# Computational Neuroscience

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# Ribeirão Preto, SP, pop. ~703,000 (2019), alt. 547 m (1,791 ft)


Campus of USP Ribeirão Preto


Laboratory of Neural Systems – www.sisne.org

# Part 0

## Presentation of Computational Neuroscience

# Neuroscience: fast-growing young science

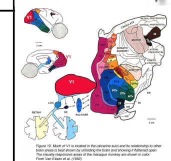
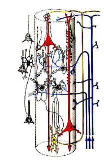
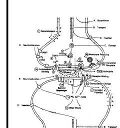
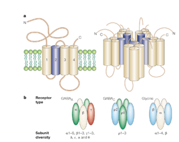
- Neuron discovery:
  1889, Ramon y Cajal

- Concept of synapse:
  1897, Sherrington
- 1st "official" use of the term *neuroscience*, *circa* 1965
- 1st *Society for Neuroscience* (SfN) congress: 1971 (1100 participants)
- 50th SfN congress: 2019 (~30,000 participants)

# Brain: complex system

- **~86 billion** neurons
- **Trillions** of synapses

# Brain: many (interrelated) levels of organization

| | | |
|---|---|---|
| $\sim$10cm | Whole brain |  |
| $\sim$1cm | Brain structure/cortical areas |  |
| 100$\mu$m- 1mm | Local network/‘column’/‘module’ |  |
| 10$\mu$m- 1mm | Neuron |  |
| 100nm- 1$\mu$m | Sub-cellular compartments |  |
| $\sim$10nm | Channel, receptor, intracellular protein |  |

# Brain: lots of data, poor understanding

**<u>Types of data</u>**:

- Anatomical: cell shapes, connections
- Physiological: bioelectrical properties
- Biochemical: molecular processes
- Psychological: behavior
- Recent techniques: molecular biology, imaging, optogenetics, **mathematical and computational modeling**

- *In vitro*

- *In vivo*

- *In silico*

# Computational Neuroscience

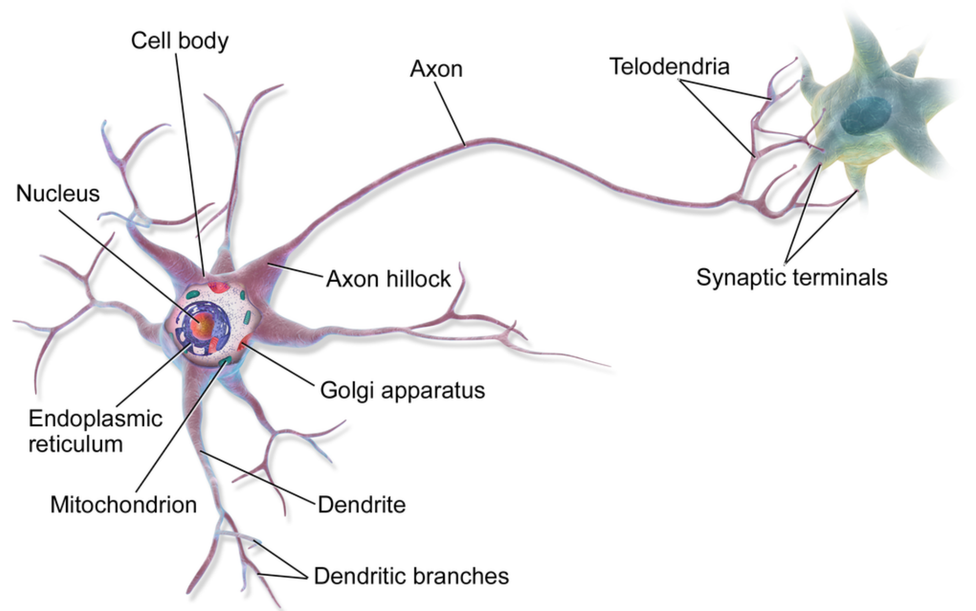
- Theoretical part of neuroscience: also called theoretical neuroscience
- Objective: to determine and articulate the principles and mechanisms behind the functioning of the nervous system
- It is assumed that this functioning involves "computations"
- Due to their complexity, most models are explored with the use of computer simulations

# Part 1

## Basic Concepts

# Neuron

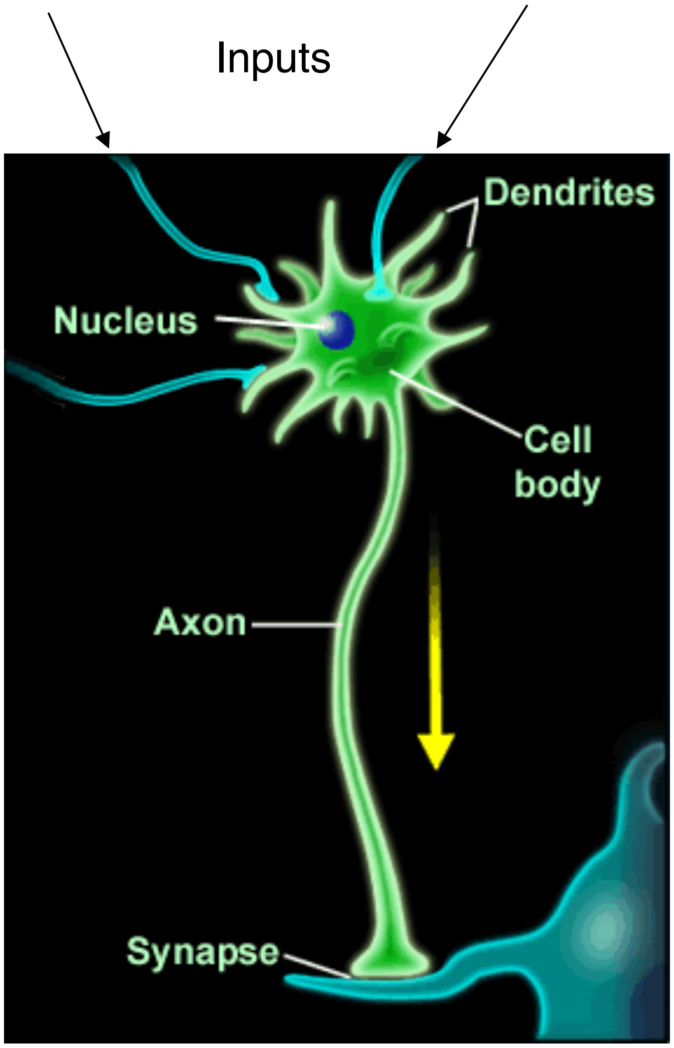
- The brain is made of isolated cells – neurons and glia –, which are structurally, metabolically and functionally independent.
- **Neuron doctrine** (Ramon y Cajal, 1894): The neuron is the **basic functional unit of the nervous system**
- Neurons are specialized for intercellular communication



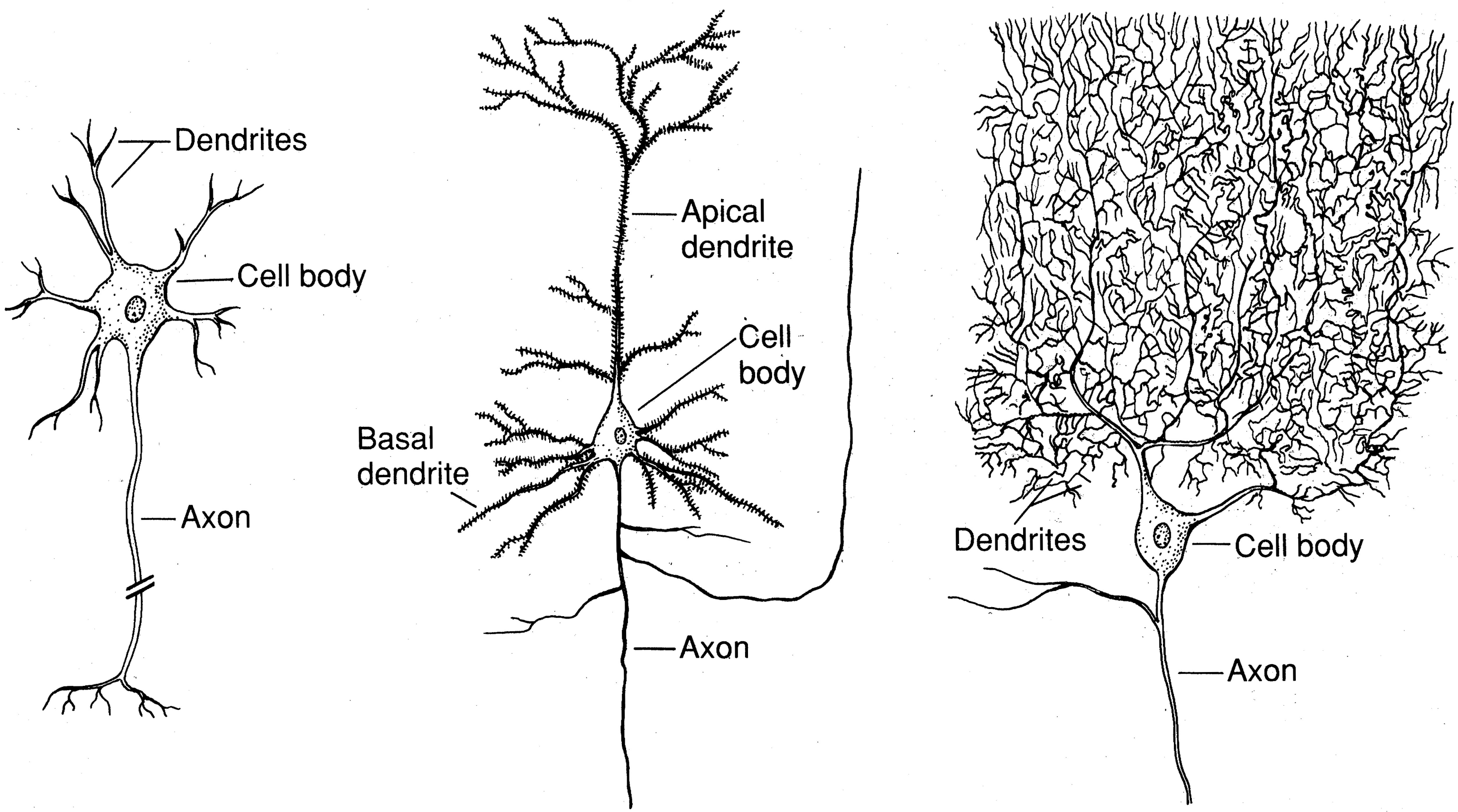

https://en.wikipedia.org/wiki/Neuron

# Structure of a neuron

- A typical neuron consists of three main parts:
- Dendrites: receive and process inputs
- Soma (cell body): integrates inputs
- Axon: generates output (at the initial segment) and transmits it to target neurons
- The connection from an axon of one neuron to a dendrite of another neuron is called a synapse



# Variability of neuronal structures



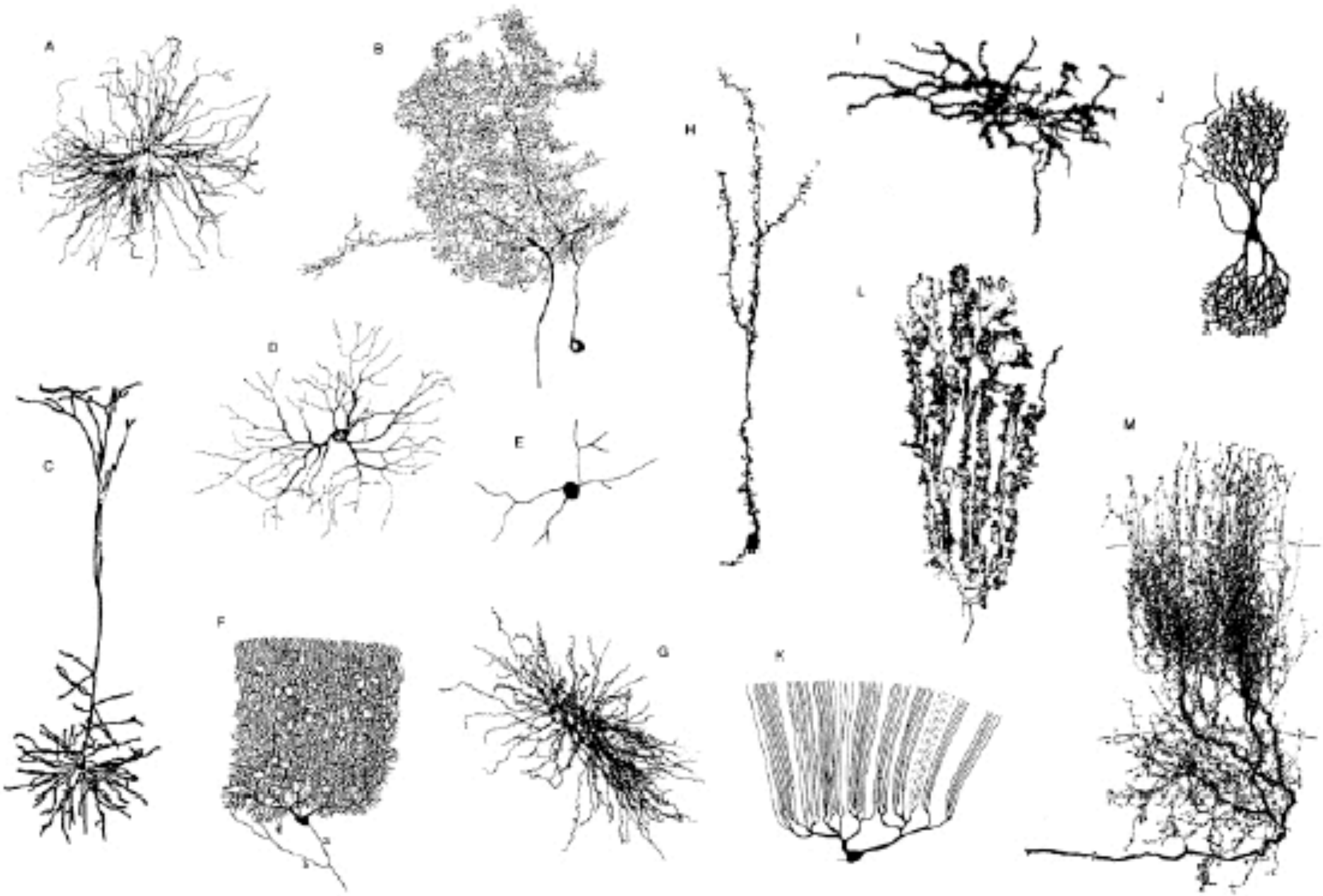

Spinal motor neuron

Hippocampal pyramidal cell

Purkinje cell of cerebellum

In addition to synapses from axons onto dendrites, there are also synapses from axons onto cell bodies (somata) and onto other axons.

