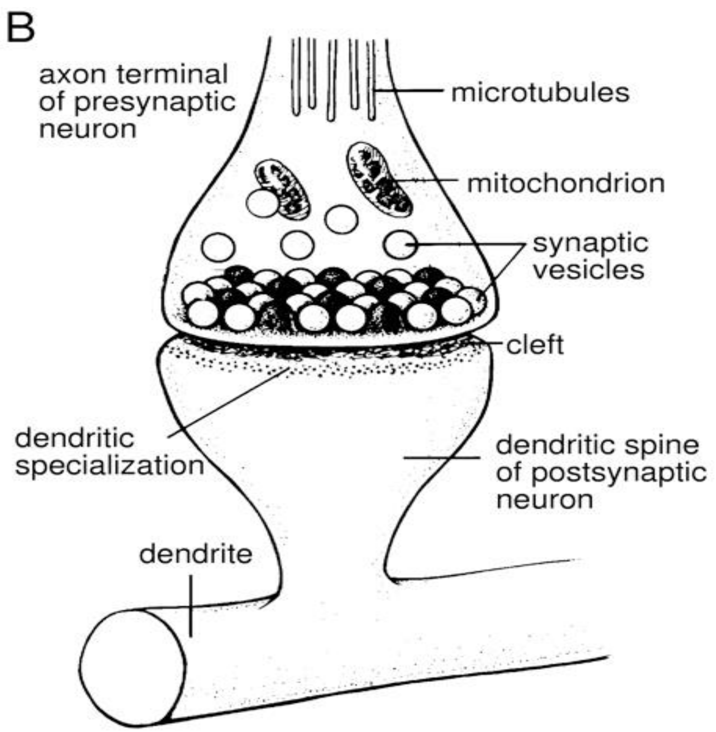
Membrane Potential and Action Potential

- Ions channels across the membrane, allowing ions to move in and out, with selective permeability (mainly Na+, K+, Ca2+,Cl-)
- Vm: difference in potential between interior and exterior of the neuron.
- at rest, Vm~-70 mV (more Na+ outside, more K+ inside, due to N+/K+ pump)
- Following activation of (Glutamatergic) synapses, depolarization occurs.
- if depolarization > threshold, neuron generates an action potential (spike) (fast 100 mv depolarization that propagates along the axon, over long distances).





Synapses



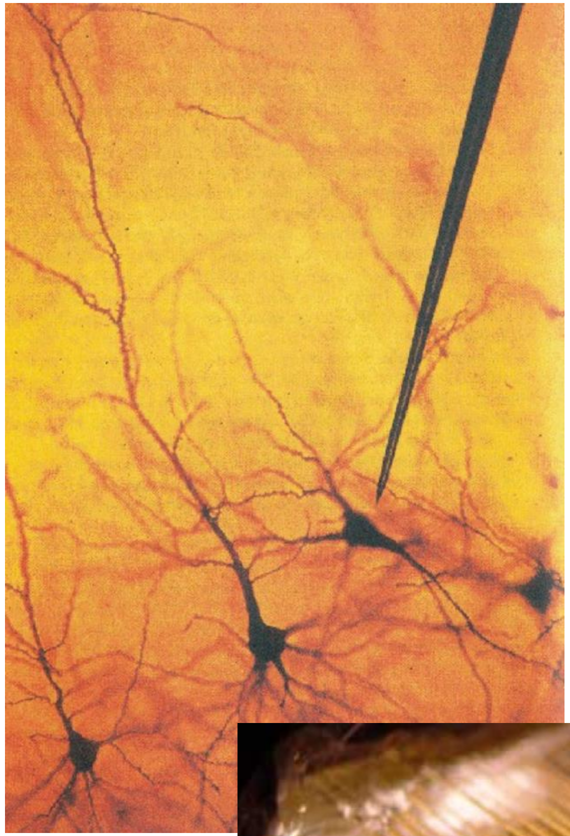
- Axon terminate at synapse.

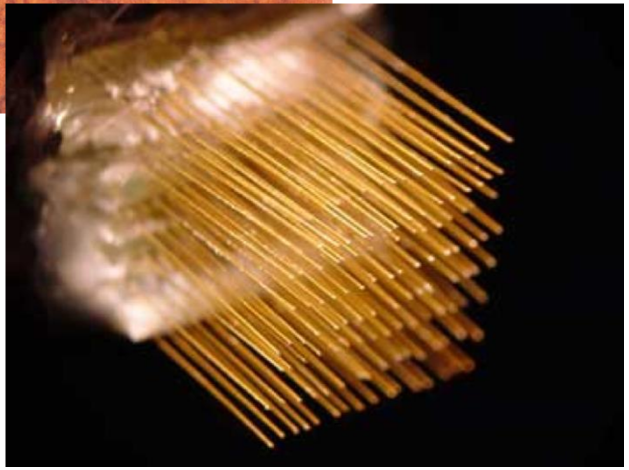
AP-> opens ion channels, influx of calcium (Ca2+), release of neurotransmitters in the synaptic cleft, which bind at the post-synaptic receptors, causing ion-conducting channels to open.

- Glutamate: main excitatory neurotransmitter -- bind to AMPA, NMDA, mGlu receptor, induces depolarization.

- GABA: main inhibitory neurotransmitter -- GABA receptor, induces hyperpolarization.

