MSc in Artificial Intelligence and Robotics
MSc in Control Engineering
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Neuroengineering

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4- ELECTRICAL CORRELATES OF THE BRAIN ACTIVITY

Learning objectives of the lesson

1. Describe the different scales at which electrical correlates of the brain activity are produced and can be measured
2. Compare intra- and extra-cellular single neuron recordings
3. Illustrate the origin of the electrical correlates of the collective activity of groups of neurons
4. List the different acquisition methods
5. For each of them, describe their origin, their spatial resolution, and which neuronal groups are involved
6. Explain the generation of the EEG signal at the neuronal and tissutal level
7. List the advantages and the main issues of scalp EEG measures

they are the non invasive technique that we study in this lesson

summary of method from the more detailed to the less

Brain Electrical Measures

spatial resolution is achieved by means of invasiveness, so we can achieve very high spatial resolution only with more invasive methods, that are those that imply going into the brain tissue. So for the single cell measure we can touch or go into the membrane of single cell is the maximum invasive method

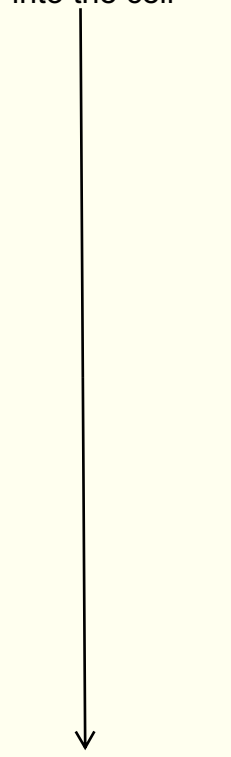
Spatial Resolution

when we move into this list the spatial resolution decreases, so we move from cm to mm

- IP: Intracellular Potentials
- EP: Extracellular Potentials
- LFP: Local field potentials
- S-EEG: Stereo-electroencephalography
- ECoG: Elettrocorticography
- EEG: Electroencephalography

Non-invasiveness

into the cell



out of the head

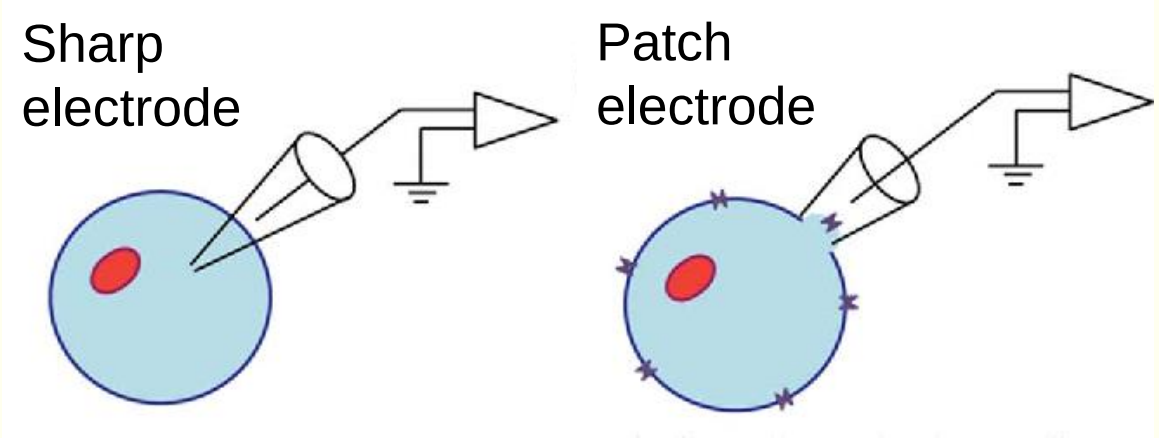
first method

Single-cell Recordings

In both extra and intra cellular we record brain activity but in this case we are actually recording the neural activity. What we have at the end of this procedure is the behaviour of the neurons. In particular what we mesure with intracellular recordings is the membrane potential. To make this measure we need to have an elechtrode inside or at least in elechtrical contact with intracellular fluid and a reference elechtrode in the extracellular fluid or just outside the cell

Intracellular recordings

- Hollow glass electrodes filled with a conducting electrolyte
- A reference electrode placed in the extracellular medium
- Intracellular recordings can be made with:
  - it reach the intracellular fluid
  - sharp electrodes inserted through the membrane into the cell
  - patch electrodes sealed to the surface of the membrane providing electrical contact with the interior of the cell



Adapted from Unal et al, Nanobiomedicine, 2014

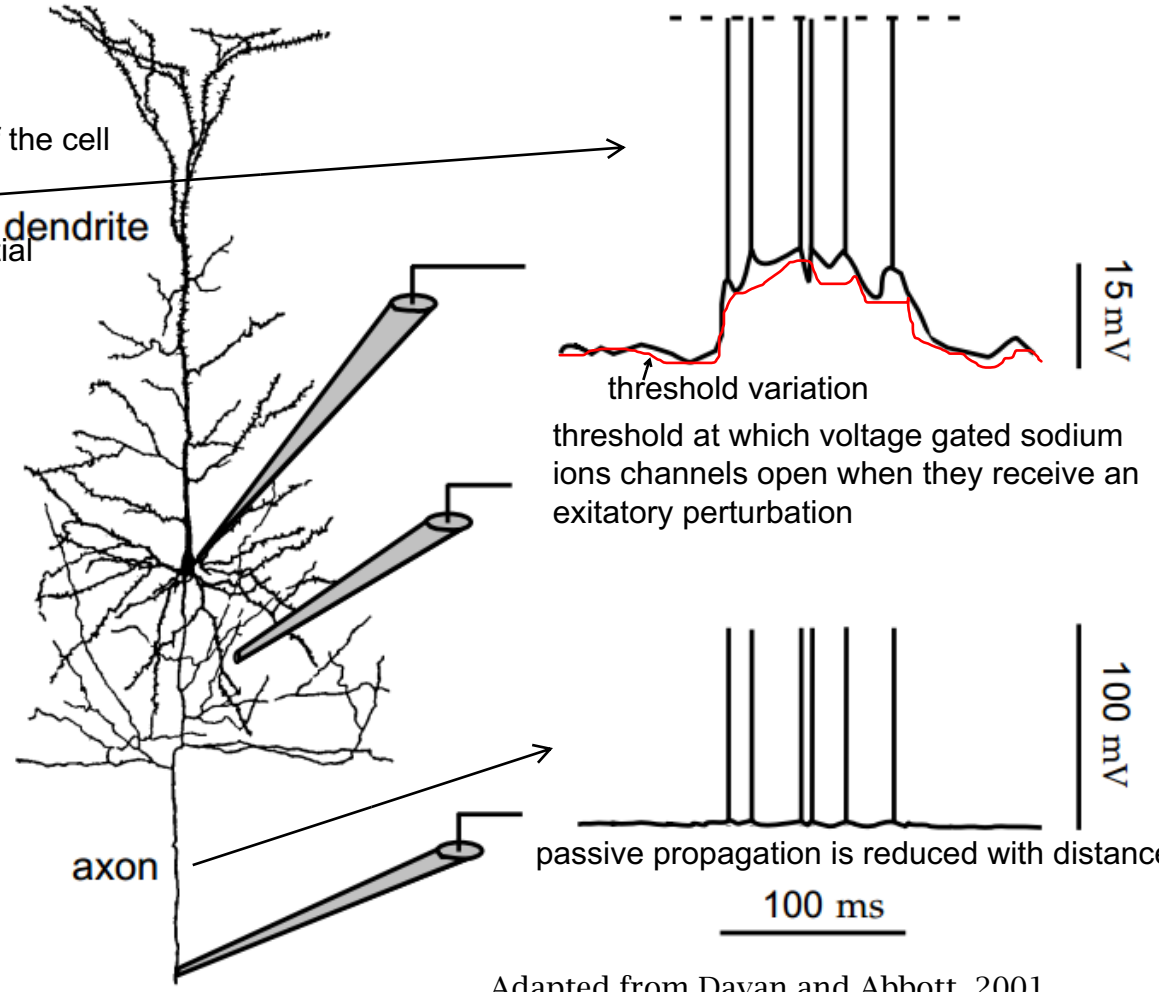
We have a different potentials in different part of the cell so it isn't omogeneous.

Intracellular recordings - 2

- More complex than the extracellular recordings
- Usually performed in the soma, sometimes in the dendrites, very seldom along the axon
- They record the actual membrane potential (graduate and action potentials)
- Usually performed in in vitro experiments

it's more easy because is a bigger part of the cell

if we measure the potential in the dendrites we can actually measure the postsynaptic potential

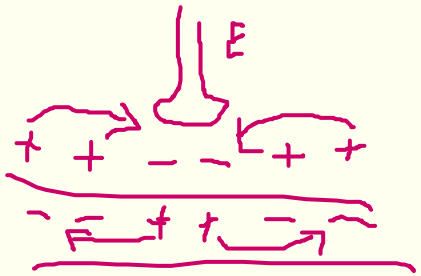


Adapted from Dayan and Abbott, 2001

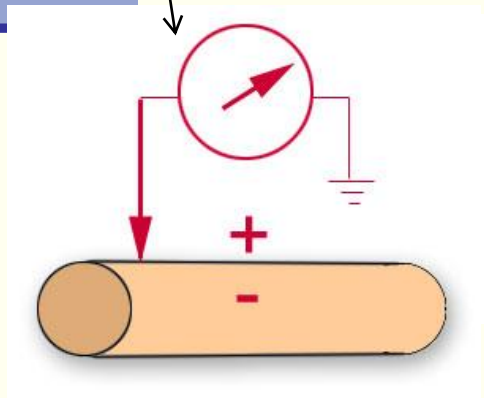
we put the elechtrode close to the cell membrane but outside of this
we measure the difference not between the intracellular and the extracellular fluid but between the extracelluar fluid close to the membrane and the extracellular fluid far from the membrane

