What is real? How do you define 'real'?

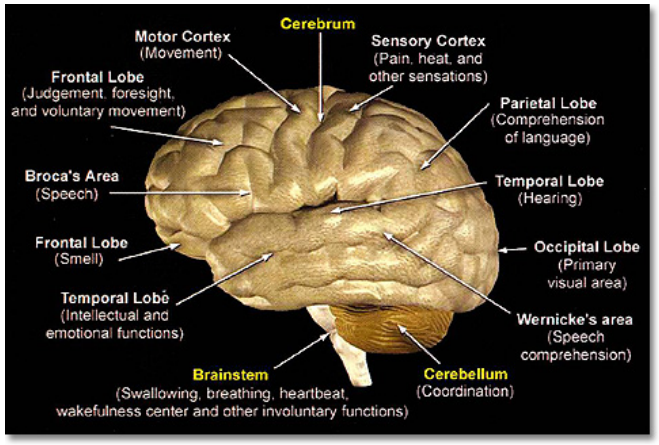
" If you're talking about what you can feel, what you can smell, what you can taste and see, then 'real' is simply electrical signals interpreted by your brain. This is the world that you know."

Morpheus, in *the Matrix*.

1. Encoding:
How is information encoded in the brain?

Readings: Encoding D&A ch.1

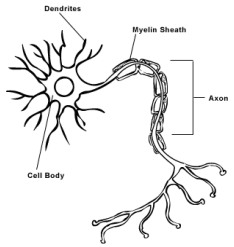
The Brain

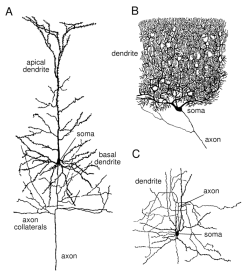


- **Neurons and Glial cells (insulating, supporting, nourishing neurons).**

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

Neurons



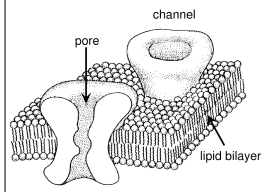


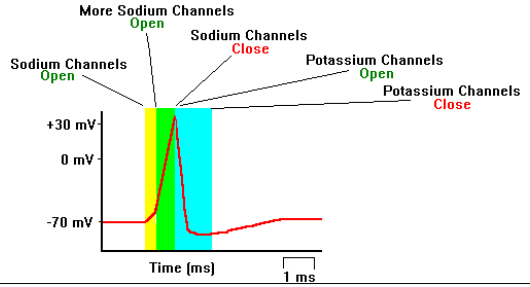
- neuron = cell, diverse morphologies
- **Dendrites**: receive inputs from other cells, mediated via synapses.
- **Soma** (cell body): integrates signals from dendrites. 4-100 micrometers.
- Action potential: All-or-nothing event generated if signals in soma exceed threshold.
- **Axon**: transfers signal 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)

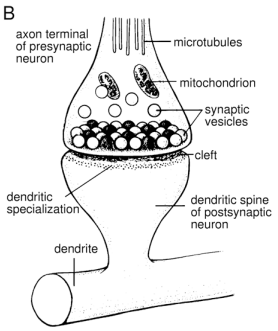
Membrane potential and action potential

• 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

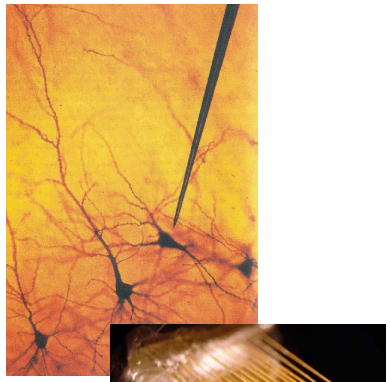


• Axon terminate at synapse.
AP-> opens ion channels, influx of Ca2+, release of neurotransmitters in the synaptic cleft, which bind at the post-synaptic receptors, causing ion-conducting channels to open.

