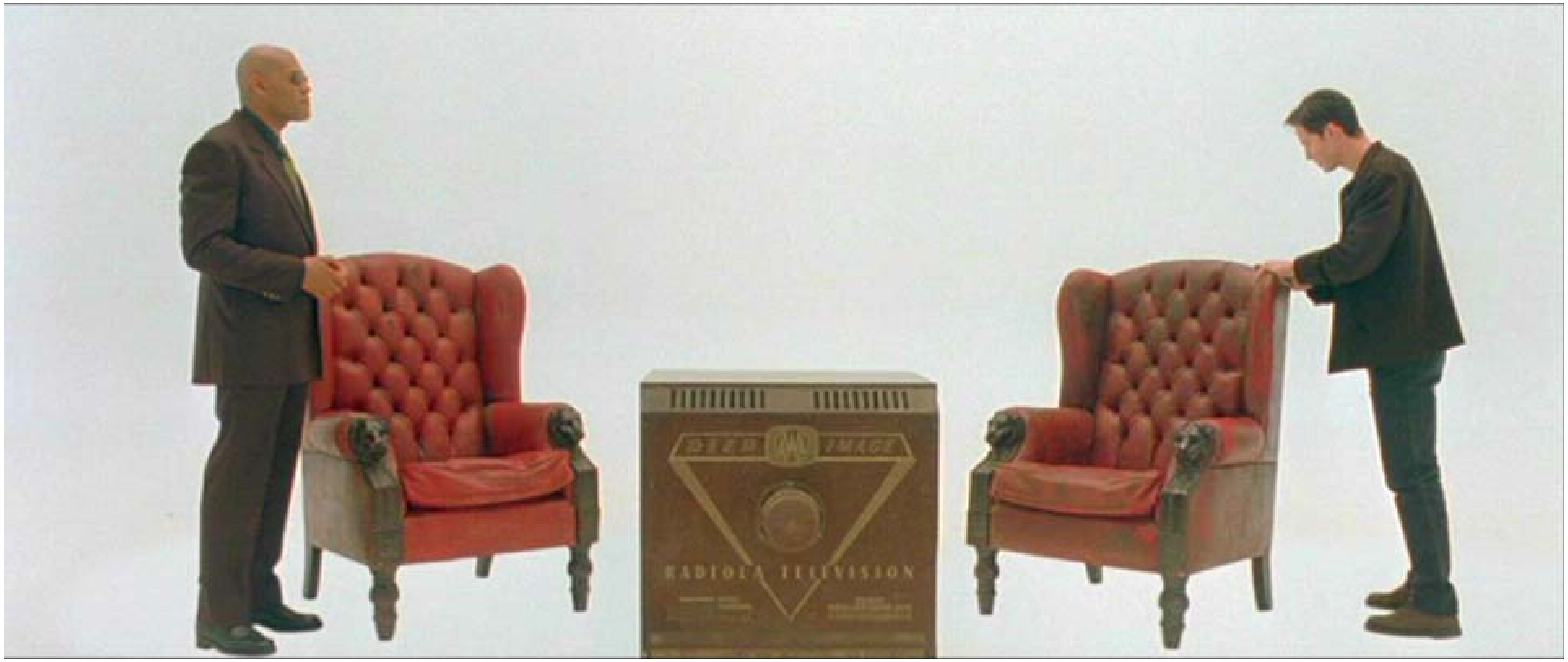
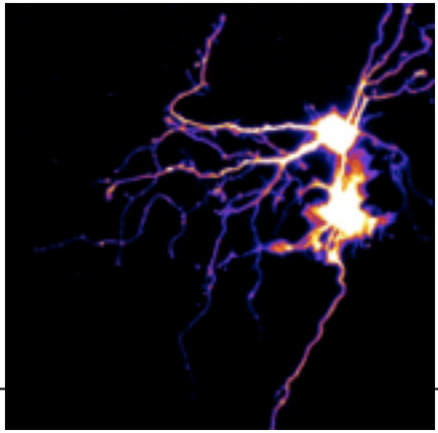
What is real? How do you define ‘real’?



“ 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 and How is information encoded in the brain?

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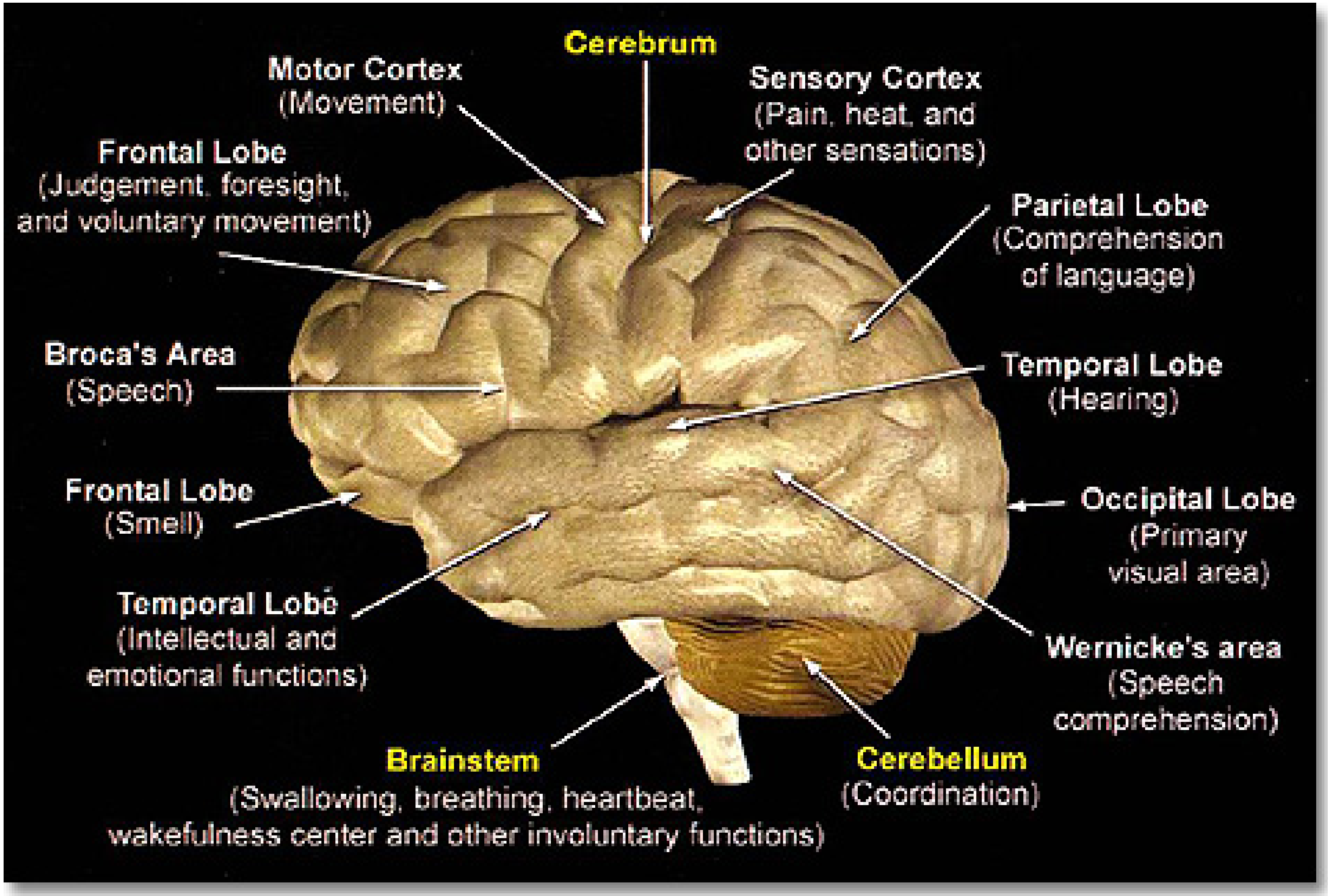
CCN lecture 2

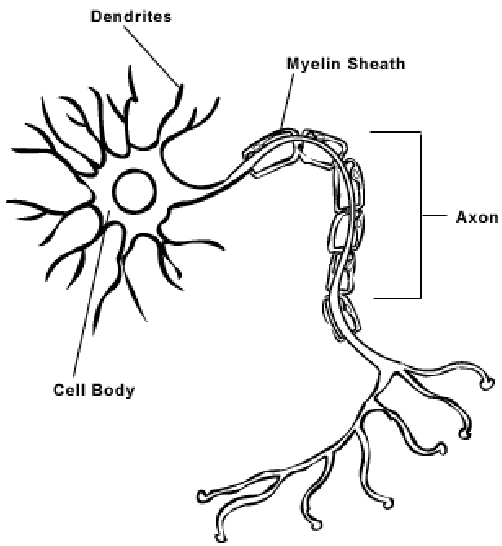
The Brain

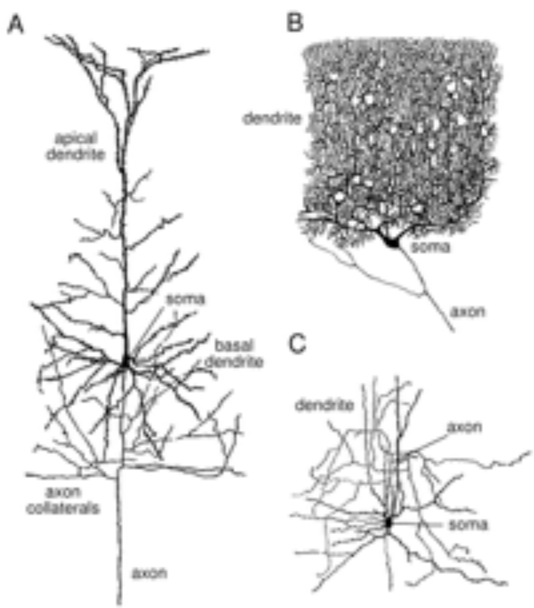


- **Neurons and Glial cells (insulating, supporting, nourishing neurons).**

- **10^11 neurons** in human brain, each link to up to 10,000 other neurons.

