

Neuroengineering

Simone Palumbo's Notes 2023/2024

MSc in Artificial Intelligence and Robotics



Introduction

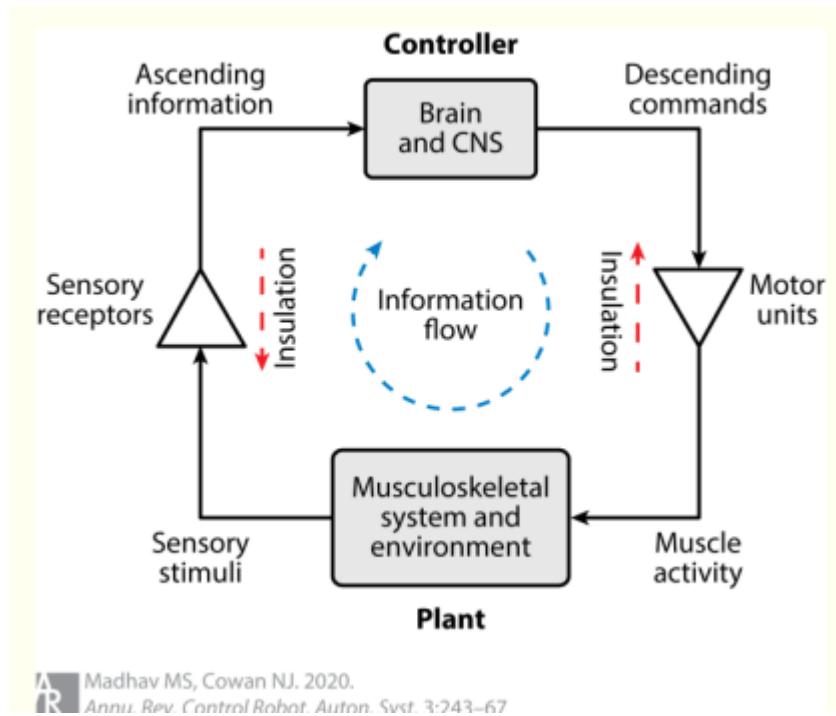
28/02/2024, 5/03/2024

Neuroengineering means quantitative understanding of neural systems in order to advance medical technology in applications related to the nervous system.

The brain is a complex learning system that can process information at millisecond level. It produces an excellent trade off between energy and effectiveness. There are a lot of open questions in clinical but also non-pathological applications.

How can neuro-engineers help neuroscience:

1. Control Theory:

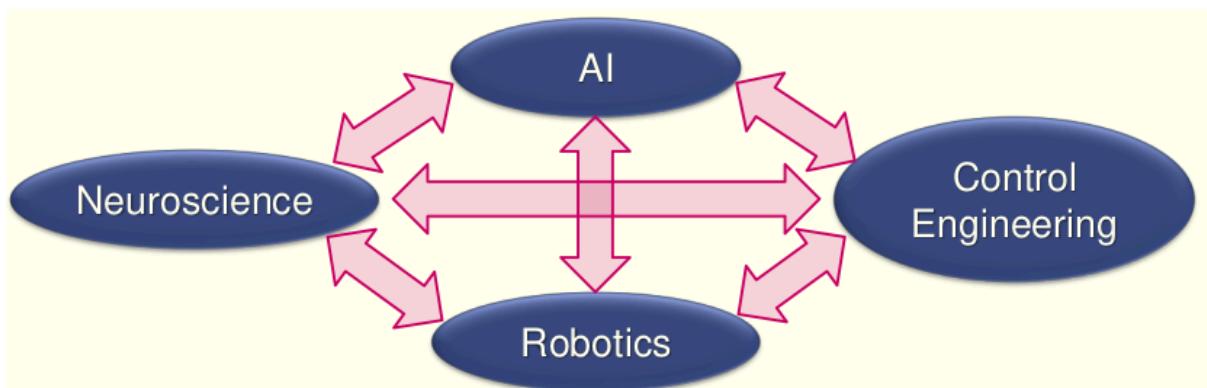


The nervous system is basically a control system. We have inputs received in the form of sensory stimuli coming from the external or even the internal mental world of the subject. These stimuli are processed and reach the controller, that is the brain. The brain produces an output. Usually our output is a muscular contraction, a movement or even just a contraction without a movement. The one and only natural way we have to interact with the external world is movement. Even speaking or changing facial expressions means contracting muscles. This is modeled with control theory.

2. Robotics: neural prostheses and BCIs¹. Brain decoding: I measure something from the brain and I decode what the signal tells about the intention of the subject. BCI is used to interface the human brain with a machine. The idea is to do brain decoding and get information to control in real time an external device, that can be a computer, a domotic house, or a prostheses.
3. Artificial intelligence: analyze vast and complex dataset coming from the brain. We can acquire a huge amount of data in term of spatial localization, network

¹ Brain Computer Interfaces

organization of the brain, anatomical information, functional data and so on. We end up with very noisy data (SNR = 1 is considered good). How to deal with this complex dataset?



Cincotti's Part

The electroencephalogram (EEG)

28/02/2024, 6/03/2024, 13/03/2024, 20/03/2024

The brain generates current and we can record potential differences from the surface. When you measure potential difference on the surface of the scalp we can observe an oscillation, this oscillation is linked to the function of the brain. These oscillations are related to something the human does.

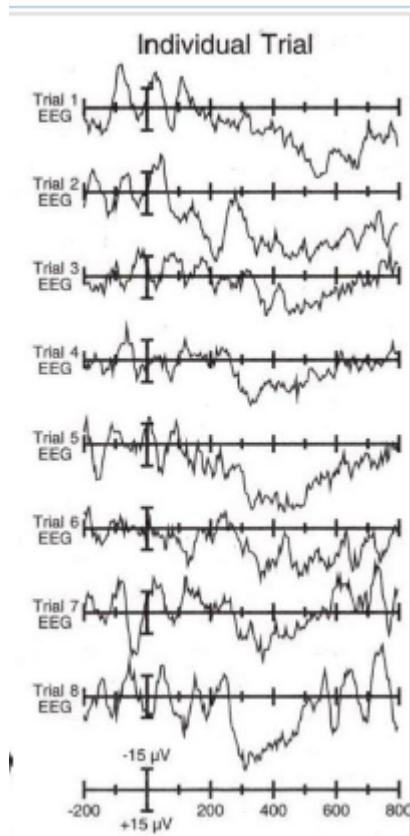
For instance, if you measure the potential difference on the primary² visual cortex (occipital part of the brain), that is directly connected to the eyes, you can see from the EEG a persistent idling 10-hz rhythm named “alpha”

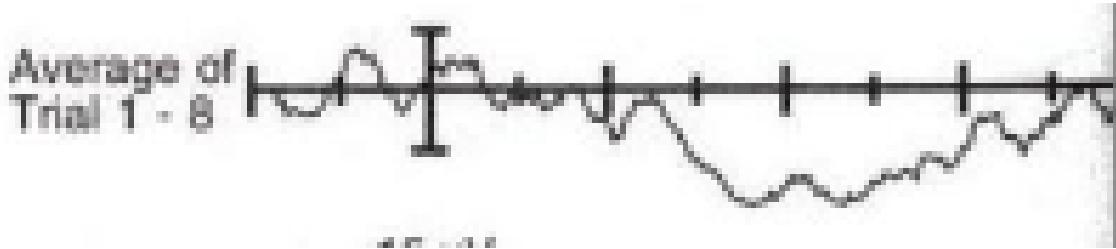


when you close your eyes the oscillations appear, when you open them the oscillations disappear. This phenomenon is called alpha blocking. This is due to the fact that when the visual cortex is involved in a task it desynchronizes, and the higher the oscillations amplitude the more synchronized there is. So even if when your eyes are open there is more activity on the single neurons, the synchronization is lower. When the cortex is idling, so there are no visual inputs, there is more synchronization.

Besides spontaneous brain activity (like the alpha rhythm) EEG can show time-locked responses to various sensory stimuli.

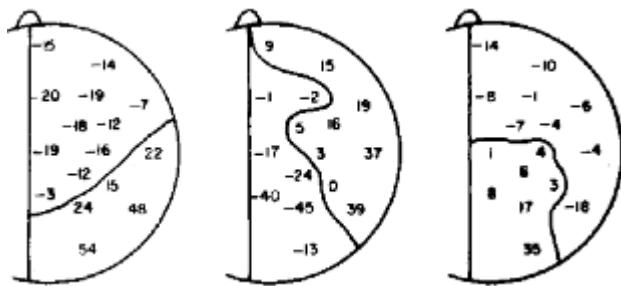
² It is called the “primary” visual cortex because it is the first point in which the sensory visual arrives. Then these inputs are propagated to the secondary visual cortex.





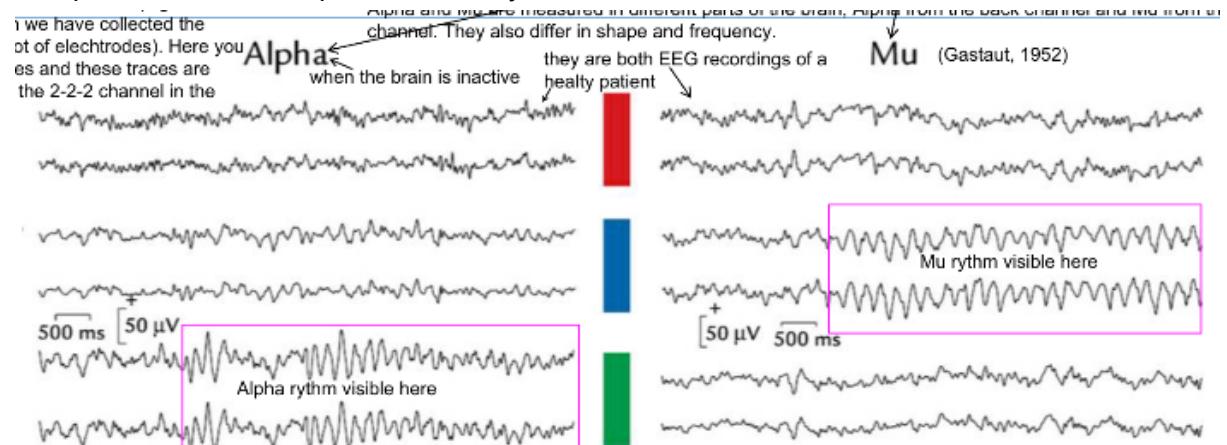
With a computer you can average EEG signals time-locked³ to various stimuli. A stimulus can be a loud sound that makes the human jump. The response to a stimulus is low in amplitude (since it has lower order of magnitude than the alpha rhythm it is overridden by it) and transient: 200 ms later, for instance, is gone. It is necessary to do the average between several responses to several stimuli since with just one measurement we can't really measure the response of the human. Doing the average, the response is more visible.

Another important thing we can do with computers is plot maps of several channels acquired



Another rhythm is the mu rhythm. It oscillates around 10 hz and it blocks when the area is functioning, but, differently from the alpha rhythm, it is generated by the motor area, that is the central⁴ area of the brain. So if you make a movement the mu rhythm stops.

Comparison between alpha and mu rhythm:



³ Time-locked means that the same response follows with the same delay of the stimulus. So you just take the time of the stimulus as the 0

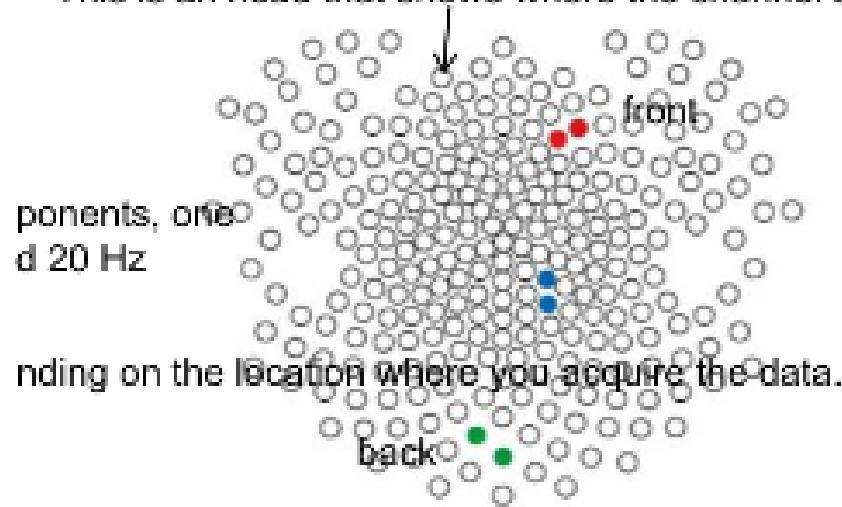
⁴ Central means that it is not anterior nor posterior, while mesial is between the left and the right

while the alpha rhythm is more or less symmetrical, the mu rhythm has an arc-shape (a me non sembra actually). These graphs doesn't have x and y axis, but they have calibration bars:



for instance you can see from above that the amplitude of the alpha rhythm is 500 ms and the distance is 50 microVolt, with positive upwards⁵. In this case there are 6 traces for alpha and mu. The three colors, red, blue and green indicate the position of the brain in which the signal was recorded. Since red is associated with the front signal, we can see that this one is more regular than the back one.

This is an head that shows where the channel are taken.



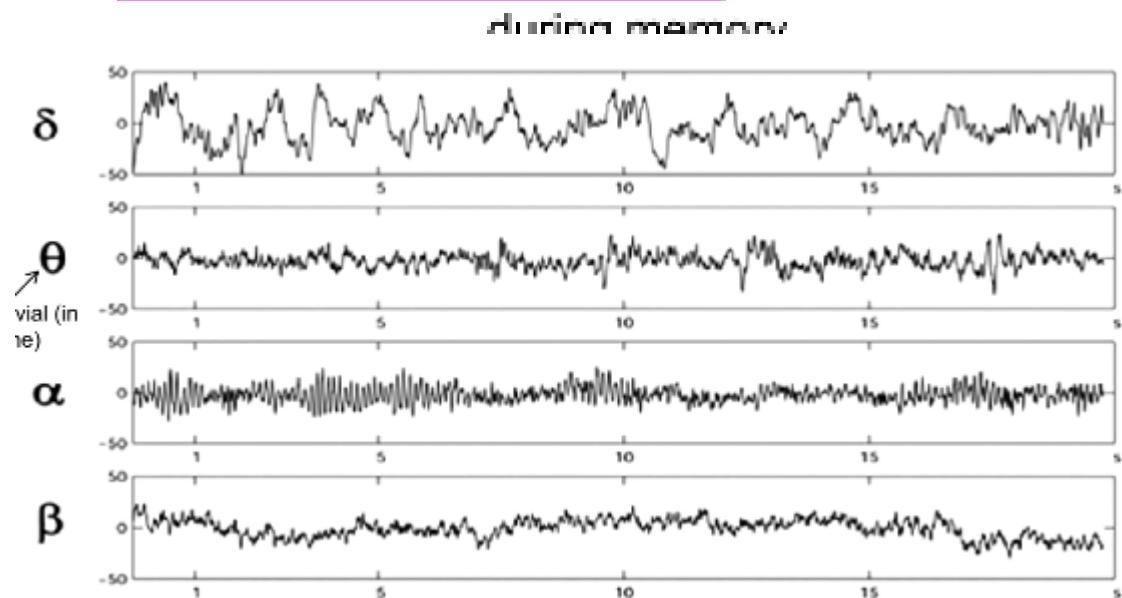
Actually you can put electrodes in other parts of the body, not only in the head, since you may not have enough space in the head to place them all. Indeed, the canonical number of electrodes is 19, but for research purposes you use at least 32, if not 64, 128 or even 256.

In the map above, you have the vertex in the center, at the side the holes indicate the ears, while the holes upfront are for the eyes.

⁵ commonly in neurophysiology the y axis is positive downwards.

While rhythms are associated with functions of the brain, we have frequency bands: we know from the Fourier Theorem that any shape of a function can be decomposed into sine wave oscillations (**FOR HAVING THAT, THE SIGNAL MUST BE PERIODIC, IS THE EEG PERIODIC?**). So I can take the EEG, apply the fourier theorem, and say that is the sum of sine waves. More precisely, the EEG is composed of the following sine waves (**ARE THESE SINE WAVES?**):

- Delta: < 3.5 Hz
- Theta: 4–7.5 Hz
- Alpha: 8–13 Hz
- Beta: 14–30
- Gamma: > 30 Hz



Note that the alpha band includes the alpha rhythm, but also the mu rhythm. These bands are not to be taken as exact, they are just convention and they are not 100% precise.

Evoked and Event-Related Responses:

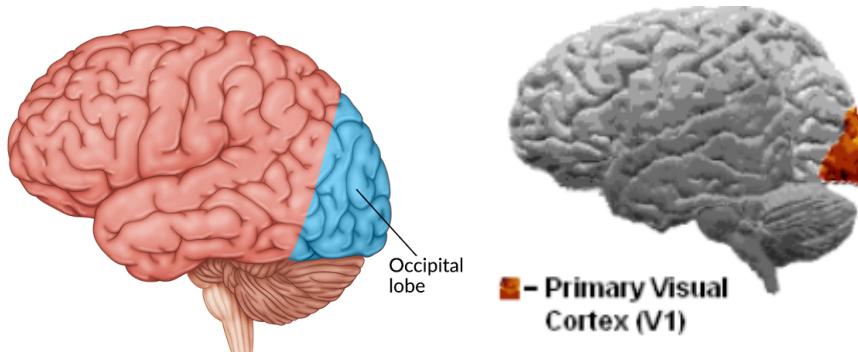
- Evoked Potential (EP) are stimulus-driven activity

- Event-Related Potential (ERP) are EEG signals triggered by external stimuli or stimuli related to internal mental events or task-related events. This leads to the difference between:
 - a. External Stimulus: independent by the subject
 - b. Internal Stimulus: caused by the subject itself.
 - i. Internal Mental Events
 - ii. Task-Related Events: e.g. moving a finger (I put it here but I don't know maybe it's internal mental events? I am sure is an internal stimulus though)

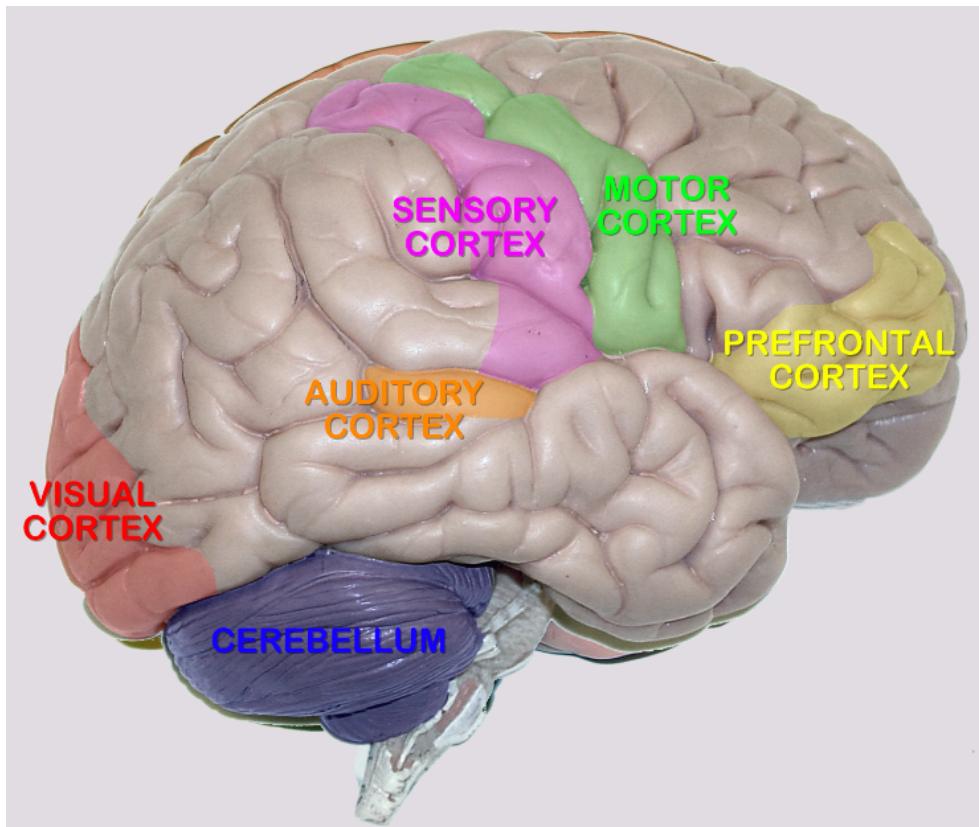
So that means that Evoked potential (EP) is a subtype of Event-Related Potential (ERP) where the event is a sensory input. Is there any other chance? Namely, are there any other subtypes of ERP? Yes: for instance, you can estimate an event potential correlated to a movement. Not only the movement of the wrist follows the event but also it proceeds since the brain has to think about the movement.

True Statement of 1.01 EEG

1. The alpha rhythm is an oscillatory component of the spontaneous EEG. Yes, the alpha rhythm is part of the spontaneous brain activity
2. The frequency of oscillation of the alpha rhythm is around 10 Hz.
3. The amplitude of the EEG in the alpha band decreases when the generating region of the cerebral cortex becomes engaged in a functional task (visual, motor). Yes, for instance if you open your eyes, the primary visual cortex is engaged in a visual task and the alpha rhythm amplitude is decreased
4. The proper (visual) alpha rhythm is generated in the occipital lobe of the cerebral cortex. Yes:



5. The mu rhythm is an oscillatory component of the spontaneous EEG, whose frequency is in the alpha band. Yes, as the alpha rhythm
6. The mu rhythm is generated in the central regions of the cerebral cortex. Yes, as you can see from here the motor cortex is in the central part of the brain



7. The oscillations of mu rhythm are more “arc-shaped”, rather than resembling a regular sine wave. **I don't see this thing actually**
8. The amplitude of the alpha rhythm is not constant, but rather “waxes and wanes” (**ALTI E BASSI**) with irregular periods, with changes occurring often after an interval in the order of 1 second
9. The alpha band of the EEG is conventionally limited between 8 and 13 Hz
10. The delta and theta frequency bands identify frequencies lower than those in the alpha band. Yes, in fact:

Delta: < 3.5 Hz

Theta: 4–7.5 Hz

Alpha: 8–13 Hz

11. The beta and gamma frequency bands identify frequencies lower than those in the alpha band. Yes, in fact:

Alpha: 8–13 Hz

Beta: 14–30

Gamma: > 30 Hz

12. The alpha rhythm can be observed by filtering the spontaneous EEG signal using a narrowband filter, with cutoff frequencies at 8 and 13 Hz. **This doesn't seem right since we have several different rhythms in the alpha band, so if I consider only this frequency band I should see not only the alpha rhythm but also the mu rhythm for instance. MAYBE IS THE FACT THAT I SAMPLE THE SIGNAL ON A SPECIFIC BRAIN AREA SO I DON'T SEE THE MU RHYTHM IF I RECORD ON THE VISUAL CORTEX**
13. Evoked Potentials are deflection of the EEG signal following the presentation of a sensory input.
14. Event related potentials include evoke potentials, as well as EEG responses to motor or cognitive events. (**SO THERE IS A DIFFERENCE BETWEEN EVOKE AND EVENT RELATED POTENTIALS**)
MAYBE EVOVED COMES FROM AN EXTERNAL INPUT WHILE EVENT RELATED COMES FROM INTERNAL INPUT (?)

EEG Instrumentation:

EEG electrodes transduce the ionic currents to electric current



The most commonly used EEG electrodes are made of silver and silver chloride⁶. The silver chloride electrode has the following advantages:

1. nonreactivity with biological tissue

⁶ The silver chloride electrode has this metal covered with a layer of salt.

2. accurate reproduction of extremely slowly changing potentials
3. low polarization potentials, drift, and noise.
4. replicates the potential in the biological medium to the electronic circuit (is this equal to 2?)

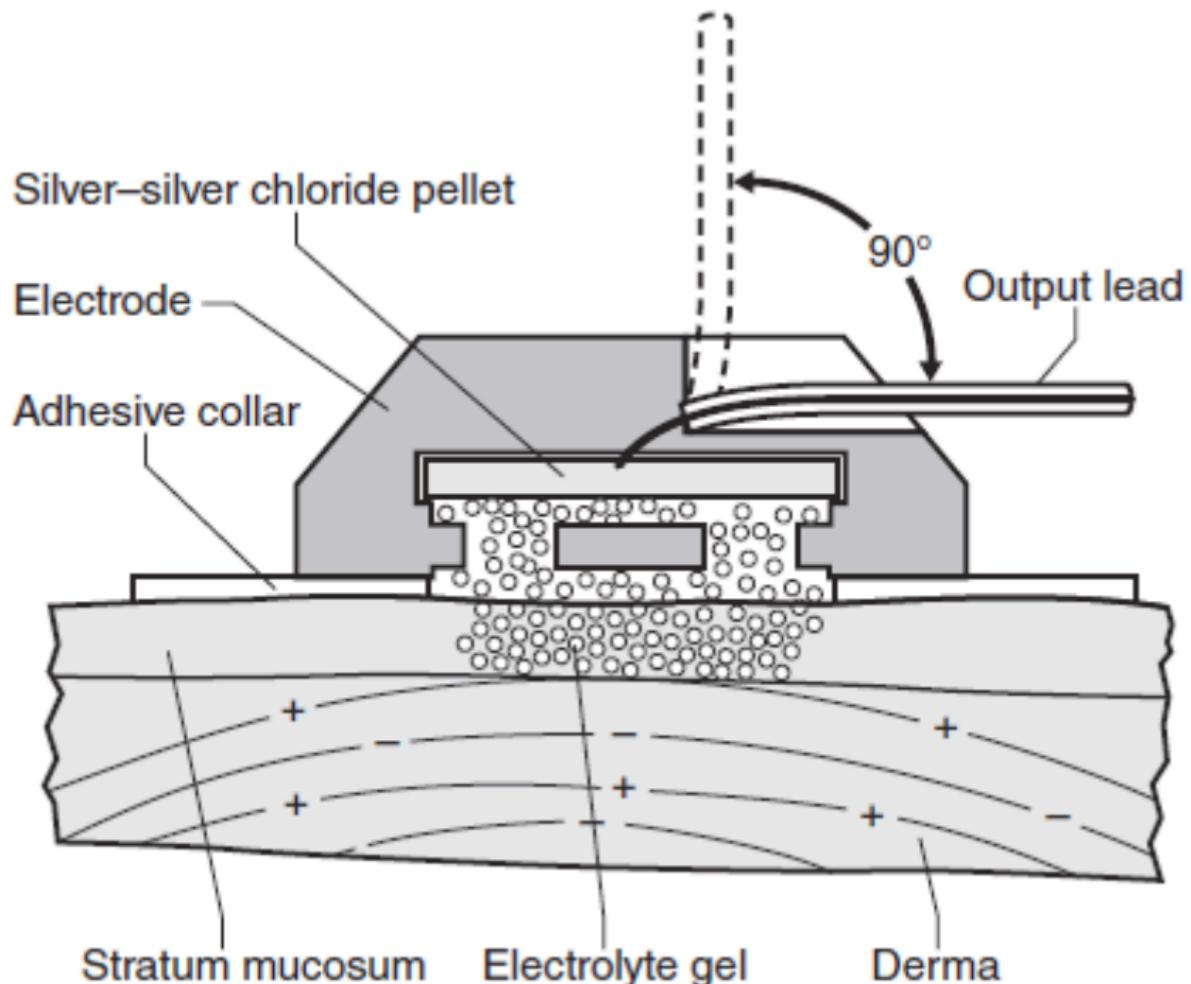
The impedance is a measure of the quality of the contact between the scalp, electrode, and conducting medium. It is the resistance + the reactance, but for our purposes we can just call it resistance. It must be measured with alternating current (AC), since some electrodes have a very poor performance in continuous currents (DC). This requirement is not a problem since the EEG is has its most important part at 10 Hz, and so the DC is not really relevant I DON'T KNOW WHY THE FACT THAT THE EEG IS AT 10 HZ MEANS THAT THE DC IS NOT RELEVANT.

there are circuits that measure impedance

They apply alternating current and the measurement is done in AC, at around 10 to 20 Hz.

gold, tin, and silver-chloride electrodes

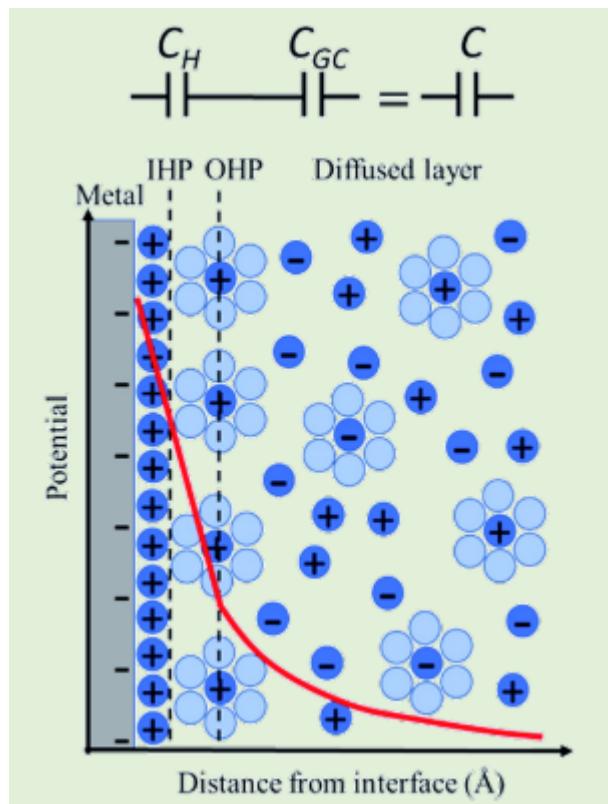
There are modern electrodes with the same behavior as silver chloride but that require less maintenance:



Between the metal and the skin there is no contact: the contact is mediated by the electrolyte gel, just a gel of ions. The top part of the skin is dry, and is a poor conductor. So we wet it with the gel. The gel diffuses into the skin to create a conductivity part between the deep part of the skin. This gel is ionic conductive, as the human skin. **The metal cannot touch the skin directly, for a reason that we will see in the possible section.**

You need a way to put the gel, the conventional way is use a syringe with a needle injecting the gel you move it in a way that is spread so it touches all the walls of the electrodes.

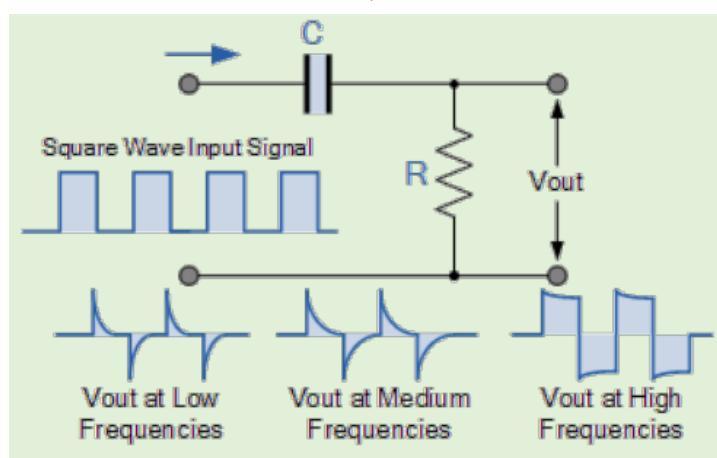
Metal-electrolyte interface: at the interface of metal and the biological medium (the gel) there is a potential difference (positive at the biological medium and negative at the metal). Since this potential difference exists, all positive ions tend to move toward the metal creating a layer. **Some of them will catch an electrode from the metal, and this will make it more difficult for other positive ions to get closer.** That means that the flow of current is hindered by this layer.



This obstacle would be avoided if the energy for an ion to get an electron was very low. Silver with chloride has low energy and so the current is less hindered. Gold on the other hand has a high energy so the flow of currents is hindered.

In fact, this metal-electrolyte interface, with a wall of ions, is like a capacitor. We know that the capacitor blocks the DC (as we said). The gold is like a capacitor without leakage, while the silver-chloride is like a capacitor with resistance in parallel, so with a leakage.

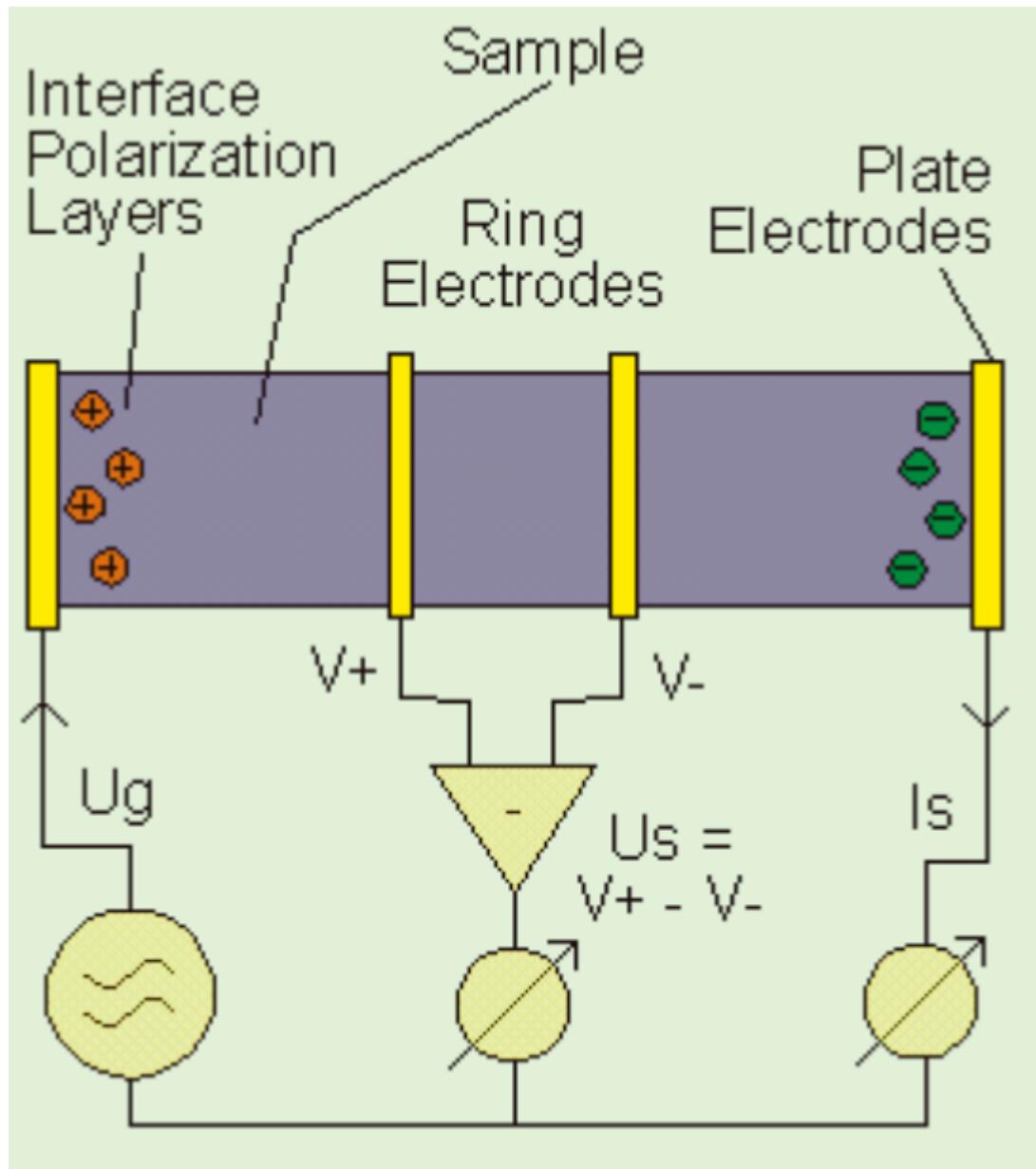
Ma che è sta roba? Sarebbe un gold material? CREDO SIA L'INTERFACCIA, CHE PUÒ ESSERE MODELLATA IN QUESTO MODO



Since this is a high-pass RC circuit, if the square wave in input has high frequencies squares most of the signal will pass through. If the frequency is lower the plateau cannot be reproduced and so an exponential behavior is reproduced.

We want to control this interface and this is the reason why we can't put the skin directly in contact with metal, since we can't perfectly control the skin: the human skin can be more or less conductive, for instance.

When you have a metal touching a biological medium, since the potential is not zero, there is a polarization effect. When there is polarization, we want to measure potential and currents.



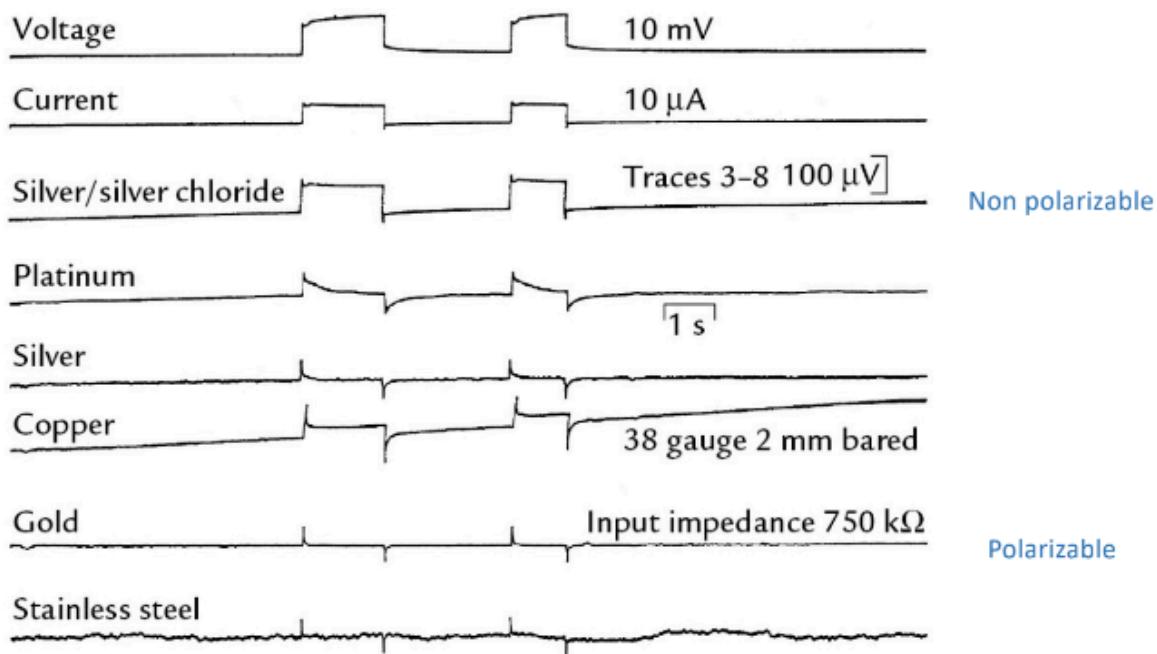
TO UNDERSTAND BETTER

solution: 4 electrodes apparatus, decoupling the injection of the current from the measurement of the potential

using two more electrodes the current is guaranteed to
since you have a generator and an amperometer

you measure the potential between V+ and V-

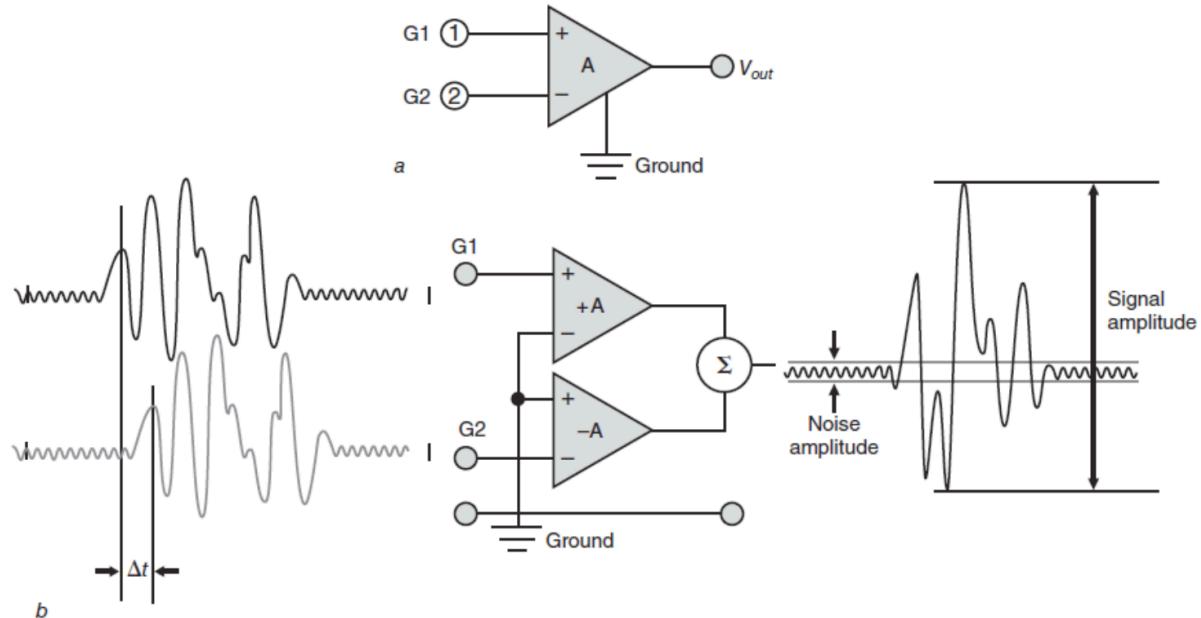
Output of the amperometer, the potential of the generator and measurement with the two electrodes on V+ and V-



From the third line there are the measurements where we change the material. Silver and Silver Chloride are quite good for our task: the waveform is preserved quite well, since, as we said, they are capacitors with leakage, so the plateau is preserved. This means that the silver/silver chloride is *non polarizable*. On the other hand, the gold is a good high-pass filter and in fact the plateau doesn't pass, and this means that the gold is *polarizable*.

