3

Cerebral Electrogenesis

Hans Berger was the first to use electroencephalography to record electric brain activity in humans at the end of the 1920s [BER 29]. However, the idea that these signals do indeed originate in the brain was not immediately accepted, and only after Lord Adrian, the eminent British physiologist from Cambridge, reproduced Berger's results at the beginning of the 1930s, did the scientific community become interested in the technology [ADR 34]. Since then, medical and scientific applications of electroencephalography have proven to be of considerable importance.

However, although it is now well established that electroencephalogram (EEG) measurements record brain activity, it is important to note that they only reveal a small portion of brain activity. Understanding what type of brain activity can or cannot be revealed by EEG is fundamental (1) in order to accurately interpret EEG recordings and (2) in order to know what information they can (or cannot) provide.

3.1. Electrical neuronal activity detected in EEG

For the most part, electrical brain activity is produced by neurons, so EEG essentially records neuronal activity. The following paragraphs describe this activity in detail.

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Brain–Computer Interfaces 1: *Foundations and Methods*, First Edition.
Edited by Maureen Clerc, Laurent Bougrain and Fabien Lotte.

3.1.1. *Action and postsynaptic potentials*

Electrical neuronal activity includes action potentials (APs) and postsynaptic potentials (PSPs).

APs are produced at the initial segment of the axon, from which they propagate in an active (regenerative) manner toward the peripheral end, without being attenuated, at a speed (ranging from a few meters to several dozen meters per second) that depends on the axon's myelination and diameter. A typical action potential lasts between 1 and 3 ms for an amplitude of about 100 mV. PSPs are produced at the synapses, in the dendrites and the neuron cell bodies[1]. For the most part, they propagate instantaneously, and in a passive (non-regenerative) manner[2] and for that reason, they attenuate with distance. Unlike APs, PSP amplitudes are not fixed, but rather depend on the intensity of synaptic activity. However, their amplitude remains far weaker than that of APs around 10 mV. On the other hand, PSPs last far longer than APs in the order of 20 ms [KAN 00]. At first sight, we might think that APs contribute most to EEG, since they are far stronger than PSPs. However, we will see that their short duration makes their contribution rather weak. We will see, on the other hand, that the relatively long duration of PSPs makes them prime contributors to EEG activities, despite their low amplitude.

EEG records brain activity at a distance through the bone and the scalp. Metaphorically, it is similar to hearing a conversation between people located far away, on the other side of a wall. A single person speaking loudly would not be heard. Several people speaking at a normal volume while taking turns would not be heard either. Instead, several people speaking at a normal volume *at the same time* would be audible. In the same manner, it is necessary for several neurons to be active at the same time in order for the sum of their elementary activities to reach an intensity sufficient to be measured at the surface of the scalp. In other words, EEG is only sensitive to the activity of neurons when enough of them are active at the same time.

1 There are also synapses between a dendrite and an axon.

2 There are also cases of regenerative transmission outside of the axonal compartment, but these are the exception.

When an afferent volley reaches a certain structure, it activates its target neurons synchronously. However, taking into account the inherent variability of any biological phenomenon, this synchrony is not perfect and the resulting activity is only *quasi*-synchronous. Given this variability, APs' short lifespan makes their summation unlikely[3]. On the other hand, even when they are set off in an imperfectly synchronous manner, PSPs last long enough to effectively be added-up, even if a part of their activity is lost in the variability of neuronal activity.

It is therefore PSPs that produce the most important contribution to EEG activity, and we will study them in more detail.

3.1.2. *Resting potential, electrochemical gradient and PSPs*

Active transport of some ions through the plasma membrane, on the one hand, and differences in membrane permeabilities to different ions, on the other hand, produce differences in concentrations among intra- and extracellular compartments, as well as polarization in the membrane, which becomes positively charged on the outside and negatively charged on the inside [KAN 00]. The difference in transmembrane potential due to this asymmetric distribution of charges constitutes a neuron's "resting potential".

Differences in concentration between intra- and extracellular compartments create a chemical gradient that drives ions to move from the most concentrated compartment to the least concentrated. Moreover, the resting potential pushes them toward (or keeps them in) the opposite charge compartment. The combination of these chemical and electric gradients, which is known as an "electrochemical gradient", determines the direction (and the strength) of each ion's spontaneous tendency to move toward one compartment or another. As an example, the potassium ion, since it is positively charged, is retained by the electrical gradient in the intracellular milieu; but that same potassium ion, since it is more concentrated in the intracellular milieu, is pushed by its chemical gradient to the extracellular milieu. Potassium's chemical gradient being stronger than its electrical

3 We will see later that it is also necessary to consider the "quadrupole" nature of the field produced by classic axonal APs, which attenuates strongly with distance from the recording position, thus further reducing their contribution to EEG.

gradient, the resulting electrochemical gradient pushes it toward the extracellular compartment.

