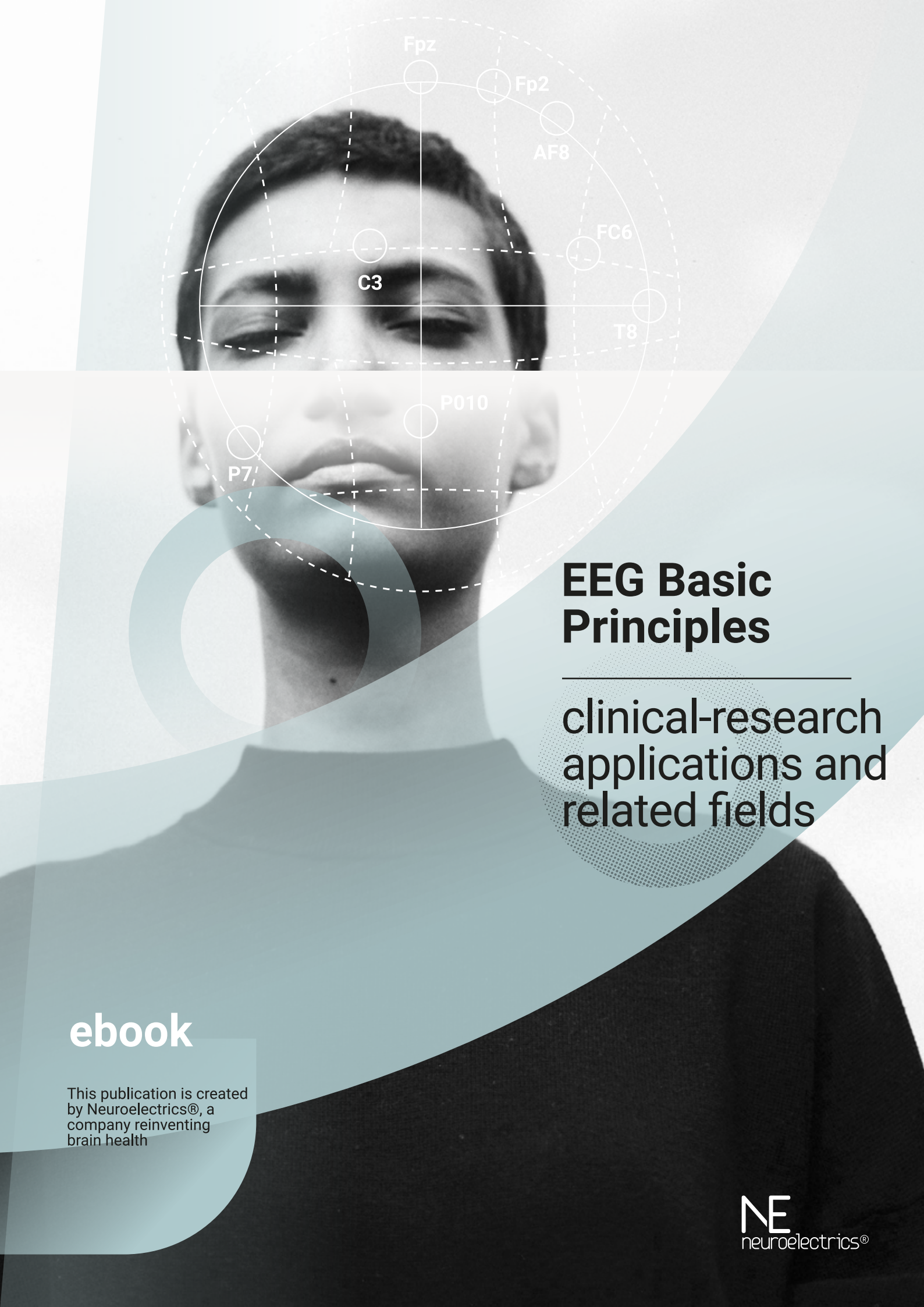

EEG Basic Principles

clinical-research applications and related fields

ebook

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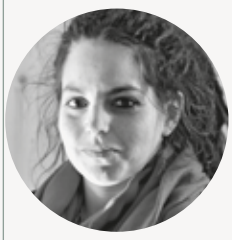
EEG Basic Principles, clinical-research applications and related fields



Marta Castellano
Neurotech Expert

1 What is an EEG?

1.1. The electric brain – from neurons to EEG

The human brain is composed of 100 billion neurons (i.e. 100.000.000.000) - but its complexity does not only come from the sheer number of neurons. To put it into perspective, an elephant's brain has about 250 billion neurons, while chimps and seals both have about 6 billion neurons. Neurons come in different shapes and sizes – but they do share a similar structure: a cell body (soma) that extends into axons and dendrites. Dendrites and axons in turn contain synapses, which are highly specialized junctions connecting two neurons [2][18].

Neurons make up 10% of our brain tissue and are regarded as the 'basic computational unit' of the brain due to their ability to transmit electrical signals [2][10]. Neurons, like muscle cells, are electrically excitable cells that integrate and transmit signals through the generation of **action potentials or spikes** [2]. In contrast to other electrically excitable cells, a neuron produces action potentials (i.e. brief changes in the voltage of the membrane) that are rather similar in terms of intensity and duration: a 100mV voltage change that lasts 1-2ms. These action potentials are triggered by electrochemical signals called neurotransmitters, such as dopamine or serotonin, that control the release of ions [2]. Depending on the type of ions that are being released, synapses can be considered excitatory or inhibitory.