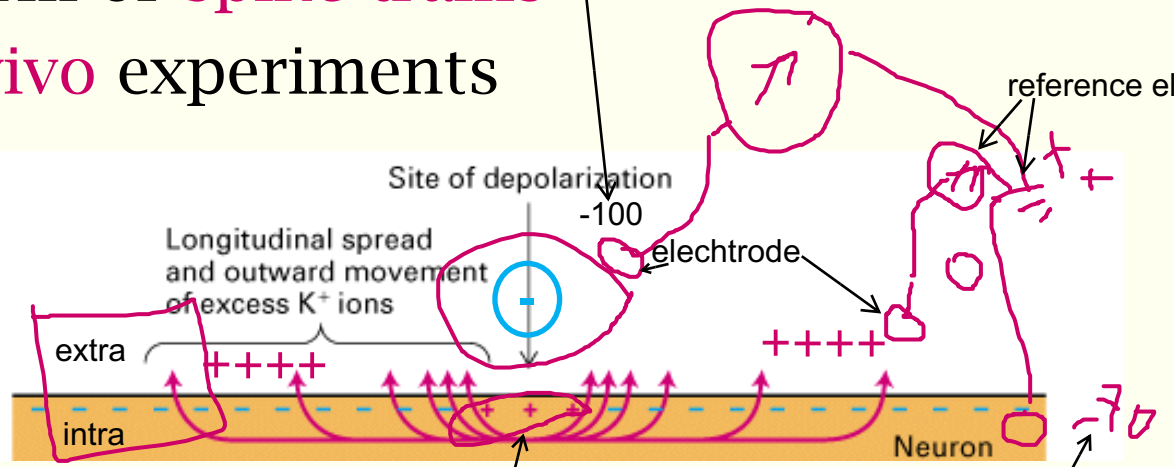
Extracellular recordings

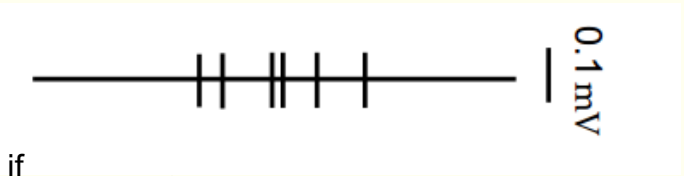
- Electrodes are placed near the membrane, but do not penetrate it
- They detect (don't measure!) the action potentials fired by a neuron, but not its subthreshold membrane potentials
- They measure the exact moment in which an action potential occurs, not its shape or amplitude
- Reduced amplitude (0.1 mV instead of 100 mV)
- Take the form of spike trains
- Used in in vivo experiments



this is not the resting potential but the difference between the peak of the action potential and zero

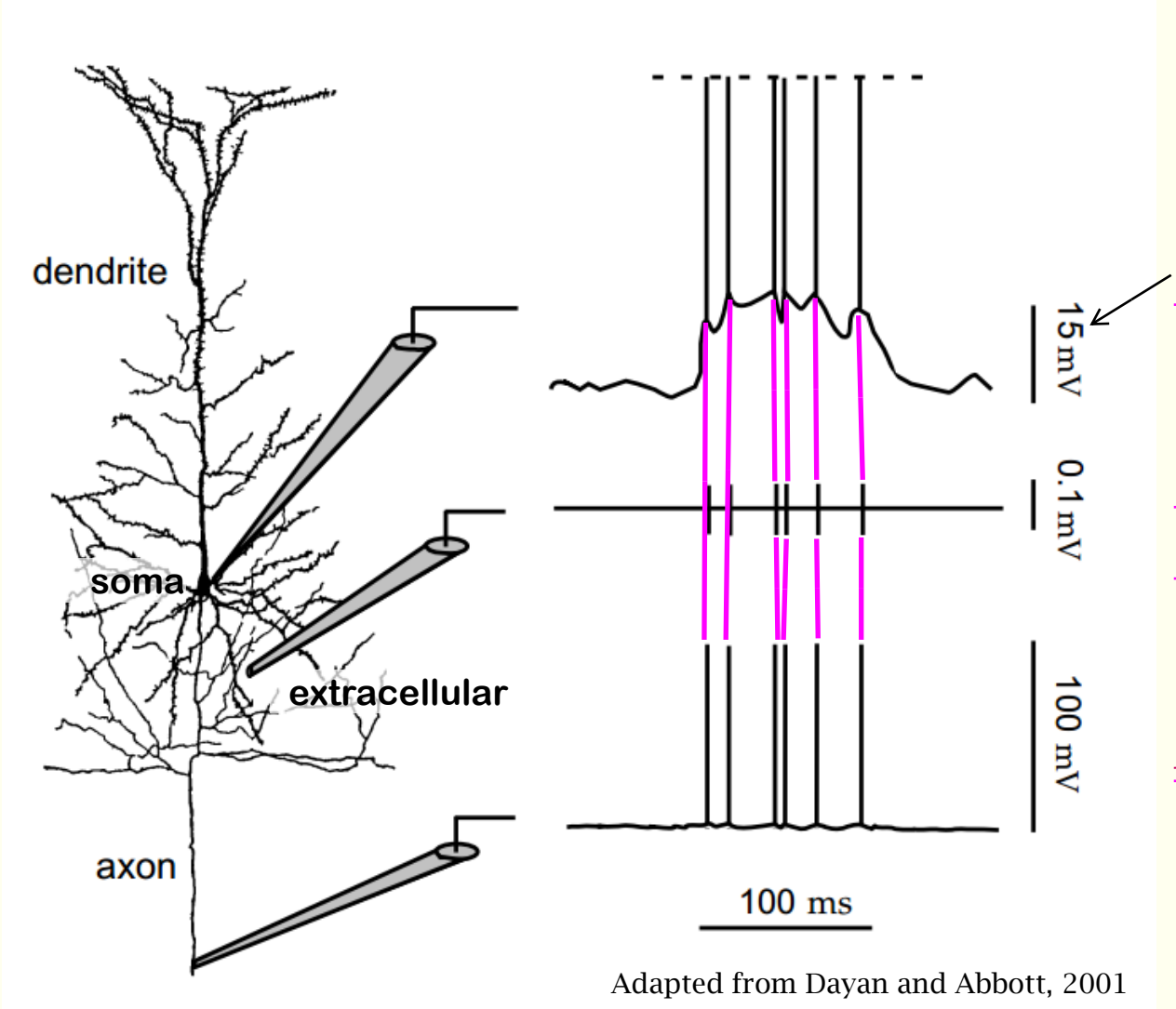






Adapted from Dayan and Abbott, 2001

Comparison between intracellular and extracellular recordings



Adapted from Dayan and Abbott, 2001

RED:intracellular
BLUE:extracellular

we are interesting on its peaks and in with what frequency it appears

Subthreshold + action potentials

Signal temporally correlated with the action potentials

Action potentials (in the axon)

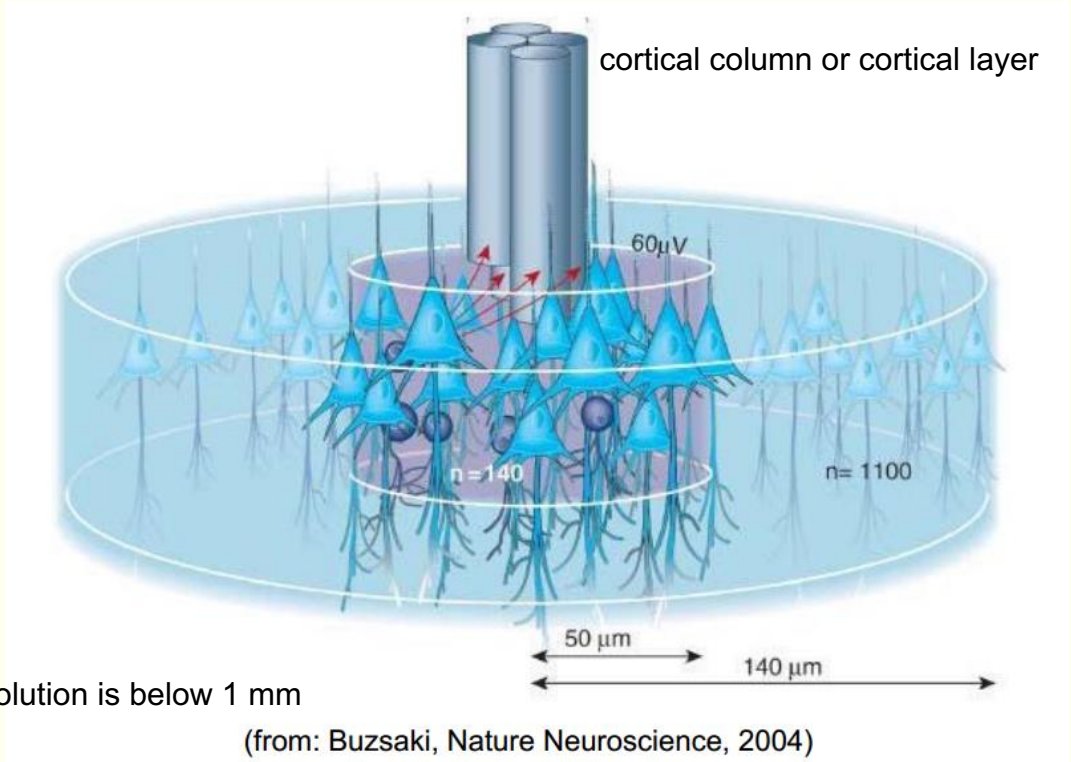
Recordings from Neural Populations

studying the single neuron is not useful for any purpose, we need to study a group of neurons

Local Field Potentials (LFP)

they are measures of the elechtrical activity especially of the cortex because is more easily accessible

if we put an elechtrode close to a group of neurons, we are able to measure the sum activity of the correlated signal which is produced by the activity of the single neuron



(from: Buzsaki, Nature Neuroscience, 2004)

- Extracellular current flow resulting from the linear summation of PSP of neuronal groups

post synaptic potential

- Electrodes put inside the cortex
- Frequency range: 0-100 Hz
- Spatial resolution: 10^{-3} to 1 mm^3

spatial solution is below 1 mm

EEG in a nutshell

only synchronous activity of large number of neurons produce signal that is strong enough to be detected at distance sources. What we measure is a signal which is produced by the sources and propagated through the tissues of the brain and the head. This propagation is based on ion currents.

