Introduction to Computational Neuroscience

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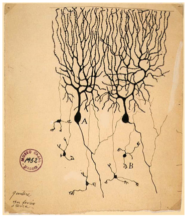
Part 0

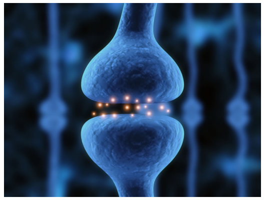
Presentation of computational neuroscience

Neuroscience: fast-growing young science

- Neuron discovery:
  1889, Ramon y Cajal



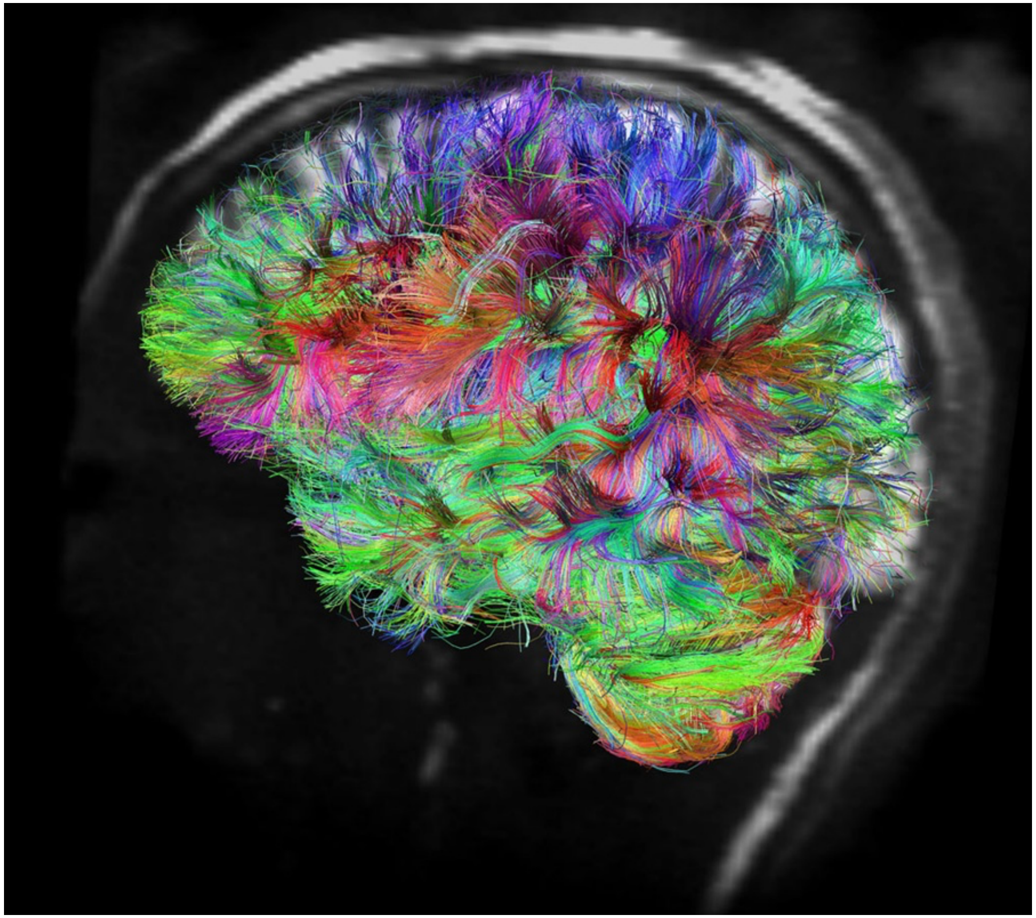

- Concept of synapse:
  1897, Sherrington




- First “official” use of the term *neuroscience*, *circa* 1962
- 1st *Society for Neuroscience* (SfN) congress: 1971 (1100 participants)
- 50th SfN congress: 2019 (~30,000 participants)

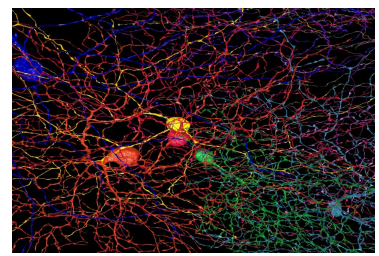
The brain: complex system

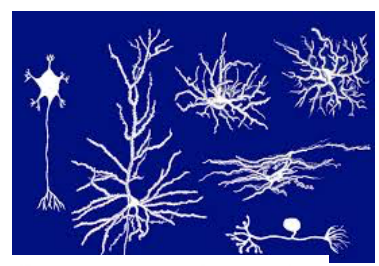
- **~86 billion** neurons
- **Trillions** of synapses

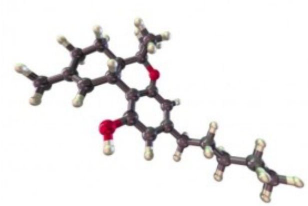


The brain: many (interrelated) levels of organization

1 m	Sist. Nervoso Central
10 cm	Sistemas
1 cm	Regiões
1 mm	Redes
100 μm	Neurônios
1 μm	Sinapses
1 Å	Moléculas







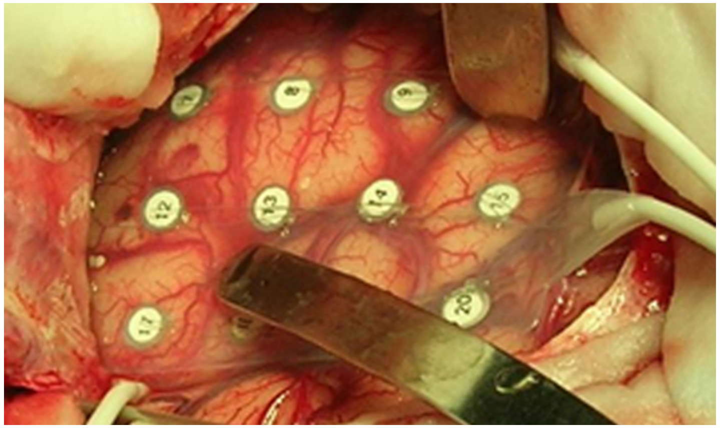
The brain: a lot of data, poor understanding

Types of data:

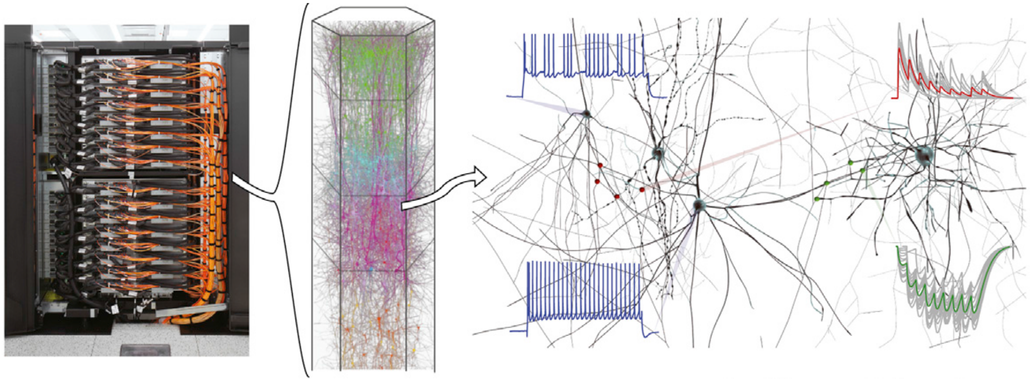
- Anatomical: cell shapes, connections
- Physiological: bioelectrical properties
- Biochemical: molecular processes
- Psychological: behavior
- Recent techniques: molecular biology, imaging, optogenetics, **mathematical and computational modeling**

- *In vitro*

- *In vivo*



- *In silico*



Models

- **Deliberate** simplifications of phenomena;
- **Intuitive understanding** of processes;
- Relate the **hypotheses** made with the **results** observed experimentally;
- Allow **integration** of data from different levels;
- Should be capable of explaining new phenomena: **robustness**.

All models are wrong, but some are useful

(George E. P. Box)

Computational Neuroscience

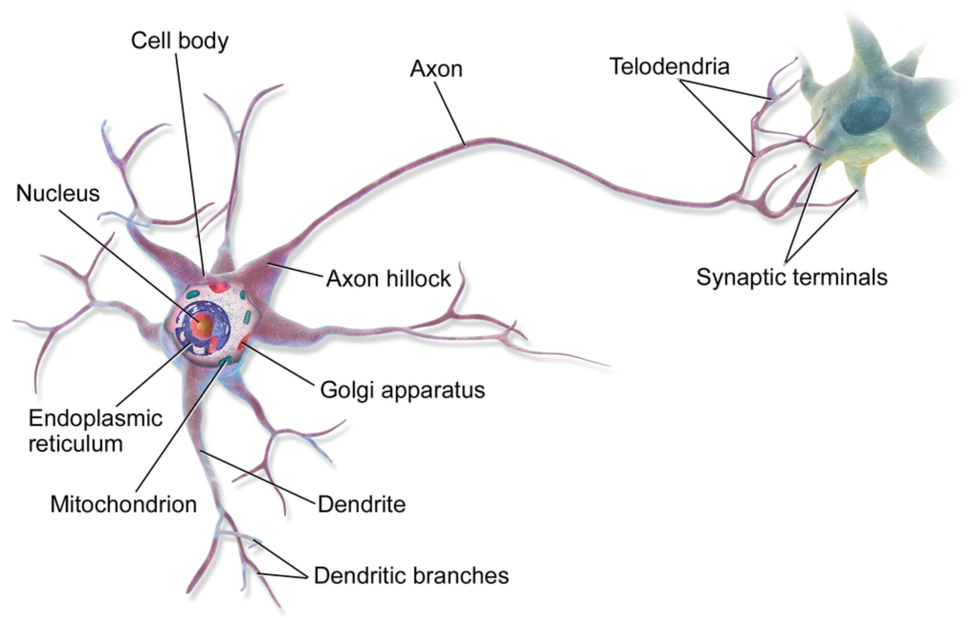
- Theoretical part of neuroscience: also called theoretical neuroscience
- Objective: to determine and articulate the principles and mechanisms behind the functioning of the nervous system
- It is assumed that this functioning involves "computations"
- Due to their complexity, most models are explored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