Electrophysiological Recordings

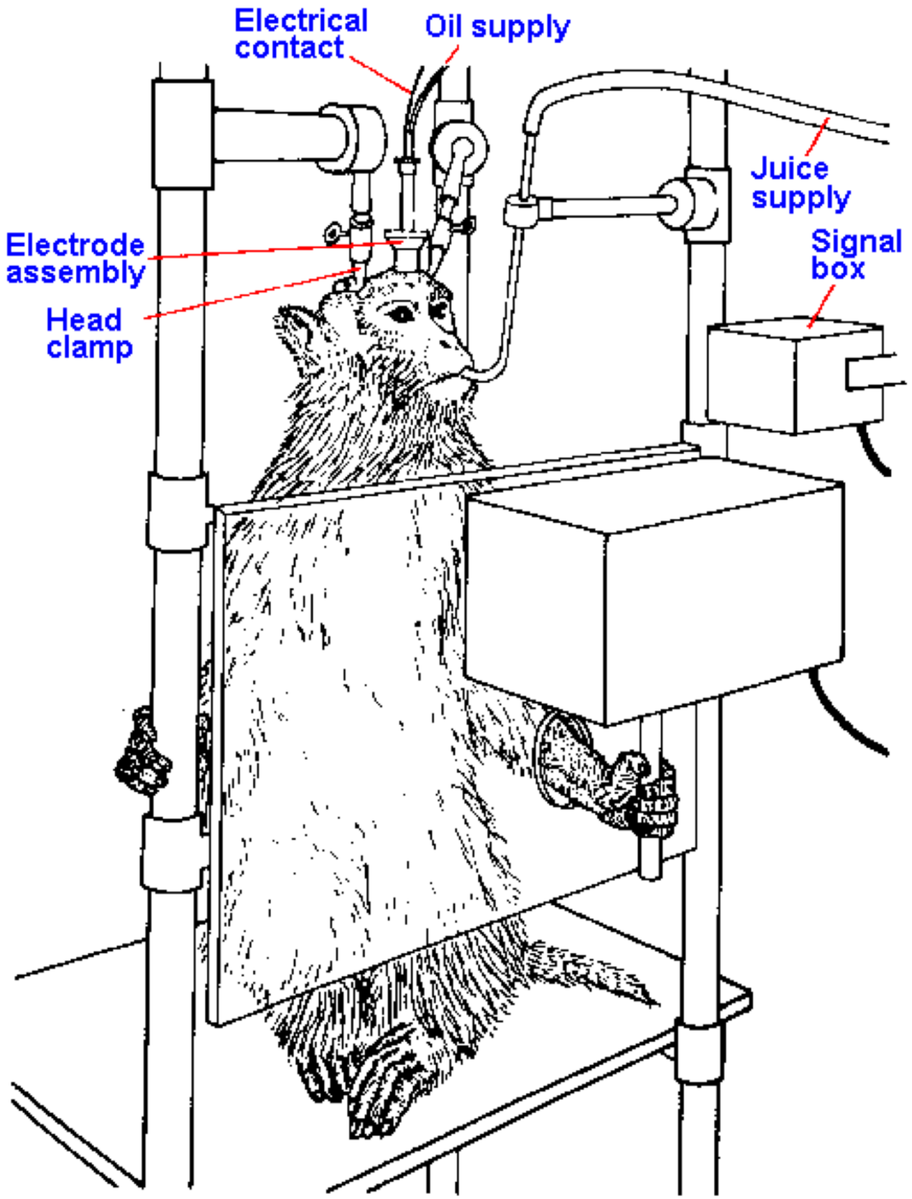


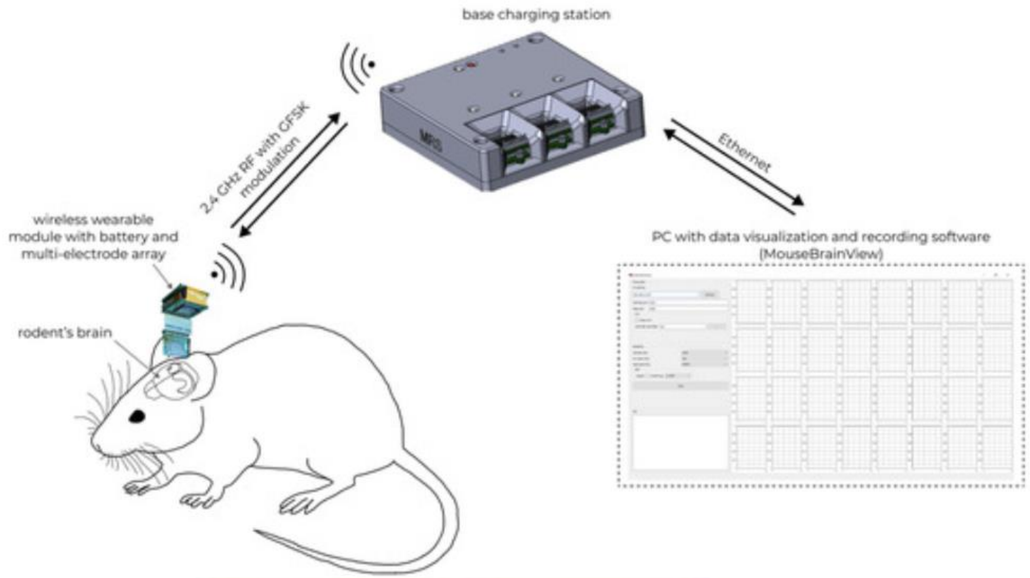


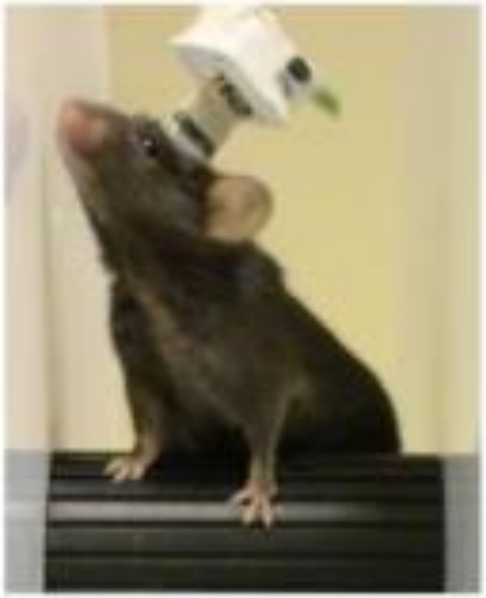
• intracellular recordings (commonly *in vitro*, sometimes *in vivo* (anesthesized, paralyzed))
sharp electrode placed inside the neuron
patch electrode, sealed to the membrane.
view Vm.

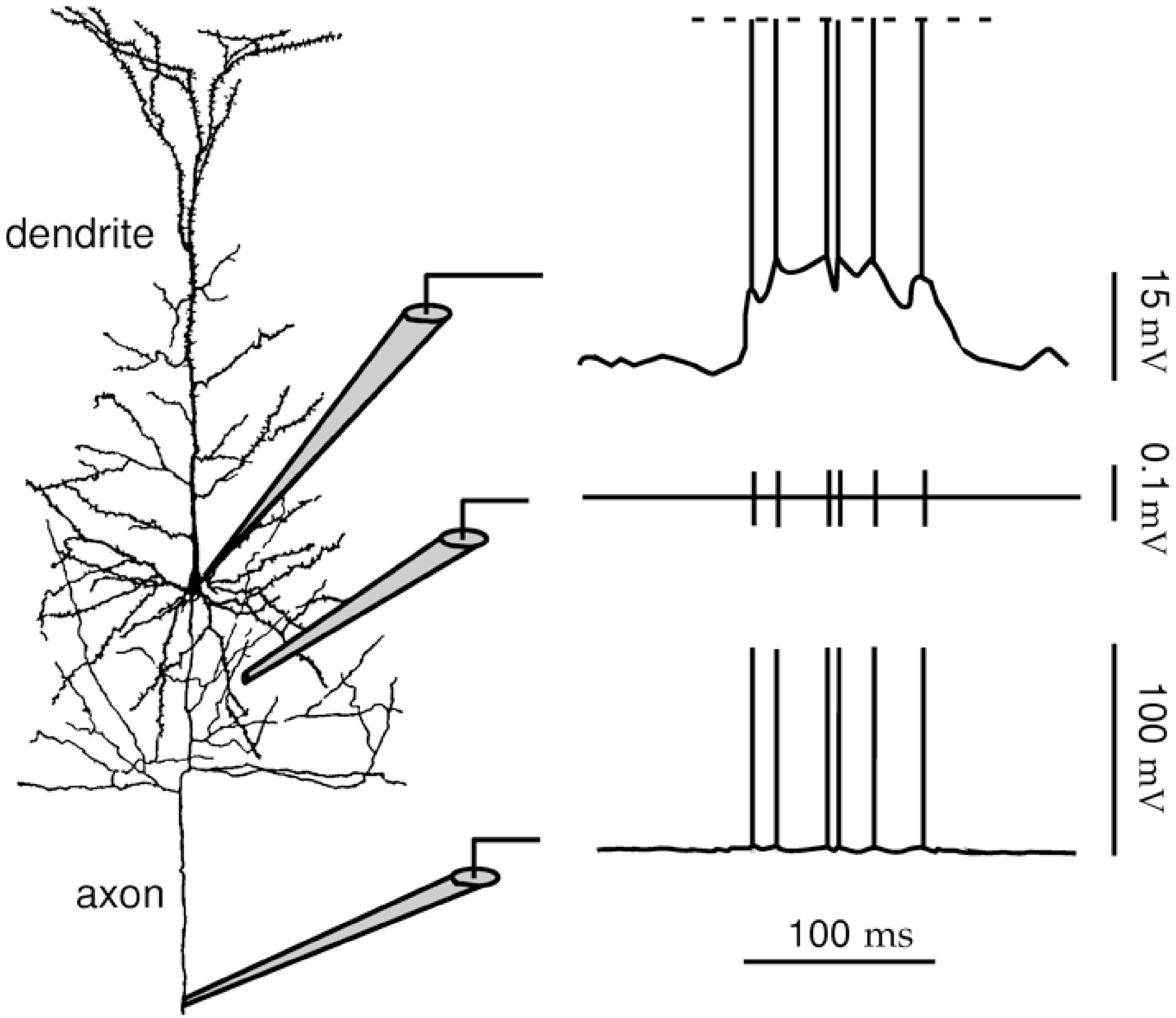
• extracellular (often *in vivo*, possibly awake behaving animal)
electrode is placed near a neuron.
view action potentials.

• Commonly, one neuron at a time, now use of arrays of electrodes.