- Originates from synchronous postsynaptic cortical currents (sources) of millions/ 1 billion neurons

it's what happen in our head and body each time that elechtrical signals are produced by excitable cell

- Volume conduction: tissues contain salt water, so ion currents can spread → effects of the electrical activity of excitable cells at a large distance (cm)
- Electric fields produced by local currents spread instantaneously (at the light speed) and sum up linearly
- Amplitude on the scalp = μV (very feeble, membrane potentials = mV)

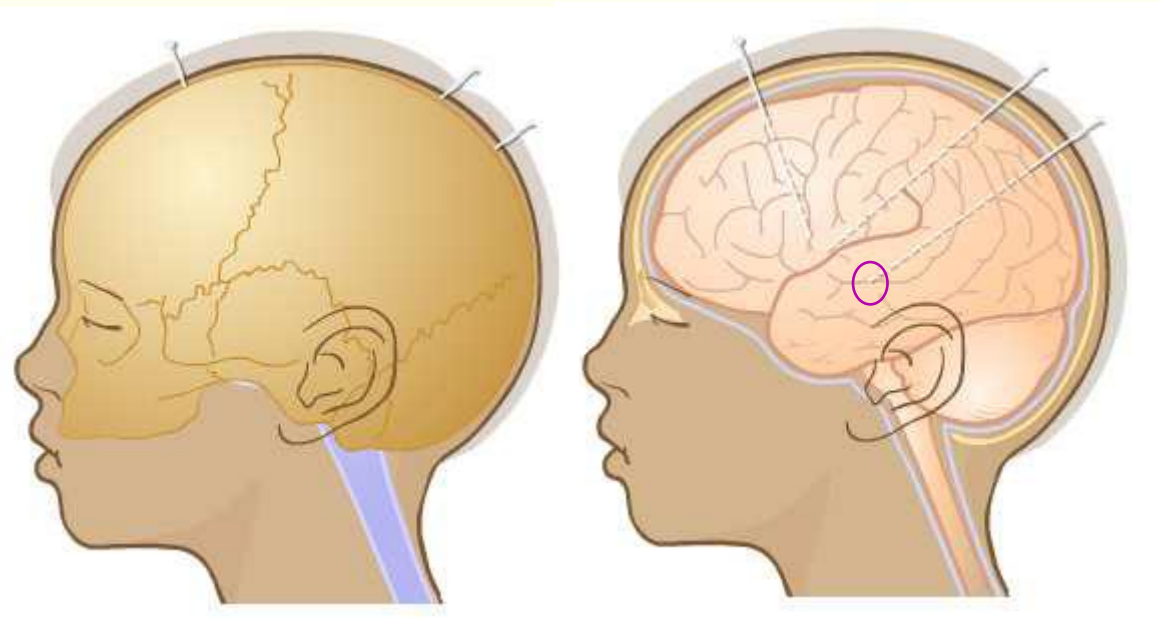
in millions of cells

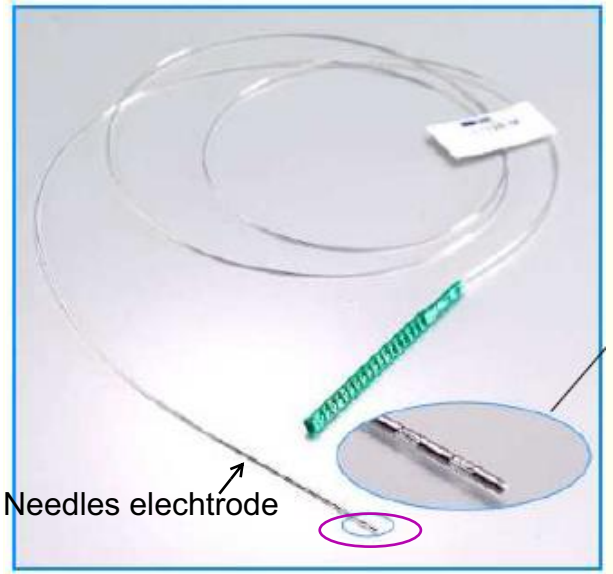
in a single cell

- Temporal resolution = milliseconds (very high)

Stereo-Electroencephalography (S-EEG)

very invasive method. With this method we access to the subcortical region



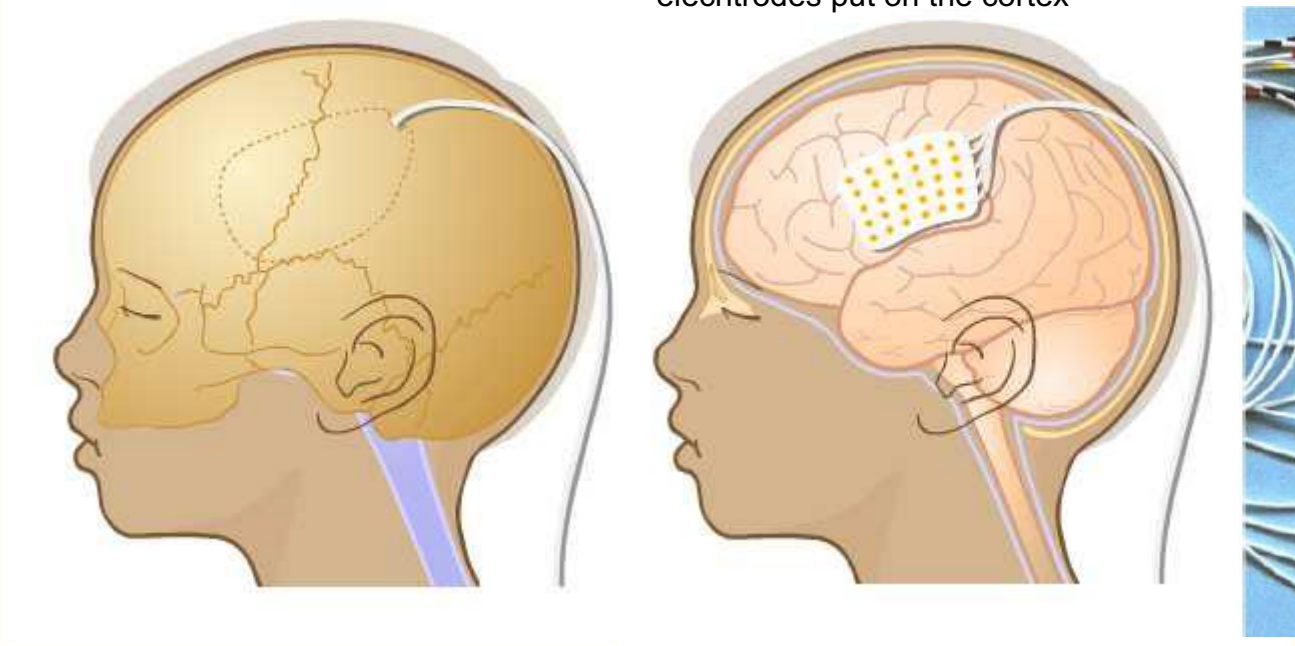


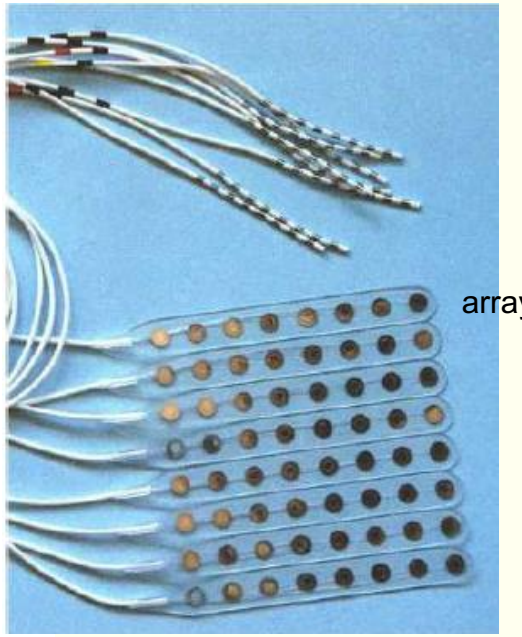
- Spatial resolution: 1-4 mm^3
- Electrodes deeply implanted in the brain
- Can measure the activity in subcortical regions
- Used in epileptic patients when the epileptogenic zones are located in depth

more used of the previous and it is less invasive

Electrocorticography (ECoG)

elechtrodes put on the cortex





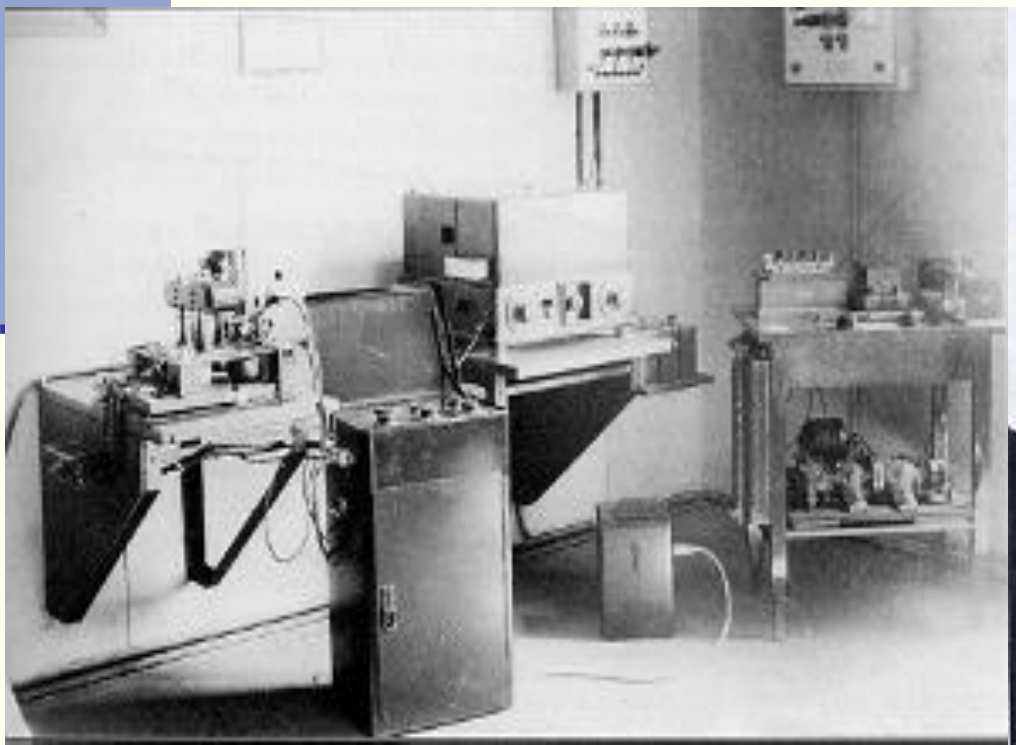
array of elechtrodes

- Spatial resolution: 1-20 mm^3
- Synaptic activity in macrocolumns
- Electrodes arrays put above the pia mater (below the dura, intracranial)
- Mainly produced by cortical neurons
- Volume conduction (distance + shape + conductivity of the tissues)

