

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



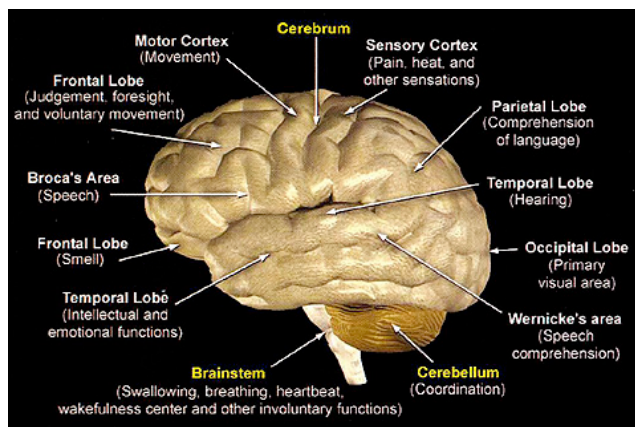
“ If you're talking about what you can feel, what you can smell, what you can taste and see, then 'real' is simply electrical signals interpreted by your brain. This is the world that you know.”

Morpheus, in *the Matrix*.

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## 1. Encoding

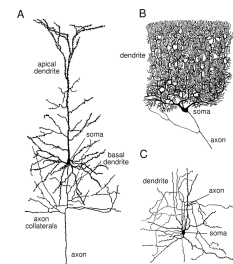
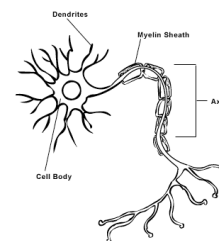
## The Brain



- **Neurons and Glial cells (insulating, supporting, nourishing neurons).**
- **10<sup>11</sup> neurons** in human brain, each link to up to 10,000 other neurons.

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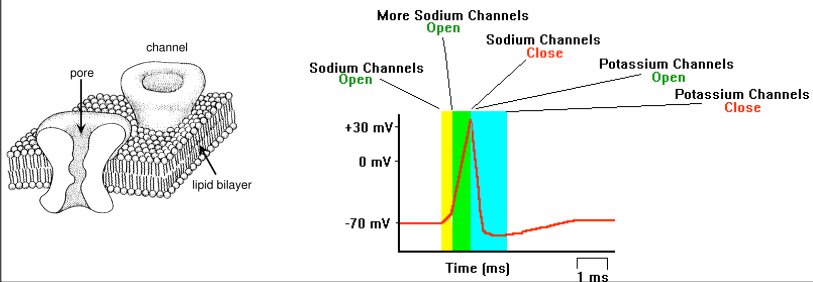
## Neurons



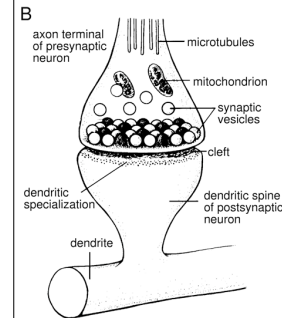
- neuron = cell, diverse morphologies
  - **Dendrites:** receive inputs from other cells, mediated via synapses.
  - **Soma** (cell body): integrates signals from dendrites. 4-100 micrometers.
  - Action potential: All-or-nothing event generated if signals in soma exceed threshold.
  - **Axon:** transfers 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<sup>16</sup> synapses in young children (decreasing with age -- 1-5x10<sup>15</sup>)

## Membrane potential and action potential

- **Ions channels** across the membrane, allowing ions to move in and out, with selective permeability (mainly Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup>)
- **V<sub>m</sub>**: difference in potential between interior and exterior of the neuron.
- at rest, V<sub>m</sub> ~ -70 mV (more Na<sup>+</sup> outside, more K<sup>+</sup> inside, due to Na<sup>+</sup>/K<sup>+</sup> 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).