The structure of a neuron provides a direction for the propagation of the action potential. Namely, neurons typically receive signals from other neurons through synapses within the dendritic tree (post-synapse, the afferent side), which accumulates within the soma. Once a threshold is reached, the electrochemical molecules travel along the axons (pre-synapse, the efferent side) and generate an action potential. This newly generated action potential in turn, will spread over the neural tissue and mix with the transmembrane currents of nearby neurons, generating an electric field [1]. In fact, the exchange of ions across any excitable membrane is what contributes to an extracellular electric field. And the electric field spreading across brain tissue is what we can monitor from the scalp with a specific type of technology: electroencephalography or EEG. But what is the etymology of EEG? Electroencephalography literally means 'writing electrical activity of the brain', which gives a hint towards the first EEG technology, which was a set of galvanometers drawn on paper.

Given that neurons are directional, the relative position of nearby cells will condition how their electric moves is superposed across brain tissue. Thus, neurons with similar spatial orientation in the brain with synchronized activation would produce an electrical activity detectable from the surface of the scalp, as this electric field would be different than the one generated by un-synchronized or orthogonally oriented neurons.

“The human brain has 100 billion neurons, each neuron connected to 10 thousand other neurons. Sitting on your shoulders is the most complicated object in the known universe.”

Michio Kaku

When placing sensors on the scalp to monitor electric fields generated by neurons (i.e. EEG recording), the electric field we record is a *smoothed* version of the original electric field, as the signal attenuates and distorts as it passes through soft and hard tissues (i.e. bone, skin, CSF, muscles, etc…).

All these distortions in the neural signal before it reaches the electrodes placed on the scalp are grouped into the concept of **volume conduction effects**. Because of these distortions and attenuations through tissue, scalp sensors can only record brain activity generated at several centimeters below the recording positions. Or from another perspective, at every position where you put a sensor on the scalp, the recorded brain activity will reflect a weighted sum of the underlying brain sources that span about 5-10cm² around that position [1][5] – which correspond to about 30.000 neurons [9].

Measuring the brain activity of 30k neurons is useful as it reflects how a population of nearby neurons communicate. However, it is not only the local activity within a brain area that is important for cognition as most of the cognitive processes arise from how distant areas interact – the connected brain. Hence, in the section 2, we will shed light on the relevance of brain connectivity metrics.

1.2. Strengths and limitations of the EEG

There are several reasons why EEG is an exceptional tool to study neural underpinnings of cognition and disease. However, there are also reasons why sometimes it may not be the best tool to analyze the brain and cognition. In fact, whether you use EEG, MEG or other neuroimaging technology to monitor the brain depends on the study's question and resources. Let's analyze several aspects of EEG technology:

Strengths

- **EEG captures brain activity in a millisecond time scale:** Behavior occurs at several timescales. For example, learning to play a new song on the piano could take days to weeks while the motor action of playing the piano itself is separated by milliseconds between notes. Yet if your research focuses on the study of processes that occur in the millisecond to second timescale, such as studying language, executive function, sensory processing (i.e. vision) or emotions, both EEG and MEG can capture such responses. Specifically, they have the ability to monitor the brain activity with sampling frequencies of 1000Hz, typically.

- **EEG is passive and non-invasive:** To monitor electroencephalography, electrical sensors (the electrodes) are placed on the scalp to constantly monitor ongoing electrical activity from the brain. Thus, by definition, the technology is, non-invasive and passive.

- **EEG is portable and inexpensive:** In contrast to other monitoring technologies, like MEG or MRI, most EEG devices are lightweight and portable, allowing for real-world brain monitoring *(see section 3.4)*. Costs will

depend on the EEG technology provider, but you can find EEG tech from 100 Euros to more than 25.000 Euros.

Limitations

- **EEG captures brain activity of a 5-10cm²**: An intrinsic limitation of EEG is that it allows for the monitoring brain activity of a 5-10cm² brain patch – or about 30.000 neurons [9]. This poor spatial resolution is a limiting factor for this neuroimaging technique.

Overall, in comparison to the available techniques to monitor brain activity (MEG, MRI, PET, etc..), EEG has a clear advantage of being a portable, inexpensive and non-invasive tool to monitor brain activity with excellent time resolution. And only recently, this flexibility is becoming more relevant as EEG manufacturers are shifting EEG devices towards home monitoring.