# More neuronal structures

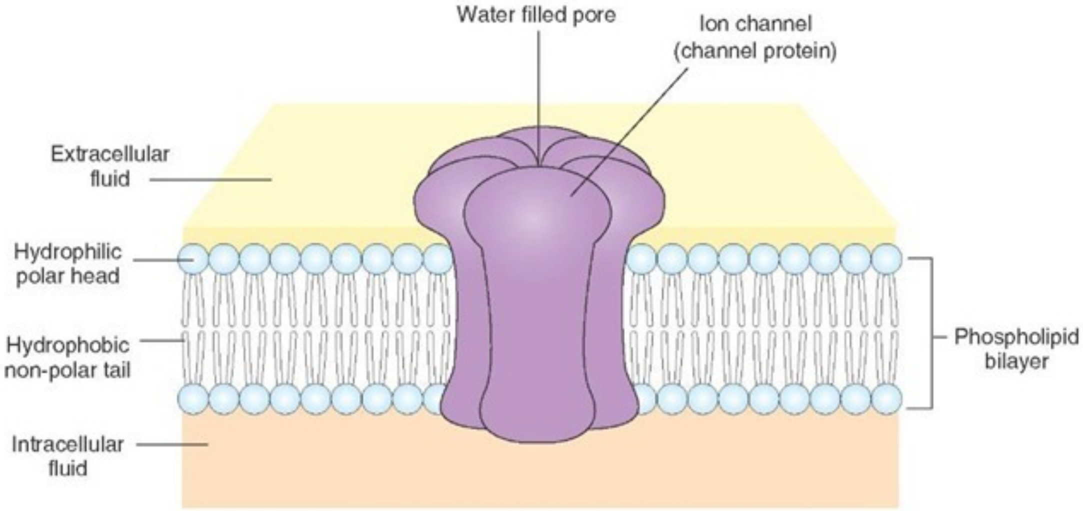



The functional implications of these different structures are still not clear!

# Neural circuits and networks

# Neuronal Membrane

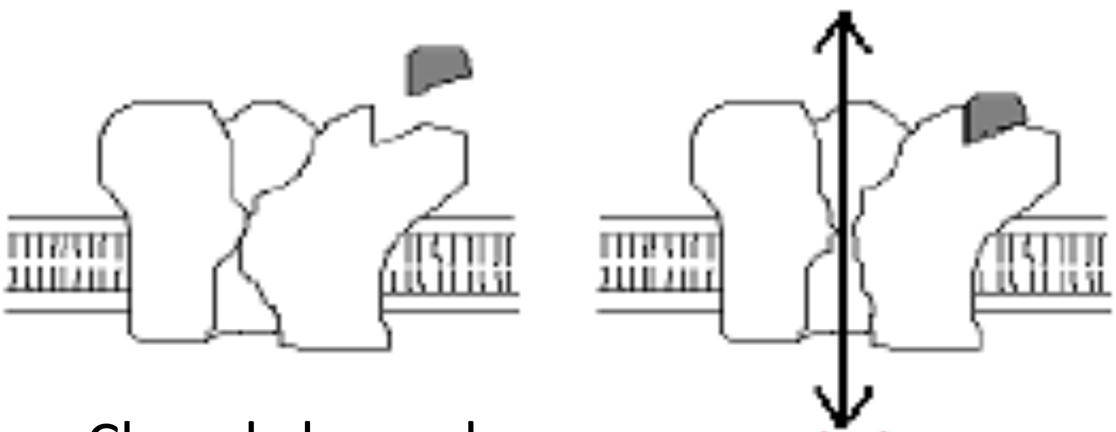
- Thin membrane (60-70 Å) that separates the cytoplasm from the extracellular space
- Made of a lipid bilayer in which proteins are immersed
- Some proteins cross the membrane forming ion channels




http://what-when-how.com/neuroscience/electrophysiology-of-neurons-the-neuron-part-1/

# Ion channels

- Membrane proteins may undergo conformational changes under electrical and chemical control, thus regulating ionic flux
- The figure below illustrates a channel opening due to a protein-ligand binding

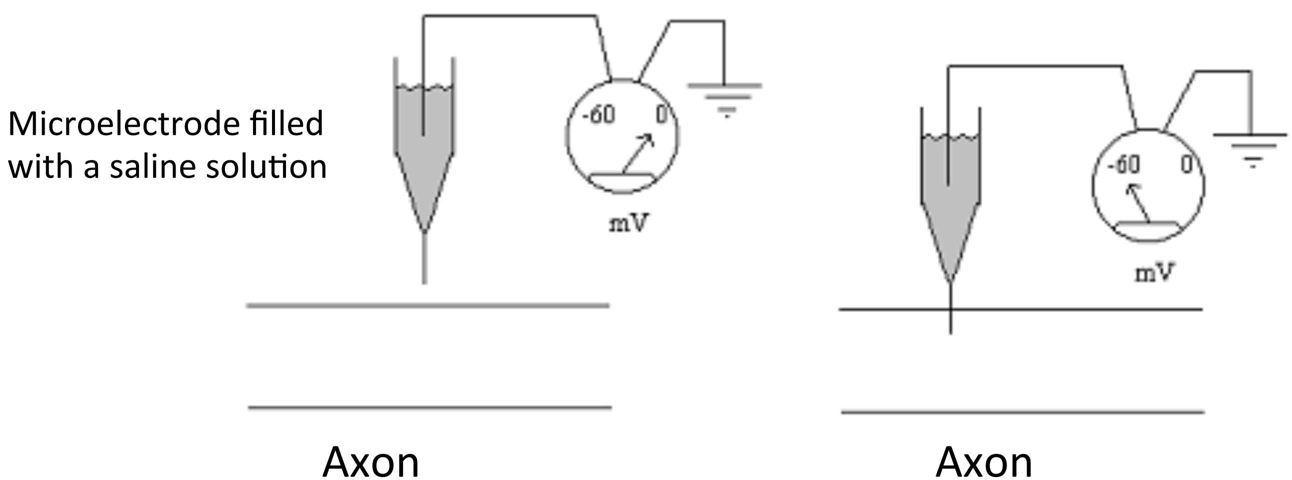


Closed channel

Open channel

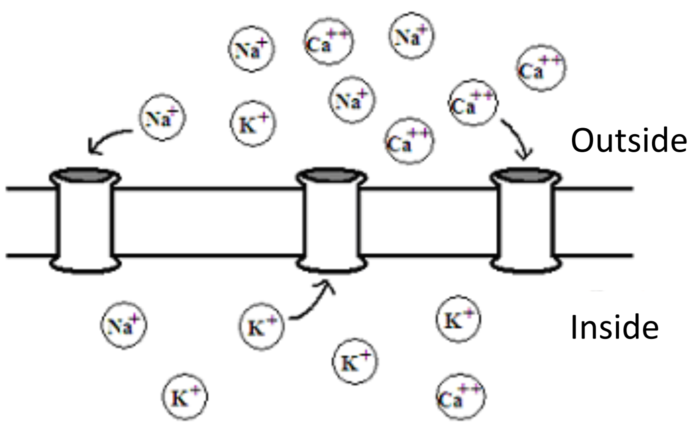
# Membrane potential

- There is a difference of electrical potential between the two sides of the neuronal membrane
- Defining the zero of potential at the outside the inside is, in general, at a potential of –50 to –90 mV



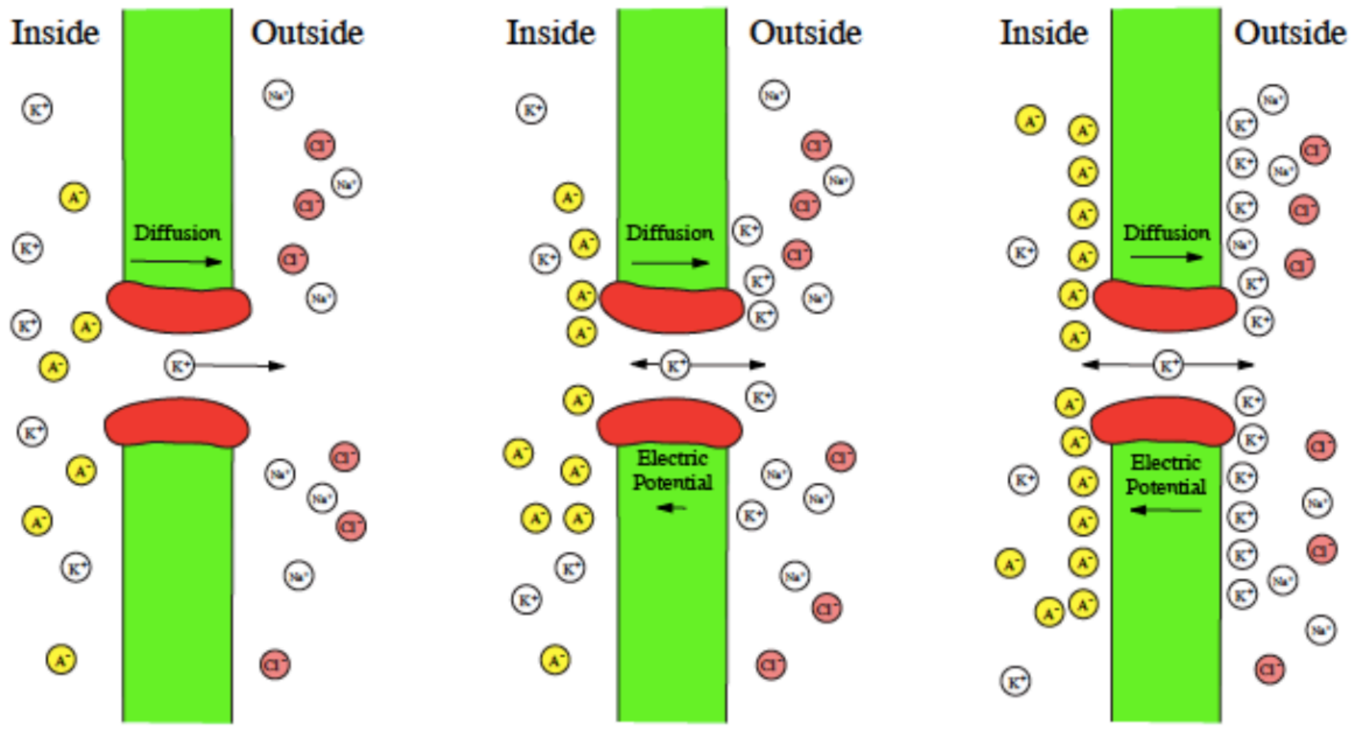
# Ionic concentrations

- Ion concentrations are different on the two sides of the neuronal membrane




| Ion | In (mM) | Out (mM) |
|---|---|---|
| **Frog muscle (20°C)** | | |
| $K^+$ | 124 | 2,25 |
| $Na^+$ | 10,4 | 109 |
| $Cl^-$ | 1,5 | 77,5 |
| $Ca^{2+}$ | $10^{-4}$ | 2,1 |
| **Squid giant axon (20°C)** | | |
| $K^+$ | 400 | 20 |
| $Na^+$ | 50 | 440 |
| $Cl^-$ | 40-150 | 560 |
| $Ca^{2+}$ | $10^{-4}$ | 10 |
| **Typical mammalian cell (37°C)** | | |
| $K^+$ | 140 | 5 |
| $Na^+$ | 5-15 | 145 |
| $Cl^-$ | 4 | 110 |
| $Ca^{2+}$ | $10^{-4}$ | 2,5 - 5 |

# Origin of the membrane potential



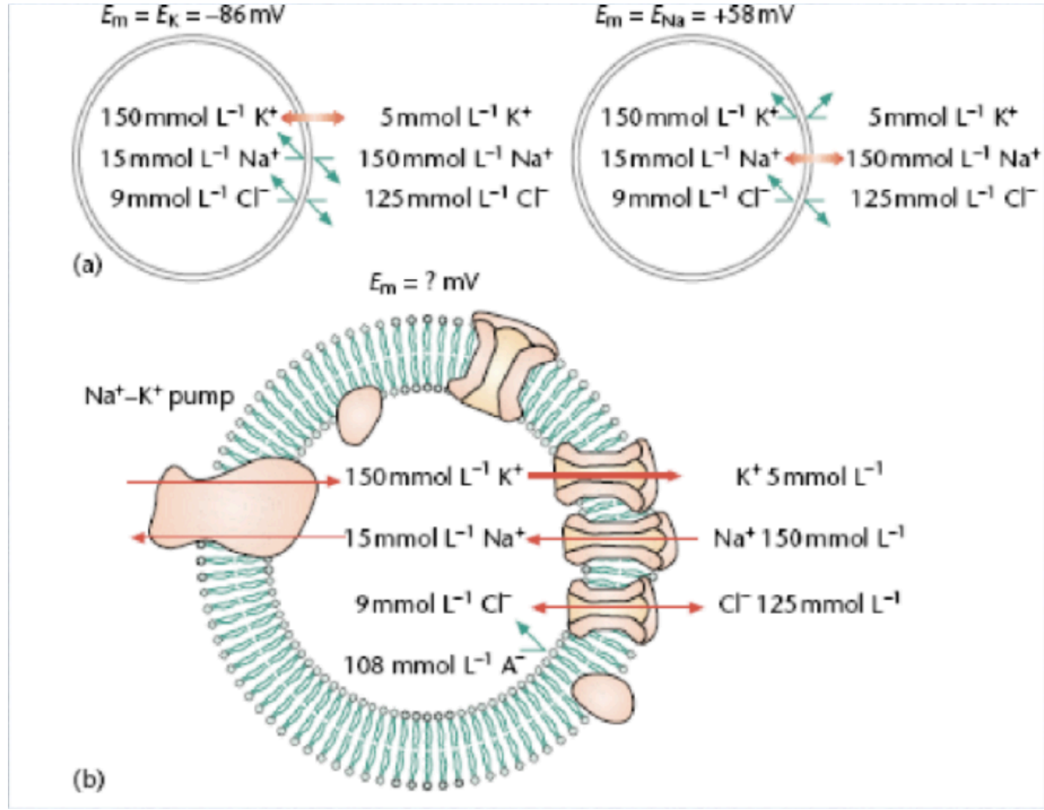

- Nernst potential

$$E = \frac{RT}{zF} \ln \frac{[C]_{out}}{[C]_{in}}$$

| | Inside (mM) | Outside (mM) | Equilibrium protential (Nernst) |
|---|---|---|---|
| **$K^+$** | 400 | 20 | -75 mV |
| **$Na^+$** | 50 | 440 | +55 mV |
| **$Cl^-$** | 40-150 | 560 | -66 a -33 mV |
| **$Ca^{2+}$** | $10^{-4}$ | 10 | +145 mV |
| **$A^-$ (organic ions)** | 385 | — | — |

