# Basics

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# Outline

Introduction

- Neuroscience concepts
- Single neurons: morphologies and electrophysiology
- Networks of neurons

Papers

- Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

# I. Neuroscience

# Short Introduction to Neuroscience: Antiquity

In order to understand what is neuroscience, we have to go back in time. The study of the brain started as an attempt to explain and treat neurological symptoms. The first written information come from ancient Egypt and Greece.

*The guiding principles of modern science—the formulation of testable hypotheses, controlled experimentation, and observer objectivity—are largely the achievements of later generations, and their application to the ancient neurosciences would be premature. From this perspective, many old theories regarding brain function and the nature of scientific evidence are decidedly* ***speculative and dubious****. In this early phase of medicine, it was also impossible to classify illnesses morphologically or etiologically. It is critical to keep in mind when studying ancient neurology that ancient science (Egyptian and Greco-Roman) differs fundamentally from modern science.* ~ Karenberg A. Chapter 5: the Greco-Roman world. Handb Clin Neurol

# Short Introduction to Neuroscience: Antiquity - Egypt

Signs and symptoms of neurological disease can be found in ancient texts and sources, including those of Ancient Egypt. However, we have only an unclear understanding of how Egyptian physicians themselves organized their observations. Egyptian doctors made careful observations of illness and injury, some of which involved the nervous system. We have three sources of information about Egyptian medicine:

- Papyri
- Inscriptions
- Mummified remains

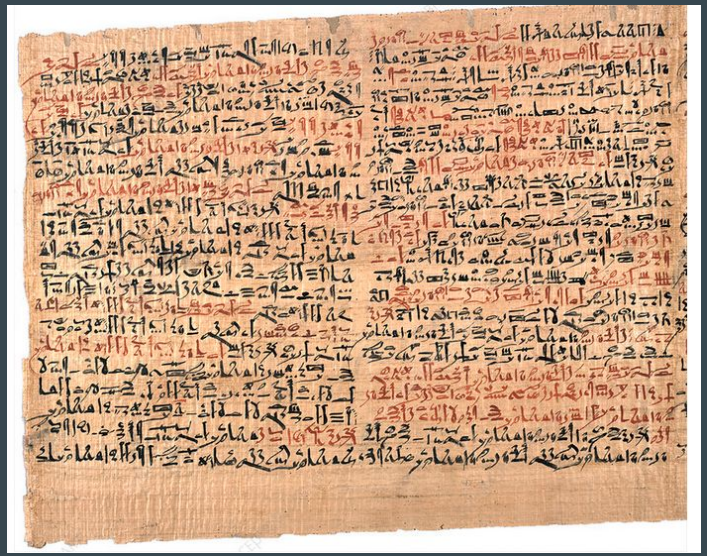
# Short Introduction to Neuroscience: Antiquity - Egypt

**Edwin Smith Papyrus** is an ancient Egyptian medical text, named after Edwin Smith who bought it in 1862 and it refers to the "**Secret Book of the Physician**".

Ancient Egypt, c. 1600 BCE

Symptoms, diagnosis, and prognosis of two patients, wounded in the head

While the symptoms are well written and detailed, the absence of a medical precedent is apparent, and magic / superstition are intertwined.



# Short Introduction to Neuroscience: Antiquity - Greece

Medical science in Greco-Roman times (8th century BCE to 4th century CE) has influenced by older beliefs. In early Greek medicine for example, we detect elements of Egyptian medicine.

As in many other cultures, the early Greeks understood health and illness as divinely bestowed. The myths Homer, Hesiod and other poets recited contained numerous healing deities, including the central healing god Asclepius which knew the medical arts.

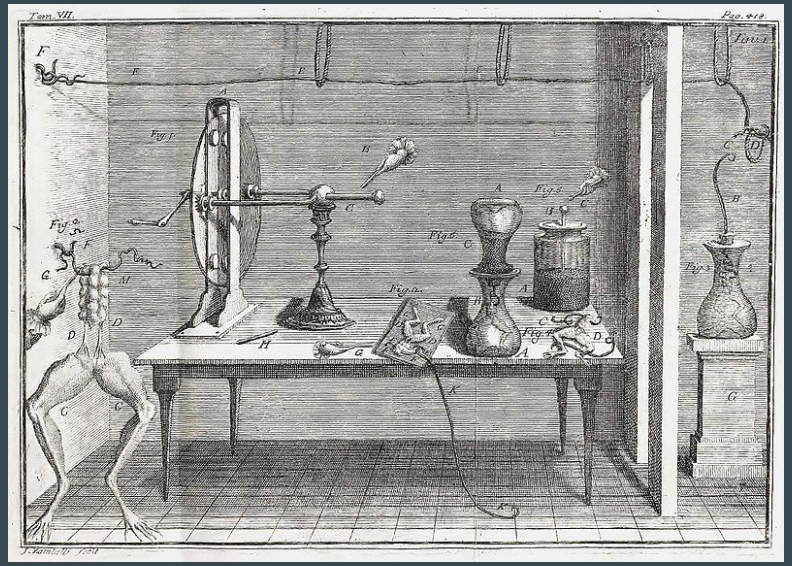
# Short Introduction to Neuroscience: Antiquity - Greece

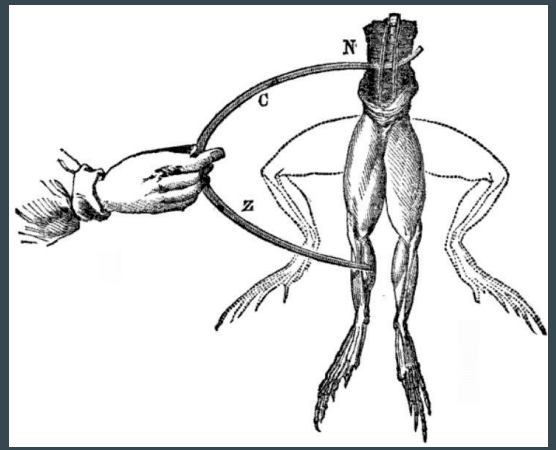
One of the first to study and dwell on the internal causes of illnesses (and especially mental illnesses) is considered to be Alcmaeon, to whom the book “On nature” is attributed - although its original title may differ as Alexandrian writers were known to have ascribed the title "On Nature" to a wide variety of works.

It is considered that Alcmaeon excised an animal eye to study the optic nerve. Based on this observation,Alcmaeon described the senses - except for the touch sense. His observations contributed to the study of medicine by establishing the connection between the brain and the sense organs, and outlined the paths of the optic nerves as well as stating that the brain is the organ of the mind.

# Short Introduction to Neuroscience - Modern

One of the first to experiment with electricity on dissected frogs was Luigi Galvani in the second half of the 18th century, exciting the imagination of how the animal body works and inspiring literature stories such as Mary Shelley's Frankenstein.





# Short Introduction to Neuroscience - Action potential

One of the main discoveries about neuron functionality was by Emil du Bois-Reymond (du Bois-Reymond, 1843): he first discovered that the peripheral passage of a nerve impulse was accompanied by an electrical discharge, establishing the foundation to describe the action potential.

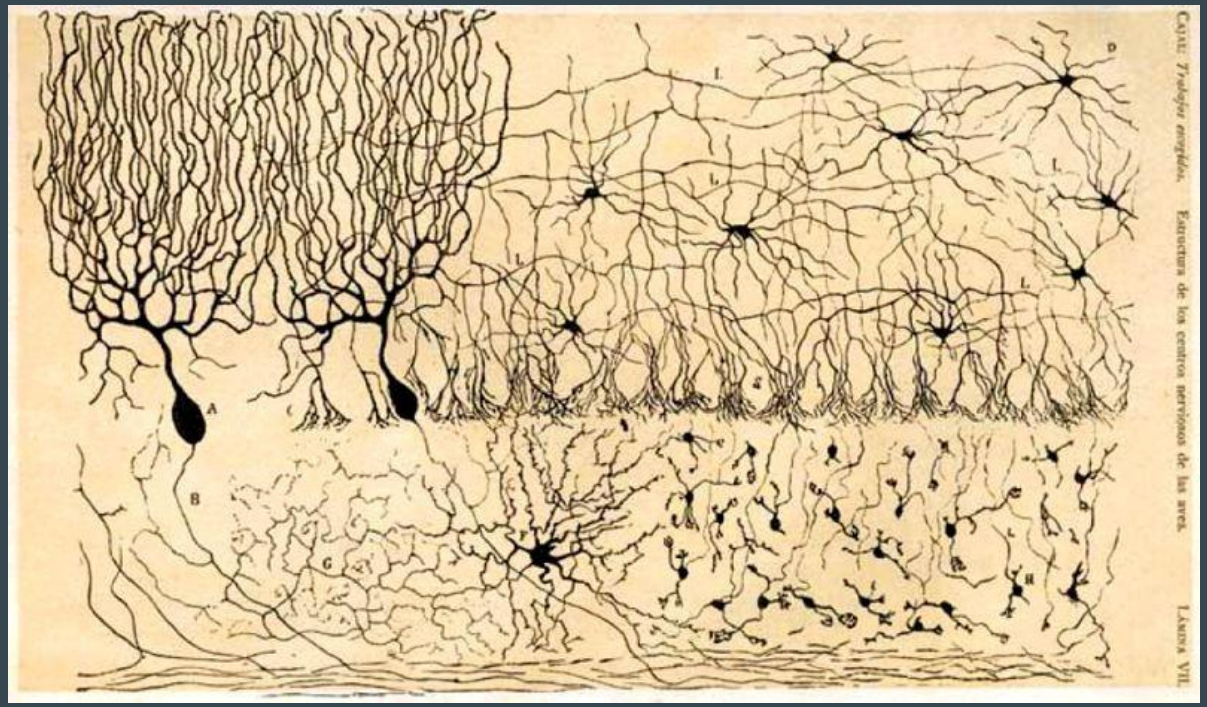
Much later, Hodgkin and Huxley (1952) formed a mathematical model that describes how action potentials are generated and propagated in excitable cells such as neurons and muscle cells. It is a set of nonlinear differential equations that approximate the electrical characteristics of neurons. The Hodgkin–Huxley model is regarded as one of the great achievements of 20th-century biophysics. Nevertheless, the Hodgkin–Huxley model is a simplification of the actual action potential generation process.

# Short Introduction to Neuroscience - Neuronal morphologies

Studies of the brain became more sophisticated after the invention of the microscope and the development of a staining procedure by **Camillo Golgi** during the late 1890s that used a silver chromate salt to reveal the intricate structures of single neurons.

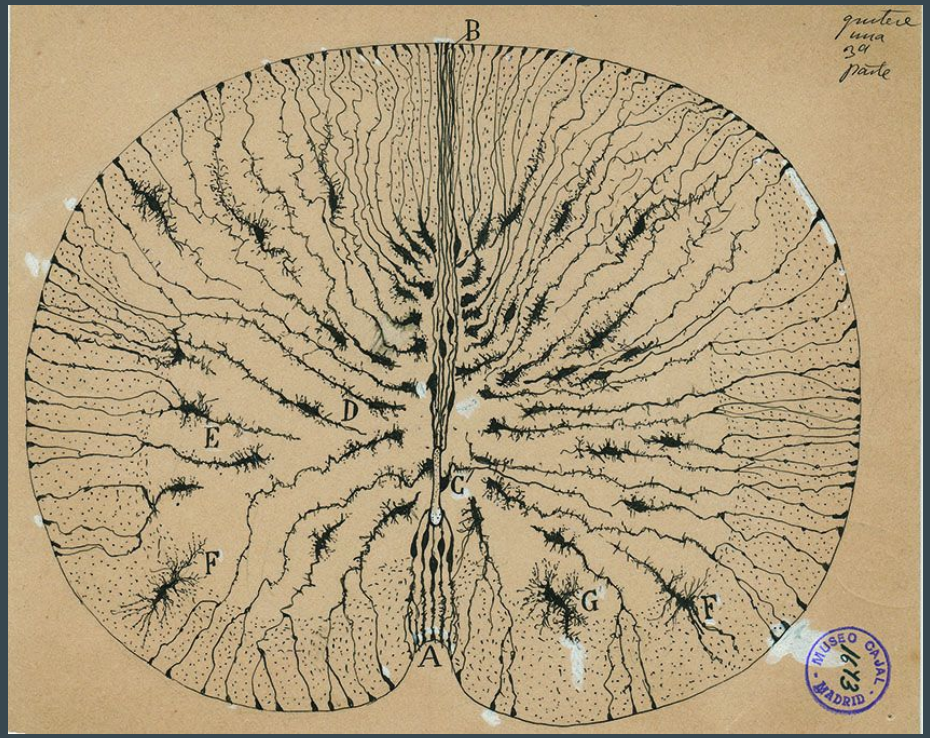
His technique was used by **Santiago Ramón y Cajal** and led to the formation of the neuron doctrine, the hypothesis that the functional unit of the brain is the neuron. The hypotheses of the neuron doctrine were supported by experiments following Galvani's pioneering work in the electrical excitability of muscles and neurons.