Scalp EEG

this is the only non invasive technique that we see today

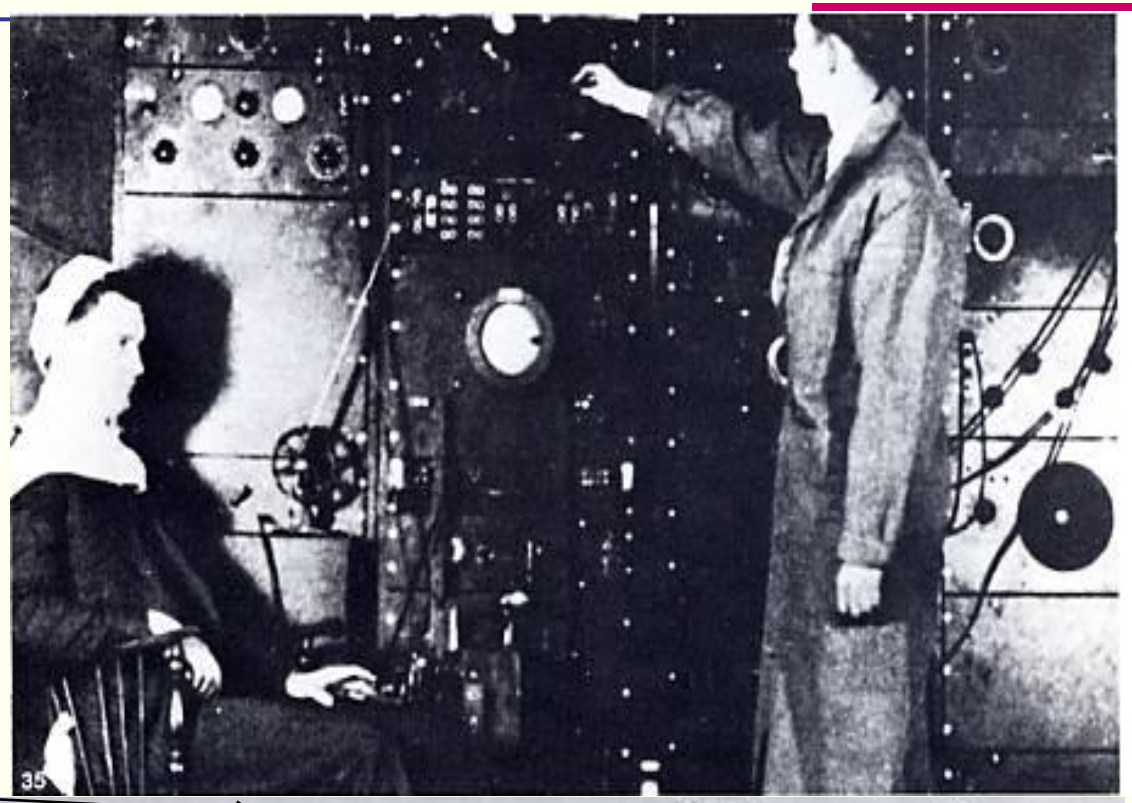
- 1929: Hans Berger, a German psychiatrist, obtained the first measure of the electrical activity on the human scalp
- He detected the alpha rythm



Harvard Medical School, 1934

- Single EEG channel
- Davis Lab at Harvard
- Hypodermic needle as electrode, head tissue band soaked with saline solution as electrical reference

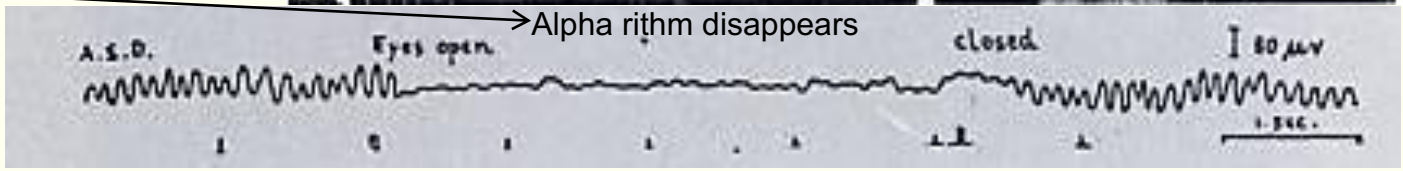
amplifier of the single channel EEG system



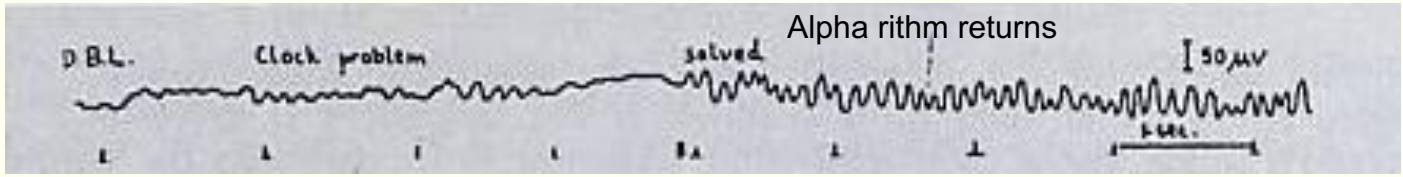
neurons which works asyncronously. When visual cortex is engaged, neurons are asynchronous, when it not works they are syncronous. This depends on the talamus

Open and closed eyes

Mental computation



Alpha rithm disappears



Alpha rithm returns

Generation of the EEG signal

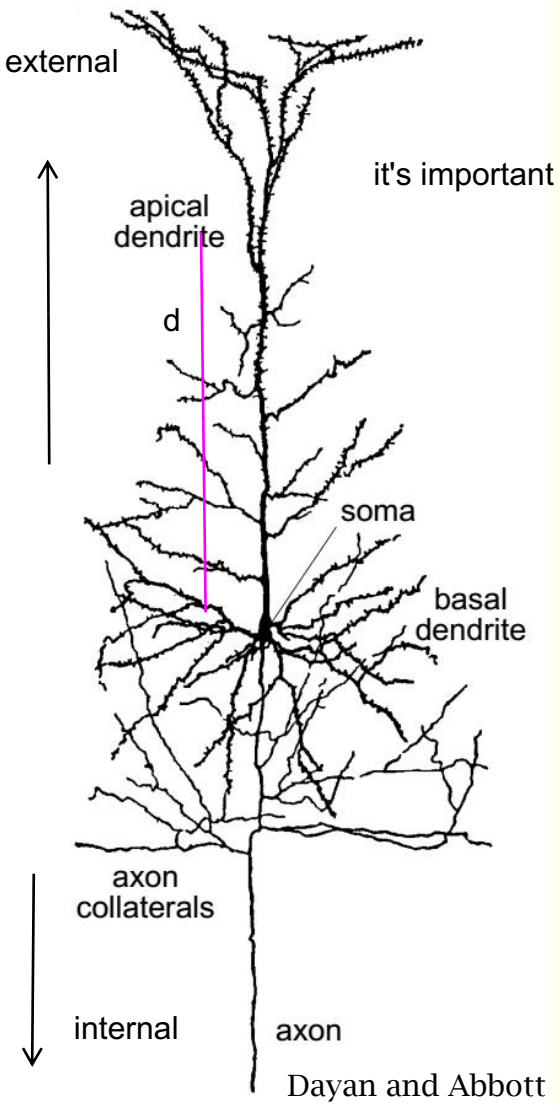
we start from the cortex because it has some specific properties that make it the most important source of the elechtroencefalografical activity
in this way we can collect also signals to long distance from their sources

Cortical pyramidal neurons

reason why we are able to measure the elechtroencefalographic signal

- Pyramidal soma
- Longitudinal shape
- Have apical and basal dendrites
- The apical dendrites are projected toward the cortical surface

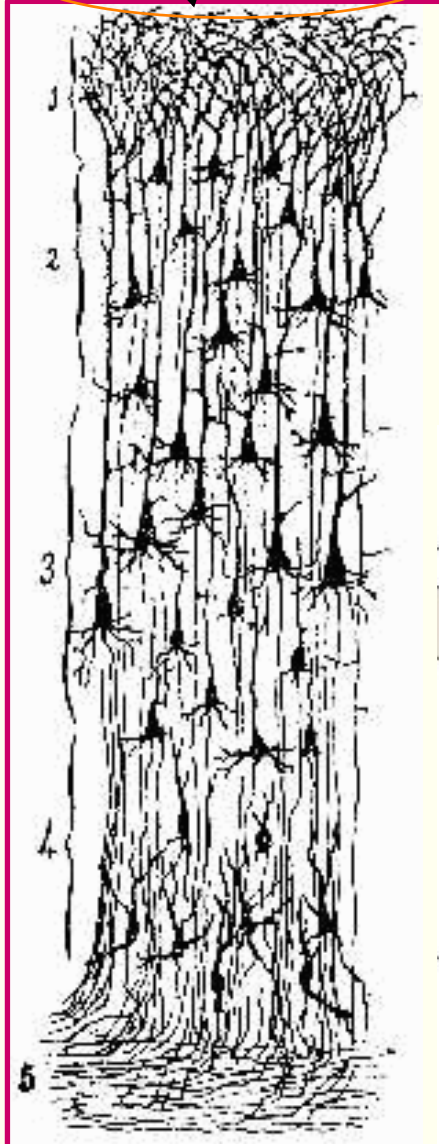
it's important the shape of the whole cell that is longitudinal