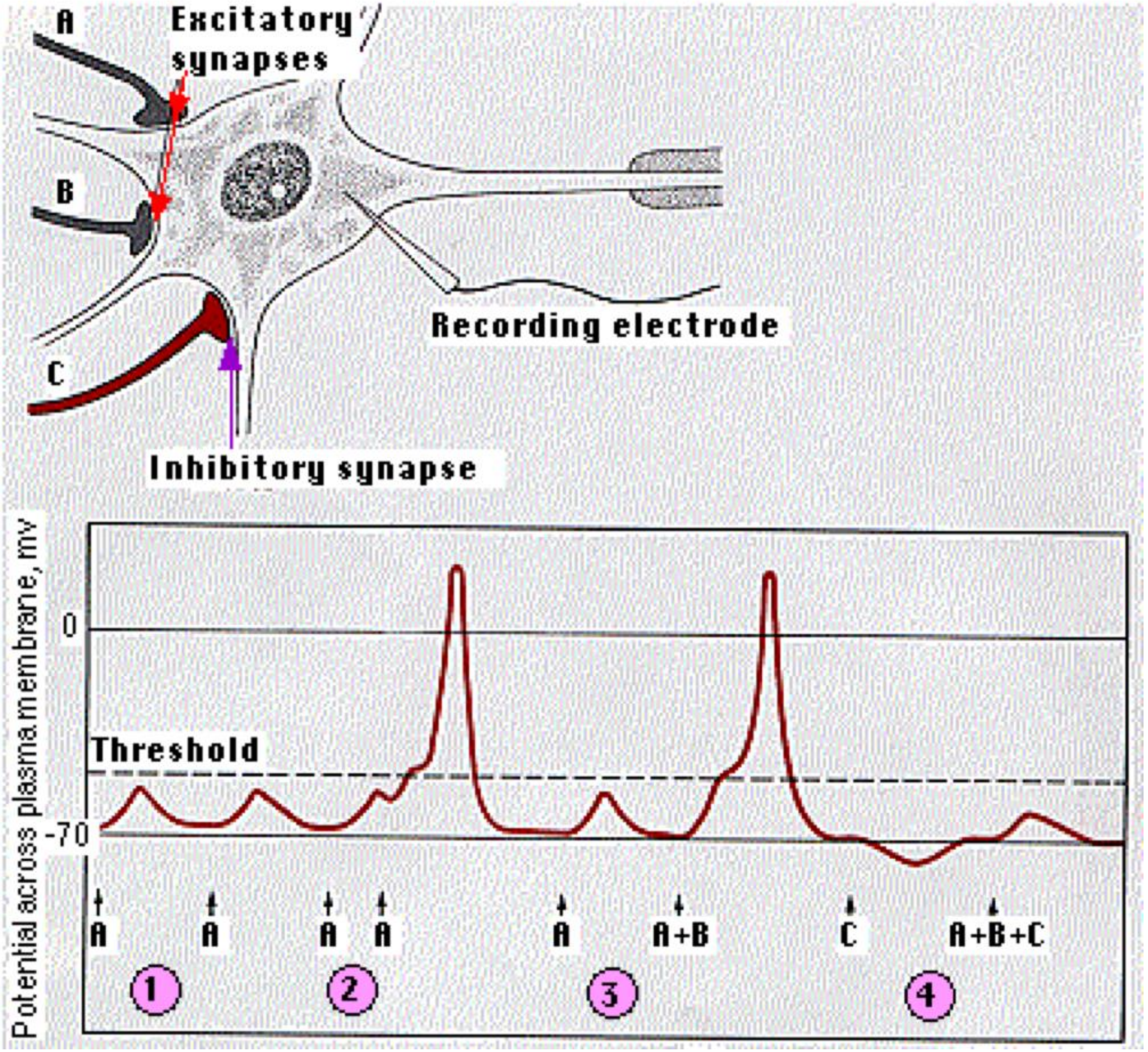

Electrical contact
Oil supply
Juice supply
Signal box
Electrode assembly
Head clamp


base charging station
2.4 GHz RF with GFSK modulation
Ethernet
wireless wearable module with battery and multi-electrode array
rodent's brain
PC with data visualization and recording software (MouseBrainView)





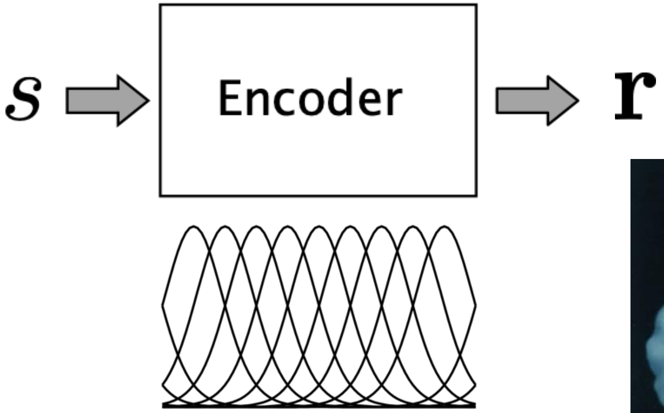
Intracellular and Extracellular electrophysiology



Excitatory and Inhibitory synapses -- EPSP and IPSP

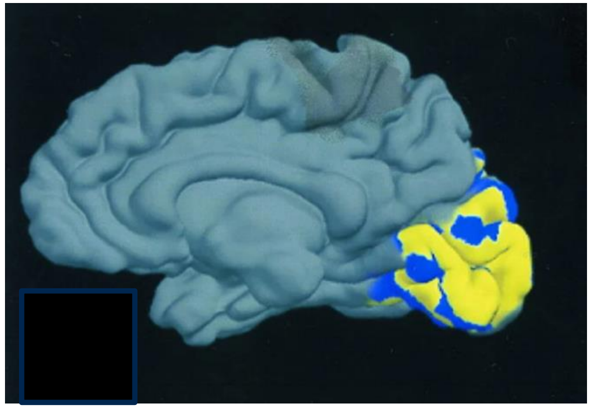
Encoding/Decoding Framework

Encoding problem P[r|s]: What is the relationship between stimuli in the world and the activity of the brain?



properties of neurons

Activity in the brain



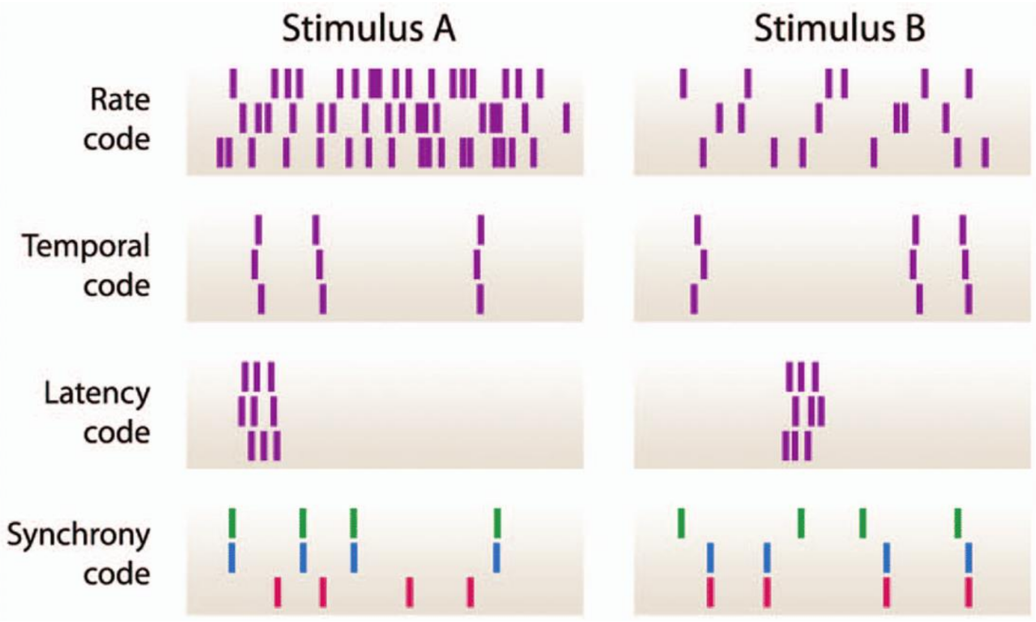
Cracking the code

• Experimental neuroscience: Describe activity of neurons as a function of sensory stimulus (visual image, skin stimulation, sound, odor etc..). What do they “respond” to?

• **What is the signal?** Assumptions about “the code”?

Describe spike sequence, or number of spikes, or rate r in time window (somewhat arbitrarily defined)?

Because information seems noisy, describe statistics **P[r|s]**

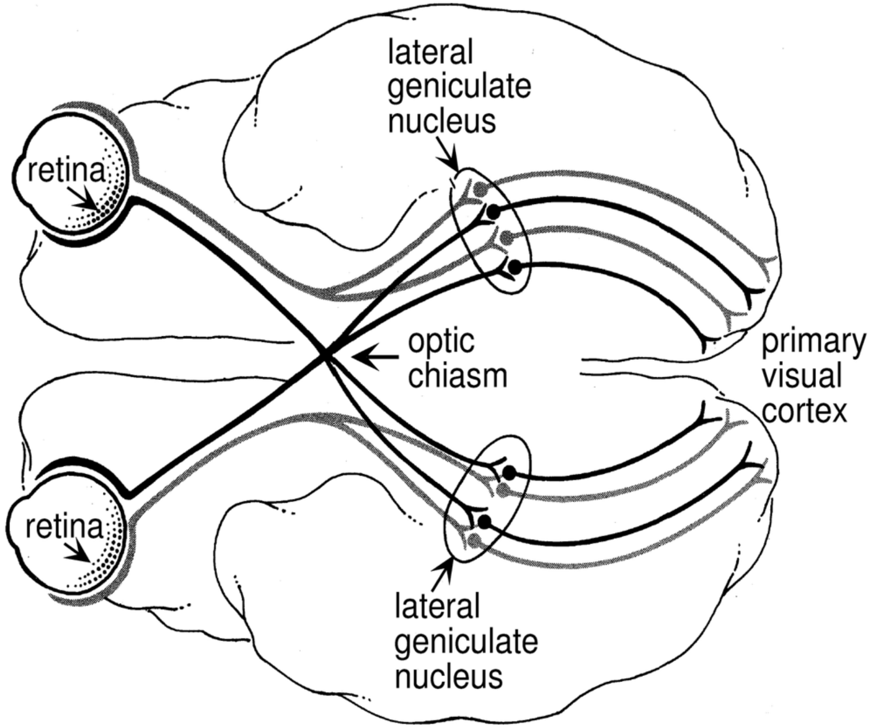


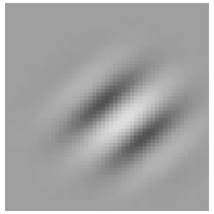
What do neurons do?
The example of Primary visual cortex (V1)

The primary visual cortex = area of the visual cortex that receives sensory input from the lateral geniculate nucleus, commonly referred to as V1 or striate cortex, located in the occipital lobe of the brain.