# Short Introduction to Neuroscience - Neuronal morphologies



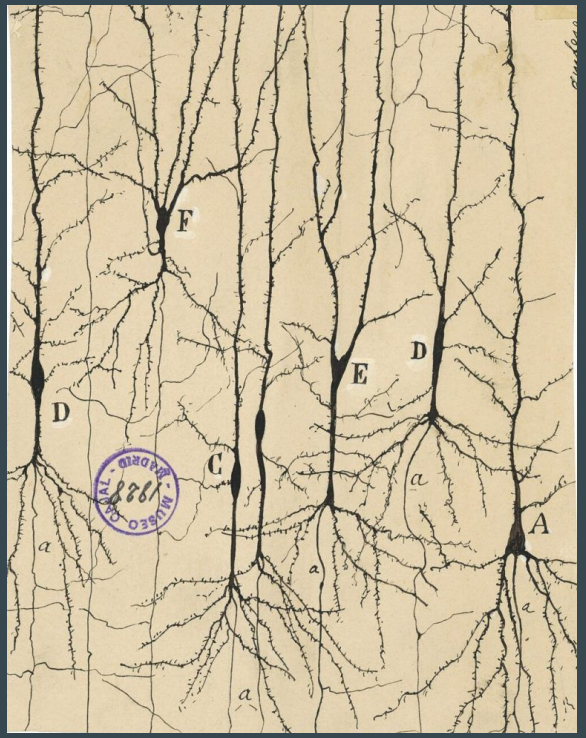

Ramón y Cajal, (Cells of the cerebellum of a chicken, 1905)

# Short Introduction to Neuroscience - Neuronal morphologies




Ramón y Cajal, Glial cells of the mouse spinal cord, 1899

# Short Introduction to Neuroscience - Neuronal morphologies




Ramón y Cajal, drawings of neurons show them as separate, individual cells

# II. Single neurons

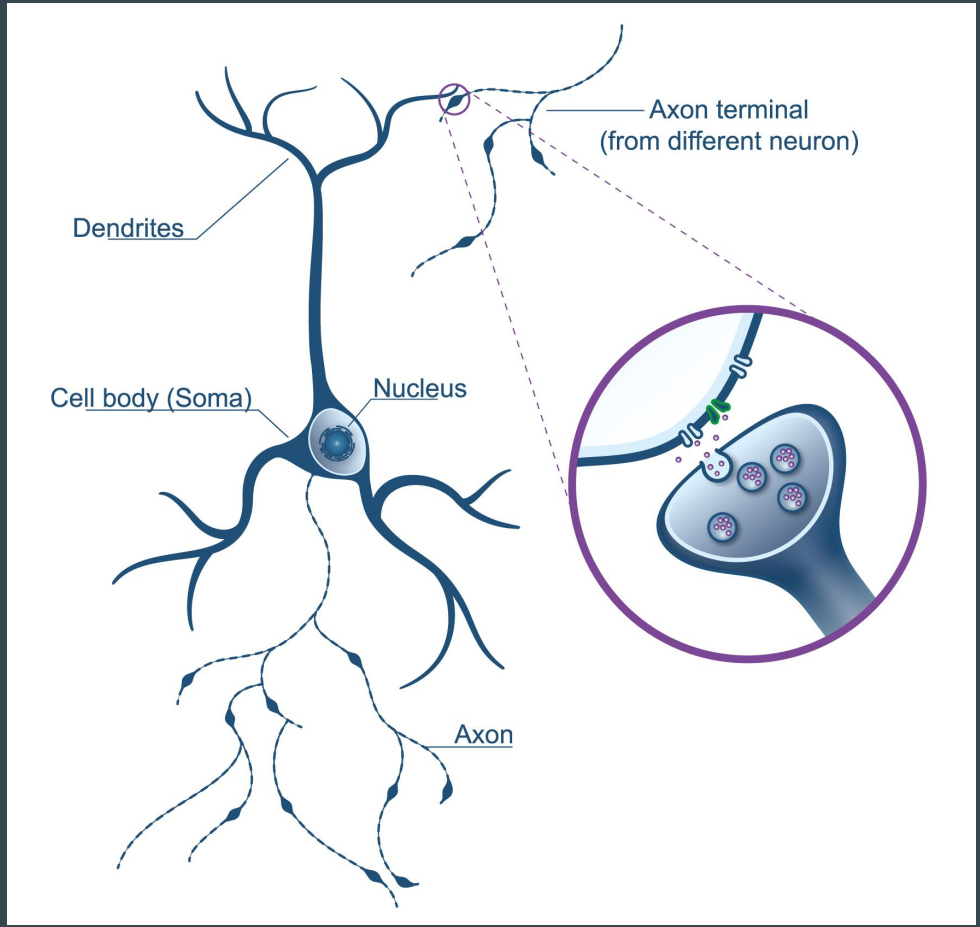
# Neuronal morphologies

Neurons are the fundamental units of the nervous system.

They are electrically excitable, i.e. they transmit electrical signals.

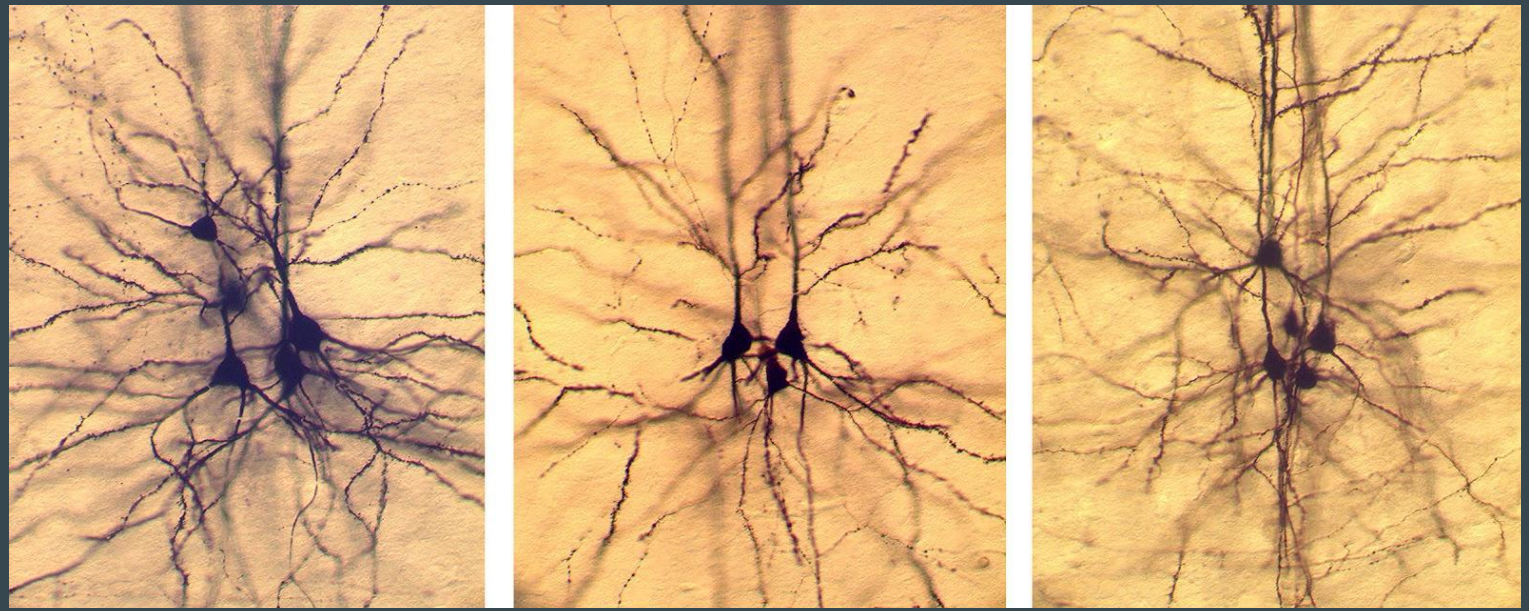
They consist of a soma, a dendrite and an axon.

They create connections with each other through synapses that form between the axons of one neuron and the dendrites of another.



# Neuronal morphologies

What does a neuron look like in real life? In the microscope stained tissue reveals neuronal structures:



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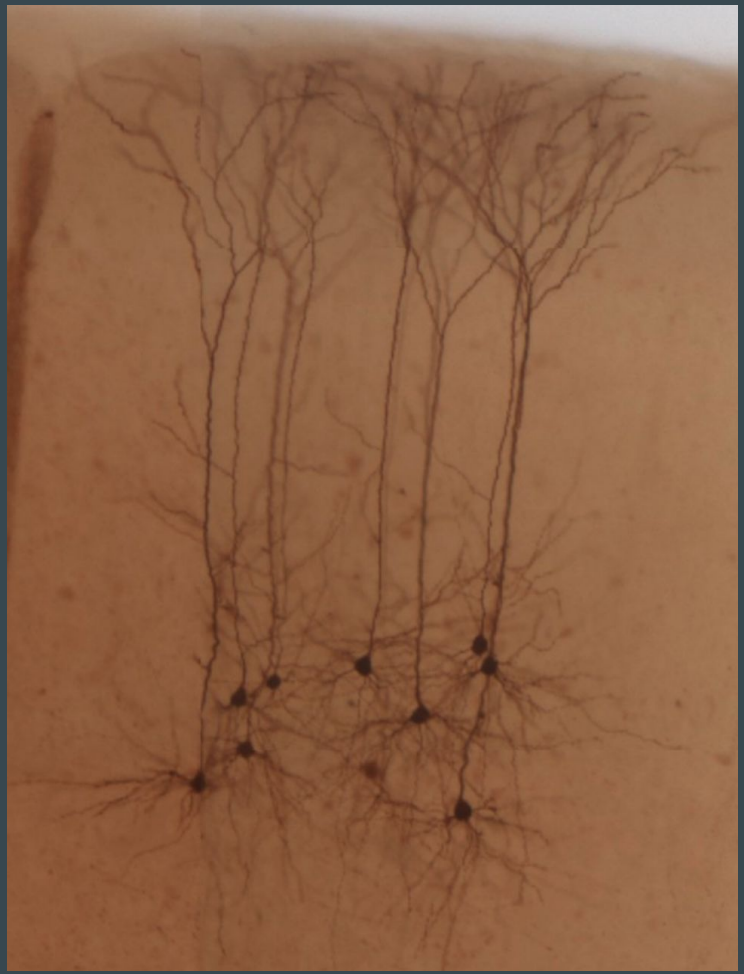

Rodrigo Perin, LNMC
pyramidal cells

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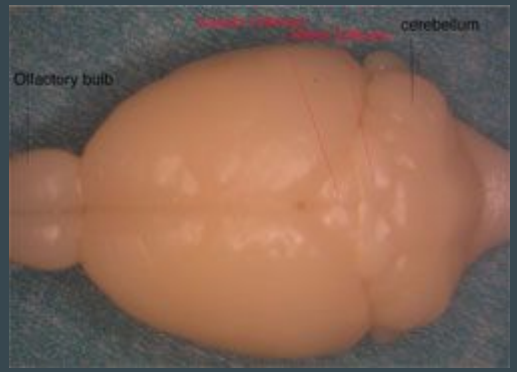



Dorsal view of fixed mouse brain, Source: Neurogenetics at UT Health Science Center

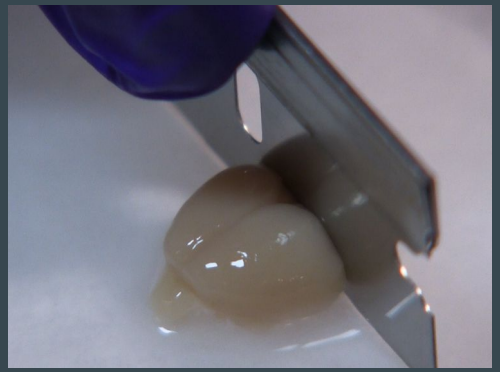
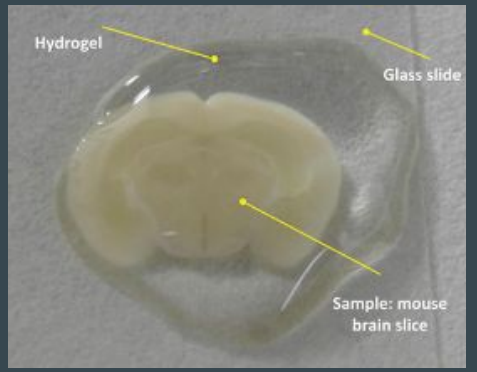


Illustration of brain slicing, Source:




Brain slice, Source: https://currentprotocols.onlinelibrary.wiley.com

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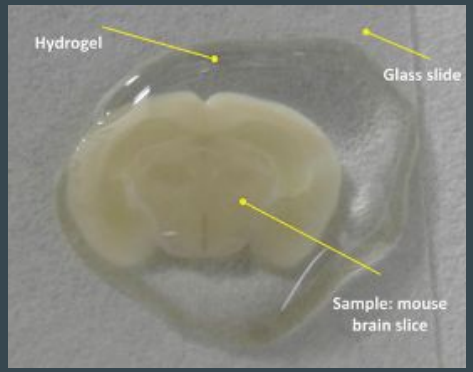


Brain slice,
Source:
https://currentprotocols.onlinelibrary.wiley.com


Slice in the microscope
Source:
https://currentprotocols.onlinelibrary.wiley.com

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# Neuronal morphologies

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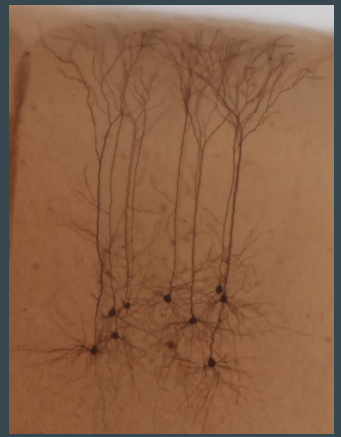
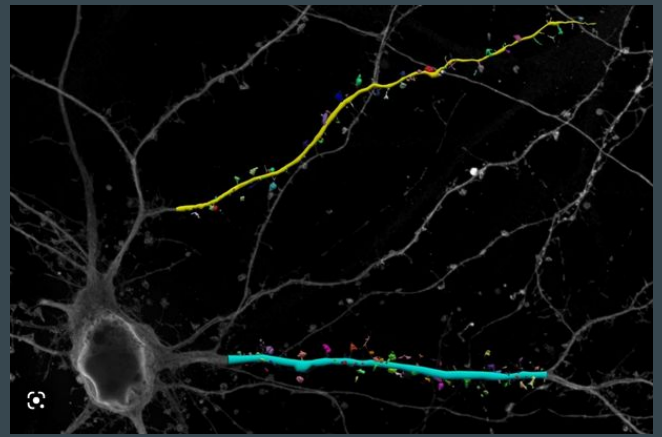
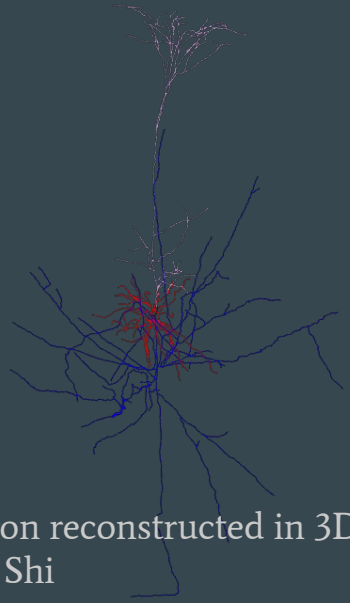


Rodrigo Perin, LNMC pyramidal cells



Reconstruction in neurolucida



Neuron reconstructed in 3D, Ying Shi

# Neuronal morphologies

1. Neurons can be separated into classes based on their shapes:
   a. Based on observations under the microscope (expert classification)
   b. Based on objective measurements (morphometrics)
2. Neurons are electrically excitable
   a. Neurons can express electrical activity when stimulated by current / voltage
   b. Neurons can be computationally simulated
3. Neuronal morphologies influence electrical activity
4. Connectivity depends on neuronal shapes

# Neuronal morphologies - open questions

1. What is the precise relation between neuron morphologies and electrical activity?
2. Is there a computational advantage for neuronal / dendritic shapes?
    a. Can dendrites be replaced by point neurons, i.e., in neural networks without loss of functionality?
    b. What can we learn from dendrites and axons?
3. What links transcriptomics to observed neuronal phenotypes?