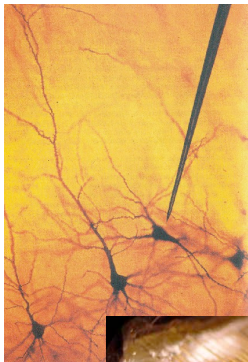


## Synapses

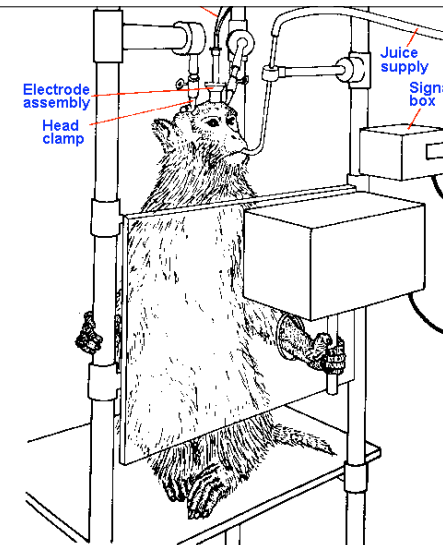


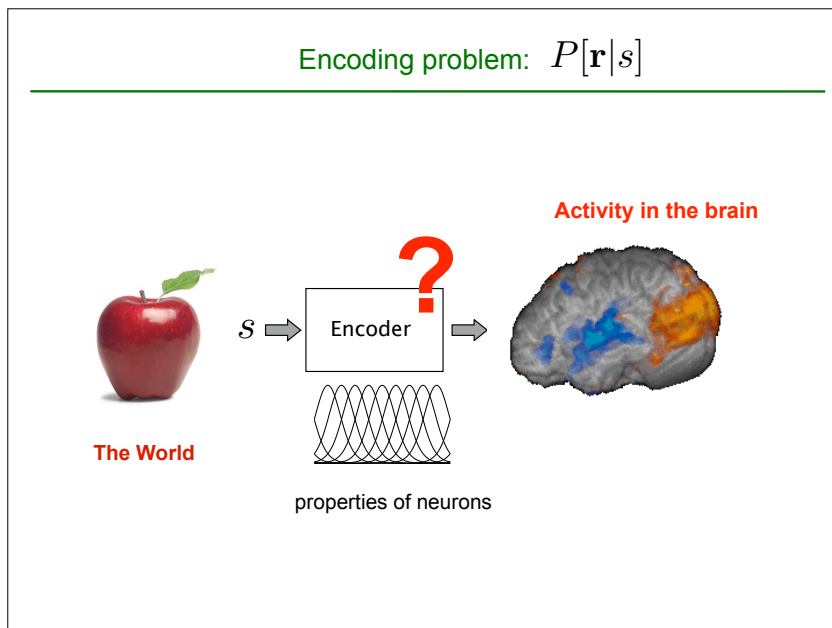
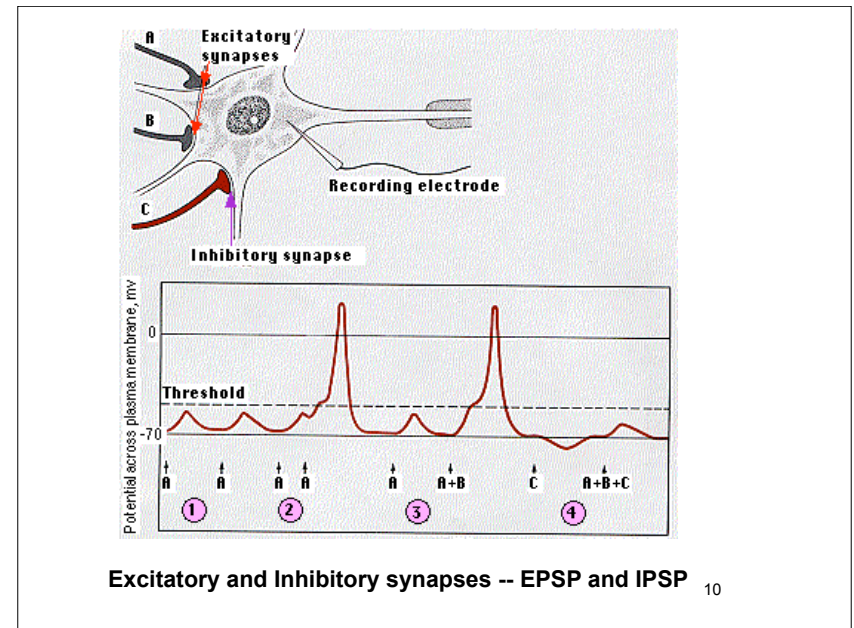
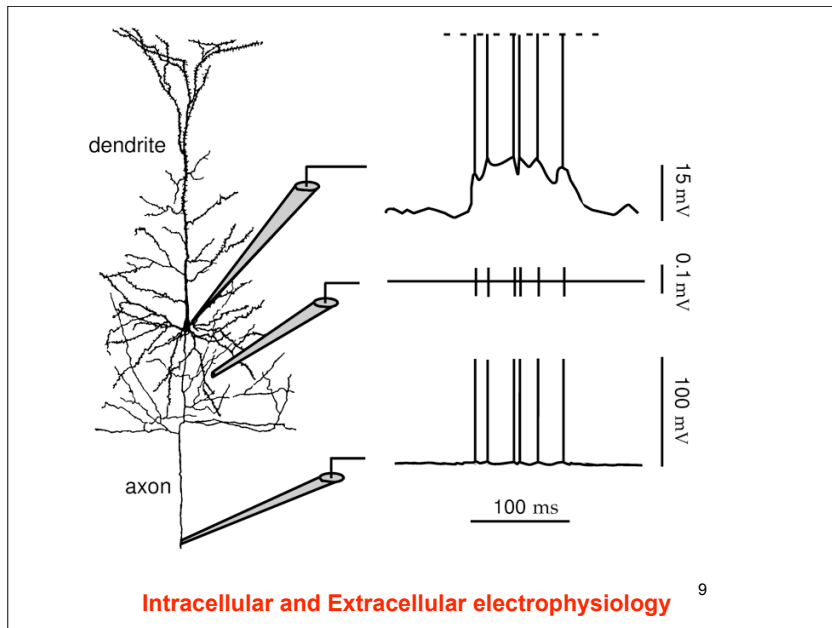
- Axon terminate at synapse. AP → opens ion channels, influx of Ca<sup>2+</sup>, release of **neurotransmitter** in the synaptic cleft, which bind at the post-synaptic **receptors**, causing ion-conducting channels to open.
- **Glutamate**: main excitatory neurotransmitter -- bind to AMPA, NMDA, mGlu receptor, induces depolarization.
- **GABA**: main inhibitory neurotransmitter -- GABA receptor, induces hyperpolarization.