Dayan and Abbott

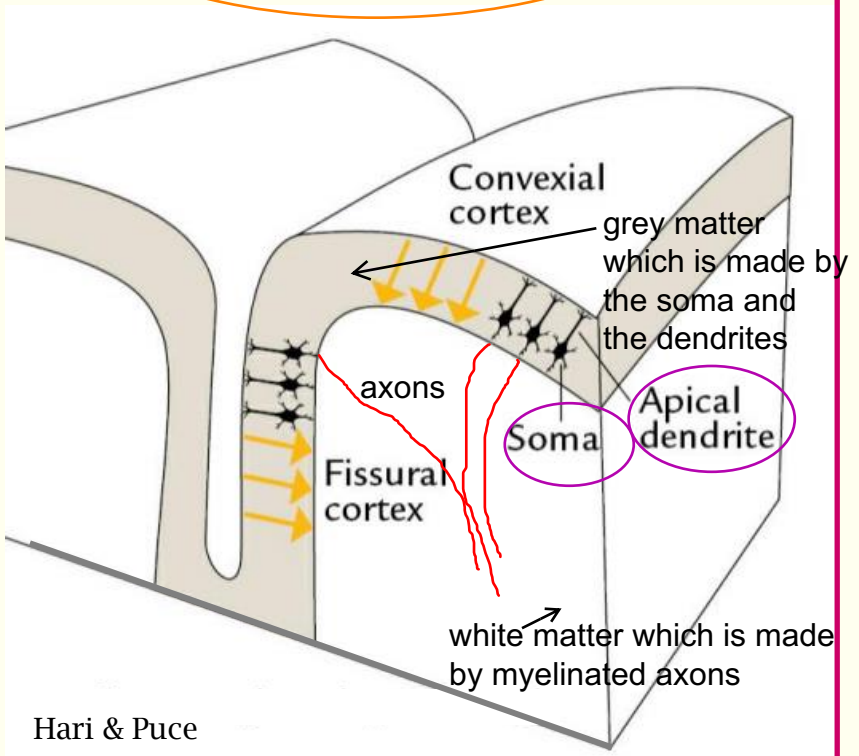
Neuroengineering - Astolfi

all parallel to the other



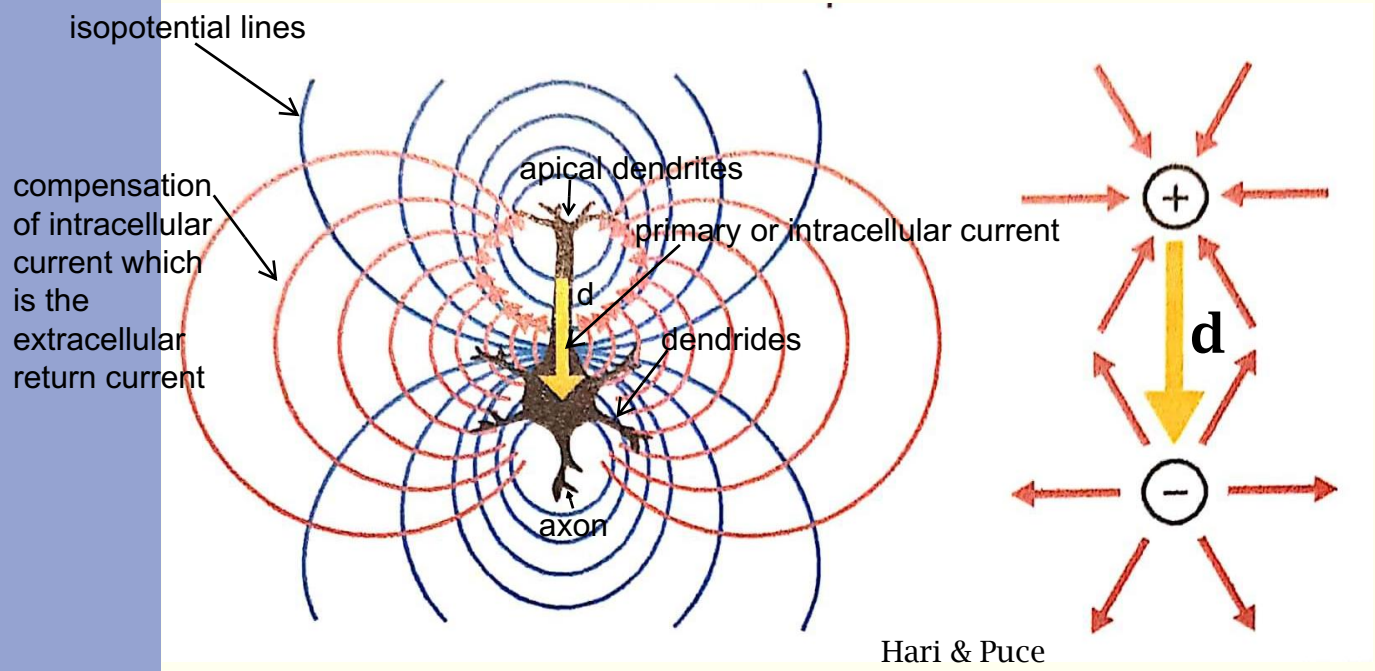
are organized in palisades

- Form palisades
- Oriented normally perpendicular to the cortical surface



Hari & Puce

Current dipole

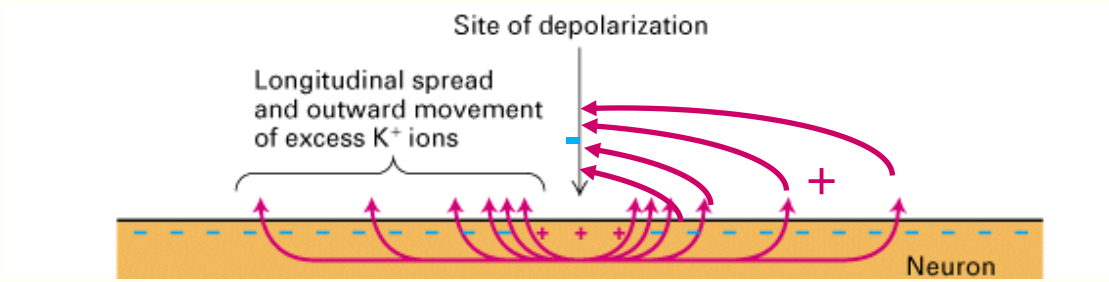


Hari & Puce

- A point source $+I$ and a point sink $-I$, separated by a distance d
- any source-sink region where the total source and sink currents are equal (local current conservation) will generate a predominantly dipole potential detectable even at a large distance (scalp)

everytime we go from source to sink

- Yellow: intracellular current
- Blue: isopotential lines
- Red: return currents
- Isopotential and return currents line are perpendicular to each other

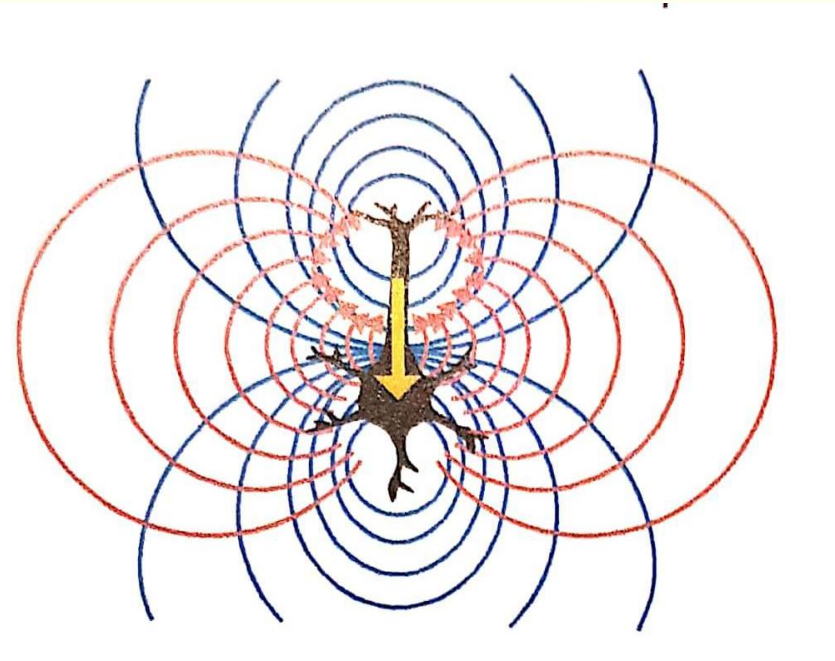


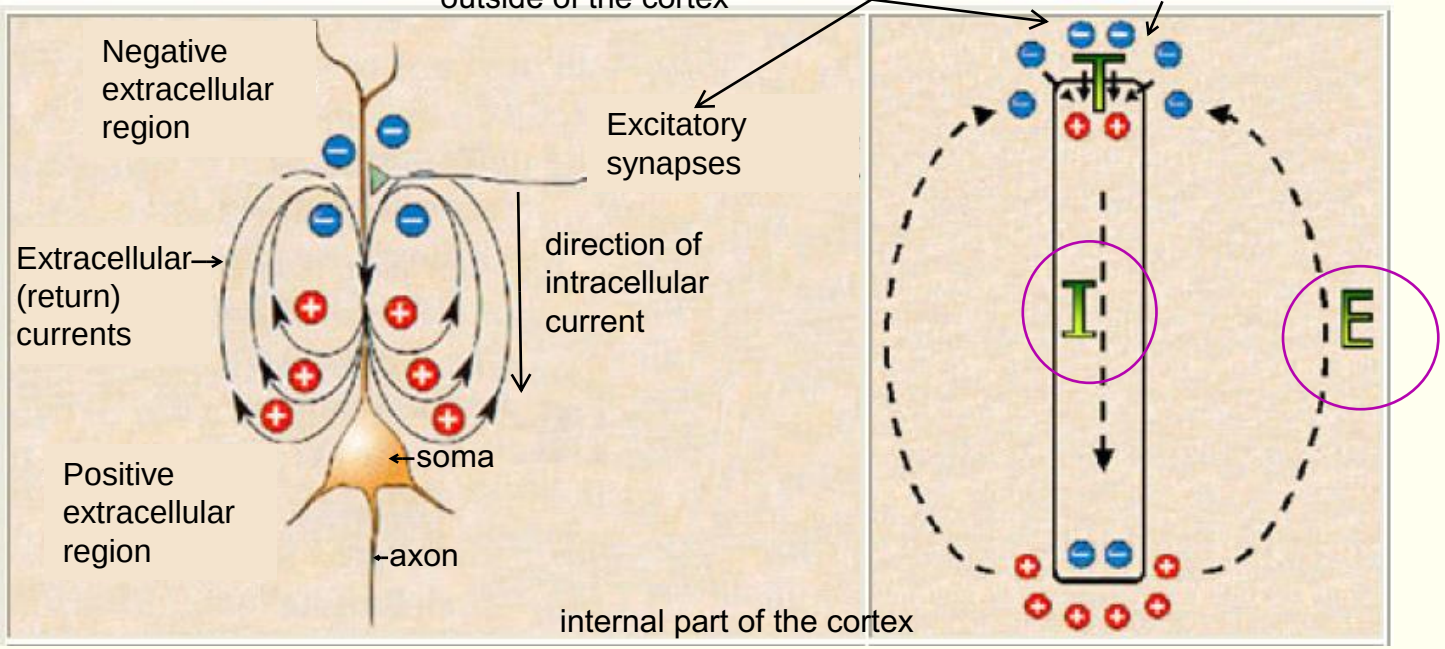
imagine we have a synapse between this neuron and another, so this neuron is the postsynaptic neuron. We focus on the dendrite. We magine that this is an excitatory synapse that produce depolarization

Dipolar nature of pyramidal cells PSPs

first factor

local depolarization of the membrane





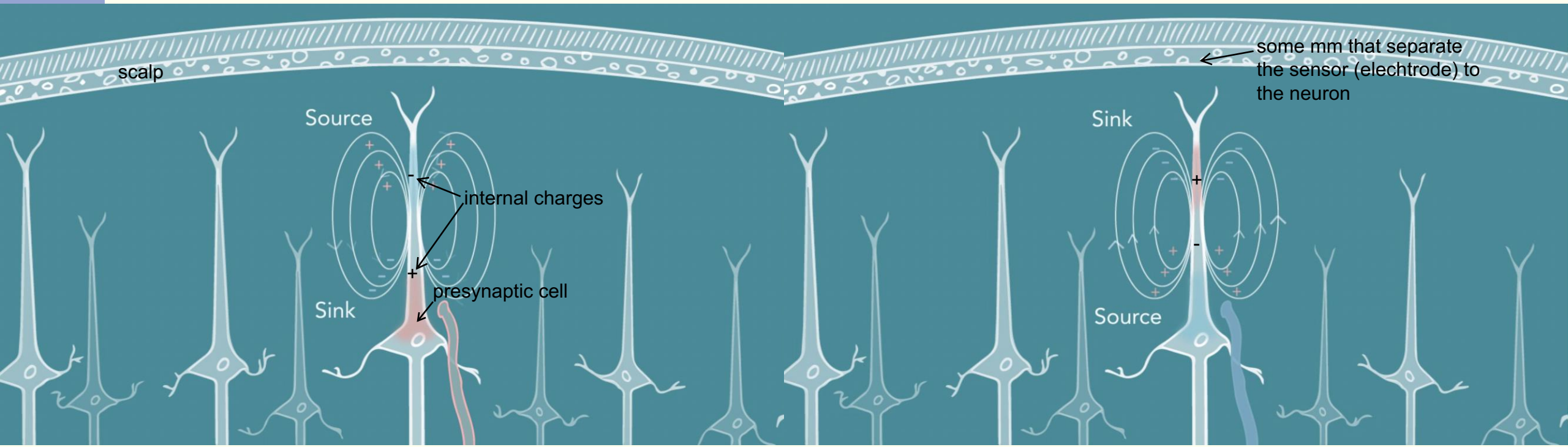
with inhibitory synapses the mechanism is the same but the current has opposite direction so also the charges are opposite