Squid giant axon at 20°C

# Multi-ion equilibrium




Goldman-Hodgkin-Katz equation

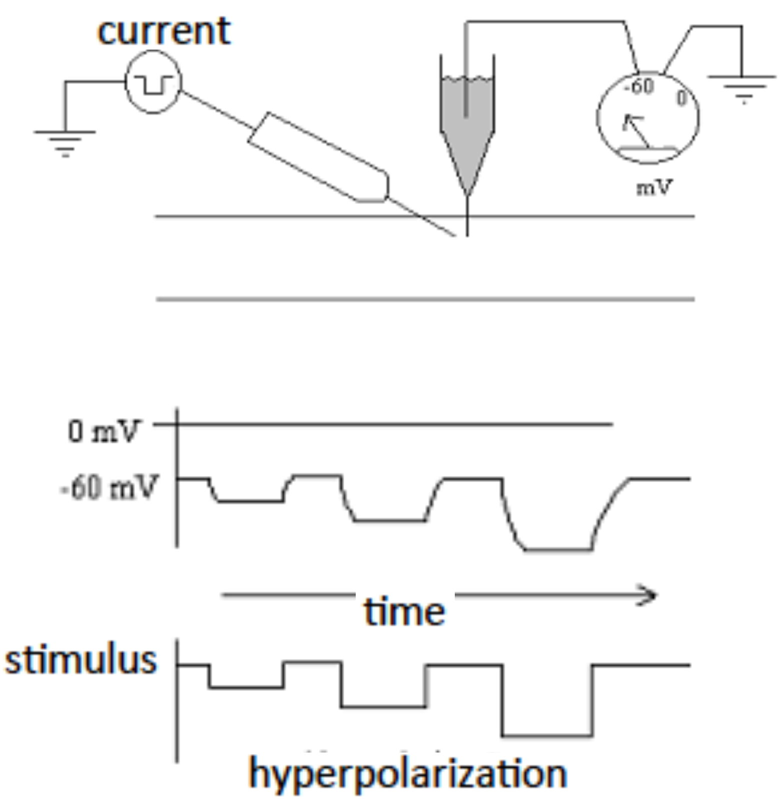
$$V = \frac{RT}{F}\ln\frac{[K^+]_{out} + (P_{Na}/P_K)\,[Na^+]_{out} + (P_{Cl}/P_K)\,[Cl^-]_{in}}{[K^+]_{in} + (P_{Na}/P_K)\,[Na^+]_{in} + (P_{Cl}/P_K)\,[Cl^-]_{out}}$$

$P_X$ = permeability of ion X

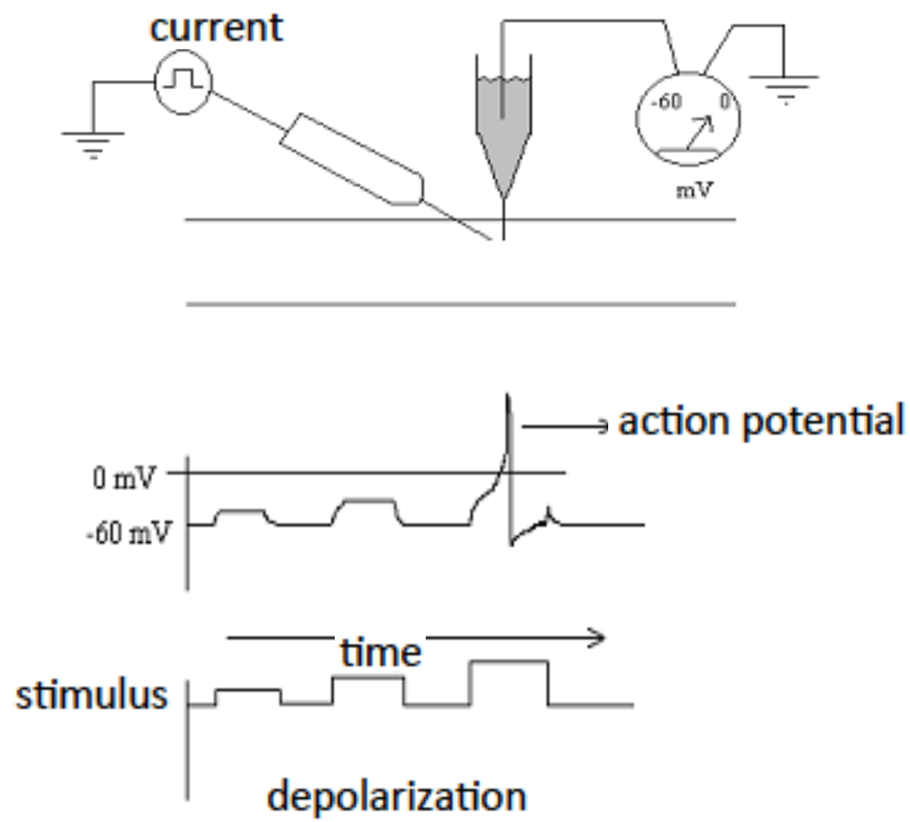
$(P_{Na}/P_K) = 0.03$; $(P_{Cl}/P_K) = 0.1 \rightarrow V = -70$ mV

Squid giant axon at 20°C

# Depolarization and hyperpolarization



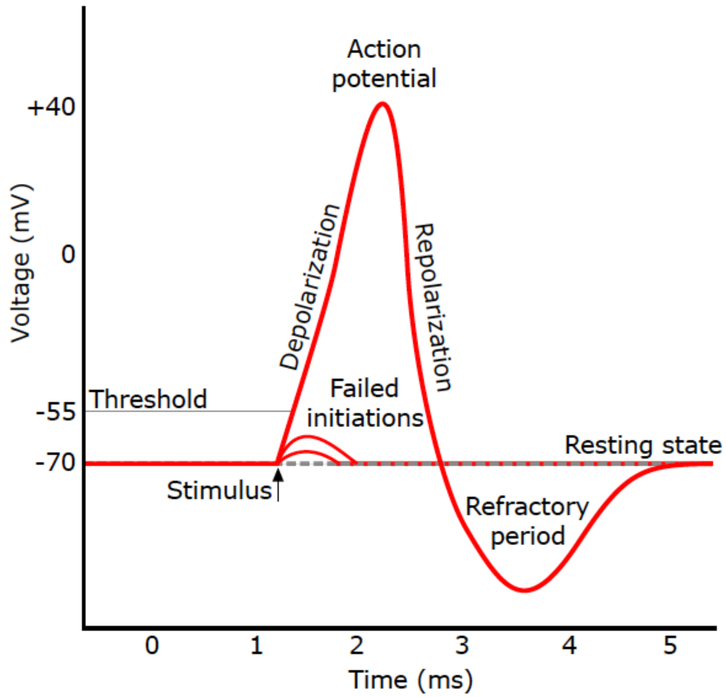

Graded variation




Action potential

# Action potential (spike)

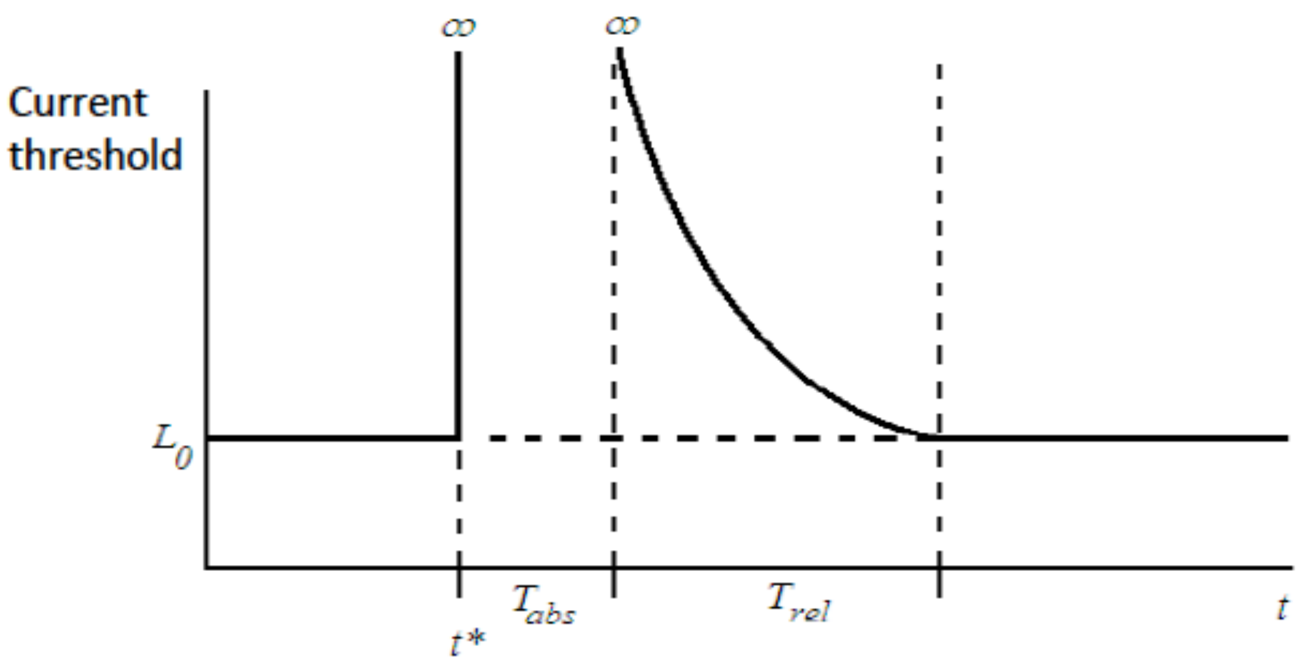
- Shape (width and amplitude) characteristic of each neuron
- Threshold phenomenon (all or none)
- Propagates unchanged along the axon while subthreshold voltage fluctuations are strongly attenuated




https://commons.wikimedia.org/wiki/File:Action_potential.svg#/media/File:Action_potential.svg

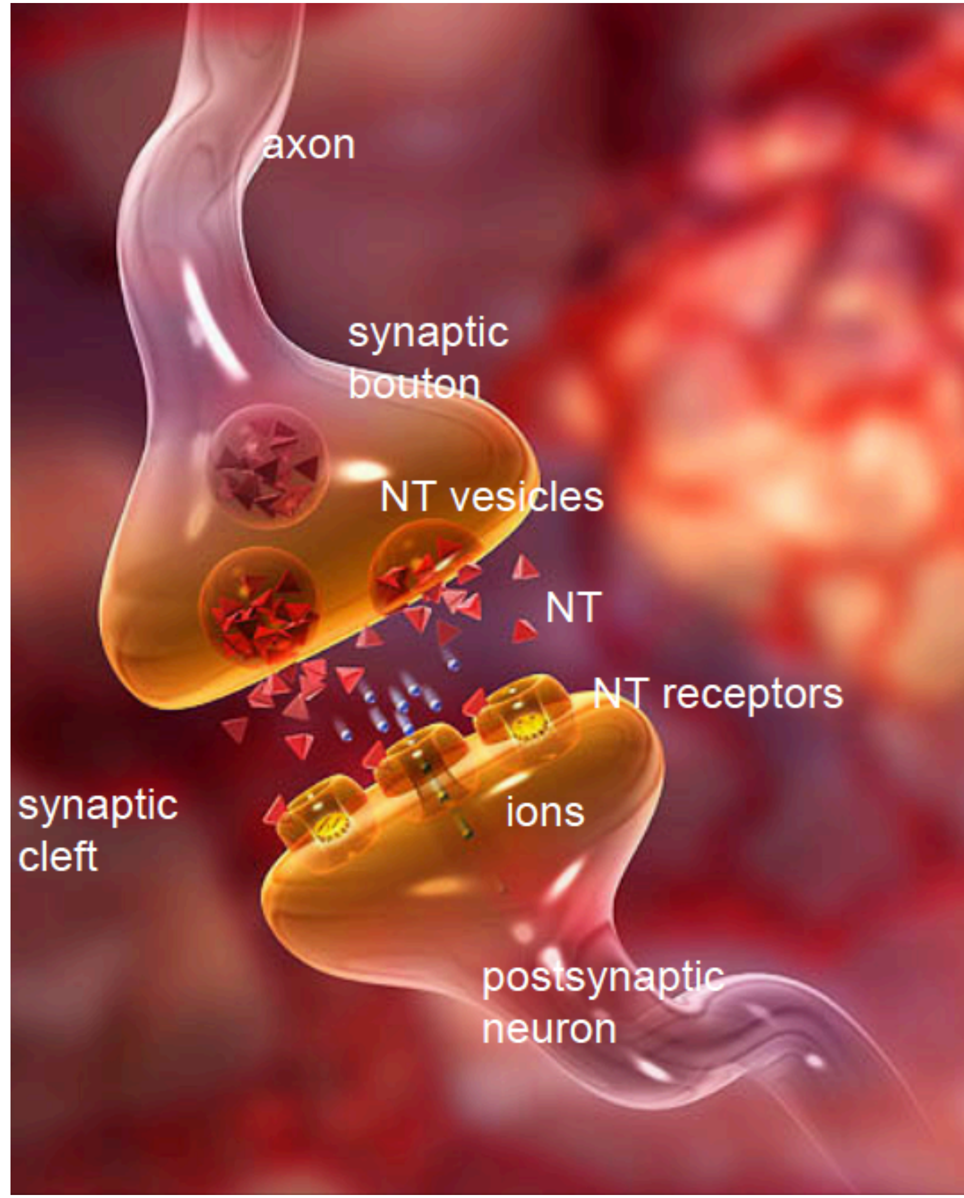
# Refractory periods

- **Absolute**: period during which a second stimulus (no matter how strong) will not lead to a second spike. It is as if the spike threshold were infinite
- **Relative**: period during which a second spike can be generated by a second stimulus stronger than the first. The strength of the second stimulus decays with time