## Electrophysiological Recordings



- **intracellular recordings** (commonly *in vitro*, sometimes *in vivo* (anesthetized, paralyzed)) sharp electrode placed inside the neuron patch electrode, sealed to the membrane. view **V<sub>m</sub>**.
- **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 is beginning.





Describing neurons' activity

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- 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?)

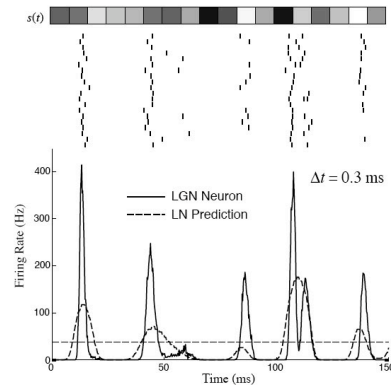
trial 1

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

number of spikes /  $T = r$

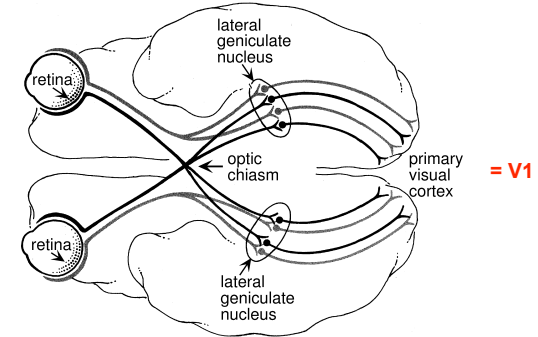
## Describing neurons' activity

- Variability is very large --> statistical measures.
- Average over many trial: trial average rate  $\langle r \rangle$ .