Part 1

Basic Concepts

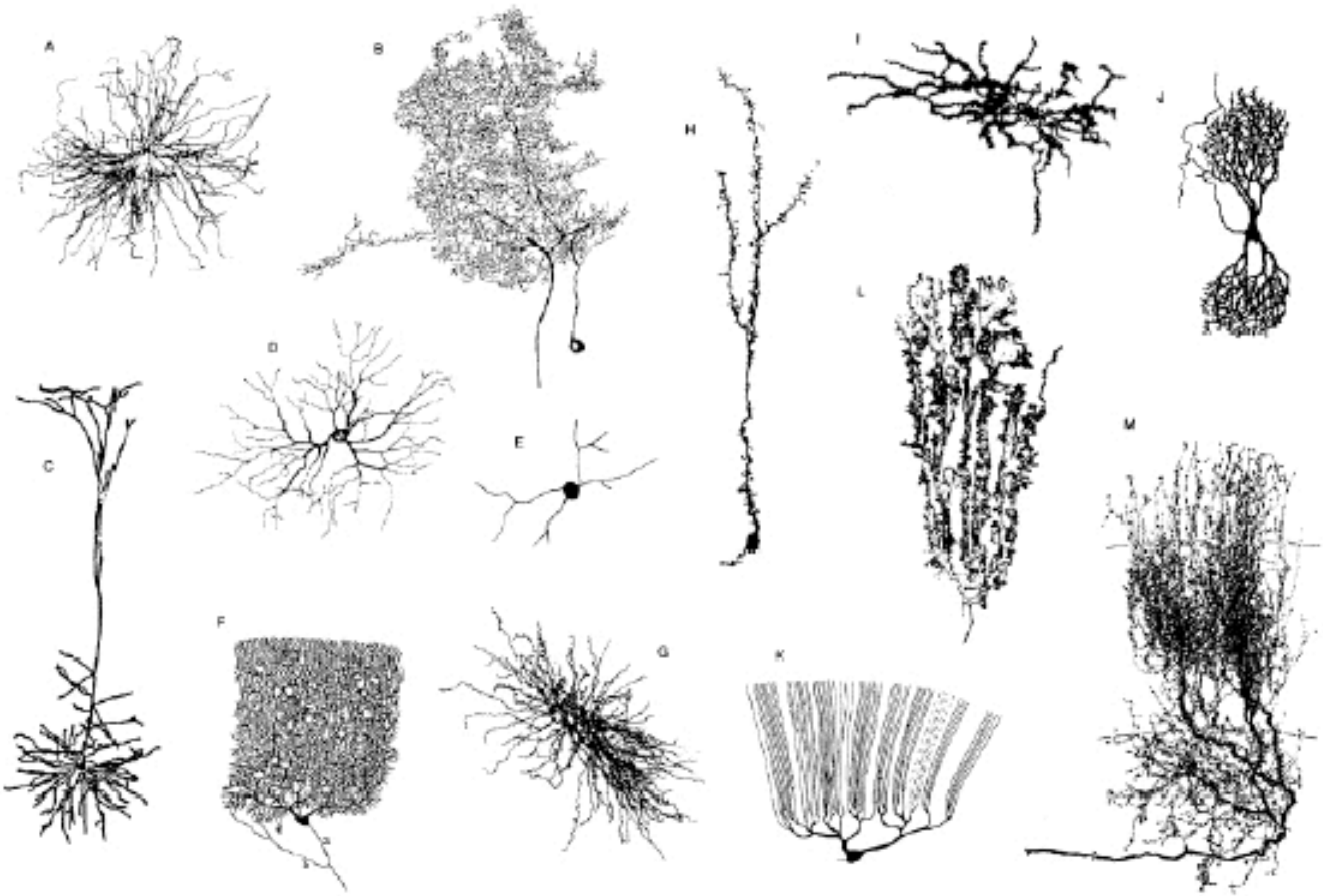
Neuron

- 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



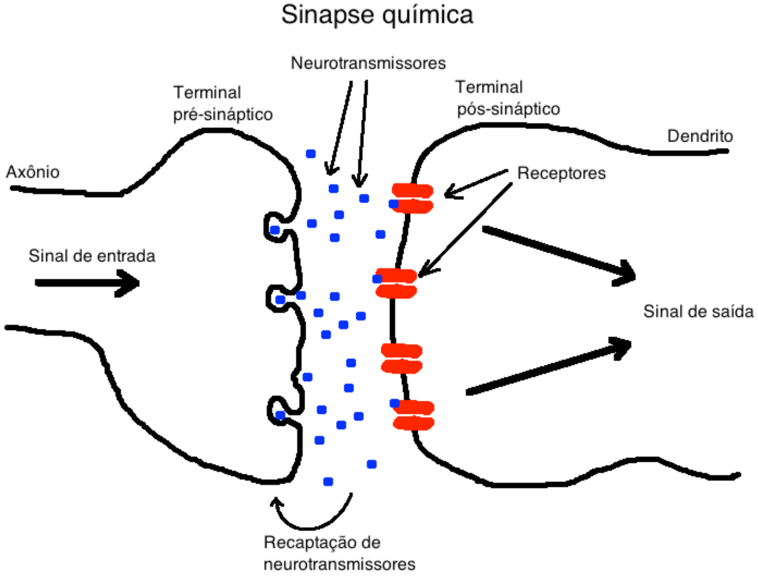
https://en.wikipedia.org/wiki/Neuron

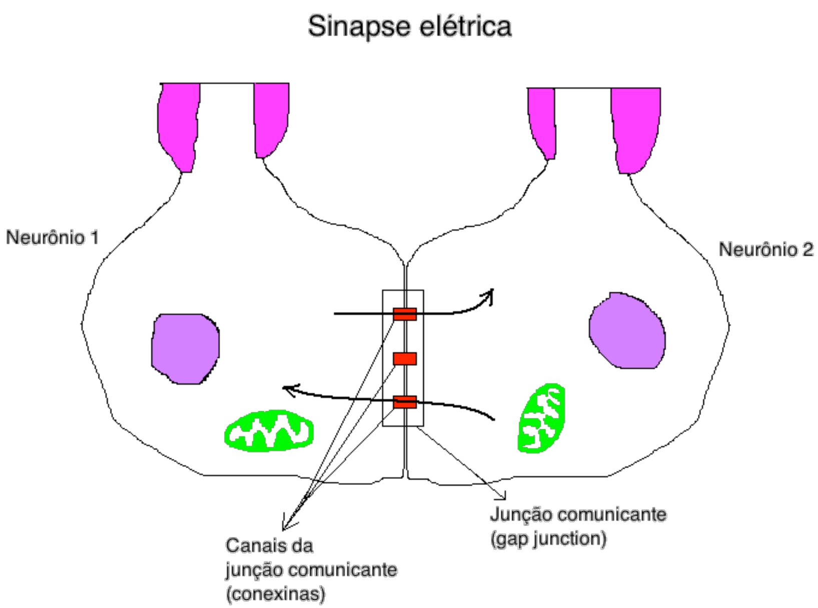
Neurons have many and diverse shapes



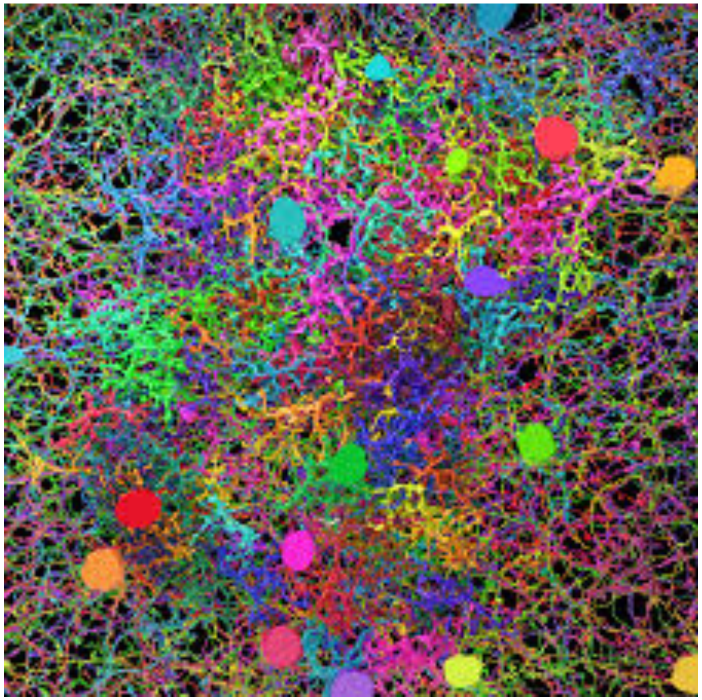
Synapse

- Specialized region in which a **pre-synaptic** cell makes contact with a **post-synaptic** cell
- Synapses may be chemical or electrical