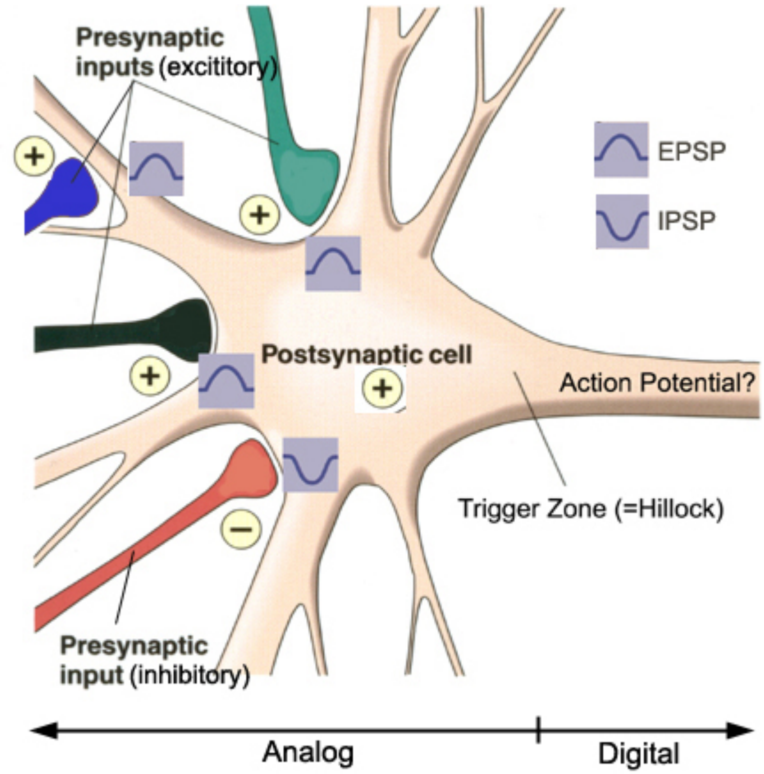
# Chemical transmission across synapses

- The spike propagates down the axon of presynaptic neuron to synaptic boutons that make contact with postsynaptic neurons.
- When the spike arrives at the synapse, a neurotransmitter substance is released from stored vesicles.
- The neurotransmitter diffuses across the synaptic cleft and binds to receptor proteins on the postsynaptic membrane.
- Many neurotransmitter receptors are ion channels. Binding of neurotransmitter opens them and results in an inward or outward flow of ions. This generates a postsynaptic potential (PSP) in the postsynaptic neuron.



# Postsynaptic potentials

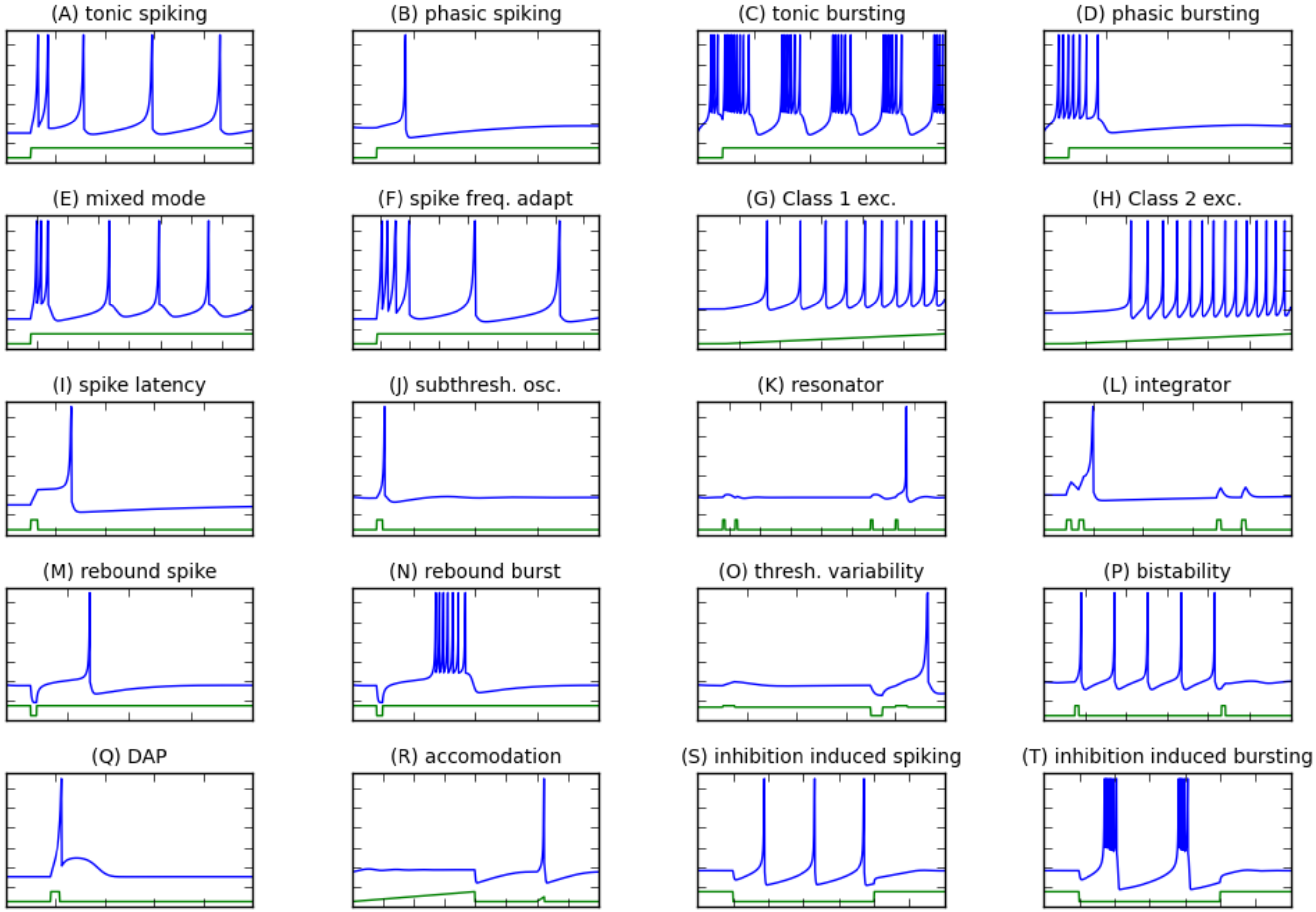
- The postsynaptic potentials (PSPs) spread along the dendrites towards the soma and axon hillock where they can result in firing of an action potential.
- PSPs can be excitatory (EPSPs, increase the probability of firing) or inhibitory (IPSPs, decrease it).
- The summation of a number of EPSPs is necessary to generate an action potential.




EPSP: excitatory postsynaptic potential
IPSP: inhibitory postsynaptic potential

# Neuronal firing patterns

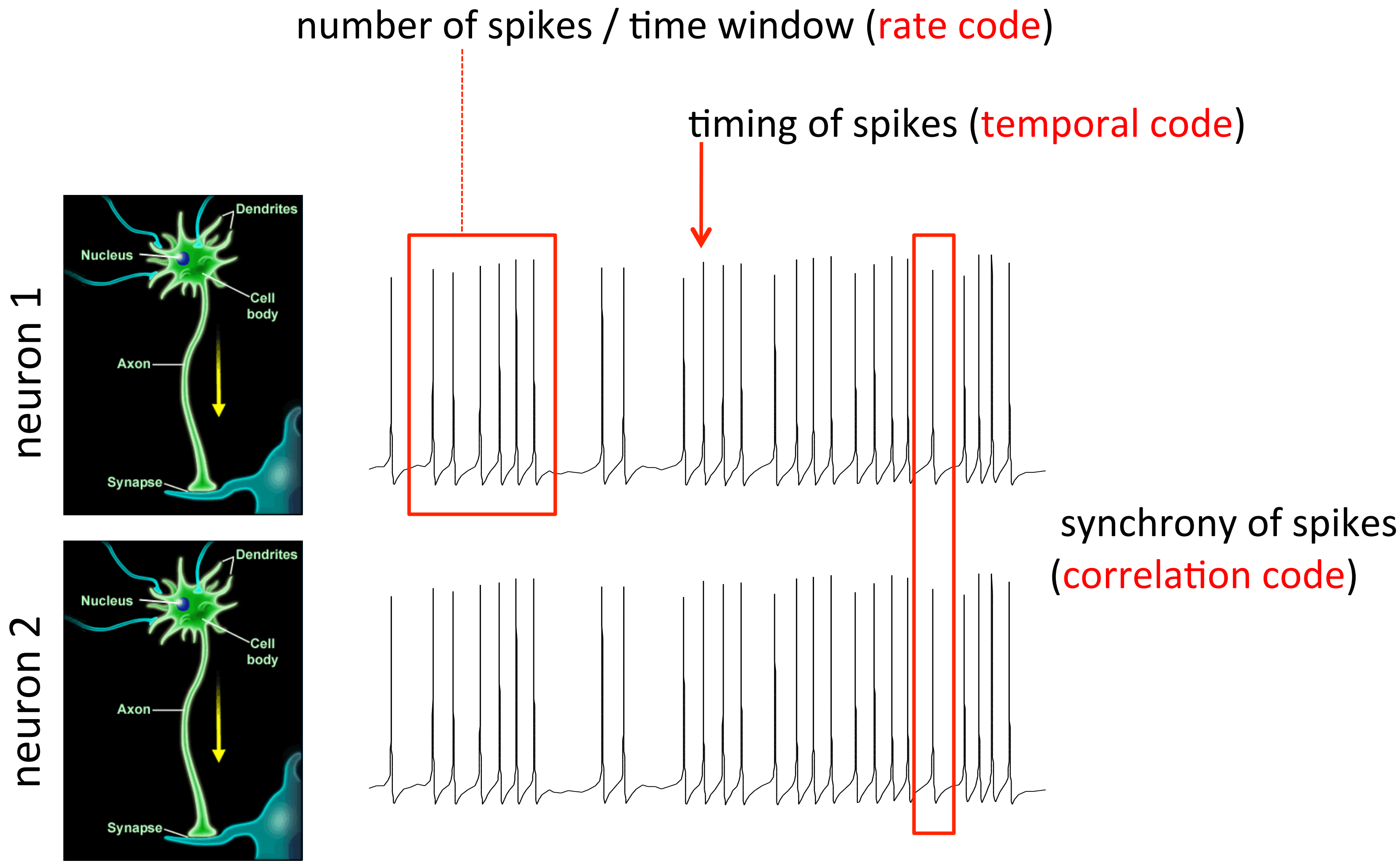
Different types of neurons fire different patterns of action potentials in response to synaptic input and application of electrical current.




How are these firing patterns used to transmit information?

# Neural coding

Spike trains can be used to represent information by the mean rate of spikes (rate coding), the timing of spikes (temporal coding), and the synchrony of spikes (correlation code).



# Examples of rate coding

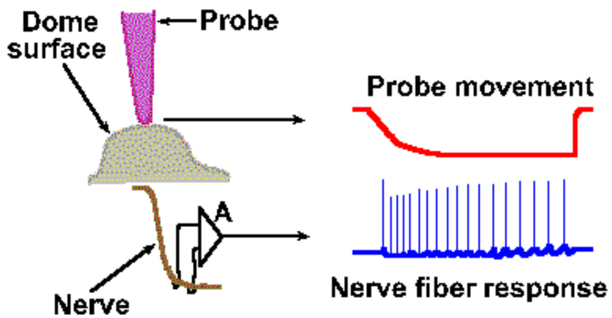



**Fig. 4-8a.** An example of a frequency code. The physical setup of the experiment illustrates how the probe is positioned over the receptor structure and how the discharges of the nerve fiber are recorded. At the right, typical response from the fiber (lower trace) to prolonged displacement (upper trace) of the receptor surface (downward deflection of the trace indicates a downward movement of the probe). Entire record is 40 msec in duration.