## 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).

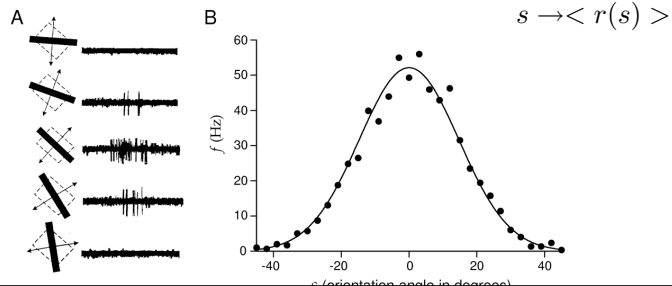


## 1. Modeling the average firing rate $\langle r(s) \rangle$

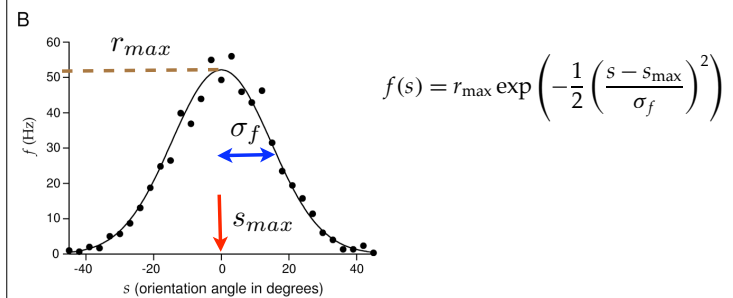
- Focus description on average firing rate  $\langle r(s) \rangle$ .
- **Tuning curves**: modify an aspect  $s$  of the stimulus, and measure  $\langle r(s) \rangle$
- V1 neurons: highly selective to the **orientation** of the stimulus (e.g. bar) flashed in their receptive field.
- Such **bell-shaped (Gaussian-like) tuning curves** are very common in the cortex.

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

<http://www.youtube.com/watch?v=Cw5PKV9Rj3o>



## a) - Gaussian Tuning Curves

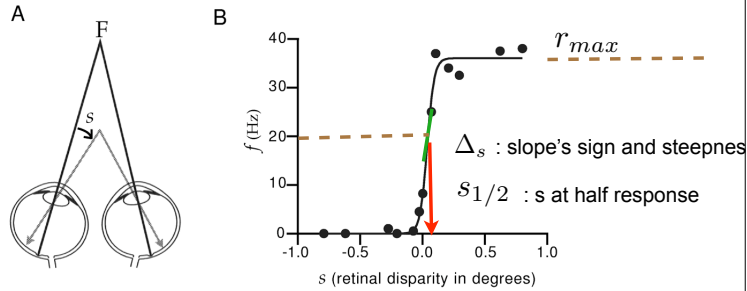


Cells are going to be described by:

- $s_{max}$  : preferred orientation;
- $r_{max}$  : maximal response;
- $\sigma_f$  : tuning curve width (selectivity)

## b) - Sigmoidal response curves

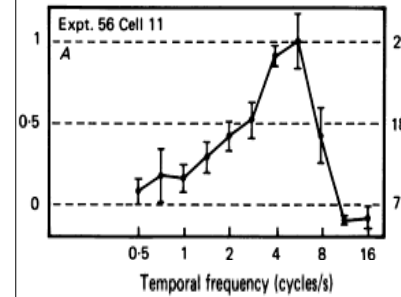
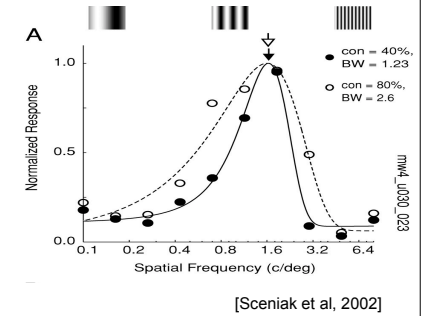
- For some other dimensions, **sigmoidal** or logistic response functions
- E.g. Luminance, Contrast, Retinal Disparity (depth / fixation point).