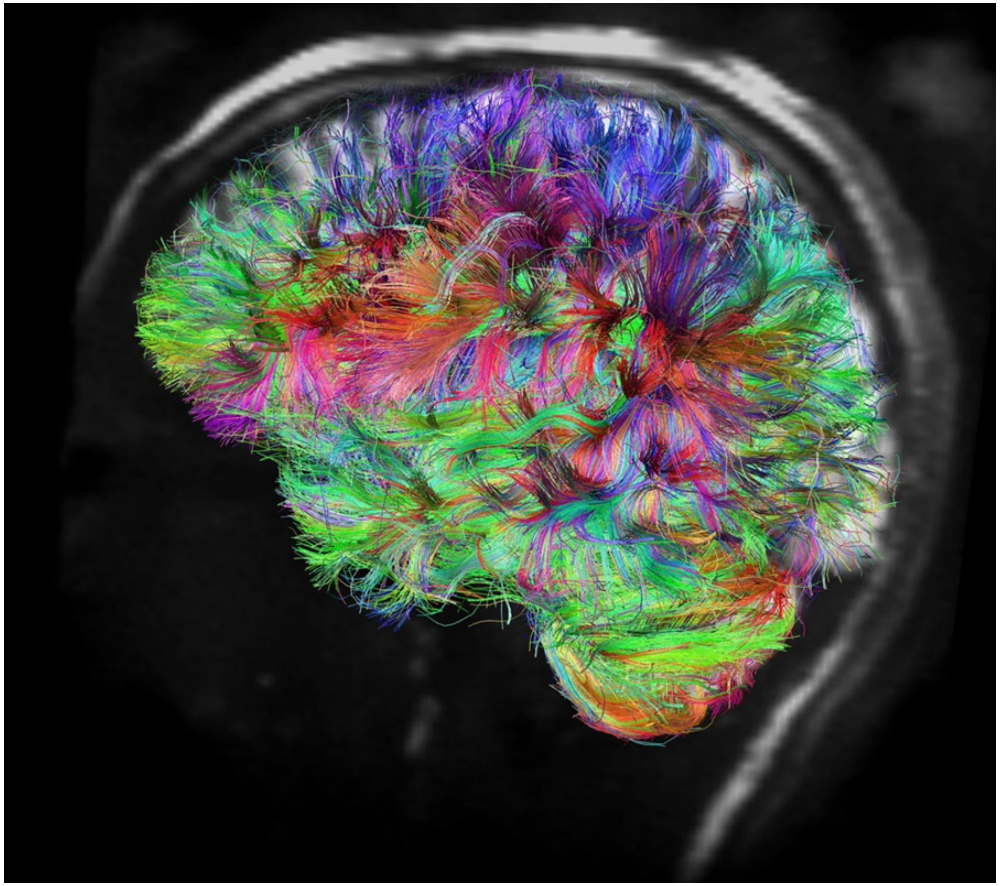




Neural circuits and networks



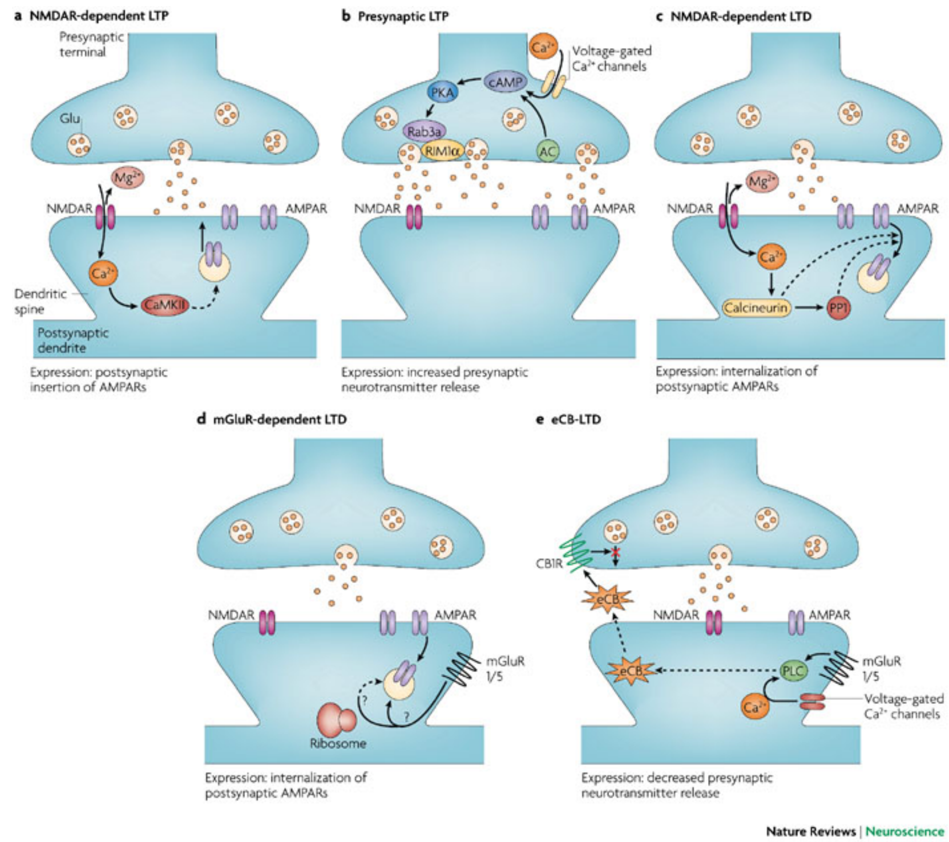
Alex Norton, EyeWire,
Seung Lab, MIT



V.J. Wedeen e L.L. Wald, Martinos Center for
Biomedical Imaging at Massachusetts General Hospital

Synaptic Plasticity

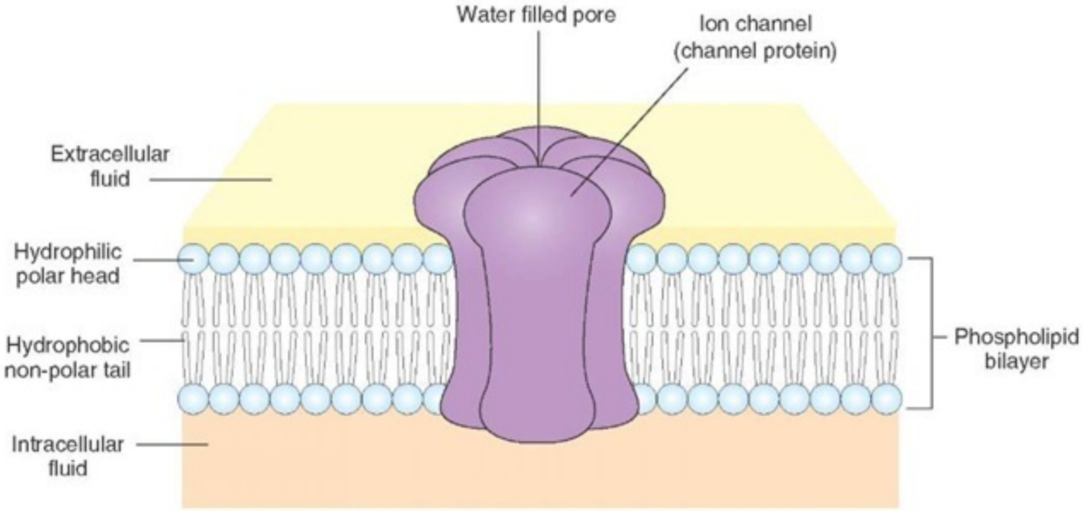
- Generic name given to any type of change (strengthening or weakening) in the efficacy of a synapse
- Synaptic plasticity can be of short or long duration
- Hypothetical mechanism underlying memory formation and learning



Kauer & Malenka (2007)

Neuronal Membrane

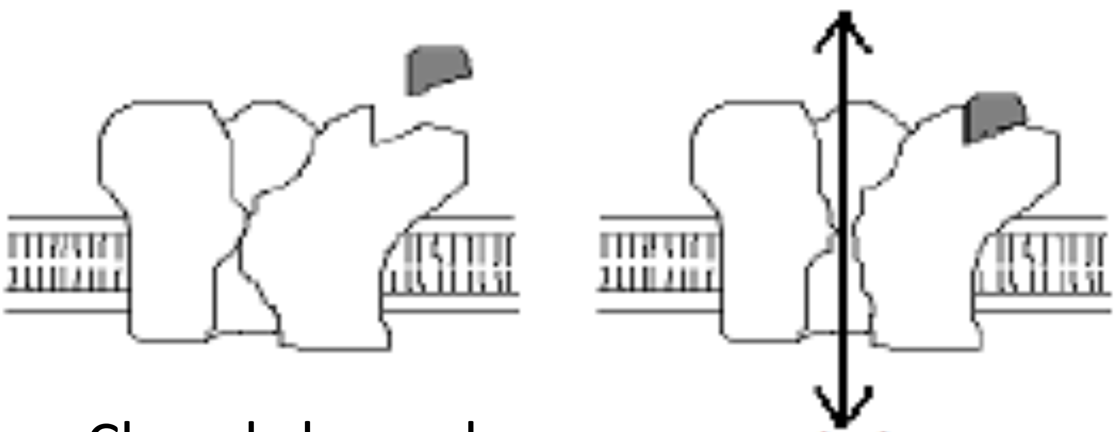
- Thin membrane (60-70 Å) that separates the cytoplasm from the extracellular space
- Made of a lipid bilayer in which proteins are immersed
- Some proteins cross the membrane forming ion channels