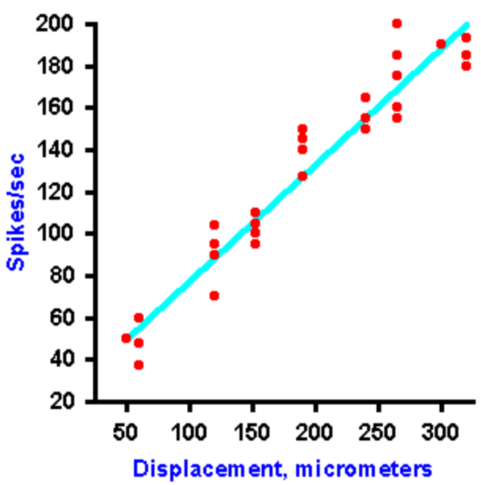
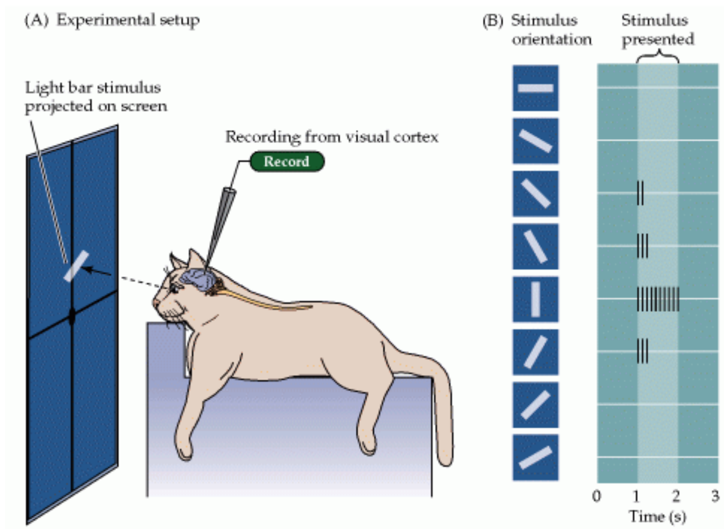
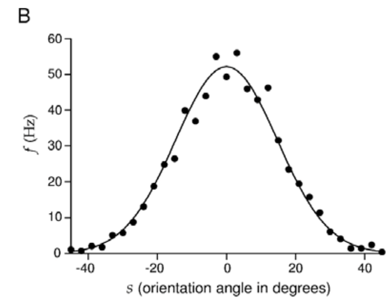


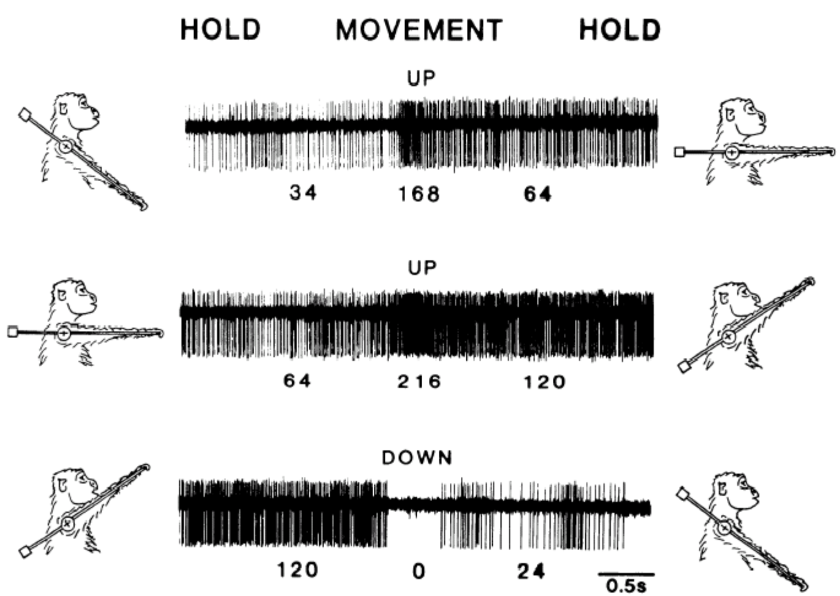

**Fig. 4-8b.** A plot of the frequency of discharge of the fiber against the amount of displacement of the receptor. Notice that the amount of displacement is coded as a linear function of the frequency of discharge (Data from Tapper DN: *Trans NY Acad Sci* 26:697-701, 1964).

Skin pressure receptor



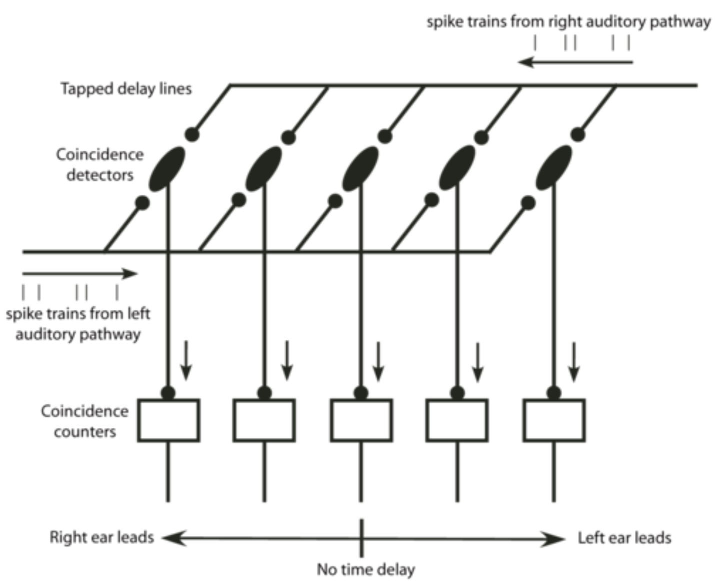




Orientation-selective cells in visual cortex




Movement direction cells in the cerebellum

# Examples of temporal coding




Echolocation in bats

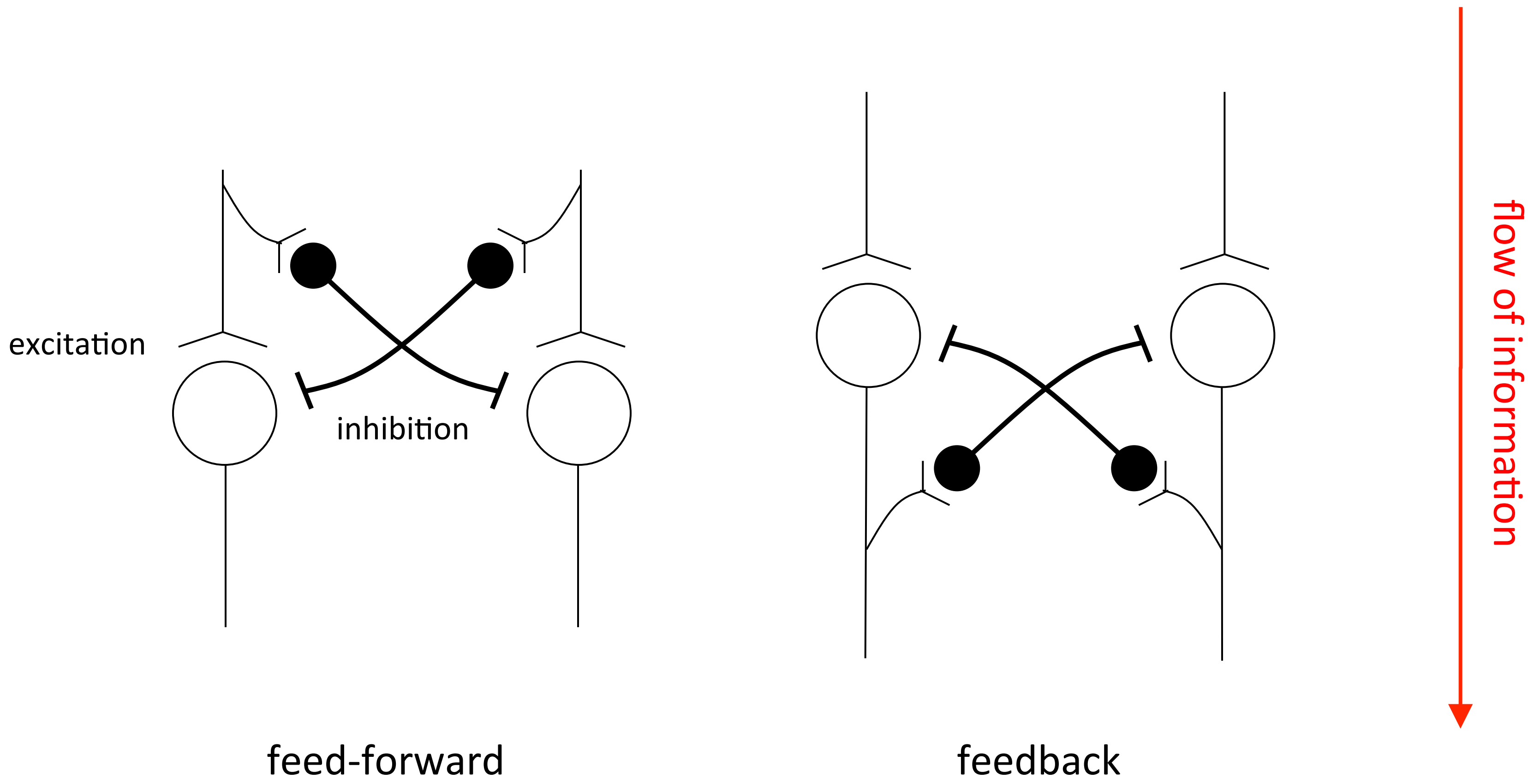
Binaural sound localization

# Example of correlation coding

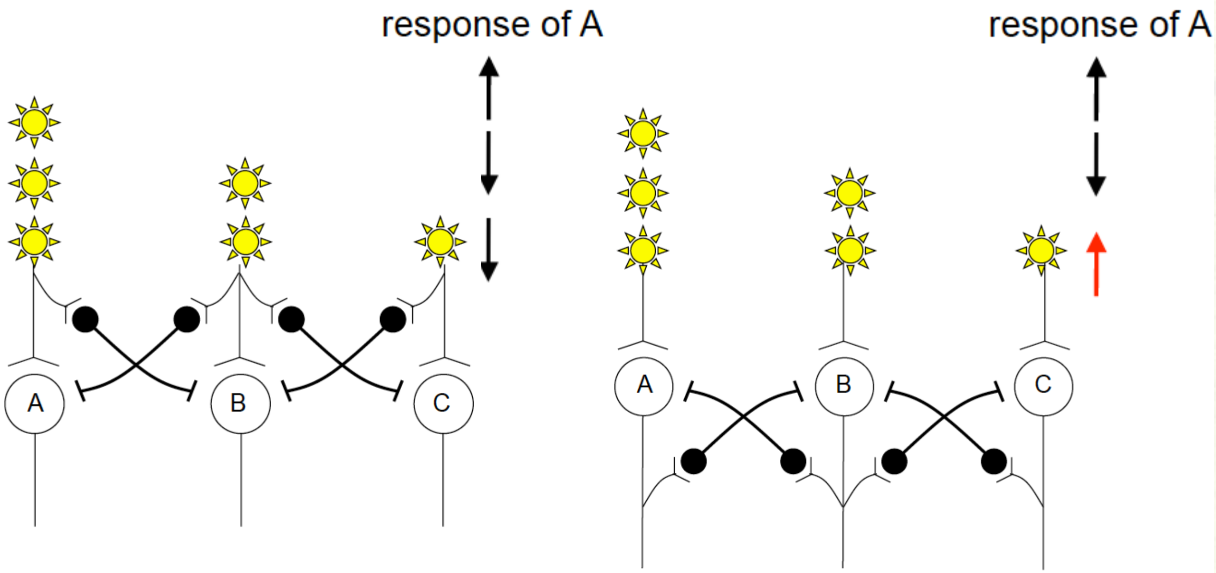
The binding problem

# Mechanisms: lateral inhibition

Lateral inhibition can be implemented by feed-forward or feedback circuits.

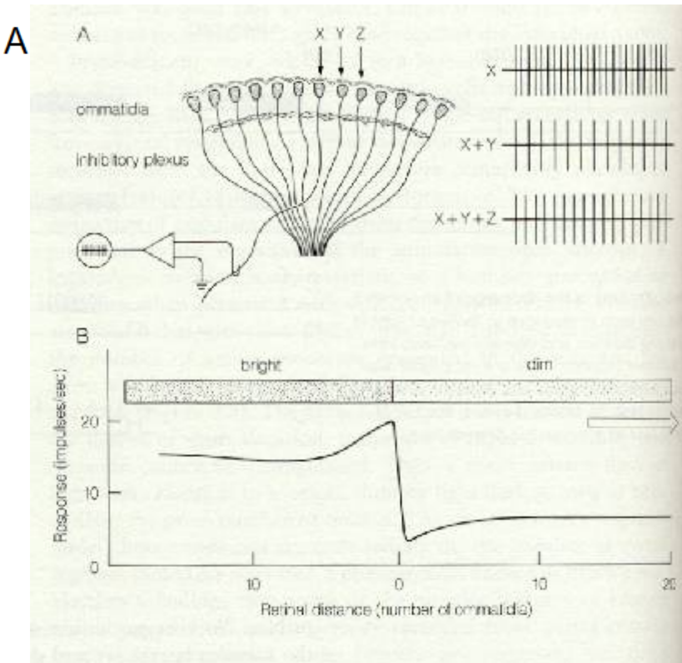


# Lateral inhibition in the *Limulus* eye




feed-forward

feedback

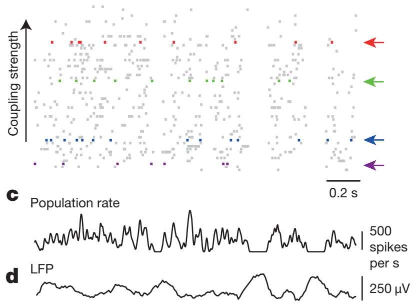


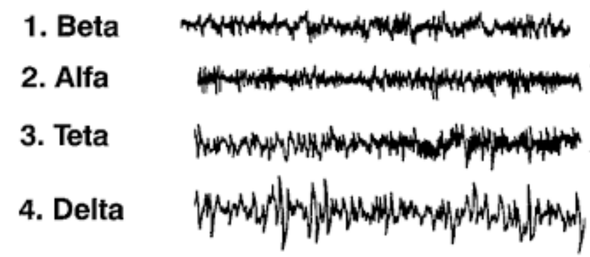

Limulus (horseshoe crab) eye is made of ommatidia that can be stimulated independently: experiments by Ratliff & Hartline (1956)

Ratliff and Hartline observed increase in activity of A when the third ommatidium (C) was stimulated.