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

## Stimulus features encoded in V1

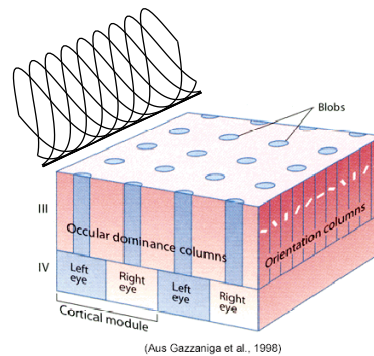
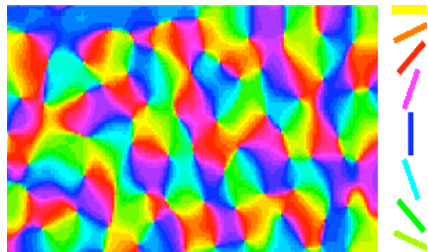
- Many different features are encoded in V1: **spatial position (retinotopy), orientation, direction, contrast, spatial frequency, temporal frequency, color, depth ...**
- a variety of tuning/ response shapes.



[Foster et al, 1985]

## 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**.

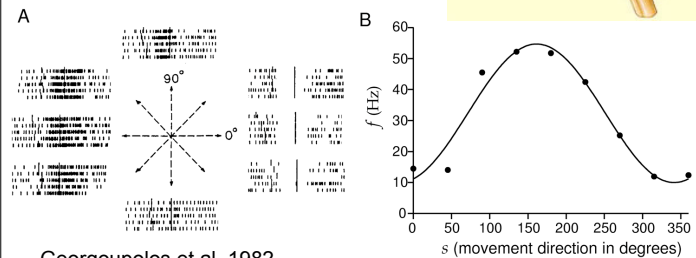
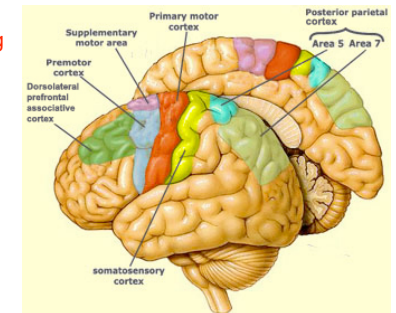


(Aus Gazzaniga et al., 1998)

## Tuning curves everywhere ...

- **Primary motor cortex (M1) -- arm reaching task**
- $\langle r \rangle$  as a function of the direction in which the monkey moved his arm
- Here described as a cosine

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



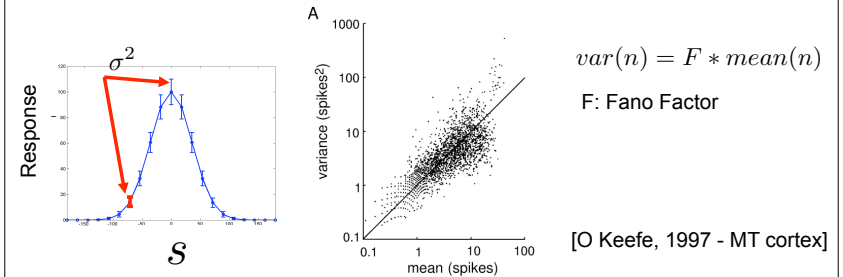
Georgopoulos et al, 1982

## 2. Describing 'the noise'

- Beyond describing only the mean spike count ...
- 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 ( $n=1,2 \dots, 10, 50$  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  $\langle n \rangle = f(s)$  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  $\sim 1$ ).
- Noise is often described as **Poisson**, or **Gaussian with a variance proportional to the mean**.