The release of a neurotransmitter by the presynaptic neuron directly or indirectly produces the opening of ion channels on the postsynaptic neuron. Opening these channels makes it possible for certain ions to pass from one compartment to another in the direction determined by their electrochemical gradient [KAN 00]. For example, opening potassium channels makes it possible for that ion to follow its electrochemical gradient toward the outside. The outflow of positive charge that results from this process increases polarization of the membrane and thereby contributes to making the neuron more difficult to excite. For this reason, PSPs resulting from opening the permeable channels are called "inhibitory". But they are not the only ones, and any channel whose opening "overpolarizes" the membrane generates, when it is opened, inhibitory postsynaptic potentials (IPSP). On the other hand, opening channels that are mainly permeable to sodium[4] makes it possible for that ion to follow the strong electrical and chemical gradients that push it toward the intracellular compartment. The resulting net inflow of positive charges reduces the difference in potentials between the interior and the exterior: it depolarizes the membrane and thereby contributes to making the neuron more easily excitable. For this reason, PSPs resulting from the opening of channels that are mainly permeable to sodium are called "excitatory". But they are not the only ones, and all channels whose opening depolarizes the membrane generate excitatory postsynaptic potential (EPSP) when they are opened.

3.1.3. *From PSPs to EEG*

Let us consider the case of EPSPs generated by opening the channels that are mainly permeable to sodium. Opening the channels enables an influx of sodium ions and that movement of positive charges constitutes an incoming current. That so-called "primary" incoming current is matched by an equivalent outgoing current, through the neuronal membrane (since the cell membrane's resistance is not infinite), distributed along the dendrites and the cell body while attenuating with distance. Incoming and outgoing currents,

4 In the following, we will neglect their permeability to potassium of those channels, since when they are open, the most important effect pertains to sodium.

which are known as “imposed”, produce an intracellular diffusion current, as well as an electrical field in the surrounding extracellular milieu [PER 07]. Since the extracellular milieu is conductive, the electrical field generated by the imposed currents also induces currents, which are passively conducted in the extracellular milieu, and called “secondary” currents. They circulate throughout the volume of the head in such a way that the current lines close, thereby respecting the charge conservation principle (see Figure 3.1). If these secondary currents reach the scalp and are sufficiently strong, they produce potential variations that are measurable by the EEG.

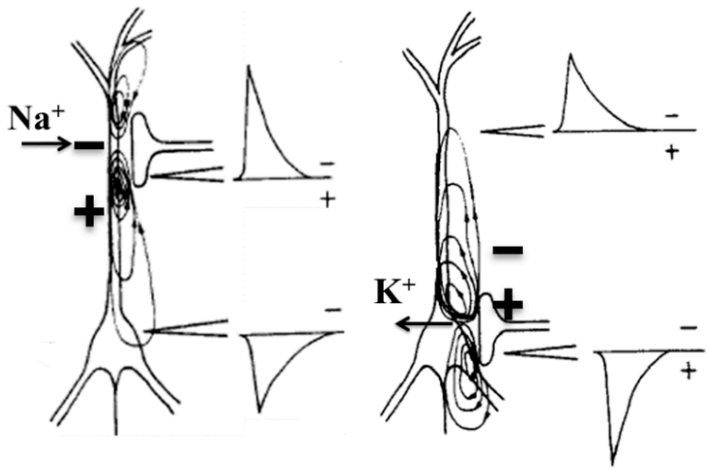

Figure 3.1. *Left: Currents created by an inflow of sodium and potential, as recorded by nearby distal electrodes. Right: Currents created and potentials recorded during a deep outflow of potassium*

The opening of ion channels is responsible for EPSPs and IPSPs[5], thereby generating the primary currents that give way to secondary currents responsible for the activities recorded by EEG by enabling ions to move in the direction determined by their electrochemical gradient.