- Apical and basal dendrites act as point source and sink
- Extracellular charges and currents are reversed with respect to intracellular ones

Dipole direction – EPSPs and IPSPs

EXCITATORY

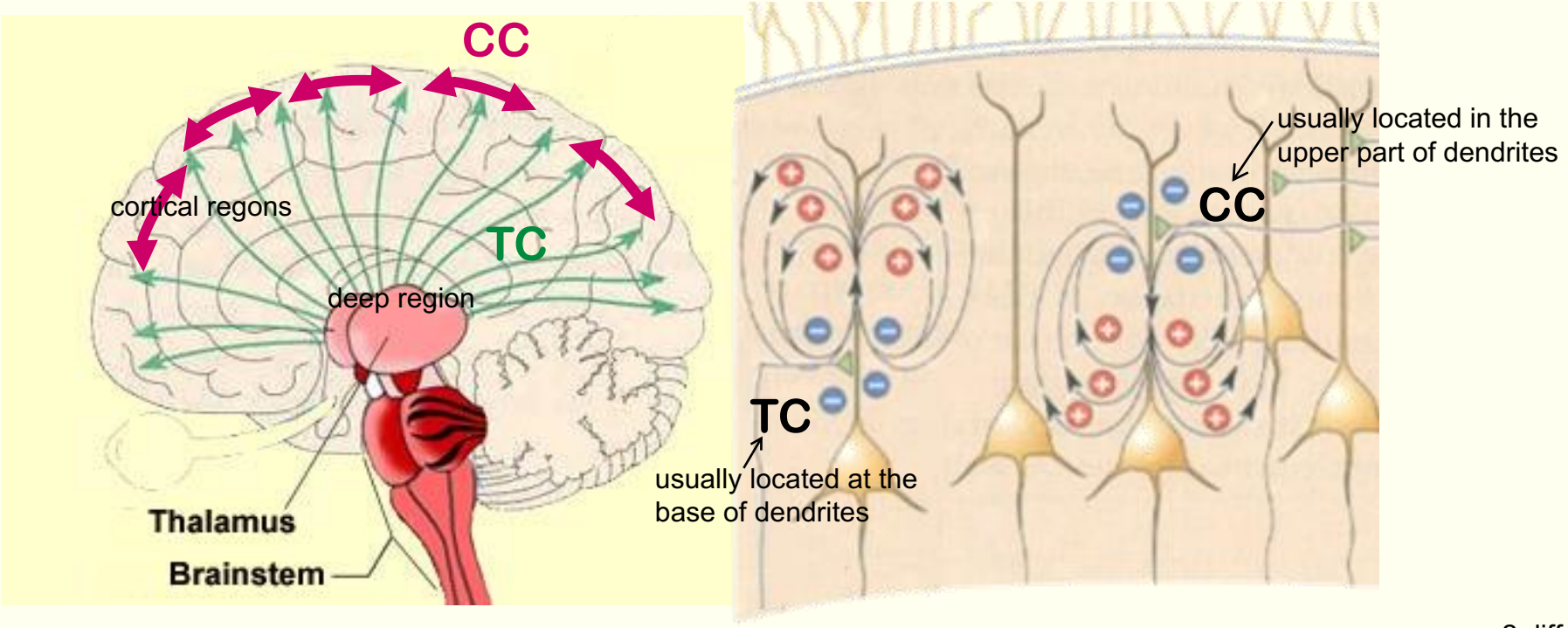
INHIBITORY



https://www.youtube.com/watch?v=rzgDOaGjjOs

second factor

Dipole direction - Position of the synapse



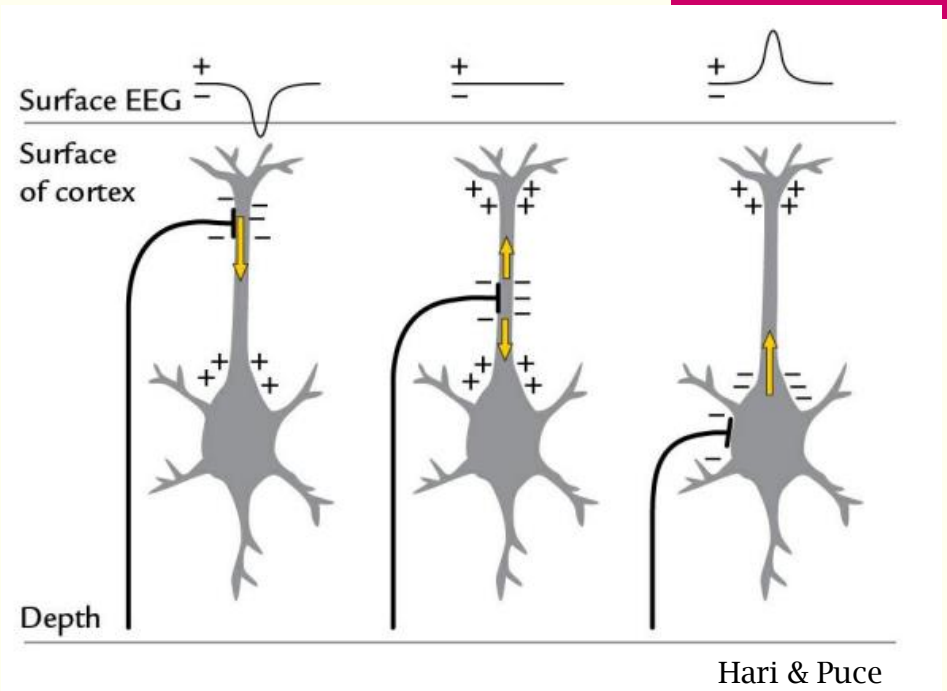
2 different positions

- Cortico-cortical (CC) synapses usually on the apical dendrites
- Talamo-cortical (TC) synapses usually on the basal dendrites

Dipole direction - Summary

equals 2 by 2

	CC	TC
E		
I		



Hari & Puce

The dipole direction depends on:

- The synapse nature (EPSP of IPSP)
- The synapse position:
  - apical cortico-cortical (CC)
  - basal talamo-cortical (TC) synapses

All of this was for a single neuron, now we see a set of neurons. If we want to measure the single cell we need to put the elechtrode very very close to the membrane. The reason why we are able to measure signals even if we put elechtrodes far from the neuron is that we are not measuring the single neuron but the signal produced by a large number of neurons(million of neurons or billions)

Orientation of the pyramidal dypoles

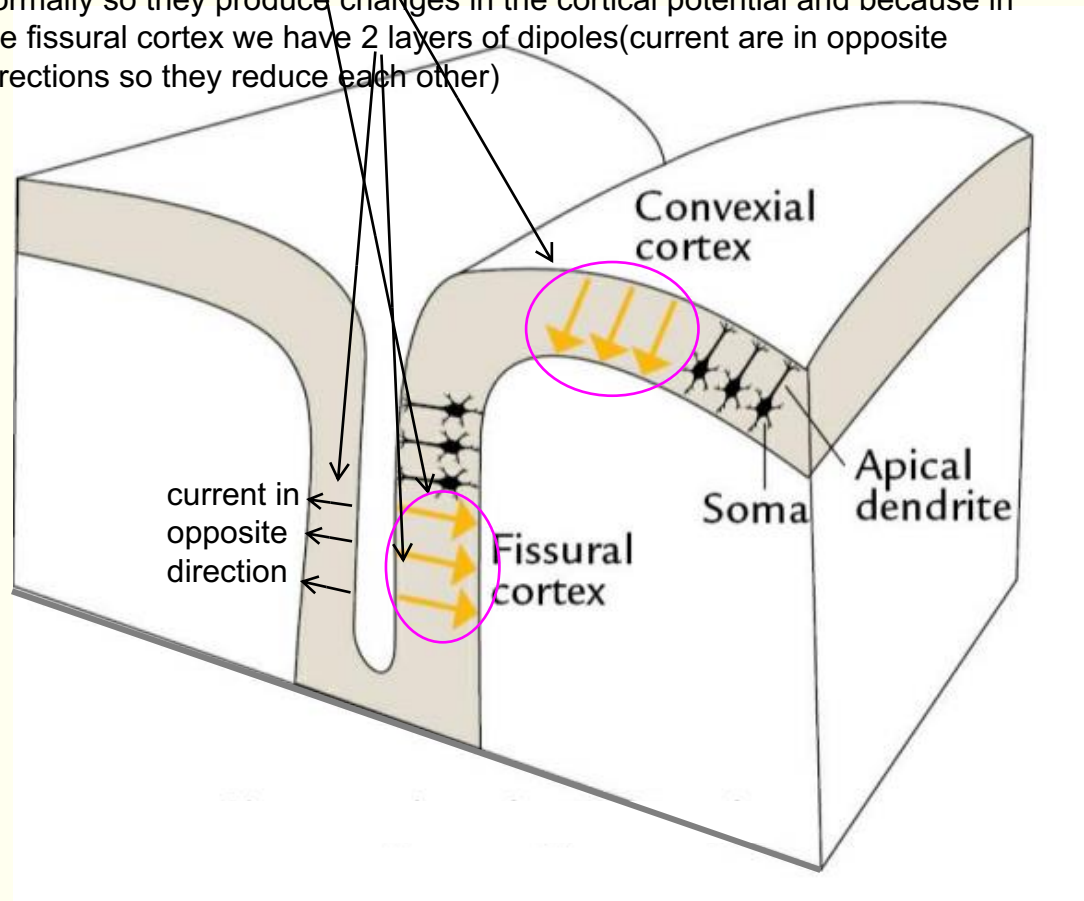
first factor

- Pyramidal neurons are perpendicular to the cortical surface

  MEG is more able to detect neurons in the fissural cortex but it is much more expensive