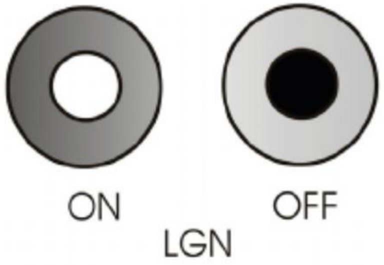
Retina and LGN neurons mostly respond to very local changes in light (contrast: bright–dark differences), not whole objects.

V1 starts extracting building blocks of image processing… and more.





V1



Neurons in V1 are selective to orientation

J. Physiol. (1959) 148, 574–591

RECEPTIVE FIELDS OF SINGLE NEURONES IN THE CAT'S STRIATE CORTEX

By D. H. HUBEL* and T. N. WIESEL*

From the Wilmer Institute, The Johns Hopkins Hospital and University, Baltimore, Maryland, U.S.A.

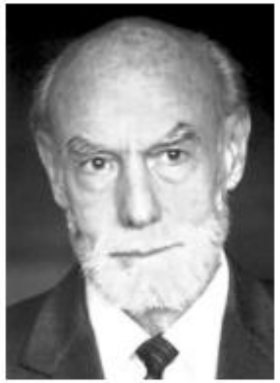
(*Received* 22 *April* 1959)

In the central nervous system the visual pathway from retina to striate cortex provides an opportunity to observe and compare single unit responses at several distinct levels. Patterns of light stimuli most effective in influencing units at one level may no longer be the most effective at the next. From differences in responses at successive stages in the pathway one may hope to gain some understanding of the part each stage plays in visual perception.

https://youtu.be/IOHayh06LJ4?si=tZfoMNitsjW1aKv3

https://www.youtube.com/watch?time_continue=115&v=Cw5PKV9Rj3o

The Nobel Prize in Physiology or Medicine 1981



Roger W. Sperry
Prize share: 1/2

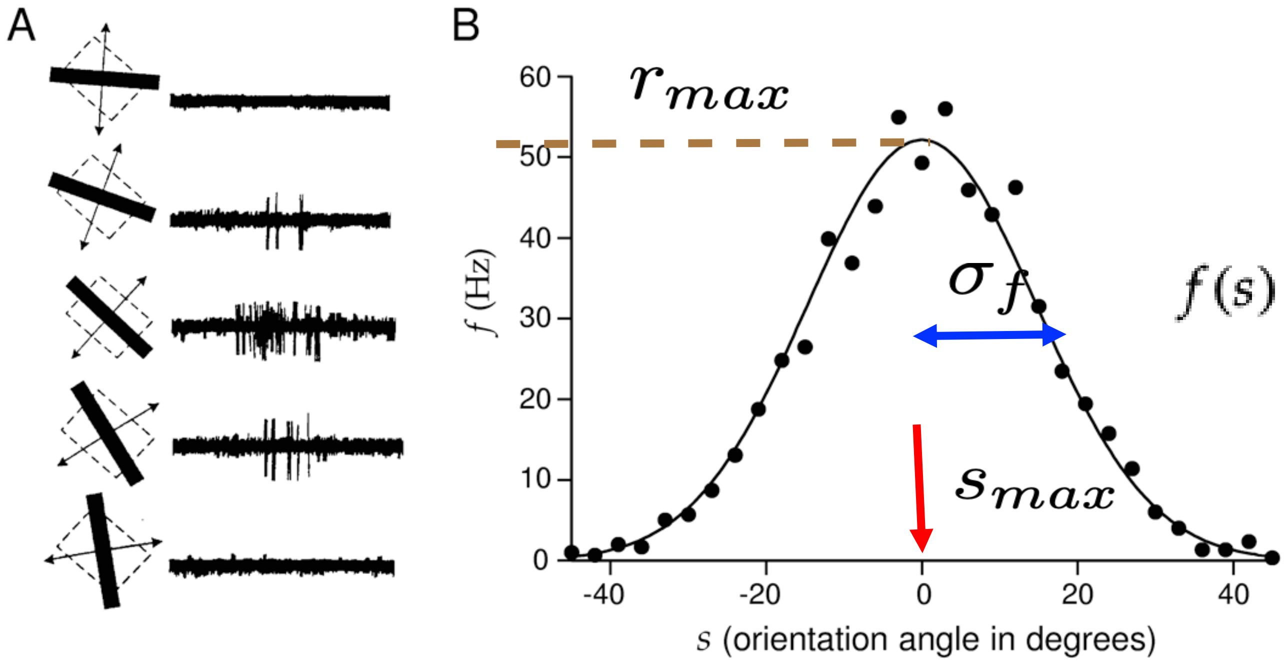
David H. Hubel
Prize share: 1/4

Torsten N. Wiesel
Prize share: 1/4

The Nobel Prize in Physiology or Medicine 1981 was divided, one half awarded to Roger W. Sperry *"for his discoveries concerning the functional specialization of the cerebral hemispheres"*, the other half jointly to David H. Hubel and Torsten N. Wiesel *"for their discoveries concerning information processing in the visual system"*.

1. First order statistics: Modeling the average firing rate <r(s)>

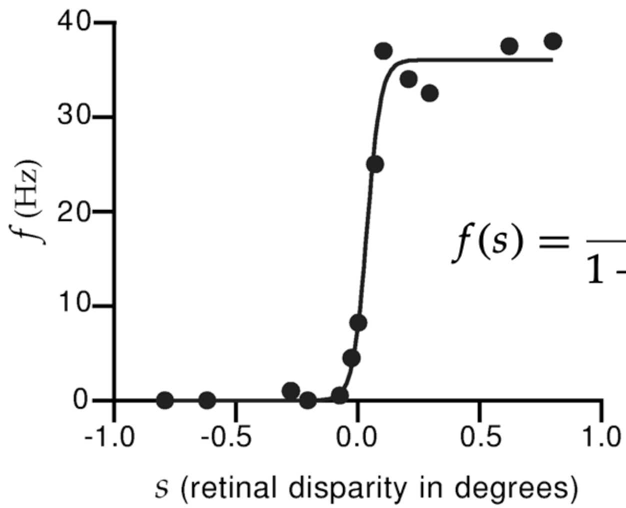
- Tuning curves: modify an aspect *s* of the stimulus, and measure <r(s)>
- V1 neurons: highly selective to the orientation of the stimulus (e.g. bar) flashed in their receptive field.
- Such bell-shaped (Gaussian-like) tuning curves are very common in the cortex.



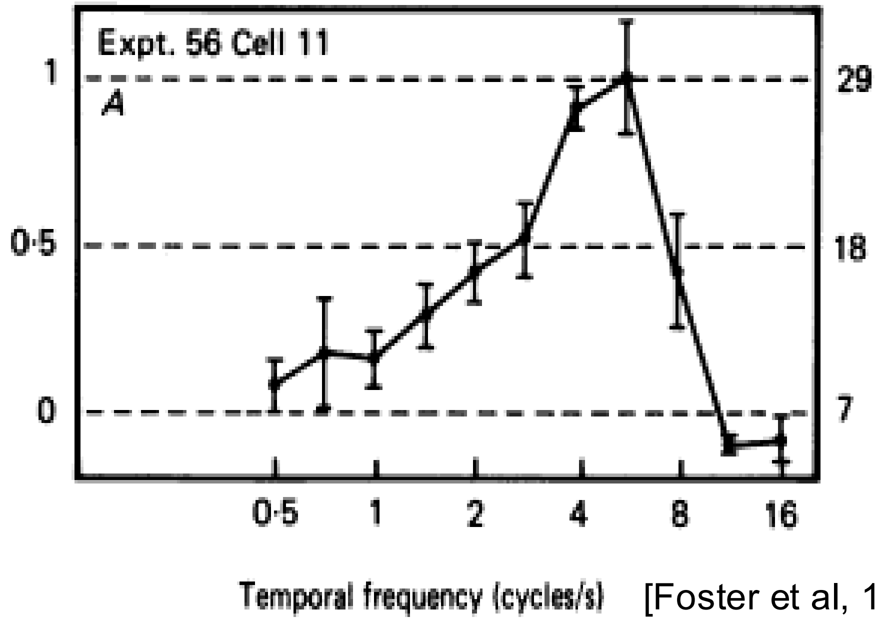
$$f(s) = r_{\max} \exp\left(-\frac{1}{2}\left(\frac{s - s_{\max}}{\sigma_f}\right)^2\right)$$