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.

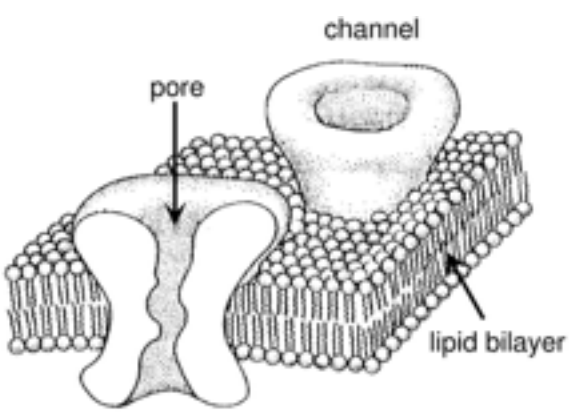
- **Synapse**: contact between pre- and postsynaptic cell.

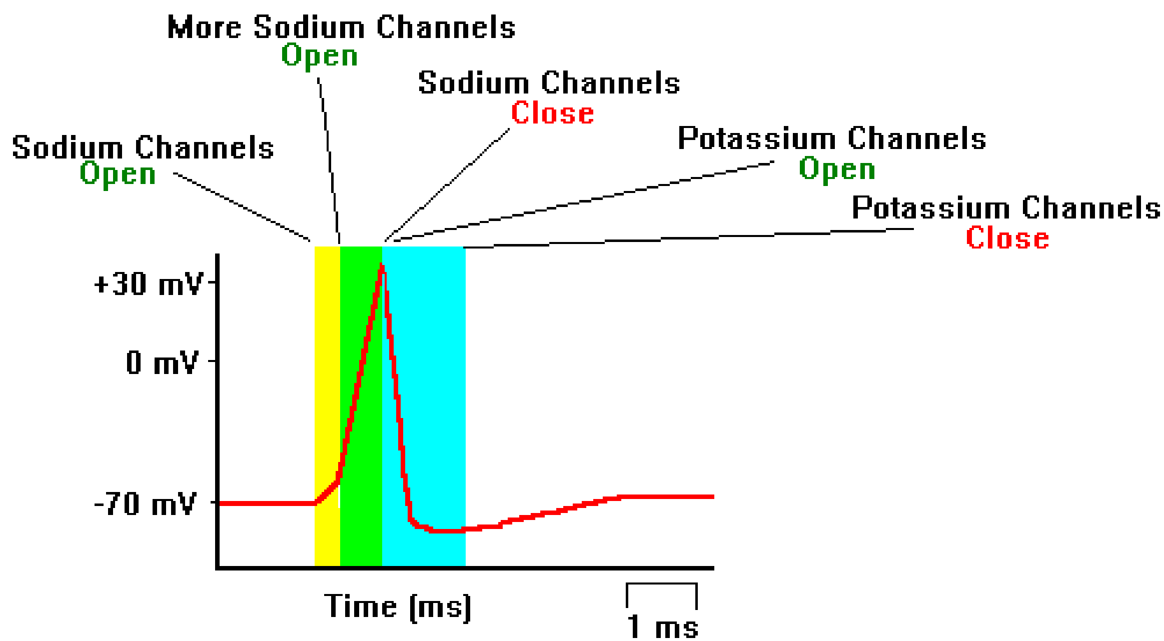
- Efficacy of transmission can vary over time.
- Excitatory or inhibitory.
- Chemical or electrical.

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

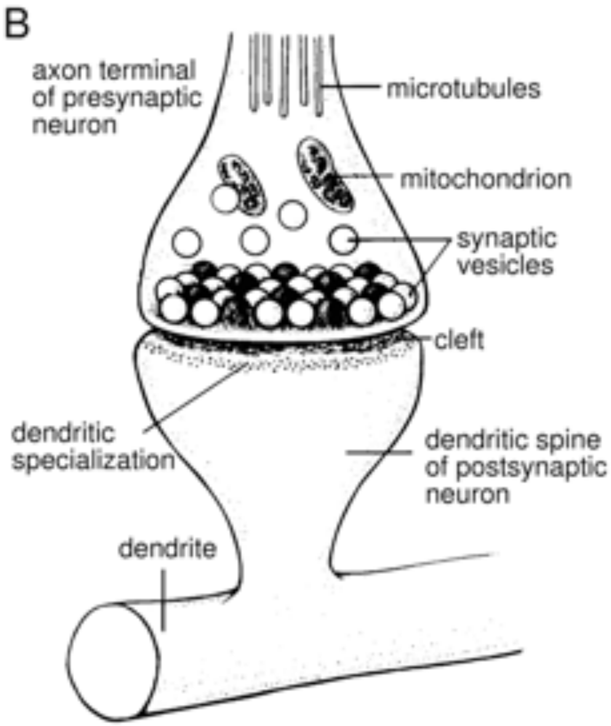
Membrane potential and action potential

- 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



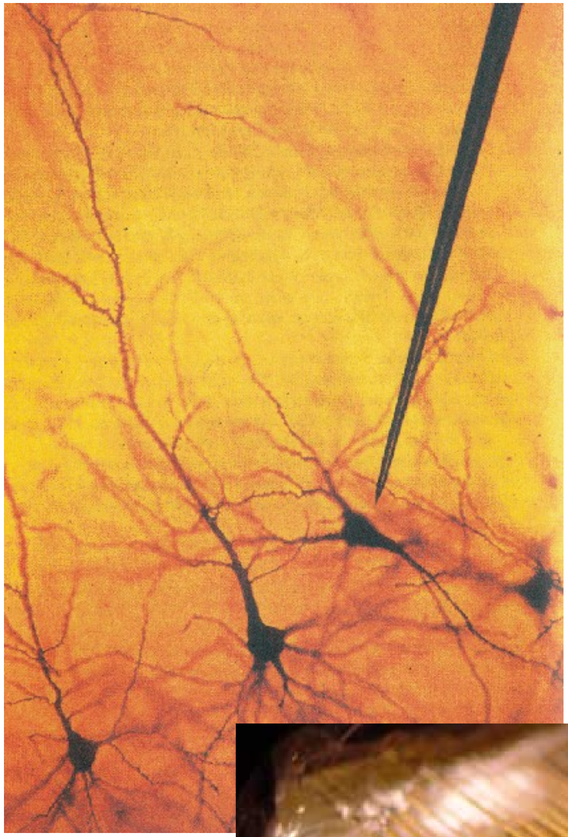
• Axon terminate at synapse.

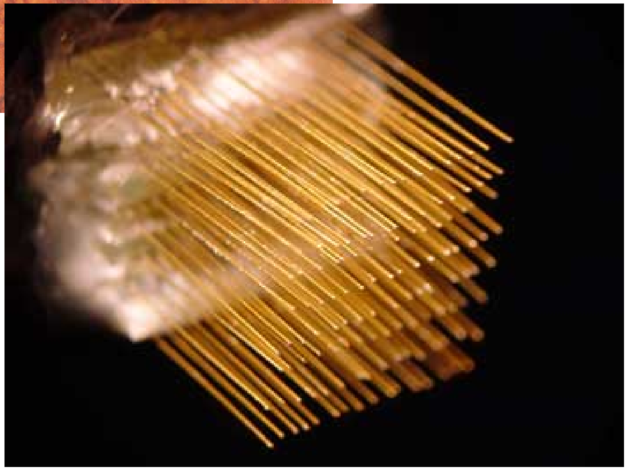
AP-> opens ion channels, influx of Ca2+, release of neurotransmitters in the synaptic cleft, which bind at the post-synaptic receptors, causing ion-conducting channels to open.