  - Gyri are more efficient generators of EEG than sulci (both because of the favorable orientation of the isopotential lines with respect to the scalp and because the dipole layers in opposing sulci cortices tend to cancel each other)
  - Palisade dipole sources line up in parallel, creating large dipole layers

neurons which are in the gyrus produce much more EEG signal with respect to those in the fissural for 2 reason: because they are oriented normally so they produce changes in the cortical potential and because in the fissural cortex we have 2 layers of dipoles(current are in opposite directions so they reduce each other)



EEG signal generation – effect of timing

second factor

- Electroencephalography measures the synchronous electrical activity of neural populations

the most

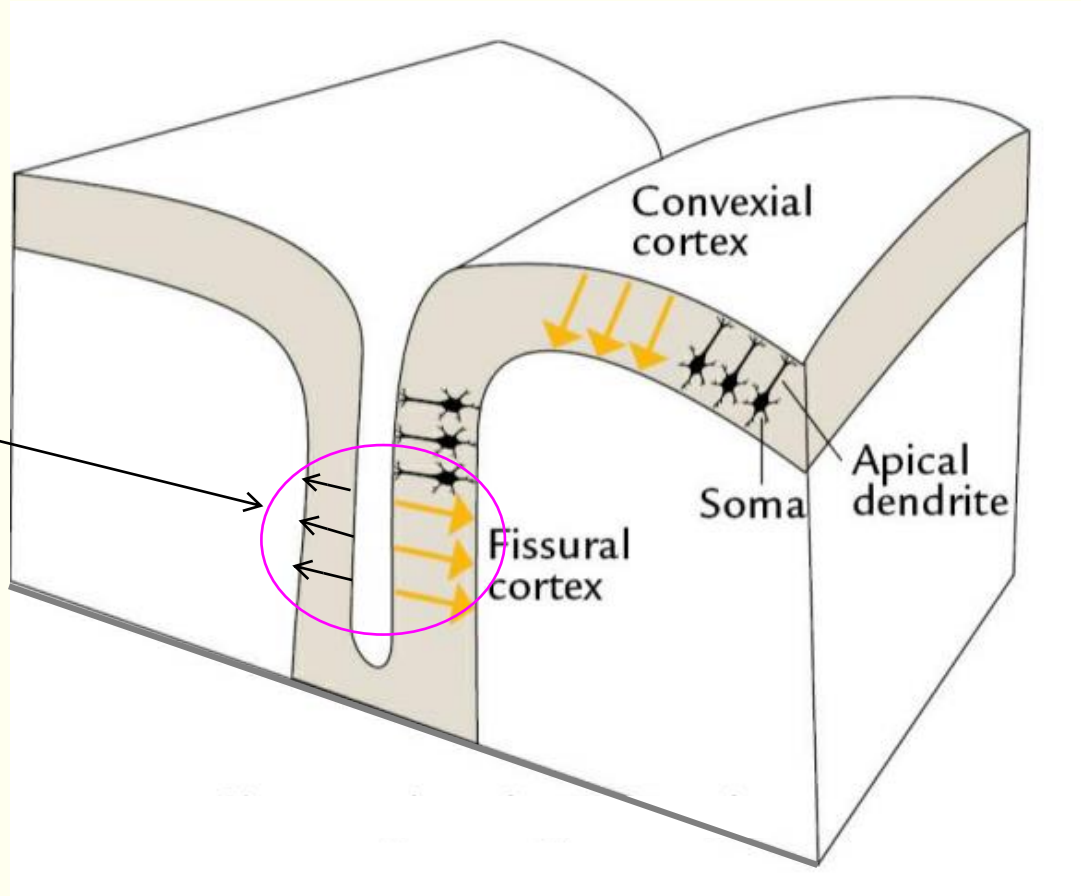
- The amplitude of the signal is:
  - linearly proportional to the amount of synchronous neurons
  - proportional to the square root of the amount of asynchronous neurons, because of intracortical cancellation
- e.g.:
  - N=10^{10} asynchronous dipoles → Signal =10^5
  - N=10^8 (1% of the previous) synchronous dipoles → Signal = 10^8

we reduce the amount of neurons of a factor of 1%

EEG signal generation – effect of orientation

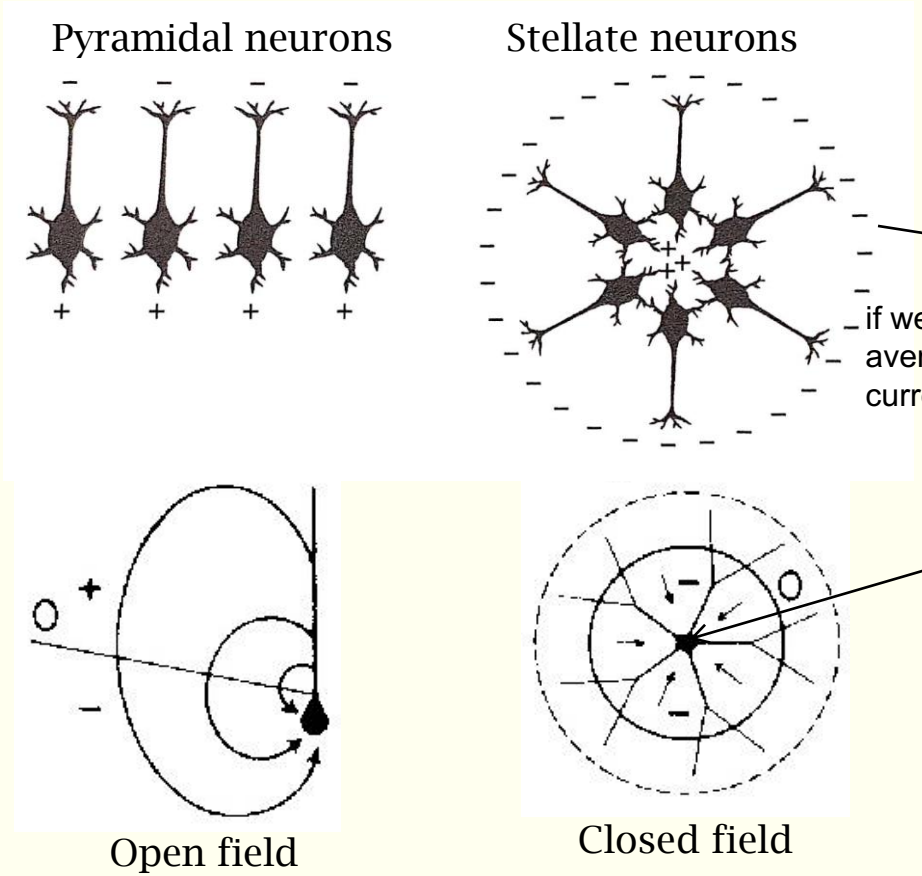
- Sulci and fissures produce **little or no** EEG signal
  - Orientation not favorable to the scalp surface
  - Mutual cancellation of opposite cortices
- Gyri produce most of the EEG signal
  - Favorable orientation
  - Summation due to the palisade disposition

orientation of the dipole is different



what about others reagions of the brain? We are not measuring only pyramidal neurons on the cortex but mainly because they produce an open field

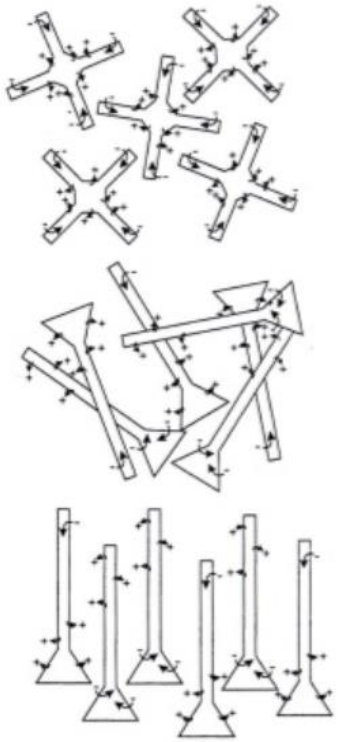
Open and closed field



not able to measuring

Closed field (cancellation before it reaches the electrodes):

- Radially simmetric neurons
- Randomly oriented neurons
- Asynchronously activated neurons

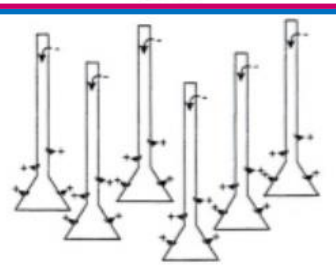


if we measure on the surface with an elechtrode the average is zero because the opposite directions of the current, so we need to put the elechtrode here

able to measuring

Open field (currents sum and conduct to the electrodes)

Aligned, synchronous neurons



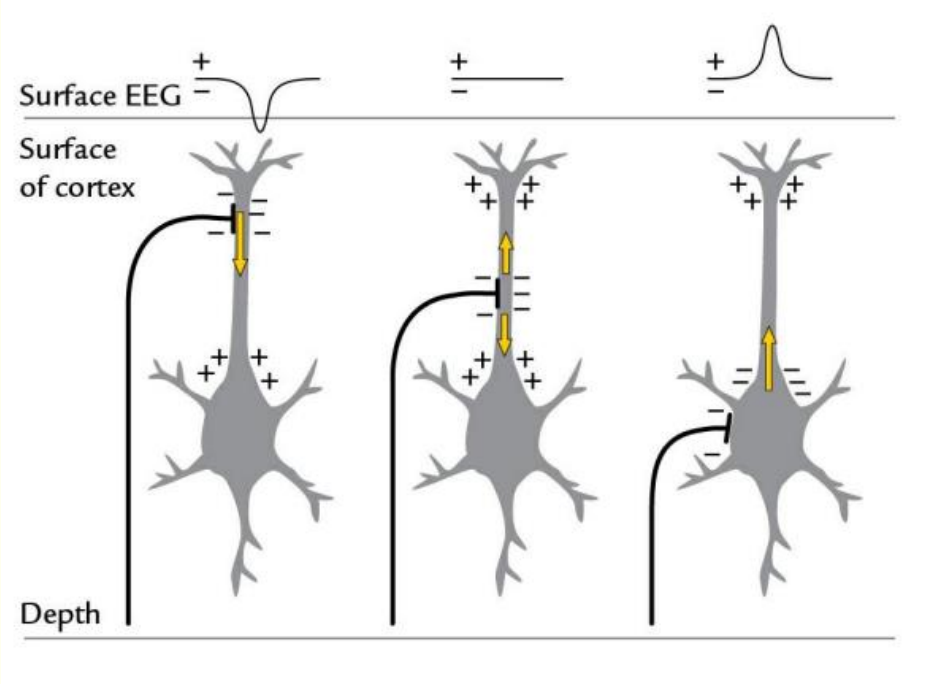
Only neurons that produce an open field contribute to EEG

EEG signal generation – which membrane potentials?