With copper you have a drift going up which may be a problem. Stainless steel has random noise.

Differential Amplifier: we use it because with the electrode we want to capture tiny potential in an environment that contains noise up to the order of volts. How to remove this noise? The good thing is that it is the same on every part of the body, so if I put two electrodes on the scalp the noise is equal on both electrodes and we can remove it with Common Mode. For doing so we use a differential amplifier, that are two operational amplifiers⁷ in parallel.



This is an amplified version of the difference between the two signals in input, as in the operational. But this time, differently from the operational, the common part will be amplified less than with an operational.

A feature of the amplifier: CMRR (common mode rejection ratio)

The amplifier has, as a measure of interest, the CMRR. This is the ratio in decibel between the differential gain (how much the difference between the inputs is amplified) and the common-mode gain (how much the common signal is amplified).

$$V_{out} = \boxed{\text{ideal amplifier}} \quad G_d(V_+ - V_-) + \boxed{\text{non-ideal component}} \quad G_c \left(\frac{V_+ - V_-}{2} \right)$$

$$CMRR = \left. \frac{G_d}{G_c} \right|_{dB} = CMRR = 20 \log_{10} \left(\frac{\text{gain for difference signal}}{\text{gain for common mode signal}} \right)$$

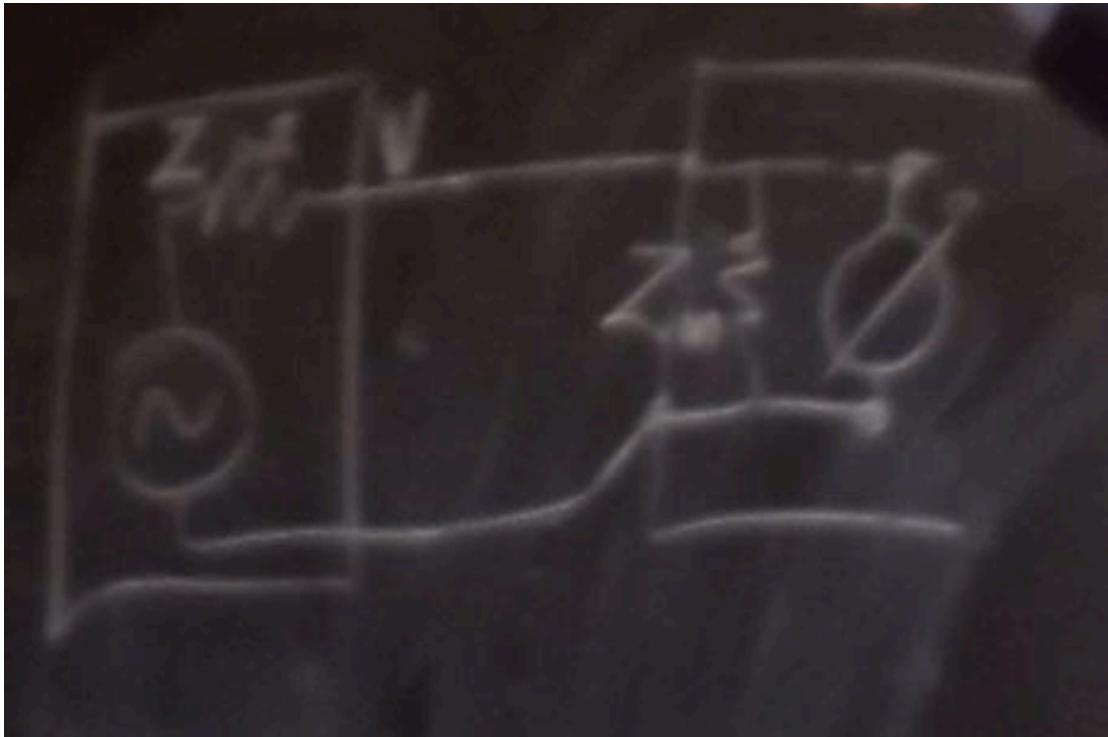
The gain of the differential part is G_d , while the gain of the common part is G_c and we want it the lowest possible.

⁷ An operational amplifier is something that takes the difference, measures it and amplifies it.

Another feature of the amplifier: Input Impedance

The impedance of the amplifier is different from the impedance of an electrode. The impedance of the electrode, as we said, is the amount of resistance that the electrode proposes.

The fact is that the path from one electrode to another is not free, there is some resistance, given by the impedance of the electrode, the resistance of the scalp and so on. Since we are engineers, we create a model of it: an equivalent circuit composed of a generator + impedance represents the black box of the head with electrodes.



If the input impedance is much higher than the output impedance you will be measuring exactly V_{in} (questo perché non c'è il partitore di corrente vero?)

I think this model is an operational amplifier, I think that since we are using differential amplifier, you have this circle repeated twice

$$V_{out} = V_{in} * (z_2 / z_1 + z_2)$$

The problem is that z_{out} contains $z_{impedance}$

We want an impedance of the electrode below 5 khm, in this way you are not moving much the denominator. If you allow the electrode impedance to be 100 khm you will be comparing 100 khm with ... that is not that much of a difference, so you are modifying the denominator

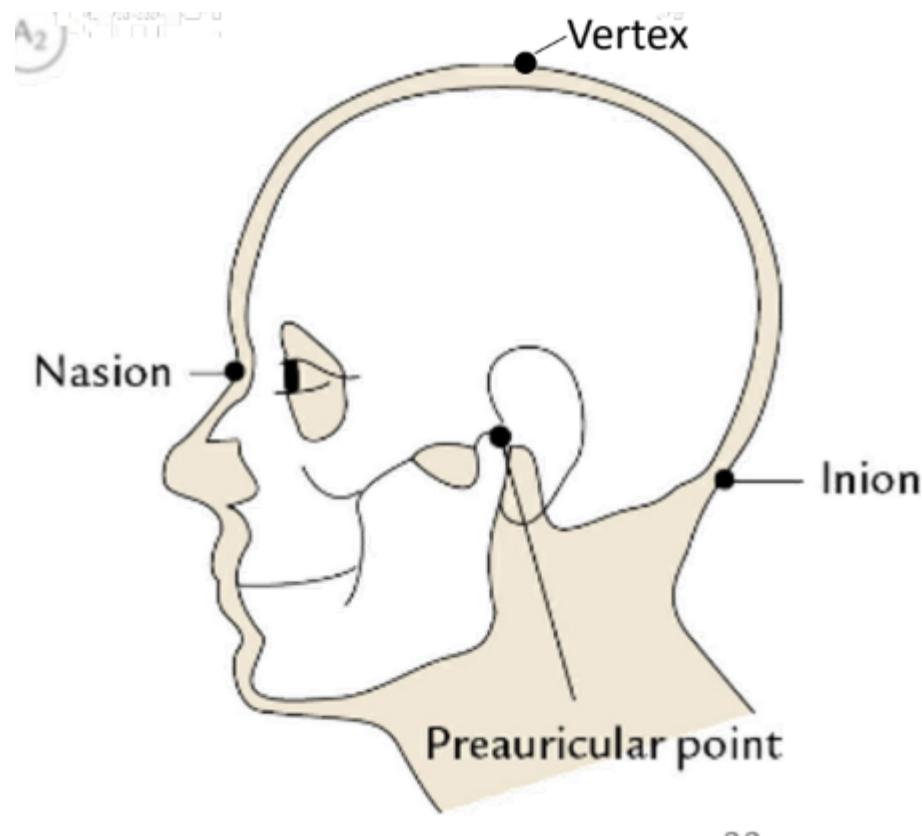
z_2 is not under your control since you can purchase an amplifier with ..
 z_1 is under your control, you want it low first for the partitore di corrente and second since you don't have 1 branch but 2 branches (one inverting and one non inverting) so z_1 must be similar to z_1 of the other branch

Voltmeters have impedance inside the instrument very high, since you don't want current inside the circuit. Currentmeters have impedance very low, since you don't want negligible potential difference.

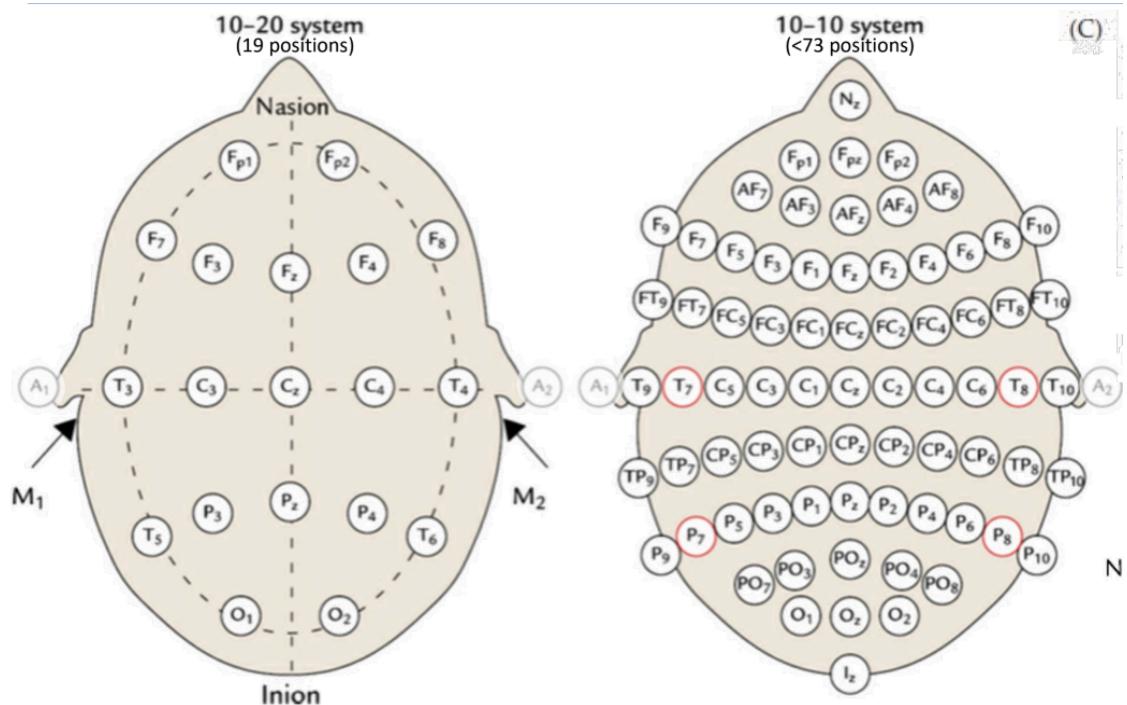
ma che c'entra?

Where do I put the electrodes:

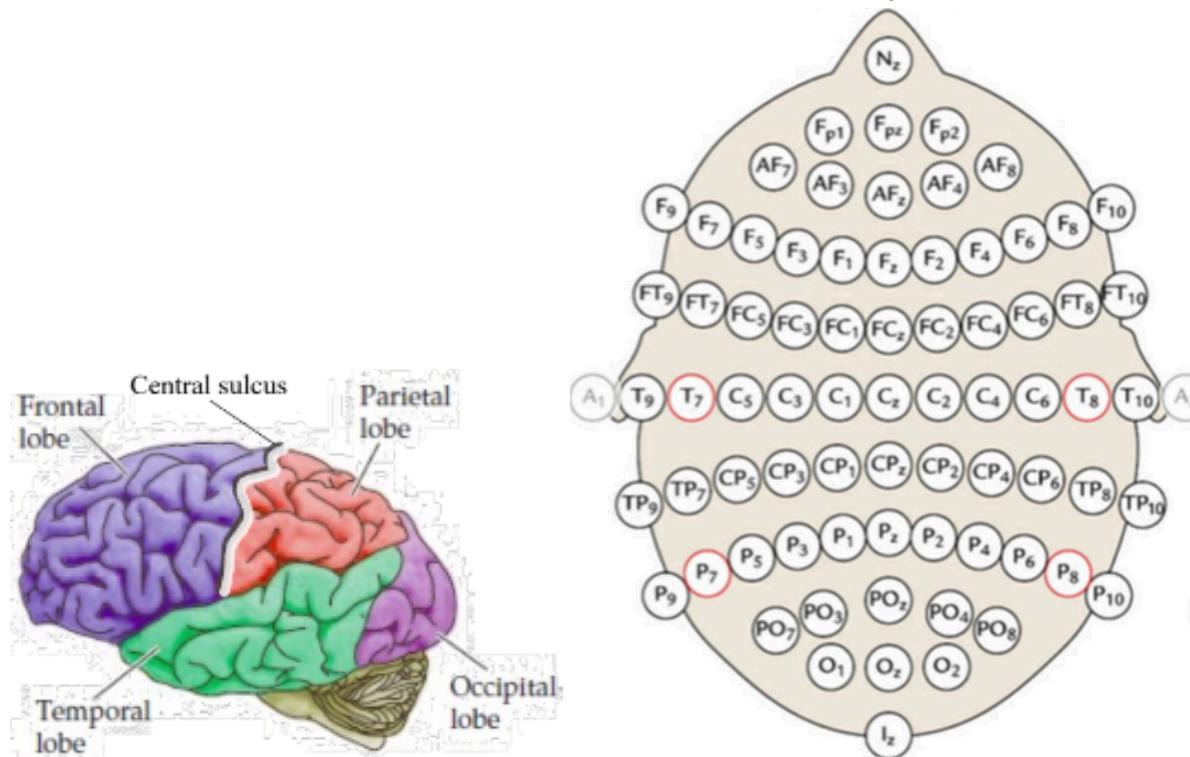
The skull has some reference point. For instance, the Vertex is at 50% of the distance between the Nasion and the Inion.



The 10-20 system takes the distance between the Nasion and the Inion and divides it in parts in the [following way](#): 10%, 20%, 20%, 20%, 20%, 10%. The same thing must be done side to side, from ear to ear. In this way you use 19 electrodes. Since nowadays we need more electrode we use the 10-10 system, that uses the same principle as the 10-20 system. In this way we define up to 73 positions.



In both systems, the line from the Nasion to the Inion is the 0 so the electrodes have the z subscript, all subscript with odds number are on the left, while even are on the right. To understand the letters of the electrode, we need some neuroanatomy:



- The electrodes placed on the temporal lobe⁸ have a T
- The electrodes placed on the central sulcus have a C
- The electrodes placed on the frontal lobe⁹ have an F
- The electrodes placed on the occipital lobe have an O

⁸ The temporal lobe doesn't cover only the "tempie"

⁹ The frontal lobe doesn't cover only the "fronte", so the forehead. But it's much bigger

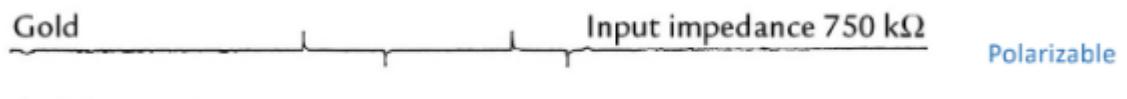
True Statement of 1.02 EEG

- EEG electrodes made of silver with a layer of Ag/AgCl are non-polarizable, thus they allow recording of extremely slow-changing potential. Yes, as shown here:



They are capacitors with leakage so the low frequencies pass through. The fact that they allow low frequencies to pass through means that they allow recording of extremely slow-changing potential, since “extremely slow-changing” means “low frequency”.

- In the EEG terminology, impedance is a measure of the quality of the contact between electrode and scalp, through the conductive gel. The impedance of the electrode (not of the amplifier!) is resistance + reactance that the electrode proposes, and for some reason this is a measure of the quality of the contact between the electrode and the scalp.
- Contact impedance of the electrodes is measured in kiloOhm and sum be measured using an alternating current. Yes: some electrodes have very poor performances in DC, I think because they are good capacitors, so they don't let DC pass through, e.g. gold electrodes.
- Gold electrodes are polarizable, thus they should not be used to measure slowly changing potential. Yes: they don't let low-frequency pass through.



transversal question: does low frequency mean DC and high frequency AC?

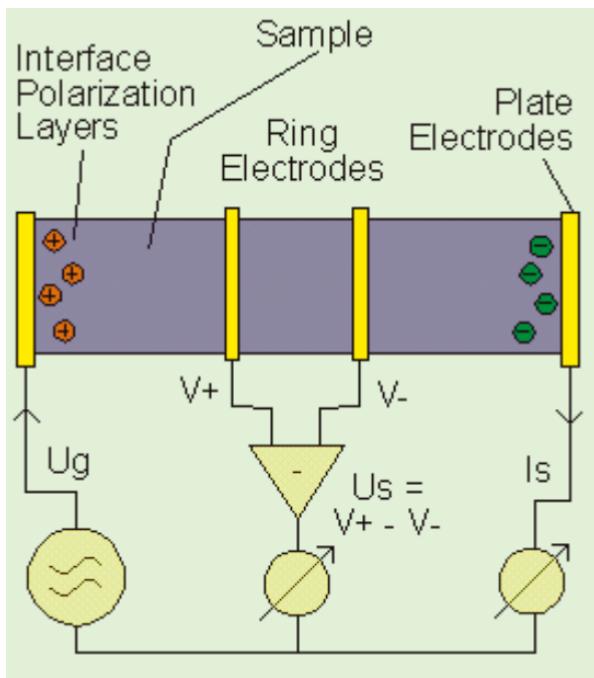
- The CMRR of a bipolar amplifier characterizes the ratio between the gain of the difference of potential between input electrodes and the gain of the common potential w.r.t. to ground. First of all: what is a bipolar amplifier? Maybe the amplifier with two inputs. Apart from that, yes:

$$V_{out} = \boxed{G_d(V_+ - V_-)} + \boxed{G_c \left(\frac{V_+ - V_-}{2} \right)}$$

ideal amplifier non-ideal component

$$CMRR = \left. \frac{G_d}{G_c} \right|_{dB} = CMRR = 20 \log_{10} \left(\frac{\text{gain for difference signal}}{\text{gain for common mode signal}} \right)$$

The input electrodes potential is subtracted



and this difference is amplified:

ideal amplifier

$$G_d(V_+ - V_-)$$

but also the common potential is amplified:

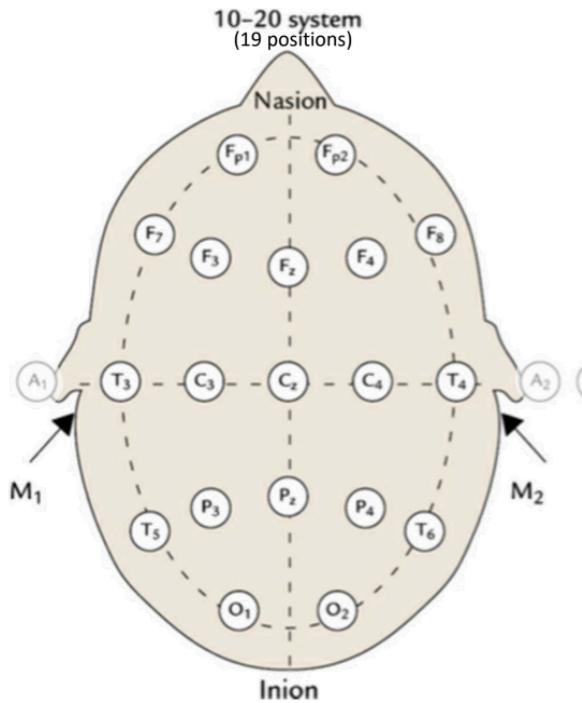
non-ideal component

$$G_c \left(\frac{V_+ - V_-}{2} \right)$$

We calculate the ratio between the gain G_d and the gain G_c

- 6. The CMRR is usually expressed in decibel (dB) and high values characterizes better amplifiers.
- 7. The advantage of a high CMRR amplifier is that it suppresses common-mode disturbances such as powerline (50 Hz) noise.
- 8. The measurement of a single EEG signal requires three electrodes - two as input to the differential amplifier and one to provide the ground potential.

9. The input impedance of a biosignal amplifier must be many orders of magnitude higher than the contact impedance of the electrodes. It is usual to have input impedances in the order of 10^8 Ohm. **Yes: in this way we don't have the partitore di corrente right?**
10. EEG guidelines suggest keeping the electrodes contact impedance below 5 kiloOhm. The use of modern amplifiers with high input impedance allow to relax this requirement.
11. One of the reason why one should keep the electrodes' contact impedance much lower than the amplifier's input impedance is that the resulting voltage divider would otherwise reduce the measured potential
12. The difference of contact impedances of electrodes should be small compared to the input difference of the differential amplifier, otherwise the resulting unbalance compromises its common-mode rejection capability.
13. The electrode labels of the international 10-20 System uses the first letter of the four lobes of the cerebral cortex (Frontal, Parietal, Occipital, Temporal), plus "C" (central) to designate electrodes over the central sulcus



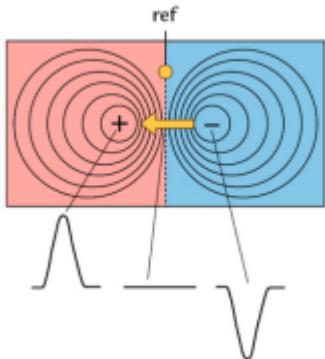
14. In the electrode labels of the international 10-20 System, odd/even number designate electrodes on the left/right side, respectively
15. The international 10-20 System for EEG electrodes placement takes its name because the distance between adjacent electrodes is 10% or 20% of the distance between pairs of reference points on the skull (Nasion and Inion, or preauricular points)

Effect Reference Electrode On Potential Distribution:

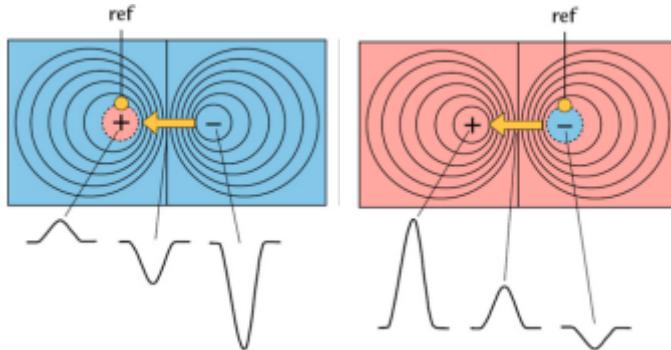
For a single measurement, three signals are necessary: active, reference and ground signals. So to acquire a 1-channel EEG we need at least three electrodes. For a 2-channel EEG required at least four electrodes: active₁, active₂, reference and ground.

The choice of the reference signal influences an EEG. Ideally the reference electrode should be neutral and not contribute to the measurement. Unfortunately there is no point in the human body with zero electrical activity.

To understand how the choice of reference signal affects the measurement, consider a water basin with two terminals (+) and (-) of a 12 v battery. Using a voltmeter we measure the potential at each point between the + and the -. Ideally, there is a point between the two battery terminals that has zero potential. This is the point at infinity that we can, ideally, take as reference.



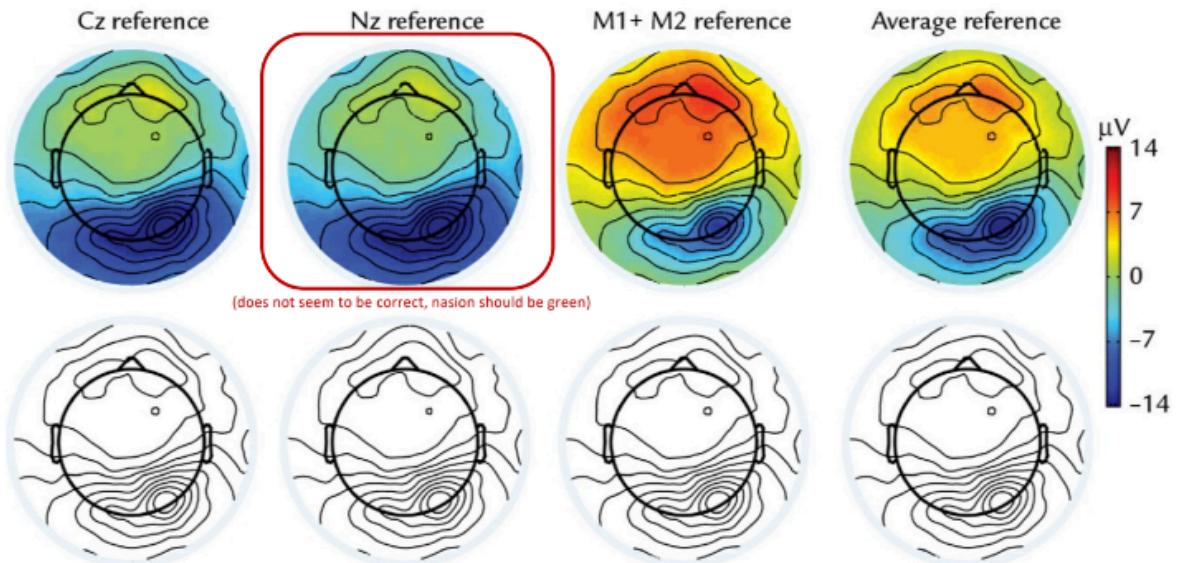
In practice we are not able to place ref at the point at infinity, so our measurements will look like the following:



Note: changing the reference will just shift all the potential values, but the potential distribution will remain the same.

Let's consider the following example. The figure below shows EEG changes w.r.t to the reference used. The data were collected with 256-channel [geodesic net](#) w.r.t the vertex (C_z). Then with a digital re-reference we get the data using nasions (N_z) as a reference and linked mastoids¹⁰ M1 + M2. Then, to obtain the best approximation of the *reference at infinity* we use Common Average Reference (CAR) technique: we average the results of C_z, N_z and M1 + M2.

¹⁰ M1 and M2 must be acquired singularly and not short circuited.

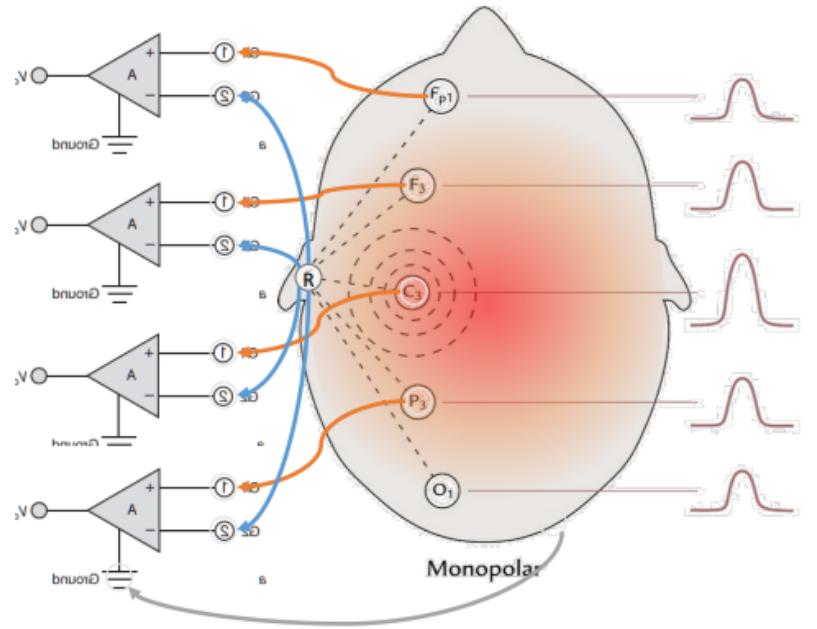


Note: it seems that the figure for N_z reference is wrong since the nasion (near the nose of the subject) should have green color, since green is 0 v, and the reference should be at this voltage.

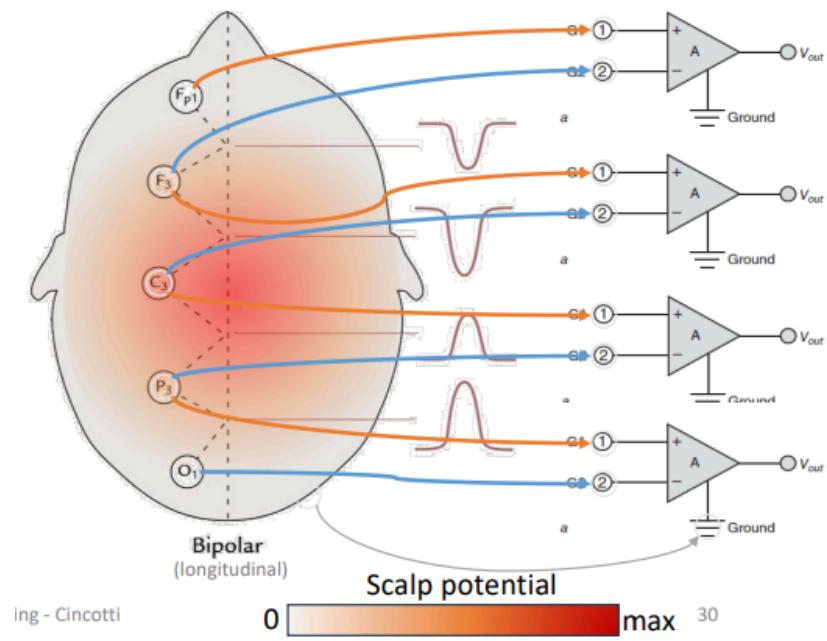
Note also that the figures at the bottom are always the same since if you change reference point you change the potential values, but the potential distribution remains the same.

Monopolar and Bipolar Recording:

With monopolar recording we measure the potential at each electrode w.r.t a single electrode that is a reference. Until now, we have considered monopolar recording. In the following image the reference is put on the left ear:

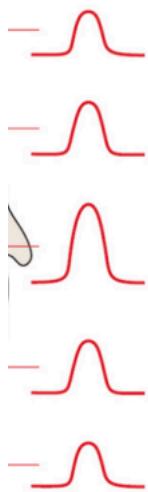


In a clinical setting it is usual to use bipolar recording in which potentials are measured between neighboring electrodes in pairs. In the following image a longitudinal bipolar derivation is used:

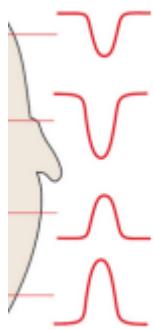


The main difference is that:

- In the monopolar recording there is an amplitude variation



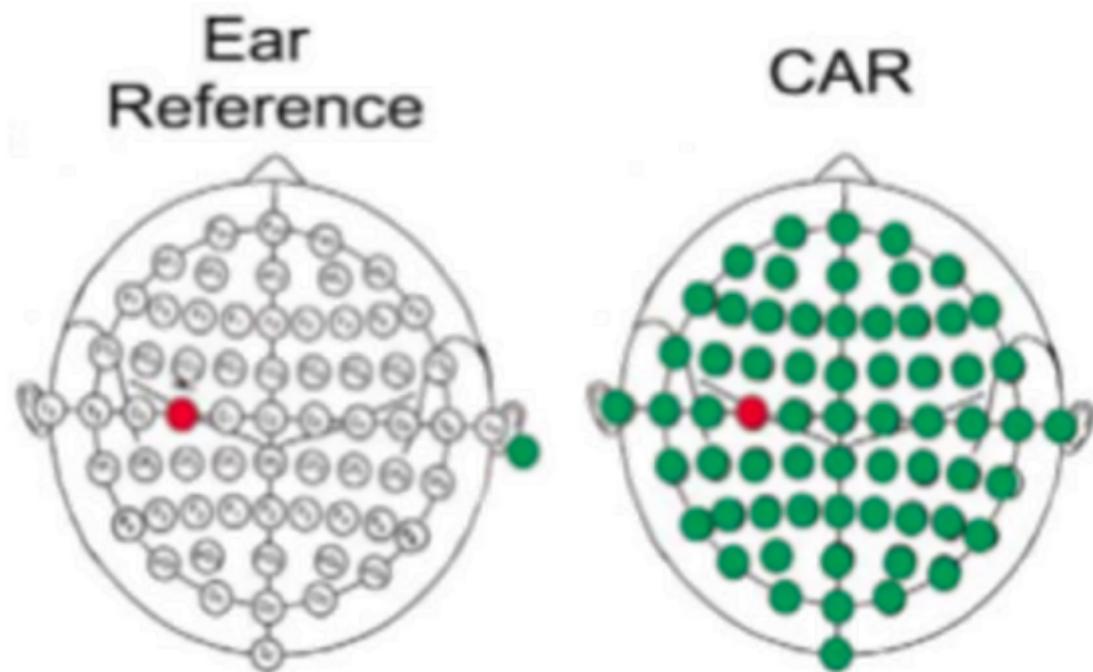
- In the bipolar recording there is a variation of polarity between the front and the back part of the scalp



Re-Referencing Relative to an Average Reference:

NON HO BEN CAPITO STA COSA

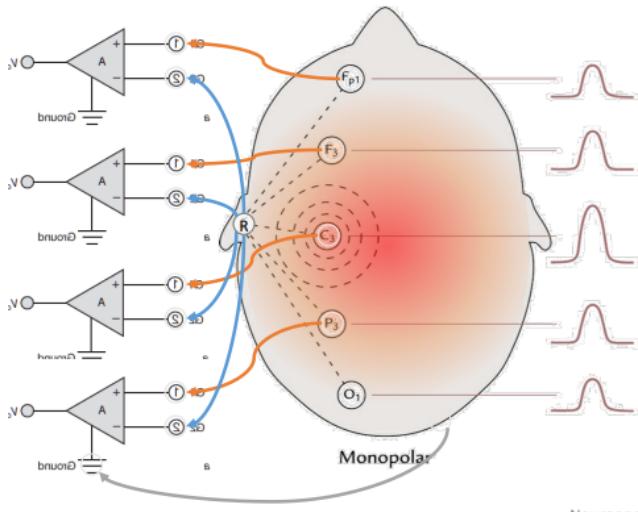
- The integral of the potential over the surface of a sphere that contains only concentric inhomogeneities is zero
- The summed potentials of evenly spaced electrodes across the entire surface would be null as well
- In practice these conditions are never exactly met



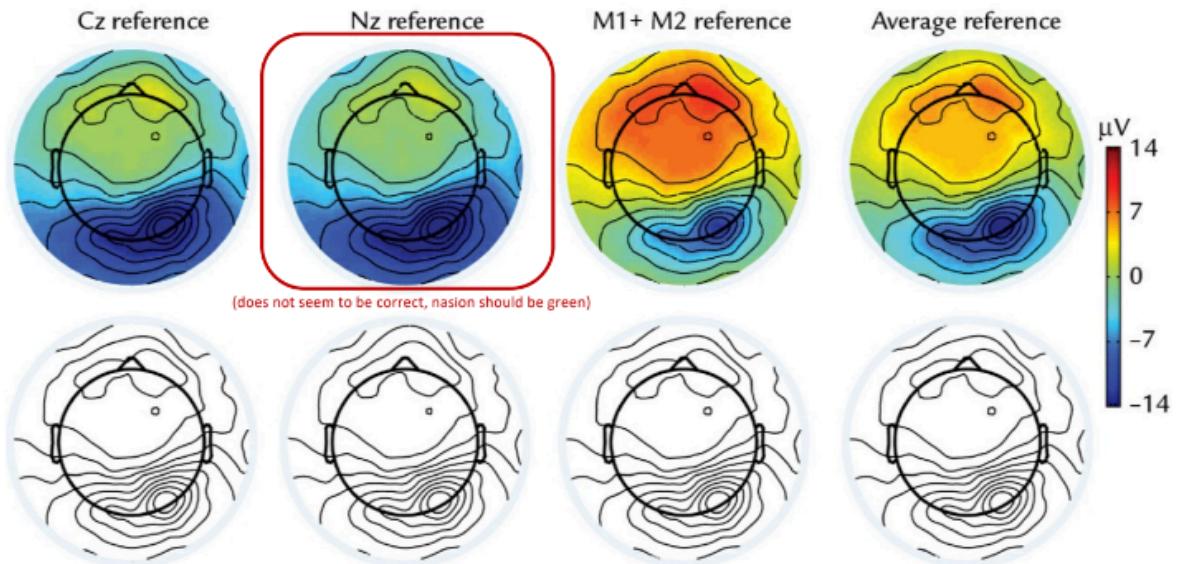
True statements 1.03 EEG

I just consider the last four, since the others are equal to the 1.02 EEG true statements:

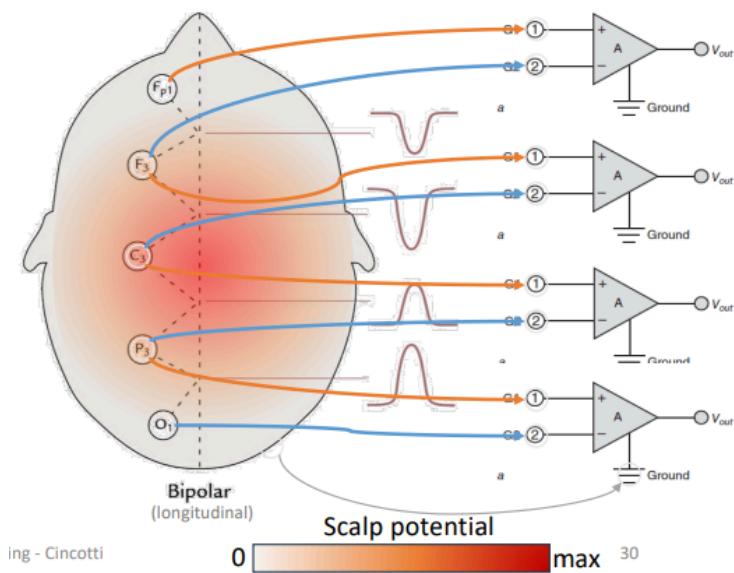
1. In monopolar EEG recordings, a single reference potential is used for all recorded channels. The reference electrode is placed on scalp position that are assumed to be far from the electrical sources of interest, such as the earlobes



2. The position of the reference electrode can strongly influence the shape and amplitude of EEG potentials. The profile (i.e. disregarding the actual potential value) of scalp topographies are not influenced.