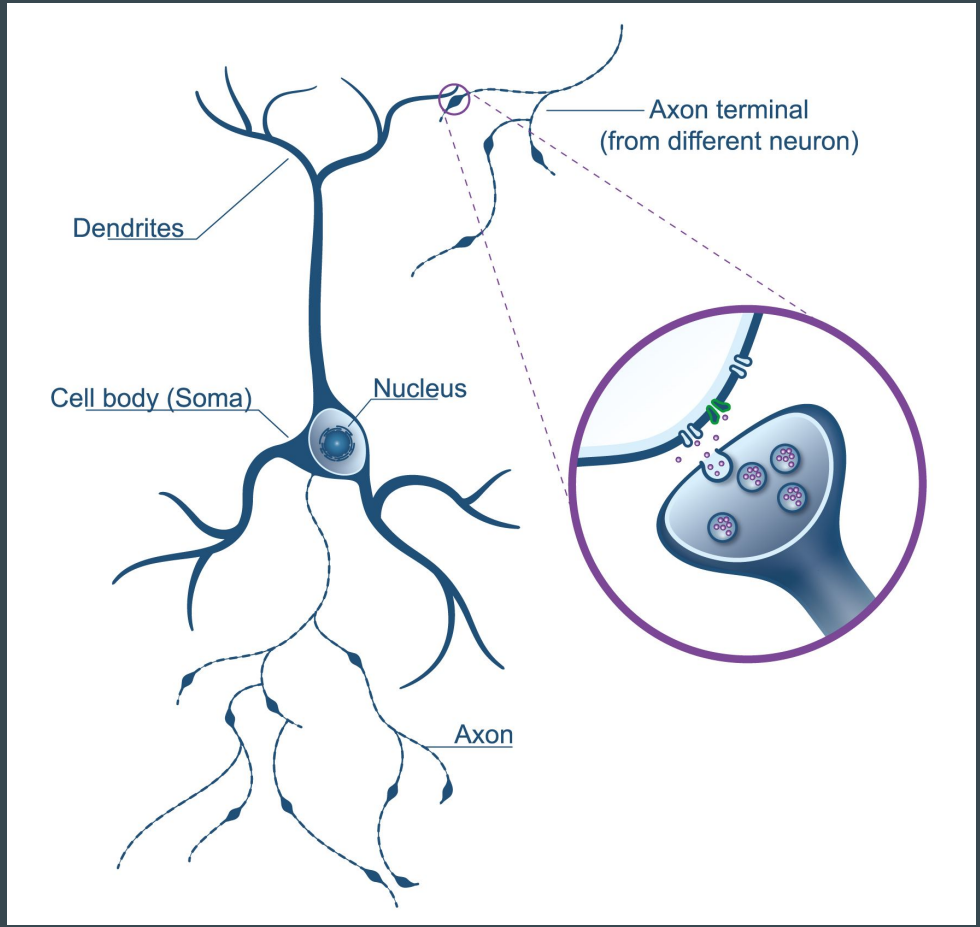
# III. Electrical activity of single neurons

# Neuronal morphologies

Neurons are electrically excitable, i.e. they transmit electrical signals.

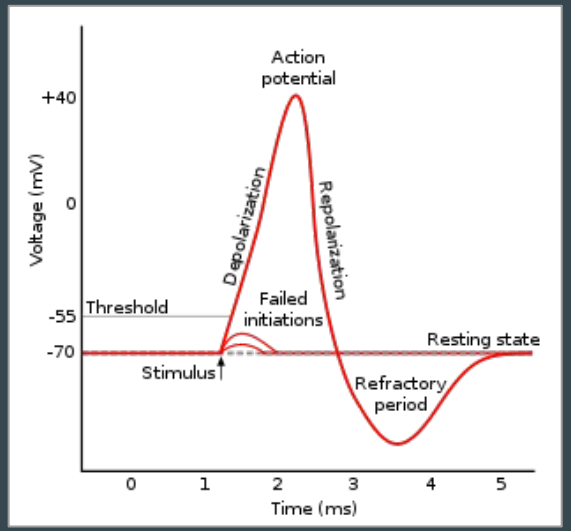
How are these electrical signals generated?

An “action potential” is transmitted from the pre-synaptic to the post-synaptic neuron through the synapse.



# Membrane potential

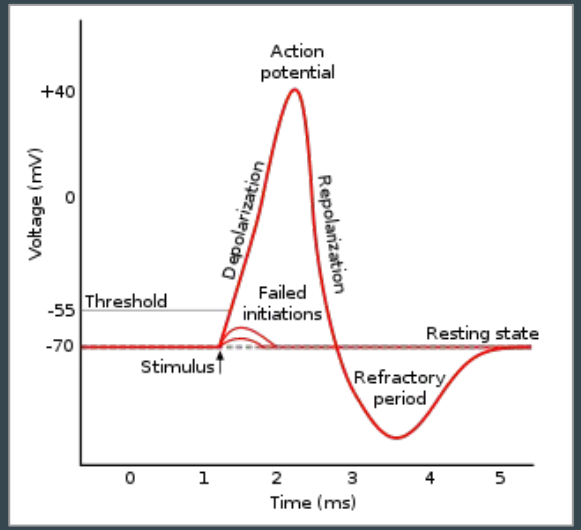
The potential difference u(t) between the interior of a cell and its surroundings is called the membrane potential. Without any input, the neuron has a stable membrane potential $u_{rest}$ which is about -65mV.




Source: wikipedia.com

# Action potential

An action potential is produced when enough spikes are received at the cell body and an electrical signal is transmitted by the neuron. It is characterised by a rapid rise and subsequent fall in voltage across a cellular membrane with a characteristic pattern. This rise and fall in the voltage causes the neuron to “fire”.




Source: wikipedia.com

# Action potential

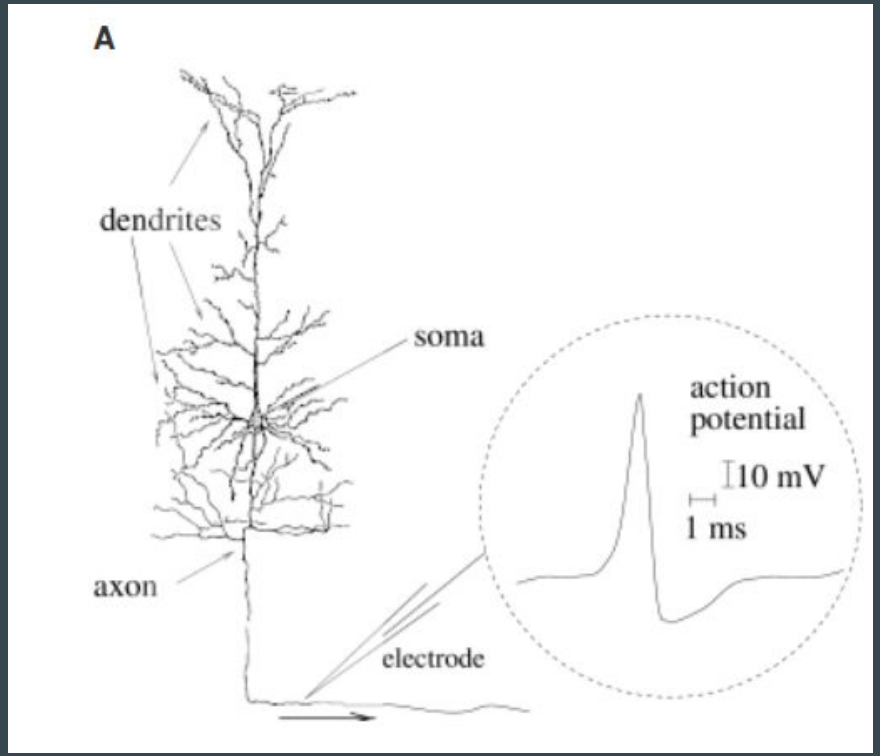
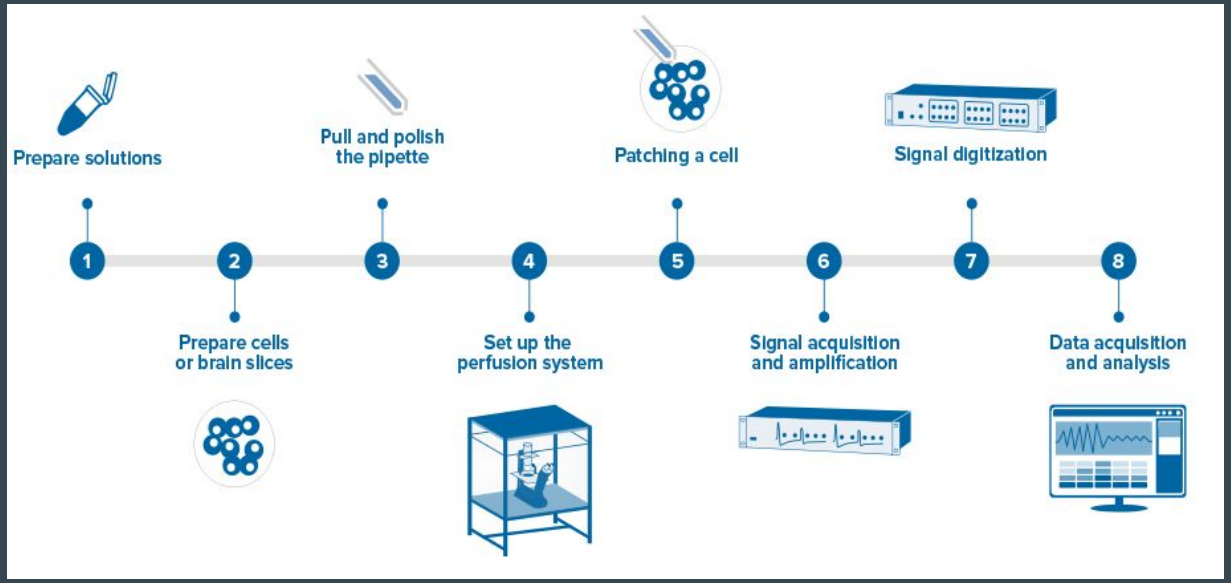



Fig. 1.2: A. Single neuron in a drawing by Ramón y Cajal. Dendrite, soma, and axon can be clearly distinguished. The inset shows an example of a neuronal action potential (schematic). The action potential is a short voltage pulse of 1-2 ms duration and an amplitude of about 100 mV

https://neuronaldynamics.epfl.ch/online/Ch1.S1.html

# Electrophysiology: experimental data

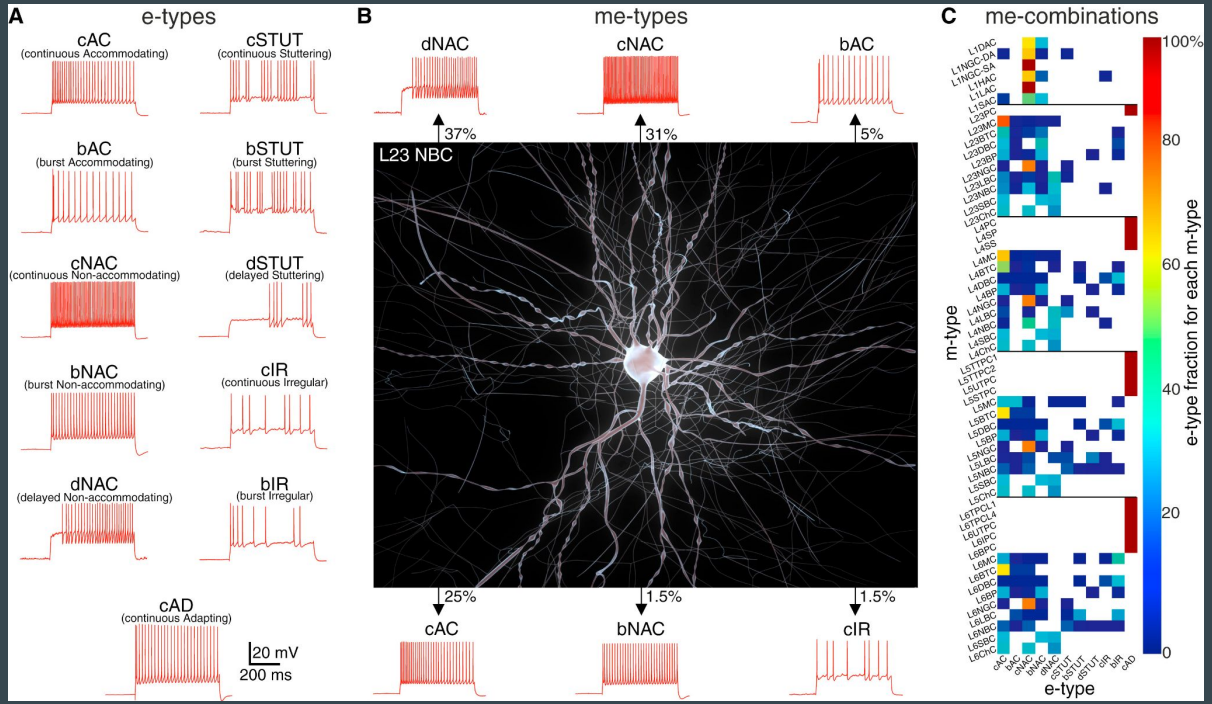
The potential difference u(t) can be recorded by an intracellular electrode which is inserted to the cell body.



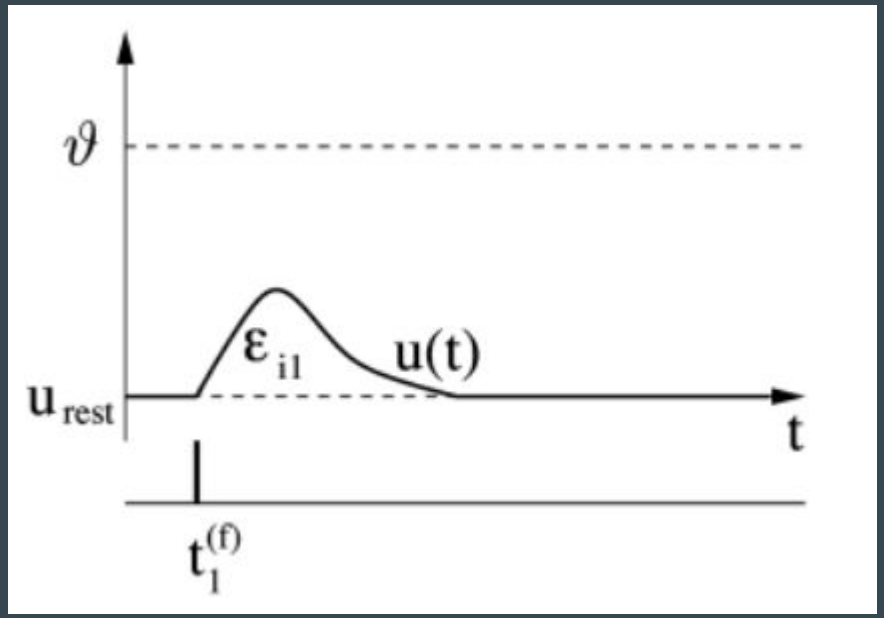

www.moleculardevices.com

# Action potential

Different cell types are characterized by specific firing patterns.