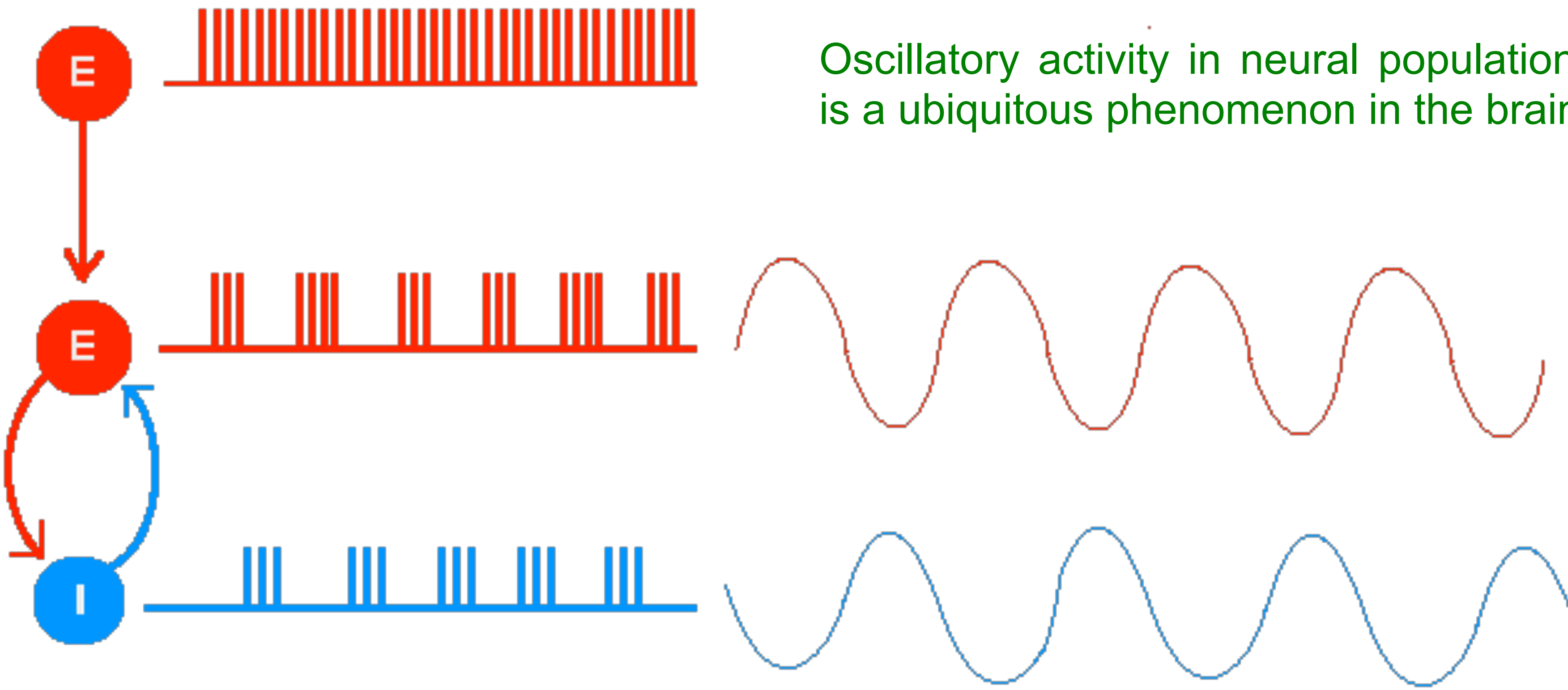
This indicated that lateral inhibition is implemented by a feedback circuit.

# Mechanisms: oscillations



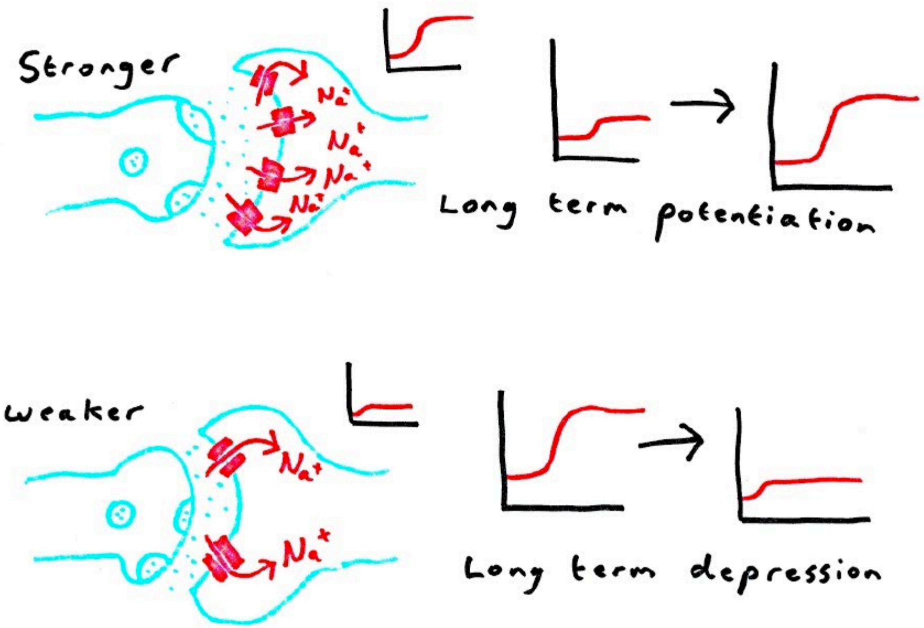




Oscillatory activity in neural populations is a ubiquitous phenomenon in the brain.



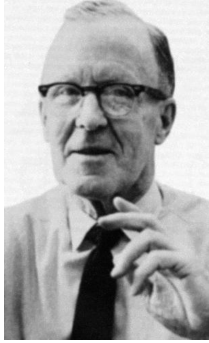
# Synaptic Plasticity

- Generic name given to any type of change (strengthening or weakening) in the efficacy of a synapse
- Synaptic plasticity can be of short or long duration
- Hypothetical mechanism underlying memory formation and learning

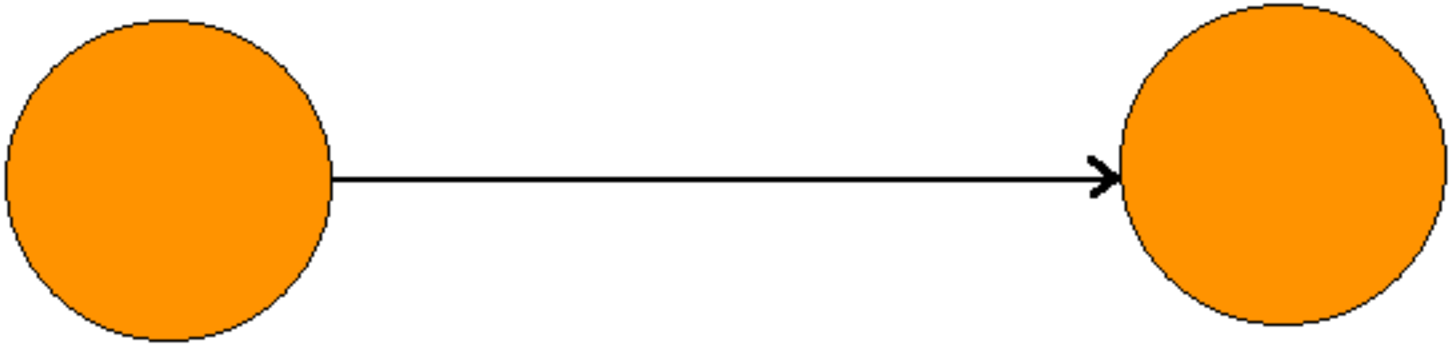



https://qbi.uq.edu.au/brain-basics/brain/brain-physiology/long-term-synaptic-plasticity

# Hebbian plasticity

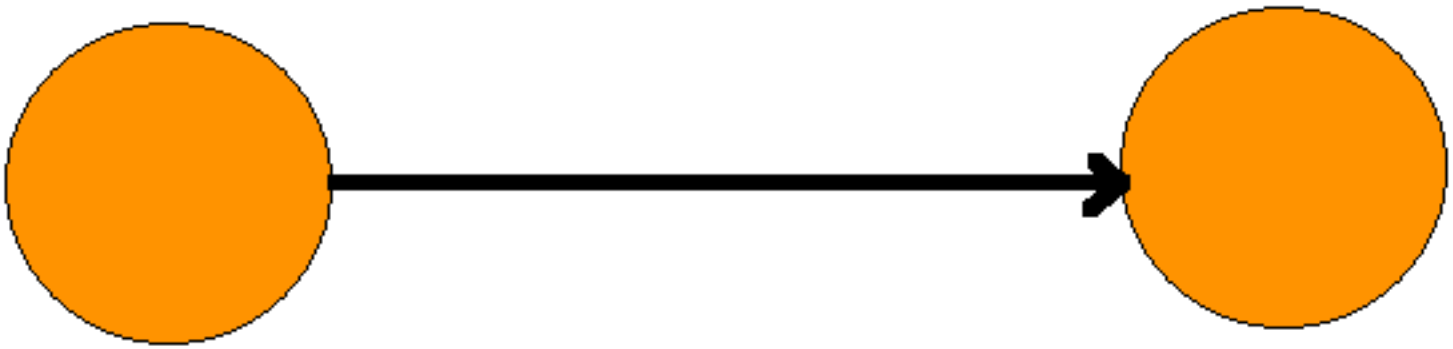


Donald Hebb



# Hebbian plasticity

# Hebbian plasticity



# Hebbian plasticity

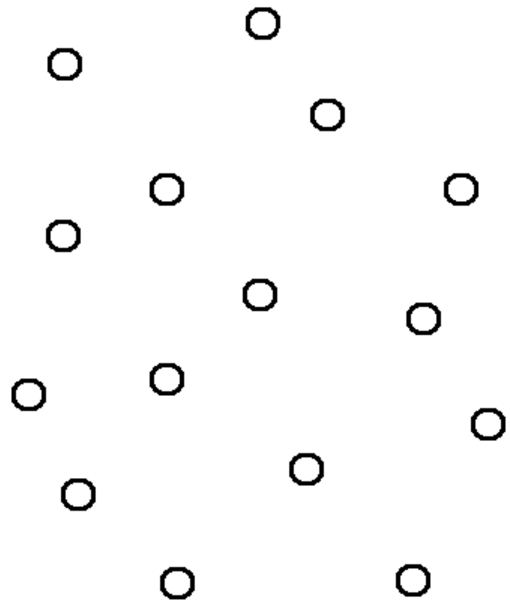
# Hebbian plasticity

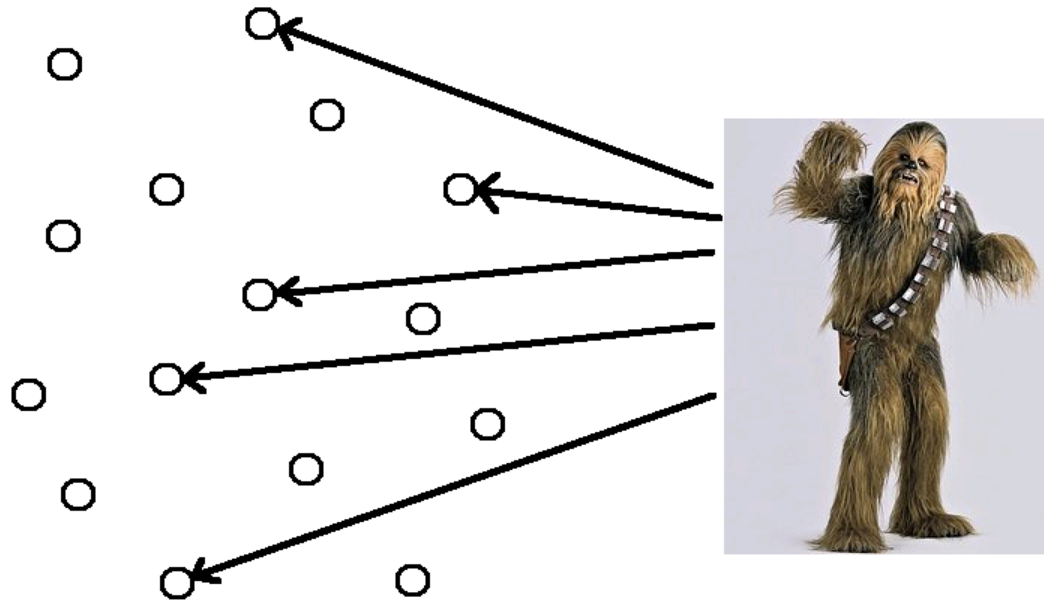
# Hebbian plasticity

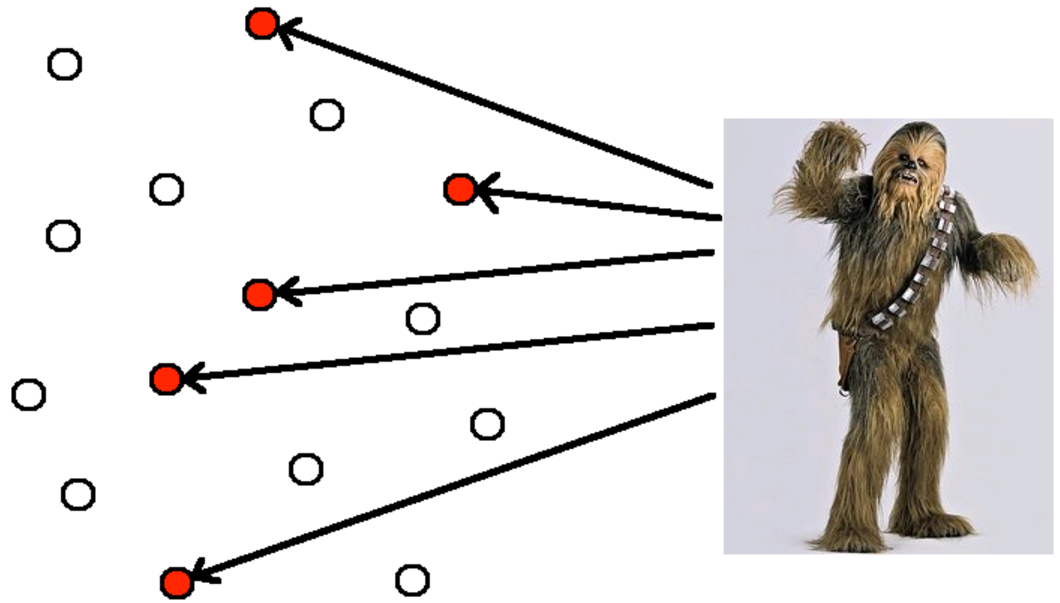
# Hebbian plasticity

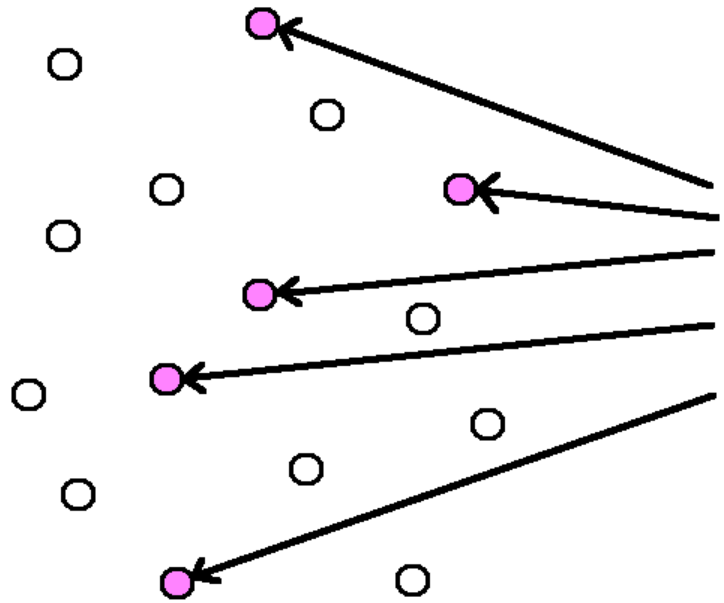
*Neurons that fire together wire together*