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

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

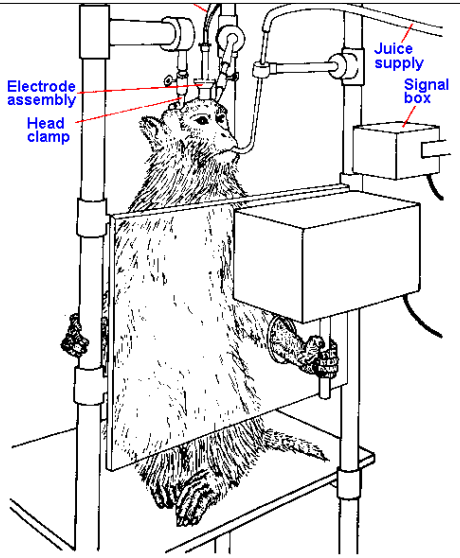
Electrophysiological Recordings

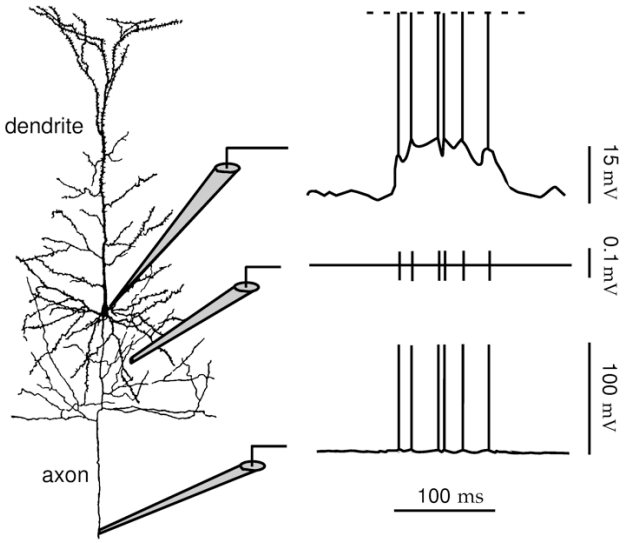


• intracellular recordings (commonly *in vitro*, sometimes *in vivo* (anesthesized, paralyzed))
sharp electrode placed inside the neuron
patch electrode, sealed to the membrane.
view Vm.

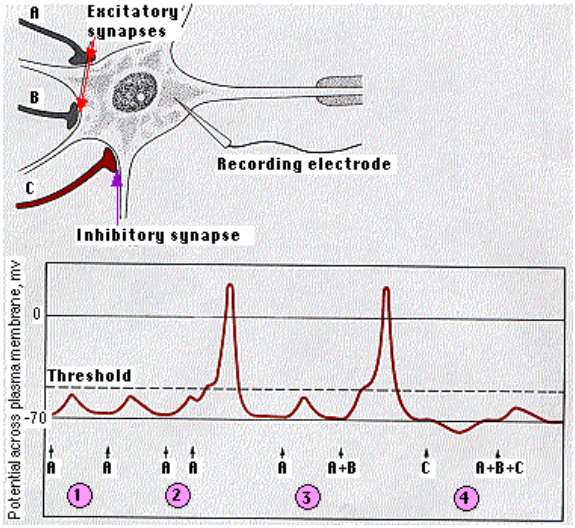
• extracellular (often *in vivo*, possibly awake behaving animal)
electrode is placed near a neuron.
view action potentials.

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



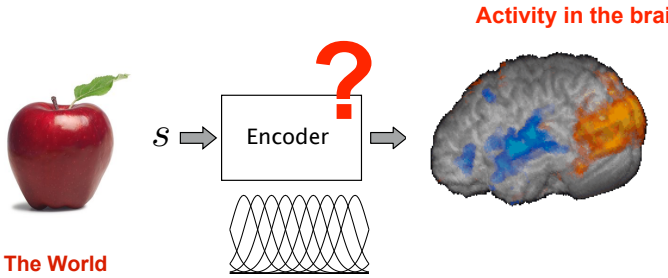


Intracellular and Extracellular electrophysiology



Excitatory and Inhibitory synapses -- EPSP and IPSP

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



properties of neurons

Describing neurons' activity

- 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

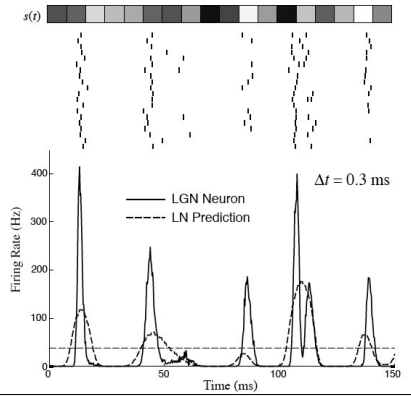
$$\rho(t) = \sum_{i=1}^{n} \delta(t - t_i)\,.$$

number of spikes /T=r

Describing neurons' activity

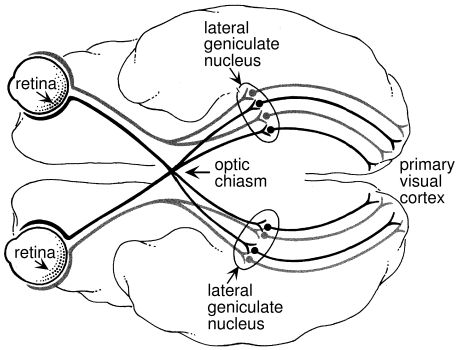
- Variability is very large --> statistical measures.

Average over many trial: trial average rate <r>.