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

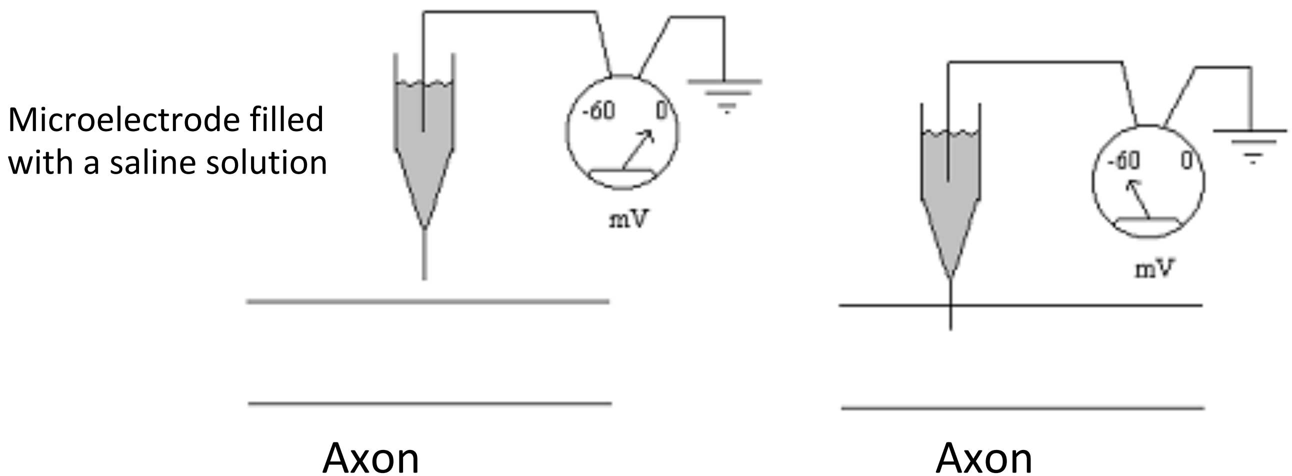


Closed channel

Open channel

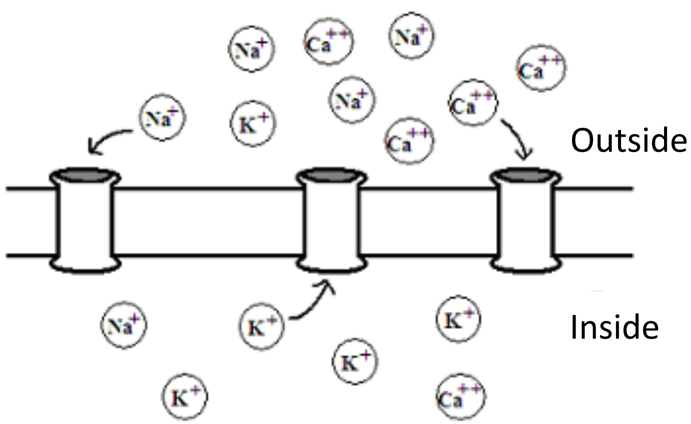
Membrane potential

- 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



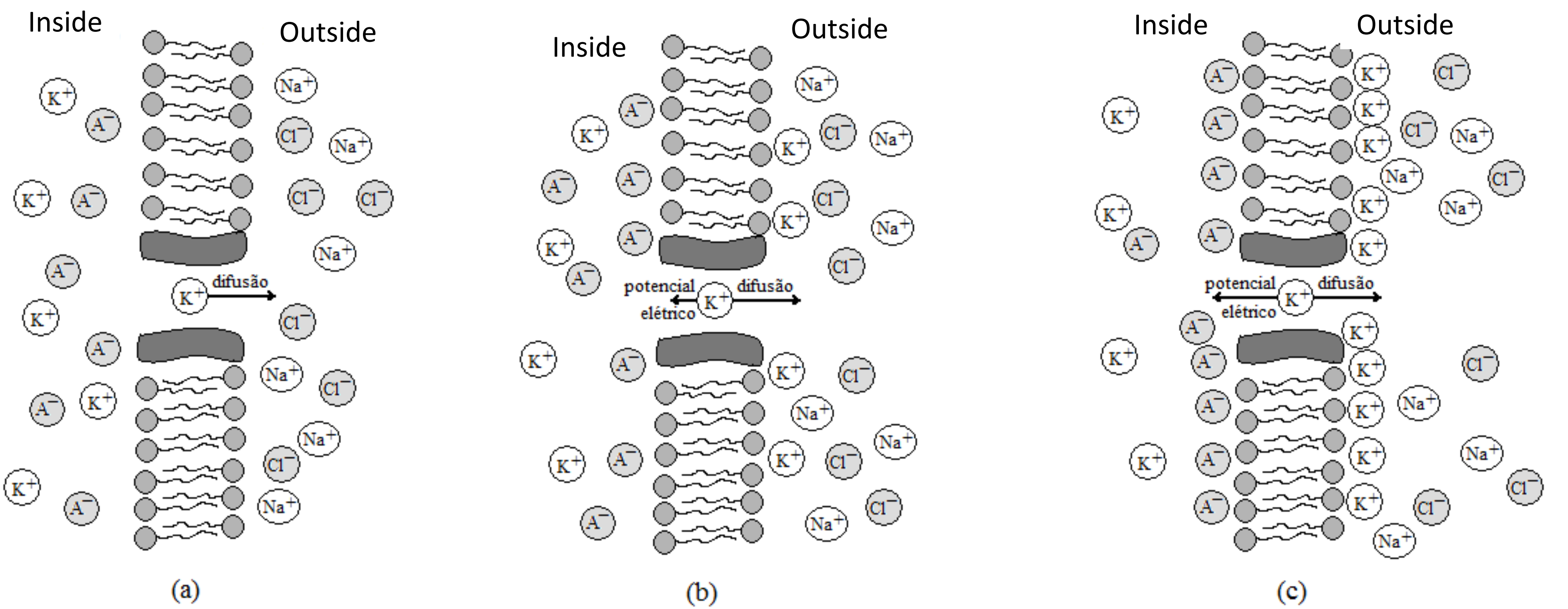
Ionic concentrations

- 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



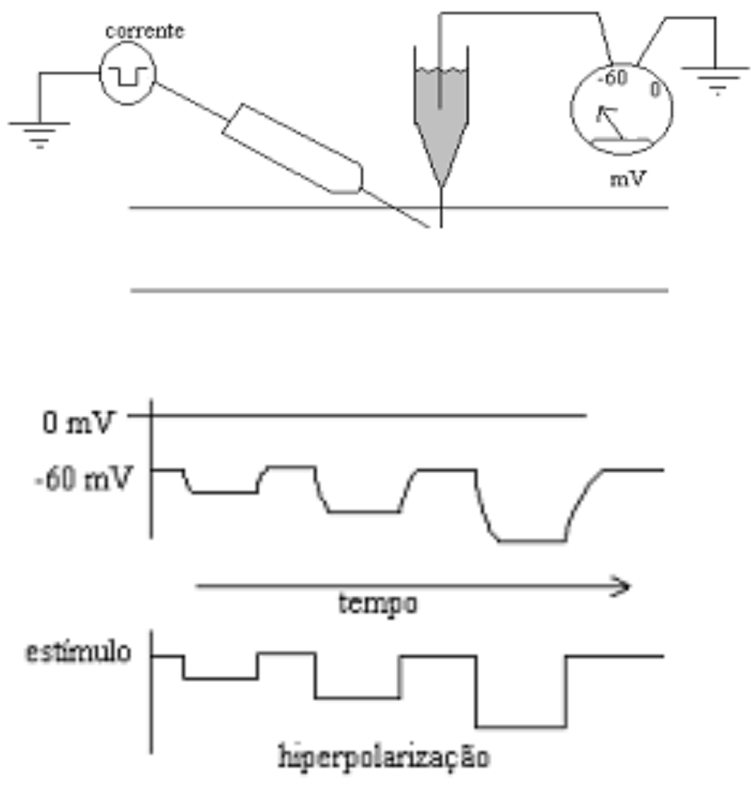
- Nernst potential

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

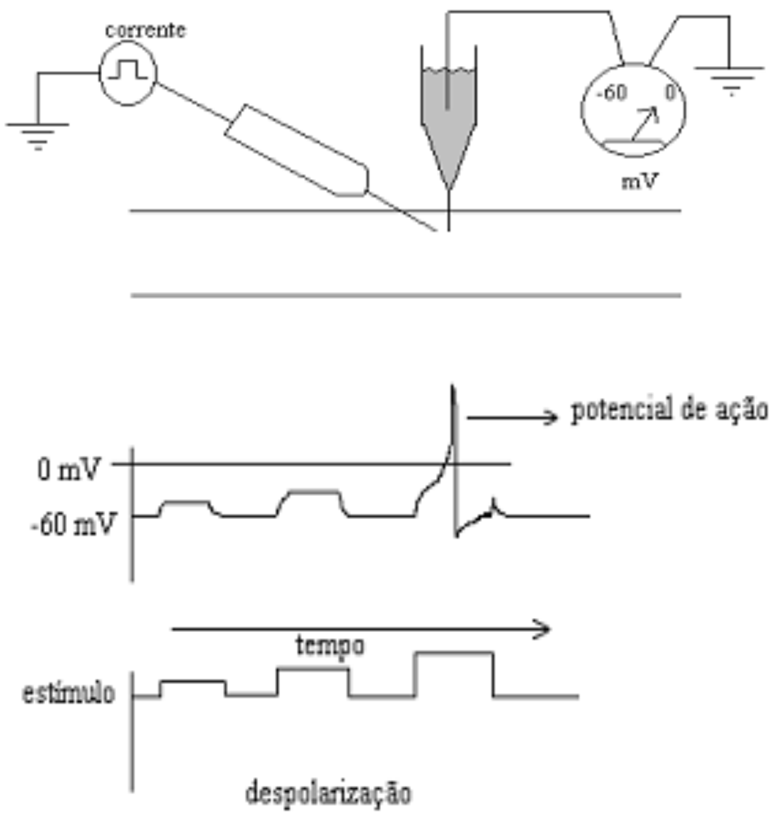
	Inside (mM)	Outside (mM)	Equilibrium protential (Nernst)
K^+	400	20	-75 mV
Na^+	50	440	+55 mV
Cl^-	40-150	560	-66 a -33 mV
Ca^{2+}	10^{-4}	10	+145 mV
A^- (organic ions)	385	—	—

Squid giant axon at 20°C

Depolarization and hyperpolarization



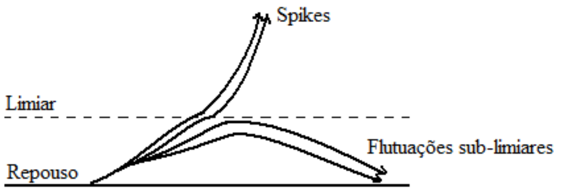
Graded variation



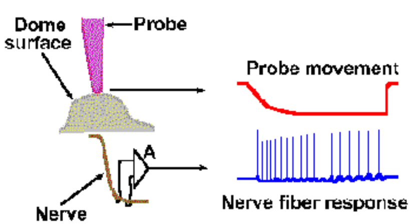
Action potential

Action potential

- Shape (width and amplitude) characteristic of each neuron
- Threshold phenomenon (all or none)



- Propagates unchanged while subthreshold voltage fluctuations are strongly attenuated
- Used by neurons to code and transfer information



Na figura da esquerda ilustra-se como a ponta de prova pressiona a superfície em forma de domo do mecanoreceptor e como as respostas do nervo são registradas. Na figura da direita, mostra-se um trem de disparos típico do nervo para uma pressão prolongada. O registro inteiro dura 40 ms.

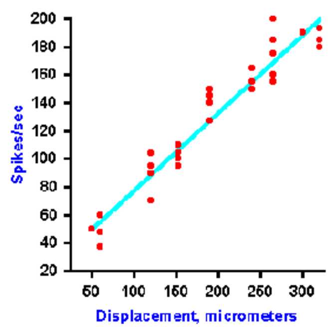
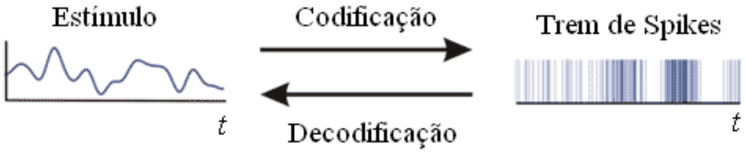
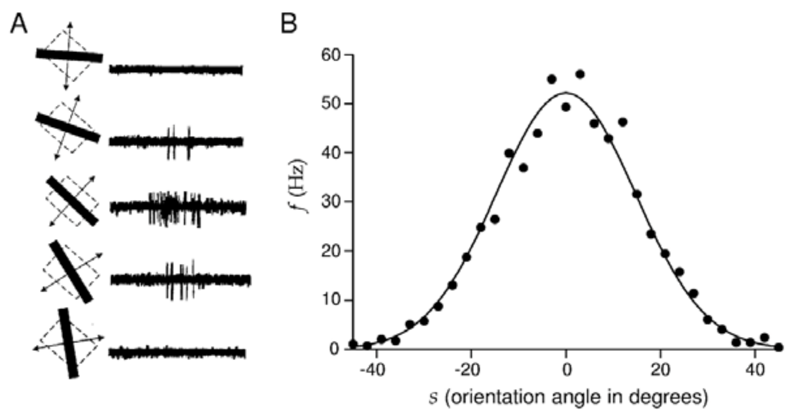
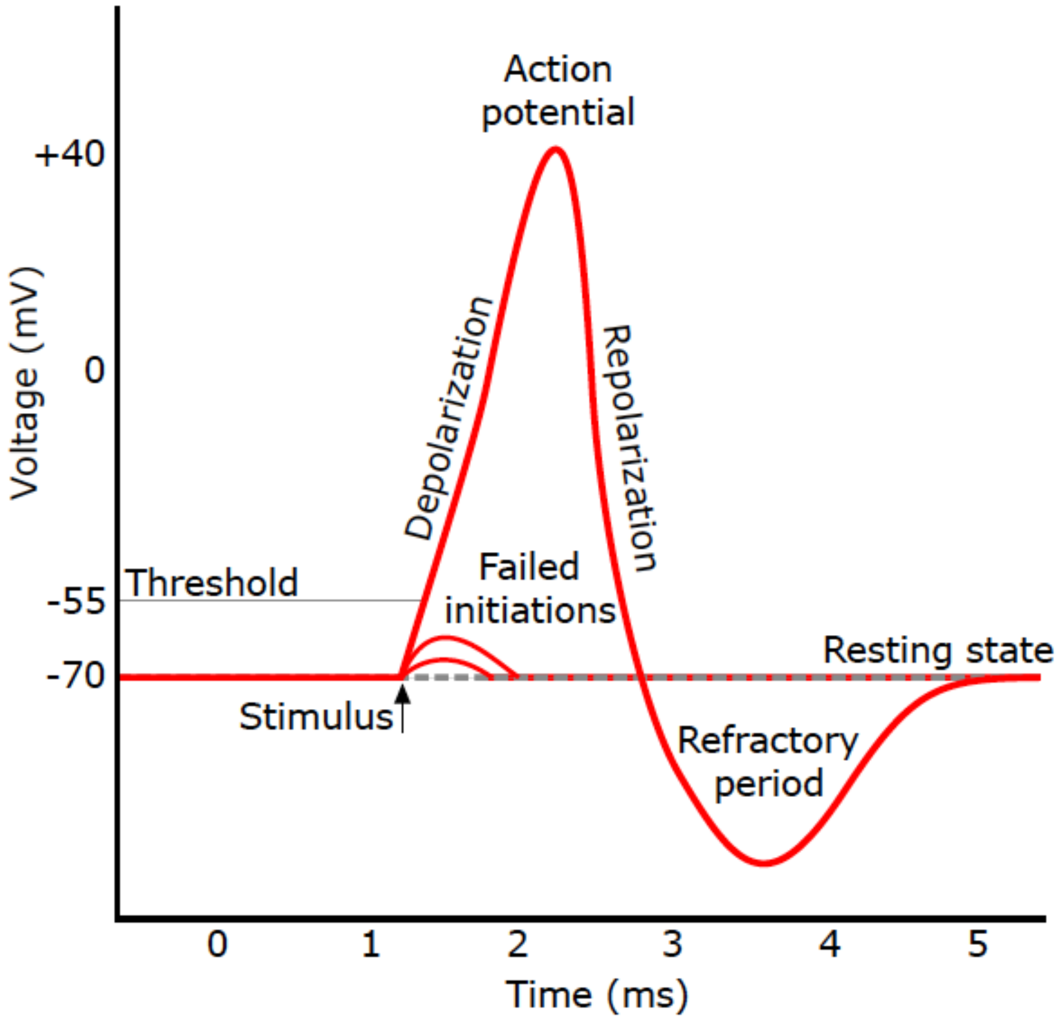


Gráfico da freqüência de disparos em função do deslocamento do receptor. Cada ponto corresponde a uma medida feita durante todo o tempo em que o deslocamento foi mantido constante (o platô na figura da esquerda). Dados adaptados de Tapper, D.N., Trans. NY Acad. Sci., 26:697-701, 1964.