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

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

Electrophysiological Recordings

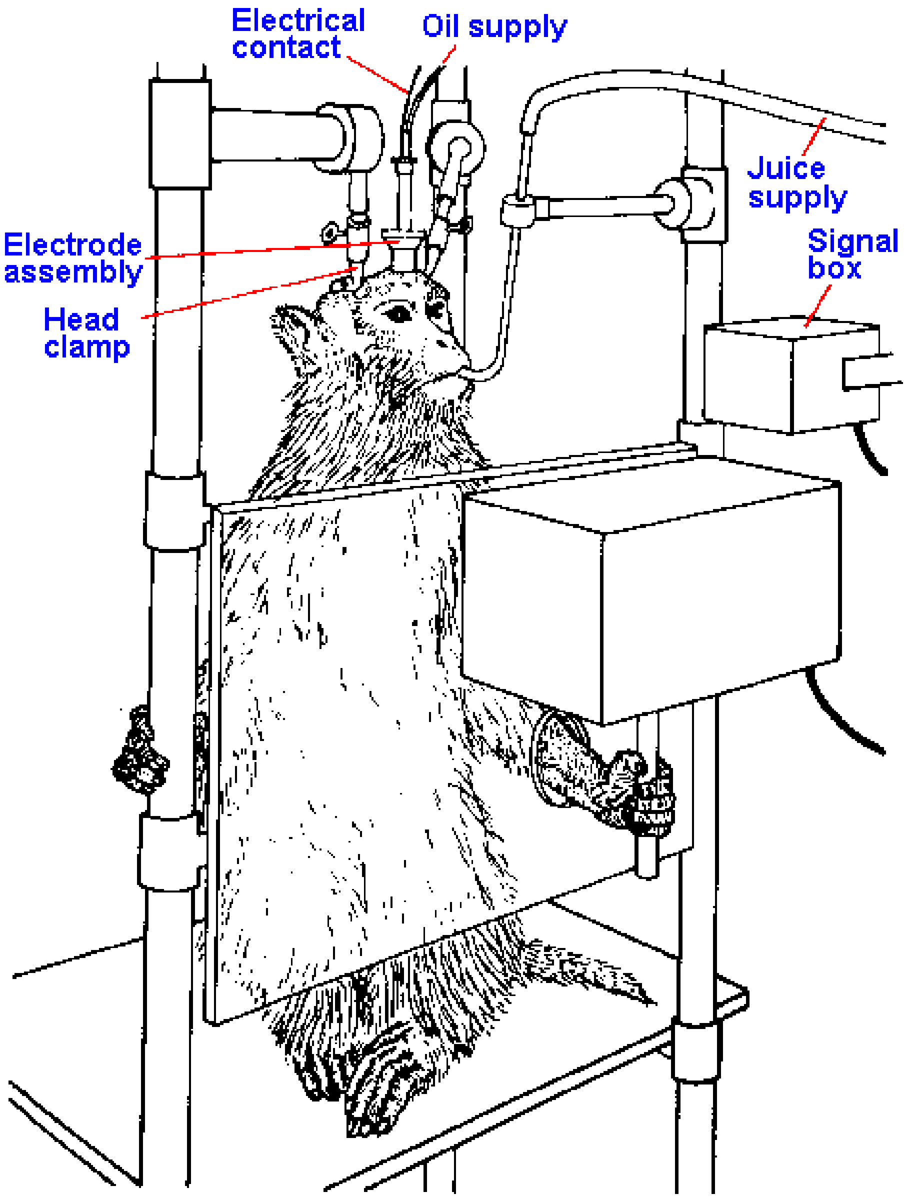




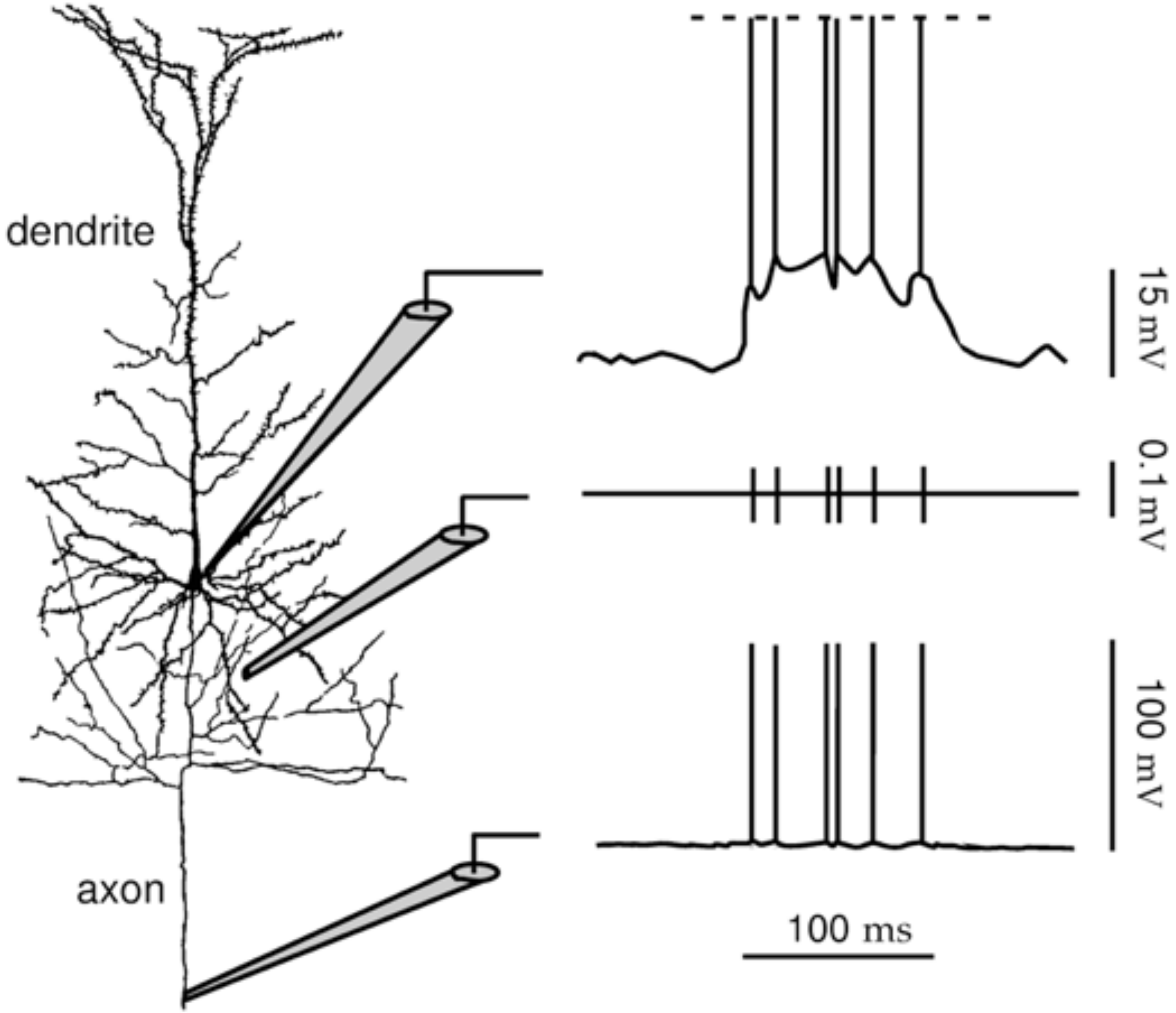
• intracellular recordings (commonly *in vitro*, sometimes *in vivo* (anesthesized, paralyzed))
sharp electrode placed inside the neuron
patch electrode, sealed to the membrane.
view Vm.

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

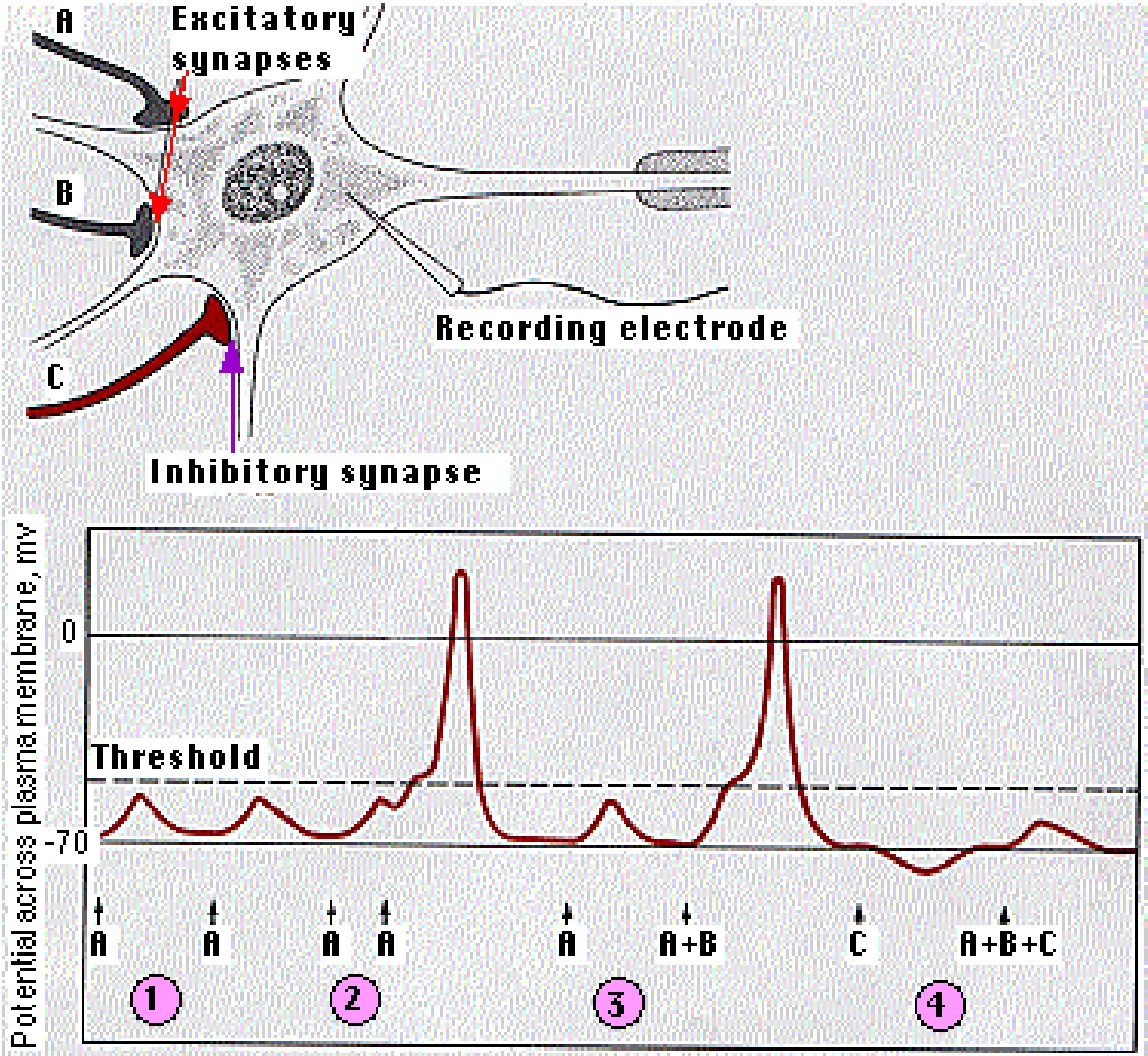
• Commonly, one neuron at a time, now use of arrays of electrodes.