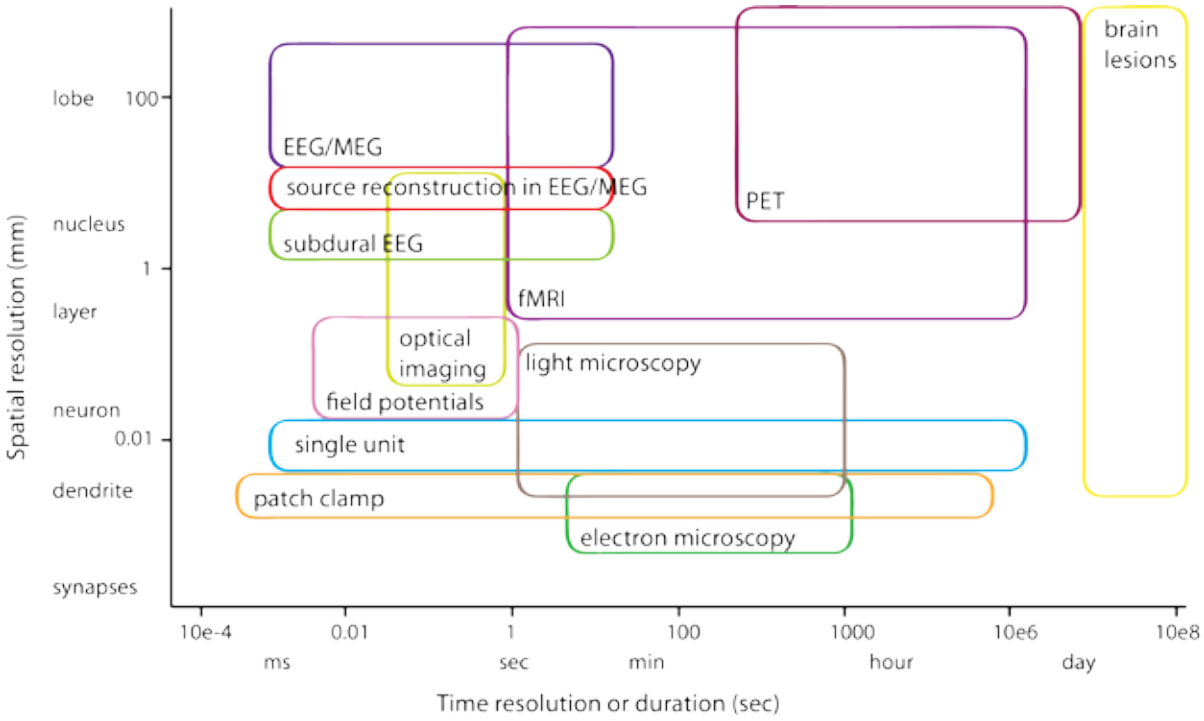


Figure 1: Comparison of brain monitoring techniques in terms of their spatial and temporal resolution, where EEG has a clear advantage.

2 What to take into account for an EEG test?

2.1. Measuring EEG

An EEG scan or an EEG test refers to the procedure of monitoring and reading electrical brain activity with an EEG device. To monitor electrical brain

activity with EEG, typically an array of sensors (the electrodes) are placed on the surface of the scalp. The number of electrodes ranges between 3 and 256, and its positioning and naming follows international naming systems – the most common of them being the 10-20 system [11]. In this system, electrodes are named according to the brain region where they are placed (i.e. F=frontal, C=central, etc…), and a number that indicates the distance to the midline - so that distance between adjacent electrodes are either 10 or 20% from the nasion/inion or between ears. In this naming system, zero (z) would correspond to all electrodes positioned in the line between the nasion and the inion, while indexes 7 and 8 would be located at the temporal regions just on top of the ears. While other electrode nomenclatures exist (i.e. Modified Combinatorial Nomenclature, 10-5 system for higher resolution recordings, or the 10-10 system), they all follow a similar naming system that utilizes anatomical landmarks as measuring points *(see Figure 2)*.

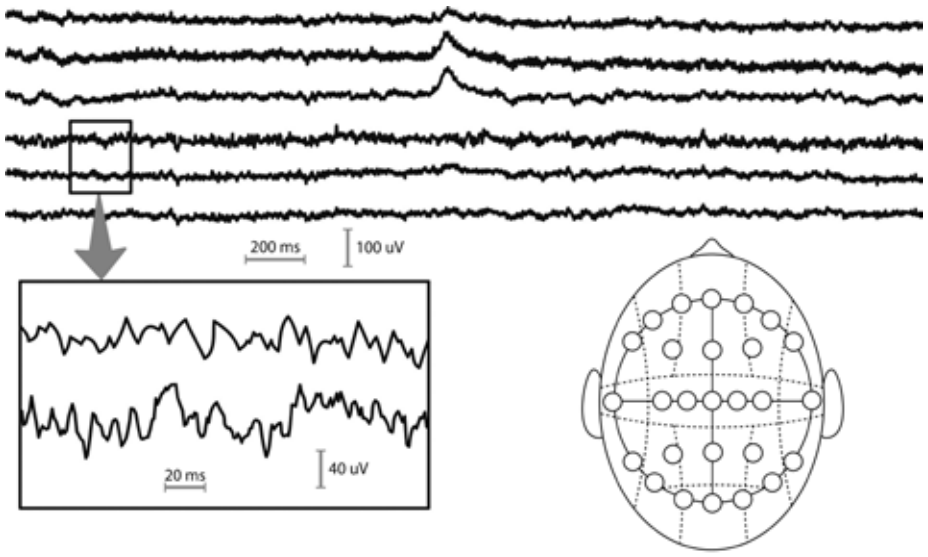


***Figure 2**: Electrical signals recorded by an EEG at different temporal resolutions and the electrode positioning system referred as the international 10-20 system, where the distance between electrodes are either 10 or 20% distance from the midline (nasion to inion) and the coronal plane between mastoids.*

The number of electrodes for an EEG recording depends on the type of experiment. Typical cognitive neuroscience applications make do with 32-64 electrodes (see section 3.3), while clinical applications (where set-up time is a constraint) might do well with as few as 8 electrodes *(see section 3.2)*. Many EEG systems use caps or nets that work as a 'helmet', where electrodes are attached; although some of the systems that are used in clinical settings typically have the electrodes attached to individual wires.

Electrodes are wired to an amplifier, which increases the voltage between a pair of electrodes: the recording electrode and the reference. Thus, the signal collected at each of the EEG locations is in fact a voltage difference between the electrode of interest and a reference signal. The positioning of

the reference electrode is up to the investigator and depends on what properties of the EEG are paramount for the study (e.g. whether symmetry needs to be enforced). Some common placements for reference electrodes include the linked mastoid, earlobe, or the Cz position [21]. And finally, how long does an EEG take? As you will see in Section 3, the duration of the EEG recording depends on the application but it can go anywhere from 3 minutes to several hours.

2.2. Artefacts in the EEG

EEG electrodes monitor electrical potentials, but not all electric potentials that you monitor will come from the brain. One of the biggest challenges in EEG analysis is to recognize and eliminate those artefacts – so do not underestimate the effort you would need for filtering when analyzing your EEG data. Sources of artefacts can include the following:

Physiological artefacts: these come from the participant and involve muscle artefacts (EMG), heart beat (ECG or EKG), sweating (i.e. skin impedance changes) or eye blinks and movements (EOG).