3. In bipolar EEG recordings, each channel is the difference of potential between two adjacent electrodes. It is mostly used in clinical settings, to highlight features of interest at visual inspection of the waveforms.



4. EEG signals recorded in monopolar configuration can be re-referenced to the CAR, by subtracting from each channel the instantaneous average of all channels. In ideal conditions, this would approximate taking the reference potential at infinity

Bo non l'ho capito benissimo

Data Collection:

Let's see some good practices to follow during an EEG recording session.

General Principles of Good Experimentation:

- Since the signal measured for acquiring EEG are very small, it is important to record the data from alert and cooperative subjects in as artifact¹¹-free and noise-free conditions as possible.
- Maintaining the subject a good practice is to divide the recording session to smaller runs (blocks).
- Monitor the brain signals continually for any artifacts or technical issues
- Remind subjects about relaxing their muscles, minimizing blinking and avoiding head and body movements.

Electrodes Preparation:

- The first thing to do is to ask subjects to wash their hair and skin prior to arriving for the EEG study and to not apply any cosmetic products on the skin
- Skin preparation and electrode application: a blunted needle/syringe is used to insert a conductive gel in the electrode

¹¹ Artifacts are signals that are not related to the EEG. So we want to reduce them as much as possible.

- The blunted needle allows light scalp skin abrasion to be performed, if needed
- After skin preparation, impedances of less than 5-10 komh can be easily obtained

Electrode-impedance measurement: the electrodes impedance must be as low as possible and very similar between them (symmetry). We need to use AC.

Planning and Logging: scientific experiments have strict protocol.

- Plan your recording
- Log the conditions occurring in each run. For instance, if there are issues with some electrodes
- Possibly save metadata (e.g. time markers)

Artifacts:

An artifact in EEG is any potential difference due to an extracerebral source. They can have:

1. Technical origin (non-physiological), e.g. power supply, noise from electrical engines, bad electrode contact...
2. Biological origin (physiological):
 - a. eye-related artifacts (blinks and eye movements)
 - b. muscle artifacts
 - c. cardiac artifacts
 - d. sweating artifacts
 - e. ...

We know that the EEG has an amplitude in the order of tens of microvolts, while, as you can see from the picture below:

BODY PART	SIGNAL TYPE	FREQUENCY CONTENT	AMPLITUDE
Brain	Electroencephalogram (EEG)	0.5–75 Hz	50–100 µV
Heart	Electrocardiogram (ECG)	0.5–100 Hz	1 mV
Muscle	Electromyogram (EMG)	10–5000 Hz	0.3–1 mV
Eyes	Electro-oculogram (EOG)	Variable (slow)	0.5–1 mV

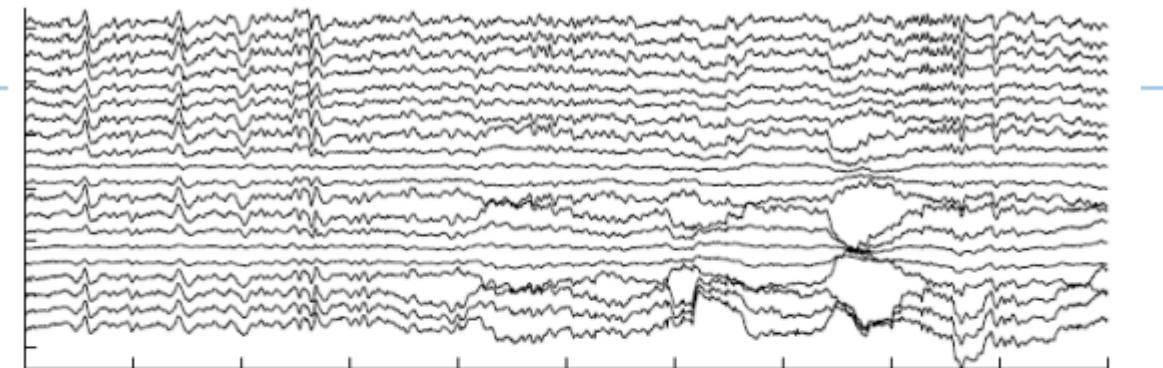
heart, muscles and eyes signals are in the order of millivolts, so they are bigger and their amplitude can overcome the amplitude of the signal of interest.

3. There is a third way of generating artifacts: if you move the electrode (or the subject) during a recording, you disturb the ions double layer on the electrode surface, creating potential shifts

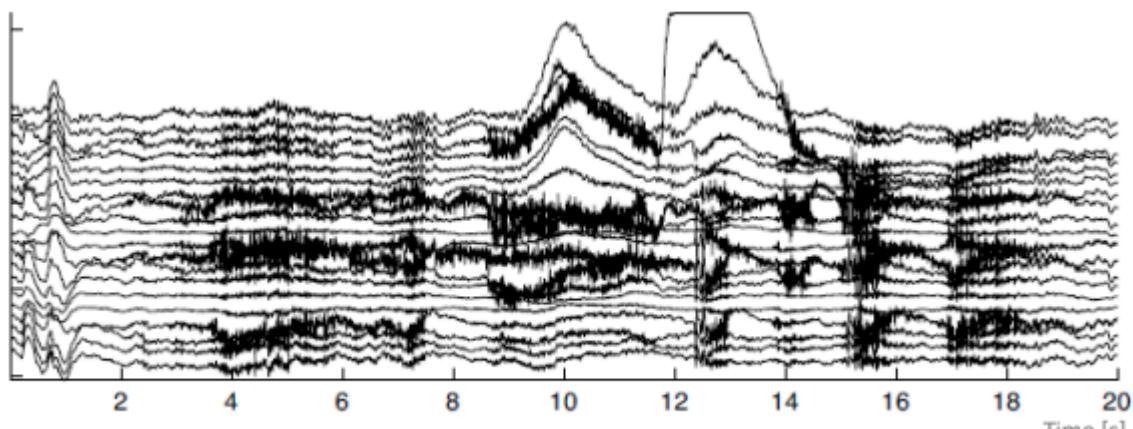
They are recorded together with the data and make it difficult to read the EEG data. So in the first place we should avoid the generation of them, but we can at least partially remove some of them in **post-processing**. For instance, if we are not able to record artifacts, we can try to apply high-pass or low-pass filters to remove them. However, sometimes there is overlap between the bands of the signal of interest and the artifacts, so we can't filter out the artifact. Other things we can do are to reject time intervals in which artifacts happen or not

consider some electrodes (e.g. electrodes near the jaw have artifacts related to the jaw muscles activity which could be not the fault of the subject).

Let's see an example. Consider this EEG recording:



it doesn't contain any artifacts, so it's desirable. On the other hand, if this recording had artifacts:



Eye-Related Artifacts:

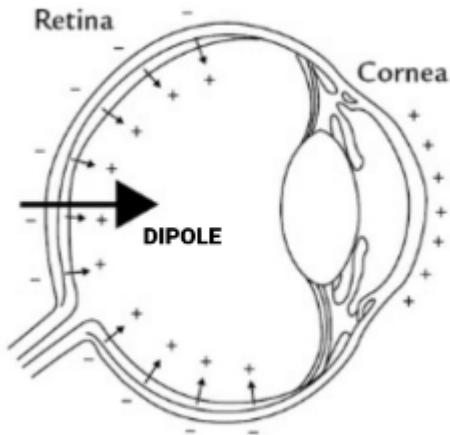
Eyes

Electro-oculogram (EOG)

Variable (slow)

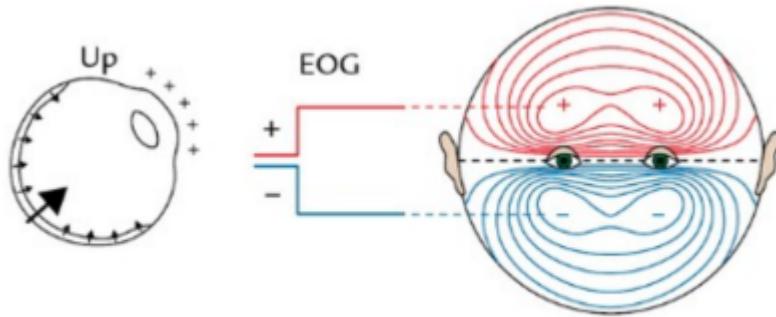
0.5–1 mV

They last 200-400 ms. So if you see a signal that is about 100 times bigger than the EEG it is likely to be an eye-related artifact (ofo it must have the right shape)

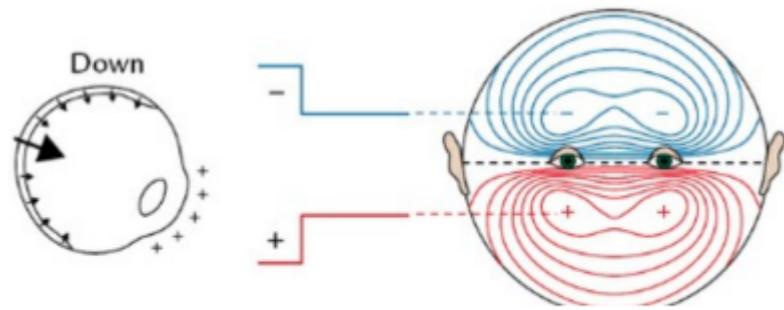


The retina is the photosensitive part of the eye. We can model the eye as an electrical dipole: the cornea is positively charged w.r.t. the back of the eyeball. That means that in our model we have a generator that creates current going from the retina to the cornea. Since ions current propagates and we can see that from a distance, we don't need to place electrodes directly on the cornea and retina, but we can put them in other parts of the head, e.g. forehead and cheekbones. We know that with electrodes we are able to measure only variations of the potential, since constant signals are DC and electrodes can't record it. So that means that a still eye doesn't affect the recording and we don't care where the eyes are (maybe they form a 20° angle with the horizontal x axis) since after a transient they have 0 potential (so as they were at 0° with the horizontal x axis). We receive information only when the subject moves the eyes or blinks.

- Eye movement. Consider a subject with electrodes put above and below the eyes (e.g. on the forehead and on the cheeks). Let's first see vertical eye movement:
 - a. If the eye moves upwards, the potential on the forehead is more positive while the potential on the bottom part of the head is more negative. This is because we are moving the generator up, from a position in which the generation was horizontal

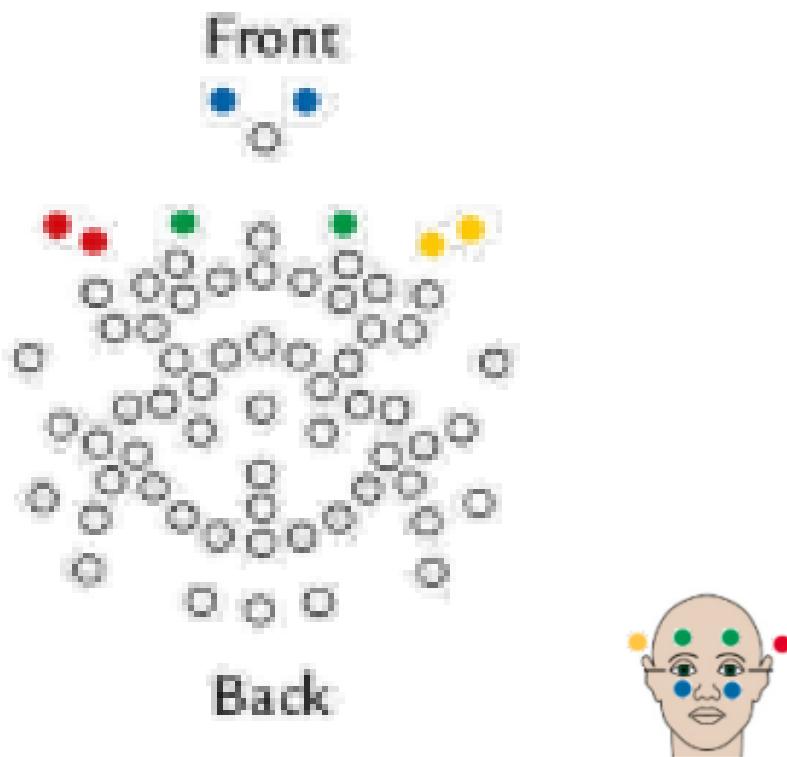


- b. If the eye moves upwards, the potential on the forehead is more negative while the potential on the bottom part of the head is more positive. This is because we are moving the generator down, from a position in which the generation was horizontal

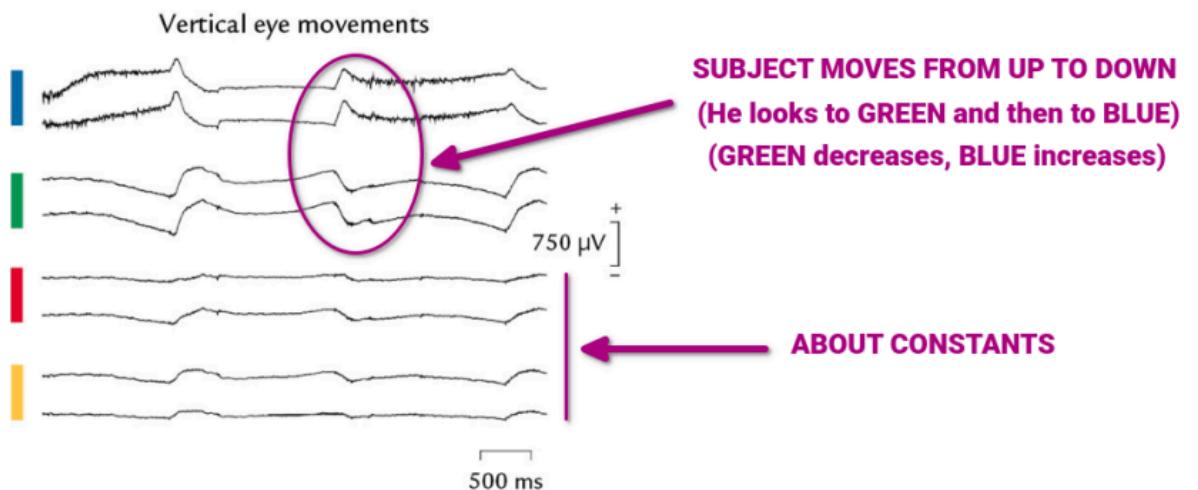


A analogous discussion can be done for horizontal eye movements, namely when the current generator moves right or left.

Let's consider this example:



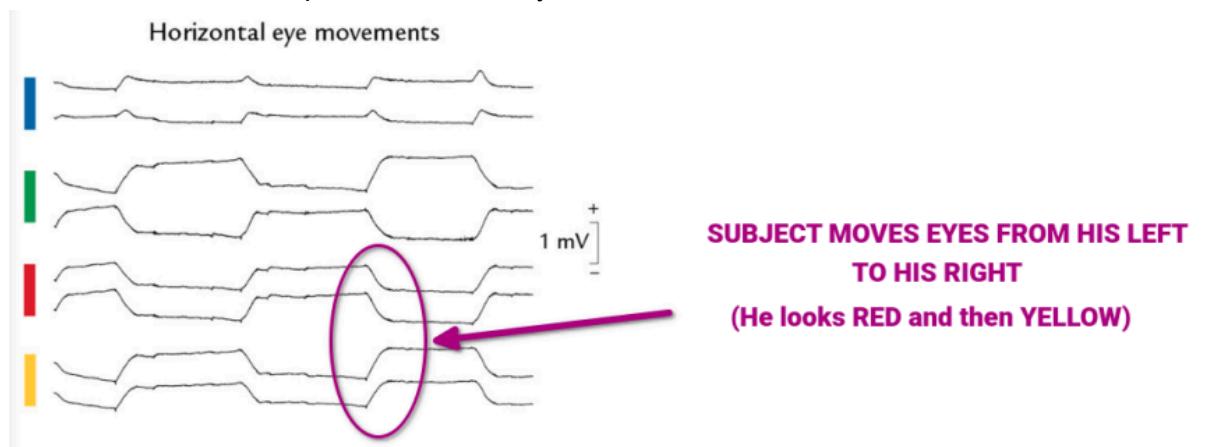
The blue electrodes are placed on the cheekbones, while the green ones are on the forehead and the red and yellow are on the sides. This above is the EEG recorded on this electrode when the subject performs a vertical eye movement:



While red and yellow curves have no relevant variation, blue and green electrodes see, respectively, a decrease and an increase in the potential.

The reason for noise at the start and at the end of the blue curves will be more clear when we talk about another topic later on

Let's see now an example of horizontal eye movement:



Red is going up while yellow is going down. Since red is on the left that means that the eyes are going to the left. Let's analyze the green, now that we know what the eyes are doing. If you look left, since you have two eyes, both the right and left eye are moving to the left. The electrode that is above the right eye doesn't feel any change, But when the left eye moves left the region becomes more positive. This is the right electrode:

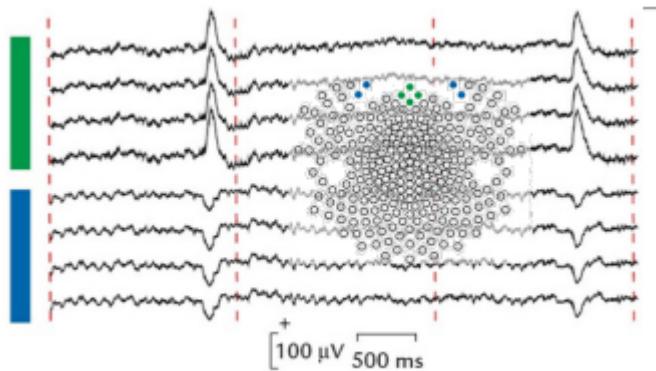


The same holds for the other electrode. The bottom trace is the left electrode



Why don't we have the same thing for the blue electrodes? It might depend on several factors, maybe the two electrodes are too close.

- Eye blinks: when the subject blinks it is putting a conductor near the eyes, so it is short circuiting the path between the cornea and - for instance, assuming there are two electrodes on it - the forehead.



This above is a blink artifact, with the green electrodes placed on the forehead and the blue ones placed on the cheekbones. As is visible, with the blink an increase of potential lasting a few milliseconds is present on the green electrodes, that are above the eyes. On the cheekbones you see a decrease in the potential.

So that means that when you close your eyes you obtain the same effects as moving the eyes up.

Where is the reference electrode? We don't know and we don't care since after a transient we have only DC for that information and due to the instrumentation DC doesn't pass.

What happens when the subject keeps their eyes closed¹²? You will have a brief positive potential, and then you will see the behavior of the instrumentation: will return to the baseline, as if the subject blinks, but not as fast as it. NOT SURE ABOUT IT

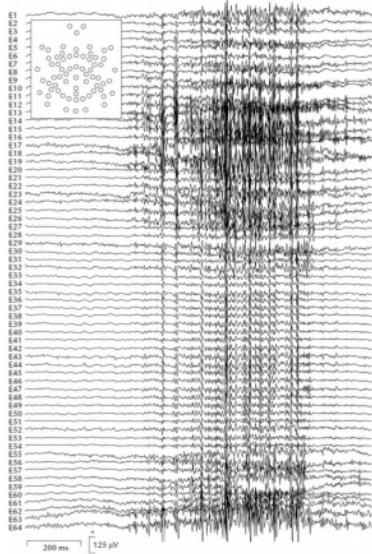
Muscle Artifacts:

Muscle	Electromyogram (EMG)	10–5000 Hz	0.3–1 mV
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The amplitude is comparable or 1 order above the EEG. That's not true: using [this scale](#) and considering that the muscle artifact signal amplitude is similar to the eyes one. The frequency is higher than the EEG. The bandwidth overlaps with the EEG Gamma band, so you must be sure there are no muscle artifacts if you are interested in this band. So no muscles of the head must be contracted during the recording. This is a problem since most of the time we are contracting muscles to keep a posture¹³. For instance, this image below could represent an EEG during a swallow of the subject

¹² So it's not blinking, which means closing and reopening the eyes.

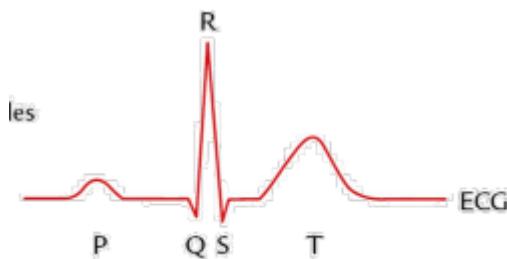
¹³ For instance the jaw muscles are used to keep the teeth closed. Also forehead, neck...



Cardiac Artifacts:

We have two different types of them.

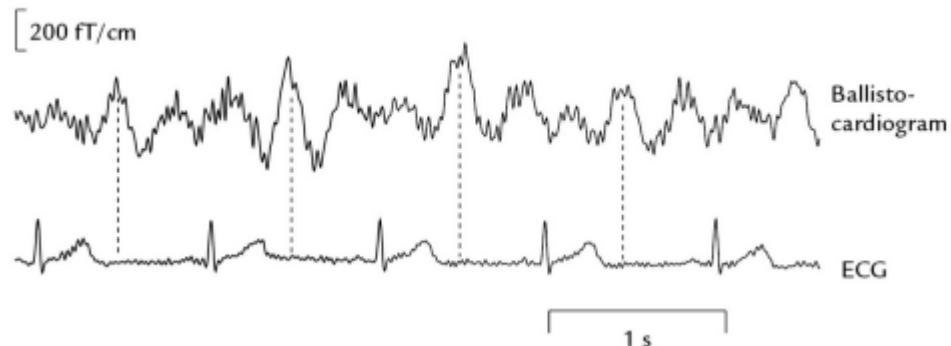
1. Heart Electrical Potential. We can record the electric potentials generated by the heart with an electrocardiogram (ECG or EKG).



The peak happens when the heart is contracting the ventricles, and it's a large artifact. However, these artifacts are not a real issue: when a cardiologist wants to record an ECG signal, they put electrodes on the two sides of the heart to see its potential variation. In our case however, since we are doing an EEG and we are putting electrodes in a way that they are both seeing the same heart potential, the heart potential difference is not visible. This type of artifacts can be a problem if the instrumentation is sensible to the Common Part, since in this case the ECG will be visible.

2. Ballistocardiogram: when an electrode is placed close to a blood vessel, it will move due to the mechanical activity of the heart. If the electrode moves, the double layer of

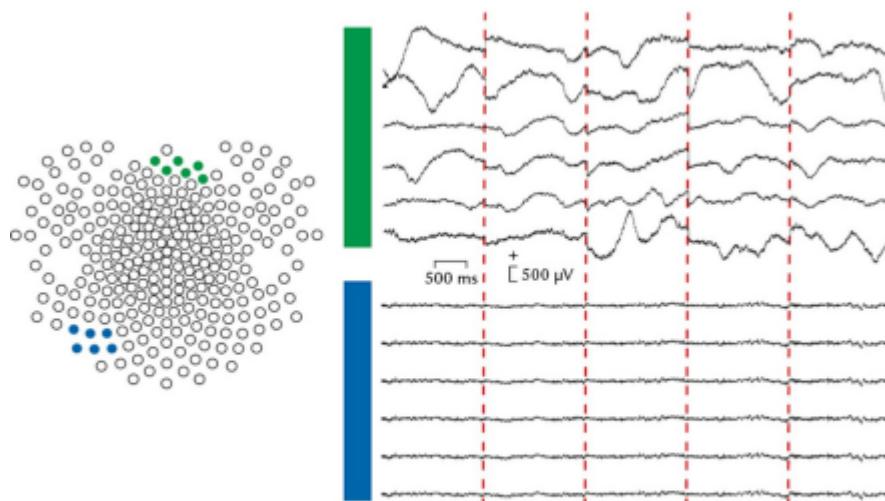
charges will move and that creates artifacts on the EEG. However, this artifact is not common and you just need to move the electrodes a bit to solve it.



fT stands for femtoTesla (ok but what is this about?)

So, when doing an EEG, we can detect heart artifacts by recording the ECG on a different channel, so to use it as a reference signal to see the correlation between the pulse of the heart and the EEG. If you see some correlation between the pulse in the ECG and peaks in the EEG (is it right? should I compare ECG with EEG?), like the one depicted in the picture above, in which you see that, starting from an ECG pulse, after a certain delay, you always have a peak in the EEG (OR IS **BALLISTO-CARDIOGRAM MEANING ANOTHER PLOT?**), it may be the case of heart artifacts in the EEG recording. By the way, the delay between the heart pulse and the peak in the **EEG/Ballisto-cardiogram** is due to the fact that it takes time for the blood to go from the heart to the head.

Sweating: sweating is accompanied by electrodermal responses with high-amplitude and low-frequency (slow, < 0.5 Hz, up to a few mV) potentials. In fact, when you sweat you are changing the resistivity of your skin¹⁴. Of course, if you are interested in the high-frequency EEG you can disregard this since it is slow and you filter it away with a high-pass filter.



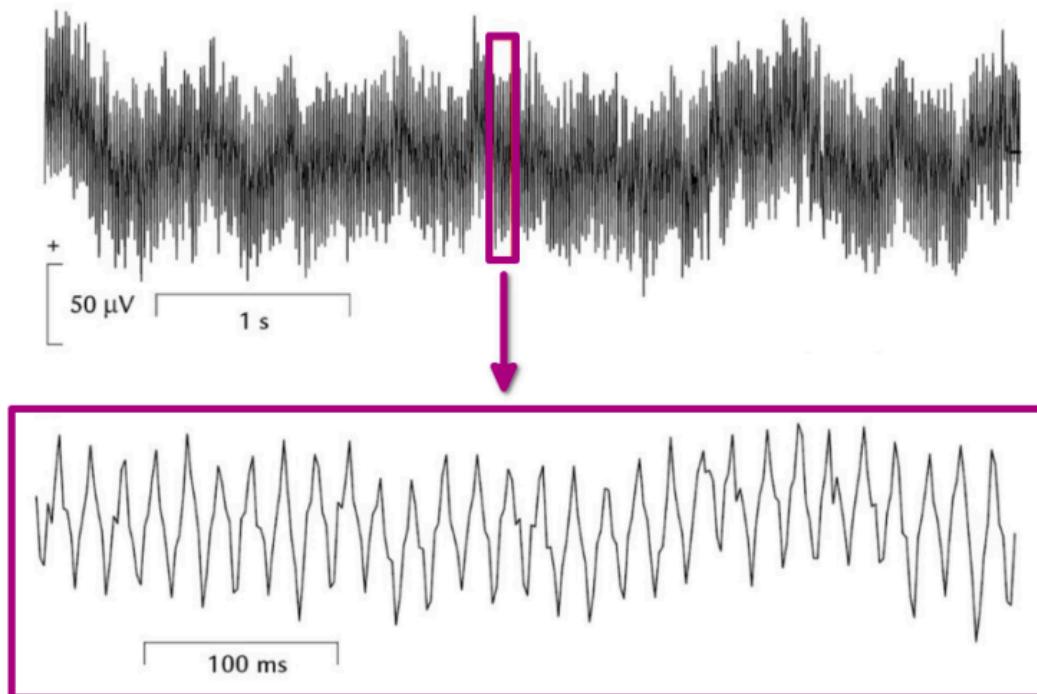
Neuroengineering - Cincotti

¹⁴ I think truth machines leverage on this

Note that in this case, the red bars represent epochs, in fact there is discontinuity between the portions of the plots.

Powerline Artifacts:

Let's now see artifacts with technical origins. The first one is Line Noise (Power-line) and arises from the capacitive coupling of alternating current supplied to electrical wall outlets. It occurs at 50/60 Hz and at their harmonics. Since sine waves have only one harmonic, it means that this signal is not necessarily a sine wave in the time domain. Electrode pairs that have a low CMRR (impedance mismatch), will have more accentuated powerline artifacts. So if you have low impedance on all the electrodes you reduce this artifact. Moreover, a digital notch filter can be used to remove this artifact, setting it at 50/60 Hz and at the signal harmonics if necessary.

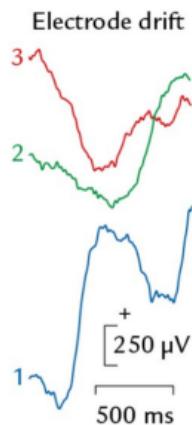


How to detect this artifact in an EEG recording? You can just zoom in and count waves. Since it is at 50/60 Hz, in 100 ms it must have 5 or 6 waves.

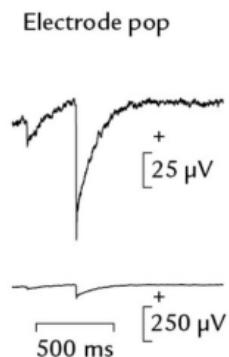
Electrode-Related Artifacts:

We can have:

1. Electrode drift artifacts. In the case above the blue channels indicates that the subject is sweating SO THIS IS A BIOLOGICAL ARTIFACT? WHAT IS THE POINT?



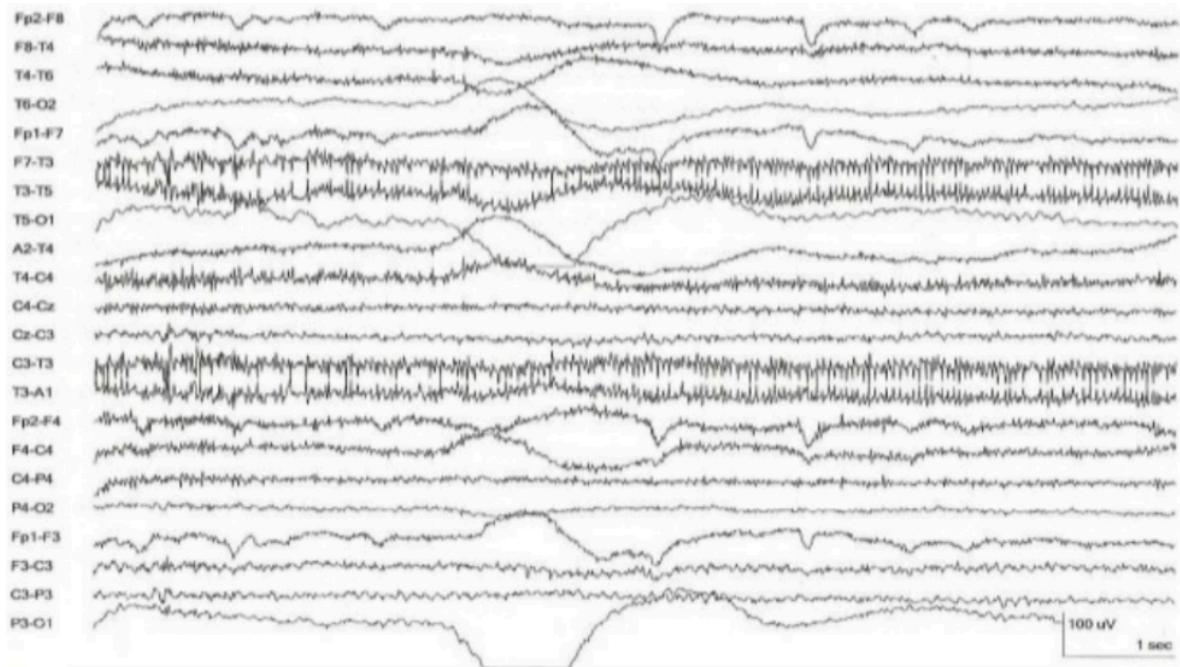
2. Electrode pop artifacts: accumulation of charges that eventually pop. A cause can be that the subject is wearing synthetic garments



Moreover, the experimenter's movements around the subject can create artifacts, especially in dry air environments creating a problem with static electricity IS THIS A THIRD CATEGORY OF ELECTRODE-RELATED ARTIFACTS OR IT IS IN ONE OF THE TWO CATEGORIES?

Movement artifacts:

We know that at the interface between the electrode and the ionic gel there is a double layer of ions that behave like a capacitor. If the electrodes are moved this double layer geometry is disturbed, producing a strong potential:

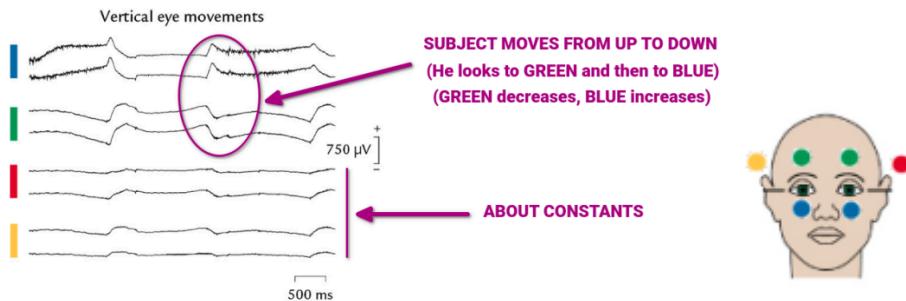


True Statements EEG 1.03 and 1.04

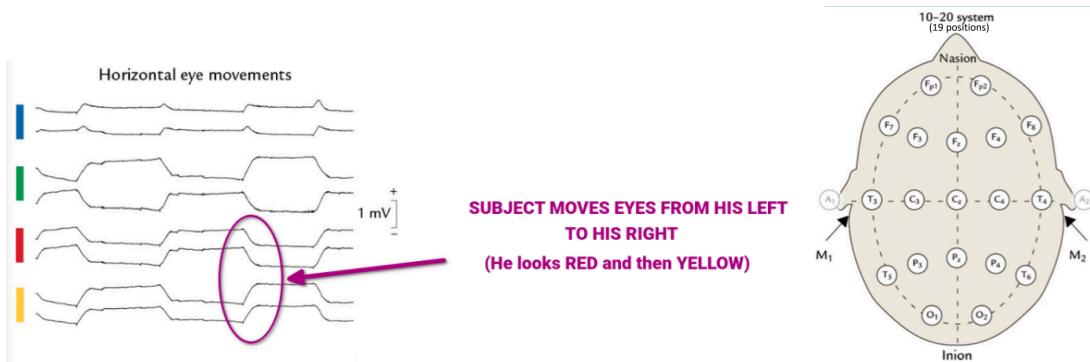
1. An EEG artifact is a potential difference due to sources outside the brain. Yes, from an extracerebral source
2. Artifacts can have biological origin (such as eyes, muscles, heart), can be due to external electromagnetic generators (power supply, engines, etc.) or to events affecting the recording setup (electrode movements or loss of contact, saturation of the ADC). Yes, these are the three origins we saw: technical, biological and body/head movements
3. Artifacts can be partially attenuated or removed through signal processing during data analysis, but it is always preferable to make all efforts to prevent them when the signal is being acquired
4. The eye is more positive in its frontal part (cornea) than its posterior part (retina), and thus its movements can generate large artifacts (EOG) on the EEG (of the order of 500 µV)
5. During an eyeblink, the eyelid shorts out the positive potential of the external surface of the eye, causing positive deflections of the EEG with amplitude of several

hundreds of microvolts and duration of a few hundreds of milliseconds. Yes, hundreds of microvolts and duration of a few hundreds of milliseconds since these are the specs of an eye-related artifact.

- A sudden upwards/downwards movement of the eyes generates a positive/negative deflection of EEG potentials (EOG) on frontal EEG channels, respectively.



- A sudden movement of the eyes to the right/left generates a positive/negative deflection of EEG potentials (EOG) on the EEG channel F8, respectively.



Yes, since F8 is on the right.

- The electrical activity of the muscles (EMG) has a spectral content starting at frequencies of 20 Hz and up, thus affecting the beta and gamma bands of the EEG signal.

Actually it starts at 10 Hz, but it's the same

Muscle	Electromyogram (EMG)	10–5000 Hz	0.3–1 mV
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Yes, it affects EEG beta and gamma bands

- Beta:** 14–30
- Gamma:** > 30 Hz

- The amplitude of the electromyogram (EMG) originated from muscles in the head can have amplitude ten times higher than the spontaneous EEG signal (thus in the order of 1 mV). Well yes, actually even more: if you consider $5 \times 10^{-5} \text{ V}$ ($50 \mu\text{V}$) for a brain signal and 10^{-3} V for a muscle signal (1 mV) you have a difference in order of magnitude of $10^2 = 100$

Brain	Electroencephalogram (EEG)	0.5–75 Hz	50–100 µV
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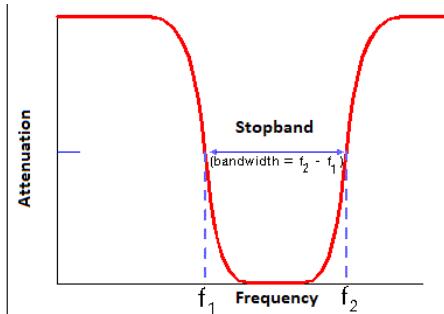
Muscle	Electromyogram (EMG)	10–5000 Hz	0.3–1 mV
--------	----------------------	------------	----------

10. EMG artifacts can easily appear on the EEG recording unless the subjects are specifically instructed by the experimenter on how to relax their face and tongue/throat muscles.
11. The heart activity can contaminate an EEG recording because an electrocardiographic (ECG/EKG) artifact can directly affect the potentials, especially if the reference electrode is not placed on the head.
12. The heart activity can contaminate an EEG recording because a ballistocardiographic artifact is indirectly generated by the pulse of a blood vessel causing movements of a nearby electrode
13. Sweating can affect the EEG, causing a slow changing and high amplitude artifact (below 0.5 Hz, up to a few mV)
14. Powerline noise is an artifact caused by the capacitive coupling between (i) the conductors carrying the alternating (typically at 50Hz) current power supply and (ii) the recording setup including the subject
15. The powerline noise affects a very narrow frequency band of the recorded signal around 50 Hz (or 60 Hz, depending on the powerline frequency). Other frequency bands can be affected at multiple frequencies that **are** multiple (typically odd multiples) of 50/60Hz.

I don't know, is this meant to refer to the harmonics? If so, can we conclude that the harmonics of the powerline signal are typically ad odd multiples of 50/60 Hz, which is the fundamental frequency?

Moreover, a guy on the whatsapp group said that odd harmonics does not cancel themselves out while even ones do

16. Powerline noise is accentuated by asymmetries in the recording electrode pairs, such as impedances and cable path, because asymmetries prevent the noise to be rejected by the amplifier's common-mode rejection capabilities.
17. Notch filters effectively remove powerline noise because they selectively reject the narrow band affected by the artifact, preserving almost entirely the useful signal.



18. Movement of the subject's head may produce **slow** (so they are slow?) artifacts on the EEG recording, whose waveform is closely related to the time course of the movement. Since the potentials originate from the mechanical displacement of the charged double layer at the electrodes interface, these artifacts are less pronounced when non-polarizable

WHY NON-POLARIZABLE (E.G. AG/AGCL) MEANS THAT THESE ARTIFACTS ARE LESS PRONOUNCED?

EEG Analysis

20/03/2024

Until now we have talked about continuous analysis of the EEG, now we will talk about trial-based analysis. Assuming we have acquired the data, now we can look at them and then do analysis. EEG data are collected in experiments using multiple trials per condition. In this way the signal, which may be quite small, can be seen better. Note that we are assuming that the signal remains the same during the whole experiment although it is masked by noise.