Neurons in the visual cortex

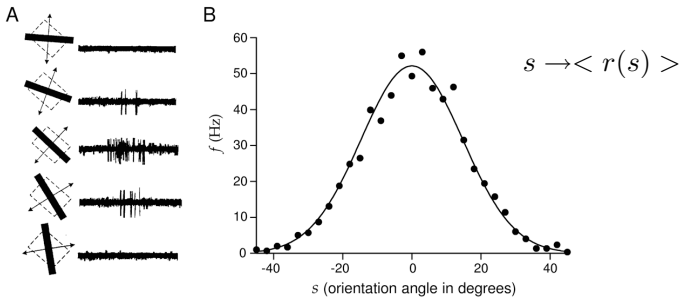
In retina, LGN and visual cortex, the activity of neurons (spike count) is correlated with some aspects of the visual image (contrast, orientation, color, spatial frequency, ... in early visual cortex ... towards more complicated features such as faces and object shapes in 'higher' areas).



= V1

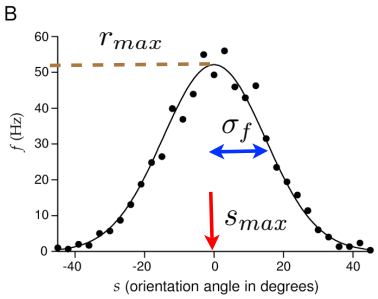
1. Modeling the average firing rate <r(s)>

- 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.



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

a) - Gaussian Tuning Curves



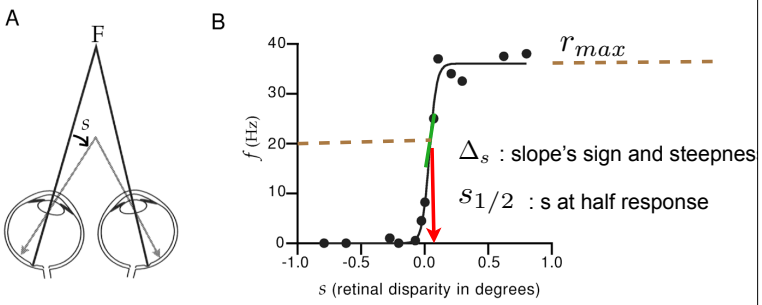
$$f(s) = r_{\max} \exp\left(-\frac{1}{2}\left(\frac{s - s_{\max}}{\sigma_f}\right)^2\right)$$

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

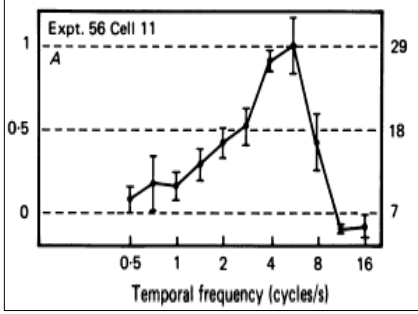
- For some other dimensions, sigmoidal or logistic response functions
- E.g. Luminance, Contrast, Retinal Disparity (depth / fixation point).



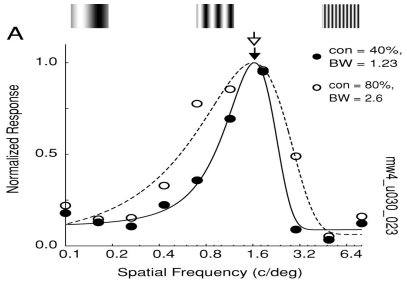
$$f(s) = \frac{r_{\max}}{1 + \exp\left((s_{1/2} - s)/\Delta_s\right)}.$$

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.



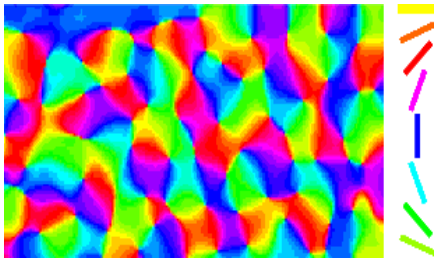
[Foster et al, 1985]

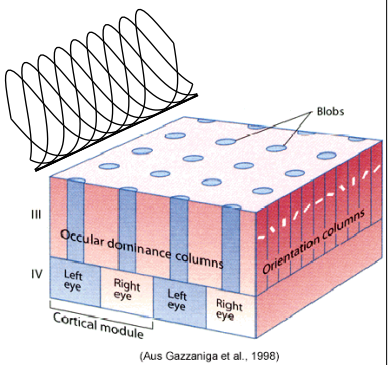


[Sceniak et al, 2002]

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.