Technical artefacts: these are produced by equipment or the environment, like cable movement, loss of connectivity with electrodes or the device, or the 50/60 Hz artefact of the electrical devices around you (i.e. fluorescent lights).

Methodologies to detect and remove artefacts from EEG signals are numerous and depend on the specific type of artefact. However, in general terms, if you want to trust your EEG test results, make sure to conduct a careful EEG preparation with the minimum amount of EEG cleaning as possible. Remember that, despite all your efforts in cleaning EEG signals, clean EEG data can only appear if you have a good quality EEG recording to start with (i.e. Garbage IN, Garbage OUT).

2.3. First steps in signal processing

EEG is rhythmic and often studied as an oscillation, which means it is analyzed by taking into account different frequency ranges at which the signals oscillate (the **frequency-domain analysis**) *(Figure 2)*. EEG oscillations (or commonly called brain waves) are classified according to a set frequency ranges: delta (0.5-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz) and gamma (30-100 Hz) *(see Table 1)*.These oscillations are thought to reflect various aspects of cortical processing: slow oscillations with strong delta component are present during sleep and are thought to be crucial for memory formation [13], while awake states are dominated by beta and gamma oscillatory activity, which have been correlated with perceptual binding, attention or multi-sensory integration [14][15]. The brain, however, is a complex non-linear system, and other methodologies that account for this complexity are also outlined in the literature [12].

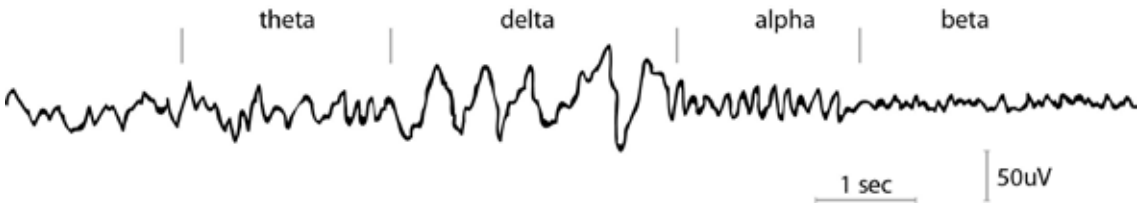
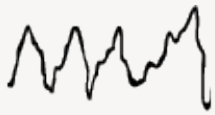
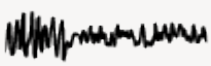


Figure 3: *Rhythmic activity of the EEG is analyzed according to its frequency.*

TABLE 1: The classification of EEG brain waves:		
Delta waves:	Up to 4 Hz. Highest in Amplitude and the slowest wave. Seen in adults in slow wave sleep and in babies. Also in patients suffering from subcortical, diffuse or deep midline lesions or metabolic encephalopathy hydrocephalus	
Theta waves:	Between 4 - 7 Hz. Seen in young children, drowsiness or arousal in older children and adults. Also found during meditative, relaxed and creative states.	
Alpha waves:	Between 7 - 14 Hz. Seen mainly in occipital regions when eyes are closed and during relaxation. This posterior basic rhythm is slower than 8 Hz in young children. Also seen in coma patients not responsive to external stimuli.	
Sensorimotor /mu rhythm:	Between 8 - 13 Hz. Seen in the motor cortex and reflects the synchronous firing of motor neurons in rest state. Mu suppression reflects the motor mirror neuron system - when an action is observed, the pattern extinguishes.	
Beta waves:	Between 15 - 30 Hz. Linked to motor behavior, active, busy or anxious thinking and active concentration. Attenuated with active movements. May be absent or reduced in areas of cortical damage.	
Gamma waves:	Between 30 - 100 Hz. Thought to represent binding of different populations of neurons together into a network for the purpose of carrying out a certain cognitive or motor function.	

2.4. Brushing over advanced EEG analysis

2.4.1. Connectivity metrics

Connectivity metrics describe relationships across signals (i.e. EEG electrodes) and can refer to the anatomical relationship (anatomical or structural connectivity), statistical dependencies across those signals (functional connectivity) or the causal interactions between them (effective connectivity)

[17]. A good review on the different methodologies that can help one understand how two brain signals depend on each other can be found in [16].

2.4.2. Source reconstruction

Source reconstruction refers to a set of algorithms that, in combination with high-density EEG, aim to improve on the spatial resolution of EEG. These methods intuitively aim to reconstruct the underlying electric fields that yield the observed EEG. In other words, they calculate from a set of observed EEG data the causal factors (i.e. electric fields) that produced them, which is known as the inverse problem *(see Table 3)*. The EEG inverse problem is an ill-posed problem; thus, there is no unique solution. To reconstruct an approximate solution, we need regularization techniques, like minimum norm estimates (MNE) or low-resolution electrical activity tomography (LORETA). These techniques make assumptions about how the electric field is distributed and conducted through the head. Although different source reconstruction methods differ on the modeling assumptions, all methods are known to improve upon the spatial resolution of EEG, reducing the **spatial resolution to 2-4 cm²** [6][7][8].

Note, however, that methodologies like Current Source Density (CSD) estimates (based on the Surface Laplacian (SL) computation) *(see Table 2)* are also known to dramatically reduce volume conduction effects and hence improve EEG spatial resolution – yet, this method does not model the electric field distribution.