# Postsynaptic Potentials




https://neuronaldynamics.epfl.ch/online/Ch1.S1.html

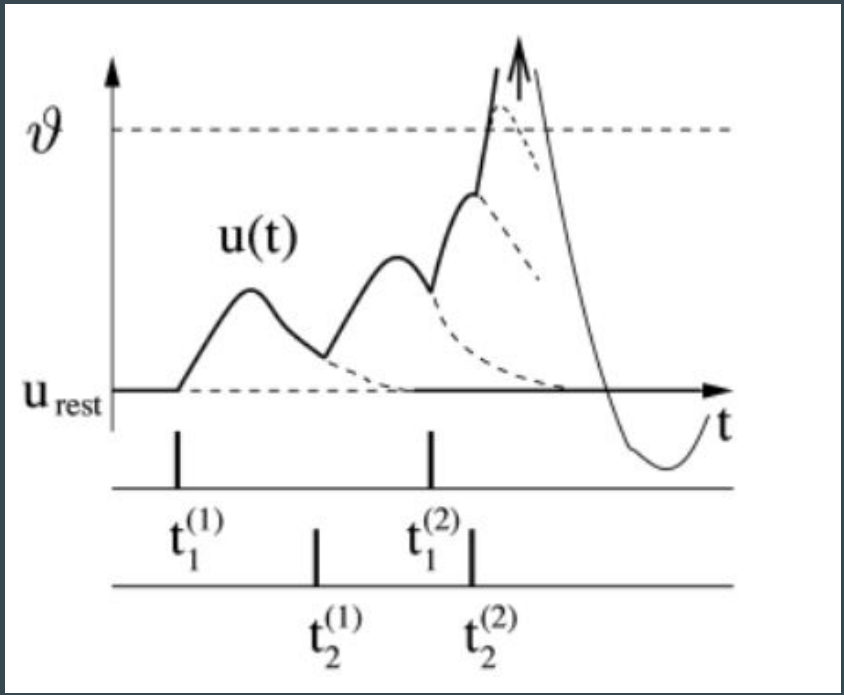
At each point in time, the difference between the membrane potential and the rest membrane potential

$$u_i(t) - u_{\text{rest}} =: \epsilon_{ij}(t)$$

defines the postsynaptic potential (PSP). It can be summed up to compute the total change in the potential of a cell.

$$u_i(t) = \sum_j \sum_f \epsilon_{ij}\left(t - t_j^{(f)}\right) + u_{\text{rest}}$$

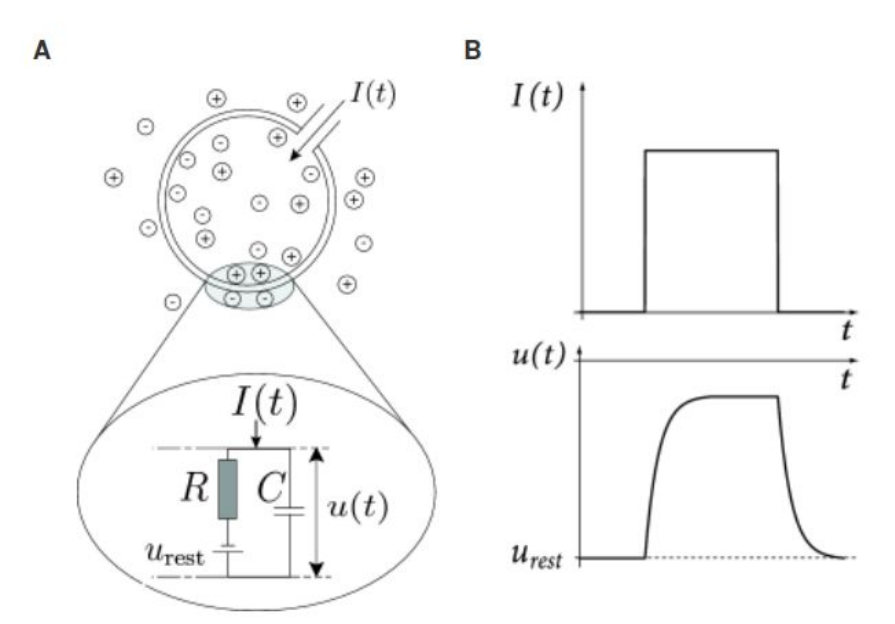
# Firing Threshold and Action Potential




https://neuronaldynamics.epfl.ch/online/Ch1.S1.html

Linearity breaks down when many inputs are received at the soma during a short interval. If the firing threshold θ is surpassed, the membrane potential exhibits a pulse-like excursion with an amplitude of about 100 mV. This short voltage pulse propagates along the axon to the synapses with other neurons. After the action potential, the membrane potential does not directly return to the resting potential, but typically passes through a phase of hyperpolarization below the resting value.

# Integrate-And-Fire Models




https://neuronaldynamics.epfl.ch/online/Ch1.S3.html

The current in the neuron, if seen as an electrical circuit, it can be described by an equation:

$$I(t) = \frac{u(t) - u_{\text{rest}}}{R} + C\frac{\mathrm{d}u}{\mathrm{d}t}$$

When solved it gives a way to compute u(t):

$$u(t) = u_{\text{rest}} + R\,I_0\left[1 - \exp\left(-\frac{t}{\tau_m}\right)\right]$$

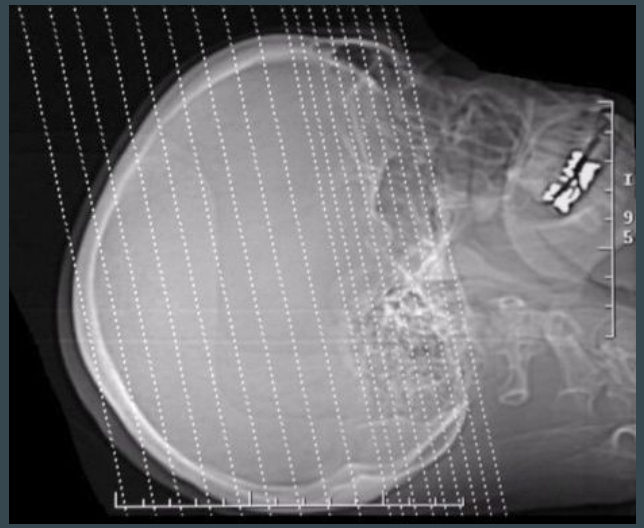
To learn more you can visit:

https://neuronaldynamics.epfl.ch/book.html

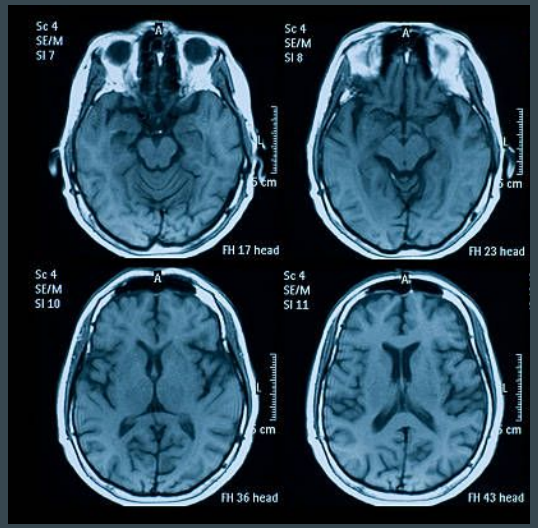
# IV. Networks

# How can we study neuronal networks?

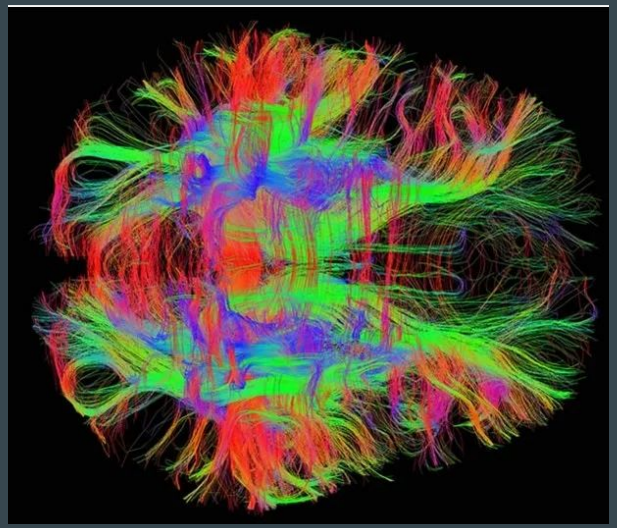
1. Medically accessed with large scale anatomical brain imaging: CT, MRI, DTI



CT imaging
https://case.edu/med/neurology/NR/CT%20Basics.htm



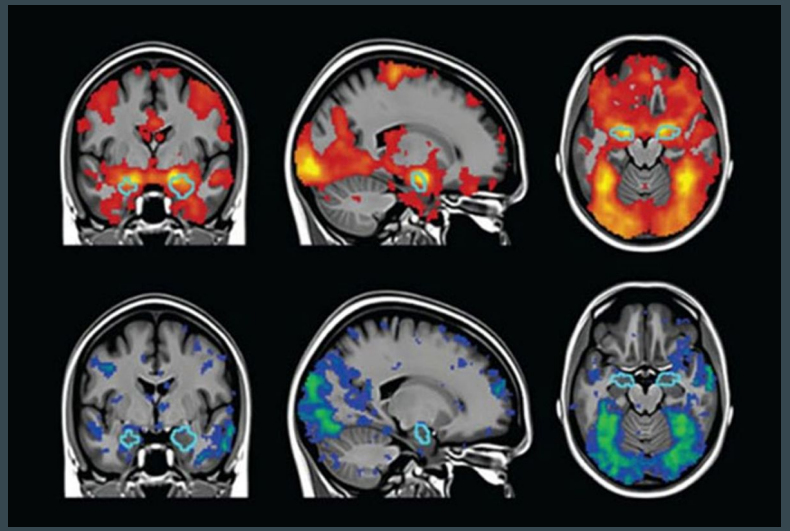

MRI



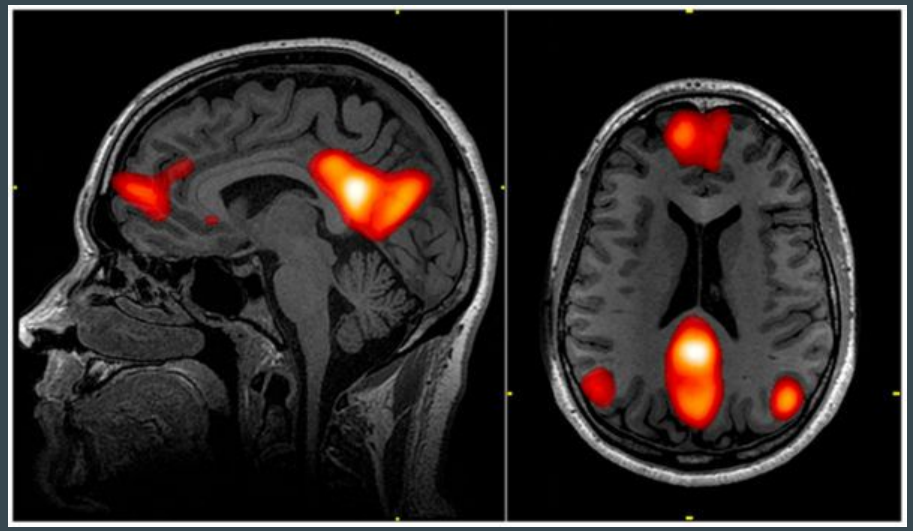
DTI
Image Credit: Zeynep Saygin, mcgovern.mit.edu

# How can we study neuronal networks?

1. Medically accessed with large scale anatomical brain imaging: CT, MRI, DTI
2. Medically accessed with large scale functional imaging: fMRI BOLD, EEG



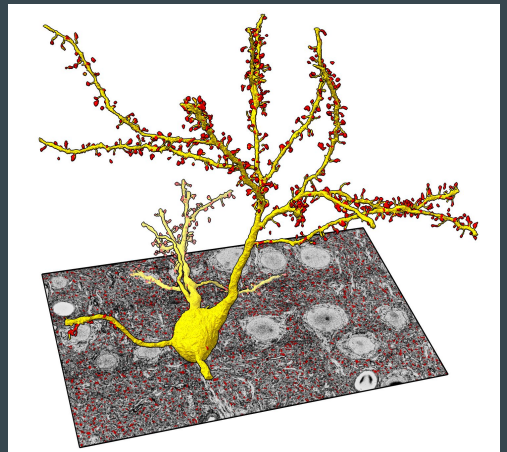
fMRI, https://www.the-scientist.com/



BOLD MRI, https://www.practical-patient-care.com

# How can we study neuronal networks?

1. Medically accessed with large scale anatomical brain imaging: CT, MRI, DTI
2. Medically accessed with large scale functional imaging: fMRI BOLD, EEG
3. (Animal experimentation): Electro-Microscopy (EM)



https://www.rbvi.ucsf.edu/chimerax

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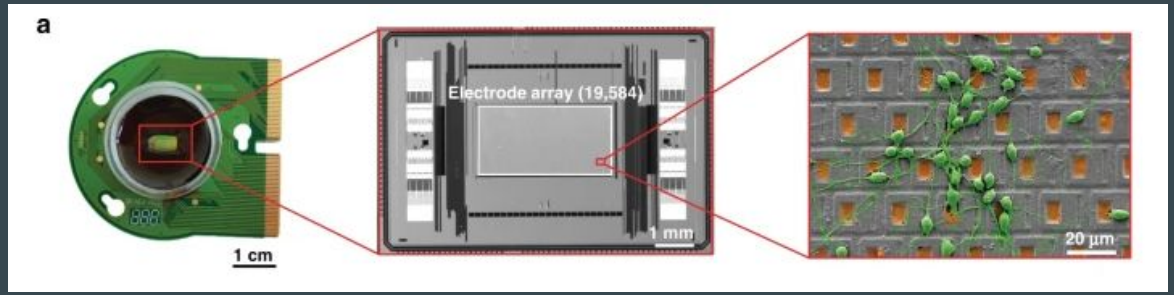
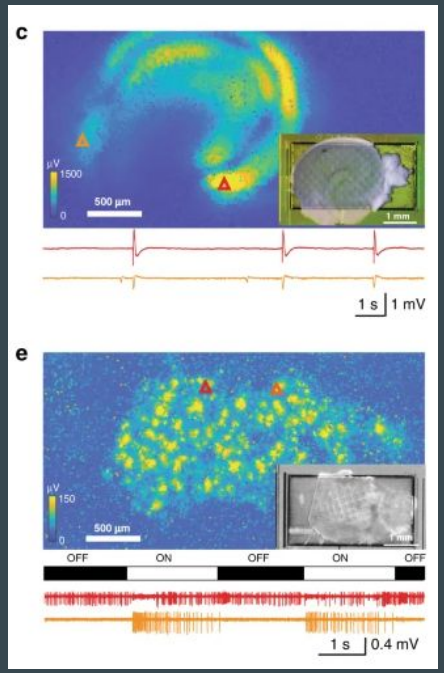
4. (Animal experimentation): Multielectrode Array (MEA)