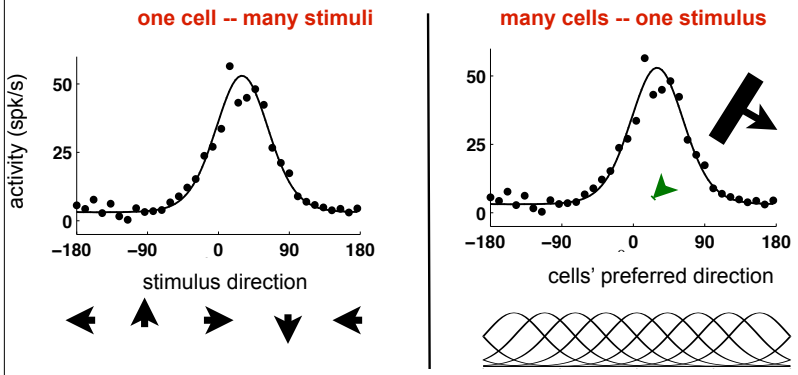


(Aus Gazzaniga et al., 1998)

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



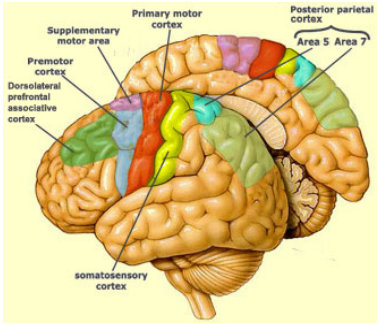
Tuning curves everywhere ...

• Primary motor cortex (M1) -- arm reaching task

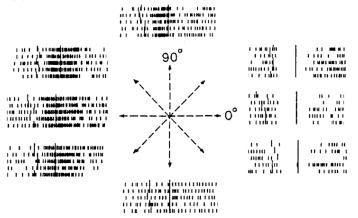
• <r> as a function of the direction in which the monkey moved his arm

• Here described as a cosine

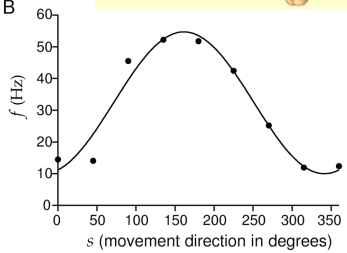
$$f(s) = r_0 + (r_{\max} - r_0)\cos(s - s_{\max})$$



A



B



Georgoupolos et al, 1982

2. Describing 'the noise'

• Beyond describing only the mean 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 for which we want to find a suitable model.

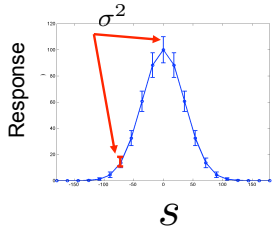
• To do that, we use known statistics of *n*: the mean *<n>=f(s)* and 2d order statistics (variance, correlations).

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.



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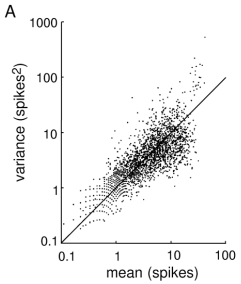


$$var(n) = F * mean(n)$$

F: Fano Factor

[O Keefe, 1997 - MT cortex]

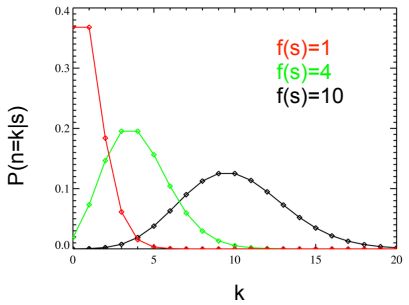
a) Poisson Distribution - P(n|s)

• Probability of a spike count (positive integer -- discrete probability distribution) occurring in a fixed period of time, knowing average spike count f(s)

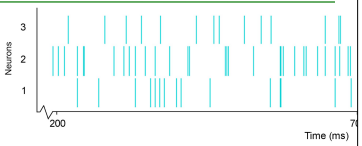
• The assumption is that the generation of each spike (and its stochasticity) is independent of all other spikes

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

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



a) Poisson Distribution - 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.

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).

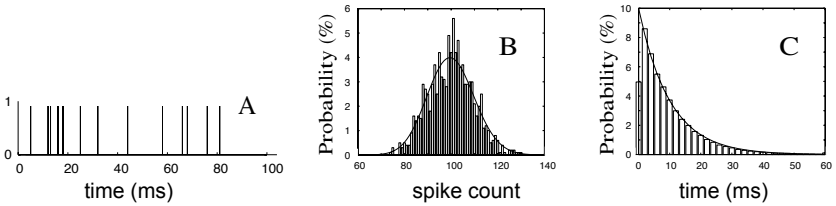


Figure 1: A. Snippet of a Poisson spike train with $r = 100$ and $\delta t = 1$ msec. **B.** Spike count histogram calculated from many Poisson spike trains, each of 1 sec duration with $r = 100$, superimposed with the theoretical (Poisson) spike count density. **C.** Interspike interval histogram calculated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