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



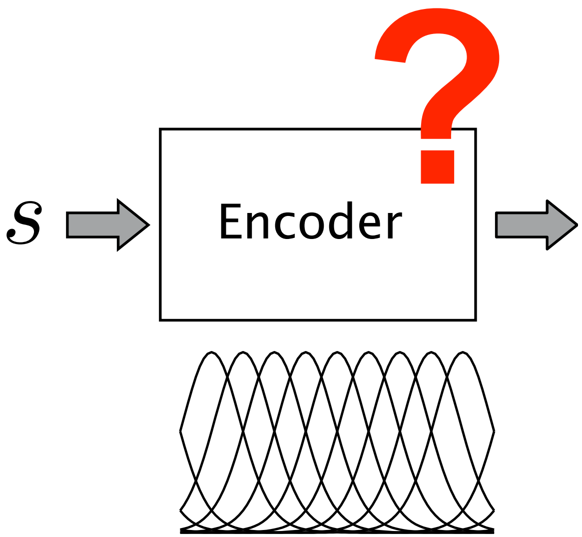
Intracellular and Extracellular electrophysiology

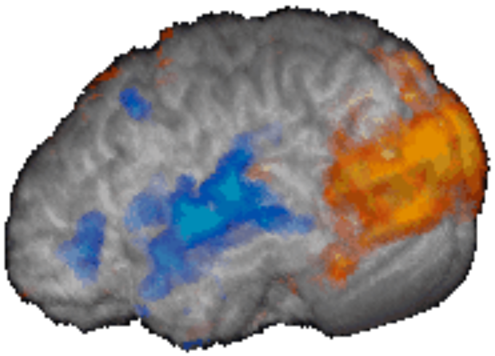


Excitatory and Inhibitory synapses -- EPSP and IPSP

Encoding problem: $P[\mathbf{r}|s]$

Activity in the brain





The World

properties of neurons

Cracking the code

• one aim of experimental neuroscience: describing the activity of neurons: what are they 'responding to'?

• sensory neuroscience: activity as a function of sensory stimulus (eg. visual image, skin stimulation, sound, odor etc..).

• 2 alternatives: describe spike sequence, or number of spikes, or rate r in time window (somewhat arbitrarily defined) -- depending on assumptions about the code (spike times or rate?)

trial 1

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

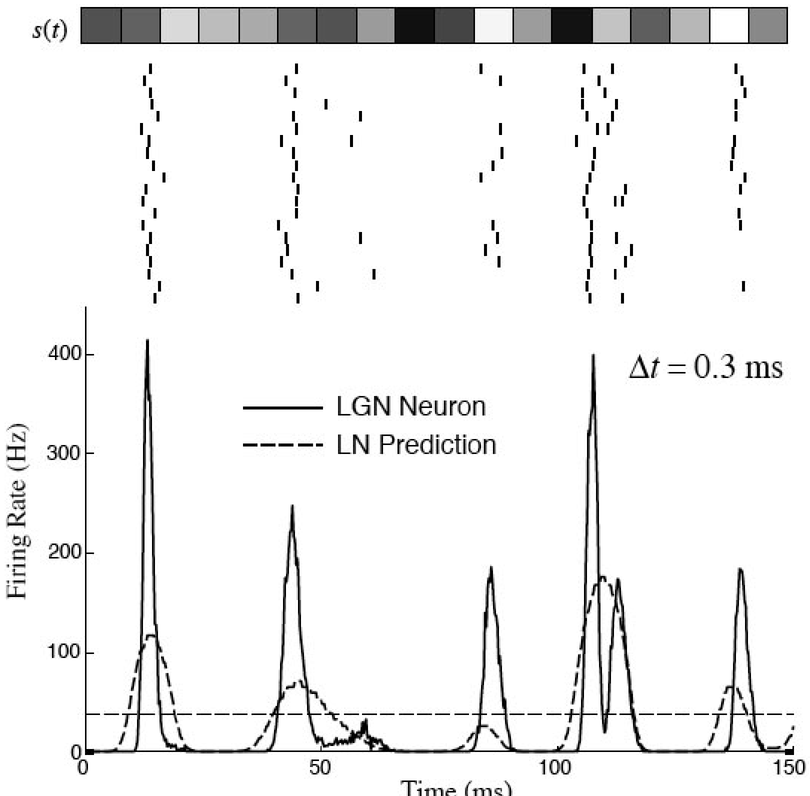
number of spikes /T=r

Cracking the code

- The alternative to spike counting is that **each spike time matters (?)**.
- **Variability** is very large --> statistical measures.

Average over many trial: trial average rate <r> seems more robust to this noise

- Which **time window** should we average from though??



frontiers in Systems Neuroscience

REVIEW
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Philosophy of the Spike: Rate-Based vs. Spike-Based Theories of the Brain

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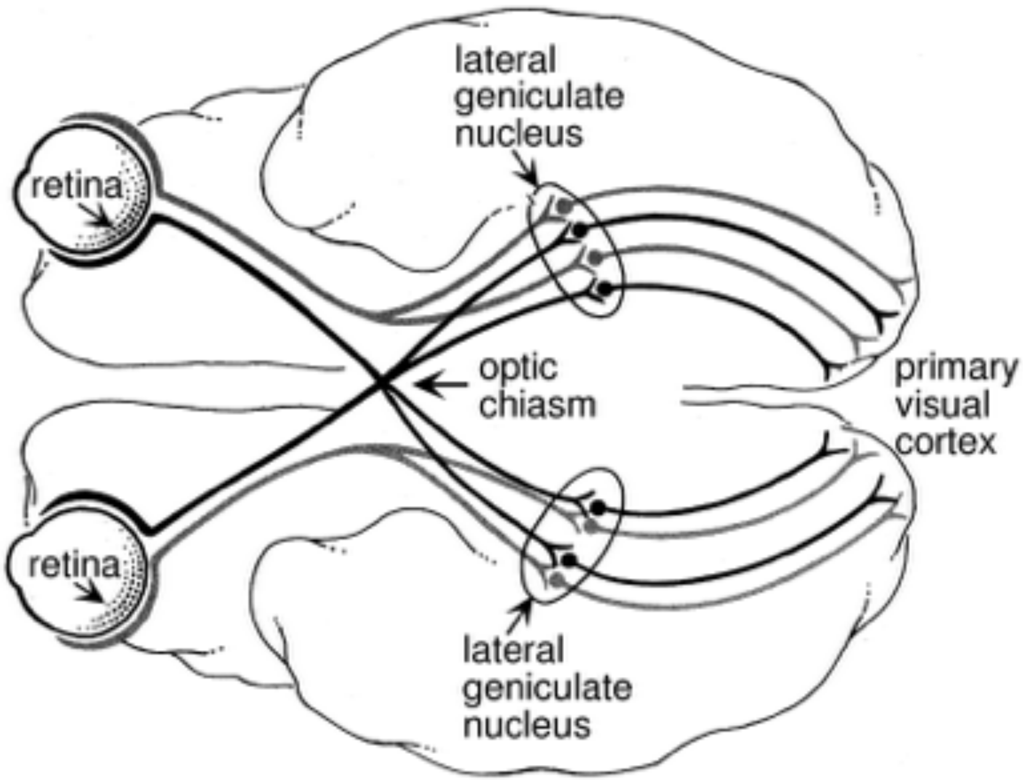
Does the brain use a firing rate code or a spike timing code? Considering this controversial question from an epistemological perspective, I argue that progress has been hampered by its problematic phrasing. It takes the perspective of an external observer looking at whether those two observables vary with stimuli, and thereby misses the relevant question: which one has a causal role in neural activity? When rephrased in a more meaningful way, the rate-based view appears as an *ad hoc* methodological postulate, one that is practical but with virtually no empirical or theoretical support.

Keywords: action potentials, firing rate, information, neural coding, neural computation, neural variability, spike

Neurons in the visual cortex

In retina, LGN and visual cortex, the activity of neurons (spike count) is correlated with some aspects of the visual image (contrast, orientation, color, spatial frequency, ... in early visual cortex ... towards more complicated features such as faces and object shapes in 'higher' areas).



= 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.

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

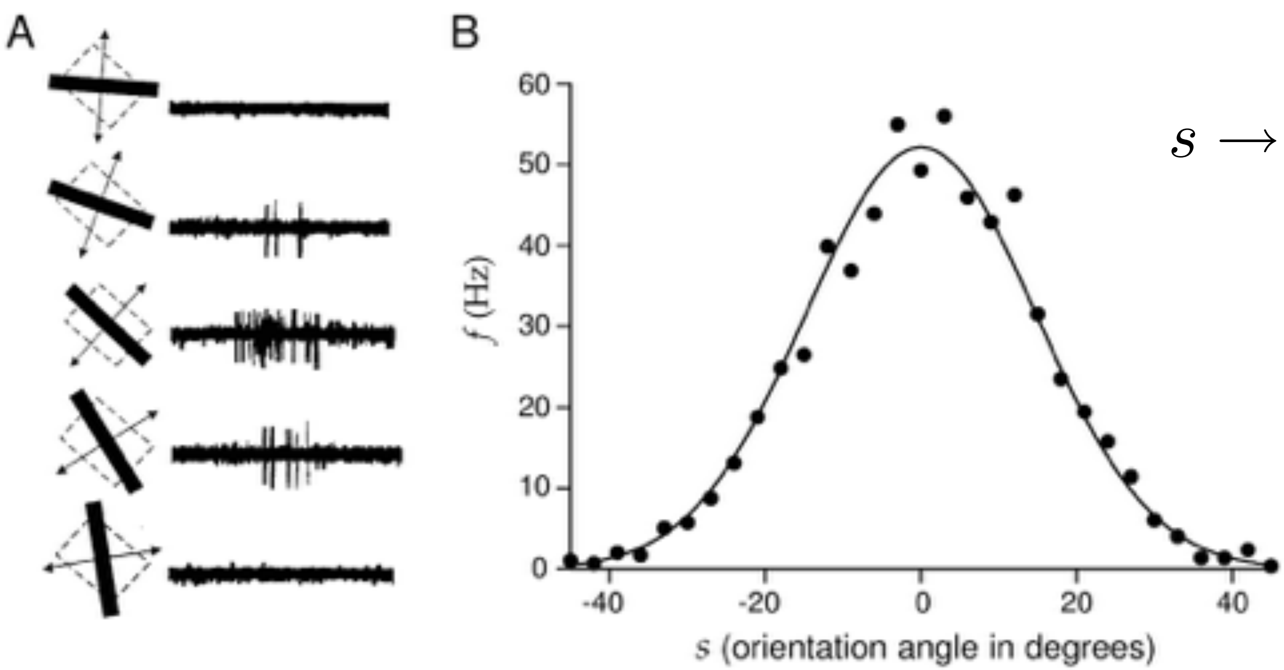
The Nobel Prize in Physiology or Medicine 1981 was divided, one half awarded to Roger W. Sperry *"for his discoveries concerning the functional specialization of the cerebral hemispheres"*, the other half jointly to David H. Hubel and Torsten N. Wiesel *"for their discoveries concerning information processing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