Yuan, Schröter,et al. 2020



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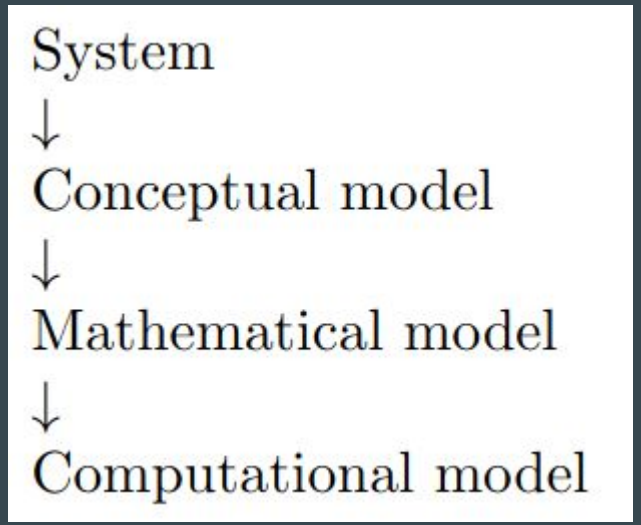
An alternative technique is computational modelling

# Computational modeling of neuronal networks

What is computational modeling?



# Computational modeling of neuronal networks

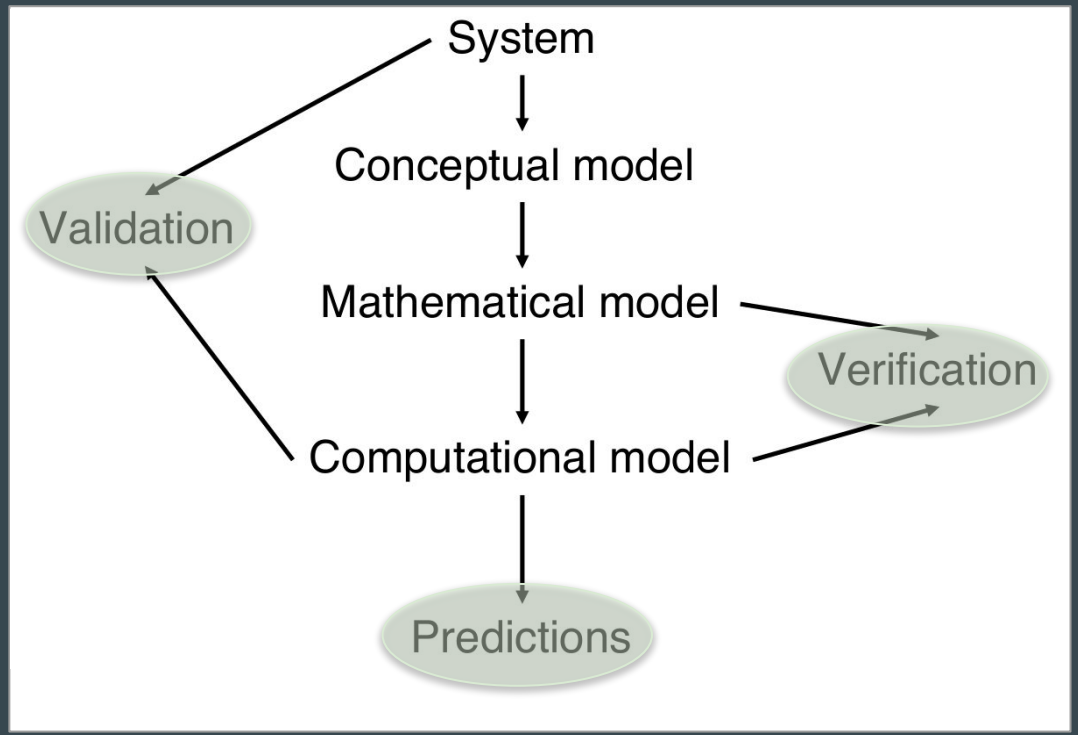
What is computational modeling?

System
↓
Conceptual model
↓
Mathematical model
↓
Computational model

Biological neurons
↓
Electrical excitability
↓
Leaky Integrate and Fire (LIF) model
↓
NeuroN

# Computational modeling of neuronal networks

For a computational model we need verification, validation and predictions



# Computational modeling of neuronal networks

Advantages of computational modelling:

- Complexity: they allow access to the full complexity of a system
- Control: explicit about parameters
- Usability: easy to manipulate, explore parameters, explore unexpected effects
- Universal: provide a unified framework, can explore different time scales

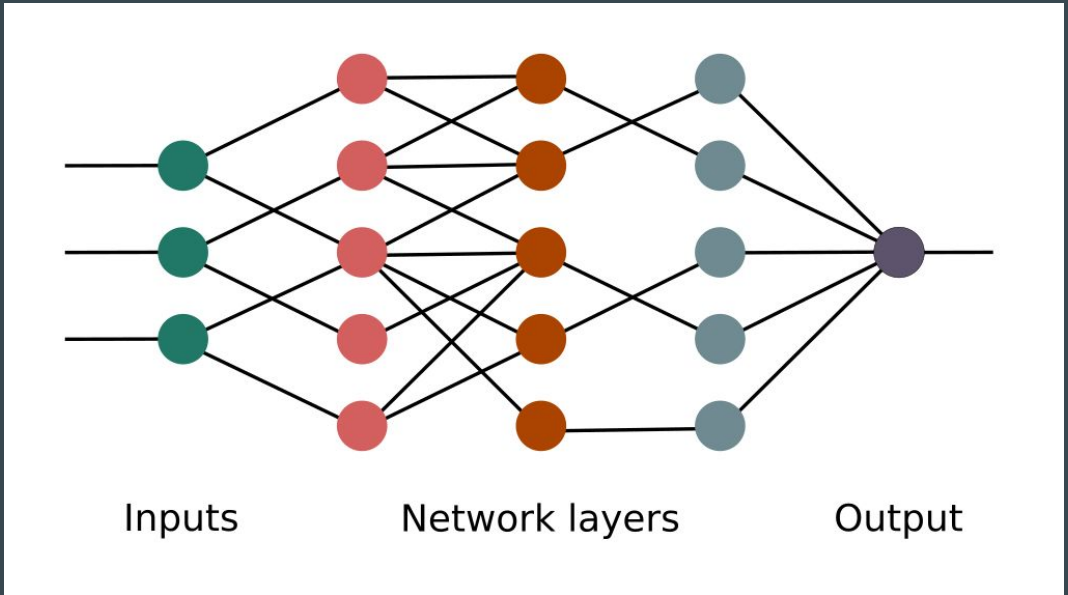
# Computational modeling of neuronal networks

Disadvantages of computational modelling

- Correctness: Computational models are wrong (no model is universally correct, the choice of model is important for what we learn and what questions we are allowed to ask)
- Data availability: Experimental data may not be readily available, of sufficient quantity or of good quality
- Time limitations: may be too complex to simulate in realistic times
- Interpretability: it might be hard to analyze or understand the results

# Neuronal networks

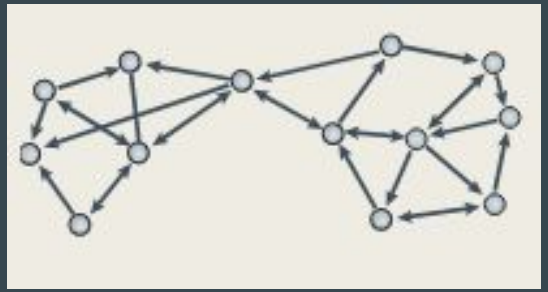
So what is a neuronal network? In the context of machine learning neural networks might look like:



# Neuronal networks

So what is a neuronal network?

A neural network in the brain is a complex network of neurons that communicate with each other to process and transmit information throughout the body. These neurons are interconnected by synapses, and the strength of these connections can be modified by experience, allowing the network to learn and adapt over time.



# Neuronal networks

1. Multiple experimental techniques to access higher level networks
2. Local and Global scales hard to access simultaneously
3. Computational models can help understand a system in a more holistic approach

# Neuronal networks - open questions

1. How neuronal morphologies constrain brain networks?
2. What are the precise computational properties of each brain region?
    a. Many brain regions are very well understood: for example the visual system of flies
    b. Other brain regions are well studied but not yet fully understood: cortical brain regions of mouse
    c. Some brain regions are still largely unknown: temporal association cortex of the mouse
    d. Especially in species such as humans, speculations are still highly predominant
3. How brain regions connect to each other

# V. Neurotransmission

# Neurotransmission

Electrical signals can be *excitatory* or *inhibitory*. An **excitatory** synapse is a synapse in which an action potential in a presynaptic neuron increases the probability of an action potential occurring in a postsynaptic cell. An EPSP (excitatory postsynaptic potential) will increase the probability of a cell to produce an AP while an IPSP (inhibitory postsynaptic potential) will decrease the probability for an AP. If excitatory signals in a neuron exceed inhibitory signals by a threshold, then the neuron will generate an action potential that will travel through it's axon to transmit the signal to other neurons. Excitation and inhibition are controlled by neurotransmitters.

# Neurotransmission: modulatory

*Excitatory neurotransmitters* have excitatory effects on the neuron. This means they increase the likelihood that the neuron will fire an action potential.

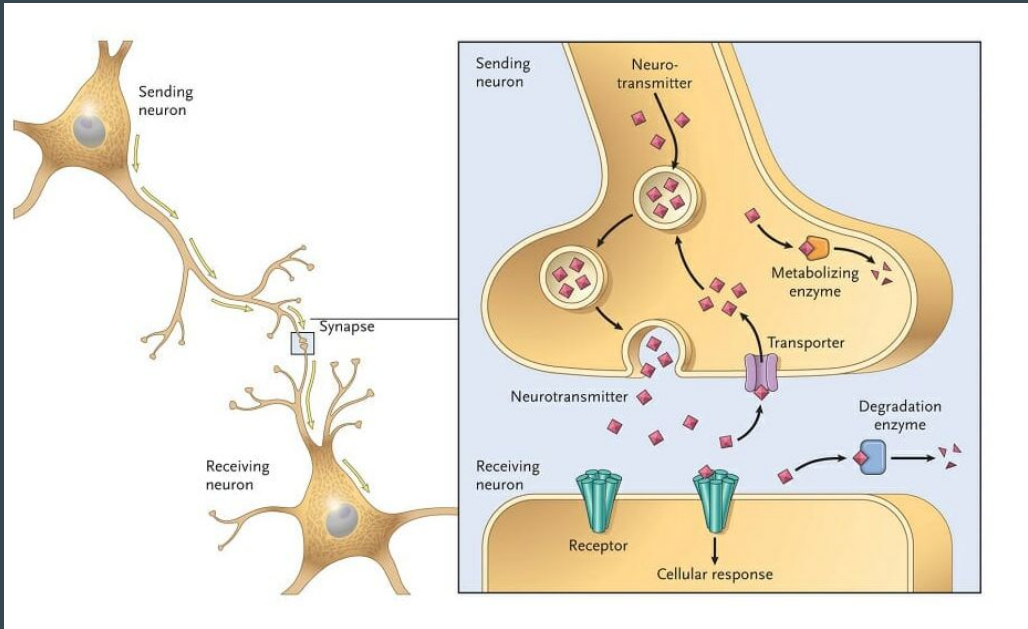
*Inhibitory neurotransmitters* have inhibitory effects on the neuron. This means they decrease the likelihood that the neuron will fire an action.

*Modulatory neurotransmitters* can affect a number of neurons at the same time and influence the effects of other chemical messengers.

# Neurotransmission

Examples:

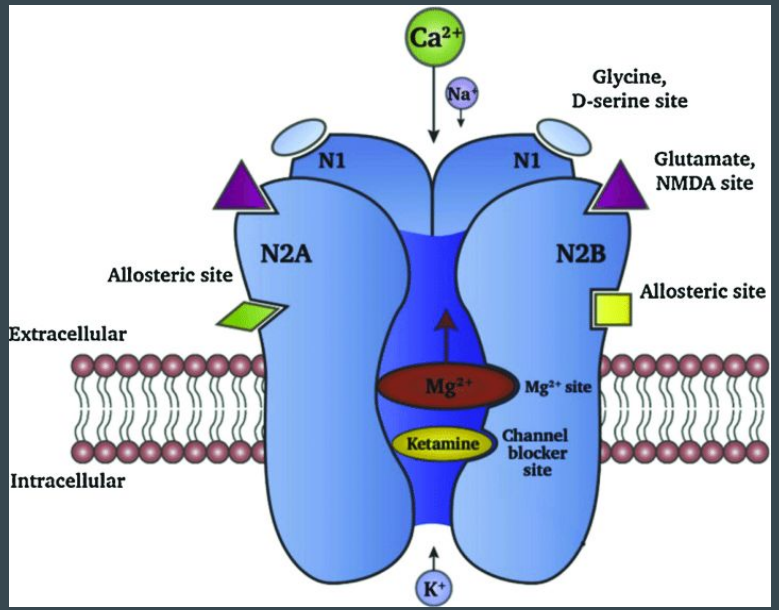
Glutamate
Gamma-aminobutyric acid (GABA)
Acetylcholine
Epinephrine (adrenaline)
Histamine
Dopamine
Serotonin



# Neurotransmission: excitation

Excitatory receptors:

NMDA: a receptor of glutamate, the primary excitatory neurotransmitter in the mammalian brain. It plays an essential role in synaptic plasticity, a neuronal mechanism believed to be the basis of memory formation.