Off-line data inspection:

Review raw data before processing and analysis:

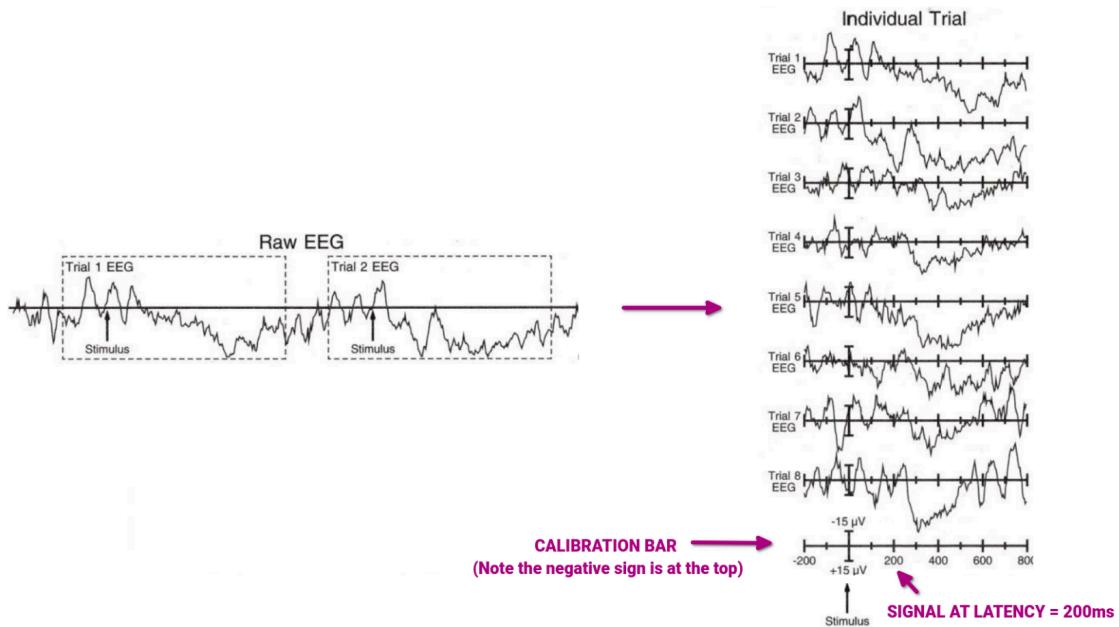
1. Bad EEG segments or channels must be removed
2. Understand which artifacts mostly affect the analysis, so that we don't waste data by rejecting too much of it (what does this last sentence mean? Maybe that if an artifact doesn't affect much the analysis we can keep the segments and channels in which it's present so we don't remove useful data)

Types of EEG Analysis:

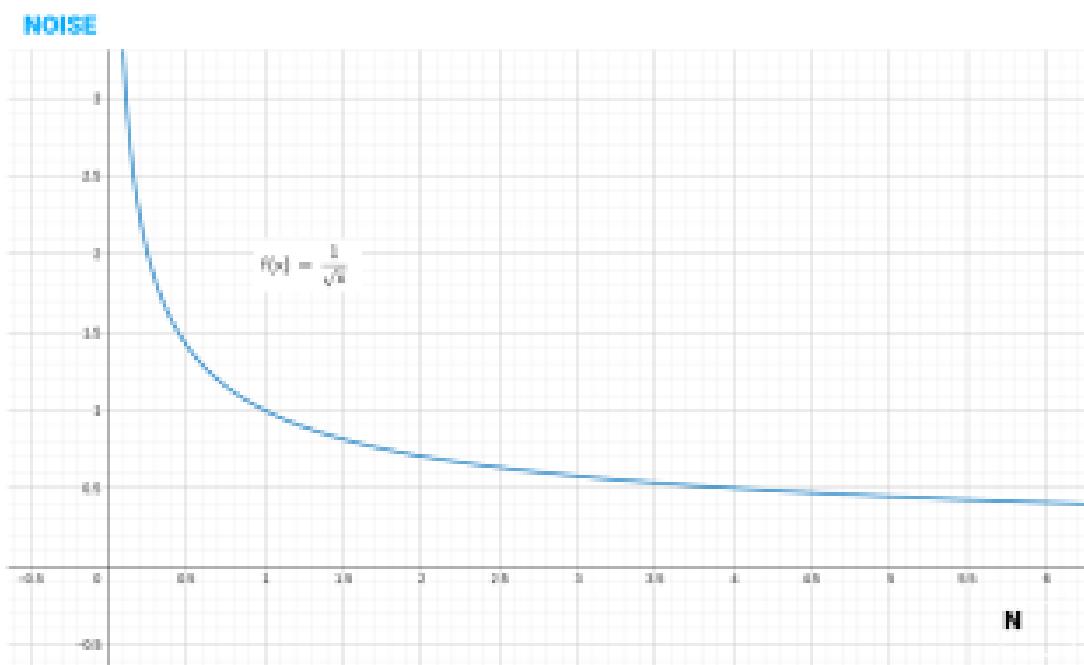
- Analysis EP EEG: EEG recordings during external stimulation
- Analysis Spontaneous EEG: EEG recordings without external stimulation

Analysis EP EEG: Synchronized Averaging:

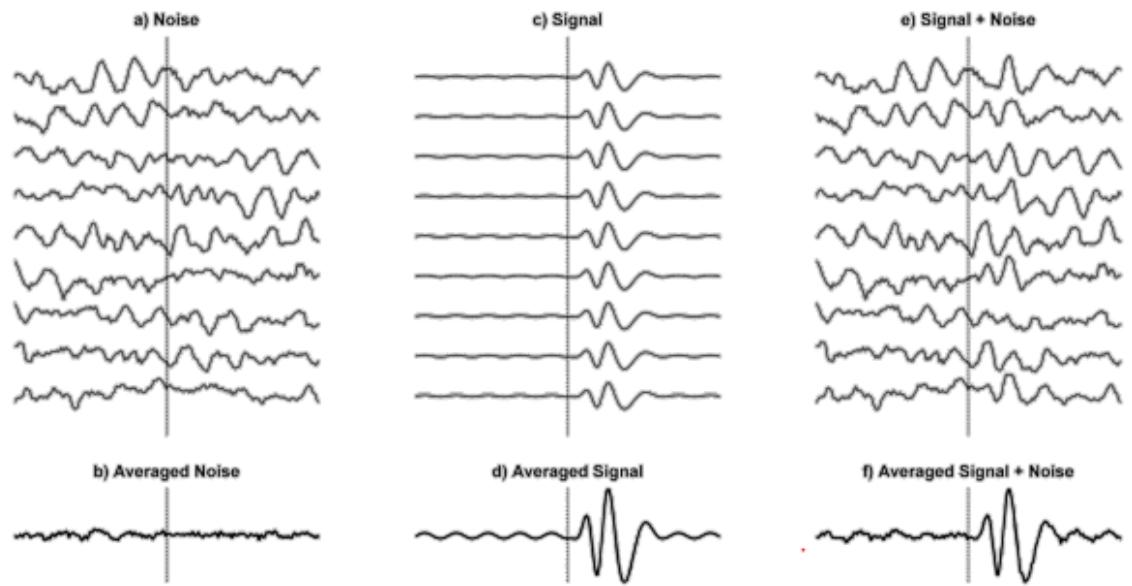
1. Segmentation: After EEG recording, we are left with a continuous recording that must be cut up into segments (or epoch). Each segment has a pre-stimulus (or pre-event) period, followed by the activity of interest.



2. Averaging: consider $x(t)$ (the entire EEG). There exists a noise function $f(x)$, for instance:



RIVEDI STA PARTE NON SONO SICURO

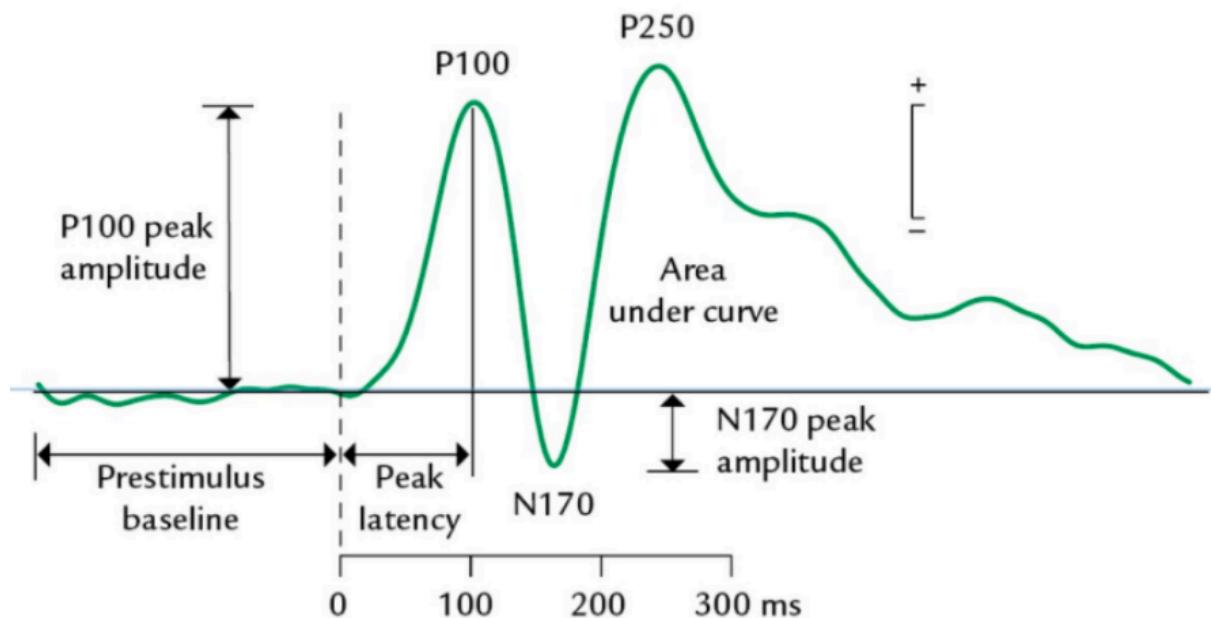


For this to work, we have to assume that the EP is superimposed upon, and independent of, the background EEG. Namely, we are assuming that $x(t)$ comprises a distinct signal embedded in noise. You see that if you average the noise you get a function with low amplitude. If you average the EP you get a function with low amplitude except for the point in which the EP is present, so if you average the sum of the noise and the EP (namely, the EEG recording), you can see clearly where the EP is happening.

Nomenclature of ERP components and Standard Times:

We want to measure:

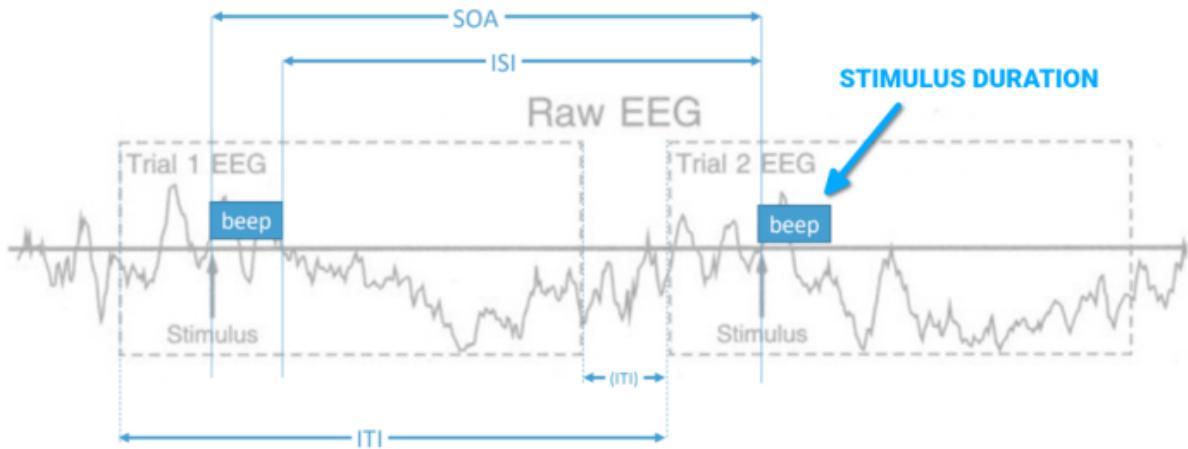
- Peak amplitudes w.r.t pre-stimulus baseline
- Latency w.r.t stimulus onset or motor event



In the literature, the nomenclature is diverse and confusing. An old naming convention numbered successive deflections separately for polarities (P for scalp-positive and N for scalp-negative) with an incremental number and possibly letters added. A less ambiguous way: combine the polarity (N or P) of the response peak with the nominal peak latency¹⁵ in milliseconds, as shown in the photo above.

Now let's see some standard time quantities:

- SOA (Stimulus Onset Asynchrony): the time between two successive stimulus onsets
- ISI (Interstimulus Interval): the time between the offset of one stimulus and the onset of another
- ITI (Intertrial Interval): the time between the beginning of subsequent trials, during which multiple stimuli may be presented. Note that some authors define the ITI as the pause between the end of a trial and the beginning of the next one.



It's clear that we have the following relationship:

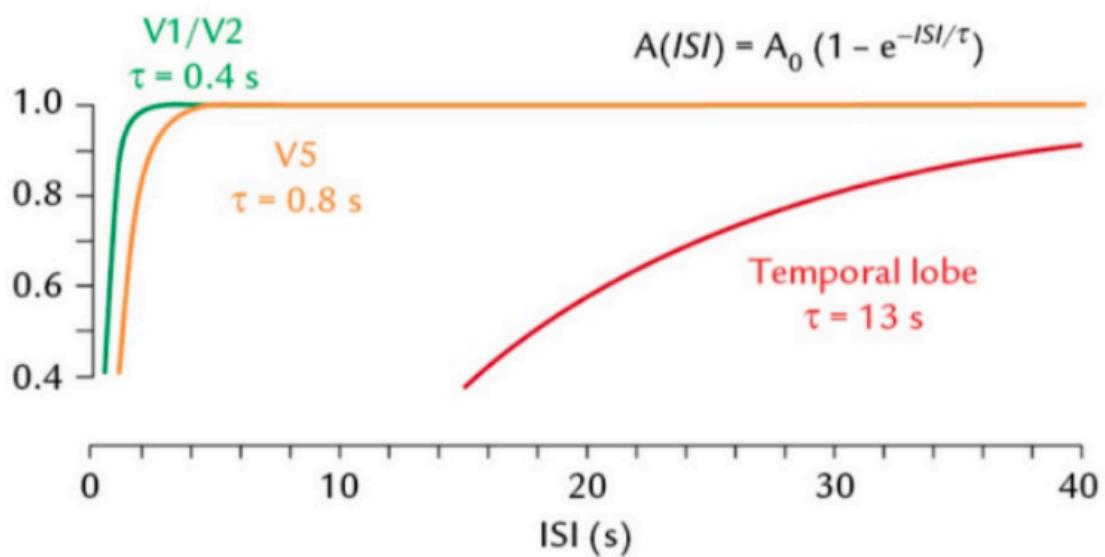
$$ISI = (SOA - \text{stimulus duration})$$

Effect of stimulus timing (Tradeoff between N and SOA):

The shape and amplitude of the ERP depend on the timing of stimuli. The longer the latency the more sensitive the response is to stimulus repetition rate. In other words, for long-latency components of the ERP the brain tends to respond less strongly to the same stimulus repeated several times in a short interval, namely when the SOA is too short. Since we want to reduce the overall time of the EEG recording, we can't do a too high number N of stimuli or the response to them will be less sensitive, although the more stimuli we do the better, since the noise decreases with N (on the slides is written \sqrt{N} , shouldn't it be $1/\sqrt{N}$?). So we have a tradeoff between the number N of stimuli and the SOA, since:

$$\text{Total Time of EEG recording} = N * \text{SOA}$$

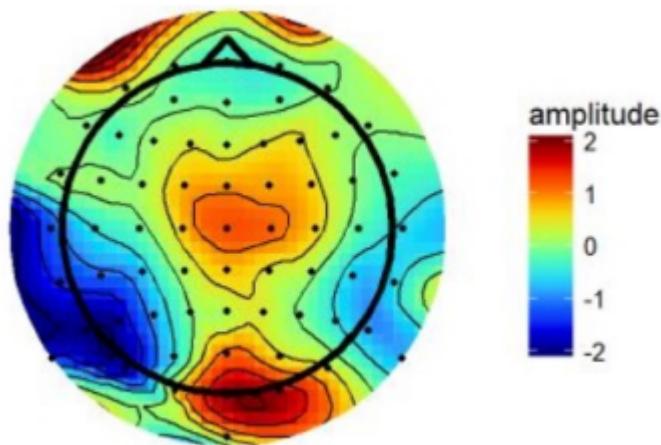
¹⁵ We use the approximate (nominal) latency and not the measured individual latency. That means that the mean peak latency of N100 may vary between, say, 90 and 110 ms. **IF I UNDERSTOOD CORRECTLY IT'S SAYING THAT WE ARE USING THE LATENCY AVERAGED ON THE DIFFERENT TRIALS, WHILE THE LATENCY OF EACH INDIVIDUAL TRIAL MAY NOT BE 100ms (CHECK TRUE STATEMENTS)**



I don't know what is this image representing

Mapping:

We can see ERPs in a topographic scalp voltage map. These maps depict interpolated voltages between the electrode locations at any time point, so if we display them at times of response peaks and troughs we can see the amplitude of the ERP.



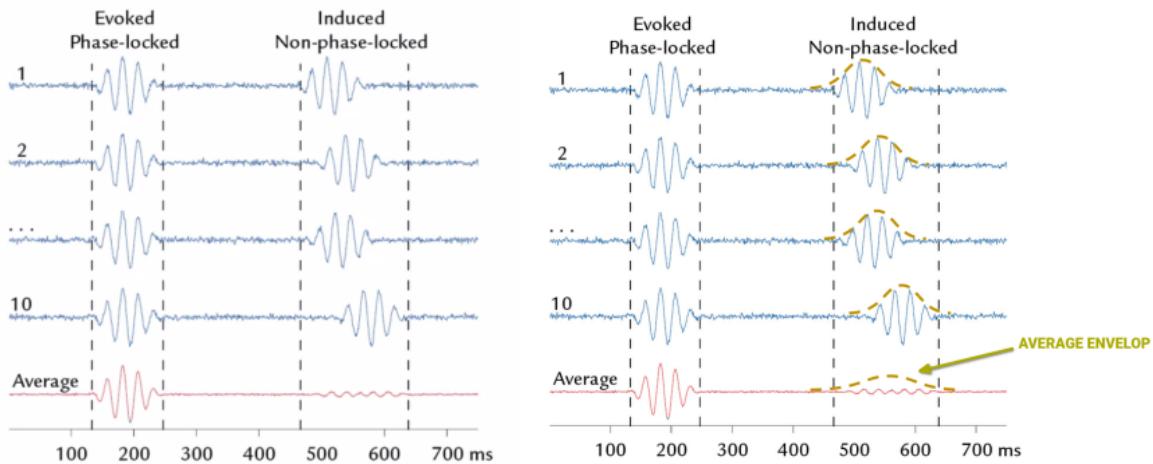
Analysis Spontaneous EEG:

Now let's see the second type of EEG analysis we can do. Here we are interested in studying the EEG response after an internal stimulus.

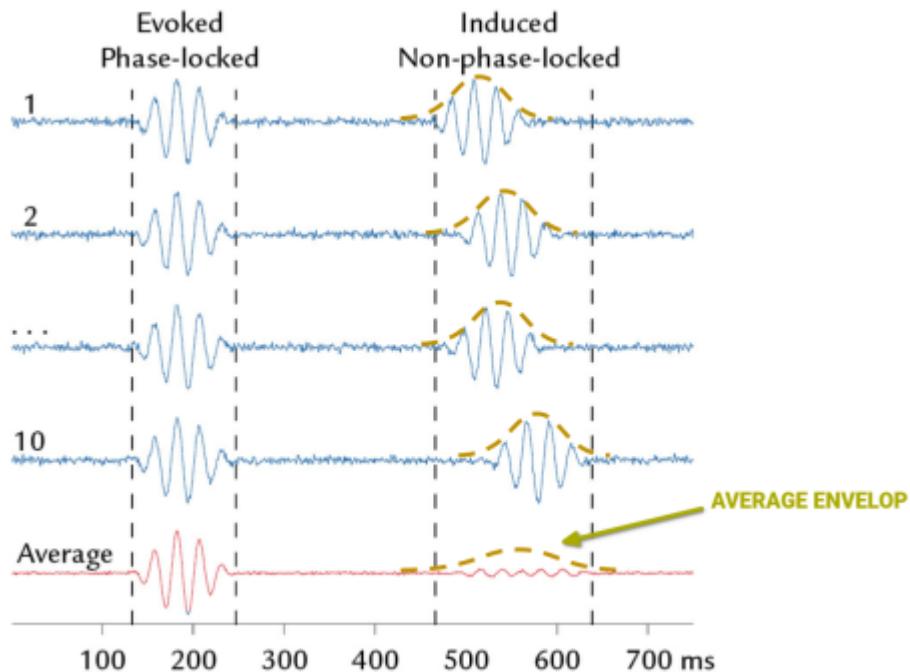
Non-Phase locked response:

Differently from the external stimulus, in internal stimulus the time between the stimulus delivery and the EEG signal response it's not always the same, so the response is called non-phase response, while the time quantity that passes from the stimulus delivery to the response is called jitter.

We know that time-locked¹⁶ (phase-locked) activity, in response to the stimulus, can be uncovered from the whole EEG recording by synchronized averaging. In this case, we can't apply this technique due to jitter. To have a proof of this:



So you can see that the final non-phase response average is so low that it will be lost behind the spontaneous (ongoing) EEG activity. An idea may be to align the responses of each trial, but is not so easy in practice. A more simple technique is to compute the average envelope:



We call:

- A negative envelope ERD (Event Related Desynchronization): is a negative variation of the EEG power w.r.t. a baseline period

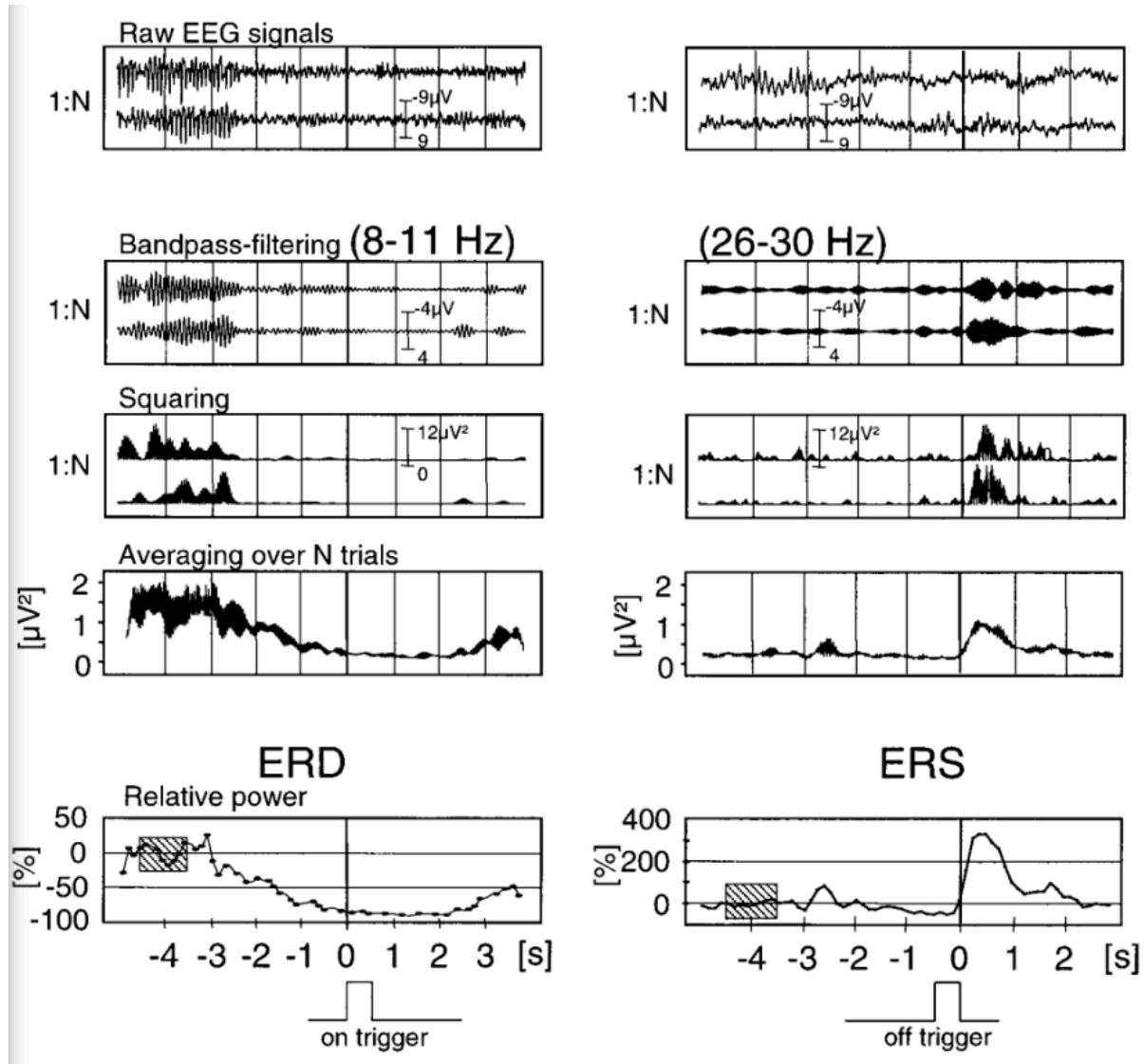
¹⁶ reminder: time-locked means that the same response follows with the same delay the stimulus

- A positive envelope ERS (Event Related Synchronization): is a negative variation of the EEG power w.r.t. a baseline period

How to obtain ERD and ERS from N raw EEG trials:

1. Bandpass filtering of all event-related trials
2. Squaring of the amplitude samples to obtain [power](#) samples
3. Averaging of power samples across all trials
4. Averaging over time samples to smooth the data and reduce the variability

At the end you have a percentage variation of the signal power w.r.t. to the baseline. Let's see two examples:

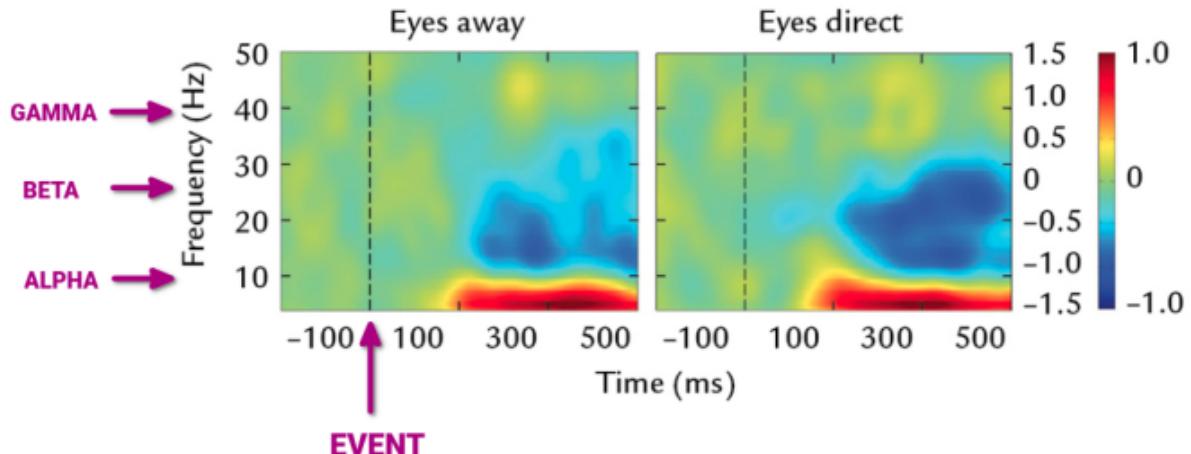


The dominant ERD is in the alpha band. Precisely, we are interested in the mu rhythm, indeed the shown stimulus corresponds to a finger movement by the subject. The dominant ERS on the right side is in the beta band.

Note that the recording is started several seconds before the stimulus, since we have to detect the baseline signal to then obtain ERD and ERS. The baseline is “faraway” from the stimulus since the brain prepares in advance to perform a task, e.g. move the finger, since it's a voluntary movement.

Time-Frequency EEG Analysis

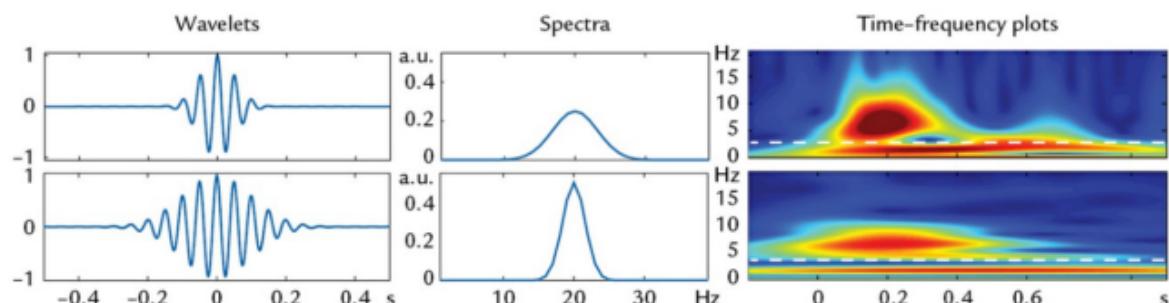
We can compute and visualize the spectral and the amplitude content of the signal as a function of time. Using Fourier transform, Hilbert transforms and wavelet-based approaches we can visualize features in MEG/EEG data in both time and frequency.



This above is a time-frequency plot, showing frequency of the EEG signals during a visual task with two conditions: face gazing away (eyes away) and at the subject (eyes direct). The horizontal axis is, as indicated, time, while the vertical axis is frequency and the vertical color scale indicates power in dB. It is visible that the two conditions show very similar profiles of activity: a prolonged increase in theta and alpha activity and decrease in beta activity.

Time-Frequency Resolution Trade-Off (Indetermination Principle):

Improving time resolution worsens spectral resolution and vice versa



Which of the two is the high-time/low-frequency resolution?

True statements EEG 1.04

1. As a preliminary step to EEG data analysis, the following data can be discarded
 - one or more channels, if it is extensively contaminated by artifacts
 - all time intervals (epochs) in which artifacts appearBoth strategies can be applied on the same dataset.
2. The estimation of event-related or evoked potentials (ERPs, EPs) requires the acquisition of numerous repetitions (typically tens or hundreds) of the stimulus or event which evoked or induced the potential

3. When recording ERPs or EPs (whose peak amplitudes are a few microvolts down to a fraction of microvolt), the spontaneous EEG (whose amplitude is of tens of microvolt) is to be considered a noise that completely masks the EPs or ERPs on the recorded waveform.
4. In ERP analysis, the averaging procedure consists in
 - a. segmenting epochs (trials) with fixed duration from the raw recording, each aligned to a repetition of the event
 - b. performing a synchronized average, i.e. averaging all corresponding samples sharing the same latency across the set of trials.
5. Synchronized averaging of N trials preserves the amplitude of the ERP and reduces the amplitude of the background spontaneous EEG activity by a factor \sqrt{N} , under commonly verified hypotheses.
6. The amplitude of ERPs is measured with respect to a baseline epoch (usually preceding the stimulus), in which the amplitude is assumed to be zero.
7. The latency of an ERP peak is measured with respect to the relevant event, usually the presentation of a stimulus, rather than with respect to the beginning of the waveform.
8. In an ERP, peaks are named with a leading P (N) if the peak has positive (negative) polarity.
9. In an ERP, peaks are often named with a trailing number indicating the nominal latency in milliseconds. In older conventions, the trailing number represents the order of the peak within the ERP.
10. **A negative peak in an ERP recorded on a specific subject with a latency of 108 ms may still be named N100, if it matches the physiological phenomenon of the nominal N100 component. (CHECK NOMENCLATURE OF ERP COMPONENTS SLIDE AND NOTES)**
11. The Stimulus Onset Asynchrony (SOA) measures the time interval between the onset of two successive stimuli in a train. If each trial only contains a stimulus, it is equivalent to the Inter-Trial Interval (ITI)
12. The Inter-Stimulus Interval (ISI) measures the time interval between the end of a stimulus and the beginning of the following one. It equals the SOA minus the stimulus duration.
13. In an ERP, the response to a stimulus has a reduced amplitude when the SOA is too short. Long-latency components of the ERP are especially sensitive to this decrease.
14. Brain activity in response to a stimulus can be phase-locked to the event, meaning that the whole time course (including positive and negative peaks) of the response has the same latency in every repetition. This activity is called evoked (???????)
evoked e basta?)
15. Brain activity in response to a stimulus can be non-phase-locked, meaning that they show variable latency (jitter) at each repetition. This activity is called induced.
(???????) evoked e basta?)
16. The averaging procedure can reliably uncover components of an ERP corresponding to evoked activity of the brain.
17. Induced activity is often examined by analyzing the envelope of the EEG in a relevant frequency band, i.e. by rectifying or squaring the pass-band filtered trials before averaging them.
18. In the EEG terminology, synchronization (desynchronization) is synonymous with an increase (decrease) of the waveform amplitude (and thus power).

19. Event-Related Desynchronization/Synchronization (ERD/S) quantifies changes of the power of EEG relative to a baseline period, expressed as percent change. ERD/S is usually evaluated on a whole range of relevant latencies with respect to the event.
20. Computation of ERD/S from a set of N EEG trials requires the following steps:
- band-pass filtering in the relevant frequency band;
 - take the square of each sample;
 - take a synchronized average across trials;
 - smooth by averaging samples within each short time window in a set of adjacent ones covering the whole time course
 - compute the relative percentage change with respect to the average value in a baseline period.

Clarification: An alternative algorithm to evaluate the ERD/S uses rectification instead of squaring in step b., thus estimating the amplitude of the signal rather than its power.

21. Time-frequency analysis allows to analyze and visualize changes of the spectral components of a signal over time. Time resolution and frequency resolution cannot be freely chosen – the higher the one, the lower the other.

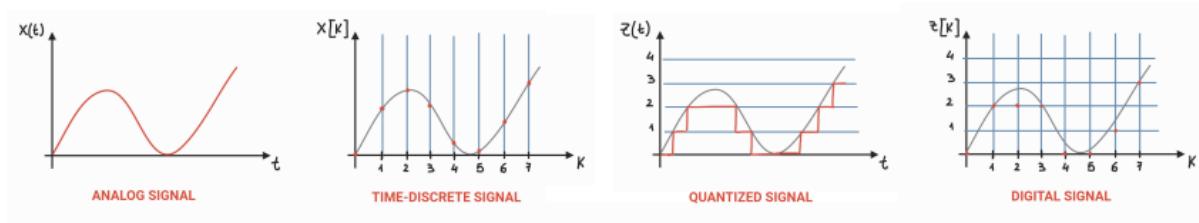
Basic of Signal Processing (Part 1):

Matlab notebooks are available [here](#).

Analog to Digital Conversion (ADC):

During an analog to digital conversion we perform two discretization step:

- Sampling: Discretization of the signal w.r.t. to time
- Quantization: Discretization of the signal w.r.t. its value at each instant



Quantization:

It is the discretization of signal amplitude. We must take into account:

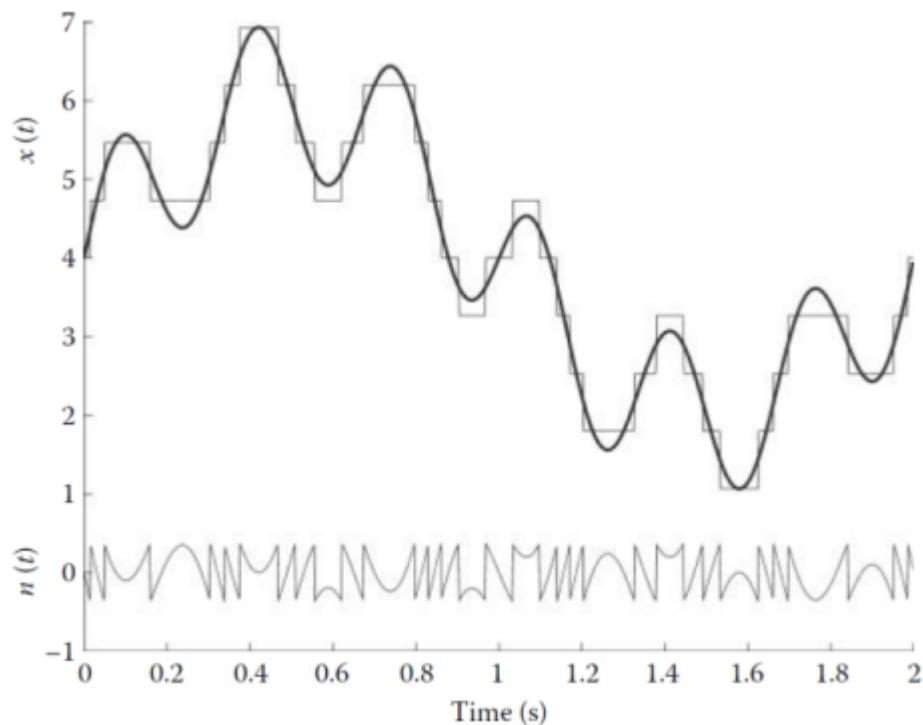
- Noise: introduced during analog to digital values conversion
- Precision (LSB, Least Significant Bit) of the conversion from analog to digital
- Full scale (Range): is the highest analog input amplitude manageable

Noise:

During the quantization, at each instant t we approximate the value of the analog signal in input to a digital value. This approximation introduces an error that we can model as a random noise $n(t)$, precisely:

$$n(t) = z(t) - x(t)$$

with $z(t)$ being the quantized signal and $x(t)$ the analog input signal. We can assume the noise is uniformly distributed in the range $[|n_{\min}| = -\frac{1}{2}V_{\text{LSB}}, |n_{\max}| = +\frac{1}{2}V_{\text{LSB}}]$. Consider this example:



Since $n(t) = z(t) - x(t)$, we have $z(t) = x(t) + n(t)$, so we can say that the noise $n(t)$ is additive.

Using different bits we get different rms noise¹⁷

- 8 bit ADC \rightarrow rms noise = $0.29/256 \approx 1/900$ range.
- 12 bit ADC \rightarrow rms noise = $0.29/4096 \approx 1/14,000$
- 16 bit ADC \rightarrow rms noise = $0.29/65536 \approx 1/227,000$

The more bits you use the lower is the range.

¹⁷ root mean square value of the noise

Precision (LSB):

The precision indicates the distance between adjacent quantization levels. The lower is this distance, the more precise is the quantization. The precision is also called LSB, from Least Significant Bit (LSB), since the Least Significant Bit is the smallest change in the analog signal that the ADC converter can detect.

The quantization noise depends on the precision, precisely:

$$n(t) \in \left[+\frac{1}{2} \text{LSB}, -\frac{1}{2} \text{LSB} \right];$$

Moreover:

$$\text{mean}(n(t)) = 0; \quad \sigma(n(t)) = \frac{1}{\sqrt{12}} \text{LSB}$$

In addition to the quantization noise, we also have the **intrinsic noise** that is caused by the measurement procedure. The overall noise is:

$$\sigma_{int+quant} = \sqrt{\sigma_{int}^2 + \sigma_{quant}^2}$$

We want the LSB to be small enough. In this way we have that the quantization noise is smaller than the intrinsic noise of the signal. In this way the quantization noise becomes negligible w.r.t. to the overall one.