Other types of tuning/response curves

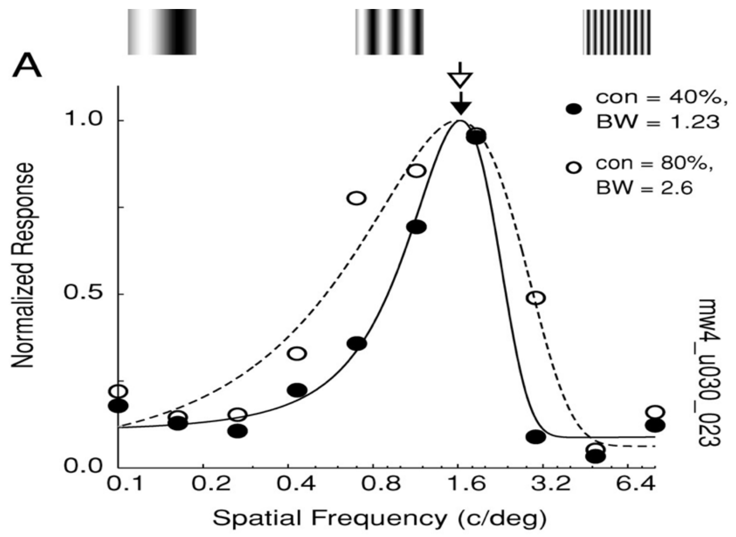
- Many different features are encoded in V1: spatial position (retinotopy), contrast, depth, direction, spatial frequency, temporal frequency, color ..
- variety of tuning/ response shapes.



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



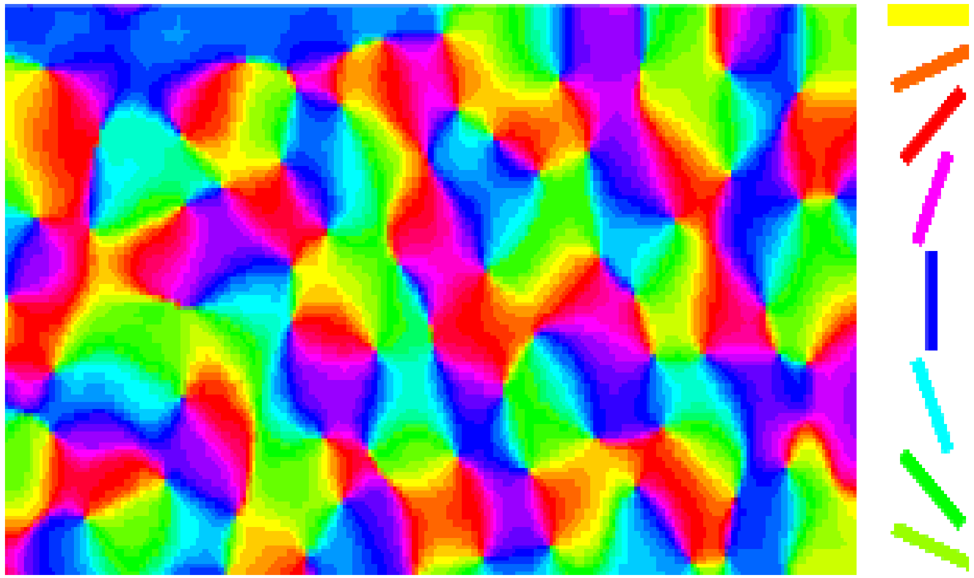
[Foster et al, 1985]



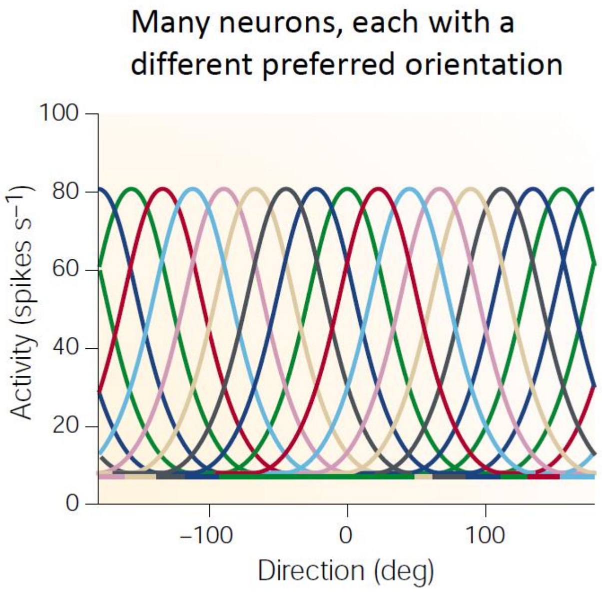
[Sceniak et al, 2002]

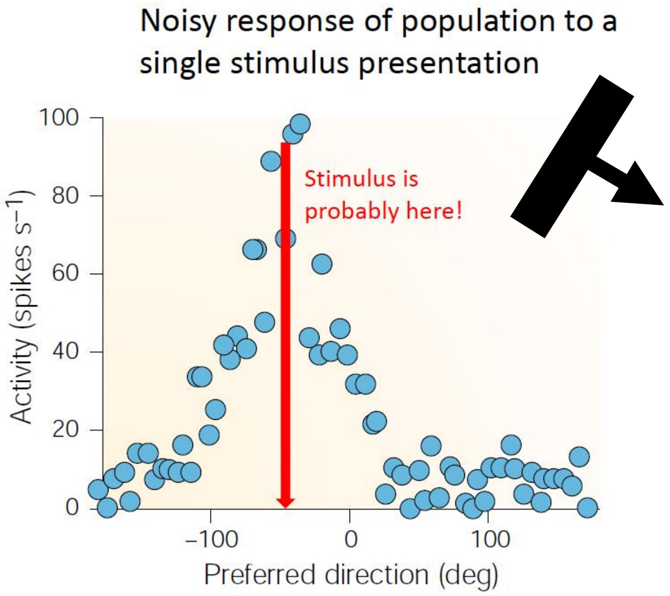
A Population Code: information lives in patterns over many neurons

- in V1, neurons of every preferred orientation, direction, spatial freq. etc.. can be found: population code.
- Retinotopy, preferred orientations, directions are very precisely organized, forming columns and maps.
- A population response to a stimulus is a point is a high dimensional space