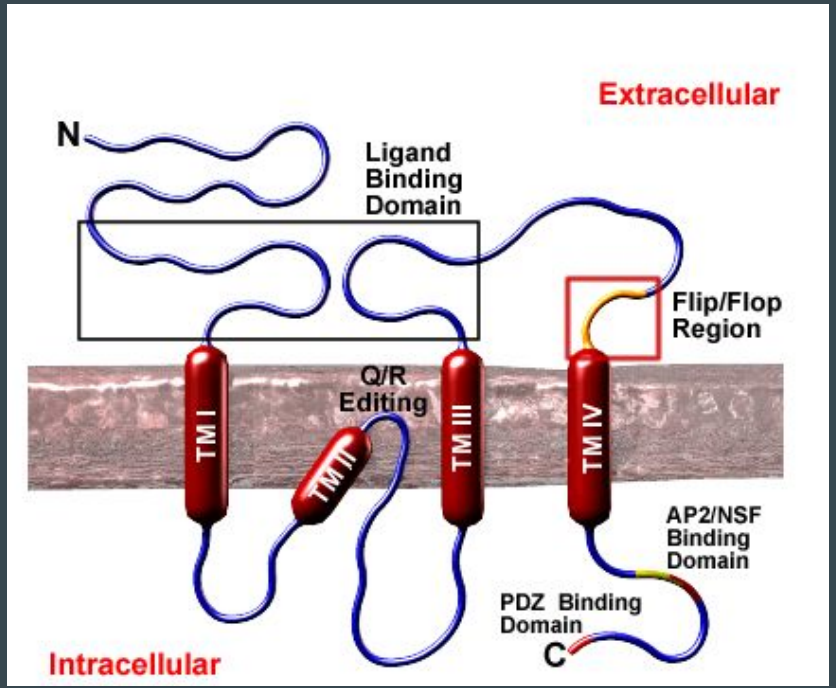


# Neurotransmission: excitation

Excitatory receptors:

NMDA

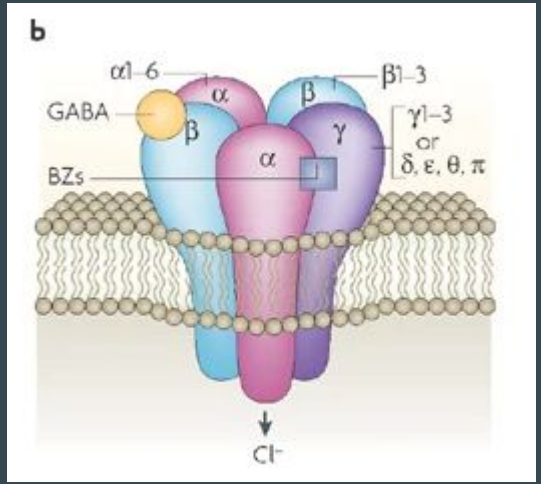
AMPA: is a receptor for glutamate (iGluR) that mediates that mediates fast synaptic transmission in the CNS. AMPA receptor modulation is one of the main mechanisms of plasticity of excitatory transmission in the brain.



# Neurotransmission: inhibition

Inhibitory receptors:

GABA: Neurons that produce GABA as their output are called GABAergic neurons, and have chiefly inhibitory action at receptors in the adult vertebrate. This is not the case in fly neurons or during brain development.



# Summary

Neurons are the fundamental units of the nervous system, they express a variety of shapes and they can transmit information through electrical signals (action potentials) that are generated in the cell body and are transmitted through the axons of a neuron to all the dendrites that it connects to through synapses. Depending on the neurotransmitters on the neuron (excitatory: NMDA, AMPA or inhibitory: GABA) an action potential might increase or decrease the likelihood of a neuron to fire. The graph of connectivity between neurons defines a neural network, which represents the connections between neurons within a brain region (or between brain regions).

# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Dmitri B. Chklovskii

# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Neurons often possess elaborate axonal and dendritic arbors. Why do these arbors exist and what determines their form and dimensions? To answer these questions, I consider the wiring up of a large highly interconnected neuronal network, such as the cortical column. Implementation of such a network in the allotted volume requires all the salient features of neuronal morphology: the existence of branching dendrites and axons and the presence of dendritic spines. Therefore, the requirement of high interconnectivity is, in itself, sufficient to account for the existence of these features. Moreover, the actual lengths of axons and dendrites are close to the smallest possible length for a given interconnectivity, arguing that high interconnectivity is essential for cortical function.

# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Wiring of 3D neuronal network, approximating a cortical column

Assumptions:

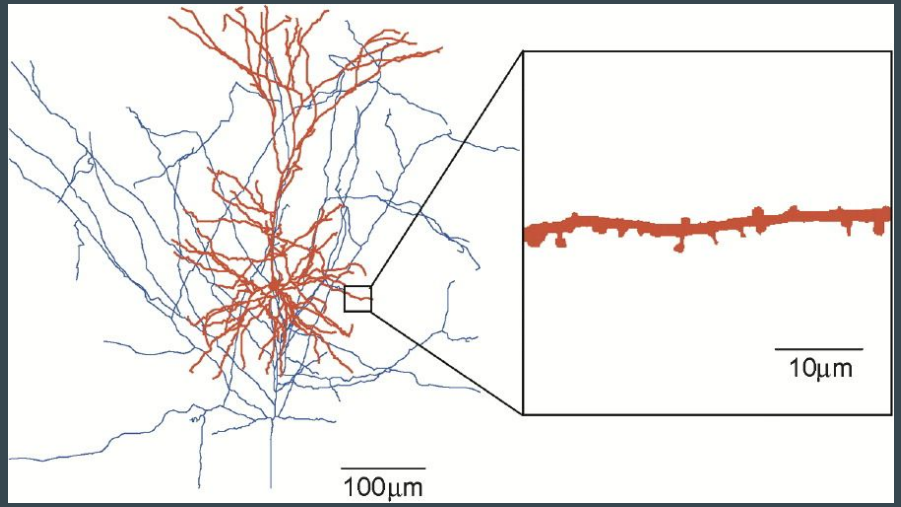
- Each neuron connects to all other neurons (all-to-all)
- Number of neurons: N
- Wire diameter: d
- Wiring cost will be approximated with wiring volume

The network volume depends on the chosen wiring design.

# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Figure 1. Reconstruction of a Pyramidal Neuron from Rat Neocortex

Axons are shown in blue, dendrites and cell body are shown in red. Spines are small protrusions on the dendrites shown in the inset. Image is courtesy of G. Shepherd, Jr. and K. Svoboda; inset is courtesy of A. Holtmaat and K. Svoboda.

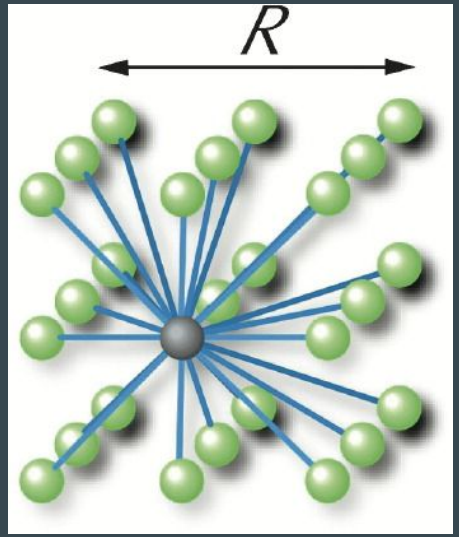


# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design I: Point-to-Point Axons

Each axon connects to all other neurons directly, therefore each neuron forms N connections. If the average axon length is R, then the wiring length per neuron would be:

$$l = NR$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design I: Point-to-Point Axons

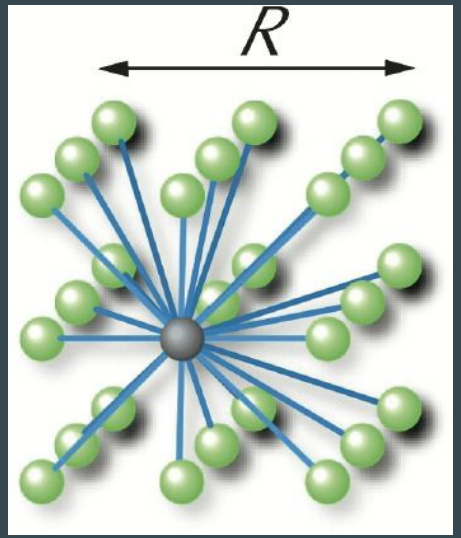
$$l = NR \quad (1)$$

$$R^3 = Nld^2 \quad \text{d=axon thickness} \quad (2)$$

$$R^3 = N \times NR \times d^2 \rightarrow$$

$$R^2 = N^2 d^2 \rightarrow$$

$$R^3 = N^3 d^3 \quad (3)$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design I: Point-to-Point Axons

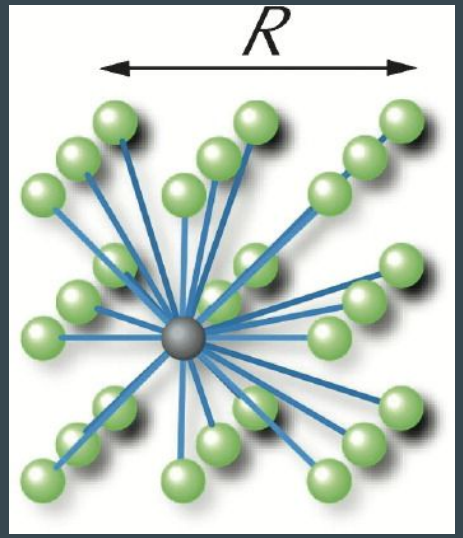
$$V = N^3 d^3 \qquad (3)$$

For a cortical column of $V_0 = 1mm^3$

$$N = 10^5$$

$$d = 0.3\mu m$$

$$V = 30KV_0$$



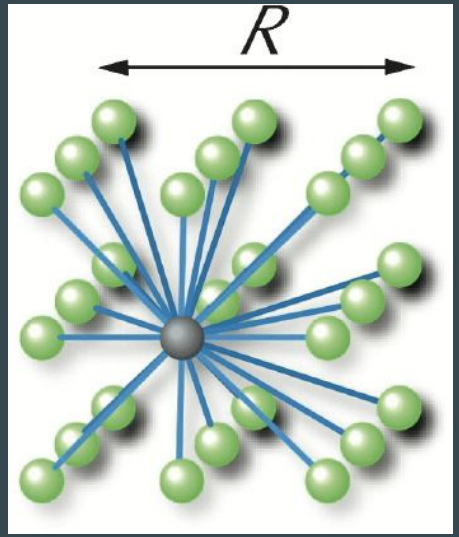
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design I: Point-to-Point Axons

$$V = 30KV_0 \qquad (4)$$

This model is insufficient to explain the actual cortical volume. What is missing? Axonal branching.

More sophisticated wiring designs are needed.



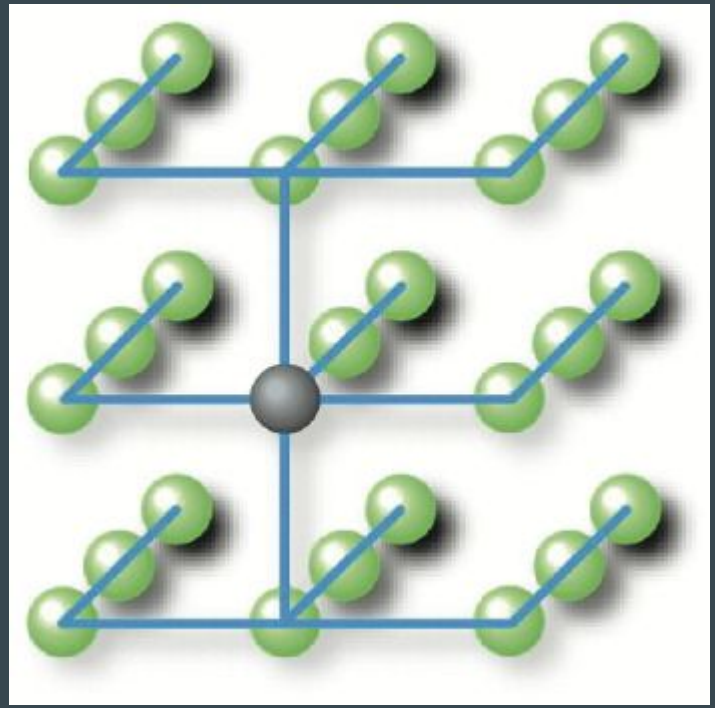
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design II: Branching Axons

In this case, the axonal length is estimated to be N * iterneuron distance.