Probability Recall:

- The variance of a random variable X is:

$$Var[X] = \sigma_X^2$$

- If two random variables are uncorrelated, we have that:

$$Var[X + Y] = Var[X] + Var[Y]$$

Range (Full Scale):

The third and last specification of the instrumentation is the range of values that can be accepted in the input signal. Values outside this range are saturated. This range can be calculated in the following way:

$$Range = \text{LSB} * 2^{bits}$$

So we need the information about the precision and the number of bits we use for the quantization.

Sampling:

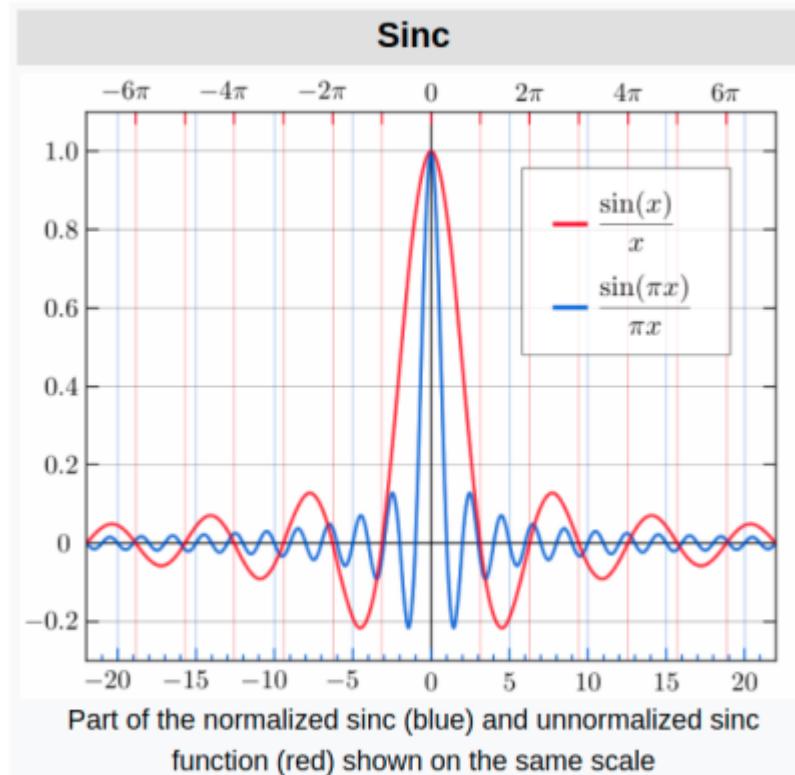
The sampling consists in the discretization of the signal over time. When considering sampling, we have to consider the sampling frequency (or sampling rate), that is the number of samples acquired in a second.

Nyquist-Shannon Theorem: this theorem tells us which is the proper sampling frequency to use. Precisely, we have that a continuous signal can be properly samples **only if** it doesn't contain frequency components above the Nyquist frequency f_{Nyquist} :

$$f_{\text{Nyquist}} = \frac{f_{\text{sampling}}}{2}$$

where f_{sampling} is the sampling rate. With properly we mean that we are able to reconstruct the analog signal from the sampled with no error. This exact reconstruction, with no error, is guaranteed only if we sample the signal without quantizing it, otherwise the theorem doesn't hold anymore.

How to reconstruct the signal? You can place a sinc() function for each sample, properly scaled and shifted in function of that sample, and then summing all functions (convolution).



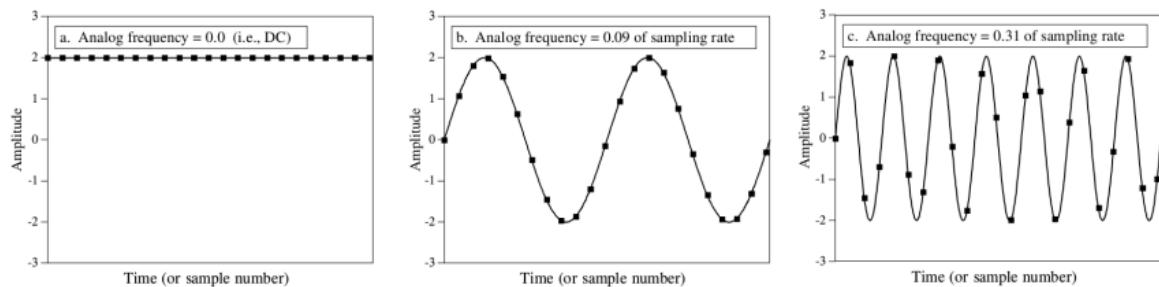
So, from the Nyquist-Shannon theorem, what we can say is that, given a signal with the highest frequency component f_{max} , the sampling rate sampling must satisfies:

$$f_{sampling} \geq 2f_{max}$$

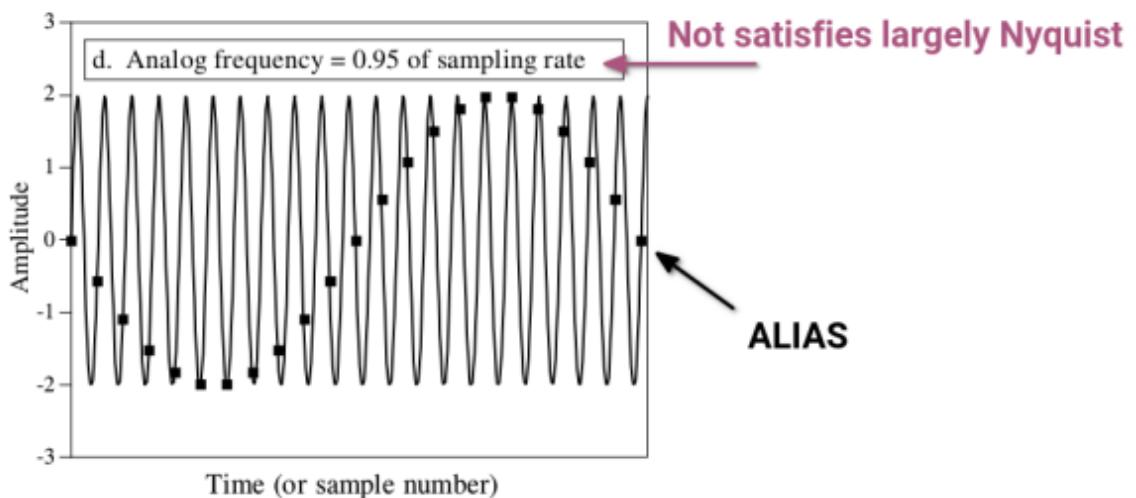
Aliasing:

If you don't respect the Nyquist theorem, we are not able to reconstruct the sampled signal properly during the digital to analog reconversion. More precisely, we reconstruct another signal that acts like an *alias* of the original one. This phenomenon is called aliasing.

Let's consider this example:



In these cases above, we don't have aliasing, since the analog frequency (f_{max}) is less than half of the sampling rate ($f_{sampling}/2$). In the case below, instead:

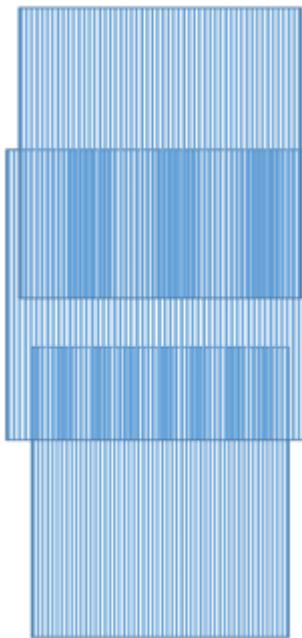


The inequality is not respected, and so there is aliasing. Precisely, since the input signal frequency is 0.95 of the sampling rate, we are able to take only 5% of the input signal samples. In other words, the reconstructed signal, namely the *alias*, has a frequency equals to 0.05 of the original signal.

SE HO CAPITO BENE DICE CHE SE LA FREQUENZA È TROPPO ALTA POI DAI SAMPLES (I PUNTINI) NON RIESCI A RICOSTRUIRE PROPERLY LA FUNZIONE MA SOLTANTO LO 0.05 PERCENTO DI QUELLA CHE ERA LA FUNZIONE ORIGINARIA. LO

VEDI DALL'IMMAGINE SOPRA IN EFFETTI, IN QUANTO DAI QUADRATINI NERI RICOSTRUISCI UNA CURVA CHE NON C'ENTRA NULLA (PRECISAMENTE, C'ENTRA PER IL 5%) CON LA FUNZIONE ORIGINARIA.

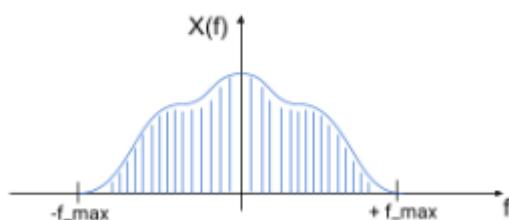
This visual artifact:



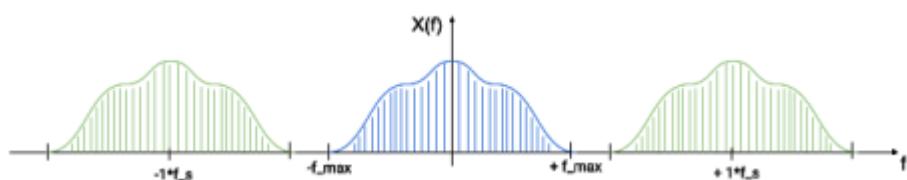
is due to aliasing.

Frequency Spectrum (the reason behind Nyquist theorem):

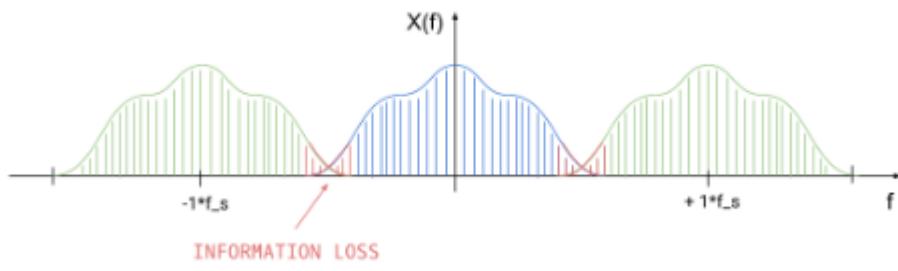
Representing the input signal in the frequency domain:



when we perform sampling, we replicate the signal spectrum along the frequency axis by shifting the original spectrum to multiples of f_s .



This above is the case in which we have respected the Nyquist theorem. Instead, if we don't respect it, when sampling:



we have overlapping between spectra and that causes loss of information. So we have aliasing.

Note that since real analog signals have frequencies also at infinity, we apply an analog filtering before the Analog to Digital circuit.

True Statements of 2.01 (and 2.02?):

1. Shannon's theorem (sampling theorem) states that a continuous signal can be properly sampled only if it does not contain frequency components above one-half of the sampling rate.
2. In Analog to Digital Conversion (ADC), the Nyquist frequency equals half of the sampling frequency.
3. The reconstruction of an analog signal from its sampled version is equivalent to the sum of a set of sinc() functions, one for each sample, each centered on the time of the respective sample, whose amplitude equals the sample value.
4. Aliasing occurs when an analog signal is sampled outside the conditions set by the Shannon's theorem.
5. When aliasing occurs in ADC, a sinusoidal component with frequency

$$f_0 \in (f_{Nyquist}, f_{sampling})$$

is reconstructed as a sinusoidal component at

$$f_{aliasing} = f_{sampling} - f_0 \in (0, f_{Nyquist})$$

6. Aliasing can be prevented by applying an analog low-pass filter with cutoff frequency lower than $f_{Nyquist}$ to the analog signal (i.e. before it is converted).
7. Quantization (i.e. approximation of the analog value of a sample to the nearest among the allowed quantization levels) introduces a noise whose amplitude is proportional to the width of the quantization interval:

$$\sigma_{quant} = \frac{1}{\sqrt{12}} LSB$$

8. Quantization divides the input range of the ADC into (approximately) 2^{N_BITS} intervals, where N_BITS is the number of bits of the ADC.

9. Given a fixed number of bits N _BITS of the ADC, choosing a large input range increases the quantization error, while choosing a small input range increases the chance that the signal is clipped (i.e. the input range is saturated).
10. Appropriate application of an analog filter (i.e. before the analog signal is converted) may prevent saturation by removing high amplitude artifacts in specific frequency bands.

Basic of Signal Processing (Part 2):

STATISTICS, PROBABILITY AND NOISE

INTRODUCTION

Signals can be entirely deterministic, or they can be known only by means of their statistical properties. We will introduce a number measurements to characterize both types of signals.

Probability theory deals with the mathematical modeling of random variables (numbers) and processes (signals). Statistics deals with the description of empirical observations, and with the estimation of the (usually unknown) parameters of the mathematical models of the variables and processes (stochastic signals).

Fundamental to several analysis algorithms, the Central Limit Theorem states the relevance of Normal (Gaussian) distributions in empirical sciences.

BASIC MEASURES FOR SIGNAL CHARACTERIZATION

Mean:

$$\bar{X} = \frac{1}{N} \sum_{i=0}^{N-1} x_i$$

When the number of samples N tends to infinity, the empirical mean \bar{x} tends to the mathematics mean of the stochastic variable X:

$$\lim_{N \rightarrow +\infty} \bar{X} = \mu_X$$

So \bar{x} is essentially an estimator of μ_X

Amplitude: there are two quantities that tell us about signal power

Average Rectified Value (ARV)

$$ARV_X = \frac{1}{N} \sum_{i=0}^{N-1} |x_i|$$

Root Mean Square (RMS)

$$RMS_X = \sqrt{\frac{1}{N} \sum_{i=0}^{N-1} x_i^2}$$

Deviation: also in this case we have two different quantities used to measure deviation of the signal with respect to signal mean. The first one has been defined by engineers, the second one instead is the mathematical definition.

Average Deviation

$$AD_X = \frac{1}{N} \sum_{i=0}^{N-1} N - 1 |x_i - \bar{X}|$$

Variance and Standard Deviation

The estimator of the mathematical **variance** is the following:

$$s_X^2 = \frac{1}{N-1} \sum_{i=0}^{N-1} (x_i - \bar{X})^2$$

Similarly to the mean:

$$\lim_{N \rightarrow +\infty} s_X^2 = \sigma_X^2$$

NOTE: ($N - 1$ division)

At denominator we have $N - 1$ instead of N due to mathematical reasons. In a nutshell, since s_X^2 is computed through an estimator \bar{X} , in order to be *unbiased*, s_X^2 has $N - 1$ at denominator. Anyway, if we know exactly μ_X then we can use it and divide by N instead $N - 1$.

So actually, average deviation is not mathematical correct but still be used for historical reasons.

Then, we have estimator for **standard deviation**:

$$s_X = \sqrt{s_X^2} = \sqrt{\frac{1}{N-1} \sum_{i=0}^{N-1} (x_i - \bar{X})^2}$$

In this case, estimator of standard deviation does not converge exactly to the mathematical standard deviation σ , this is due to root square that is a non-linear operator that transforms an unbiased quantity to a biased one.

$$\lim_{N \rightarrow +\infty} s_X \cong \sigma_X$$

NOTE: (Zero mean signal)

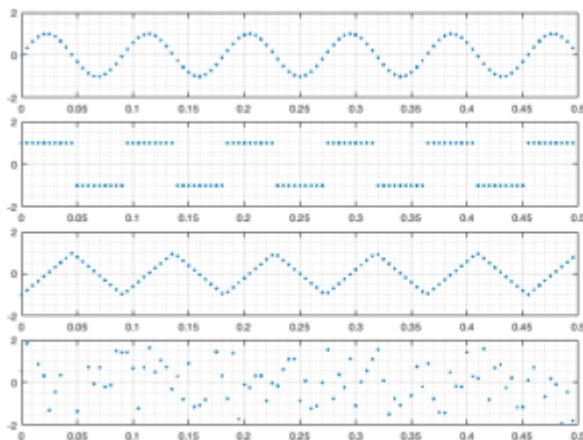
Note that when a signal has zero mean, $RMS_X \cong \sigma_X$, and $ARV_X \cong AD_X$

Example Signals:

We introduce here four signals that we will analyze in the following:

1. Sinewave (Deterministic)
2. Square wave (Deterministic)
3. Triangular wave (Deterministic)
4. Gaussian white noise (Stochastic)

The first three are deterministic waveforms, oscillating at fundamental frequency. The last one is a stochastic signal, characterized by having uncorrelated samples (whiteness, i.e. no statistical prediction can be made on the value of a specific sample by knowing the value of the others) and Gaussian distribution of the sample values (see below).



Sinewave

Square wave

Triangular wave

Gaussian White noise

NOTE: (Uncorrelated samples)

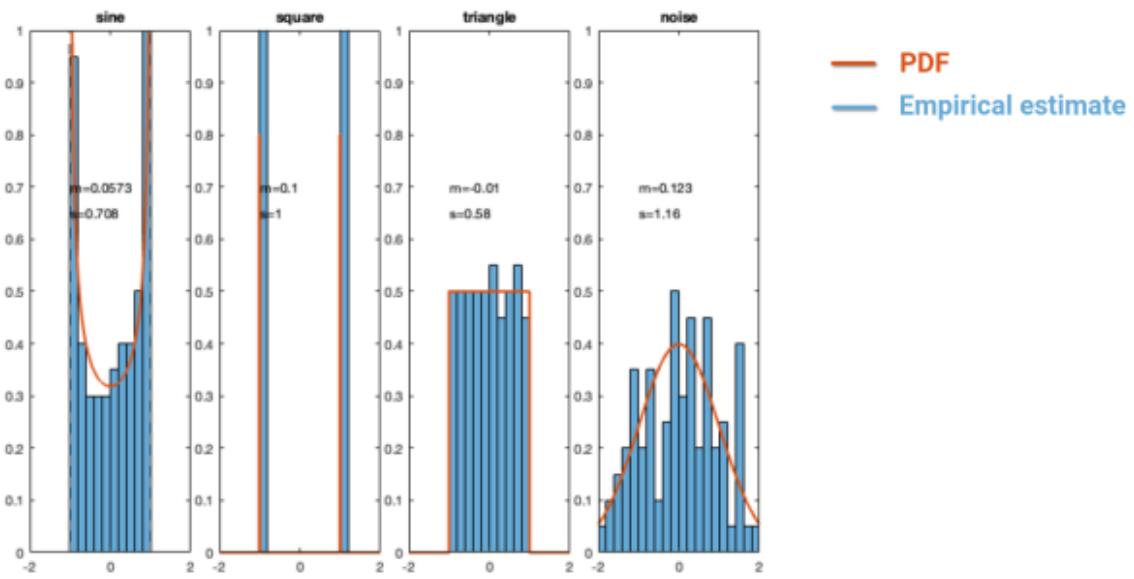
The main difference between the first three signals and the last one, is that in the first ones each sample is correlated to their neighbors, namely given a sample, we can predict the next one. This is not possible in an uncorrelated signal like Gaussian white noise.

Amplitude Distribution:

We want to characterize here how the samples are distributed on the vertical axis: the central tendency (mean), the dispersion (standard deviation), the shape of the distribution (probability density function, PDF).

Note that we have perfect knowledge of the mathematical model we used to generate the deterministic and stochastic signals. Nevertheless, even for deterministic signals there are sources of non-deterministic outcome (e.g. finite number and uncontrolled position of time samples) which make the empiric and ideal results to overlap only in part.

As for the stochastic signal, each time we repeat this simulation, we obtain different values of mean, standard deviation, and histogram. We can only assess the compatibility of empirical observations with the mathematical model in a statistical sense.



Values in for PDF of square signal are not correct due to an intermediate normalization step performed in MATLAB.

NOTE: (PDF Continuous variable)

Probability Distribute Function (PDF) in the case of continuous variables, is used to get the cumulative probability of a set of values that the variable can assume, namely the probability for which the variable assumes values on a specific range. Therefore, the PDF in a single point x is infinitesimal (about 0), however is defined in a small interval like

$$[x - \epsilon, x + \epsilon].$$

THE CENTRAL LIMIT THEOREM (CLT)

When N independent and identically distributed random variables X are averaged, the resulting variable Z tends toward a normal distribution even if the original variables themselves are not normally distributed. (Normal distributions are sometimes called Gaussian distributions.)

$$Z = \frac{1}{N} \sum_{i=1}^N X_i \rightarrow \mathcal{N}(\mu_Z, \sigma_Z^2)$$

The mean of Z equals the mean of X , the variance decreases by a factor N , the standard deviation by a factor \sqrt{N} .

$$\mu_Z = \mu_X \quad \sigma_Z^2 = \frac{1}{N} \sigma_X^2 \quad \sigma_Z = \frac{1}{\sqrt{N}} \sigma_X$$

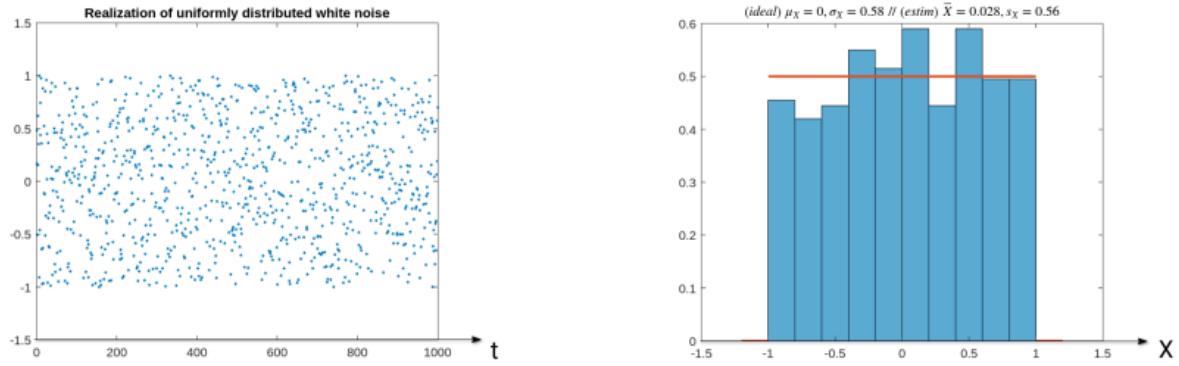
Example Noise:

To visualize the consequences of the CLT, we first show the amplitude distribution of a (uniformly distributed) white noise, and its standard deviation. By design, the expected value of this noise's mean and standard deviation are respectively:

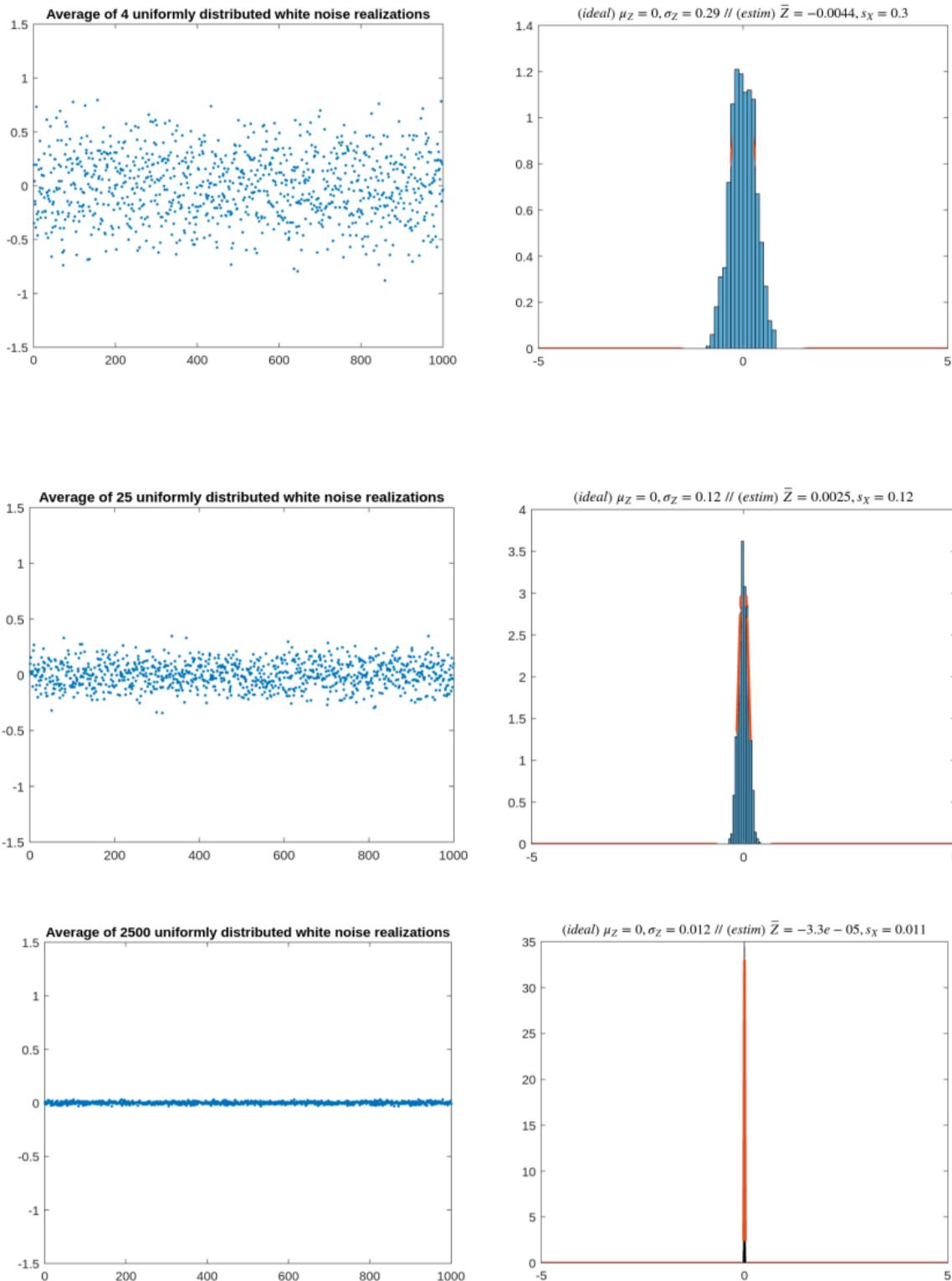
$$\mu_X = 0 \quad \sigma_X = \frac{2}{\sqrt{N}} \cong 0.57735$$

N.B. when we estimate these parameters from empirical data we can only approach the modeled values.

Let's consider a trial in which we collect only a white noise without any signal of interest in the recording:

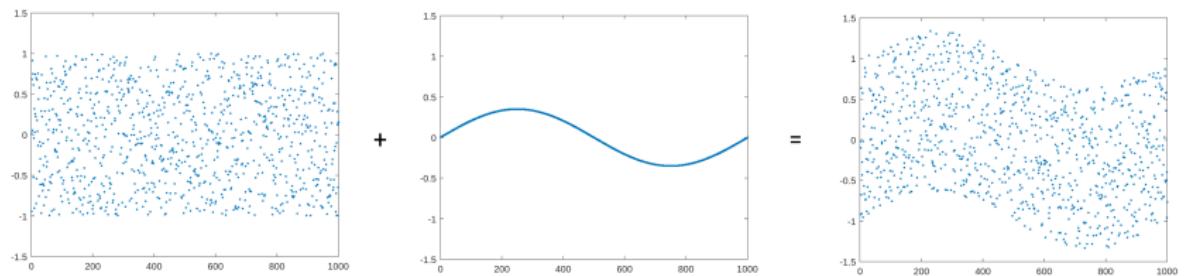


Then computing the average of N trials we can observe CLT effect, namely the random average signal is a normal distribution with the same mean of the white noise and with a lower standard deviation.

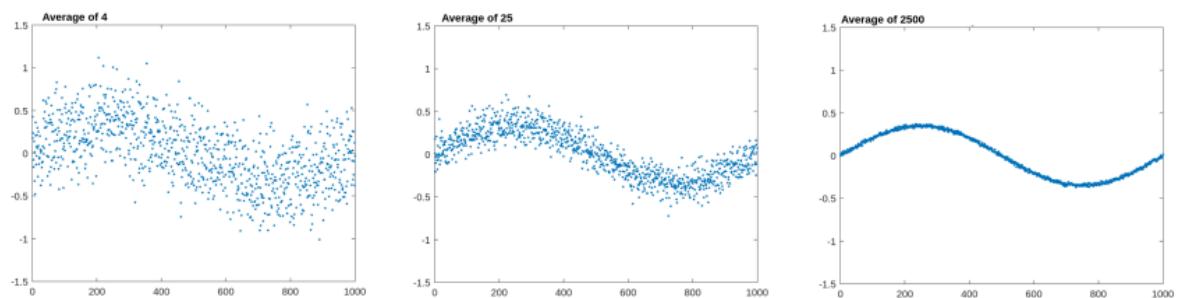


Example Noise + Signal:

Let's consider now a trial in which we collect data affected by a white noise during the recording:



If we collect and average an high number of trials, then we are able to extract signal of interest from noisy recordings



True Statements Basic of Signal Processing Part 2: TODO

TRUE STATEMENTS

- The Average Rectified Value (ARV) is a measure of the amplitude of a signal, and it is obtained by summing the absolute values of all samples and dividing the result by the number of samples.
- ARV_X is defined as:

$$ARV_X = \frac{1}{N} \sum_i |x_i|$$

where the sum extends on the N samples of the signal X

- The Root Mean Square (RMS) is the square root of the average of the squared value of the samples of a signal
- The variance of a signal is estimated by summing the square of all deviations of the N sample values from the sample mean, and then dividing by $(N - 1)$
- s_X^2 is defined as:

$$s_X^2 = \frac{1}{N-1} \sum_i (x_i - \bar{X})^2$$

where the sum extends over the N samples of the signal X .

- The variance σ^2 and the square of the RMS of a zero-mean signal have the same value. (Consider $N \rightarrow +\infty$)
- The standard deviation σ of a signal is the square root of its variance.
- In white noise, all samples are uncorrelated, i.e. when given the value of one sample we have no increased knowledge to predict the value of another sample.
- The frequency spectrum of white noise is flat, i.e. it has the same power at any frequency.
- In a Gaussian noise, the probability [density] that a sample has a given amplitude value follows the normal (Gaussian) distribution with zero mean.
- Given two ranges of equal width $A = [-0.5, +0.5]$ and $B = [0.5, 1.5]$, it is more likely that samples of a Gaussian noise will have amplitude in A rather than B [because the gaussian probability density function is highest around 0]
- Given two ranges of equal width $A = [-0.1, +0.1]$ and $B = [0.8, 1.0]$, it is less likely that samples of a sinewave $x = \sin(t)$ will have amplitude in A rather than B .
- The amplitude of the samples of a triangular waveform have uniform probability density function, i.e. samples have the same probability [density] of taking a value between the $-A$ and $+A$ (being A the peak value of the waveform) and zero probability of taking a value outside $[-A, A]$.
- The Central Limit Theorem (CLT) states that the probability distribution of the average of N independent and identically distributed random variables tends to a normal distribution for N approaching infinity.
- The probability distribution of the average of N independent and identically distributed random variables is a normal distribution independently of the value of N .
- Given N independent and identically distributed random variables with variance (or standard deviation) equal to σ^2 (or σ), the variance (standard deviation) of their average is: σ^2/N (or σ/\sqrt{N})

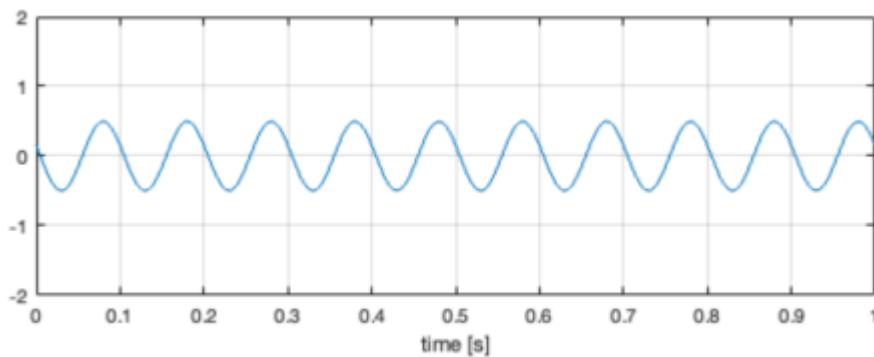
- The synchronized average of N trials containing only spontaneous EEG whose $RMS_{trial} = \sigma^2$ is a signal $RMS_{avg} = \sigma^2/N$

Basic of Signal Processing (Part 3):

Spectral Analysis:

A sinewave is a function of time, with parameters frequency f, amplitude A, initial phase ϕ :

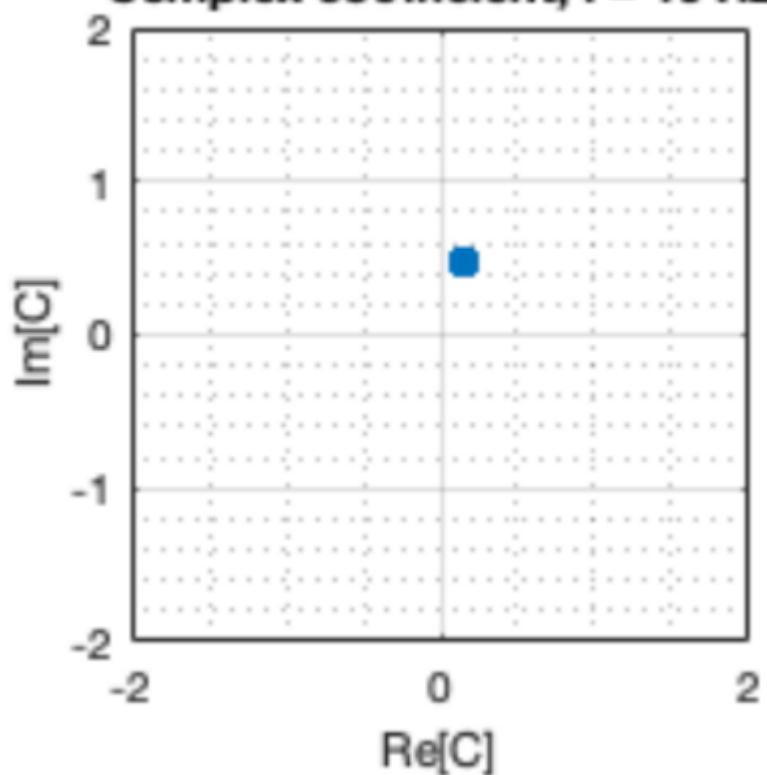
```
sinewave = @(t, f,A,phi) A * cos(2*pi*f*t + phi);  
t = (0:.005:1)'; % seconds  
f = 10; % Hz  
A = 0.5;  
phi = 0.4 * pi; % radians
```



A sinewave can be represented as a complex number C:

$$C = Ae^{j\phi} \Leftrightarrow A = |C|, \phi = \angle C$$

Complex coefficient, $f = 10$ Hz



Sinewaves can be composed to create more complex waveforms:

```

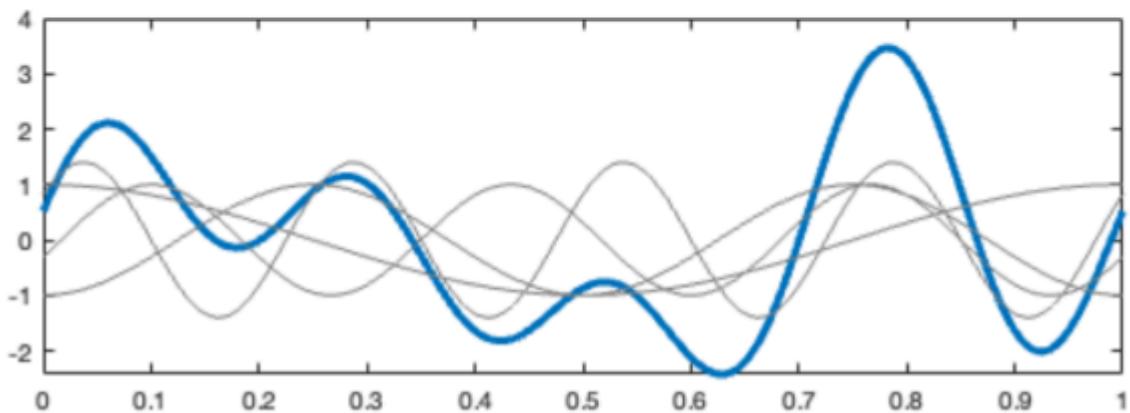
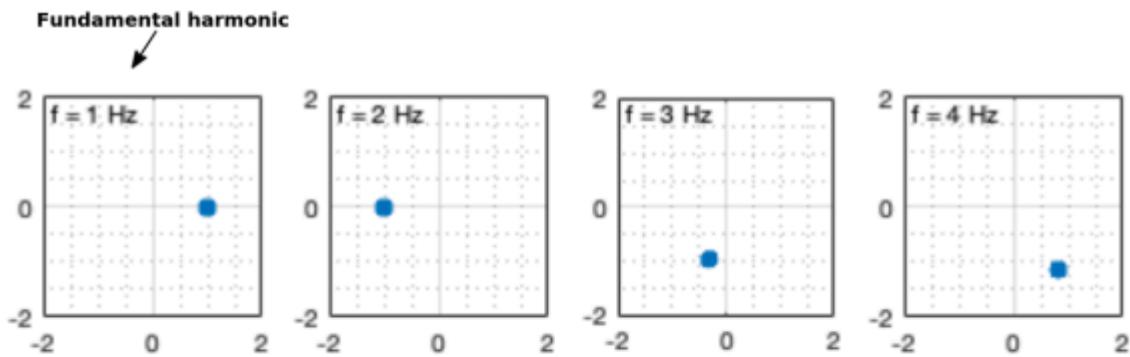
f1 = 1; % Hz
ff = f1 .* [1 2 3 4];
CC(1) = 1 * exp(1j * 0 * pi);
CC(2) = 1 * exp(1j * 1 * pi);
CC(3) = 1 * exp(1j * -0.6 * pi);
CC(4) = 1.4 * exp(1j * -0.3 * pi);

waveform = @(t) ...
    sinewave(t, ff(1), abs(CC(1)), angle(CC(1))) + ...
    sinewave(t, ff(2), abs(CC(2)), angle(CC(2))) + ...
    sinewave(t, ff(3), abs(CC(3)), angle(CC(3))) + ...
    sinewave(t, ff(4), abs(CC(4)), angle(CC(4)));

figure(2)
clf
for k=1:4
    subplot(2,4,k)
    plot_complex_coefficient(CC(k), ff(k));
end

subplot(2,1,2)
plot(t, waveform(t), "Linewidth", 3)
hold on
for k=1:4
    plot(t, sinewave(t, ff(k), abs(CC(k)), angle(CC(k))), "Color", "#808080");
end
hold off

```



FOURIER TRANSFORMATION

Fourier Analysis, i.e. decomposition of signals into sum of sinewaves. Since each sinewave carries power at exactly one frequency, the decomposition can be used to analyze the signal in the frequency domain.

Specifically Discrete Fourier Transform can be used to transform the (time-limited and sampled) time- domain representation of a signal into its (bandwidth limited an sampled) representation in the frequency domain.

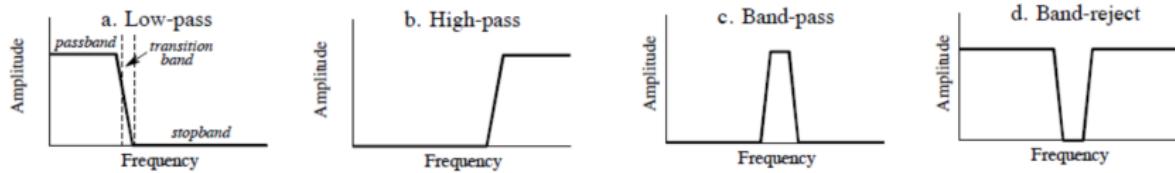
Basic of Signal Processing (PART 5) (AND THE 4?)