TABLE 2: The Surface Laplacian (SL) computation

In mathematics, the Laplacian is a differential operator ($\nabla\nabla$ or ∇^2) that describes the divergence (the first ∇) of the gradient (the second ∇) of a function f on a point in the space. This means that the Laplacian of a function f is defined as follows:

$$\mathrm{Lap}(f) = \nabla^2 f = \nabla\nabla f$$

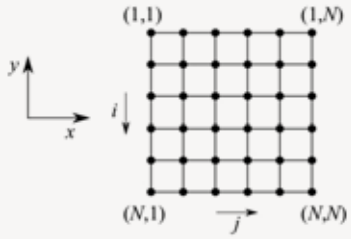
It was first proposed in s. XVIII in the study of movement of objects in outer space, but in fact, it's used to measure many physical phenomena, like quantum mechanics, wave propagation or electric potentials. The starting point in EEG applications is the Ohm's law:

$$I = V/R$$

where I refers to the electrical current that passes through conductor material, V is the voltage measured between two points and R refers to the resistance of this material. Thus, the Ohm's law establishes a relationship between the measured voltage by the EEG sensors (V) and the underlying electric currents (I) of the brain.

TABLE 2: The Surface Laplacian (SL) computation *(continuation)*

To put these two concepts together, we start by considering that we can describe the surface of the brain (where the EEG electrodes are placed), by a continuous variable x and y (see figure below) - a surface that is discretized into a regular-grid that is indexed through the variables i and j. Thus, an electrode corresponds to a position i, j in the grid.



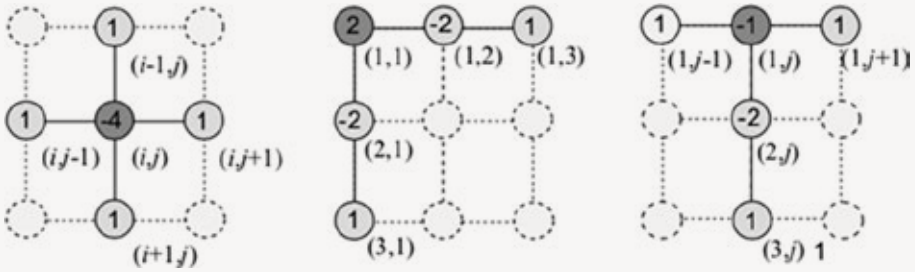
The fact that we assume the surface of the scalp can be described by the continuous variables x and y implies that the Laplacian can be computed as follows:

$$\mathrm{Lap_S}\,(\mathrm{V}) = \frac{\partial^2 \mathrm{V}}{\partial \mathrm{x}^2} + \frac{\partial^2 \mathrm{V}}{\partial \mathrm{y}^2}$$

And the fact that we assume that those continuous variables x and y can be discretized by the variables i and j, which are equidistant, implies that the Laplacian can be computed as follows:

$$\mathrm{Lap_S}\,(\mathrm{V})|_{(\mathrm{i,j})} \approx \frac{\mathrm{V_{(i\text{-}1,j)}} + \mathrm{V_{(i+1,j)}} + \mathrm{V_{(i,j\text{-}1)}} + \mathrm{V_{(i,j+1)}} - 4\mathrm{V_{(i,j)}}}{\mathrm{h}^2}$$

where h corresponds to the size of the grid. With this, we are able to approximate the voltage from electrodes around $i+1$ and $j+1$ at the central node iand j. Now, this is not the only way of computing the Surface Laplacian, but several geometric arrangements between points in the grid can be used to approximate the Laplacian at different electrode locations. Take for instance the different configurations below:



The one on the left is usually referred to as Hjorth's approximation and while it works well for electrodes located at the center of the EEG sensor grid, it doesn't account for border effects, which is what the other two SL approximations aim to address. Other SL approximations would allow for a five-point approximation (for EEG sensor grids that have more electrodes) or account for unevenly-spaced electrodes. For further detail, see [33]

2.4.3. Setting up an EEG experiment – the brain and the brain's context

In setting up your EEG experiment and considering the millisecond resolution of the EEG *(see Table 4)*, you may want to include monitoring of other signals in your experiment, such as eye tracking, motor activity, heart rate, external stimuli like videos or audio, or even other participants' simultaneous EEG recordings (what is referred to as hyperscanning).

The ability to synchronize these signals to millisecond resolution makes EEG an ideal technology to study neural processes associated to a very particular context. In these types of experiments, the EEG can provide information about the neural response that occurs at the onset of a particular event, like the appearance of a visual stimulus and the subsequent change in heart rate. In fact, this type of experiment is well established in the field and is commonly referred to as event-related potentials (ERPs), which aim to study brain responses time-locked to the specific sensory, cognitive, or motor events. It is difficult to view a single EEG response from a stimulus or event as the ERP amplitude is usually much smaller than the amplitude of background EEG. Therefore, scientists would apply several trials and average the results together. In such case the signal-to-noise ratio increases as the square root of numbers of averaged trials. This procedure allows to filter out the noise or the rest of uncountable brain processes and leaves the desired waveform for analysis. This waveform is known as the ERP. Almost any psychological computerized test with consequently presented trials can be used for ERP recording. However, in order to record ERPs, the recording set-up must be accurately synchronized with both the stimuli presentation and EEG recording devices.

TABLE 3: Maxwell's equations and the inverse problem

What are inverse and forward problems?

Think about baking bread. The forward problem is how to combine known ingredients into the final bread elaboration. The inverse problem is how to take the final bread and deconstruct it into the ingredients. It should be apparent with our bread example that the inverse problem is very often far more complex than the forward problem.

The inverse problem for EEG is that you're taking a very small number of measurements about a very complex phenomenon and you'd like to determine what the most likely underlying phenomenon is. To understand source reconstruction methodologies, it is crucial to understand Maxwell's equations. The process of source estimation in EEG is known as the EEG source localization problem. Solving the EEG source localization problem requires solving the forward and inverse problems. Solving the forward problem requires estimating the potentials at the electrodes on the scalp, given some source distribution inside the head. The forward problem is solved repeatedly for different distributions of the source(s). The EEG inverse problem is solved using the forward solution to estimate the distribution of source(s) from an EEG recording.