Interneuron distance (id) is

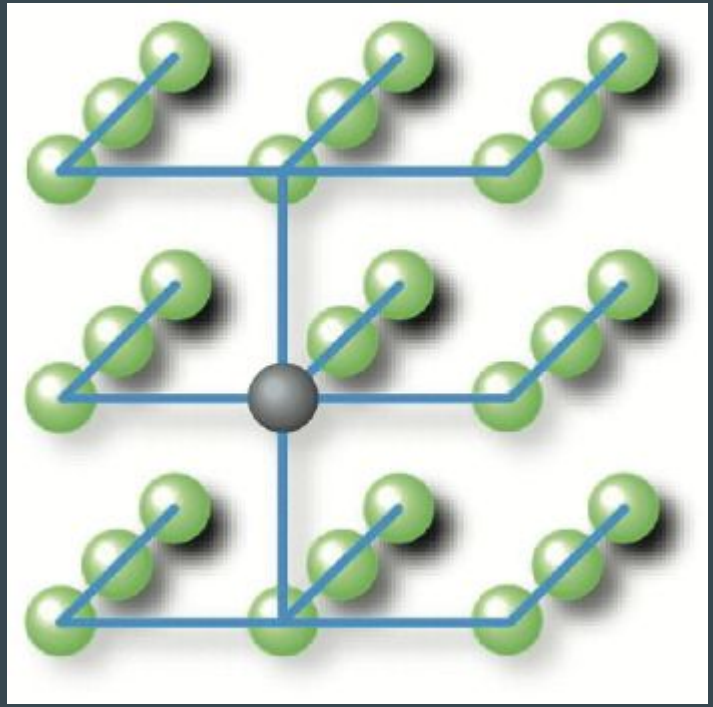
$$id = R/N^{1/3}$$
$$l = Nid = RN^{2/3}$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design II: Branching Axons

$$l = Nid = RN^{2/3}$$
$$R^3 = Nld^2 = N^{5/3}Rd^2$$
$$R^3 = N^{5/2}d^3$$
$$V = N^{5/2}d^3 \qquad (5)$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design II: Branching Axons

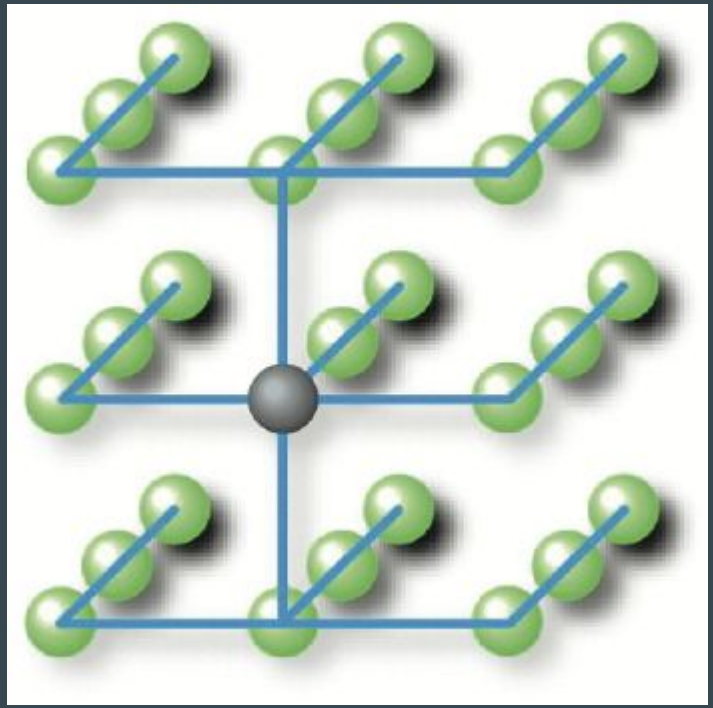
$$V = N^{5/2} d^3 \quad (5)$$

$$N = 10^5$$

$$d = 0.3\mu m$$

$$R = 4.4mm$$

$$V \approx 85mm^3 \approx 85V_0 \quad (6)$$



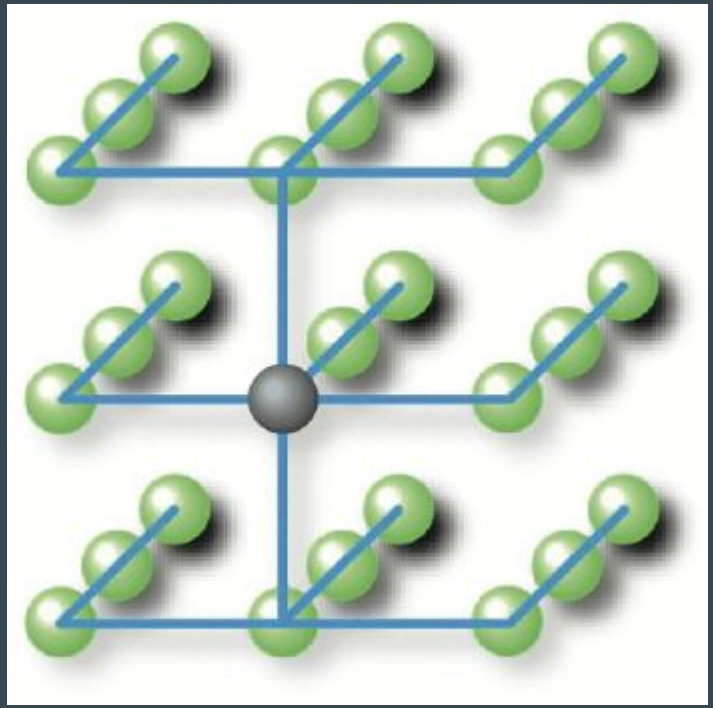
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Design II: Branching Axons

$R^3 \sim 85\ mm^3 \sim 85\ V_0$ (6)

This model still cannot explain the observed cortical volume. What is missing? Dendritic branching.

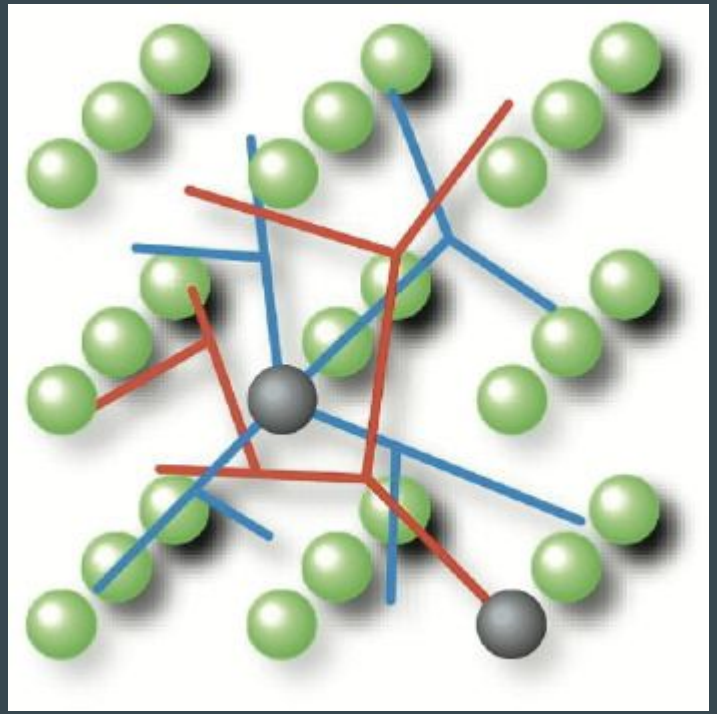
More sophisticated wiring designs are needed.



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

For axons-only network, each axon has to make its way to every cell body. The same functionality can be achieved by a single process reaching out in the direction of axons and meeting them halfway. Because a single dendrite takes up less volume than the many converging axons, this solution is more efficient. In reality, axons converge on a cell body from various directions, requiring several dendritic branches. Yet, in the limit of large convergence, adding dendrites to the wiring design lowers the wiring cost.

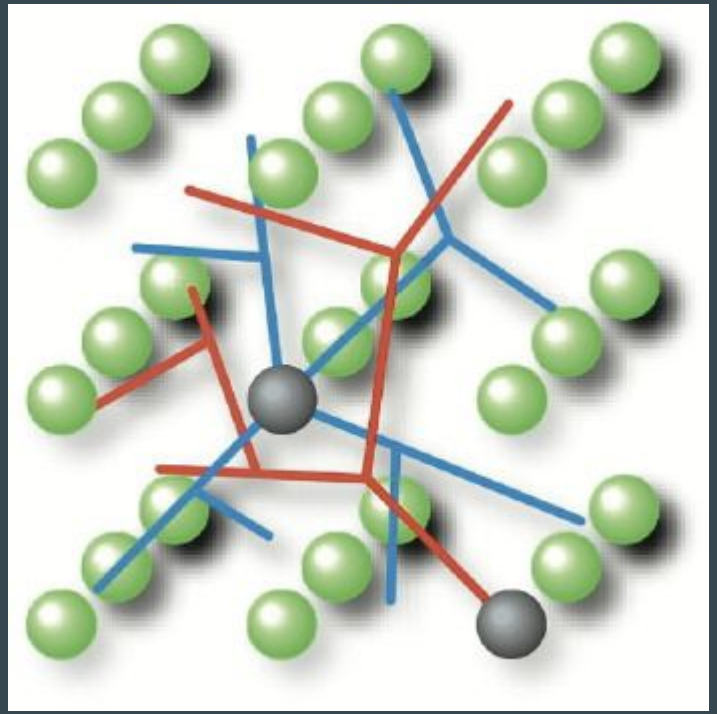


# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

In the all-to-all connected network, convergence and divergence are equal, suggesting a symmetry between axons and dendrites.

However, something to keep in mind: axons are thinner than dendrites.



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

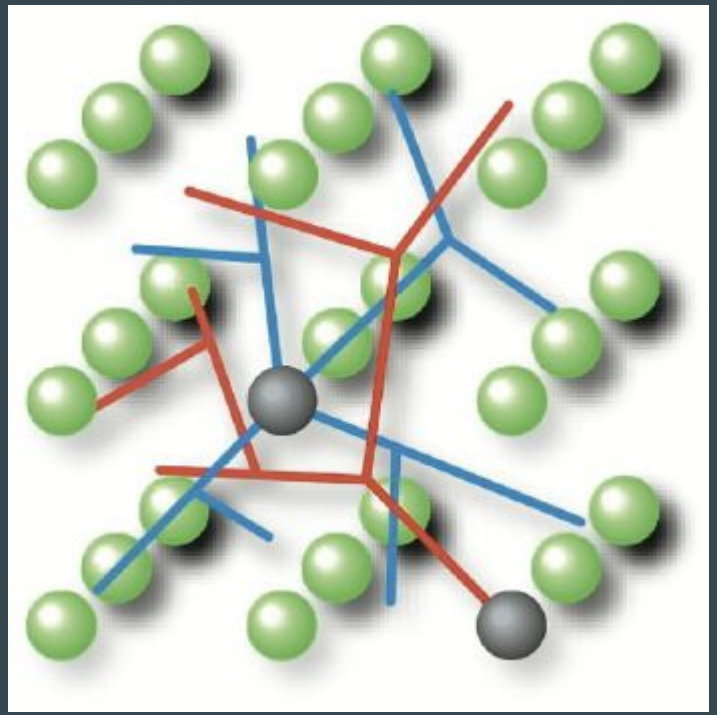
III. Branching Axons and Dendrites

If we require that axons make contact with each dendrite (to compensate for all to all connections) then we can divide V = R^3 into cubes of d^3

$$R^3/d^3$$ voxels

Each axon: l/d voxels

Each dendrite: l/d voxels



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

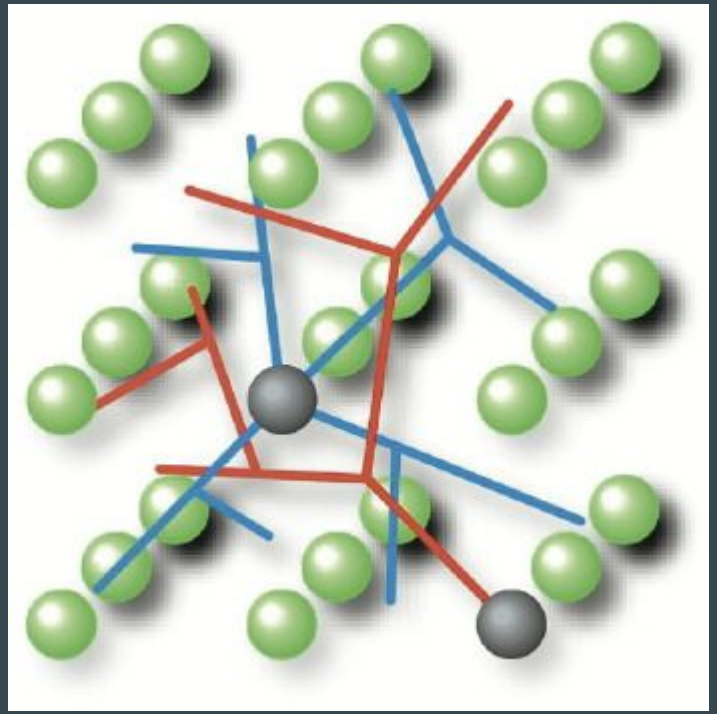
Voxels containing axons:

$$V_a = \frac{l}{d} / \frac{R^3}{d^3}$$

Similarly for dendrites:

$$V_d = \frac{l}{d} / \frac{R^3}{d^3}$$

Voxels containing both: Va * Vd



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

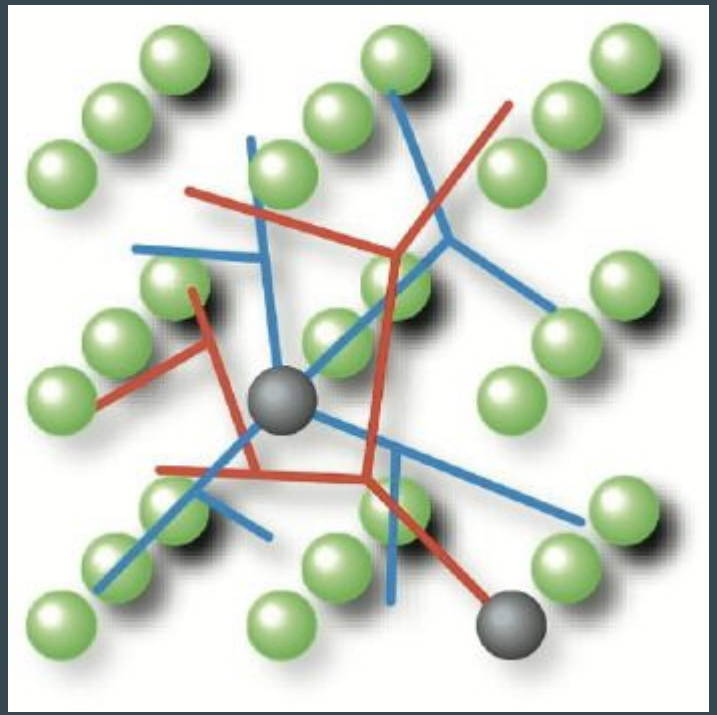
$$V_a V_d = \frac{l^2 d^4}{R^6}$$

The total number of voxels containing axons and dendrites:

$$V_a V_d * \frac{R^3}{d^3} = l^2 d / R^3$$

According to Stepanyants et al., 2002 filling fraction = 1 which translates to

$$l^2 d / R^3 \approx 1 \qquad (7)$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