http://www.youtube.com/watch?v=IOHayh06LJ4

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

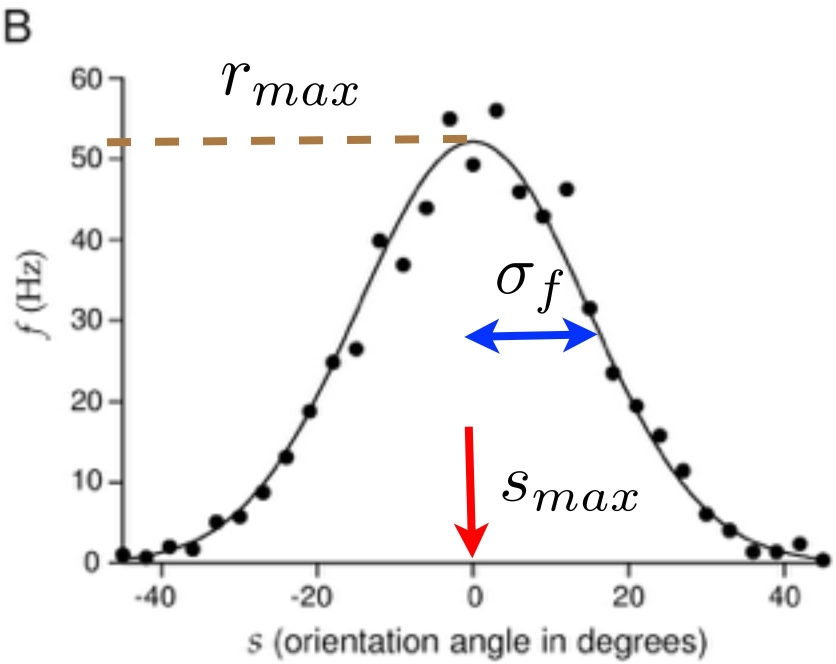
1. Modeling the average firing rate <r(s)>

- Focus description on 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.



$$s \rightarrow < r(s) >$$

a) - Gaussian Tuning Curves



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

Cells are going to be described by:

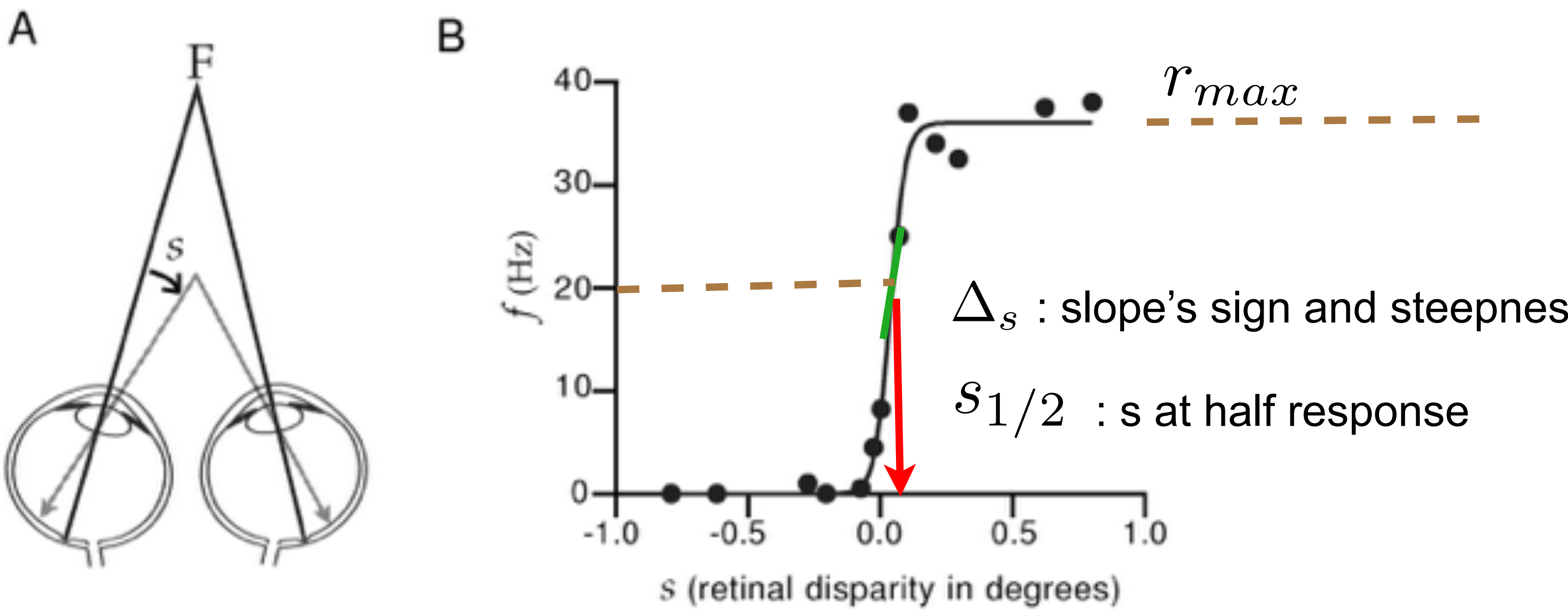
s_{max} : preferred orientation;

r_{max} : maximal response;

σ_f : tuning curve width (selectivity)

b) - Sigmoidal response curves

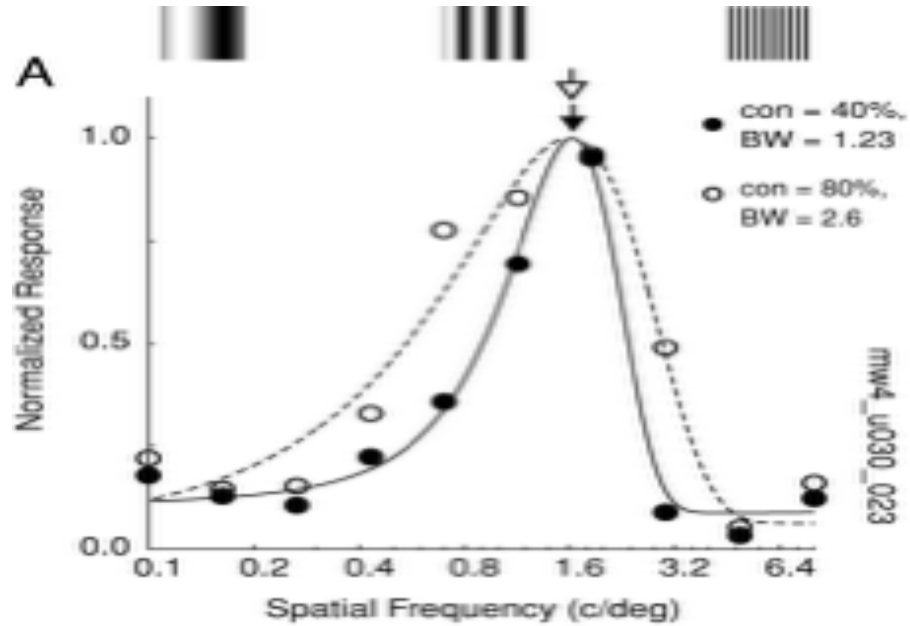
- For some other dimensions, sigmoidal or logistic response functions
- E.g. Luminance, Contrast, Retinal Disparity (depth / fixation point).



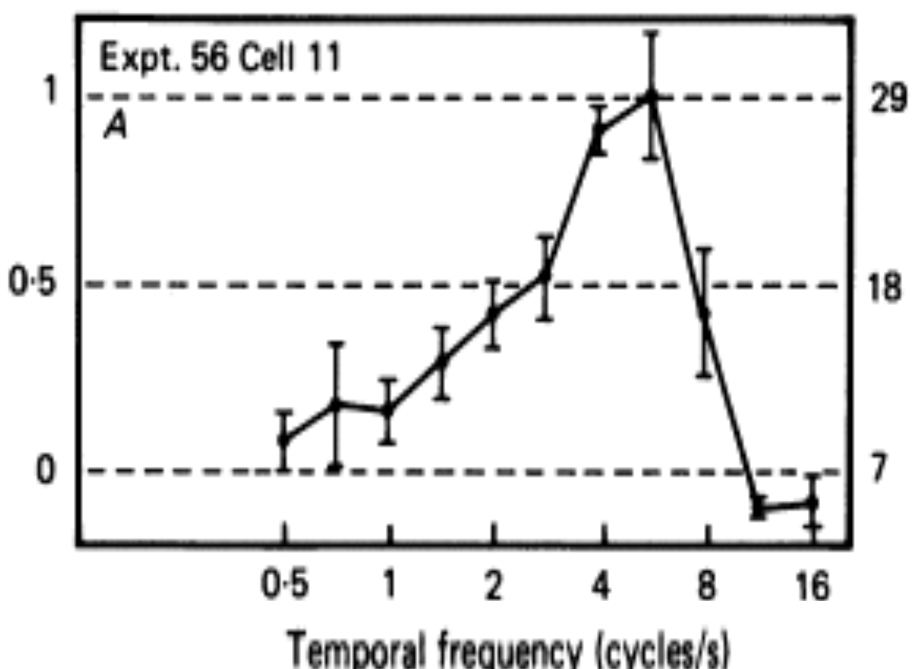
$$f(s) = \frac{r_{\max}}{1 + \exp\left((s_{1/2} - s)/\Delta_s\right)}.$$