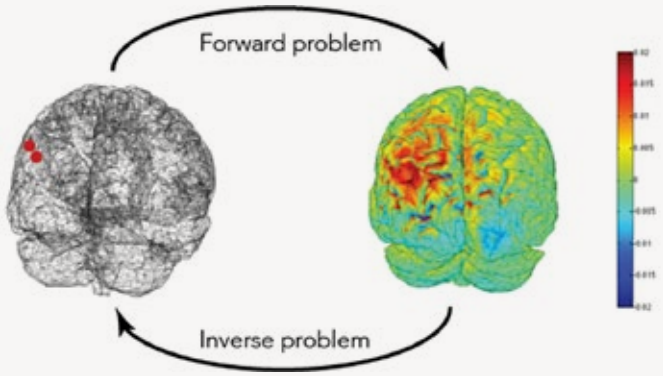


TABLE 3: Maxwell's equations and the inverse problem *(continuation)*

For that, we first need to understand how electric fields spread through the brain or, in other words, the dynamics of the electric field in various media or tissues (i.e. brain, scalp, CSF, etc.) - a behaviour that was first described by James Maxwell in 1861, in what are called Maxwell's equations, that are defined as follows:

$\nabla \times H = \frac{\partial D}{\partial t} + J$ Ampere's law

$\nabla \times E = -\frac{\partial B}{\partial t}$ Faraday's law

$\nabla \times D = \rho v$ Gauss' law

$\nabla \cdot B = 0$ Gauss' law for magnetism

Where ∇ describes the gradient or divergence. The first equation is also known as Ampere's law and describes how a magnetic field will spread on a surface. Thus, H refers to the magnetic field strength (A/m), $\partial D/\partial t$ to the displacement of the electric current density (A/m²) and J to the current density (A/m²).

Faraday's law specifies that the electric field (E, in V/m) corresponds to the negative time derivative of the magnetic field (B, in wb/m²). The last two equations, pose constraints on the electric flux density (D, in C/m²) and the magnetic flux density (B): Gauss' law constrains how the electric flux gradient (∇D) can change in relation to the total charge in that volume (ρ_υ , the charge density in that volume in C/ m³). Gauss' law states that the total magnetic flux gradient on a particular volume (∇B) has to add up to zero.

These equations will also vary depending on the properties of the tissue/media (i.e. whether is homogeneous, isotropic, etc…), as these properties will change how the tissue enables the currents to dissipate. To account for these changes, different tissues are described in terms of their permittivity, permeability and conductivity (s) - which account for tissue properties.
But, is there any way we can reduce the complexity of our attempt in relating the electric field strength (E, in V/m) and the voltage at the scalp potentials? Note that with the current nomenclature, Ohm's law reads as: $J = sE$

The first simplification, the *quasi-static approximation of Maxwell's equations*, relies on the fact that the frequencies of interest of the brain signals is rather low (typically below 1kHz). With this, we can reduce Faraday's law to $\nabla xE = 0$ and overall, segregate the dynamics of electric fields (E) from the magnetic fields (B), as well as ignoring the propagation delay between the sources of the electric fields and the scalp. With this, we can also relate the potential (V) to the electric field strength as follows $E = -\nabla V$, so that the new Ohm's equation reads as $J = s\nabla V$.

TABLE 3: Maxwell's equations and the inverse problem *(continuation)*

Next, in describing the current density (J) in a 3 dimensional plane (x,y,z) and assuming that this current density is spatially bounded to a volume (which is also isotropic) we can further constrain the quasi-static approximation, which yields to the *Poisson equation of the electric field:* $\nabla J = \nabla(s\nabla V)$. This is the forward equation for EEG source localization - and basically relates the dynamics of current density in a 3D space with the dynamics of the voltage given a conductivity's.

So far we have been able to reduce the problem of switching between neural electric fields that give rise to the observed scalp potentials to a single equation. Are we done? If we want to approximate the brain as an isotropic and homogeneous medium, yes. But if we go back to the idea that different tissues have different conductivities, we need an approach with dealing with these different tissues. To solve the inverse problem with more than one type of tissue, we need to define a set of *boundary conditions* at the interface of different brain regions. The boundary conditions would define how currents spread across surfaces with different conductivities, and thus, will define the continuity of the current from one tissue to another.

In approaching source reconstruction by looking at the electric field distribution, it is clear that one of the key steps is to obtain a 3-dimensional representation (x,y,z) of the brain: the head modelling step, as well as information on the conductive properties of the tissue. Modern approaches to head modelling consider 5-7 different tissues and advanced numerical solutions to represent the shape of the head. More information can be obtained in Jatoi, M. A., & Kamel, N. (2017). Brain Source Localization Using EEG Signal Analysis. CRC Press.

TABLE 4: 6 steps to carry out a successful EEG experiment

1	**Understand what you want to study and why**	1.1. Define your hypothesis: What exactly are you trying to learn?
		1.2. Conduct a literature review: Are there similar published works?
		1.3. Define your subject population: What is the age range? Gender? Handedness? Any pathologies you want to include or exclude?
2	**Design your experiment and prepare your experimental campaign**	2.1. Define your EEG protocol: Do you have defined electrode positioning, behavioral tasks associated with your experiment, population under study, etc...
		2.2. Make sure you have fleshed out the details of your experimental campaign: Do you have a clear idea of the possible covariates? Are your information sheets, informed consent forms and other documents ready?
		2.3. Ensure you have all the equipment necessary for the whole experimental campaign: EEG device, electrodes, gel, recording computer and stimulus computer if necessary.
		2.4. Prepare your lab: make sure you have a calm and silent environment, ideally only with the necessary equipment (if possible, computers should be placed outside of the recording room to avoid any interference). Make sure the recording room is as comfortable as possible for the participants