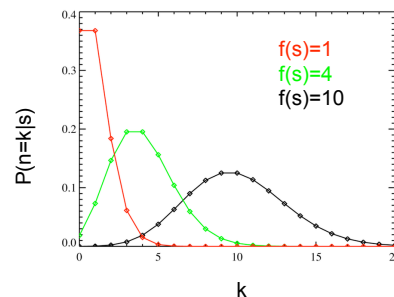


## a) Poisson Distribution

- 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  $f(s)=10$ ,  $P(n=10|s)=0.125$   
 $P(n=7|s)=0.09$   
 $P(n=3|s)=0.007$



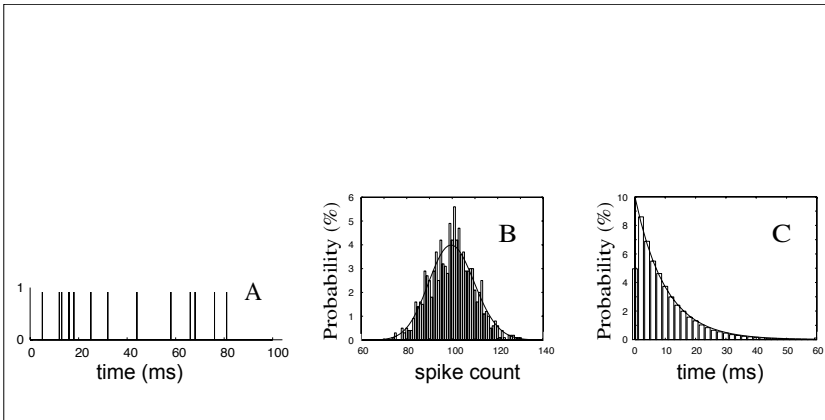
## a) Poisson Distribution

### 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  $P(\text{head})=p$ , if you get a head, record a spike.
- For small  $p$ , the number of spikes in  $T$  follows a Poisson distribution.

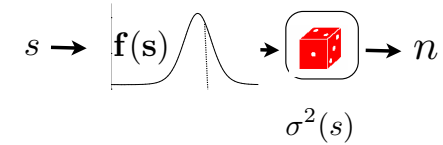
### Properties

- 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.

### b) Gaussian distribution



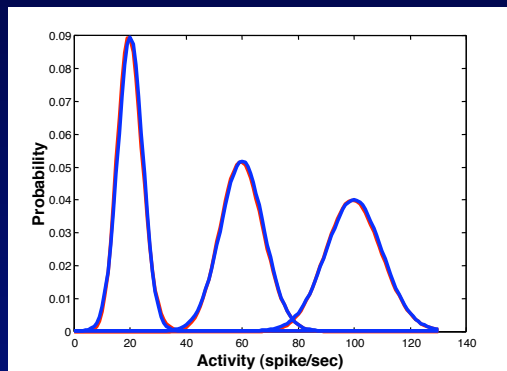
- Another model that is commonly used to describe the variability of the spike count is the **Gaussian noise model**.
- The activity of a neuron (number of spikes) can be described as:

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

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

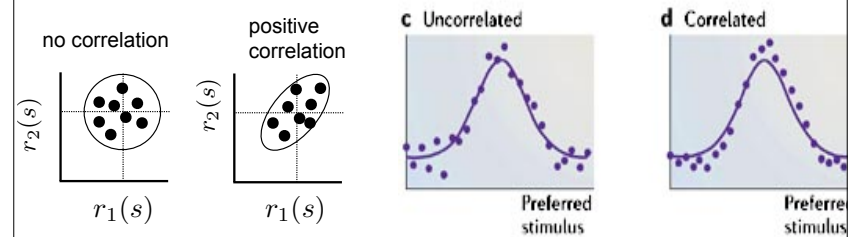
- To mimic a Poisson process, we choose  $\sigma^2(s) = f(s)$