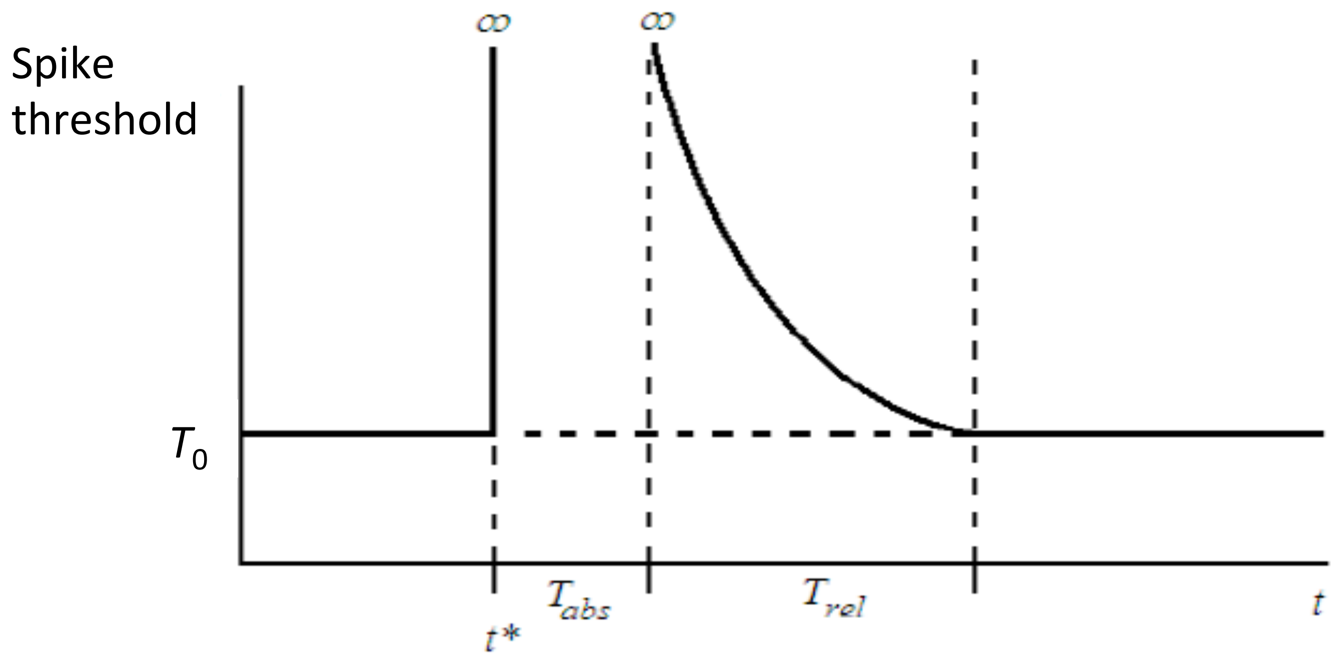




https://commons.wikimedia.org/wiki/File:Action_potential.svg#/media/File:Action_potential.svg

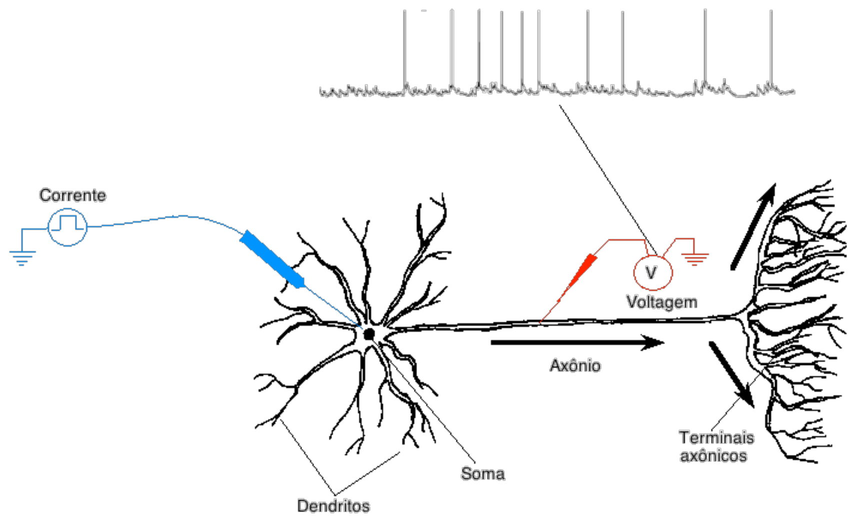
Refractory periods

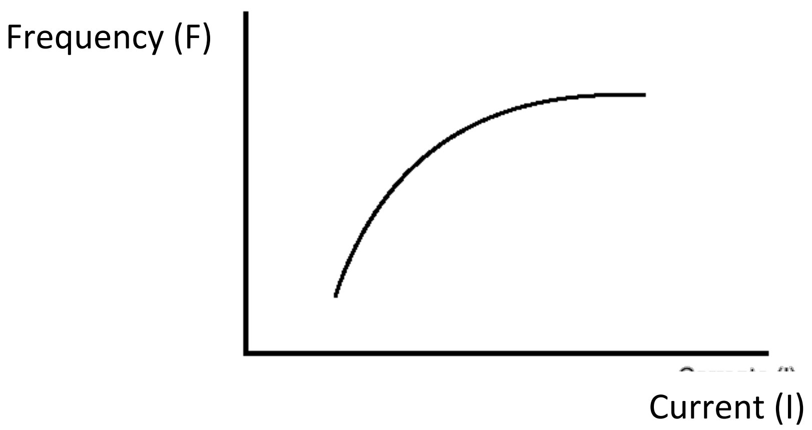
- **Absolute**: period during which a second stimulus (no matter how strong) will not lead to a second spike. It is as if the spike threshold were infinite
- **Relative**: period during which a second spike can be generated by a second stimulus stronger than the first. The strength of the second stimulus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



F-I Curve

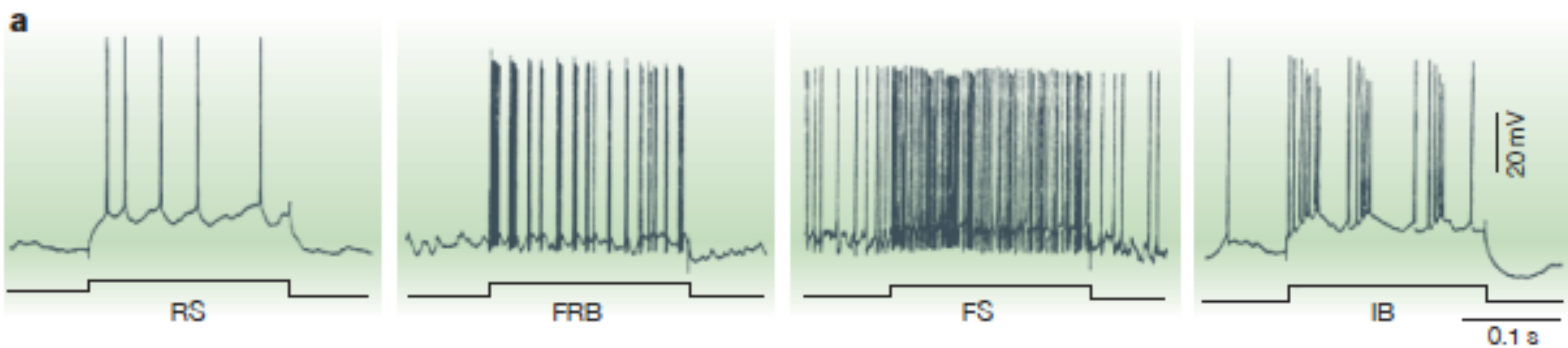
- Firing rate (F) of a neuron as a function of its input current (I)
- Each I value corresponds to a constant step current applied for a given time
- Describes the input-output transfer function of the neuron
- In general, F-I curves are nonlinear with saturation for high input values





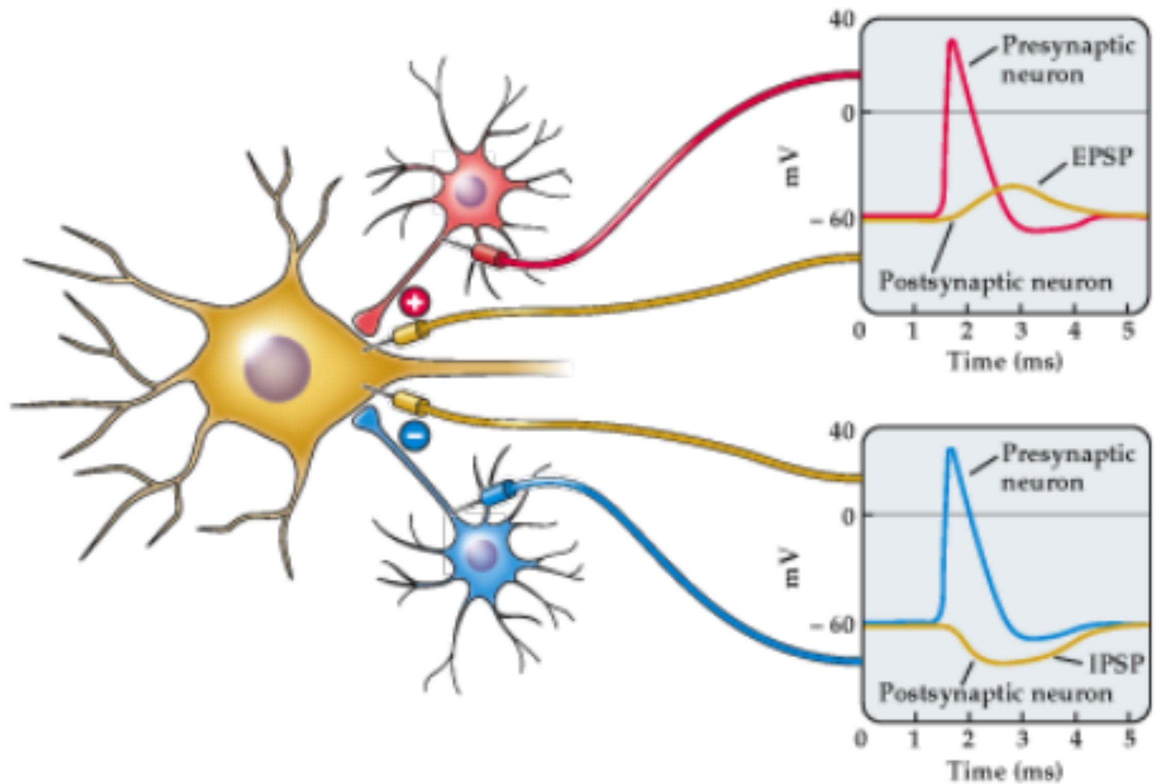
Electrophysiological classes

- Different types of neurons produce different spike train patterns in response to the same input current
- The different patterns are grouped in **electrophysiological classes** (four examples of cortical classes are shown below)