3	**Test your experimental protocol before the real experiment**	3.1. Get familiarized with the experimental protocol and the recording room: Can you execute the different steps of your EEG recording without difficulty?
		3.2. Foresee all the possible problems that might occur in the recording session and have backup plans for each of them: Do you know where all the consumables are placed? Do you have cleaning materials to easily record several participants in a row?
		3.3. Make sure that all your external sources of signals are connected and synchronized to your EEG recording (i.e. GSR, eyetracking, etc…)
		3.4. Execute the complete EEG experimental campaign from a small sample of volunteers (most of the time this is the FFF step: Fools, Friends and Family). This is the pilot campaign, which will test all the aspects of your experimental design.
4	**Perform a preliminary data analysis with the data collected in the pilot campaign**	4.1. Check for the EEG data quality: Is the data format correct? Has the data been properly recorded? Do you have triggers from external sources? Do you need accelerometer data? What is the expected size of your data files?
		4.2. Check for the coherence of your experimental campaign: Is the experimental protocol addressing your question? Do you need to add more questionnaires to control for possible confounds?
		4.3. Check the participant: Is the recording room comfortable? Do you have sources of distraction during the recording?
5	**Get ready for the experimental campaig**	5.1. Participant involvement before starting the recording: Is your informed consent ready? Do you have a timetable of the visits of the different participants? Do they have all the information they need to conduct the experiment?
		5.2. Participant involvement at the day of the recording: Note all of the relevant information that allows you to identify the participant (i.e. contact info, date and all of the details that can modify your EEG recording (i.e. electrode impedances from hair thickness)
		5.3. Monitoring experiment covariates: Make sure you have stored information about the covariates that you identified to be relevant for your experiment, including age, gender, handedness, etc...
		5.4. Monitoring the EEG recording: Supervise the recording at all times and write down any details of the recording, such as movements, falling asleep, scratching, sneezing, coughing, etc...
		5.5. Finalize your experiment: Make sure your equipment is clean and ready for the next recording.
6	**Enjoy the recording - may you gather great data!**	

3 Clinical and research applications

3.1. EEG biomarkers in brain disorders

So far, we have briefly described some metrics and features that can be used to analyze our EEG data (i.e. frequency-based metrics, connectivity metrics). But what if instead of monitoring a particular EEG characteristic, we directly monitor the trait we are interested in? Take for instance an EEG recording from all the people that live in your building – wouldn't you prefer to know whether anyone will develop Parkinson's Disease (PD) rather than knowing the oscillatory power in alpha band of their prefrontal cortex? At that point, whatever combination of EEG metrics that you have used to predict the onset of PD is irrelevant - what matters is the clinical trait. The combination of EEG features becomes a **biomarker**, which provides quantitative information about a trait that is useful for many clinical and research applications.

Current diagnoses of most neurological disorders rely on tests and questionnaires that characterize the phenotype of the disease, but often not its cause. Hence, diagnosis for complex neurological disorders, like Alzheimer's disease, remains 60-70% accurate. As a result, intensive efforts in finding quantifiable biomarkers that increase the accuracy of the diagnosis are being done (i.e. genetic causes, blood tests). But there are four factors that make EEG an increasingly effective approach to identifying biomarkers of neurological disorders: increasing accessibility of EEG devices for home use, wireless capabilities, cost-efficiency, and ongoing technical advancements that improve its sophistication.

This is particularly useful for complex neurodevelopmental diseases in, for example, accurate diagnosis of children with Attention Deficit Hyperactivity Disorder (ADHD) whose clinical criteria diagnoses 5-7% of children in the USA and 1-2% in the EU, with an overall diagnostic accuracy of 61% [19]. For that, the theta/beta ratio at frontal electrodes is monitored in rest-EEG, a quantitative biomarker that is currently under review by the FDA [20].

3.2. Cognitive Neuroscience

What is cognitive neuroscience? The field of cognitive neurosciences deals with understanding the mechanisms through which the brain implements cognition and behavior – the mental process of acquiring knowledge and understanding through thought, experience, and senses.

Cognitive processes are quick – after all, if we want to survive, we need to be able to generate a response to the environment in tens to hundreds of milliseconds – faster than what it takes for a car to crash into a bicyclist. But, how do we study cognition? Cognitive processes that ultimately lead to behavior are extensive, and usually a mixture of them are required to execute a particular task.

Take for example, the act of grasping an object – a spoon from a drawer. Such a basic motor action involves cognitive processes involved in planning, preparation, and execution of a motor action, which in turn involve processes like working memory, attention, or decision-making. All within the few seconds that it takes you to end that action. Brain oscillatory activity (within and between diverse cortical areas) has been associated with the execution of such actions and altered in disease [22]. Other aspects of cognition that are being largely studied with EEG involve memory [13], attention [14], multi-sensory integration [15] or language processing [23].

3.3. Mobile EEG in everyday applications

Over the last decades, EEG devices in the market have become more sophisticated in their design to optimize usability in out-of-the-lab settings, starting by the availability of wireless systems. Taking advantage of its portability, several applications that require free-moving brain monitoring have appeared: sports monitoring, driving or flying simulators, social gathering (e.g. through hyper-scanning), consumer neuroscience, marketing research or media testing.

Most of these applications appear not only due to the availability of mobile-EEG systems, but also from our ability to extract physiological markers from ongoing EEG. For example, sports monitoring benefits from understanding brain markers of fatigue or engagement, while marketing applications (consumer neuroscience, marketing research or media testing) classically study emotional states in terms of arousal or valence. Some mobile-EEG technology already includes the extraction and visualization of these cognitive-emotional metrics.