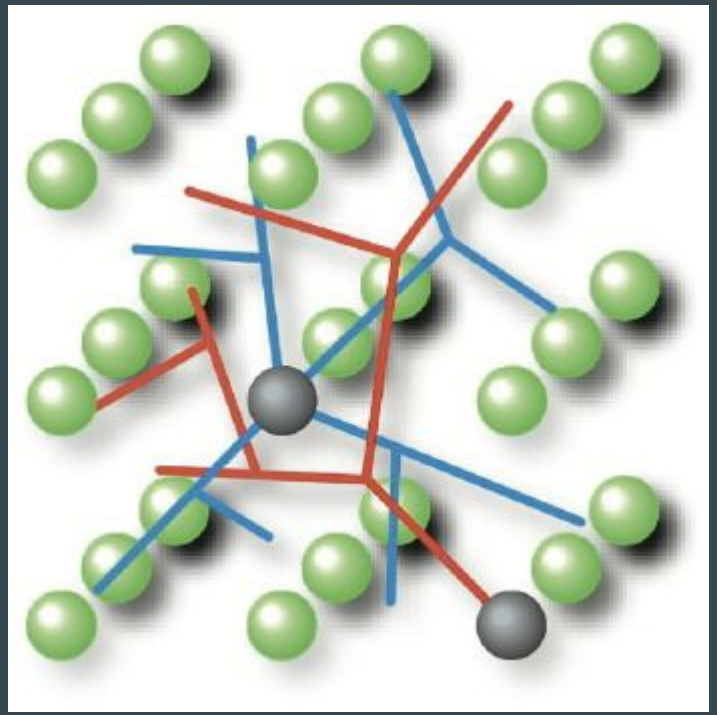
$$R^3 \approx l^2 d$$

$$R^3 = N l d^2$$

$$\boxed{V = N^2 d^3}$$

$$R = 0.65mm$$

$$V = 0.27 V_0$$



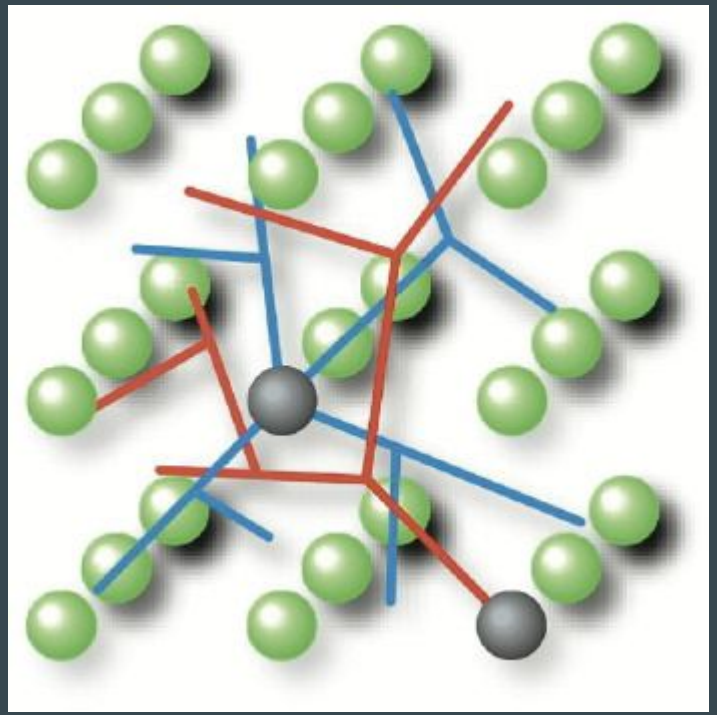
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

III. Branching Axons and Dendrites

$$V = 0.27V_0$$

However, this approximation does not account for difference in dendritic / axonal diameters. If we include a mean diameter of (0.3 + 0.9) / 2 = 0.6

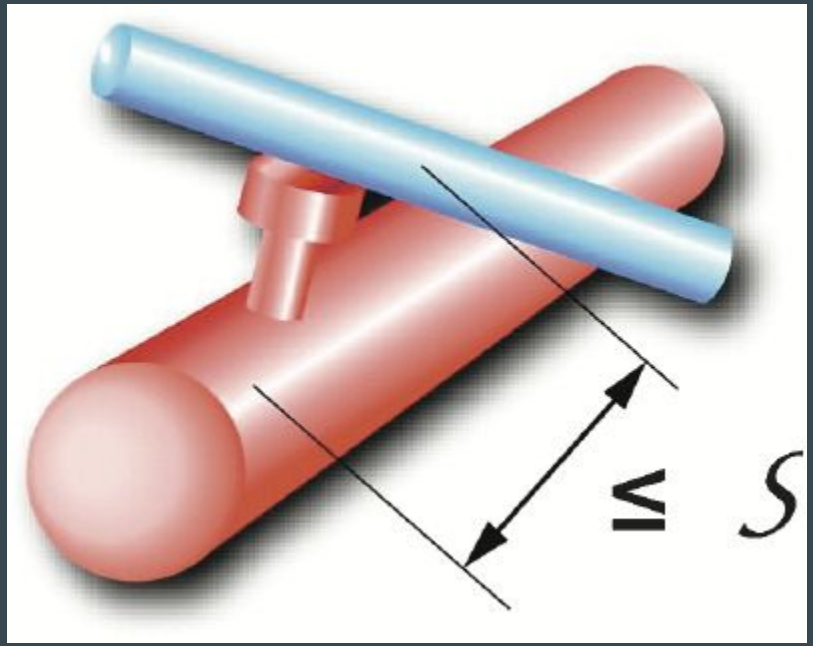
$$R \approx 1.3mm$$
$$V \approx 2.1V_0 \quad (8)$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

IV: Branching Axons and Spiny Dendrites

Adding dendritic spines reduces the size of the branching axon and dendrite network (design III) because axons and dendritic shafts do not have to touch in order to make a synapse, but can pass within the spine length, s, of each other. In addition spine volume can be considered minimal, as spine neck is small, compared to its length s.



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

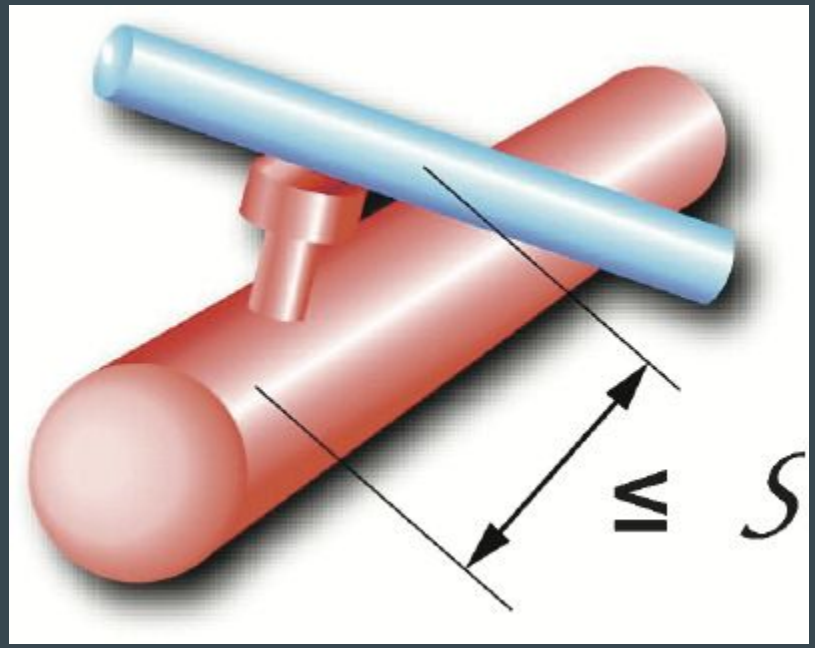
IV: Branching Axons and Spiny Dendrites

If we add the dimension of spines “s” in equation (7) we get:

$$l^2 d / R^3 \approx 1 \qquad (7)$$

becomes

$$l^2 s / R^3 \approx 1 \qquad (9)$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

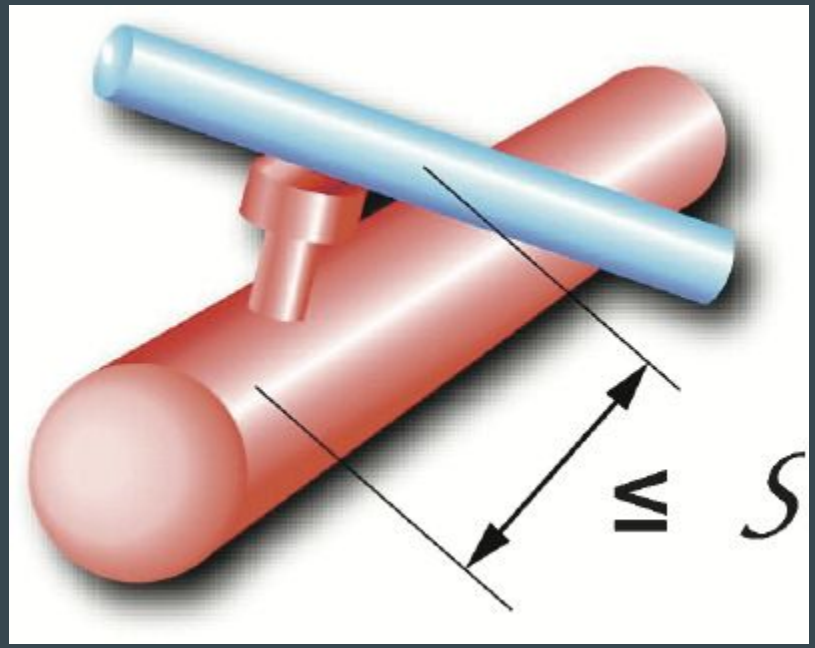
IV: Branching Axons and Spiny Dendrites

$$l^2 s / R^3 \approx 1$$

$$l = N d^2 / s$$

$$R^3 = N^2 d^4 / s$$

$$R = N^{2/3} d^{4/3} / s^{1/3}$$



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

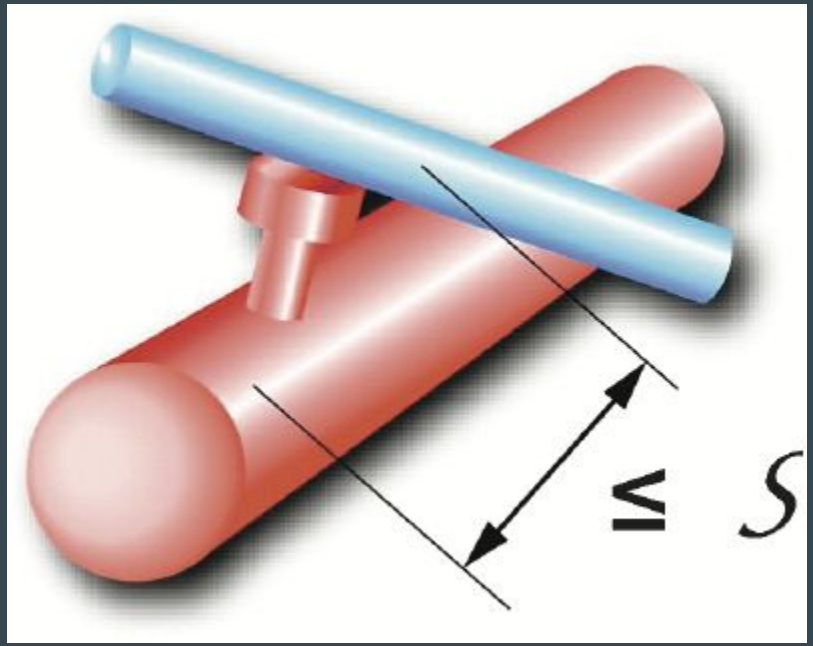
IV: Branching Axons and Spiny Dendrites

$$V = N^2 d^4 / s \quad (10)$$

$$R \approx 0.79mm$$

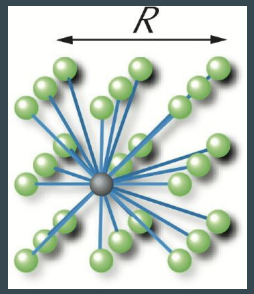
$$V \approx 60\% \quad (11)$$

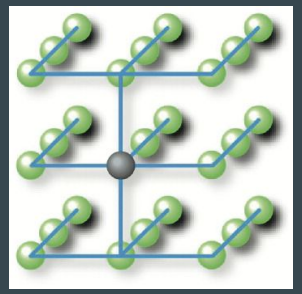
Which is comparable to the actual volume occupancy of cortex ~ 60%

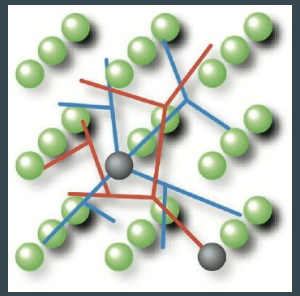


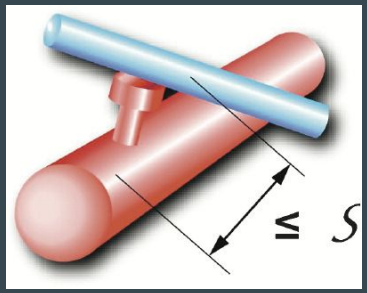
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

| | All to all | Axonal branching | Axons and Dendritic branching | Spines |
|---|---|---|---|---|
| l | N R | N ^⅔ R | N d | N d^2 / s |
| R | N d | N 5/6 d | N ^ ⅔ d | N^⅔ d^4/3 / s^⅓ |
| R^3 | N^3 d^3 | N 5/2 d^3 | N^2 d^3 | N^2 d^4 / s |
| V0 | 30 K | 90 | 2.1 | 0.6 |







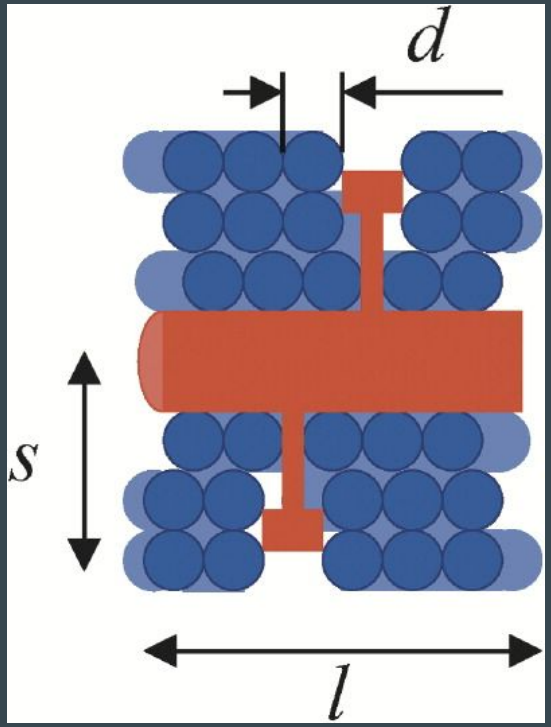
# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Proof of Design Optimality

Dendrites must be sufficiently long to ensure that every presynaptic axon can synapse with them. Because of volume exclusion among axons, the maximum number of available presynaptic axons:

$$N = ls/d^2 \rightarrow l = Nd^2/s$$

Dendritic length estimated this way coincides with that in design IV, thus proving its optimality.



# Synaptic Connectivity and Neuronal Morphology: Two Sides of the Same Coin

Only the final model, including all the salient features of the neuronal morphology, gives a correct order-of-magnitude estimate for the cortical column volume.

The existence of dendrites, axons, their branching, and the presence of dendritic spines are necessary to wire up the cortical column sufficiently efficiently to fit within the known volume.

All the proposed models oversimplify the reality of neurons that have many branches, varying thickness and local branching properties that might also contribute to mechanisms for optimal packing in space.

# Questions?