FILTERS:

The purpose of a filter is to allow some spectral components of a signal to pass (almost) unaltered, while (almost) blocking other spectral components. For some purposes like anti-aliasing or anti-saturation filtering, analog filter are used, however in most of the cases also a digital (software) filter is used for final signal processing.

BASIC FREQUENCY RESPONSES:

The figure below shows the four basic frequency responses:



We can distinguish three different regions in each frequency response:

- Passband refers to those frequencies that are passed (GAIN = 1)
- Stopband contains those frequencies that are blocked (GAIN = 0)
- Transition band is between passband and stopband (GAIN $\in (0, 1)$)

A fast roll-off means that the transition band is very narrow.

Cutoff frequency:

The division between the passband and transition band is called the **cutoff frequency**.

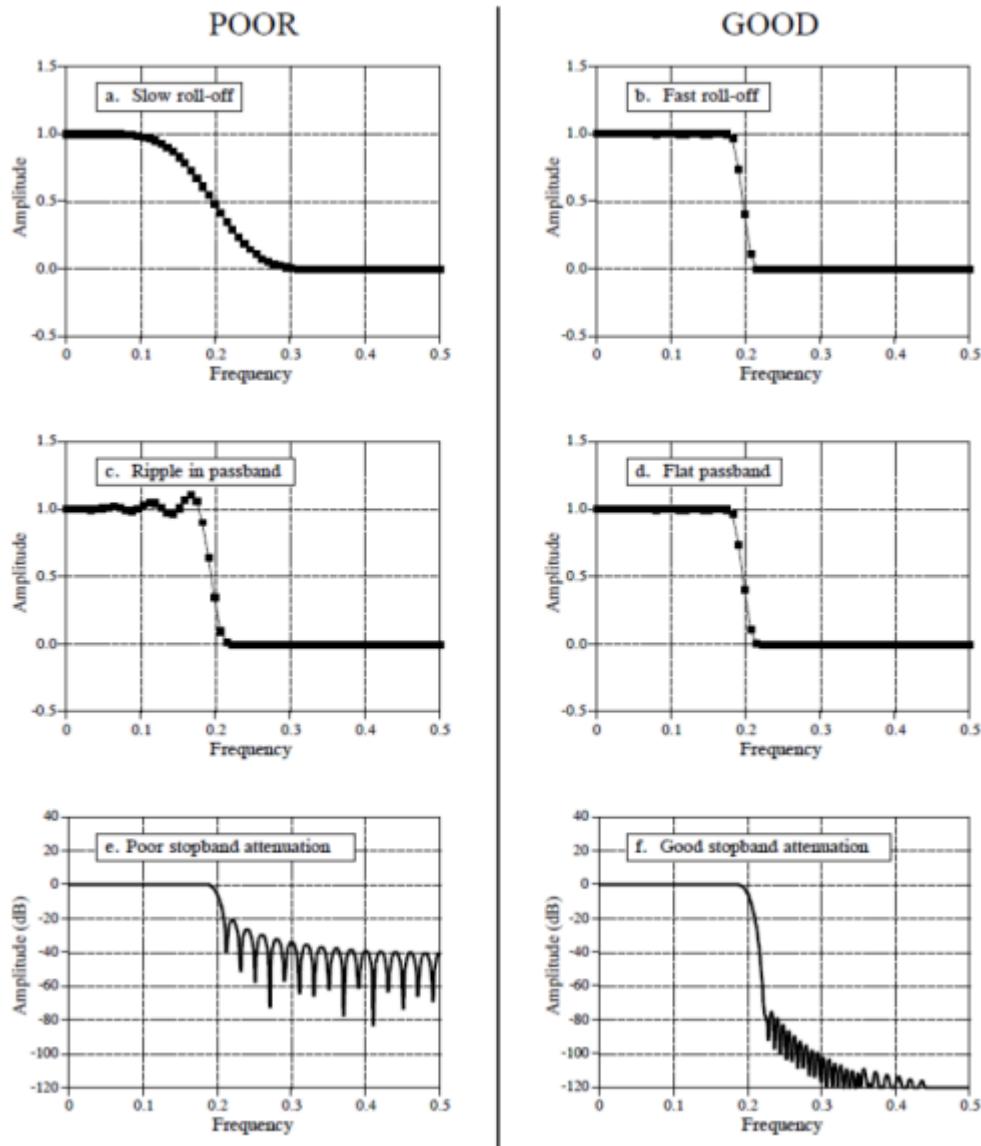
In **analog filter** design, the cutoff frequency is usually defined to be where the amplitude is reduced to 0.707 times the input (i.e. -3dB).

Digital filters often specify different attenuation at the cutoff frequency, depending on the synthesis process.

POOR-GOOD FILTERS:

The figure below shows three parameters that measure how well a filter performs in the frequency domain:

- To separate closely spaced frequencies, the filter must have a fast roll-off, (top row).
- For the passband frequencies to move through the filter unaltered, there must be no passband ripple, (middle row).
- To adequately block the stopband frequencies, it is necessary to have good stopband attenuation, (bottom row).



OBS: (Logarithmic Y-scale)

Note that in the last figure (stopband attenuation) we use a logarithmic scale for amplitude axis in order to be able to appreciate small variations (ripple)

NOTE: (Normalized X-Axis)

The X-axis of the previous figures use a normalized scale respect to the sampling frequency $f_{sampling}$, indeed they represent frequency response in the frequency interval $[0, f_{Nyquist}]$. (Recall $f_{Nyquist} = 0.5f_{sampling}$)

In the real world is impossible to have a perfect filter (No free lunch), when we design a filter we have a tradeoff between three factors:

- Ripple tolerance: Maximum ripple amplitude admissible
- Order: (Complexity)
- Roll-off slope

In practice, only two of them can be chosen. For instance, if we want a filter with fast roll-off and low ripple tolerance, then our filter must have an high order (high design complexity).

MAIN FILTERS FAMILIES:

Finite impulse response and Infinite impulse response are the two main families of filter types. The main difference between them is their response to a finite impulse:

- Given in input a finite impulse to FIR filter, it responses with a finite signal that eventually reaches zero
- Given in input a finite impulse to IIR filter, it responses with a infinite signal

Finite Impulse Response (FIR)

In a FIR filter, the output $y[i]$ at time discrete i is computed by combining samples of the input x . We essentially perform a convolution operation:

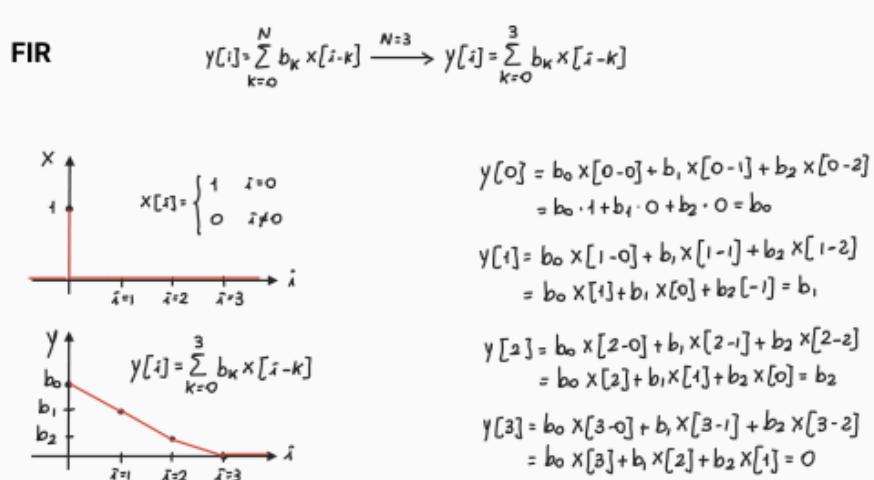
$$y[i] = \sum_{k=0}^N b_k x[i-k]$$

Where:

- b_k Convolution coefficients
- N Filter order (indicates how many recent samples are used to compute the output)

Example (FIR)

$N = 3$



We can note that y goes to zero after a while when we have an impulse x in input.

Common used FIR Filters:

Examples of design methods for FIR filters:

- Windowed sinc (using the same window types used in spectral analysis)
- Minimax (or Parks-McClellan)

Infinite Impulse Response (IIR):

In a IIR filter, the output is computed by combining samples of the input x and previous samples of the output y . In this case we have a recursive formula:

$$y[i] = \sum_{k=0}^N b_k x[i-k] - \sum_{k=1}^M a_k y[i-k]$$

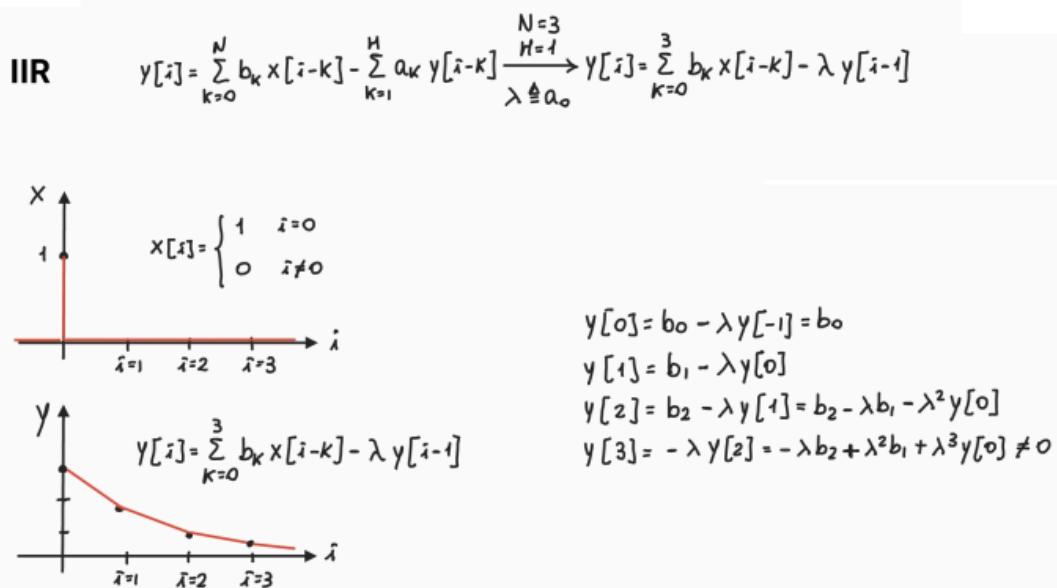
Where:

- N : Number of input samples to use
- M : Number of previous output samples to use
- b_k Convolution coefficients
- a_k Recursion coefficients

In this case the filter order is given by: FILTER ORDER = max (M, N)

Example (IIR)

$N = 3, M=1$



We can note that y does not reach zero when we have an impulse x in input.

Common used IIR Filters:

Examples of design methods for IIR filters:

- Butterworth

- Chebyshev
 - Type I (It has ripple in passband)
 - Type II (It has ripple in stopband)
- Elliptic

FILTERS APPLIED TO EEG SIGNAL

// to do
 // add some examples

EXTRACT ALPHA RHYTHM

```
load eeg.mat eeg ec_start_samp eo_start_samp
fs = 512;
num_samp_eeg = length(eeg);
time_eeg = (0:num_samp_eeg-1) / fs;
ec_trial = eeg - mean(eeg); % fix overall baseline

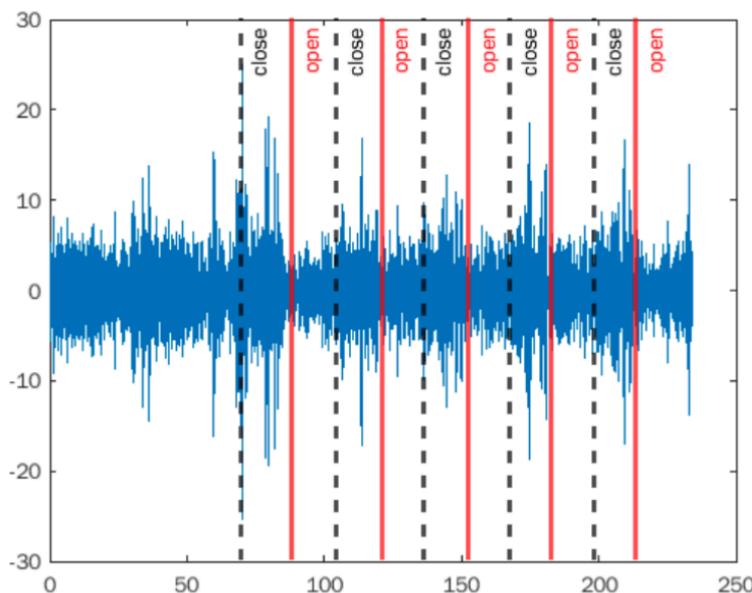
alpha_filt = designfilt('bandpassfir', 'FilterOrder', 256, 'CutoffFrequency1', 8,
'CutoffFrequency2', 13, 'SampleRate', fs);

alpha = filtfilt(alpha_filt, eeg); % filtfilt introduces no delay

figure(3)
clf
plot(time_eeg, alpha)

for smp = eo_start_samp(:)
    xline(smp/fs, 'r-', "open", "LineWidth", 2);
end

for smp = ec_start_samp(:)
    xline(smp/fs, 'k--', "close", "LineWidth", 2);
end
```



True Statements Basic of Signal Processing Part 5: TODO

TRUE STATEMENTS

- The purpose a filter is to allow some spectral component of a signal to pass (almost) unaltered, while (almost) blocking other spectral components
- Filters are categorized into four types depending on the basic shape of their frequency response: (i) low-pass; (ii) high pass; (iii) band-pass; (iv) band-reject (or band-stop)
- The passband is the interval of frequencies in which the gain of the filter is close to 1. In the stopband the gain is close to 0. In the transition band the gain has an intermediate value between 0 and 1.
- The roll-off of a filter is the slope of its frequency response in the transition band. It is high when the transition band is narrow.
- The cutoff frequency (or corner frequency) designates the limit of the passband. The gain of the filter at cutoff frequency is approximately 0.71 (i.e. $1/\sqrt{2}$, -3dB) [The gain value at the cutoff-frequency might be different for some filter designs, but this concept is beyond the scope of this course]
- The gain in the passband can monotonically decrease below 1 when the frequency approaches the cutoff frequency, or it might ripple above and below 1.
- The frequency response of a filter in the stopband should not be evaluated from a graph where the gain axis is in linear scale, because a gain of 0.001 can hardly be distinguished from a gain of 0.0001. Rather, a vertical axis in logarithmic scale (i.e. the gain is expressed in dB) should be used.
- Good features of a filter include: (i) fast roll-off; (ii) flat passband (i.e. no ripple); (iii) strong stopband attenuation (e.g. gain below -40dB, but the specific value may change depending on applications)
- Digital filters are categorized into two types depending on their implementation: (i) Finite Impulse Response (FIR); (ii) Infinite Impulse Response (IIR)
- The output of FIR filters is the linear combination of samples of the input. The output of IIR filters combines both samples of the input and past samples of the output.
- The order of a filter measures the number of recent samples of the input (or the output) are combined to compute the output. [slightly incorrect, but will do for this exam. A more accurate definition that is beyond the scope of the course states that the order of a filter is the maximum delay applied to an input or output sample, whichever is largest]
- The Butterworth filter is a design method in the family of IIR
- The corner frequency of a high-pass filter is called low cutoff frequency. The corner frequency of a low-pass filter is called high cutoff frequency. Band-pass and band-stop filters have both a low cutoff frequency and a high cutoff frequency.
- A notch filter is a type of band-stop filter which removes only attenuates the input in a narrow band around the notch frequency. Its most common use is to remove the powerline artifact at 50 Hz and its harmonics (60 Hz in some other countries).
- An IIR filter is more efficient than a FIR filter, meaning that the latter needs to be of a higher order to achieve the same quality specifications.
- A FIR filter can be designed to have “linear phase”, meaning that it will not introduce time-domain distortions in the waveform of the output signal. IIR filters cannot have linear phase.

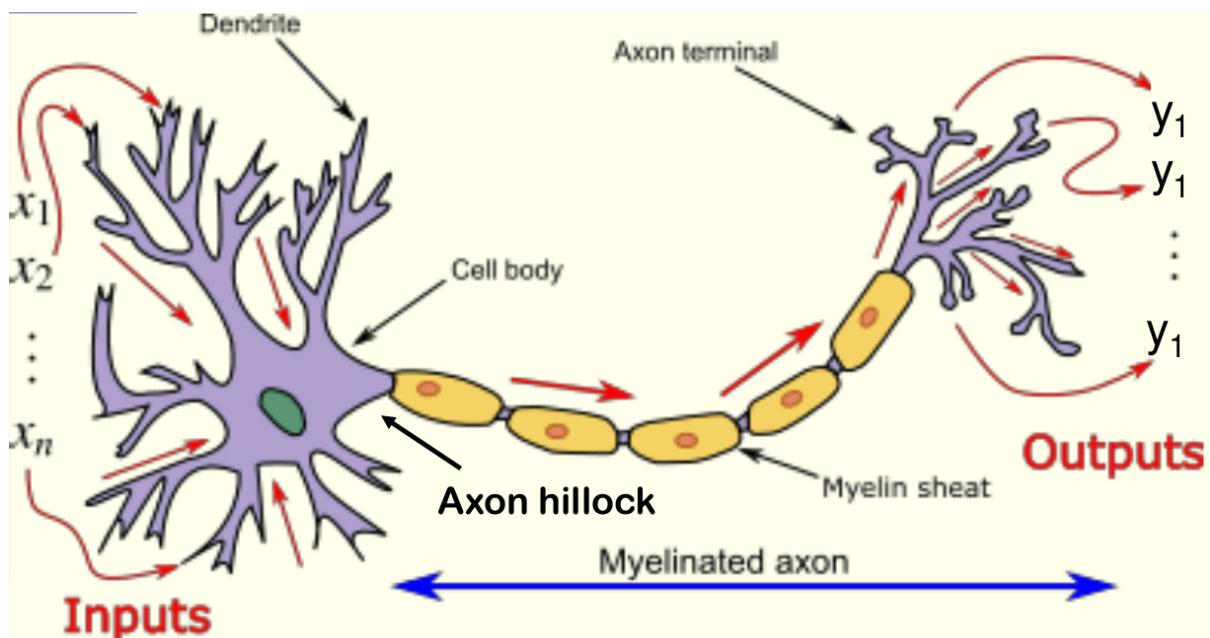
Astolfi's Part

The Neural Cell, Part I

5/03/2024, 12/03/2024

The neural cell, namely the neuron must be able to do in a simplified way the 3 main task that the brain does, but alone they can't reproduce the entire brain behavior, for that we need a network of neurons. The 3 main task are:

1. collect information from the outside world or from the past, so it's also able to store
2. process said information
3. produce output



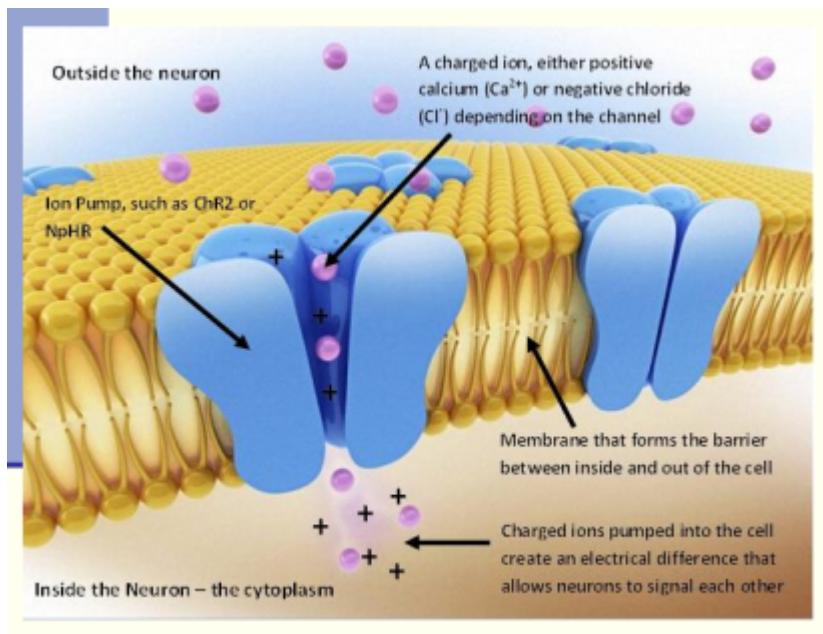
Task 1: the dendrite is the part of the cell that is devoted to collect thousand of inputs x_1, \dots, x_n , from the external, each single millisecond. It is in the shape of many branches, to have the maximum possible surface.

Task 2: the dendrite and the cell body (or soma) does the processing as integration of information. Axon hillock is where the processing usually occurs: the information is transduced in a single binary output.

Task 3: this binary output needs to reach another cell, that can be another neuron or a muscular cell. A very long and thin cable (the axon) is used to reach the other cells. This cable is insulated with myelin. The axon is divided in branches with the single signal reaching possibly multiple neurons.

So, to summarize: the cell collects multiple info, it sums up, the result is compared with the threshold and converted into a binary output, on the same axon at the same time there is a single signal traveling and reaching all the cells that are connected with the neuron considered.

The Neuronal Membrane: where is this thing?



What is different from other cells, in the neural cell, is the membrane. So it's the part responsible for the 3 main tasks we have said. The neural cells are excitable cells¹⁸, so they are able to react to some stimuli coming from other cells or from the external world.

The yellow thing with 2 tails and 1 head is the phospholipid bilayer. Inside the neuron, below the yellow wall, there is the intracellular fluid, the cytoplasm. Outside the neuron, above the yellow wall, there is the external environment.

The membrane thus keeps the external environment separated from the internal. The heads go well with water, thus they are oriented always toward the watery side: toward the external environment and the cytoplasm. The two tails are fatty, so they don't go together with water and they are internal.

If there is an ion, that is an electrically charged element, the membrane acts like a wall and cannot be crossed by the ion. Only alcohol and things that are small and not electrically charged (also some drugs can), can cross the membrane.

Those in blue are gates, **proteins** that allow some ions to pass through the membrane. For instance, calcium and iron can cross the membrane channel if there is a gate for it.

So the membrane is selectively permeable: it's a wall with gates so it's permeable only for some substances. Ions have to cross the membrane because their movement means currents, and the current makes our brain work. In this context is called membrane current.

So we have three electrical measurements: membrane potential, membrane current, longitudinal internal and external current. This will determine all the behavior of the cell.

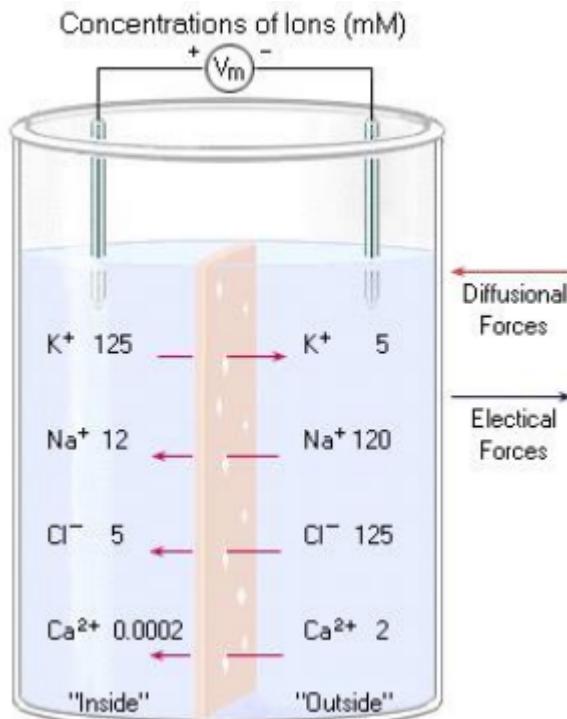
¹⁸ The other one are the muscular cells and the heart cells

The four main ion families having a role in the neuron functioning are: sodium Na+, potassium K+, chlorine Cl, calcium Ca++

We have two types of transportation:

- Passive transportation: the energy is already in the ion itself. Basically the ions can move without the need of external energy, just following the gradient. A channel is however needed to be open, to let the ion cross the membrane. This natural force that moves the ions it's a question of balance between diffusional and electrical forces.

First, let's talk about the diffusional forces: these forces are due to **chemical gradient**



The part in the middle is the membrane, and as we know there are the intracellular fluid (on the left) and extracellular fluid (on the right).

- The potassium ions are more concentrated inside the cell
- The sodium is more concentrated in the outside
- The chloride (?) is more concentrated outside
- The calcium (?) is more concentrated outside

The fact that there is a different concentration of ions in these two fluids result in a **random motion (even if there is a gradient I think it's random motion)** of the ions tends to the equilibrium.

The diffusional force is related to the thermal energy of the molecules. These:

$$Therm_{ion} = K_B * T \quad Therm_{mole} = R * T = N_A * K_B * T$$

are the thermal energy for an ion and a mole, where:

- K_B is the Boltzmann constant
- N_A is the Avogadro's number

Now let's talk about the electrical forces: these forces are due to an **electrical gradient**. This is because ions are electrically charged, so they are attracted to areas with negative potential.

The electrical force is related to the potential energy of the molecules:

$$Pot_{ion} = zq(E_A - E_B) \quad Pot_{mole} = zF(E_A - E_B)$$

with q charge of the proton.

Combining these two forces:

$$\Delta\mu = RT \ln \frac{[X]_A}{[X]_B} + zF(E_A - E_B)$$

and each ion is subjected to this electrochemical force. Precisely:

- $[X]_A$ is the ion concentration on the A side of the membrane
- $[X]_B$ is the ion concentration on the B side of the membrane
- R is the universal gas constant
- T is the temperature in Kelvin
- F is the Faraday constant
- z is the ion valence (e.g. +2 for Ca^{++} , -1 for Cl^-)
- $E_A - E_B$ is the membrane potential

This is the **electrochemical difference** between two regions A and B, for a given ion family X.

The equilibrium between these two forces is reached when the electrochemical difference between A and B is zero:

$$\begin{aligned} \Delta\mu = 0 &\Leftrightarrow RT \ln \frac{[X]_A}{[X]_B} + zF(E_A - E_B) = 0 \\ &\Leftrightarrow -zF(E_A - E_B) = RT \ln \frac{[X]_A}{[X]_B} \\ &\Leftrightarrow E_X \triangleq E_B - E_A = \frac{RT}{zF} \ln \frac{[X]_A}{[X]_B} \end{aligned}$$

If A is the extracellular region and B the intracellular region, we obtain the **Nernst**

equation, for the electrochemical equilibrium potential E_j for each ion family j:

$$E_j = \frac{RT}{zF} \ln \frac{[j]_{extra}}{[j]_{intra}}$$

where:

- $[j]_{extra}$ is the extracellular concentration of ion of family j
- $[j]_{intra}$ is the intracellular concentration of ion of family j
- z is the valency of ion of family j

So E_j is the voltage at which the forces are balanced for the ions of family j.

this quantity is important because it tells us in which direction ions moves when the membrane potential is equal to V_m

anche se c'è equilibrio non significa che non si muovono, si muovono ma non cambia nulla sull'equilibrio, quindi ci può essere una corrente!

Typical values for E_j :

- Potassium $E_{K+} = -90\text{ mV}$
- Sodium $E_{Na+} = 50\text{ mV}$
- Calcium $E_{Ca^{++}} = 150\text{ mV}$

The ions of family j when there is equilibrium with voltage E_j and they are free to cross the membrane, will flow with net currents that move the membrane potential V_m to that value (to E_j ????). the MP V_m is the electrical potential difference between the intracellular and the extracellular fluid. The extracellular is used as a reference at 0 v.

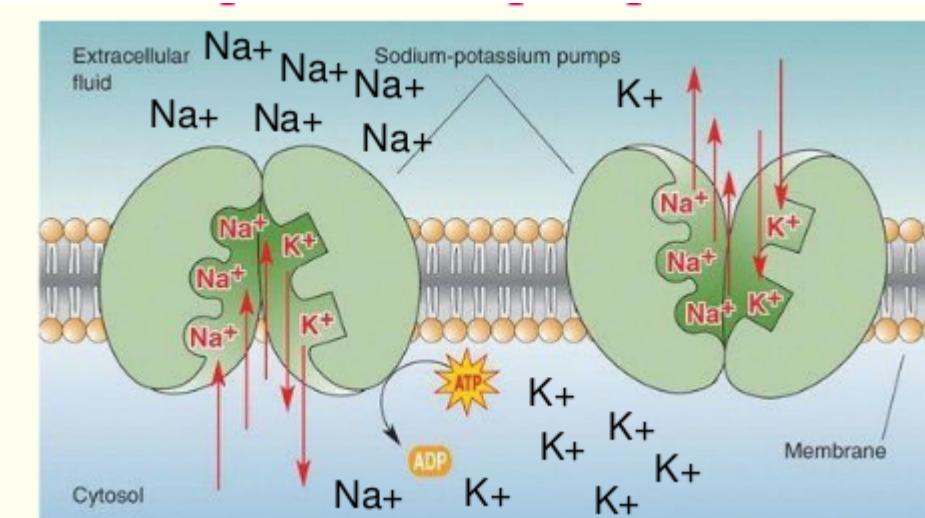
Let's assume we have a positive ion. If the ion, moving trying to reach the equilibrium potential E_j :

- goes from inside the membrane to outside, the membrane potential V_m decreases (so that means that E_j is lower than V_m right? Since V_m is decreasing to reach E_j)
- goes from outside the membrane to inside, the membrane potential V_m increases

If the ion is negative, the opposite happens.

For instance: assuming $V_m = -70\text{ mV}$, since $E_{K+} = -90\text{ mV} < V_m$, ions want to reduce V_m and so they move from inside to outside.

- Active transportation: the cell uses its own energy to move its ions against its natural direction. Usually ions move from a concentration higher towards lower, so according to the gradient. However, maybe the cell needs the difference to be maintained. So Ions pumps are used to actively move the ions against their natural gradient. The most important ion pump we have in the brain is the sodium potassium pump:



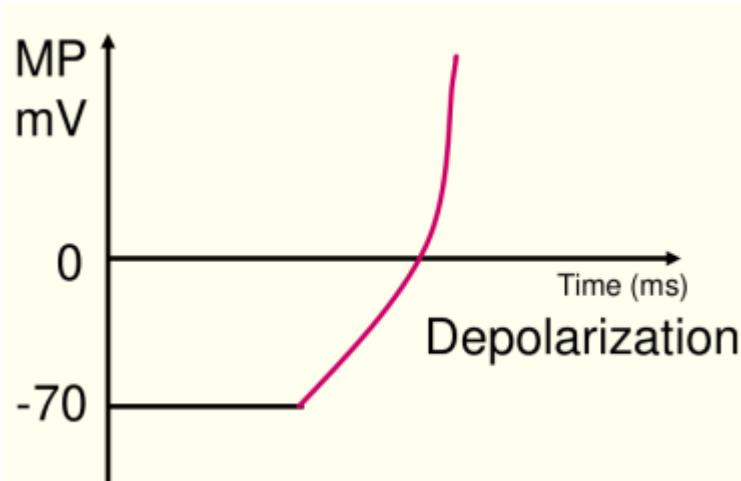
As is visible above, the ion pump is a protein that works against the electrochemical force. Potassium moves naturally from the outside to the inside, so the pump moves it in the opposite direction. For sodium it is the opposite. The sodium potassium pump at each cycle moves three ions of sodium and 2 of potassium.

But why does this active transportation exist? To work properly, the neuron membrane must have a specific potential called **membrane potential at rest**, that is about $V_m = -70 \text{ mV}$. The passive forces (diffusional and electrical) can prevent the membrane to reach this potential, so the cell uses this active mechanism of pumps. In this way, the rest potential is reached. So we can say that:

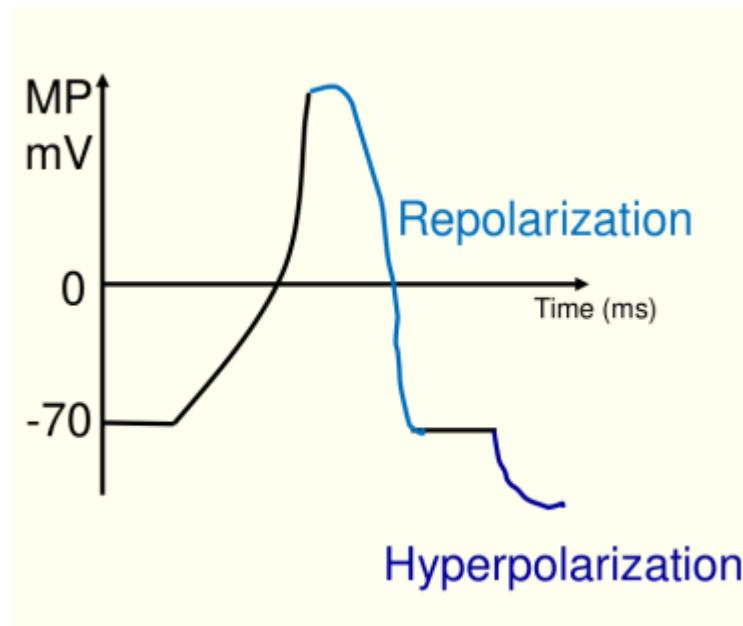
$$\text{Rest Potential} = \text{Diffusional Forces} + \text{Electrical Forces} + \text{Ion Pumps} = -70 \text{ mV}.$$

When $V_m = -70 \text{ mV}$ we say that the membrane is polarized.

1. If MP increases there is depolarization. In this case there is a current of positively charged ions flowing into the cell, or negatively charged ions flowing out of the cell.



2. If it decreases and returns to the rest potential it is polarization/repolartization
3. If it decreases above the rest potential it is hyperpolarization.



Self-evaluation Test:

1. What are the 3 main functions of the neural cell? They are:
 - a. Collection of information from multiple sources, which are other neural cells or receptors
 - b. Integration of the information to provide a binary decision
 - c. Generation and propagation of the bit information up to target cells, which are other neural cells or muscle cells
2. What are the four main ion families having a role in the neuron functioning? They are:
 - a. sodium Na^+
 - b. potassium K^+
 - c. chlorine Cl^-
 - d. calcium Ca^{++}
3. How is the resting membrane potential determined? What values does it assume?
The resting membrane potential is -70 mv, determined by the summation of diffusional forces, electrical forces, which are related to passive transportation and ion pumps, related to active transportation.

Exercise:

Given that at a certain temperature T the Cl equilibrium potential is equal to -80 mV, and the membrane potential is equal to -70 mV, the Cl net current will be:

- A. Directed from the inside of the cell toward the outside
- B. The opposite of A
- C. There will be no net current

Would this be a depolarizing or a hyperpolarizing current?

Answer: since $E_{\text{Cl}^-} = -80 \text{ mV} < V_m = -70 \text{ mV}$ the V_m will decrease. That means that a current of negative ions (since Cl^- has the minus) will flow from outside the membrane to inside, so

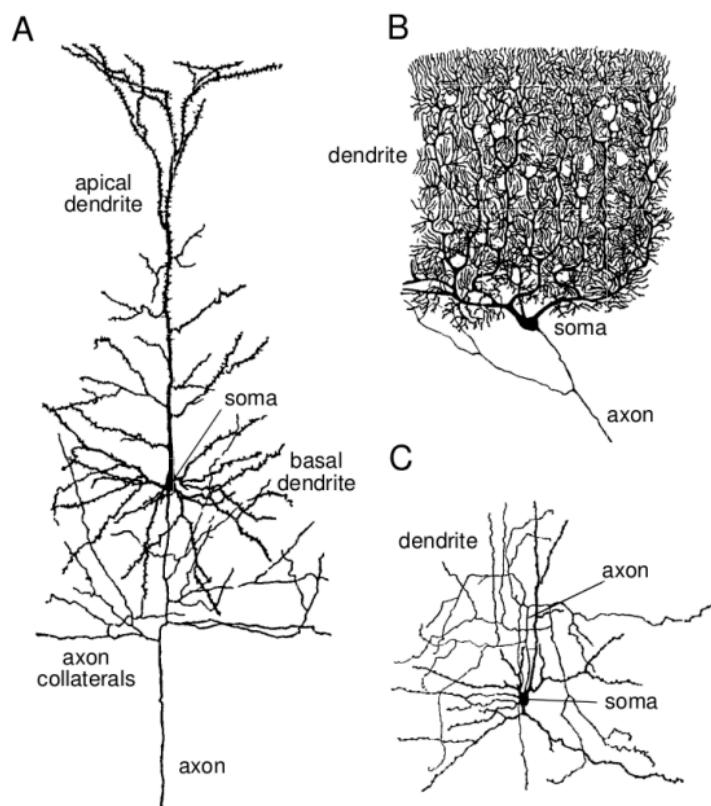
the right answer is B. Since MP is decreasing above the rest potential, this is a hyperpolarizing current.

The Neural Cell, Part II

12/03/2024, 19/03/2024

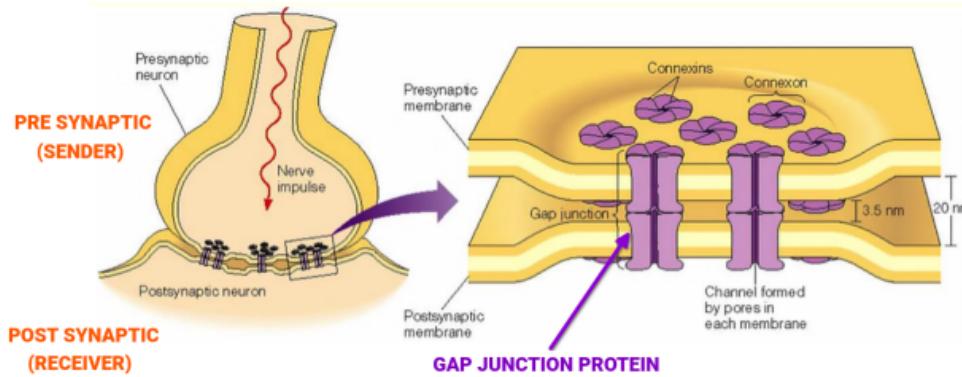
Dendritic Tree:

The first function of the neuron, the collection of information, is performed by the dendritic tree. The tree structure has the advantage of maximizing as much as possible the surface. Different kinds of neural cells have different forms of the dendritic tree:



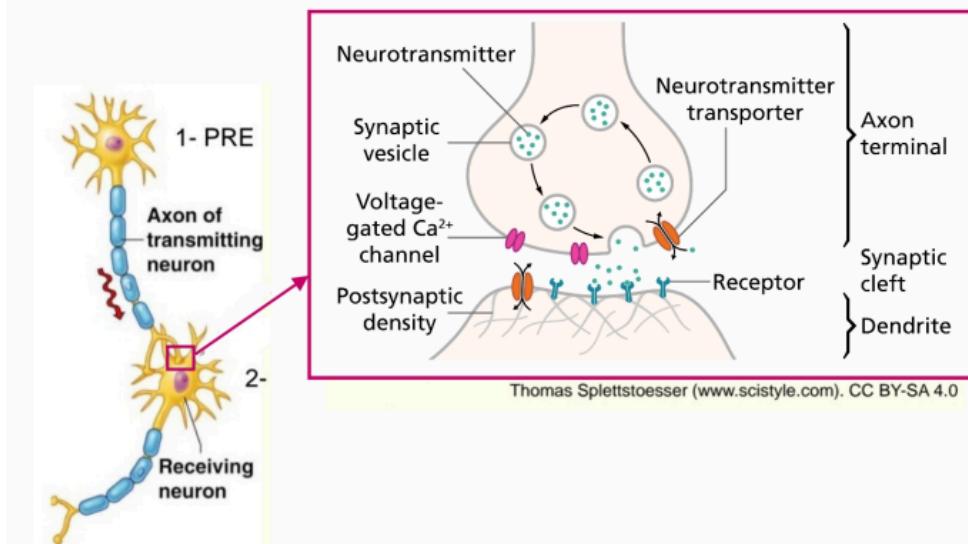
This difference influences the number of connections between neurons. And exchange of information between cells happens through the synaptic connections. The synapse is the structure that permits the synaptic connection. There exist two types of synapses:

- Electrical synapses: not common in the brain, they are based on electrical signal

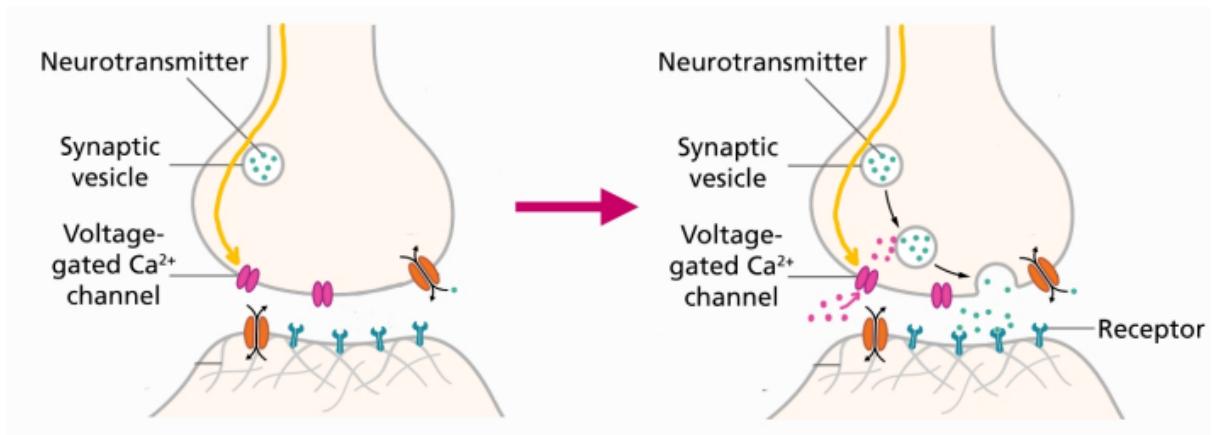


This kind of synapses allow a direct signal transmission from an electrical source, the sender, called pre-synaptic, to an electrical destination, the receiver, called post-synaptic. The exchange is mono-directional. The two cells are physically in contact through a protein called Gap Junction. Since it uses only pure electrical signals, the electrical synapse has a fast transmission.