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



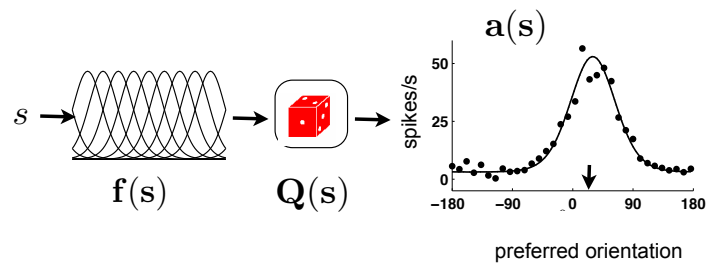
### From one neuron to the population : Describing pair-wise noise correlations

- 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.

## "Tuning Curve + Noise" Population Model



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

$$a_i = f_i(s) + \eta_i(s) \quad \eta(s) = N(0, Q(s))$$

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

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## Where does the noise come from?

- Is this 'Poisson' variability really noise? (unresolved, yet critical question)
- Where could it come from?
- Probably not in the sensory inputs (e.g. random arrival of photons)
- Probably not in the spike initiation mechanism (Mainen and Sejnowski 1995)
- Probably not in the stochastic nature of opening / closing of ion channels
- Probably not in the unreliable synapses (spontaneous AP, spontaneous release of vesicles, variability in size of PSPs).

## Where does the noise come from?

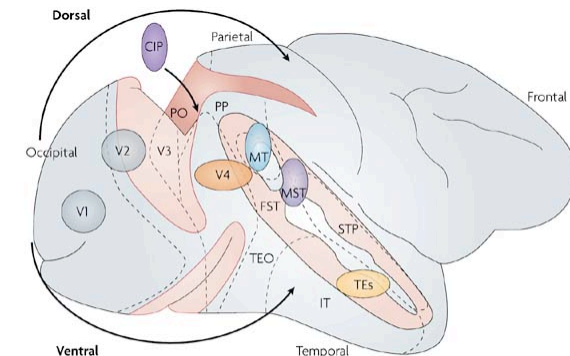
- Neurons embedded in a recurrent network with sparse connectivity and **balance between excitatory and inhibitory inputs** tend to fire with Poisson statistics (Van vreeswijk and Sompolinsky, 1997)
- a consequence of using **steady signals** (Mainen and Sejnowski, 1995, Butts et al 2007).
- Variability could offer distinct **advantages** (eg. enhance weak signals, encoding and manipulating uncertainty (Pouget))

Further reading: Neuronal variability: noise or part of the signal? Stein et al, Nature Rev Neuroscience, 2005.

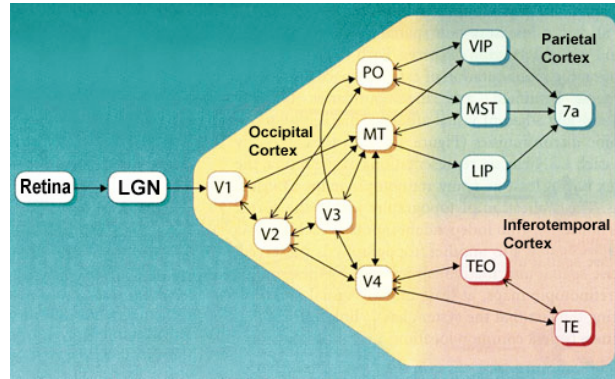
## Overview of the visual cortex

Two streams:

- **Ventral 'What'**: V1, V2, V4, IT, **form recognition and object representation**
- **Dorsal 'Where'**: V1, V2, MT, MST, LIP, VIP, 7a: **motion, location, control of eyes and arms**