Stimulus features encoded in V1

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



[Sceniak et al, 2002]

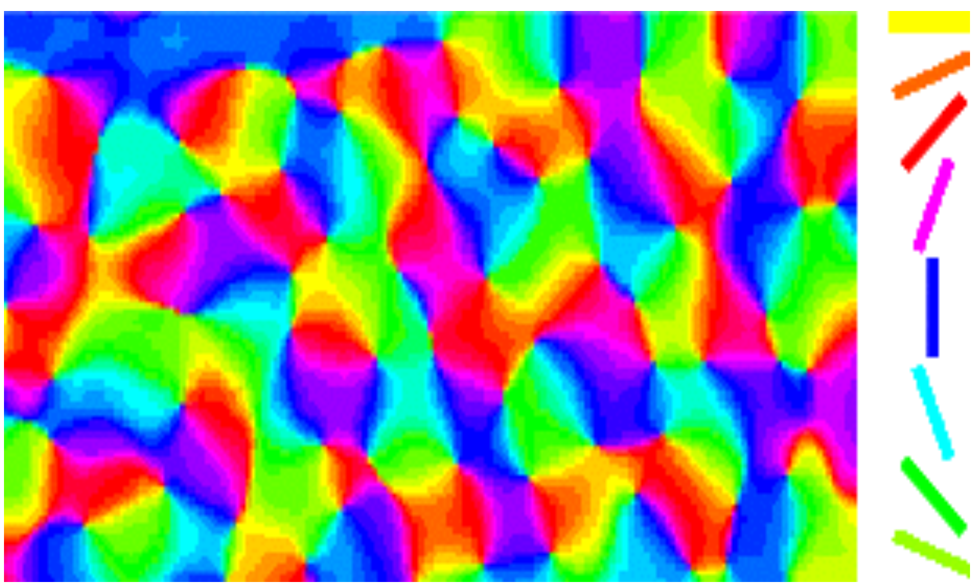


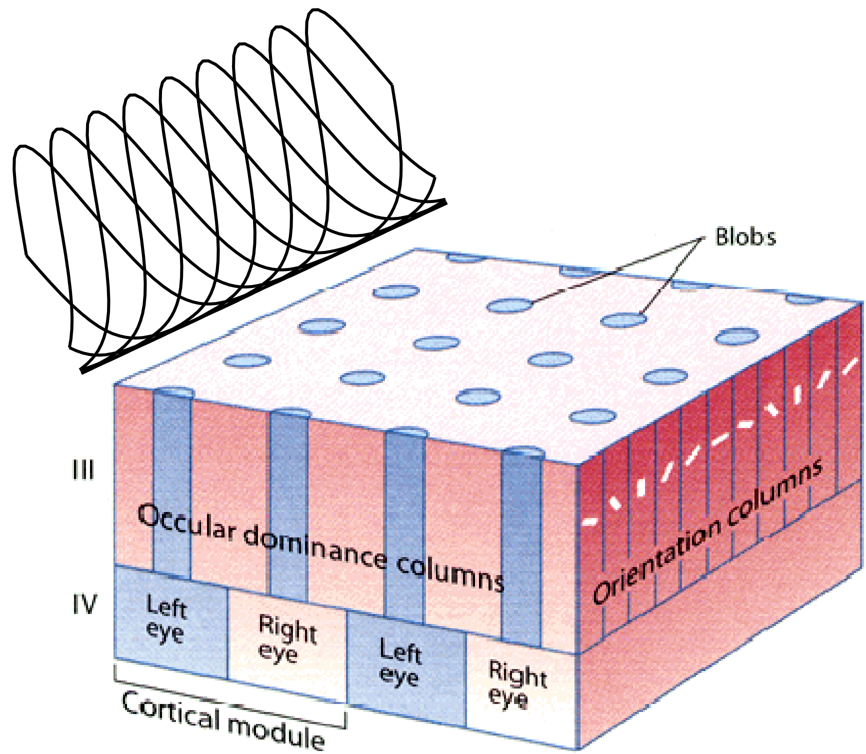
[Foster et al, 1985]

A Population Code

• 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.





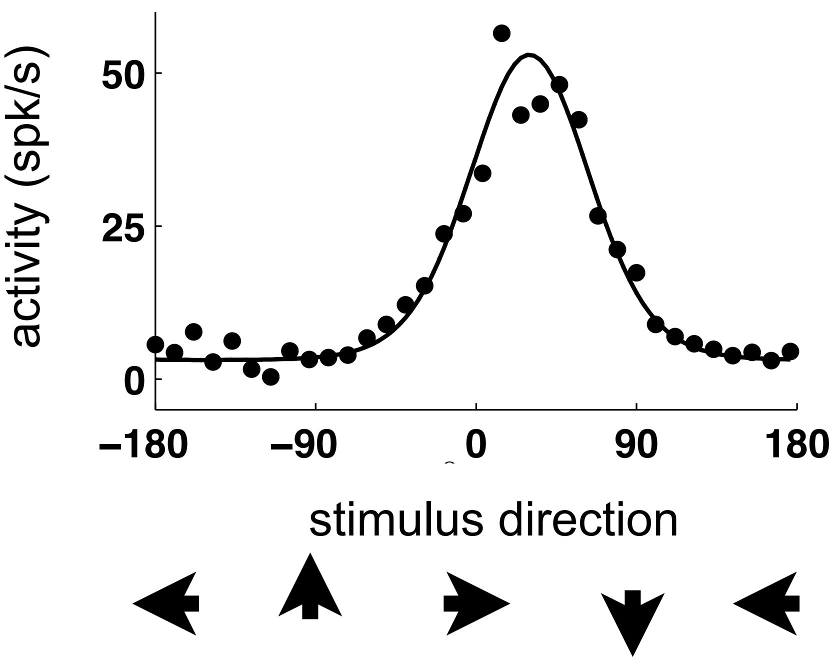
(Aus Gazzaniga et al., 1998)

Single cell tuning curves vs population response

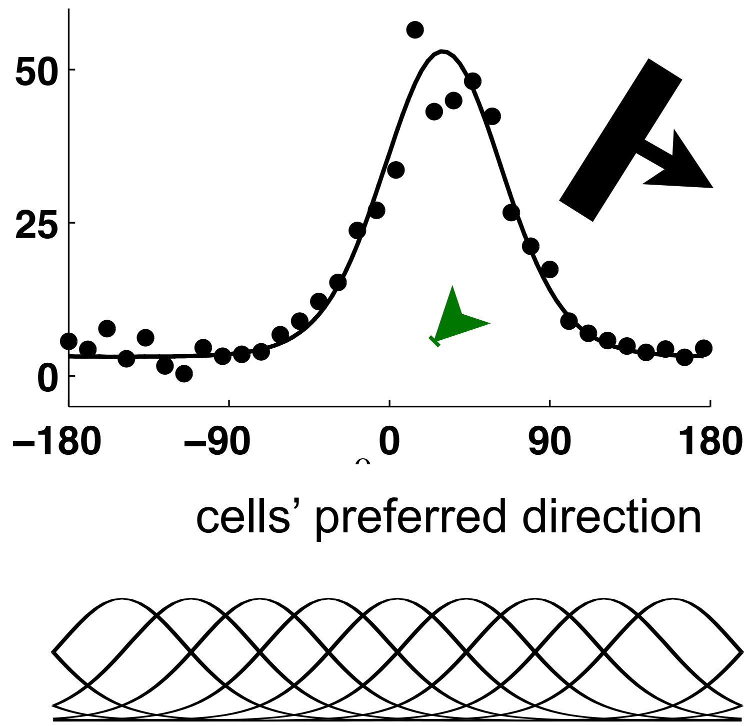
Single cell tuning curve: change stimulus, record spike count for every stimulus

Population response: keep stimulus fixed, record spike count of every neuron in the population