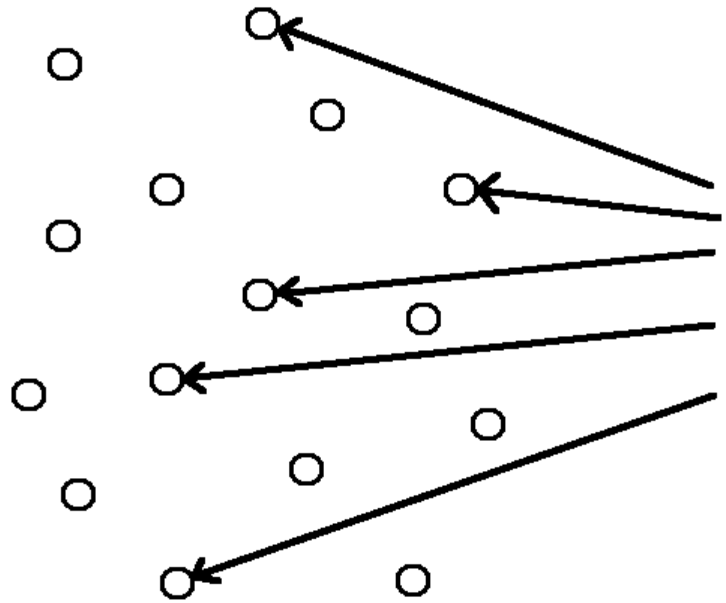
Mechanisms:
Hebbian plasticity to model
**associative learning**