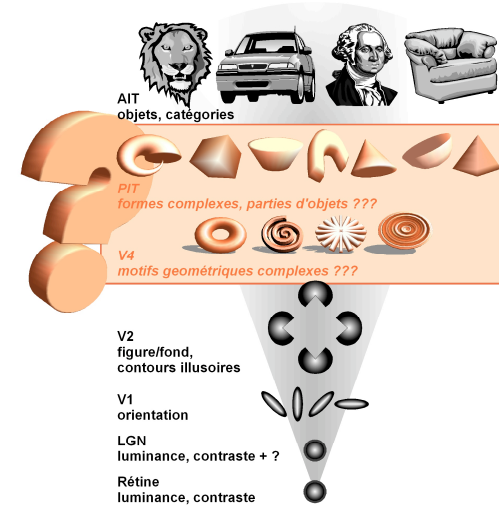


## Overview of the visual cortex



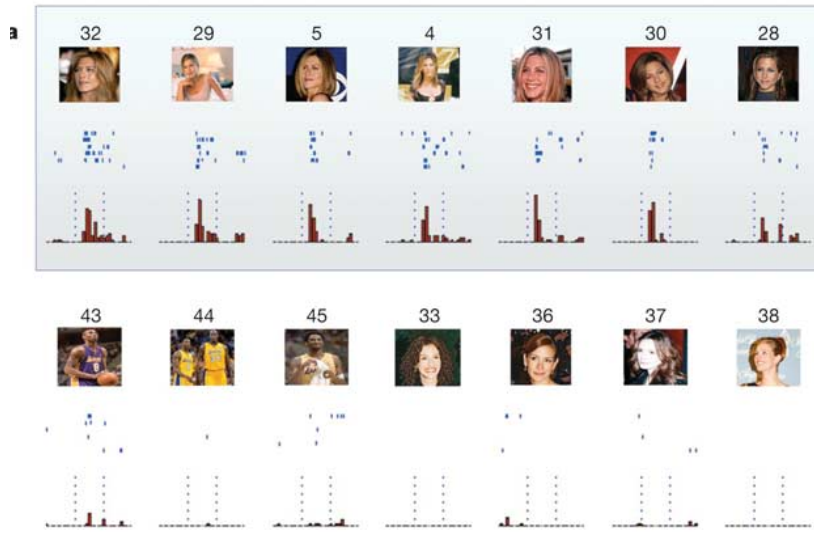
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## Ventral pathway



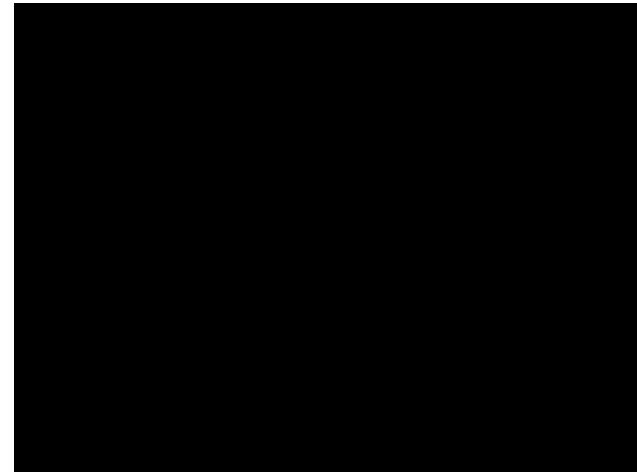
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Quiroga et al, *Nature*, 2005 -- Invariant visual representation by single neurons in the human brain (MTL), a.k.a **the Jennifer Aniston Neuron**.



## Dorsal pathway

- **MT: MOTION**. stimulus of choice: random dot patterns.



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## Dorsal pathway

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- **MST**: linear, radial, circular motion (flow field).
- **LIP**: spatial position in head-centered coordinates. spatial attention, spatial representation. saliency map -- used by oculo-motor system (the "saccade planning area"). spatial memory trace and anticipation of response before saccade.
- **VIP**: spatial position in head-centered coordinates, multi-sensory responses. speed, motion.
- **7a**: large receptive fields, encode both visual input and eye position.