Orientation Map

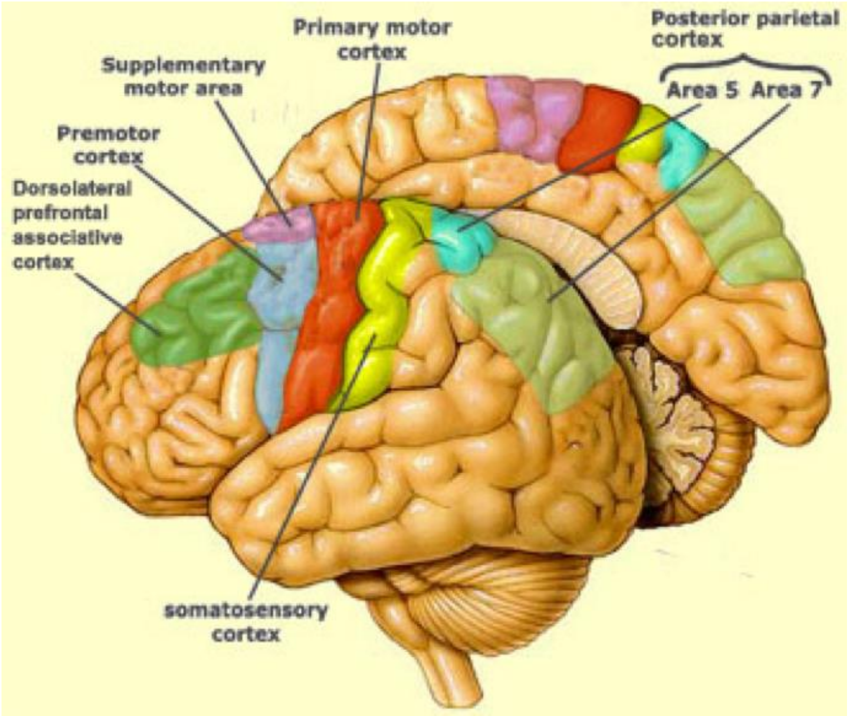


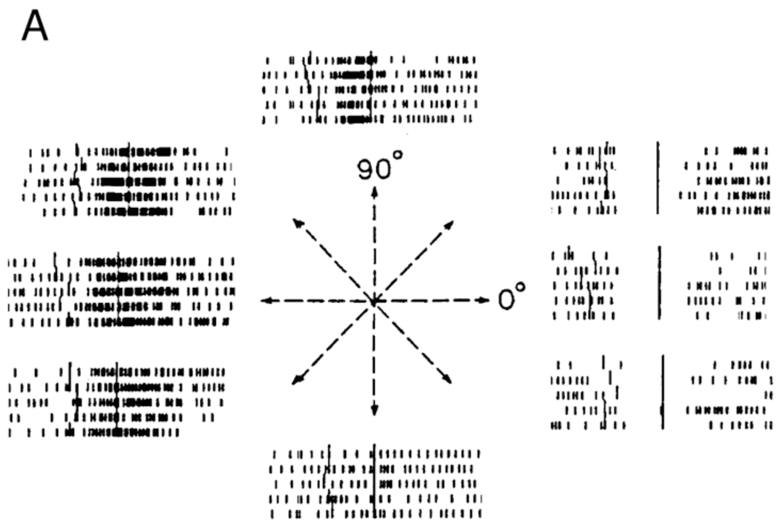


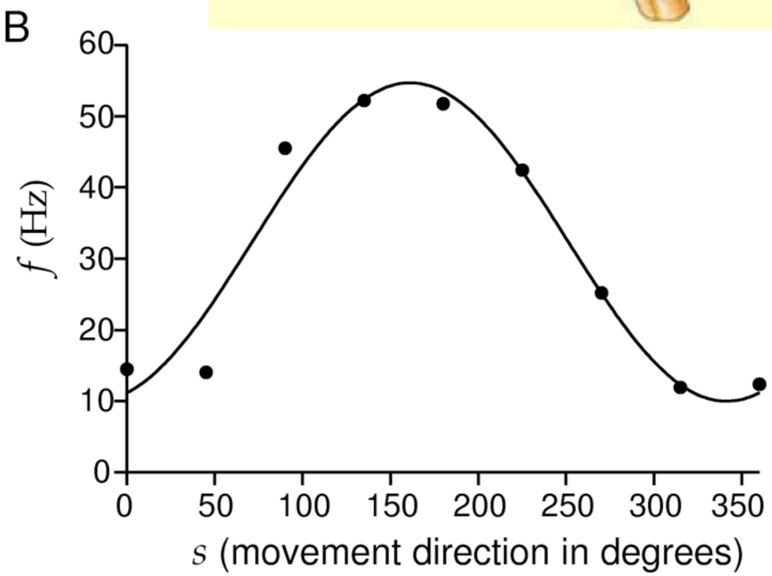
Tuning curves everywhere ...

- Primary motor cortex (M1) -- arm reaching task
- <r> as a function of the direction in which the monkey moved his arm
- Here described as a cosine

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



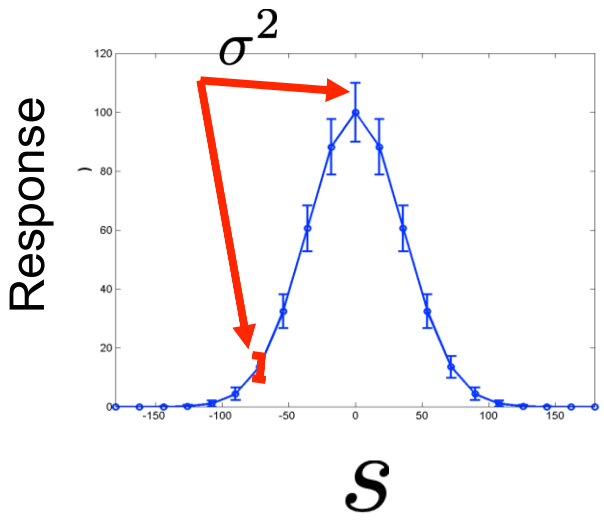


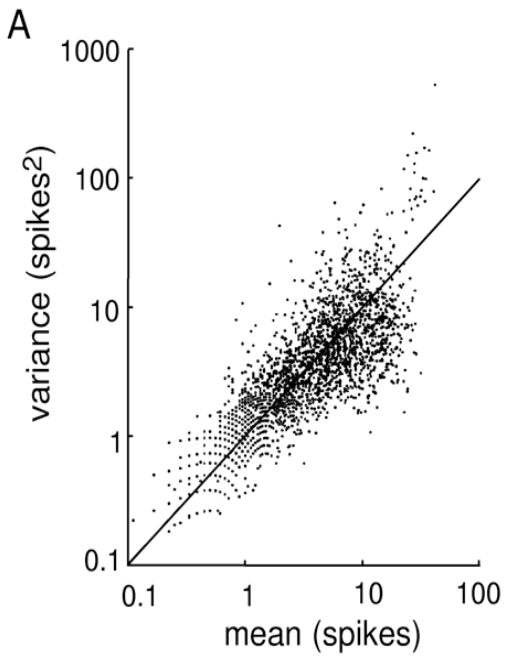


Georgopoulos et al, 1982

2.1 Describing the trial-to-trial variance of the spike count

- Model the spike count *r* on one trial as a random variable.
- What is a good model for the prob. distribution describing probability of getting each outcome (n=1,2 .., 50 spikes)?
- Measure the variance of the spike count, for a number of repetitions with the same stimulus.
- Experiments show that it is approx. linearly related to the mean spike count (with prop. const ~1).
- Noise is often described as Poisson, or, for simplicity, Gaussian with a variance proportional to the mean



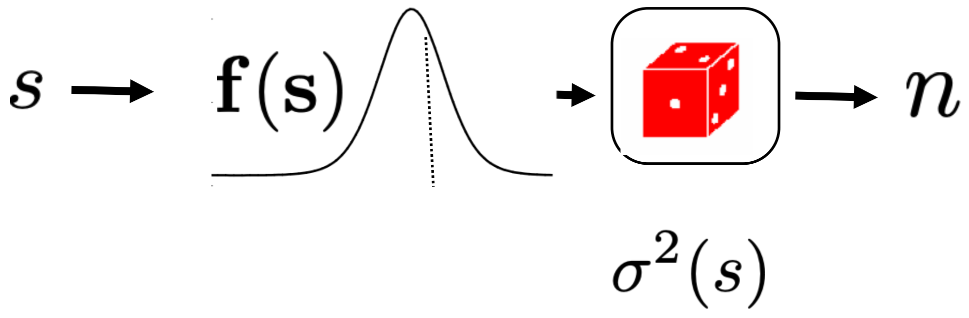


$$var(n) = F * mean(n)$$

F: Fano Factor ~1

[O Keefe, 1997 - MT cortex]

Gaussian Noise



- Commonly used to describe the variability of the spike count is the Gaussian noise model.
- The activity of a neuron (number of spikes) can be described as:

$$n = f(s) + \eta(s)$$
$$\eta(s) \simeq N(0, \sigma^2(s))$$

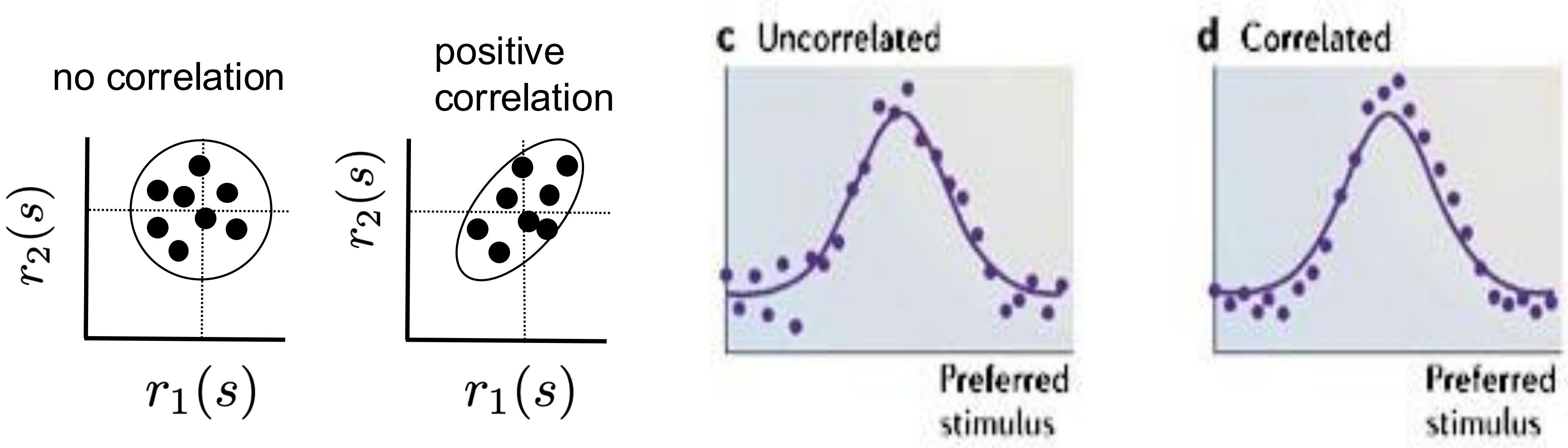
- To mimic a Poisson distribution, we choose $\sigma^2(s) = f(s)$

- [this is an approximation, in reality, better models exist e.g. Poisson with fluctuating rates, Negative Binomial / Poisson–Gamma]