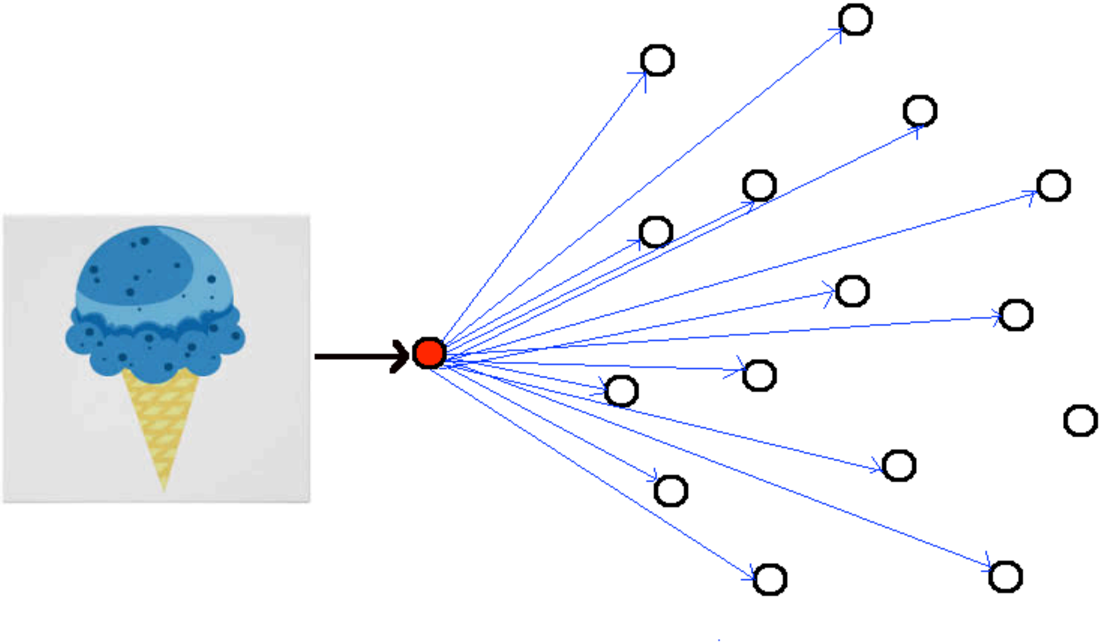


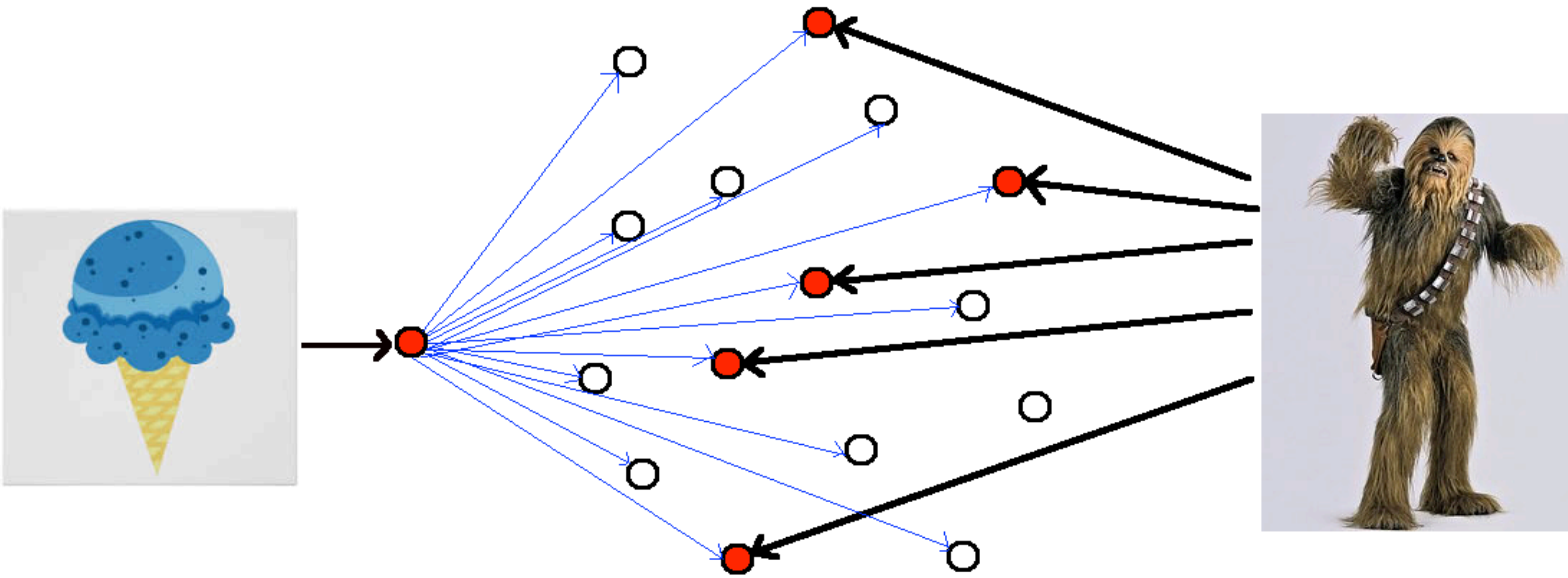


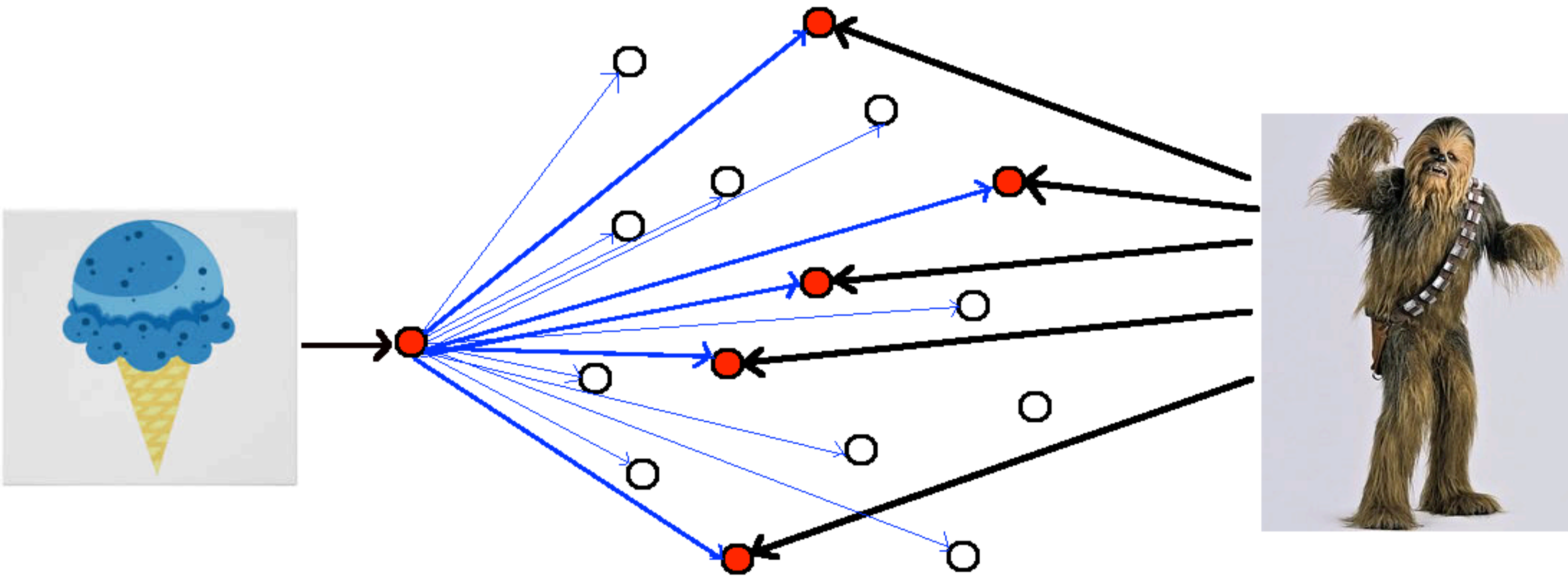


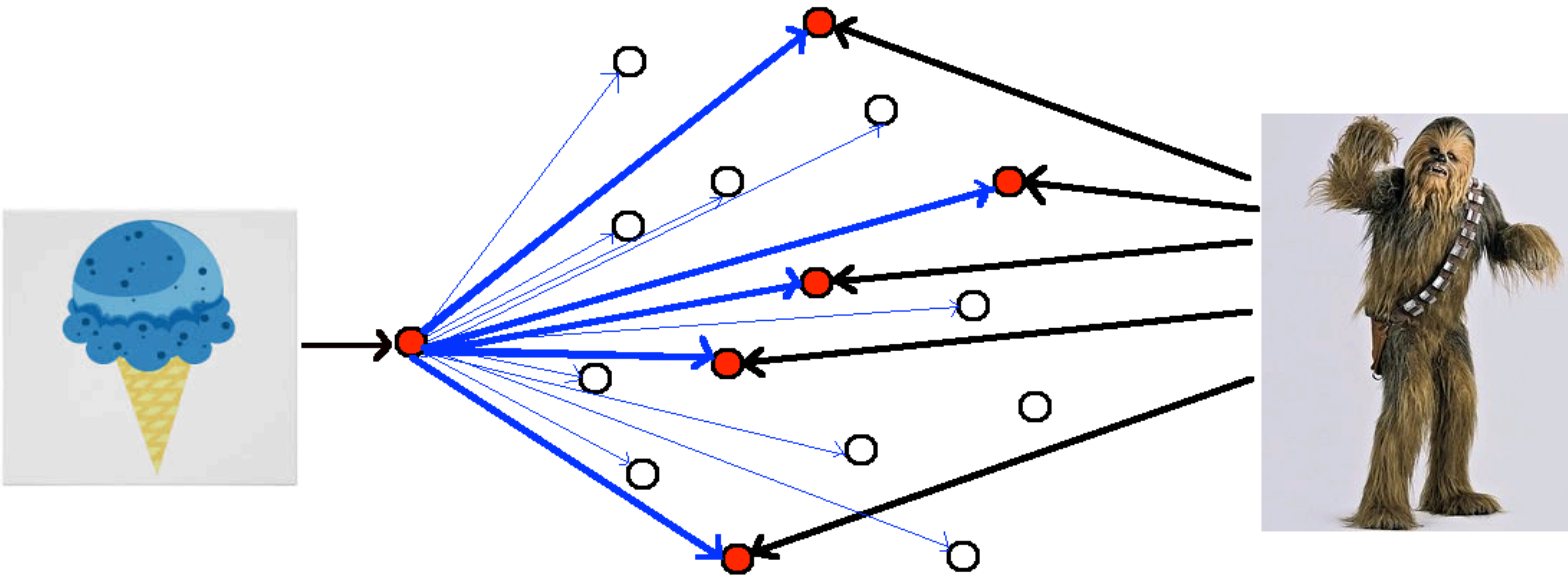


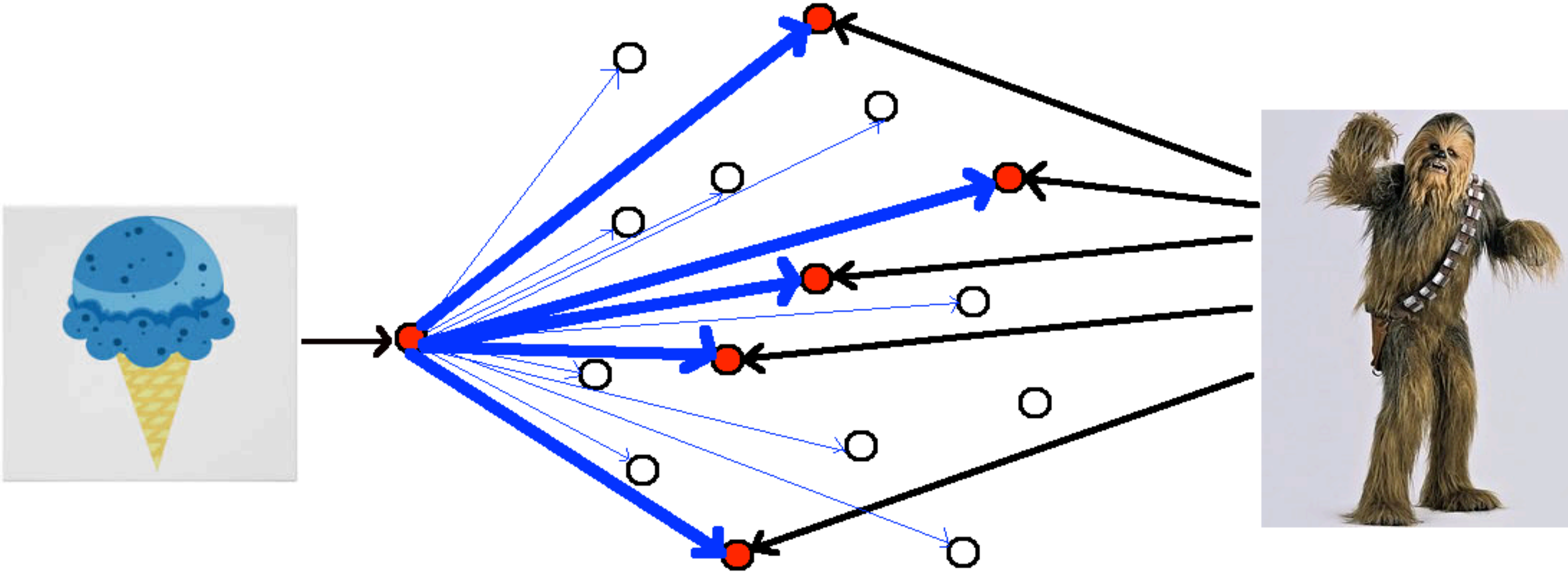


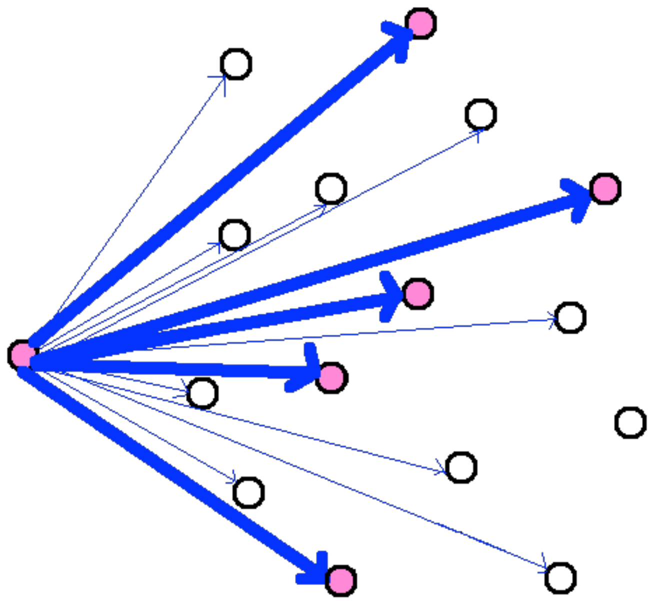


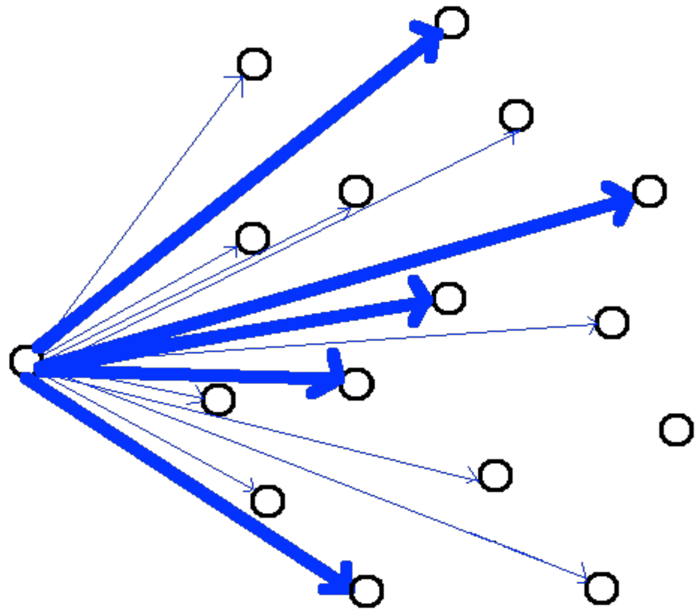


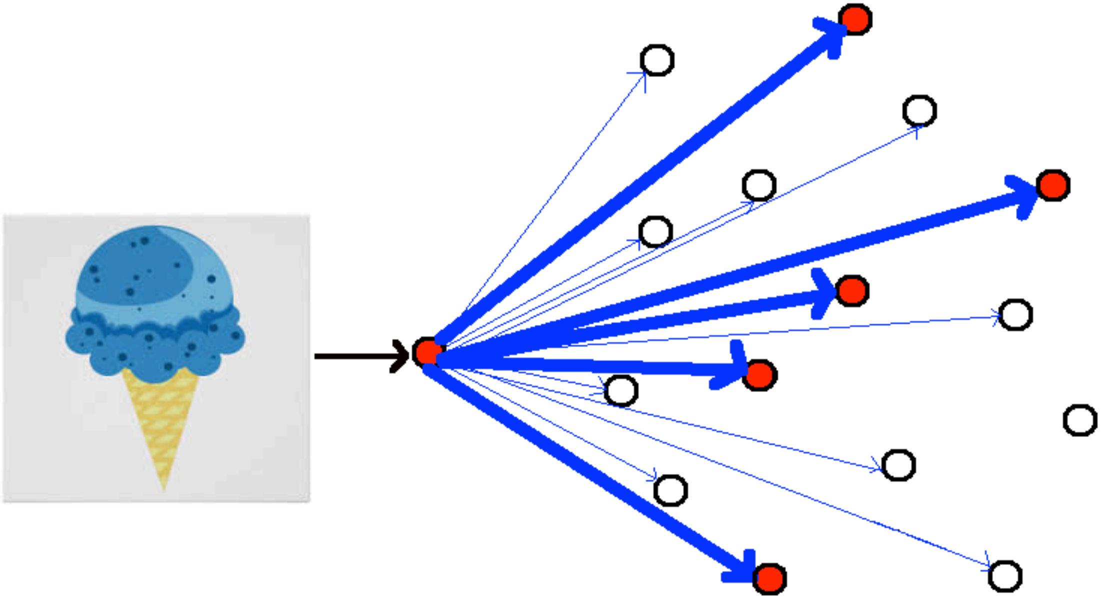


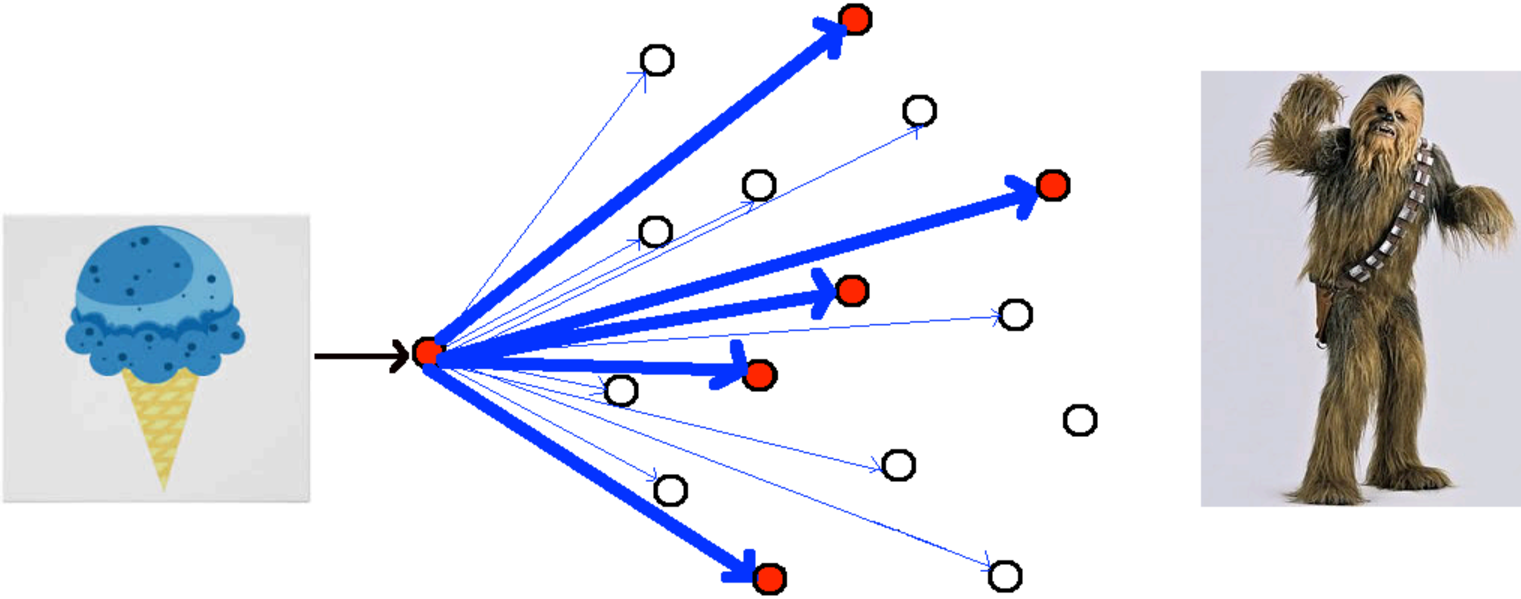












# Components of a computational neuroscience model

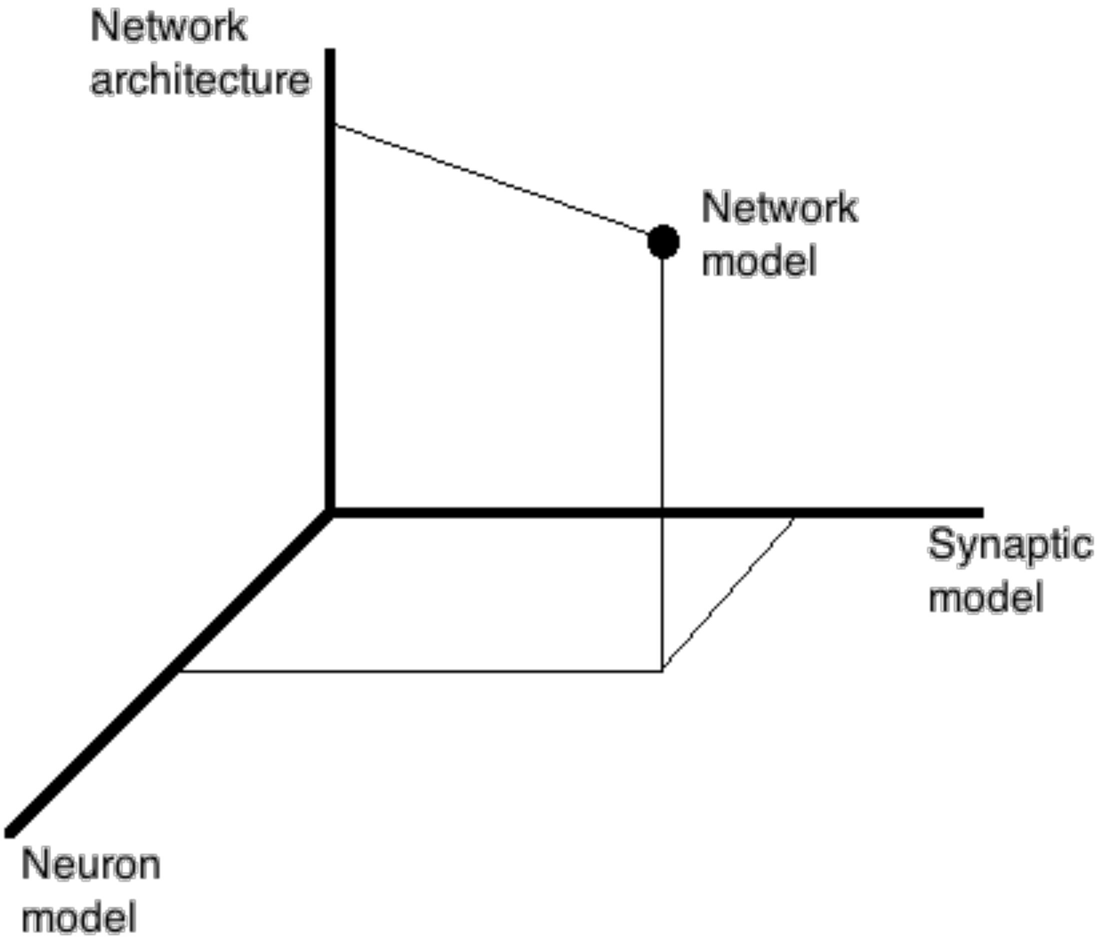
Emergent network activity

Model = structure + dynamics

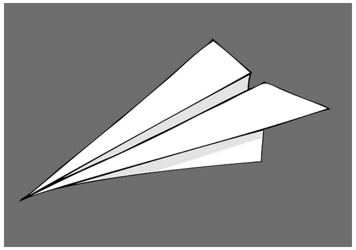
(anatomy) (activity)

Plasticity

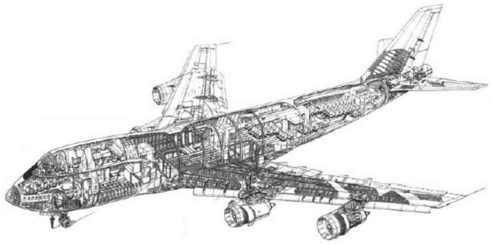
# 3D representation of a network model



# Modeling level



Simplified



Detailed

Macroscopic
(brain regions,
whole brain)

Mesoscopic
(neurons,
networks)

Microscopic
(ion channels,
synapses)

Simple models with **few** variables and parameters

Detailed models with **many variables and parameters**