one cell -- many stimuli



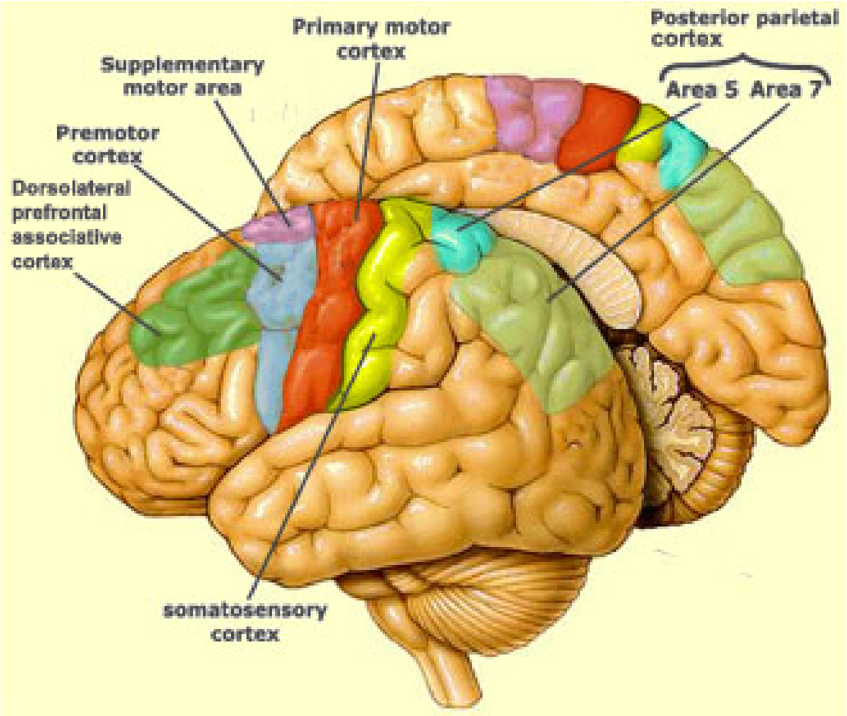
many cells -- one stimulus

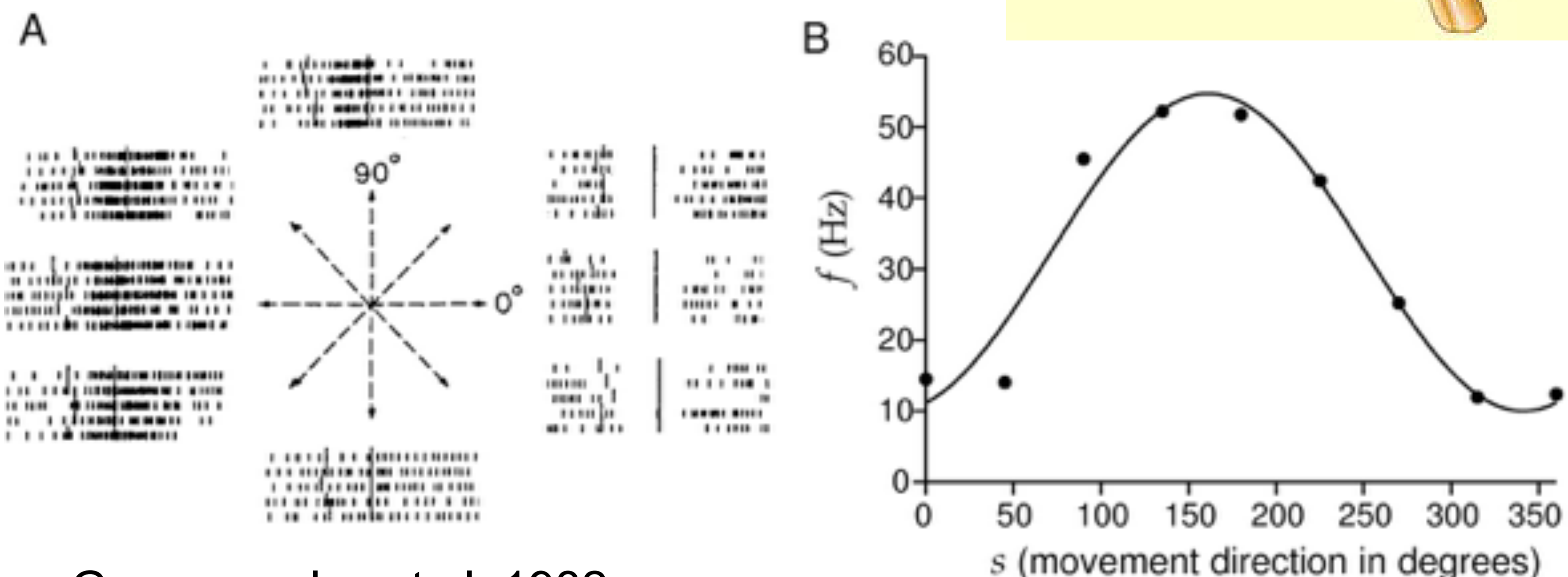


Tuning curves everywhere ...

- 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. Describing 'the noise'

• Beyond describing only the mean spike count … the variability in the spike count.

•To model the statistics of the response (one trial), we can use tools from probability theory: stochastic (random) processes.

• The spike count *r* on one trial is considered as a random variable.

• The probability of getting each outcome (n=1,2 .., 10, 50 spikes) is given by a probability distribution P(nIs) for which we want to find a suitable model.

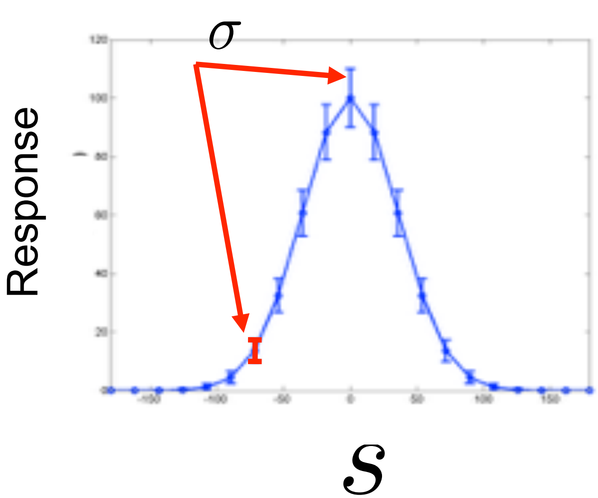
• To do that, we use known statistics of *n*: the mean *<n>=f(s)* and 2d order statistics (variance, correlations).

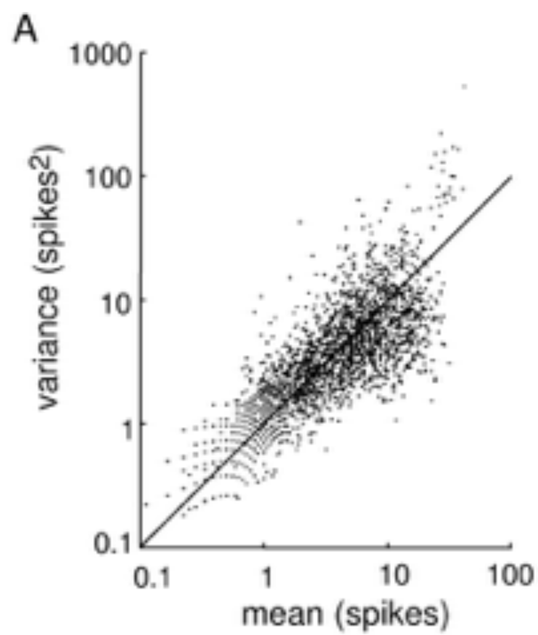
$$Var(n) = E[(n-\mu)^2]$$

$$Cov(n_1, n_2) = E[(n_1-\mu_1)(n_2-\mu_2)]$$

Beyond the rate: Describing the variance of the spike count

- Measure the variance of the spike count, for a number of repetitions with the same stimulus.
- Experiments show that the variance of the spike count is linearly related to the mean spike count (with prop. const ~1).
- Noise is often described as Poisson, or Gaussian with a variance proportional to the mean.





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

F: Fano Factor

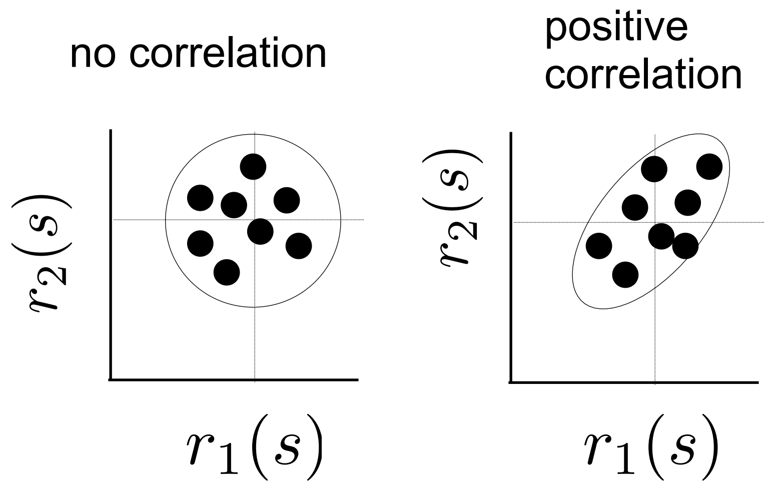
[O Keefe, 1997 - MT cortex]

From one neuron to the population : Describing pair-wise noise correlations

• An important question in neuroscience 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 is above its mean, is neuron 2 also ? or are their fluctuations independent?



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

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 ISI, 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.

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.

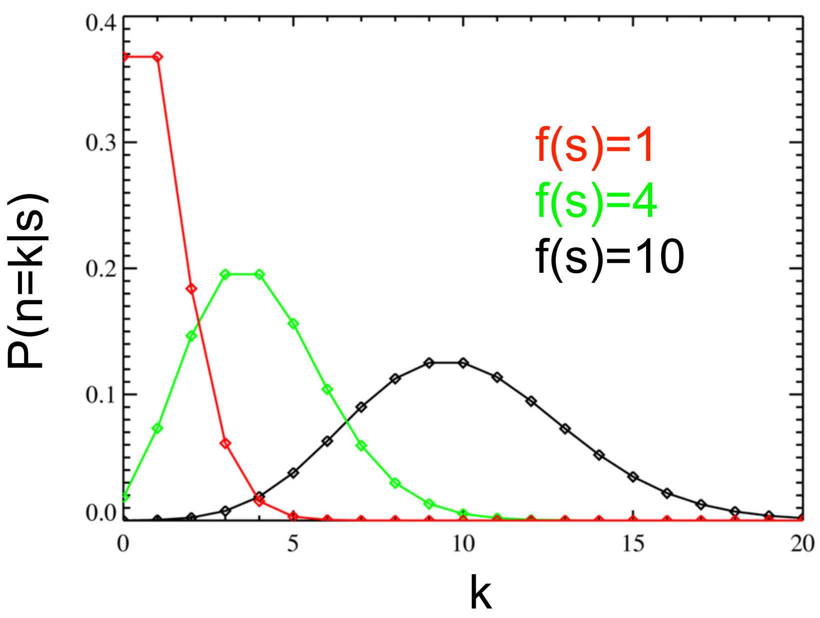
a) Poisson Distribution - P(n|s)

• 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)

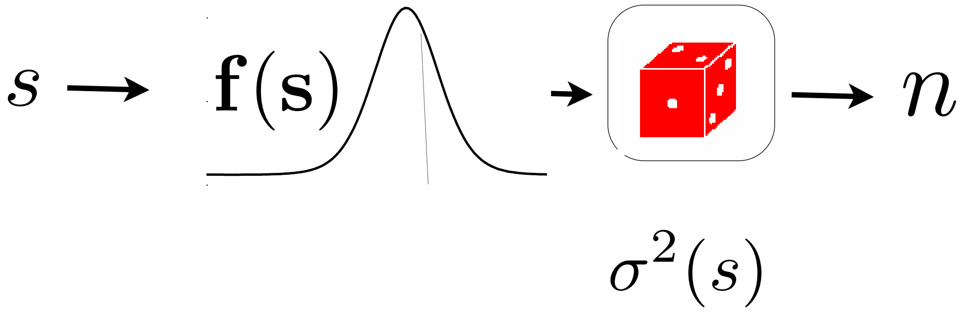
$$P(n = k|s) = \frac{e^{-f(s)} f(s)^k}{k!}$$