- Chemical synapses: common in the brain, they are based on chemical signals. They are slower, but more flexible. The two cells are not physically in contact but there is a gap called synaptic cleft, where the exchange happens.



When at rest, the neurotransmitters are in the synaptic vesicles. When the pre-synaptic neuron sends a signal to the Voltage gated calcium channels (Ca²⁺), that allows the passive entrance of calcium ions that, binding to the synaptic vesicles, permit the release of the neurotransmitters. After being released from the vesicles, the neurotransmitters bind to the receptors present on the receiver dendrites. Now ion gated channels open and the passive passage of ions is allowed.

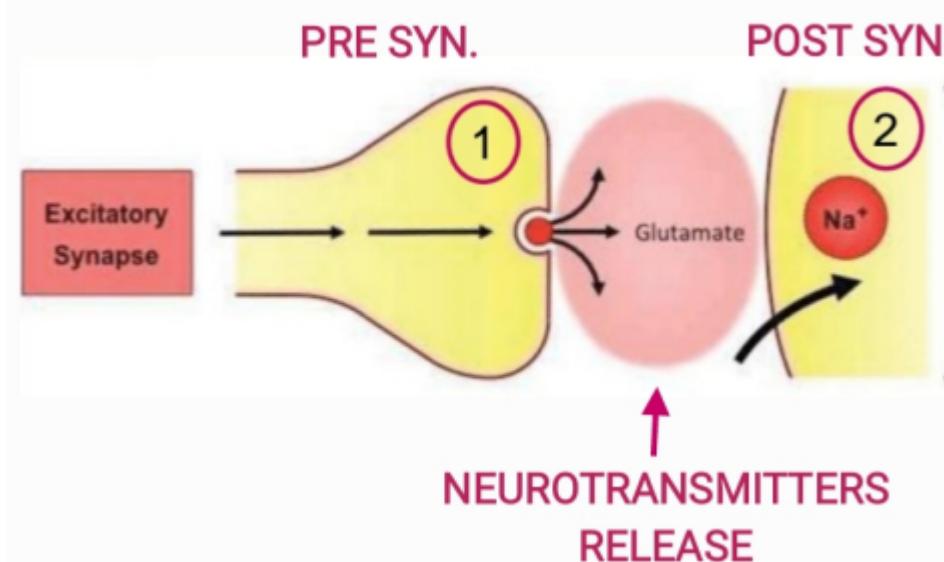


From now on, we will refer to chemical synapses

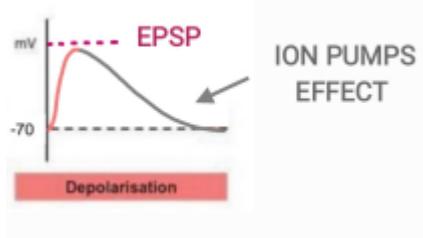
Post synaptic potential:

After the activation of the receptors on the postsynaptic neuron, the MP of the postsynaptic neuron reaches the Post Synaptic Potential PSP. More precisely, we have:

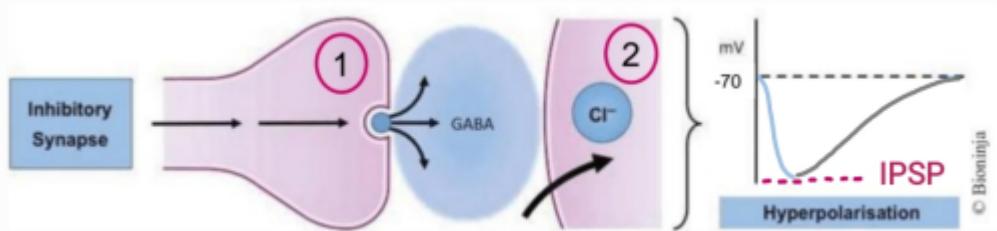
- an excitatory synapse when the pre-synaptic neuron releases an excitatory neurotransmitter like Glutamate, with which there is passive entrance of positive ions (sodium, Na^+). In this case, the PSP reached by the post-synaptic MP is the Excitatory Post Synaptic Potential (EPSP).



- After a while the MP returns to the rest potential thanks to the ion pumps action:



- an inhibitory synapse when an inhibitory neurotransmitter like GABA is released, with which there is an entrance of negative ions (Chlorine Cl⁻). In this case the postsynaptic MP reaches the Inhibitory Post Synaptic Potential (IPSP).



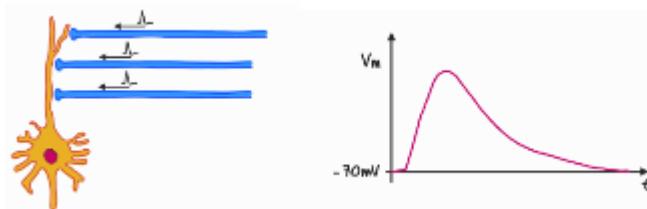
Note that the excitatory and inhibitory effects refer to the excitation and inhibition of the neuronal response: excitatory synapses stimulate the generation of electrical signals that propagate through the neurons while inhibitory synapses do the opposite.

WHO DECIDES IF WE NEED TO USE AN EXCITATORY OR AND INHIBITORY SYNAPSES? DANIELE FOUND ONLINE THAT THE NEUROTRANSMITTERS DECIDE IT BASED ON WHICH RECEPTORS THEY BIND TO

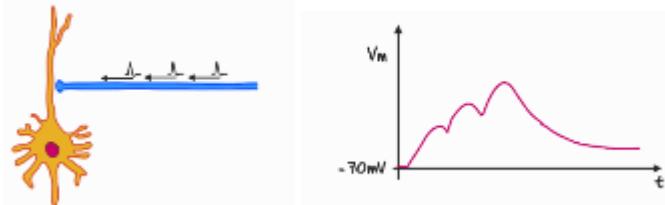
Summation of PSPs:

Since a neuron is usually connected to a lot of other cells, it has multiple chemical synapses, whose effects are summed, to get the final PSP. There are two types of PSPs summation:

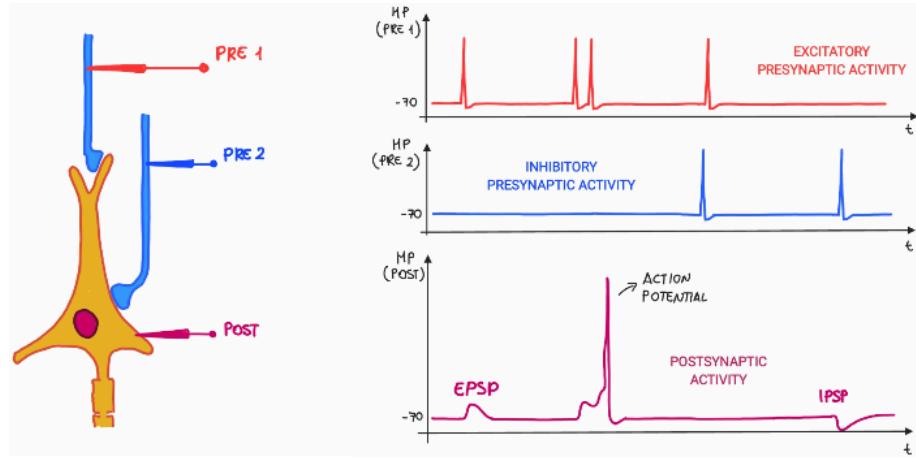
- Spatial Summation: different presynaptic neurons are firing at the same time but at different synapses. Their effects are summed (assuming only excitatory):



- Temporal Summation: the same or nearby presynaptic neurons fires multiple times in close succession. Their effect are summed (assuming only excitatory):



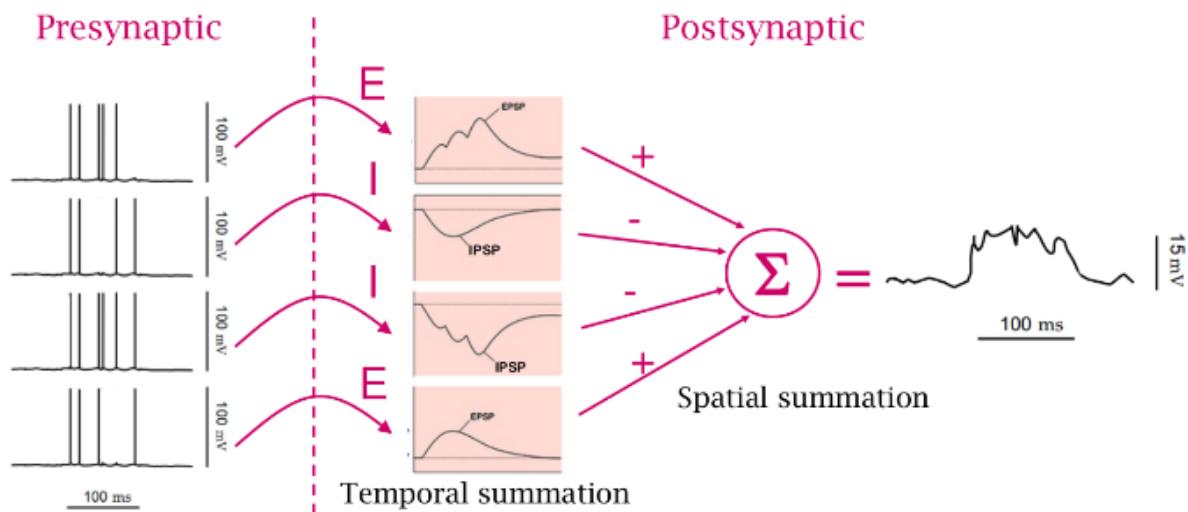
Here is a more complete example that takes into account both effects:



Looking in the postsynaptic neuron MP graph, the spike, caused by a temporal summation of the signals of the presynaptic neuron 1, is related to the **action potential**. If the signal is above a specific threshold in fact, the action potential is produced.

From discrete to continuous signal:

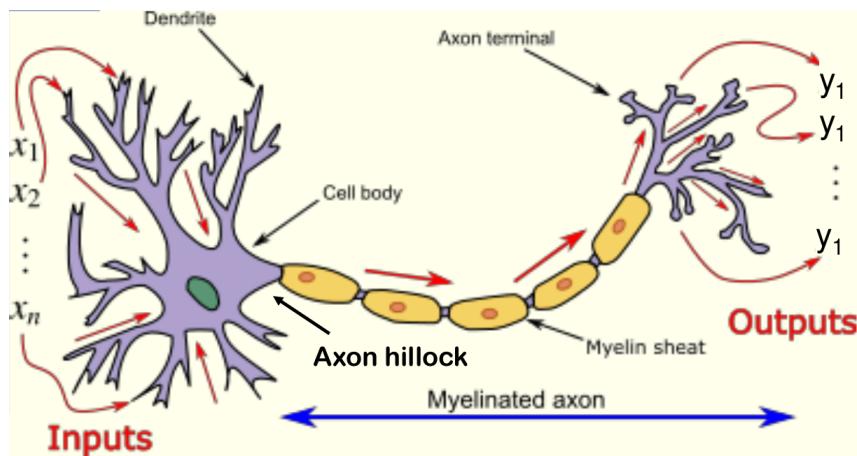
The presynaptic neurons send binary signals to the postsynaptic neuron. The postsynaptic neuron MP varies in a continuous manner, depolarizing or hyperpolarizing. So from binary impulses we obtain a continuous variation of the MP



Integration of Information:

The integration of information happens in the dendritic tree **IS THE TEMPORAL AND SPATIAL SUMMATION? SO WHAT WE HAVE STUDIED UNTIL NOW?**

Assuming the integration of information means the summation, after the integration we have a single continuous signal that is the membrane depolarization or hyperpolarization. This continuous signal is then propagated along the membrane up to the axon hillock where the binary output decision is made: firing or not an electrical signal called action potential.



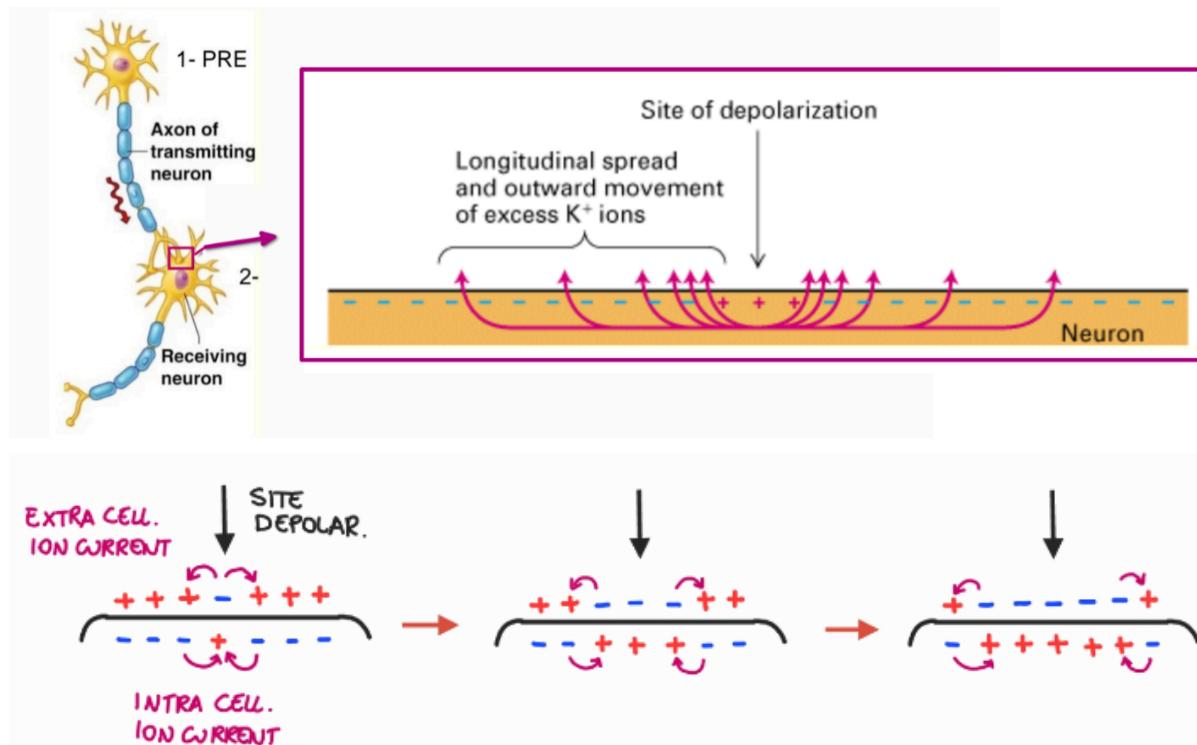
First of all, let's see the propagation of the signal in details

Propagation of the post-synaptic potential:

The depolarization or hyperpolarization inside the dendritic tree causes intracellular and extracellular ion currents. **How does it work? If it's depolarization is intracellular and extracellular if there is hyperpolarization?**

When there is de/hyperpolarization the ions are free to move, so the current is possible. At rest (**potential?**), on the other hand, the ions are not free to move, since there is an homogeneous potential: the inside of the neuron is negative and the outside is positive.

This ions current passively propagates the variation of the post-synaptic MP to the adjacent sections of the membrane. This perturbation effect decreases with distance.



The Action Potential:

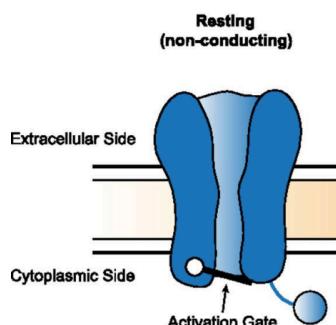
It is a variation of the MP which appears only in neural, muscular and cardiac cells (excitable cells). It's an *all-or-none* process: if the input does not reach the threshold it does not happen; if the threshold is reached, the action potential has always the same shape, duration and intensity, irrespectively to the input stimulus amplitude.

Basically, it's the binary decision, that is the output of the neuron. While the acquisition and the integration of the inputs happen in the dendritic tree, the action potential is generated (high output) or not generated (low output) in the axon hillock.

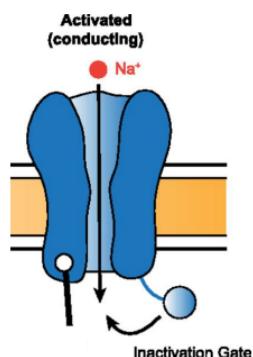
The voltage-gated Na⁺ and K⁺ channels

Two channels are at the base of the action potential generation.

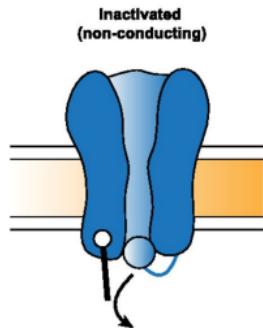
- The voltage-gated Na⁺ channel has three different states:
 - Resting State (non-conducting): the **activation gate** is closed, so Na⁺ ions cannot cross, but the activation gate can be open if the MP reaches the threshold. The MP is at rest potential (-70 mV). **ASSUMING THE ACTIVATION GATE IS THAT BLACK STICK WHILE THE INACTIVATION GATE IS THE BLUE BALL, WE CAN SAY THAT THE INACTIVATION GATE IS OPEN**



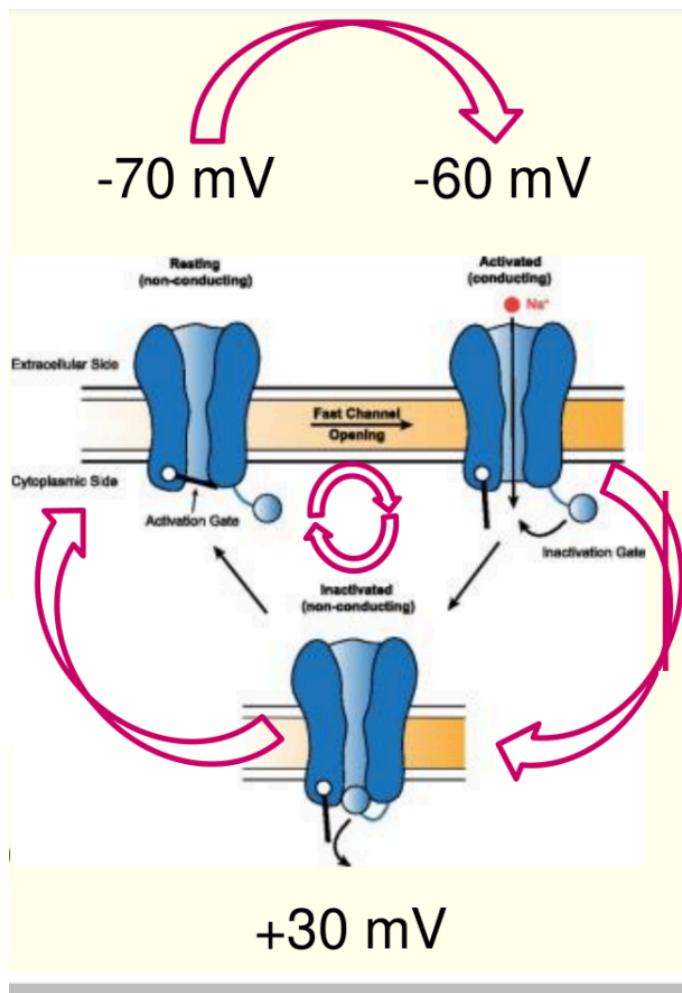
- Activated State (conducting): the **activation gate** is open and the Na⁺ ions can pass through. The opening threshold potential is -60 mV. **ASSUMING THE SAME THING AS ABOVE, WE CAN SAY THAT THE INACTIVATION GATE IS OPEN**



- Inactivated State (non-conducting): the **inactivation gate** is closed, so ions can't pass through as in the resting state, but additionally this state doesn't allow the opening of the **activation gate**. The MP is at +30 mV, so there is a strong depolarization.



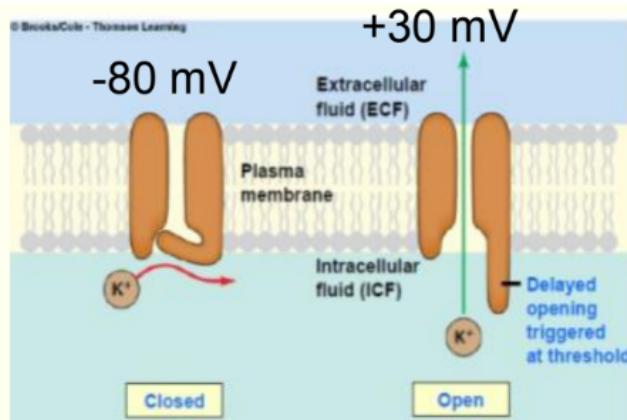
A representation of the transition between these states is represented here:



DAL DISEGNO MI SEMBRA DI CAPIRE CHE DA +30 PER RIAPRIRE IL CANALE BISOGNA SCENDERE FINO A -70 E NON BASTA RISCENDERE A -60

- The voltage-gated K⁺ channel has two states:

- Closing threshold potential (< -70 mV): the gate is closed and ions cannot cross it, but it can be open.
- Opening threshold potential ($+30$ mV): the gate is open and ions can cross it



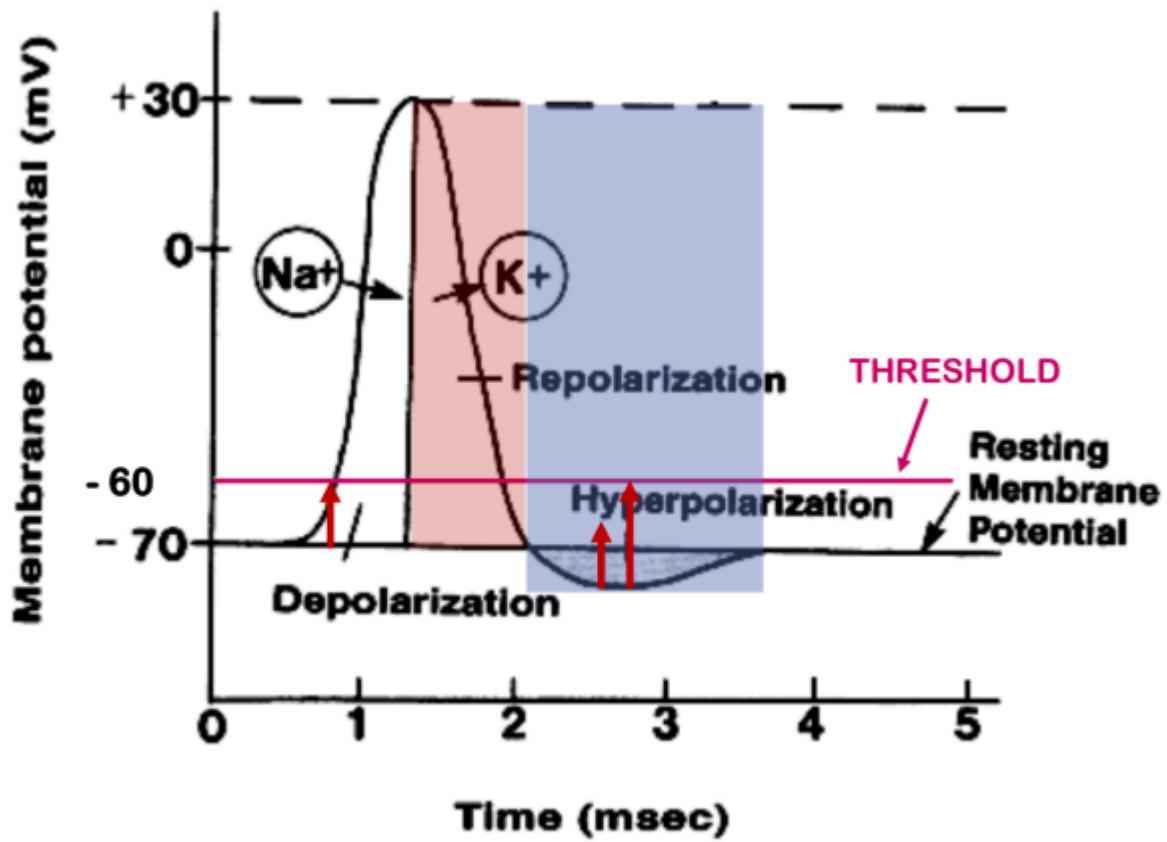
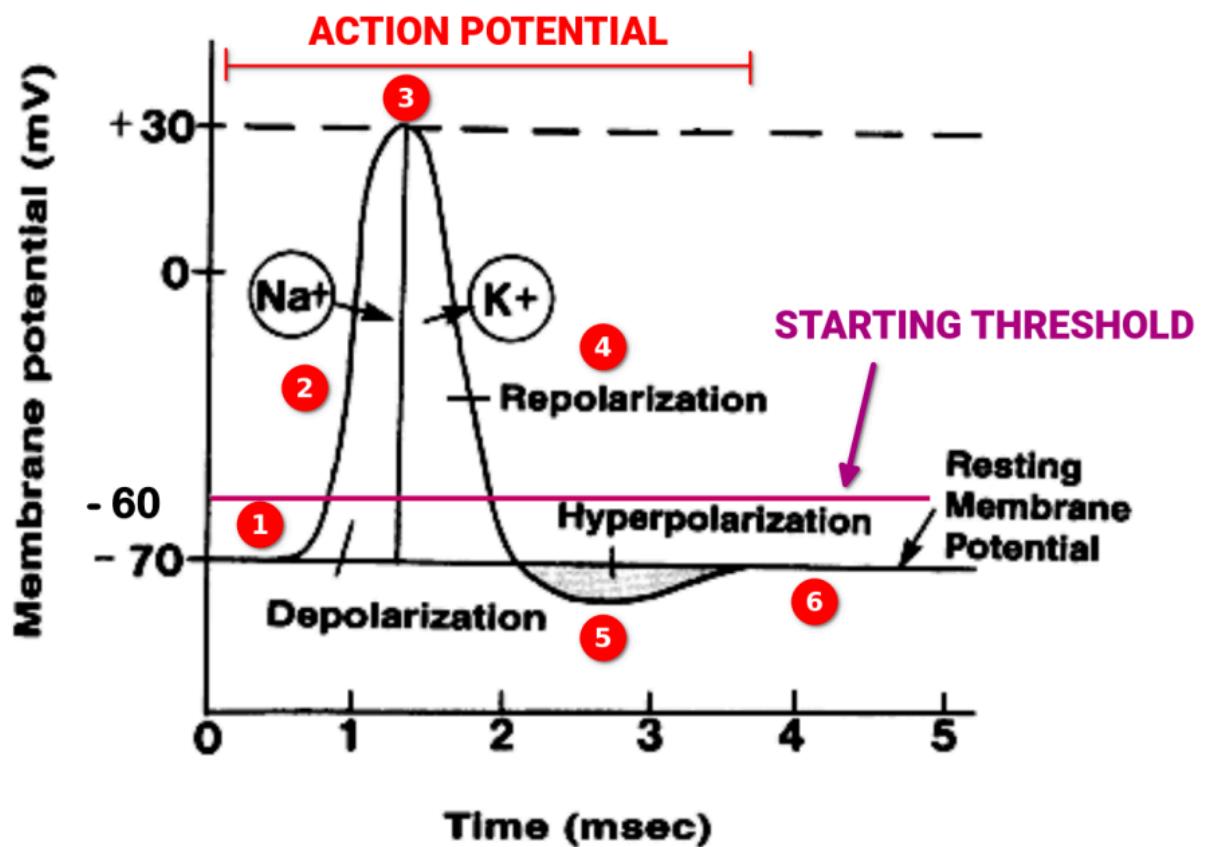
To close the gate and come back to the initial state the membrane potential has to reach a potential below the rest potential (-70 mV). SO DOES THAT MEAN THAT WE START WITH -70 mV AT REST WITH CLOSED GATE, THEN WE DEPOLARIZE AND THE GATE OPENS, THEN WHEN WE WANT TO CLOSE AGAIN THE GATE WE HAVE TO GO **BELLOW -70 mV?** OTHERWISE AT REST POTENTIAL THE GATE WILL REMAIN OPENED?

Action Potential Signal:

Now that we have understood how the gate states and their potential threshold, we can address the several phases of the action potential signal.

When the summed up signal arrives at the axon hillock, and the MP potential is above -60 mV, the action potential signal is generated. The action potential starts and ends always with same shape, timing (duration of 2 ms), and amplitude (100 mV):

1. Initial depolarization: depolarization to the Na^+ opening threshold level (-60 mV).
ACTUALLY THIS SHOULD BE SOMETHING THAT IS HAPPENING BEFORE THE ACTION POTENTIAL IS GENERATED, SINCE TO BE GENERATED, THE MP POTENTIAL MUST BE ABOVE -60 mV
2. Fast depolarization: now the voltage-gated Na^+ channel is open and Na^+ ions, **entering** the neural cell, creates a current. Due to this current the depolarization accelerates, until reaching $+30$ mV.
3. Switch channels: reaching $+30$ mV, the Na^+ channel goes in the inactivated state, so the Na^+ ions current can't flow anymore. At the same time, the K^+ channel opens, allowing K^+ ions to flow **outside** the neural cell.
4. Repolarization: due to the K^+ repolarizing currents, the MP starts decreasing.
5. Undershoot: going below -70 mV, hyperpolarization happens, and the K^+ gate closes. **Now both the Na^+ and the K^+ gates are closed.**
6. Return resting potential: due to the sodium-potassium pump, the MP returns to the rest potential $V_m = -70$ mV.

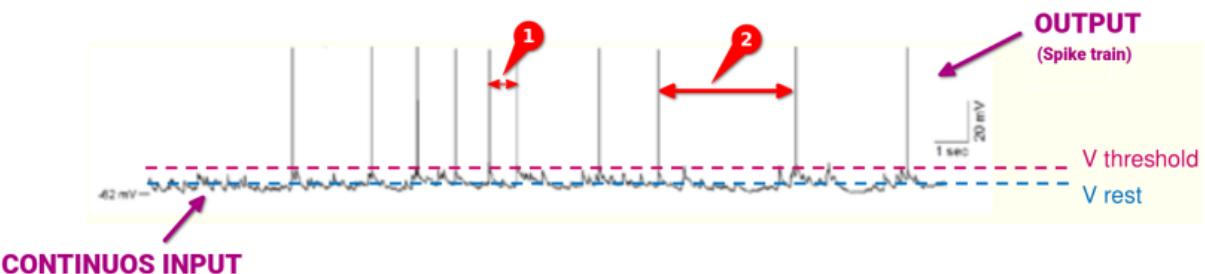


After the peak, we distinguish these two regions:

- Absolute Refractory Period (in red): since the Na^+ channels are closed, no new action potentials can be generated.
- Relative Refractory Period (in blue): now the Na^+ channels are in the resting states, so they can be opened, but the K^+ channels are opened and they provide the hyperpolarization. This means that even if a new action potential can be produced, it requires a stronger depolarization in order to fight the hyperpolarization and so it's less likely to happen.

Informative Content:

Starting from binary inputs, the post-synaptic neuron gets a continuous input by summation, and then it produces (or not) a binary output that is the action potential. Since this is a spike with always the same shape, duration and amplitude, the information content is not in the shape, duration or amplitude, but it's the temporal distance between two spikes. So a train of spikes is created and propagated to the next neuron:



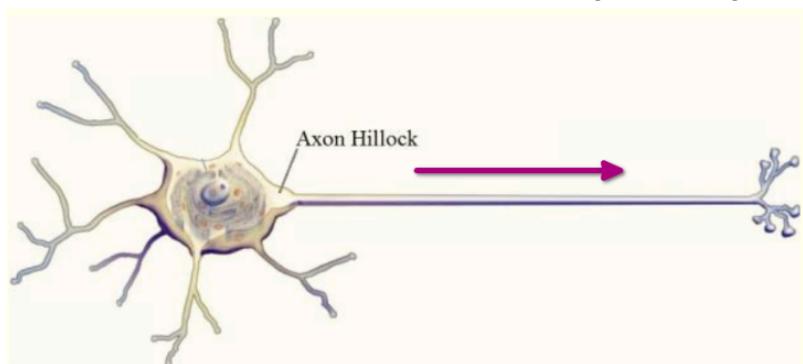
CONTINUOUS INPUT

The next neuron will produce (or not) an activation potential. Precisely:

- For case (1) in the figure the neuron produces an action potential, since the distance between the two spikes is not too big therefore the temporal summation allows to reach the depolarization threshold (- 60 mV)
- For case (2) in the figure the neuron doesn't produce an action potential, since the distance is too big therefore there is not a temporal summation that permits to reach the depolarization threshold

Propagation Action Potential:

Once the signal is generated in a specific point of the membrane, that is usually the axon hillock, the action potential needs to be propagated along the axon toward other cells.



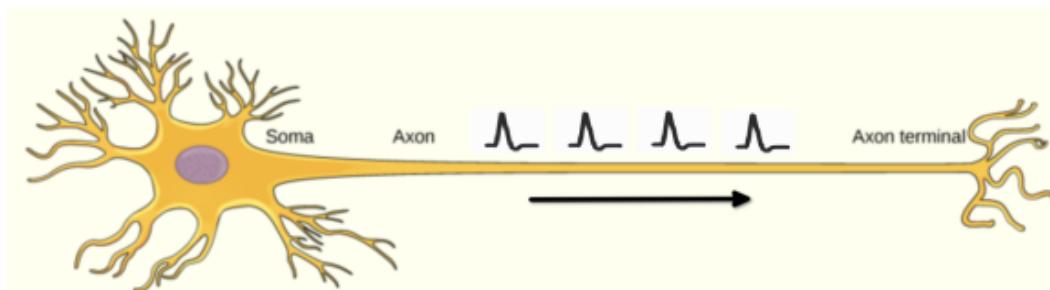
According to neuron type, there are two main mechanisms:

1. Continuous conduction (unmyelinated fibers):
2. Saltatory conduction (myelinated fibers):

Continuous Conduction:

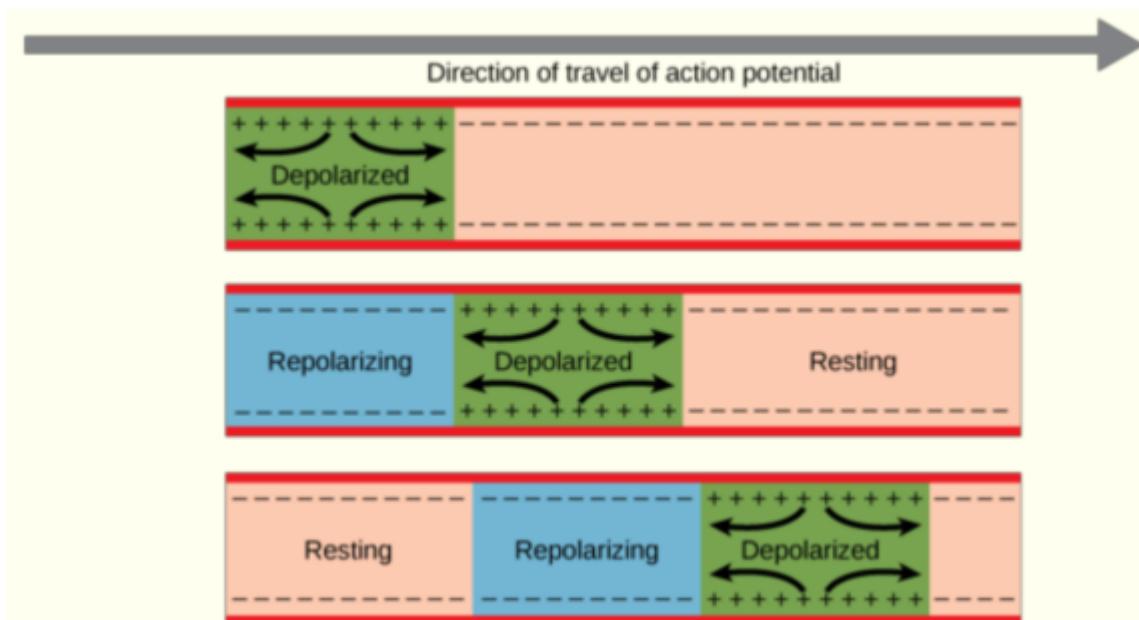
This mechanism is similar to the propagation from the dendritic tree to the axon hillock. Precisely, the action potential is continuously generated at each membrane section.

The fast membrane depolarization induces intra and extracellular ionic currents, according to electrochemical gradients, and these currents propagate the perturbation to the close membrane regions.



In these nearby regions the membrane has the Na^+ and K^+ voltage-gated channels, and so they can produce an action potential. Precisely:

- If in the region the Na^+ gate is ready to open: the depolarizing perturbation produces again an action potential (active generation)
- If in the region the Na^+ gate is inactive: it means that the membrane region has just produced an action potential, so the Na^+ channels will be in their absolute refractory period and thus a new action potential is impossible to produce



Note that the absolute refractory period (indicated with repolarizing in the figure above) is the reason why the action potential propagation is unidirectional.