3.4. Consumer Neuroscience and neuromarketing

Consumer neuroscience refers to the combination of neuroscience with marketing research where the process of linking consumer needs to producers is driven by the neuroscientific knowledge of consumer behavior. The study of consumer neuroscience is broad and classically involves a combination of psychologists, sociologists and anthropologists. Neuropsychology contributes to this aim through the study of decision-making processes, attention or affective responses [28]. When this research is focused on the understanding of marketing techniques (i.e. packaging, websites or branding), it is referred to as neuromarketing.

Neuromarketing aims to find effective and efficient marketing strategies based on the neural response of consumers. A typical neuromarketing experiment would use brain-monitoring techniques (such as EEG) to complement traditional methods of marketing by providing emotional and behavioral metrics.

Additionally, the ability to extract cognitive states like engagement, drowsiness, or motivation from EEG recordings can be useful in analyzing consumer behavior. For instance, EEG has been used to monitor emotional responses to paintings exhibited in a museum [29], or the arousal levels of different perfumes [30].

3.5. What can we learn from the raw EEG?

Is there anything we can learn by directly observing an EEG recording? Is there any direct interpretation that can be informative to us?

In **sleep labs**, the raw EEG data is examined to assess the different stages of sleep. The single most important laboratory technique for assessment of sleep and its disorders is called polysomnography (PSG). PSG consists of recordings of multiple physiological characteristics during sleep in tandem with EEG, including eye movements, muscle activity, multiple breathing variables and blood oxygen levels during sleep. For the study of sleep patterns, the EEG is examined on a scale of 30 seconds to minutes while sleep-specific EEG features are studied. In particular, sleep researchers focus on the properties of different oscillations: delta bands (1-4Hz) – the slow waves generated during sleep – appear during non-REM together with spindles (bursts of oscillations at 12-14Hz and a duration of 0.5 to 1.5 seconds), while REM sleep is characterized by a prominent theta-rhythm. These EEG features (and others) are altered in various neurological disorders like PD, Fibromyalgia or Dementia. These alterations accompany changes in sleep patterns. Monitoring with EEG during sleep can therefore provide insights into the effects associated with sleep-altering disorders.

In clinical settings, the most common use of EEG is to monitor and diagnose **epileptic activity**. Epileptologists, like sleep researchers, monitor EEG activity for long periods of time (often several hours) but in this case, the main purpose of the EEG is to assess interictal and ictal epileptiform activity and focus on EEG monitoring that can help locate the source of the epileptic seizure. EEG is also used to detect abnormal EEG activity associated with other brain disorders like head injuries, encephalitis (inflammation of the brain), brain tumors, strokes and dementia. EEG monitoring is also very important in Intensive Care Units (ICU) and Emergency Rooms (ER) for quickly differentiating the etiology and therapeutic efficacy in critically ill patients with a variety of cerebral injuries and altered states of consciousness. It is also the only procedure to diagnose nonconvulsive status epilepticus. Furthermore, the determination and diagnostic validation of brain death requires an EEG recording.

4 Related fields: real-time exploitation of the EEG

The real-time monitoring of EEG (or features of the EEG) allows for the design of **closed-loop systems**, or experiments that utilize the analysis of EEG signals in real-time.

Drawing from communication theory, in closed-loop systems, the brain would be the source of information or speaker and the link between the ‘EEG device and EEG analysis algorithm’ would be the channel that is being used to transmit the signal/information. Then, to complete the closed-loop, we just

need an adaptive system that respond automatically and immediately to these brain-states.

Thus, with this point of view in mind, applications for real-time EEG analysis is vast —but they all depend on the 'system' that listens to and utilizes the brain signal. Below, we present three different concepts— and let me propose an activity for today: can you turn brain reading in a game?

4.1. Brain Computer Interfaces

Brain Computer Interfaces (BCIs) refers to the direct communication between brain and an external device. The list of what is considered an external devices suitable for BCI is interminable, but the field of BCI has mostly focused on the development of neuro-prosthetic devices that aim to restore or support a particular function, like walking, seeing or hearing. Following years of experimentation, laboratories and hospitals working on BCI (a field that gained relevance in the 1950s) have developed several successful applications, like the control of a prosthetic robotic limb with 7 degrees of freedom [25] or the synthesis of speech from cortical activity [26].

Non-invasive brain monitoring like EEG also has success stories, despite its low spatial resolution. For instance, in the late 1990s, Niels Birbaumer presented ten amyotrophic lateral sclerosis patients (completely locked-in) who could generate a binary signal to control a computer through the self-regulation of their slow cortical potentials [24]. From this binary classifier, the most recent research reports the decoding of visual information for up to 500k different visual stimuli [27].

4.2. Neurofeedback

In neurofeedback applications, brain activity is strengthened using video or sounds with the goal of teaching the viewer to self-regulate that brain function. As such, brain activity can be monitored by any of the techniques presented in Figure 2 – and when EEG is used, visualizations display either the raw EEG or some transformation of it (like the alpha oscillatory power or motivation).

More than 70 clinical studies are being conducted right now to assess the efficacy and safety of neurofeedback with more than 100 clinical studies already completed. Typical applications include ADHD, Mild Cognitive Impairment and epilepsy, although it has been successfully used for the treatment of pain, autism and addiction.

Typical neurofeedback treatment starts by the identification of the EEG-feature of interest (i.e. beta enhancement and theta suppression in ADHD) and by establishing a way in which this feature will be visualized (usually through the use of game-like applications). From here onwards, the treatment consists of allowing the patient to identify the association between brain function and visual stimulus – and to develop strategies on how to improve it.

Neurofeedback, however, refers to the self-regulation of brain activity and thus, it has been used to enhance cognitive performance [31] and as an experimental method to investigate the causal role of specific EEG-features in behavior – an approach that is also known as brain-state dependent stimulation [32].

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