Steriade (2004)

Postsynaptic potentials



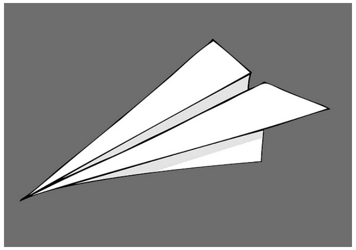
EPSP: excitatory postsynaptic potential

IPSP: inhibitory postsynaptic potential

Part 2

Types of models and their components

Modeling level



Simplified

Simple models with **few** variables and parameters

Sist. Nervoso Central

Sistemas

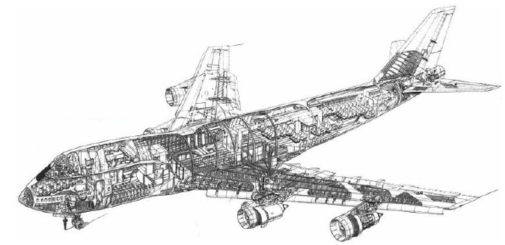
Regiões

Redes

Neurônios

Sinapses

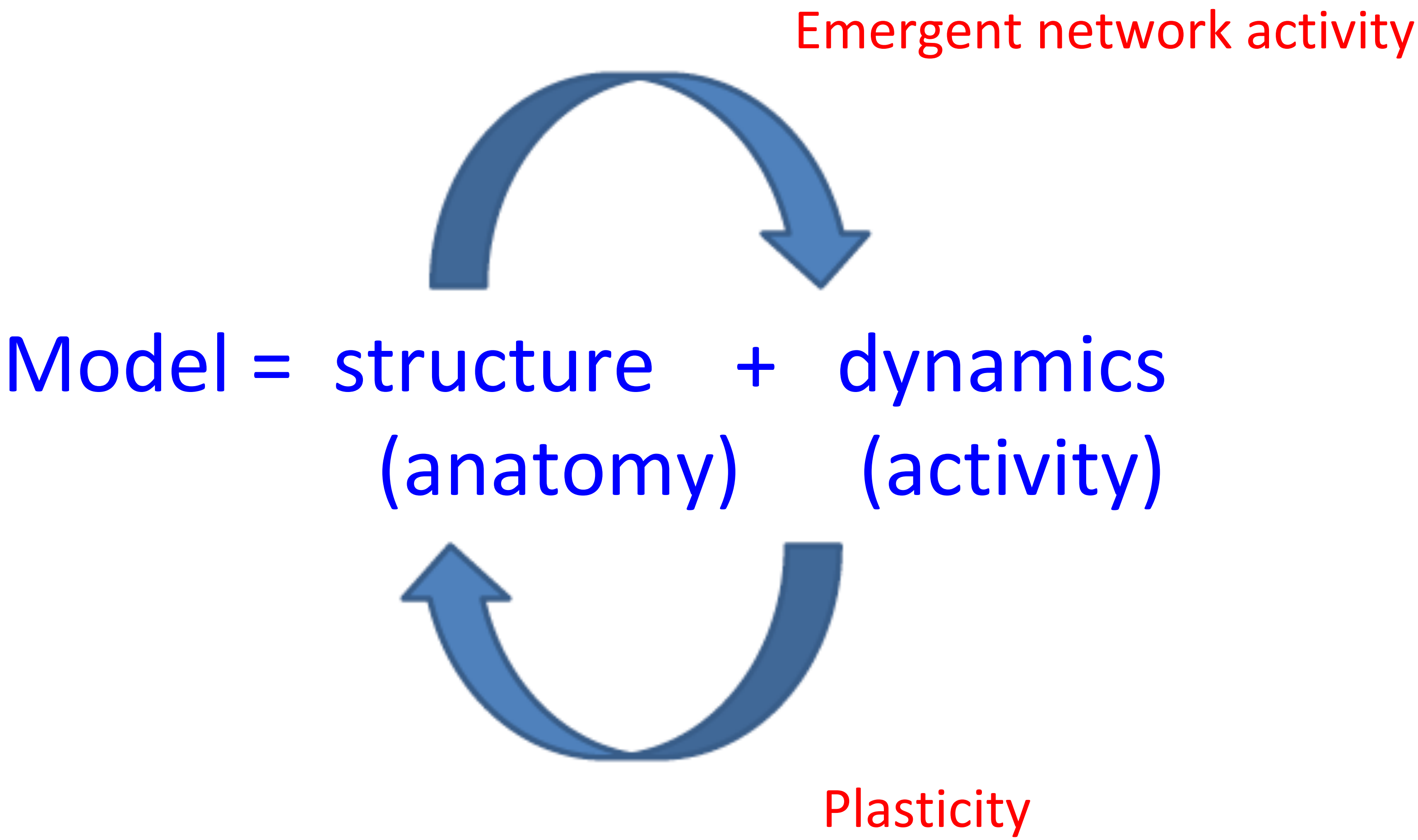
Moléculas



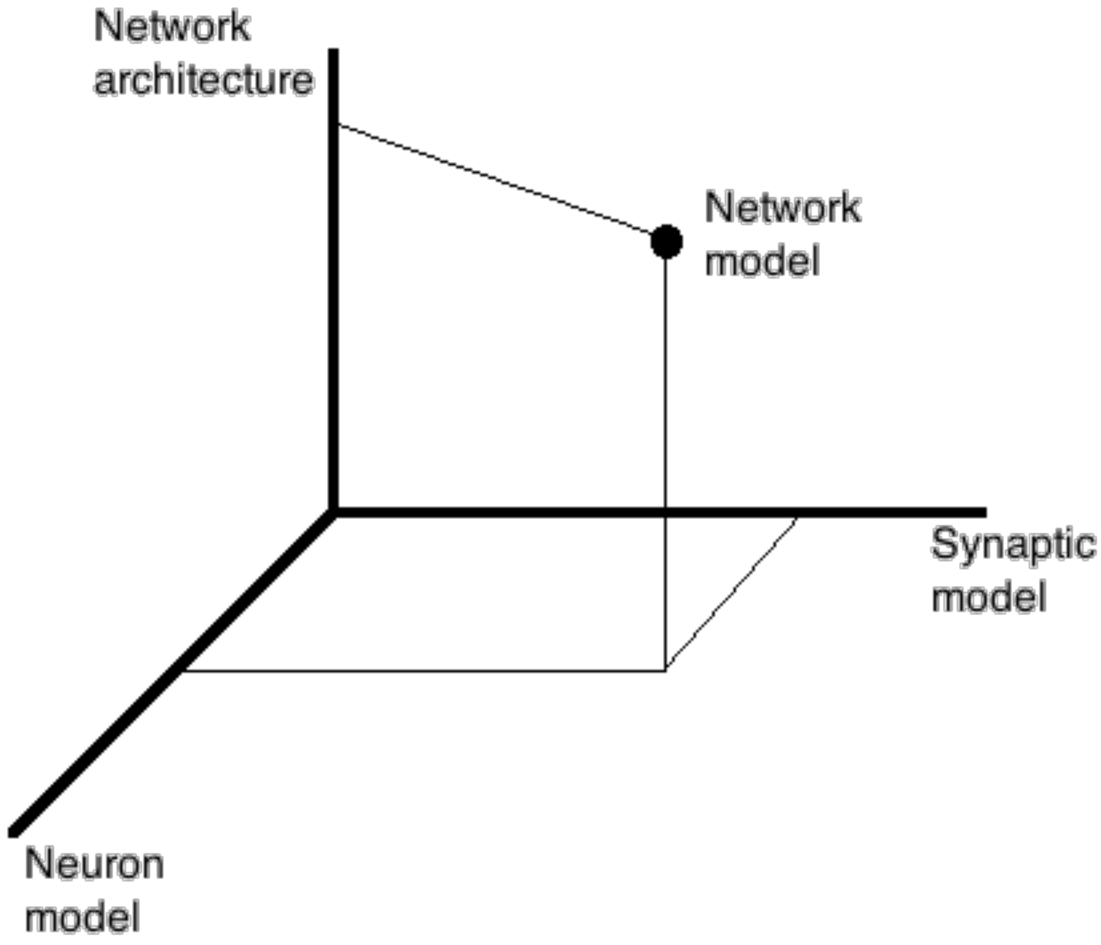
Detailed

Detailed models with **many variables and parameters**

Components of a computational neuroscience model



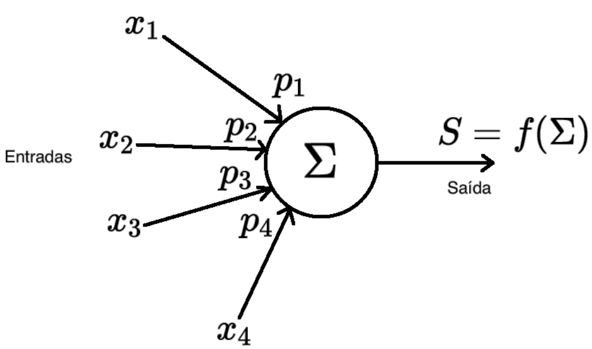
3D representation of a network model

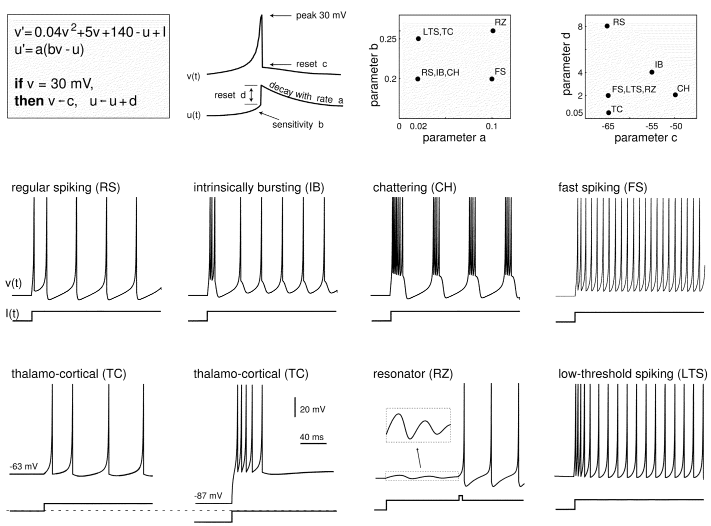


Neuron models

Simplified

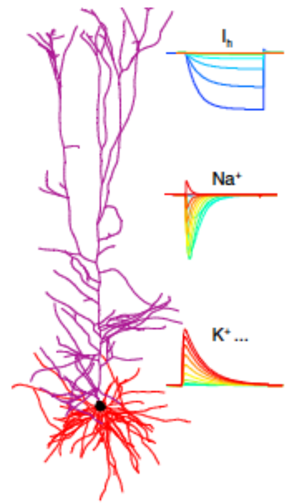
Dynamics of neuronal activity

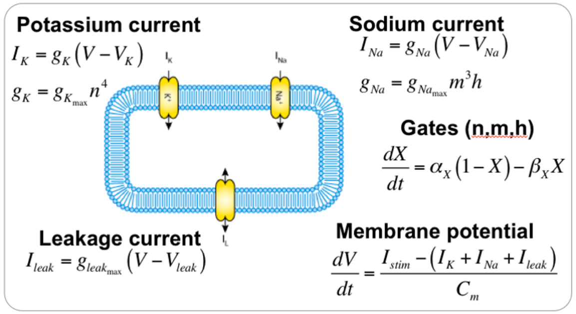


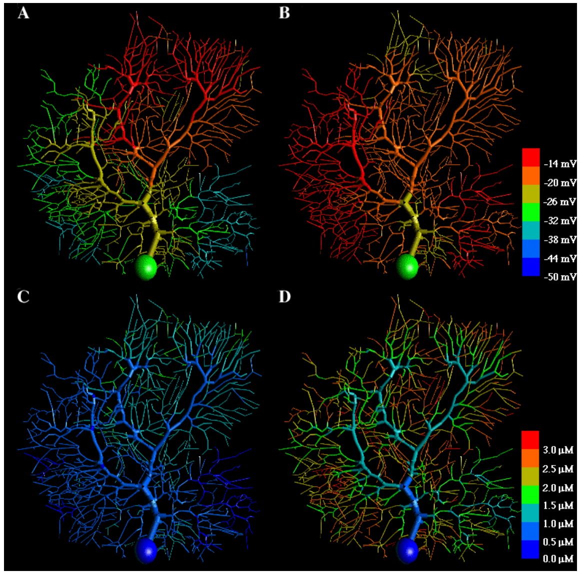


Detailed

Ionic channels; dendrites