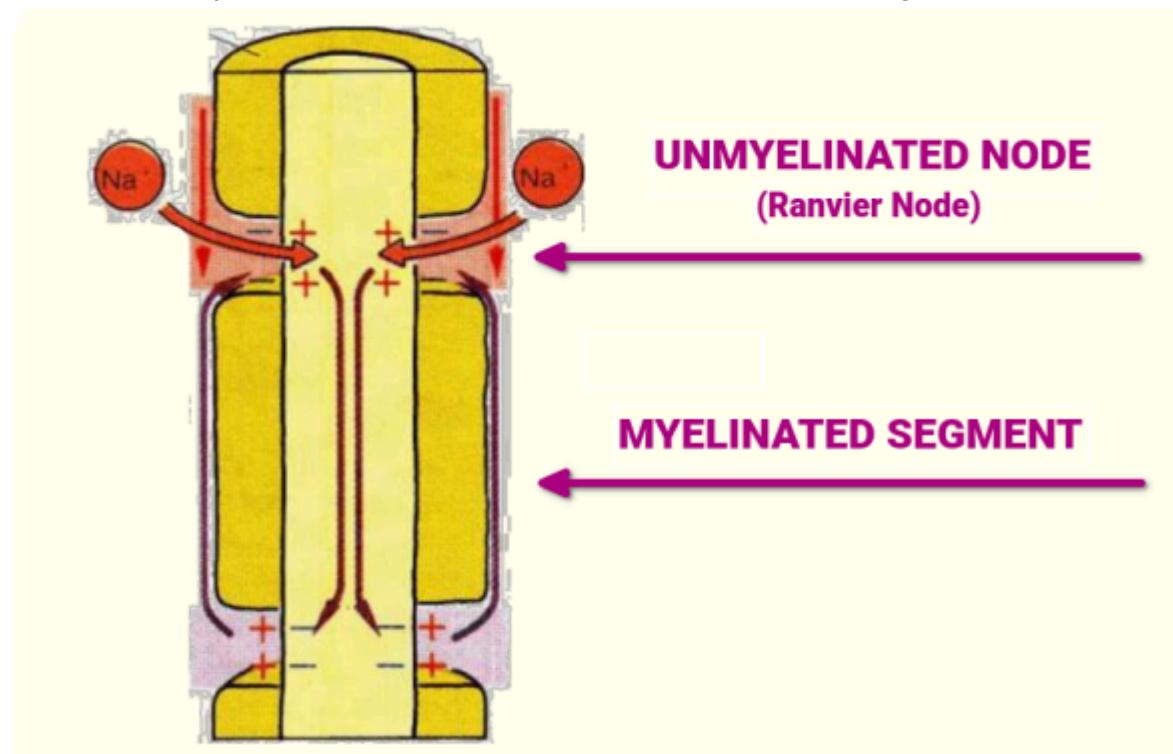
The propagation speed of this type of conduction is limited by the activation of Na^+ and K^+ channels, and it's slow (1 m/s). This mechanism is slow and inefficient since it requires generation of an action potential at each step (heavy process). For this reason it is not common in our neurons.

This conduction is used to transmit delayed signals like pain.

Saltatory Conduction:

This mechanism combines both active and passive conduction methods. It has two parts:

- Myelinated segment: this segment of the axon, surrounded by myelin (that is a lipid-rich substance) able to isolate (**isolate what? the axon?**) and avoid the generation of a new action potential.
- Ranvier nodes (unmyelinated nodes): in this part of the axon there is an interruption of the myelinated sheath, and so it allows an action potential generation



So what happens is that the action potential is generated at the Ranvier nodes (active conduction) and propagated passively along the myelinated segments, until the next Ranvier node, where there is another generation of action potential. This conduction is much faster than the continuous one and allows signal propagation along longer distances, upon centimeters.

This conduction is used to transmit rapid signals like commands to muscles.

Self-evaluation Test 1:

1. How is the membrane potential modified by an excitatory synapse? And by an inhibitory one?

Answer: assuming the MP starts from the rest potential (V_m about -70 mV), an excitatory synapse makes the MP increase until the EPSP (Excitatory Post Synaptic Potential), since the pre-synaptic neuron releases an excitatory neurotransmitter like Glutamate, with which there is passive entrance of positive ions. On the other hand, an inhibitory synapse makes the MP decrease until the IPSP, since the pre-synaptic neuron releases an inhibitory neurotransmitter like GABA, with which there is an entrance of negative ions. After a while, the MP tends to the rest potential again thanks to the ion pumps action.

2. What's the difference between temporal and spatial summation? Can they occur simultaneously?

Answer: thanks to its dendrites, a neuron receives signals from other neurons and sums it to get a single, continuous, signal: the variation of its membrane potential. There is temporal summation when the neuron sums the signals belonging to the same neuron (or nearby neurons) in close succession, while there is spatial summation when the sum is between signals coming from different neurons firing, at the same time, at different synapses of the post-synaptic neuron. Temporal and spatial summation can occur simultaneously.

3. Why is a depolarizing post-synaptic potential called "excitatory"?

Answer: the excitatory effects refer to the excitation of the neuronal response. In fact, an excitatory synapse stimulates the generation of electrical signals that propagate through the neurons

I AM NOT TALKING ABOUT DEPOLARIZATION, SO MAYBE THERE IS SOMETHING ELSE TO SAY THAT I CURRENTLY DON'T KNOW

4. What is the use of an inhibitory PSP?

Answer: the inhibitory effect refers to the inhibition of the neuronal response. That means that it inhibits electrical signals through the neurons NOT SURE ABOUT IT

I AM NOT TALKING ABOUT THE PSP PER SE, SO MAYBE THERE IS SOMETHING ELSE TO SAY THAT I CURRENTLY DON'T KNOW

- A. In a chemical synapses, when a neurotransmitter opens the Na^+ gated channels, the resulting PSP is an inhibitory one

FALSE: when there is a passive entrance of Na^+ ions, it means an excitatory neurotransmitter like Glutamate was released by the presynaptic neuron and so the resulting PSP is an excitatory one.

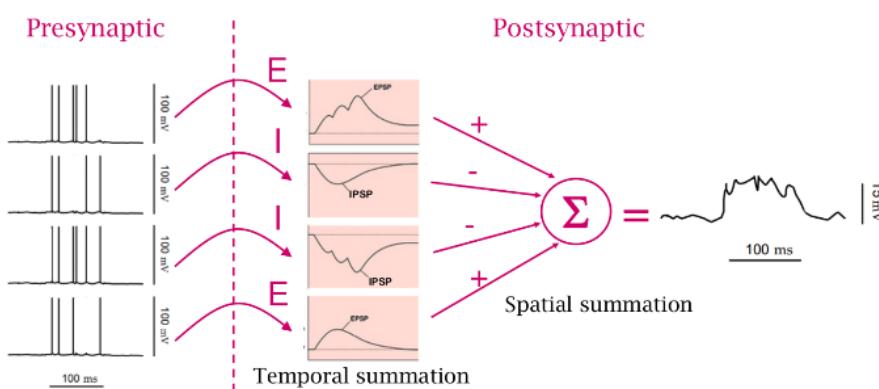
QUESTION: SO WE CAN SAY EXCITATORY SYNAPSES MAKE THE NEUROTRANSMITTER OPEN CHANNELS RIGHT? PRECISELY Na^+ GATED CHANNELS?

- B. Two PSPs can never cancel each other.

FALSE: if an inhibitory and an excitatory effects are summed, the two effects cancel each other out.

- C. The effects of temporal and spatial summation are also reciprocally summed up.

TRUE: **IF I UNDERSTOOD THE QUESTION CORRECTLY.** In the postsynaptic neuron, after the summation process, there is only one continuous signal, so the temporal and spatial summation need to be summed up to get a single signal.



Self-evaluation Test 2:

1. Do we need to measure the amplitude and duration of an action potential each time it occurs to understand the cell behavior?

Answer: the shape, duration and amplitude of the action potential is always the same, so we don't need to measure these metrics each time. The information content it's the temporal distance between two action potentials spike.

THERE IS ANYTHING ELSE TO SAY?

2. Which parameter of the spike train in output to a neuronal cell is the most informative:
 - A. The amplitude of the spikes
 - B. The duration of each spike

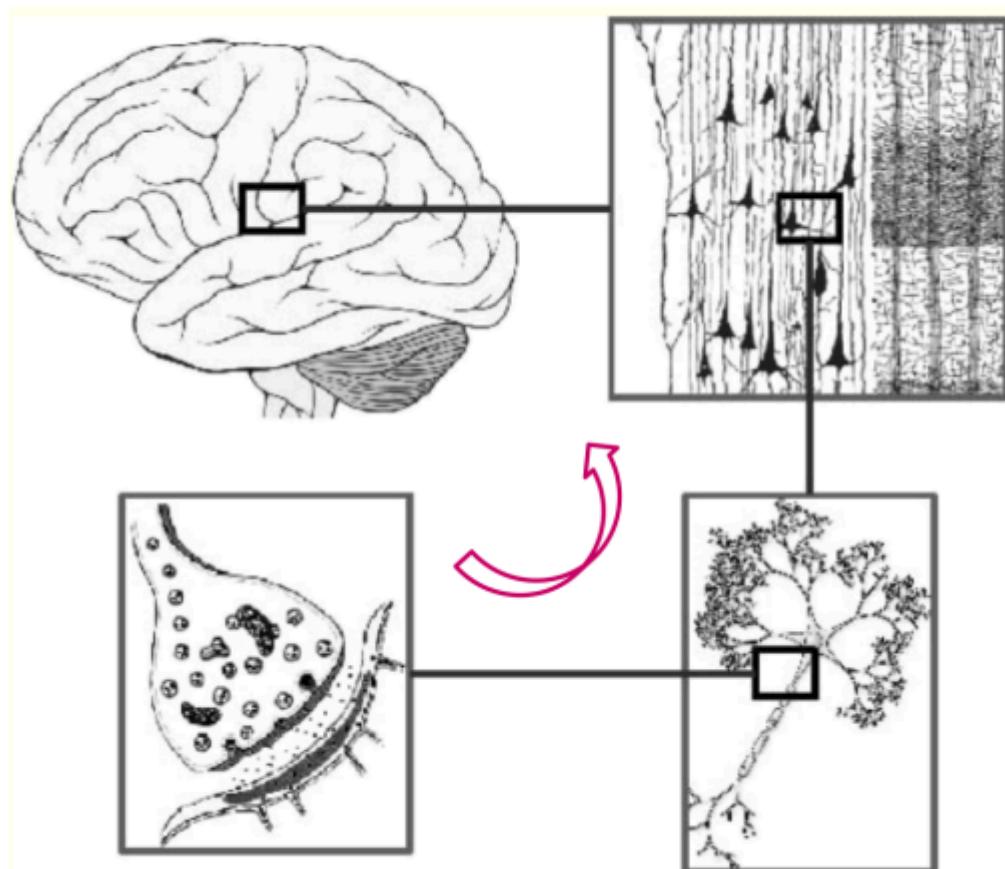
- C. The temporal distance between spikes
- D. The spatial position in which the spikes are generated
3. What will the frequency of the spikes influence:
- The temporal summations of the PSPs
 - The spatial summation of the PSPs
 - The amplitude of the resulting action potential in the post-synaptic cell
-
- CONTINUOUS INPUT**
- The next neuron will produce (or not) an activation potential. Precisely:
- For case (1) in the figure the neuron produces an action potential, since the distance between the two spikes is not too big therefore the temporal summation allows to reach the depolarization threshold (- 60 mV)
 - For case (2) in the figure the neuron doesn't produce an action potential, since the distance is too big therefore there is not a temporal summation that permits to reach the depolarization threshold
- It's not C since the amplitude of the action potential is always the same
4. The absolute refractory period is due:
- To the chemically controlled Na^+ channel
 - To the chemically controlled K^+ channel
 - To the voltage-gated Na^+ channel**
 - To the voltage-gated K^+ channel
- This period is due to the fact that Na^+ channels are closed, so new action potentials can't be generated.
5. The saltatory (myelinated) conduction is faster than the continuous one (T/F) **True**
6. A hyperpolarization of 10 mV with respect to the resting potential causes the generation of an action potential (T/F) **False: the MP must be at -60 mV (10 mV above the resting potential), so it's a depolarization that causes the action potential generation**
7. A depolarization of 20 mV causes a stronger action potential than a depolarization of 10 mV (T/F) **False: the amplitude of the action potential is always the same, so by how much the threshold is overcomed doesn't change the strength of the action potential**

Principles of Neuroanatomy and Brain Organization

28/03/2024

Introduction:

The brain structure is organized in several levels



Studying subjects with brain lesions, knowing the function they have lost and the brain areas they have lost, we were able to conclude connections between the brain areas and the functions. Now we have more modern techniques to study the brain, such as [neuroimaging](#) and neuromodulation¹⁹.

Goal of the Brain: predicts the future on the basis of the past, helping the individual to survive and perpetuate the species

The Brain in Time and Space:

At the level of a single neuron, we are:

- in the temporal scale of milliseconds
- in the spatial scale of μm and nm : the neuron soma is in the order of μm while the membrane thickness is in the order of nm .

The brain evolves both:

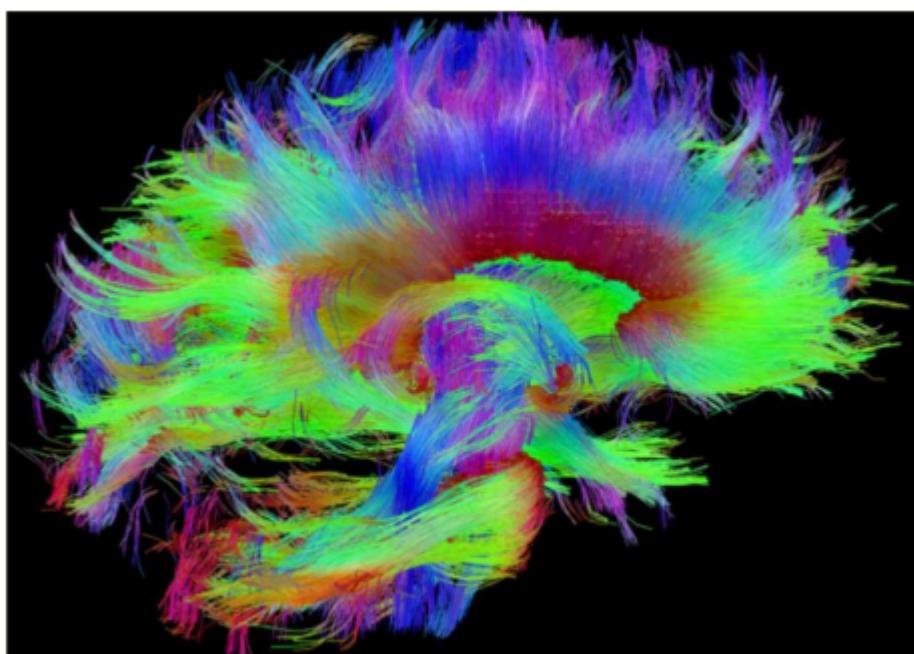
¹⁹ safely stimulate some parts of the brain

- from collective point of view, with the evolution of the human species
- from an individual one: the brain is plastic during the entire lifespan of the individual, allowing learning, memorization, spontaneous recovery and neurorehabilitation

Grey and White Matter:

Both of this matters are part of the neuron cells:

- Gray matter: cell body and dendrites of the neuron. This matter is related to information *processing*
- White matter: fibers, myelinated axons of the neuron. This matter is related to information *propagation*. Basically is the information transport system of the brain. The *corpus callosum*, the “highway” of information between the two brain hemispheres²⁰, is made of white matter. Using an *In Vivo* procedure based on DTI²¹, it is possible to obtain the white matter tractography that represents the brain network and the direction of information flow.



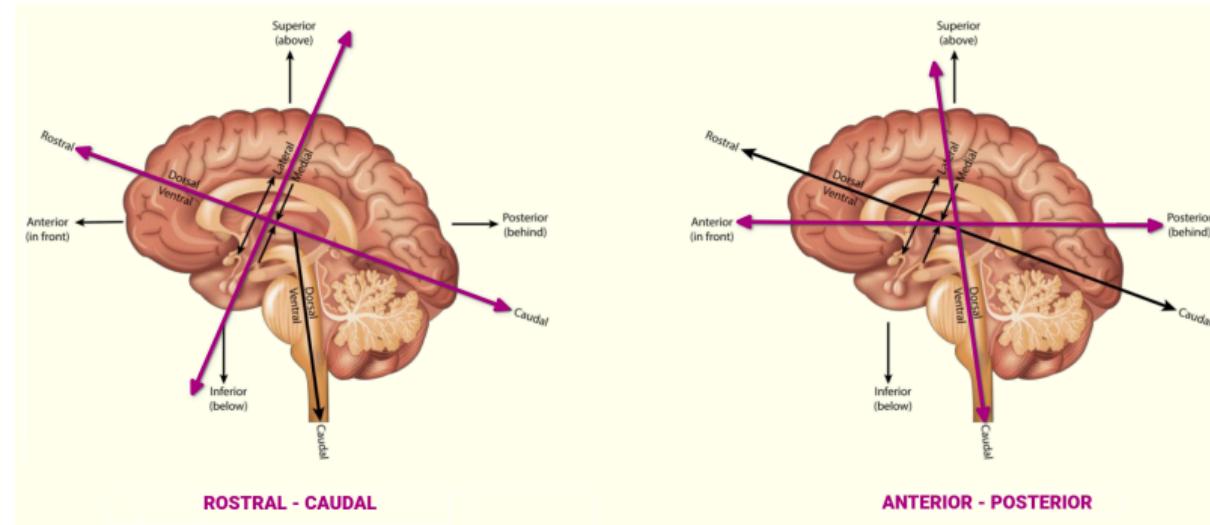
DTI image, Laboratory of Neuro Imaging at UCLA and Martinos Center for Biomedical Imaging at MGH, Consortium of the Human Connectome Project

²⁰ the brain is divided into two symmetric hemispheres. They are separated but they work together.

²¹ non-invasive procedure through a magnetic resonance machine

Terminology:

The brain can be divided into two different ways:



The following terms are used a lot in the field:

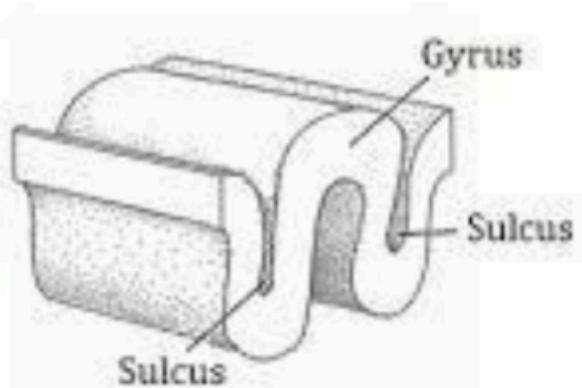
- Anterior: in front of
- Posterior: behind
- Superior: above
- Inferior: below
- Rostral: towards the front of the brain
- Caudal: towards the back of the brain
- Ventral: towards the belly (**the belly?**)
- Dorsal: towards the back (**the back?**)
- Proximal: closer to a set point
- Distal: farther from a set point
- Medial: towards midline of body
- Lateral: towards appendages
- Contralateral: on the opposite side (opposite hemisphere)
- Ipsilateral: on the same side (same hemisphere)

Brain Cortex:

The cortex is the external surface of the brain. It contains most of the gray matter of the brain. The cortex it's about 1.5% of the body weight but it uses 15% of the total blood flow, considering that the whole brain uses 20%. The brain cortex is folded in order to have, in a limited volume, more the cortical surface. There are two types of folds are:

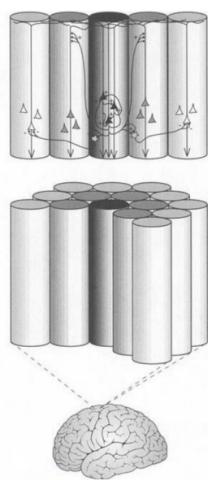
- Gyrus²²: outwards folding
- Sulcus: inward folding. Sulci represents $\frac{2}{3}$ of the surface, so most of the cortical surface is hidden.

²² gyri and sulci are, respectively, the plurals

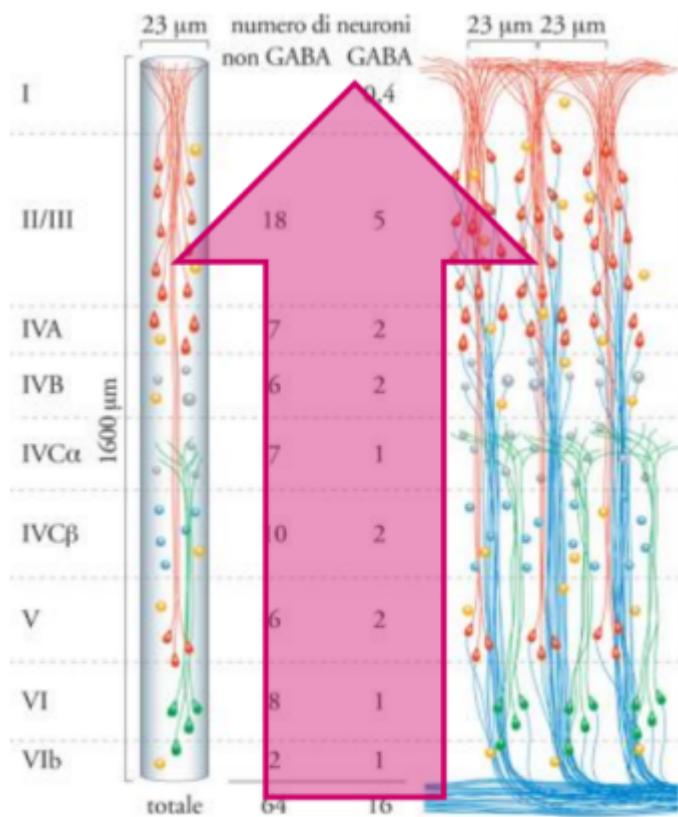


Cortical Organization:

Brain cortex is divided into 6 vertical interconnected layers. Inside each layer, neurons are organized in columns that have 0.5 mm of diameter and are perpendicular to the cortical surface. **A column has all of the 6 cellular layers (OR DOES A COLUMN BELONGS TO A SINGLE LAYER).** Inside a column there is the same type of neurons with the same function, so they have the same behavior in response to the same stimulus.



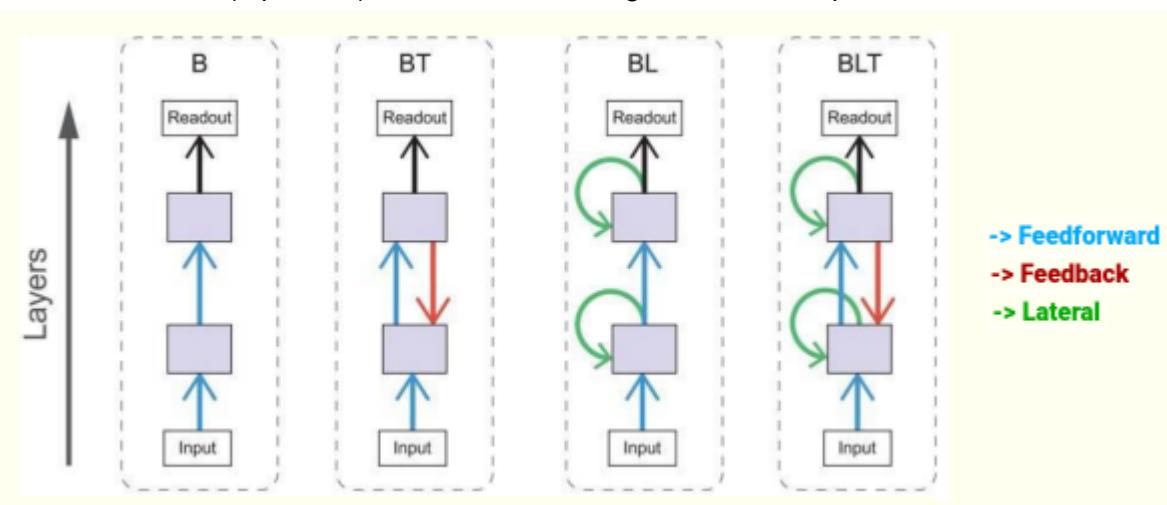
The information flow direction is the following:



Information processing

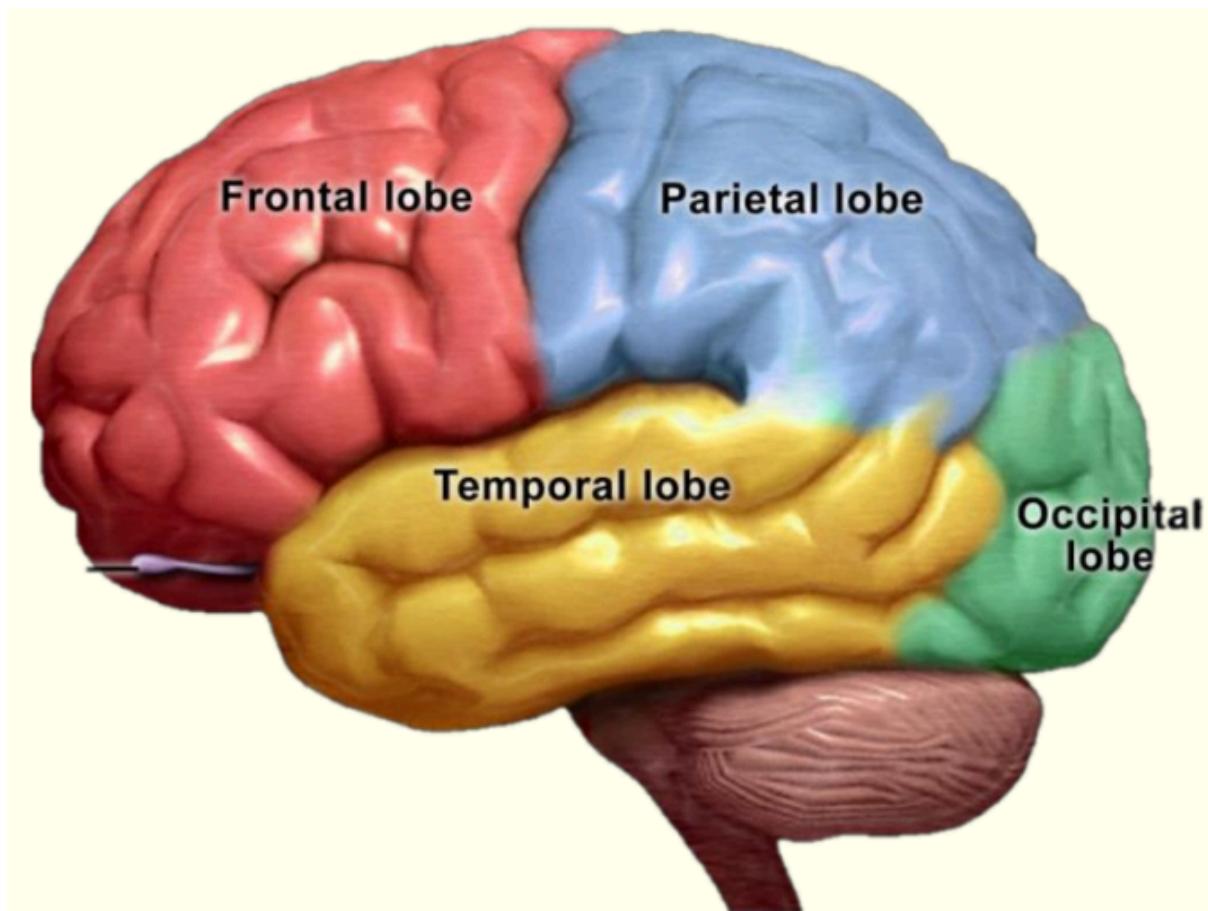
We have three main typologies of neural connections:

1. Feedforward (bottom-up): directed from regions at the first processing stages to the following ones
2. Lateral: they link same stage region
3. Feedback (top-down): from advanced stages back to the previous ones



The majority of the connections are lateral ones. All these connections can be both excitatory or inhibitory.

Brain Lobes:



1. Frontal Lobe: control center for the executive functions, namely:
 - a. reasoning
 - b. decision-making
 - c. expressive language
 - d. higher level cognitive processes
 - e. orientation
 - f. planning and execution of movement
2. Parietal Lobe:
 - a. primary and secondary somatosensory²³ cortex
 - b. spatial navigation
 - c. touch, pressure, temperature and pain
3. Occipital Lobe:
 - a. primary visual cortex
 - b. processing and interpretation of visual information
4. Temporal Lobe:

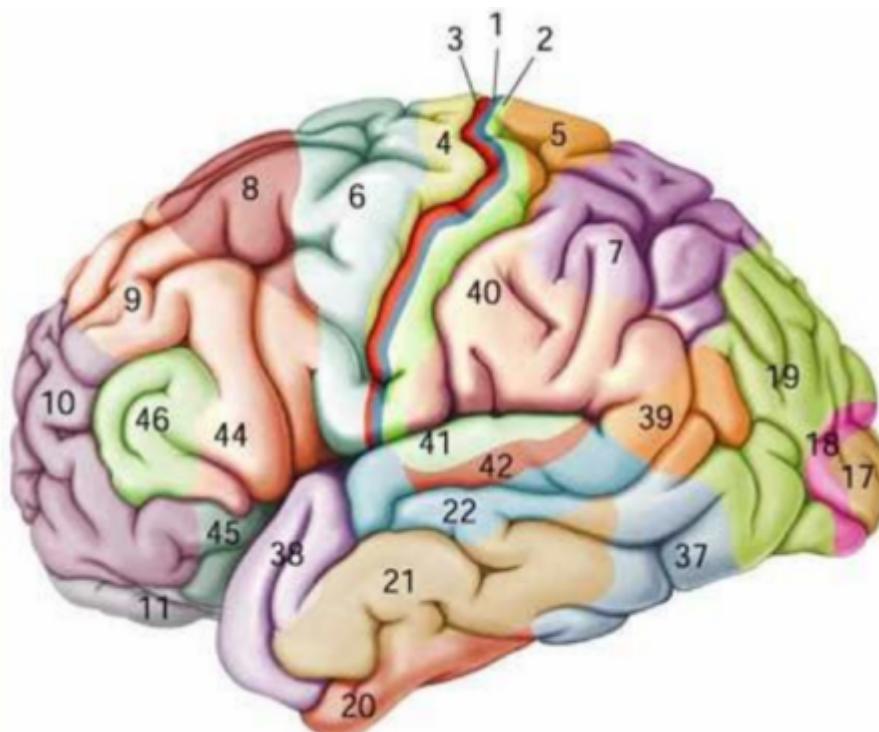
²³ The somatosensory pathways transmit impulses of tactile, proprioceptive, thermal and pain sensitivity.

- a. auditory cortex
- b. center for receptive language
- c. hippocampus (memory formation and emotion)

Note that the cerebellum²⁴ is not a part of the brain.

Brodmann Areas:

Each lobe is composed of different areas called Brodmann areas. Each of these areas is defined by its cytoarchitecture, namely its neural cells type and organization, and associated to a specific function.



Multiple areas may participate in the same function: e.g. areas 3, 1 and 2 all comprise the sensory cortex

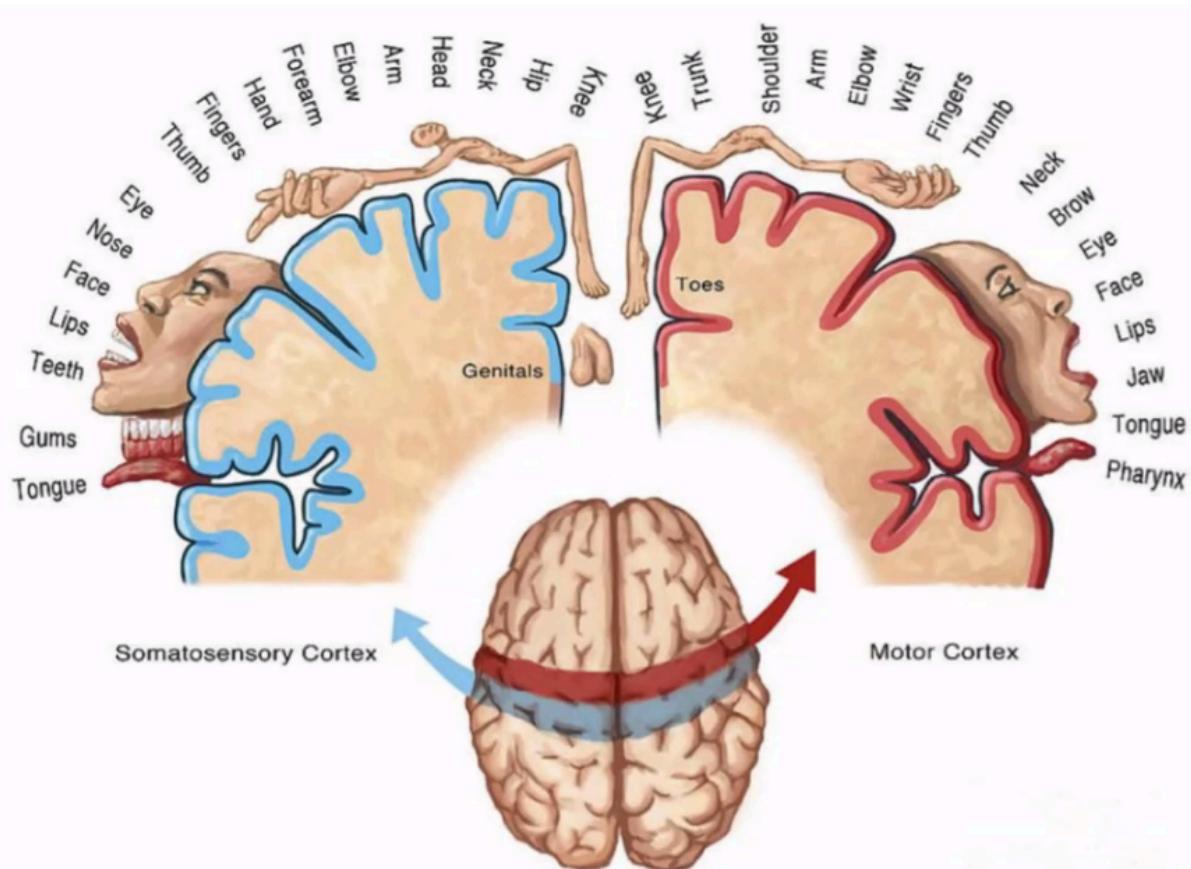
Cortical Feature Maps:

Cortical maps are areas of minicolumns (**so they are inside a column?**) in the brain cortex that perform a specific information processing function. For instance: texture maps, color maps, contour maps. Let's see two cortical feature maps:

1. Retinal Mapping (Retinotopy): **this is in the visual cortex.** This mapping is a transformation of the visual image from retina to V1 (Primary Visual Cortex) neurons. This area is highly specialized for information about static and moving objects and is excellent in pattern recognition. The neurons in this feature map are specialized for shape, movement, contrast and other things.
2. Somatotopic: this is in the motor/somatosensory cortex.

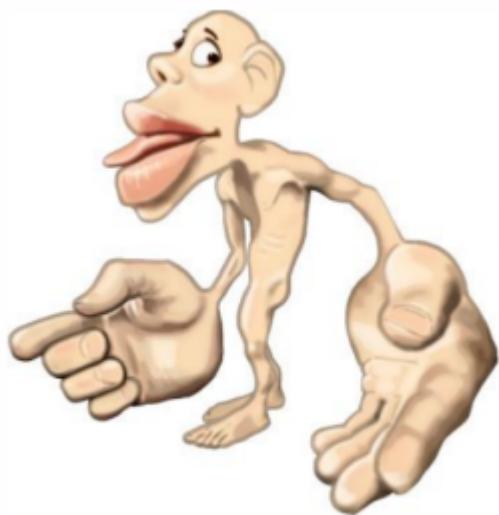
²⁴ cervelletto in italiano

- a. Motor Cortex: region of the cerebral cortex involved in the planning, control and execution of voluntary movements. This is in the pre-central gyrus of the frontal lobe (Brodmann area 4).
- b. Somatosensory Cortex: is responsible for receiving and processing sensory information from the body, such as touch, temperature and pain. This is in the post-central gyrus of the parietal lobe (Brodmann areas 3,1,2)



Note that the two red and blue stripes (respectively in the pre-central gyrus of the frontal lobe and the post-central gyrus of the parietal lobe) are dissected and shown above in detail. In the section relating to the motor cortex, it is shown which portions of the red stripe are associated with which parts of the body can be moved voluntarily. A similar question applies to the somatosensory context.

The Penfield Homunculus shows the difference in the number of neurons that are associated with each part of the body. The Penfield Homunculus is typically depicted as a distorted humanoid figure, with disproportionately large hands, lips, and face, reflecting the amount of cortical space dedicated to processing sensory and motor information from those body parts. For example, the hands and lips are much larger compared to other body parts because they have a higher density of sensory receptors and require finer motor control. This homunculus was derived from stimulating awake patients during epilepsy surgery.



PENFIELD HOMUNCULUS

A higher number of neurons is associate with a sensitive area or a requirement for high motion precision

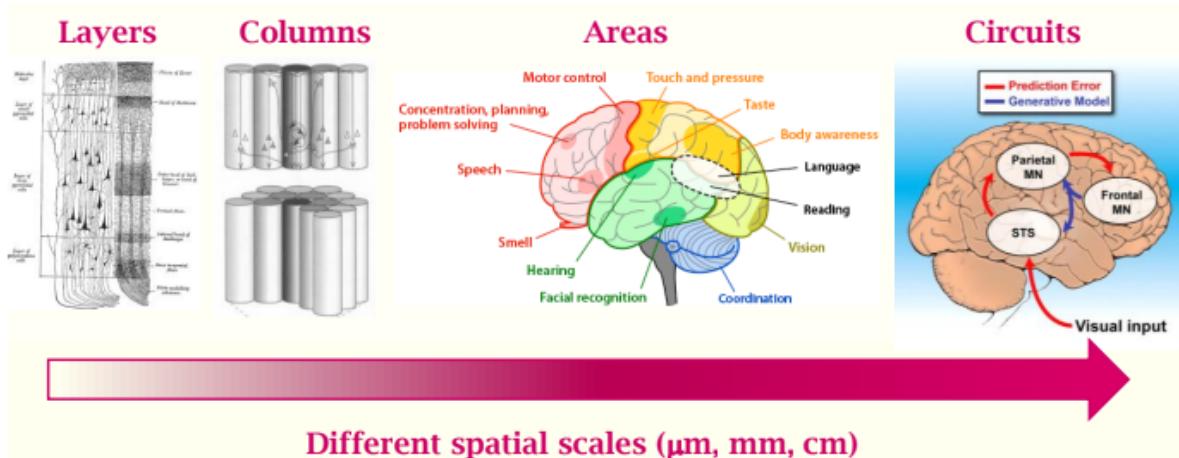
Property of the Brain (Contralateral): the left hemisphere controls the right part of the body while the right hemisphere controls the left one.

Subcortical Areas:

Until now we have talked about the cortex, so the most external part of the brain. The subcortical area is more different to reach, especially with a non-invasive method. While the cortical areas are related to advanced functions like language, subcortical areas are related to more primitive functions. Some subcortical areas are:

- Thalamus: controls traffic from most of peripheries to the cortex (**sensory afferent**)
- Brainstem (tronco encefalico in italian)
- Basal Ganglia
- Cerebellum (**didn't we say that is not part of the brain?**)

Summary Brain Organization:



Each spatial level is important, indeed, when we are interested to study a specific brain function, we focus only to a specific level. For example, to understand how action potential is generated we have reasoned at the level of a single neuron, other functions like memory instead, must be studied at higher level like areas or circuits.

THE REST IS ON THE PDF NOTES_PART_A.PDF, FROM PAGE 38