2.2 From one neuron to populations : describing pair-wise noise correlations

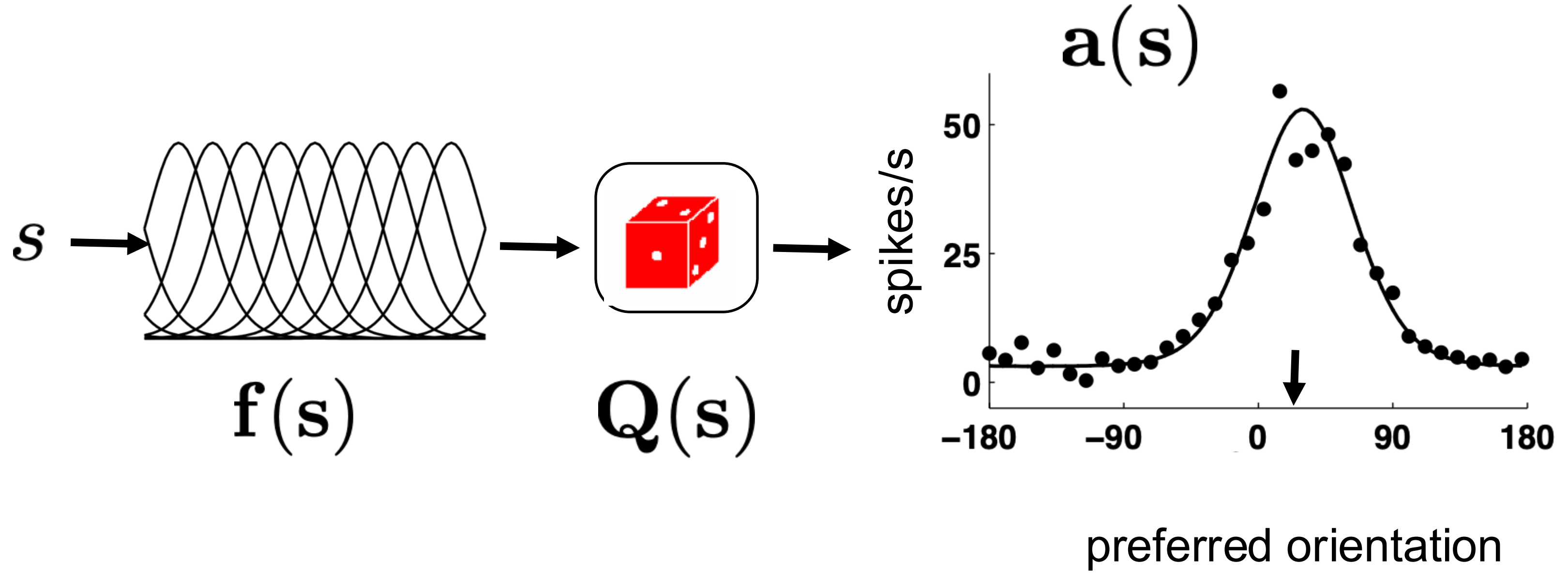
- An important question is to understand whether the noise is independent between neurons.
- Measure Trial-to-trial fluctuations of pairs of neurons, for same s.

When neuron 1's count is above its mean, is neuron 2's also? or are their fluctuations independent?



- Experimental data show weak positive correlations, which might be critical for the accuracy of the code.

"Tuning Curve + Noise" Population Model



The activity of a neuron (number of spikes) can be described as:

$$a_i = f_i(s) + \eta_i(s) \qquad \eta(\mathbf{s}) = N(0, \mathbf{Q}(\mathbf{s}))$$

$$P[\mathbf{r}|s] = \frac{1}{\sqrt{(2\pi)^N |\mathbf{Q}(\mathbf{s})|}} e^{-\frac{1}{2}(\mathbf{r}-\mathbf{f}(\mathbf{s}))^{\mathbf{T}}\mathbf{Q}^{-1}(\mathbf{s})(\mathbf{r}-\mathbf{f}(\mathbf{s})))}$$

Encoding: Summary

✤ Spikes are the important signals in the brain.

✤ What is still debated is the code: number of spikes, exact spike timing, temporal relationship between neurons' activities?

✤ Experimentalists have characterized the activity of neurons all over the brain and in particular in sensory cortex, motor cortex etc .., mainly in terms of tuning curves and response curves. A variety of well-specialized areas. Detailed wiring and mechanisms at the origins of these responses are largely unknown.

✤ The large variability (in number of spikes) is often well described by a Poisson or Gaussian model. Its origin or function is largely unknown.

✤ Applications: prosthetics - artificial ear (cochlear implants) - artificial retina / retinal implants.
e.g. https://www.youtube.com/watch?v=XZF72p1H1FA

a) Poisson Distribution - definition

- Poisson distribution, named after French mathematician Siméon Denis Poisson, is a discrete probability distribution that expresses the probability of a given number of events occurring in a fixed interval of time and/or space if these events occur with a known constant rate and independently of the time since the last event.

- if the average number of events in the interval/ rate is λ

The probability of observing k events in an interval is given by the equation:

$$P(k \text{ events in interval}) = e^{-\lambda} \frac{\lambda^k}{k!}$$

where

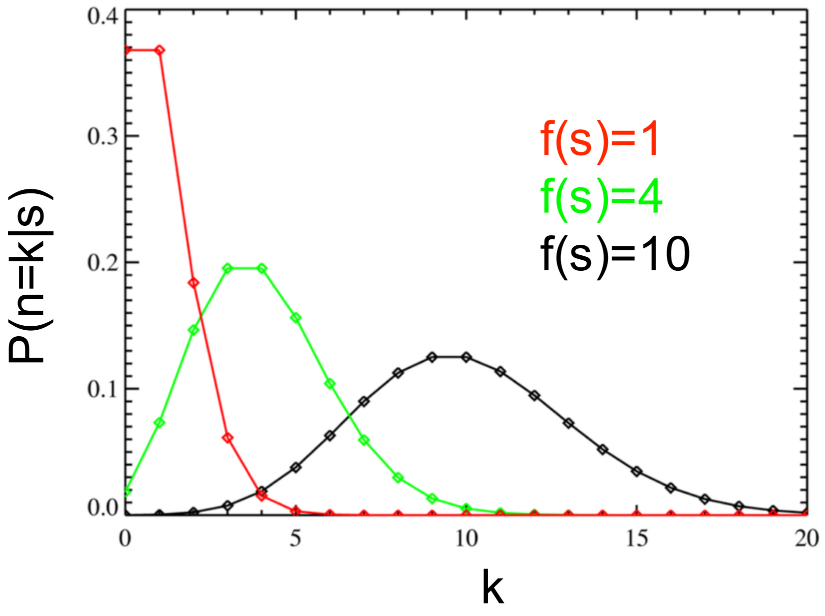
- e is the number 2.71828... (Euler's number) the base of the natural logarithms
- k takes values 0, 1, 2, …
- k! = k × (k − 1) × (k − 2) × … × 2 × 1 is the factorial of k.

a) Poisson Distribution - P(n|s)

- Poisson distribution is an appropriate model for describing the number of spikes in a time window.
- The rate / average number of spikes for a given stimulus s is also what is measured by the tuning curve f(s)

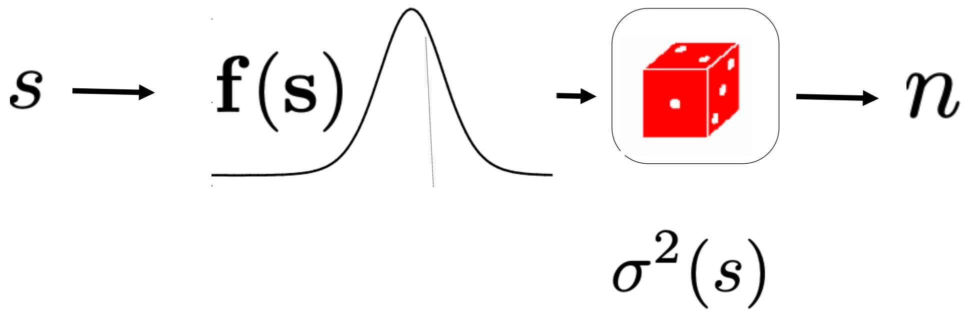
$$P(n = k|s) = \frac{e^{-f(s)} f(s)^k}{k!}$$

e.g. if f(s)=10, P(n=10|s)=0.125
P(n=7|s)=0.09
P(n=3|s)=0.007



- It is a property of the Poisson distribution that var(n)=E(n)=f(s)