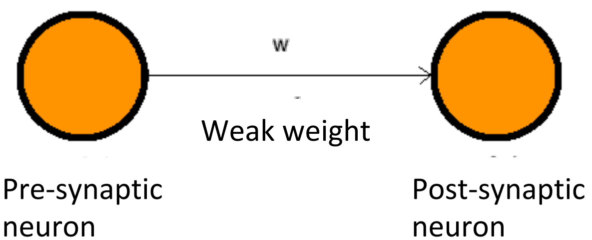


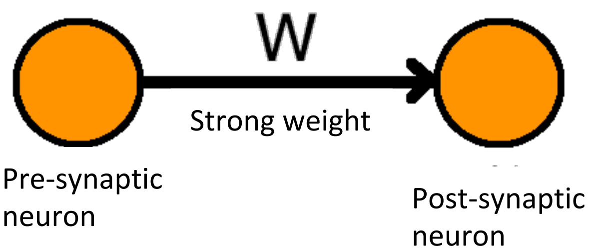


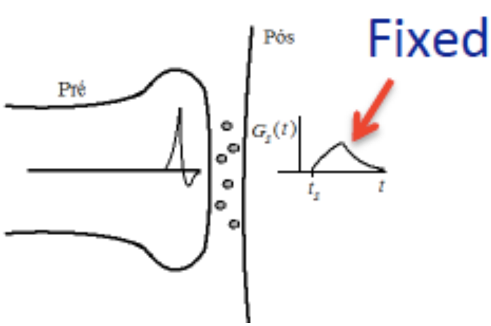
Models of synapses

Simple

Synaptic weight (a number); time course described by a fixed function

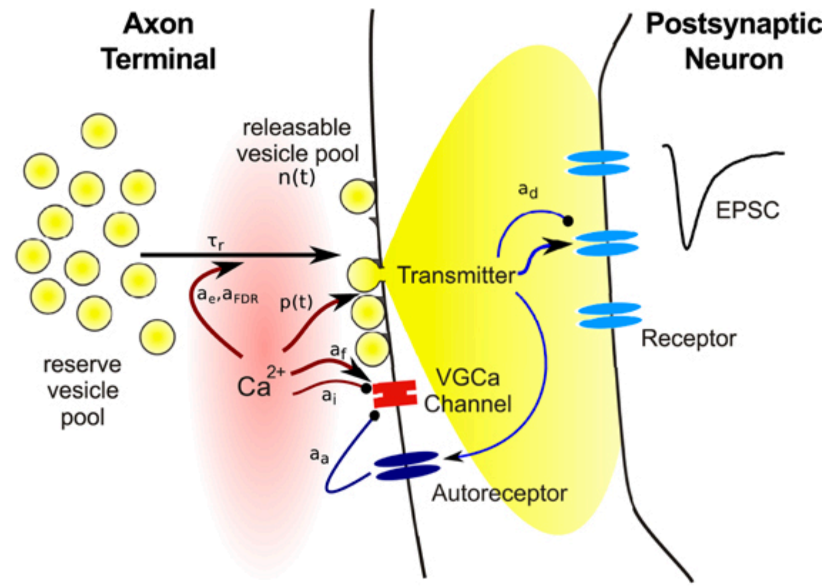






Detailed

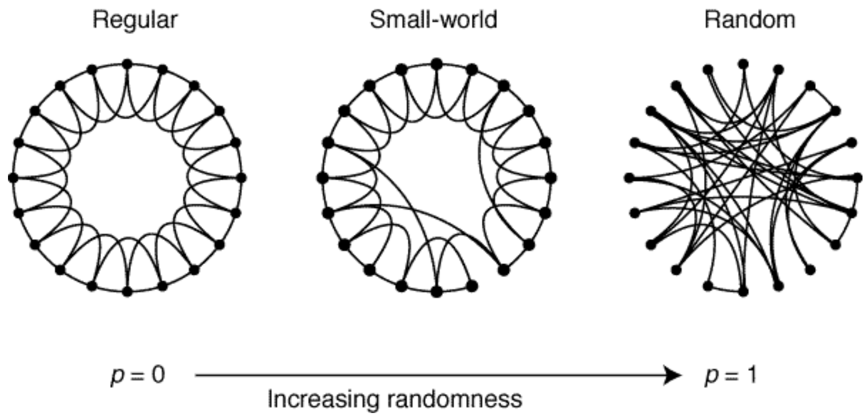
Biochemical reactions; time course modeled by kinetic equations



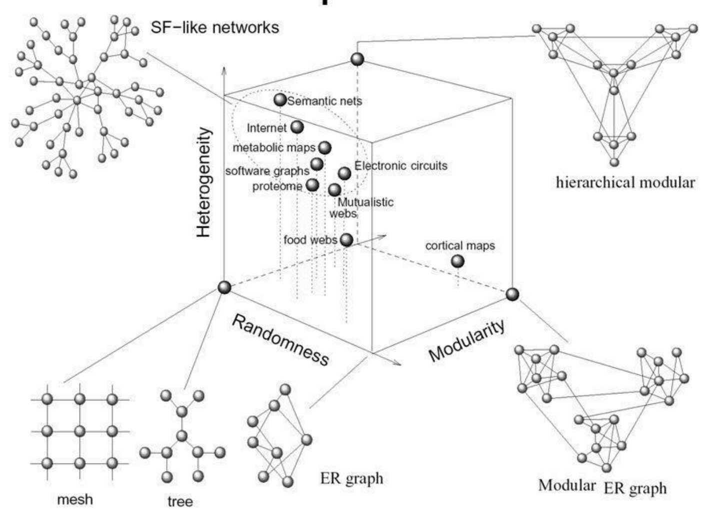
Types of network architecture

- **Artificial**: generated according to some mathematical rule
- **Data driven**: based on real data (in micro or macro scale)

Artificial architectures

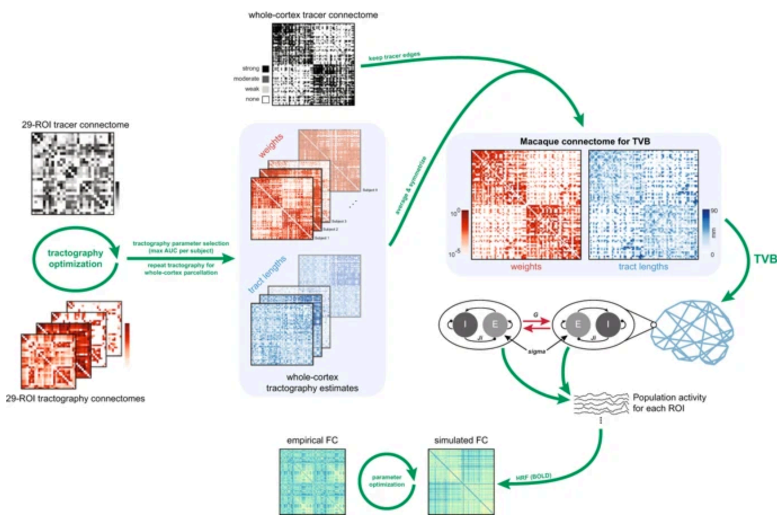


Zoo of Complex Networks

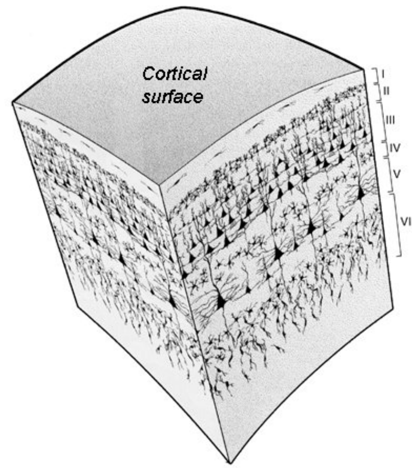


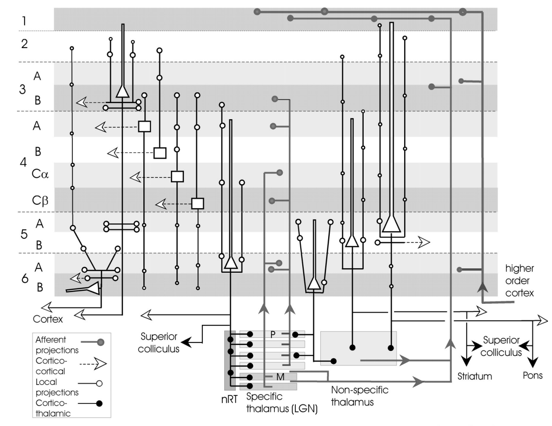
Data driven architectures

Connectivity among cortical regions

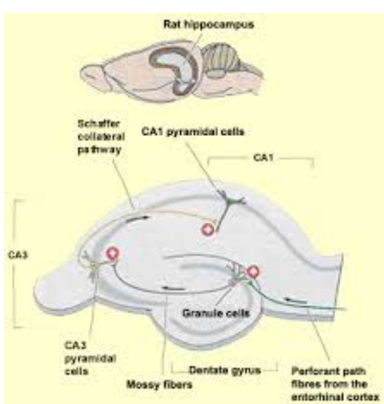


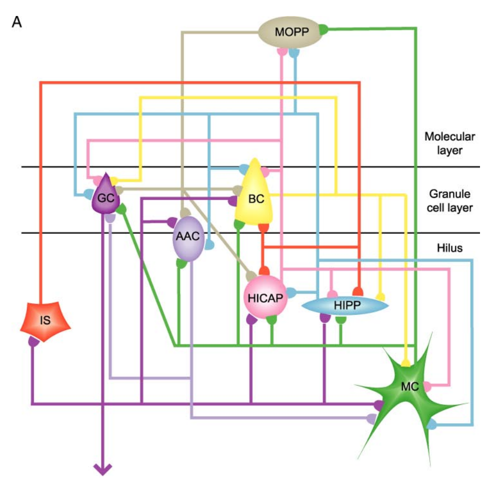
Local connectivity (microcircuitry) in a cortical column