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



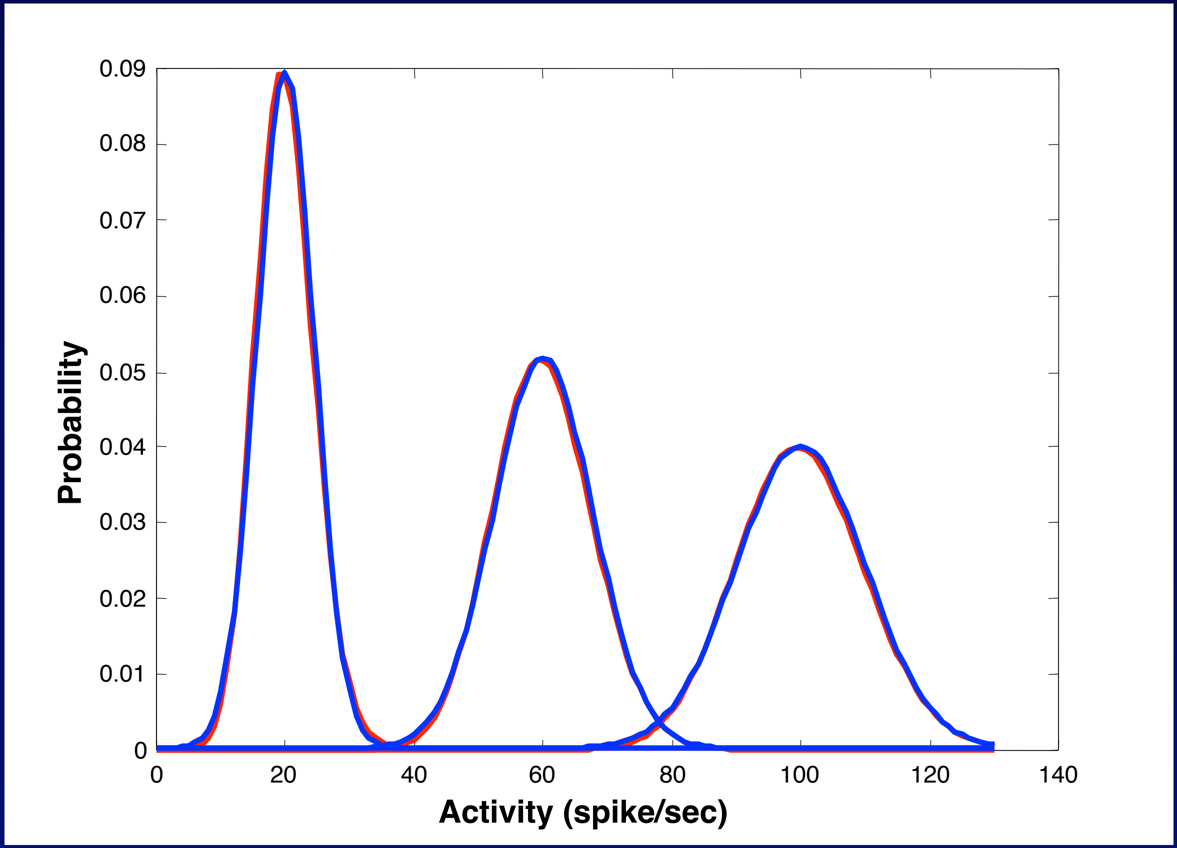
- Another model that is commonly used to describe the variability of the spike count is the Gaussian noise model.
- The activity of a neuron (number of spikes) can be described as:

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

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

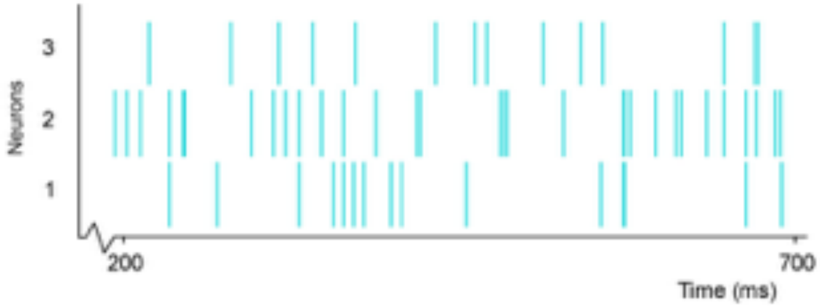
- To mimic a Poisson distribution, we choose $\sigma^2(s) = f(s)$

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.

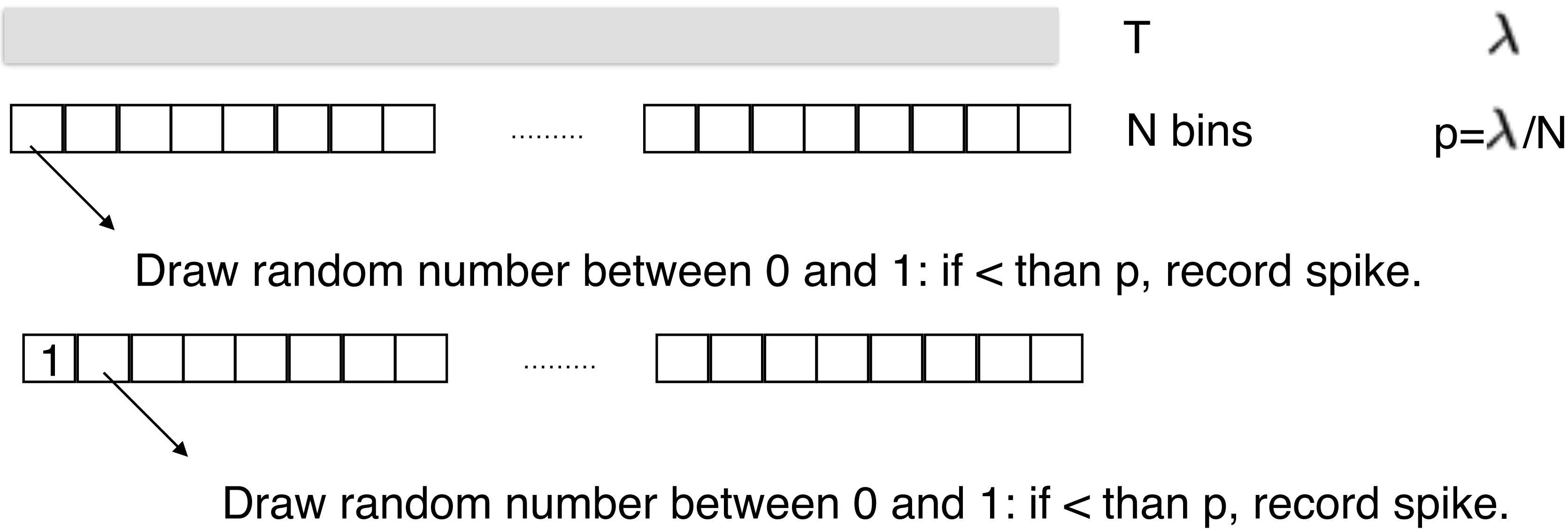
We can use the model of the Poisson Process.

c) Poisson Processes - spike sequences

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.



• 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).

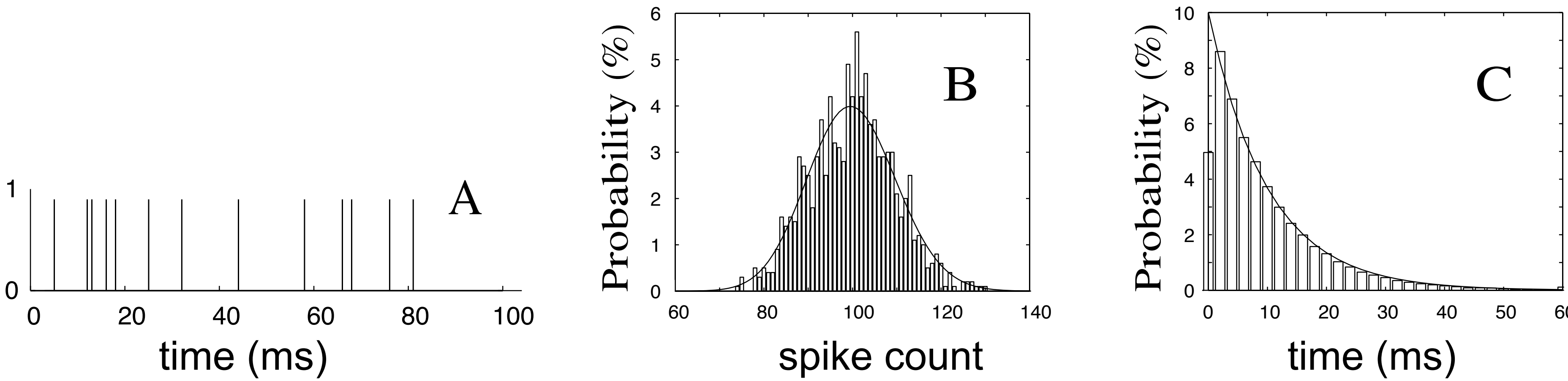


Figure 1: **A.** Snippet of a Poisson spike train with $r = 100$ and $\delta t = 1$ msec. **B.** Spike count histogram calculated from many Poisson spike trains, each of 1 sec duration with $r = 100$, superimposed with the theoretical (Poisson) spike count density. **C.** Interspike interval histogram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