While opening the (dendritic or somatic) ionic channels is indeed the primary cause of measurable differences in potentials recorded in EEG, we

5 It is necessary to also consider, in some cases, the contribution of specific channels depending on an intracellular ligand, which we will explore later (section 2.1.3).

should not imagine that any opening of ion channels, even when massive and physiologically pertinent, gives way to measurable electrical activity. Indeed, opening certain ionic channels, even when it produces a strong inhibitory effect, does not generate (or only weakly so) a PSP. This is the case when channels permeable to the chloride ion are opened. For many neurons, the chloride ion's electrochemical gradient is null or close to zero. For this reason, at or near the resting potential, massive opening of the channels permeable to chloride does not produce (or barely does so) a net flow of chloride through the membrane and therefore little or no variations in PSP are produced. On the other hand, this massive opening considerably increases the membrane's electrical conductance and, through shunting, it impedes or strongly attenuates the depolarizing effect induced by opening other channels (channels permeable to sodium, for example)[6] [KAN 00] (the majority of these channels are also permeable to the bicarbonate ion, but since their permeability to chloride is dominant, we have ignored the effect of bicarbonates – even though it is not without its functional consequences). A substantial part of the very real inhibition exerted by the chloride channels opening is therefore electrically silent; the EEG is blind to it. (Note, however, that if the neuron is depolarized or hyperpolarized, a significant electrochemical gradient for the chloride ion appears at that moment; if at the same time a synaptic activity provokes the opening of the chloride channels, it will enable a net transmembrane flow of chloride ions responsible for significant primary and secondary currents and whose direction will depend on the sign of the electrochemical gradient, determined at that moment, for the chloride ion).

Finally, there are electrical synapses which involve gap junctions: currents circulate from one neuron to the other through the junctions formed by the butt-jointed association of two pores (one per neuron). The junction of two pores forms a little "tunnel" (each pore forms half of the tunnel) that crosses each neuron's membrane as well as the extracellular milieu that separates them, thereby making the intracellular milieus of the two neurons communicate. Since the currents remain confined to the intracellular compartment, they do not generate significant extracellular currents

6 In the case of a sodium inflow, prior opening of channels permeable to Cl^- allows those ions to passively follow Na^+ toward the interior. In other words, during an incoming current carried by intake of Na^+, the previous opening of the Cl^- channels provides an outward leakage of current (shunt) carried by the inflow of Cl^- inflow.

[BUZ 12]. As a result, the electrical synapses do not contribute significantly to the EEG. On the other hand, those synapses often participate in the electrical coupling of neuronal ensembles; in this sense, they increase synchrony between the activities of connected neurons through those synapses, which facilitates summation of their activities and contributes to increase the amplitude of signals measured at a distance.

3.2. Dipolar and quadrupole fields

3.2.1. *Field created by an ion current due to the opening of ion channels*

We have indicated above that opening of ion channels, when they give way to ion currents, is accompanied by currents of the same intensity that cross the membrane in the opposite direction. The currents generated by opening ion channels (almost) always go through a single point (or points), whereas those that cross the membrane in the opposite direction are distributed throughout the neural membrane and attenuate with distance (see Figure 3.1).

Let us go back to the example of sodium inflow: an extracellular electrode will "see" current disappearing from the extracellular milieu wherever there are open channels, referred to as a "current sink". At the same time, the electrode will see current appear throughout the rest of the neural membrane, which is referred to as a "current source". An extracellular electrode thus detects the association of a current sink and a current source of the same intensity. Having equal intensity and opposite signs, if both the sink and the source occurred at individual points, they would produce a current dipole ; but since the source is distributed throughout the membrane, this sink–source configuration does not quite produce a current dipole.

In fact, the potential created at a point by such a sink–source configuration is given by an infinite sum, whose first term corresponds to the potential created by a dipole, the second to the potential created by a quadrupole, the third to the potential created by an octupole, etc[7]. [PER 07]. We should note that for a given entering current, the greater the distance between the sink and

7 In the case that interests us, according to the principle of charge conservation, charge is neither created nor destroyed in the brain; the monopolar term is therefore equal to zero and does not appear in the expression of potential created by the opening of ion channels.

the barycenter of the distributed sources, the greater the potential captured by the dipolar term. Moreover, the dipolar term decreases proportional to the square of the distance to the point where measurement is taken. The quadrupole term decreases proportional to the cube of this same distance. The octupolar term decreases proportional to this distance raised to the fourth power. Therefore, if the distance between the sink and the barycenter of the sources is large enough (on a neural scale), and if the recording point is far enough, as is the case for EEG (but not necessarily when recording local field potentials), the dipolar term dominates all the others, which become negligible for practical purposes. On the other hand, if the distance between the sink and the source's barycenter is negligible or zero, the quadrupole term will dominate.