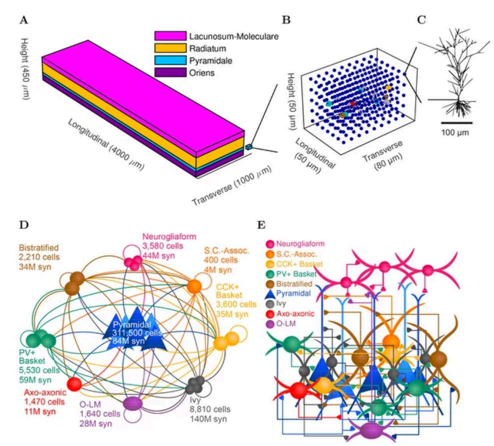




Connectivity among hippocampal neurons



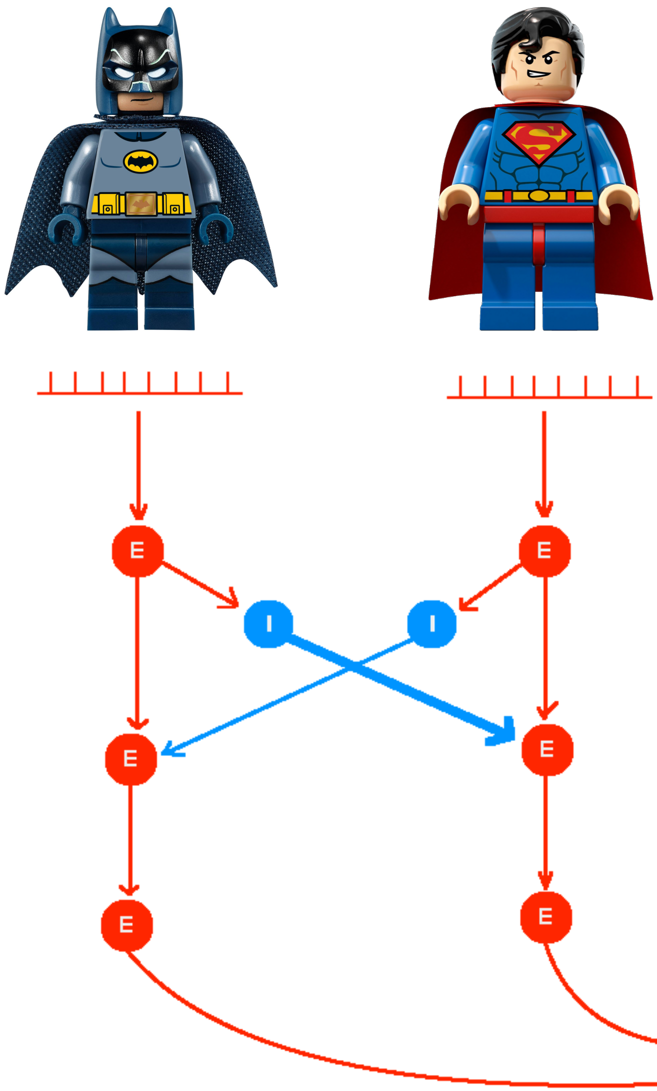




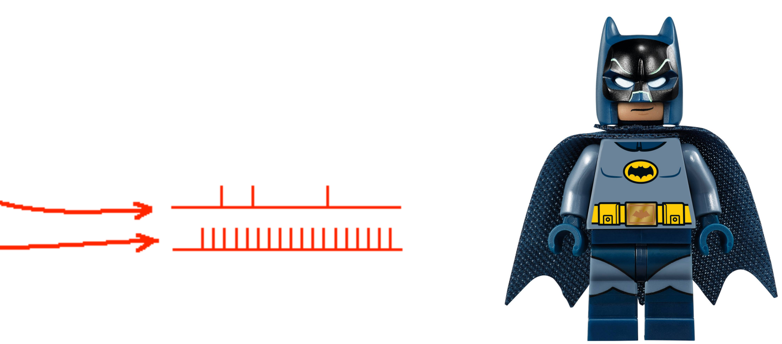
Examples of mechanisms

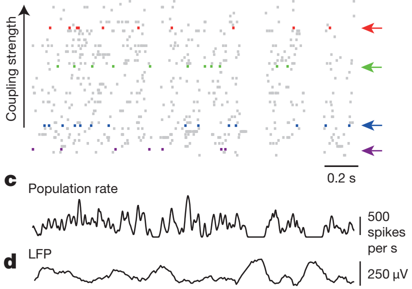
Things one can obtain combining neurons in networks

Lateral inhibition

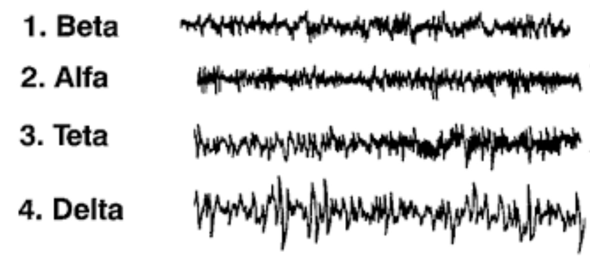


Suppression of the activity of a group of neurons by another group of neurons. Contrast enhancement mechanism used in sensory systems.

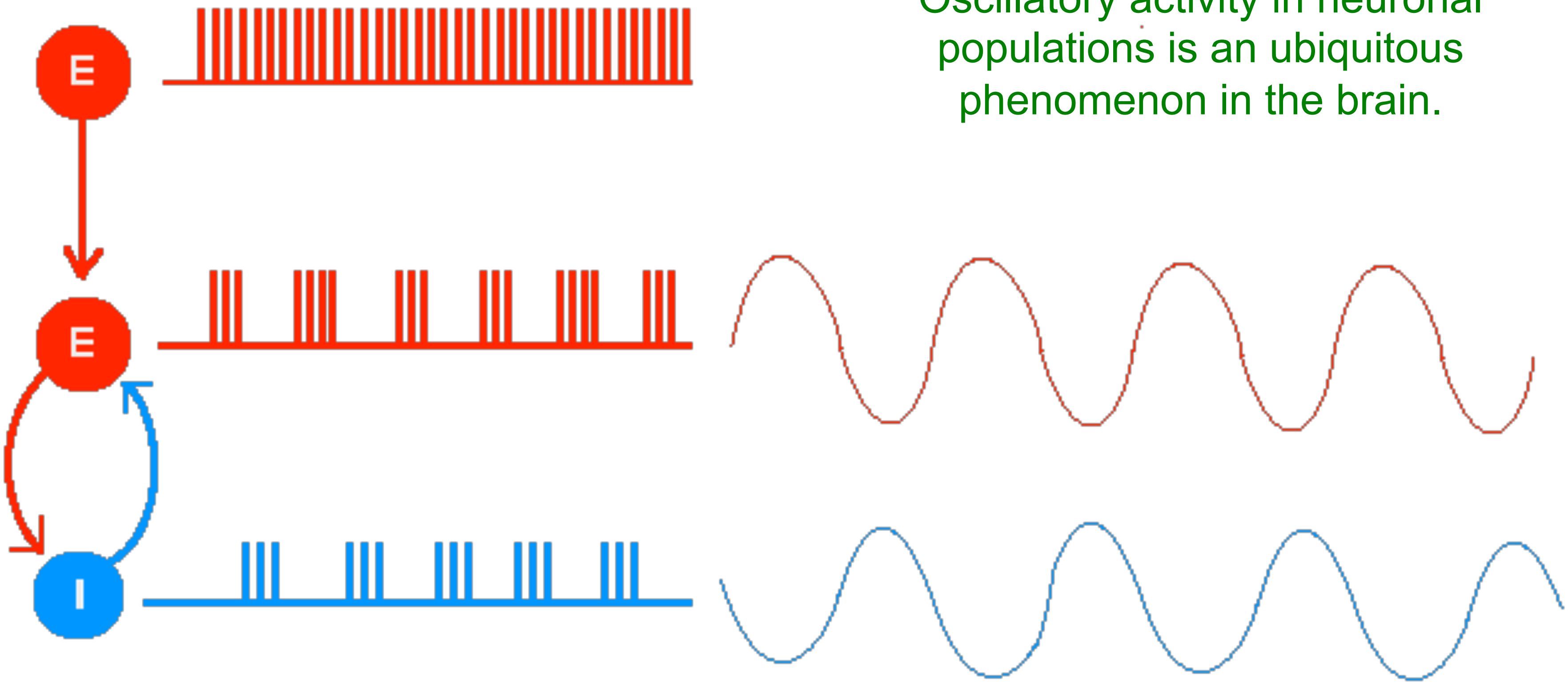




Oscillations

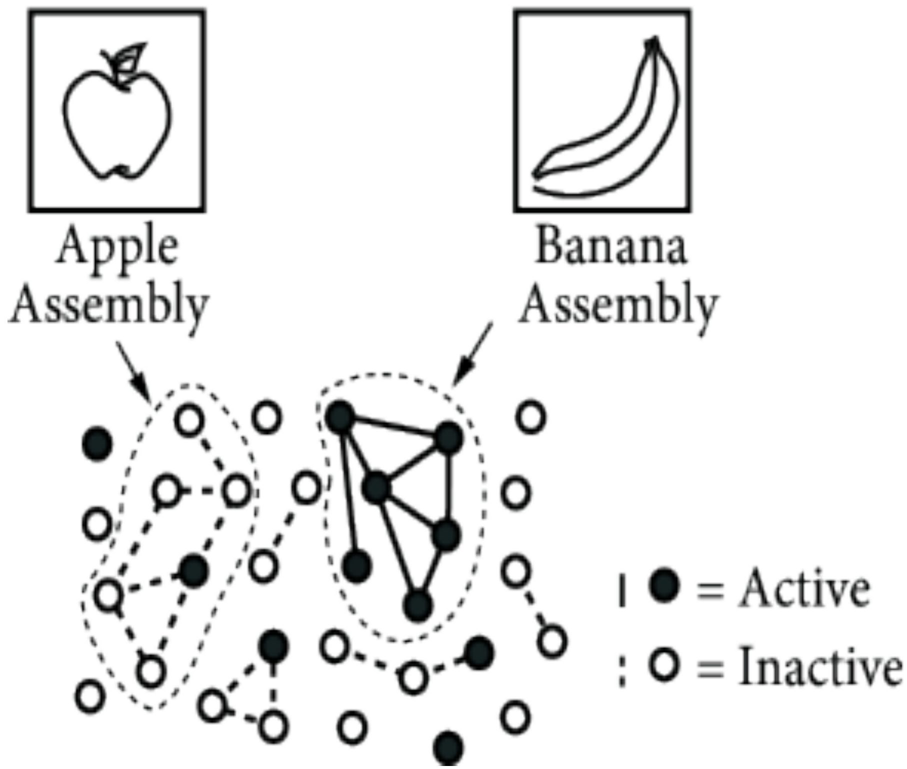


Oscillatory activity in neuronal populations is an ubiquitous phenomenon in the brain.



Hebbian plasticity

- Mechanism of **synaptic weight change** proposed by Hebb in 1949 to implement formation of cell assemblies and learning
- The weight of the synapse between two neurons grows whenever their firing activity is correlated: **neurons that fire together wire together**



Part 3

Watch and play in
the next four weeks