- Mainly constituted by post-synaptic potentials because they are slower and can sum up more easily in large groups of neurons
- Action potentials are fast and more difficult to add up in time

with respect to post-synaptic potential

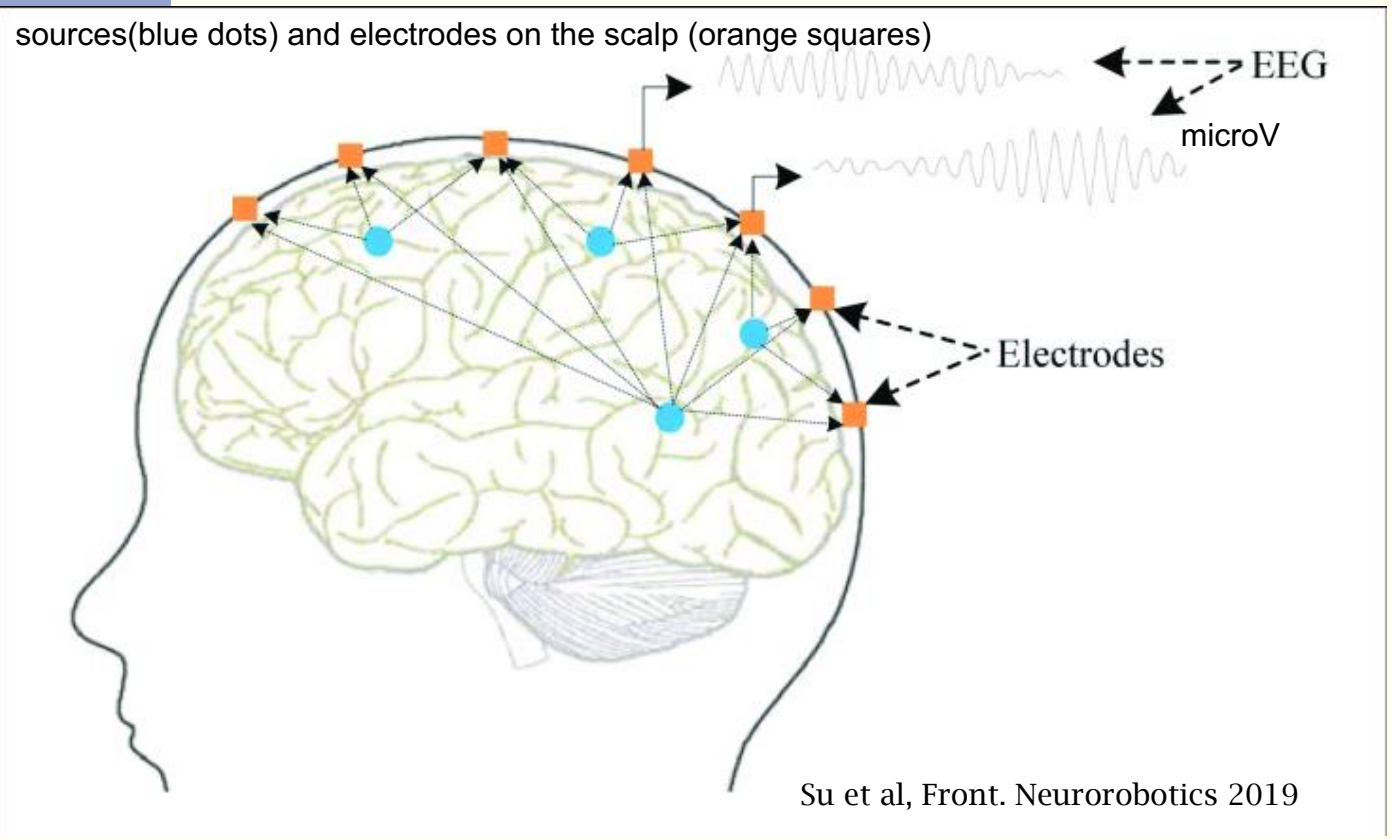
in the case in which we are measuring the single cell, it will be much easier to measure the action potential than the post-synaptic potential, but in the case of many neurons is the opposite



we summarize the consequences

Limitations of scalp EEG - 1

sources(blue dots) and electrodes on the scalp (orange squares)



Su et al, Front. Neurorobotics 2019

single source affect different electrodes

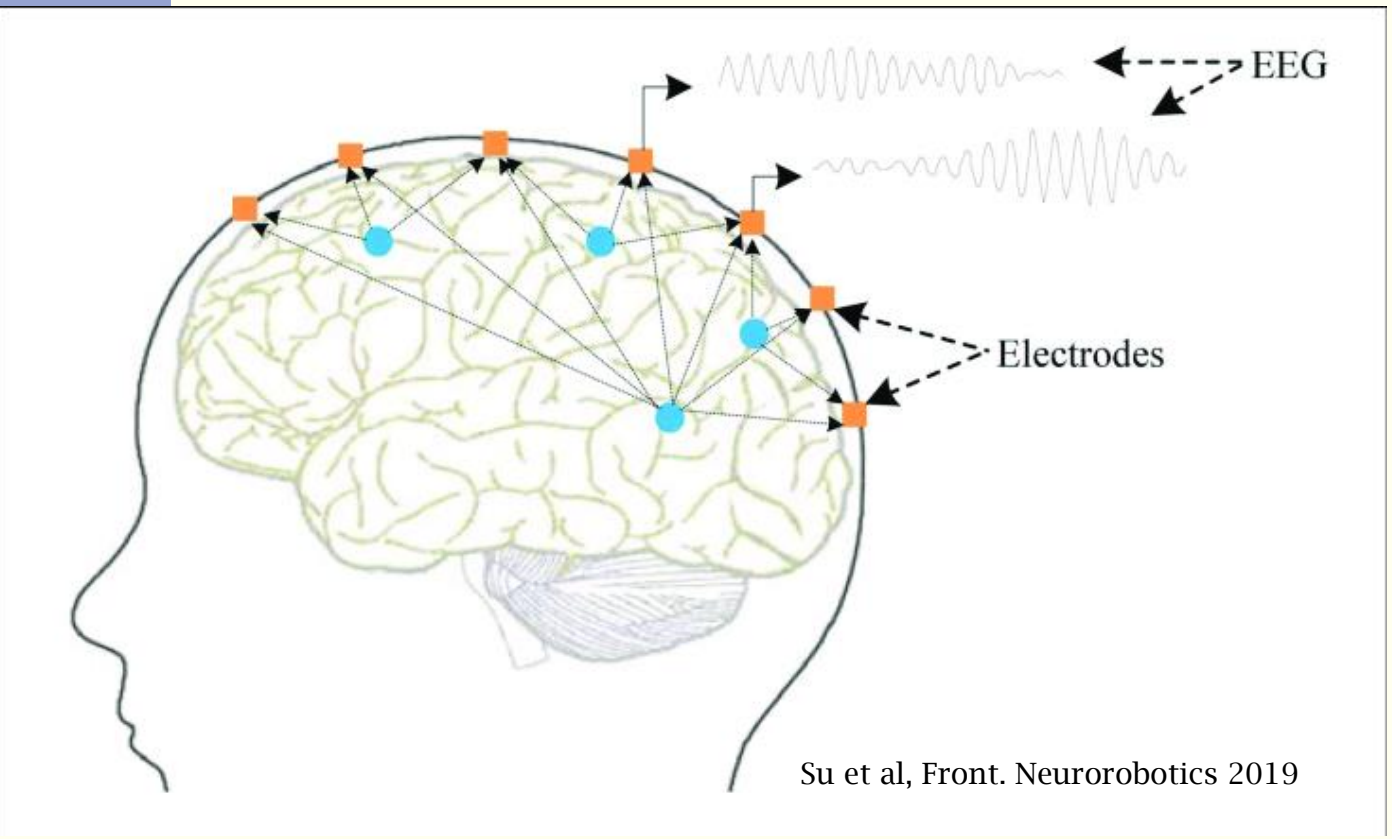
1. Spatial blur (attenuation and spread of the potential with distance)

depends on the distance

with the propagation of the current across the valium condaction we not only have a spread of potential but also an attenuation

2. Low signal-to-noise ratio
3. Multiple sources contribute to the single electrode signal
4. Near electrodes record partially overlapped (correlated) signals
5. Reference choice

Limitations of scalp EEG - 2



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Cortical sources:

- Open field (pyramidal neurons)
- closest to the scalp → stronger, more focused signals

emotional aspects of the brain function are located here

Deep sources:

- Closed field
- More distance
- Attenuation
- More spatial blur

Advantages of scalp EEG

1. Noninvasive — MEG and EEG are the only non invasive measures of the elchtromagnetic correlation of the brain activity
2. Easy to use — practical applications and researches
3. Portable — wherever you want
4. Inexpensive — few thousand of euro
5. Covers the entire cortical surface
6. Excellent temporal resolution — because the propagation is instantaneously

References

- Dayan & Abbott:
  - Chapter 1.1 (Recording Neuronal Responses)
- Wolpaw & Wolpaw:
  - Chapter 2 (Spike Recording and Processing)
  - Chapter 3, pagg. 45-57 (Electric and magnetic fields produced in the brain)
- Hari & Puce:
  - Chapter 1, pagg. 7-11
  - Chapter 3, pagg.25-27 (Charges and electric current) and pagg. 31-34 (Source currents)
  - Chapter 4, pagg. 38-40 (Early EEG recordings)

Self-evaluation test

1. Put the following levels of brain electrical correlates in sequence according to their increasing spatial resolution (from the less to the more detailed):
   A. ECoG: Elettrocorticography
   B. LFP: Local field potentials
   C. IP: Intracellular Potentials
   D. S-EEG: Stereo-electroencephalography
   E. EEG: Electroencephalography
   F. EP: Extracellular Potentials
2. To record in vitro measures of the membrane potential over the dendrites of a neural cell, you can use:
   A. Intracellular measures
   B. Extracellular measures
3. Describe which part of the pyramidal neuron acts as a current dipole and how

Self-evaluation test

4. For each of the following factors, indicate if they affect or not the amplitude of EEG signals:
   A. Open/closed field
   B. Neurons orientation
   C. Synchronicity of the neural activity
   D. Distance between the neurons and the electrodes
5. Which electrical variation of the membrane potential mainly contributes to EEG?
   A. The action potential
   B. The spike train
   C. The resting membrane potential
   D. The post-synaptic potentials
6. Which regions of the brain mainly contributes to scalp EEG? Why?
7. List at least 4 limitations of scalp EEG recordings
8. List at least 5 advantages of scalp EEG recordings