b) Gaussian Distribution



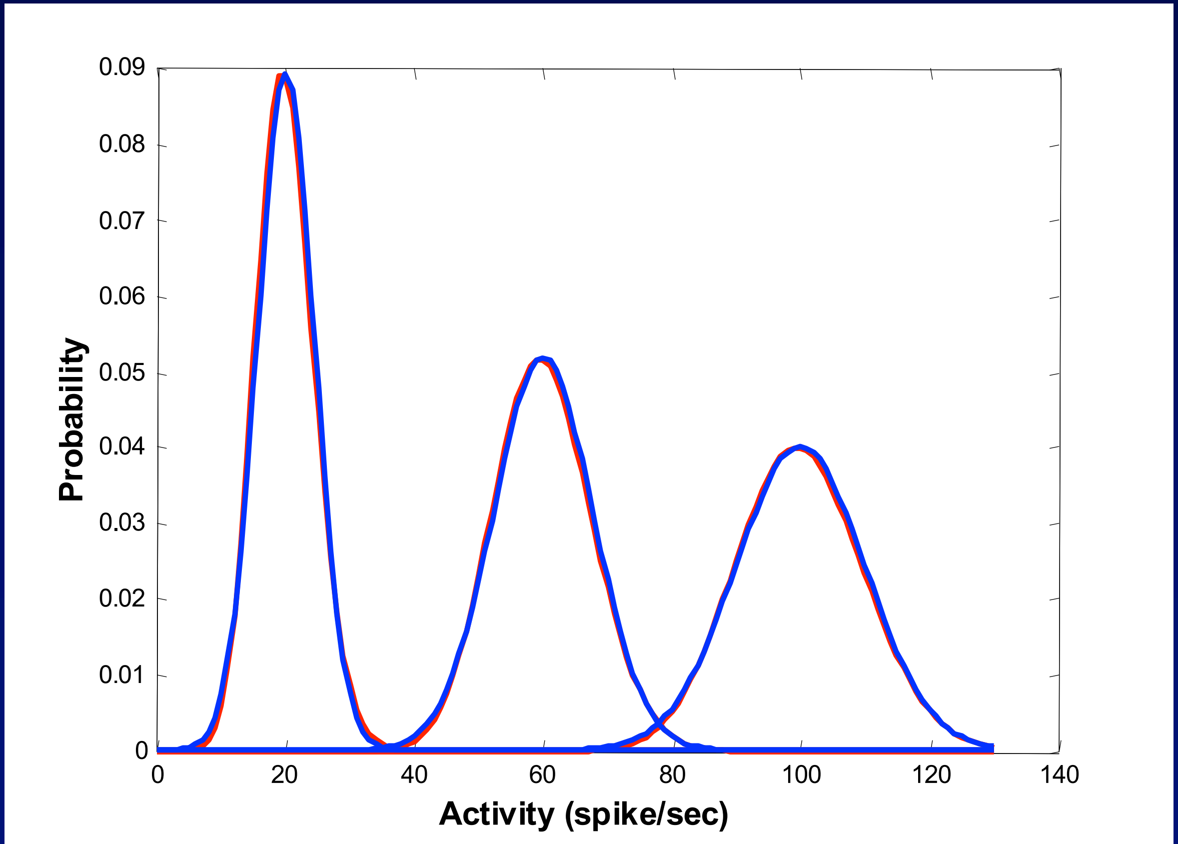
- Another model that is commonly used to describe the variability of the spike count is the Gaussian noise model.
- The activity of a neuron (number of spikes) can be described as:

$$n = f(s) + \eta(s)$$

$$\eta(s) \simeq N(0, \sigma^2(s))$$

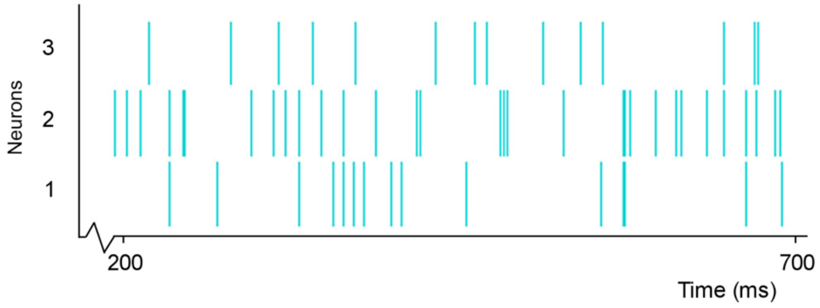
- To mimic a Poisson distribution, we choose $\sigma^2(s) = f(s)$

Comparison of Poisson vs Gaussian noise with variance equal to the mean



c) From Poisson Distribution to Poisson Process

- We can be interested to model not only the number of spikes (or any event), but the temporal sequence of such spikes.

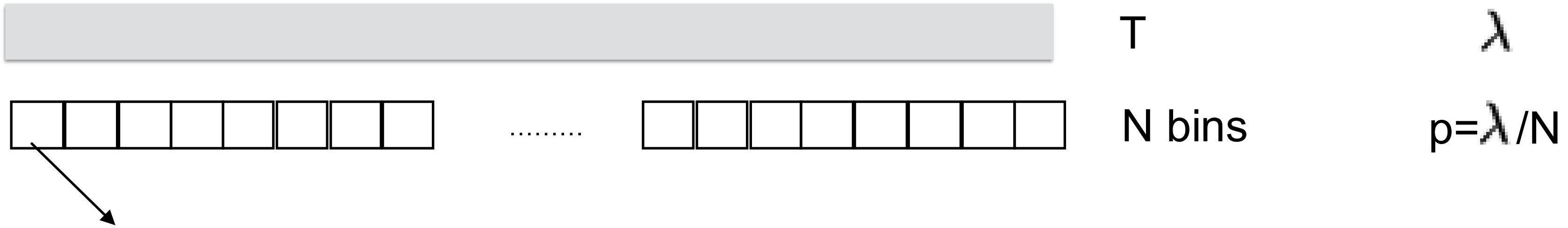


Such that the number of spikes will be described with a Poisson distribution.

We can use the model of the Poisson Process.

How to construct a Poisson Spike train

- Divide time window T into N bins. p=probability of spiking in each bin.
- In each bin, toss a coin with probability P(head)=p, if you get a head, record a spike.



Draw random number between 0 and 1: if < than p, record spike.

Draw random number between 0 and 1: if < than p, record spike.

- For small p, the number of spikes in T follows a Poisson distribution.

c) Poisson Processes - spike sequences

Properties

• variance(spike count) = mean(spike count). (~data)

• Inter-spike intervals (ISI) follow an exponential distribution (~data, except for very short intervals(refractory period) and for bursting neurons).

• Poisson model can be made to include a refractory period

• Homogeneous: mean spike count is fixed in time window f(s)

• Inhomogeneous -- changing in time window :f(s,t).

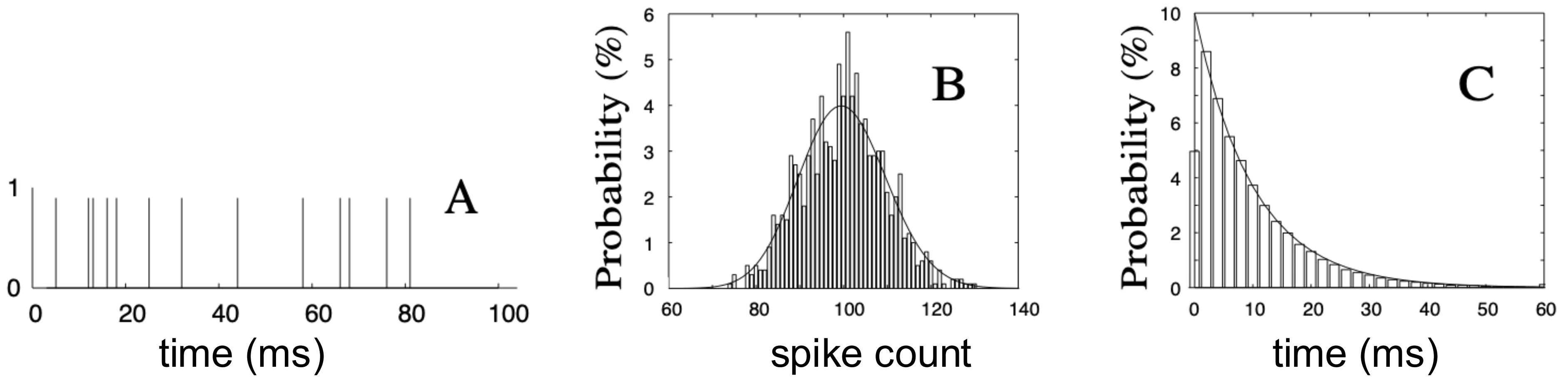


Figure 1: **A.** Snippet of a Poisson spike train with $r = 100$ and $\delta t = 1$ msec. **B.** Spike count histogram calculated from many Poisson spike trains, each of 1 sec duration with $r = 100$, superimposed with the theoretical (Poisson) spike count density. **C.** Interspike interval histogram calculated from the simulated Poisson spike trains superimposed with the theoretical (exponential) interspike interval density.