3.2.1.1. *Field created by an inflow of ions during a synapse (PSP)*

The geometry of dendrites and cell bodies is not simple, but if a neuron presents an asymmetry in its dendrites it is often possible to account for synaptic activities using a relatively simple model; this is the case for the cerebral cortex's pyramidal neurons, which we will use as an example. Let us first specify that these neurons are roughly shaped like a triangle whose base is oriented toward the deep layers of the cortex and the top toward its outer layers. They have a small basal dendritic arborization, but most importantly, they have one very long dendrite called the "apical dendrite". It stems from the apex of the triangle toward the outer layers of the cortex, being somewhat ramified in its distal end and perpendicular to the cortex's surface. A sodium inflow occurring at the apex (or the base) of the apical dendrite of a pyramidal neuron produces a point sink and a source distributed throughout the rest of the dendrite and the cell body (Figure 3.1). The current will emerge more from one side than the other (because there is more surface available for current leakage on one side than on the other). The distributed source's barycenter will therefore not coincide with the sink and, all other things being equal, even less so when we consider that the inflow of sodium will occur near one of the dendrite's ends. The dipolar term will therefore dominate the expression of potential created by the sodium inflow, and approximating this kind of generator with a current dipole is reasonable. This is why the dipolar model is often used to model the sources of EEG activity, which are essentially due to synaptic activity, that is to say to PSP. One should bear in mind that it is a model that relies on the kind of approximations we have just described.

If the dendrite's shape is similar to a straight line, which is often the case for apical dendrites in the pyramidal neurons, then the formula for the potential, $V(P)$, created by such a dipole at a point P (see section 3.2), is rather simple:

$$V(P) = \frac{1}{4\pi\sigma}\frac{M\cos(\theta)}{r^2} \qquad [3.1]$$

where σ is the medium's conductivity, M is the module of the dipole's moment, r is the distance from point P to the middle of the segment connecting the sink and the barycenter of the source and θ is the angle formed by the dipole and the segment connecting its midpoint to the point P (Figure 3.2) [PER 07]. This expression relies on an additional approximation made possible by representing the apical dendrite as a straight line because it is possible to assume that the distribution of the potential generated by an inflow of sodium is symmetric by rotation [PER 07]. For more complex dendritic geometries, where this assumption would be invalid, the formula would be less simple.

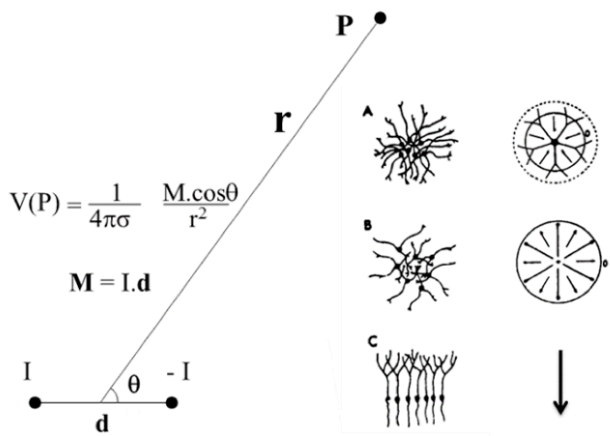

Figure 3.2. *Left: Potential created by a current dipole. Right: a) Null equivalent dipoles resulting from stellate neuron activation b) or from neurons without a specific orientation; c) non-zero equivalent dipole resulting from the activation of parallel-dendrite neurons (adapted from [LOP 82])*

3.2.1.2. *Field created by an ion inflow at the axon (AP)*

Let us stick to the example of sodium inflow, but this time, during the propagation of the AP in the axon. The inflow of sodium through the voltage-gated ion channels produces an outflow of current on both sides of the sink. Since (1) it is possible to locally represent an axon as a straight line, and (2) the same amount of current outflows on the left and the right hand sides of the sink, the distributed source's barycenter is located at the exact same point as the sink. The distance between the source's barycenter and the sink being equal to zero, the dipolar term is also zero. The dominant term in the expression of the potential generated by an AP is therefore the following term in the series, namely the quadrupole term. We have seen that it decreases proportional to the cube of the distance between the generator and the recording point. This very sharp decrease with distance is one of the reasons why APs contribute little to EEG, as compared to PSP. Another reason, as we have seen above, has to do with the fact that typical APs do not last long enough for their activity to be added together effectively.

A third reason can be added to the two previous ones: for the most part, axons have a small diameter (as compared to that of dendrites or the soma); their membrane's external surface is therefore relatively small and there is therefore relatively little surface available for transmembrane currents to pass. The transmembrane resistance of a portion of a given axon is thus relatively high. For this reason, despite high AP values (of about 100 mV), they do not produce intense currents (for a more detailed explanation see Chapter 8 in this volume, which studies extracellular recordings).

Let us also note that in the case of local field potentials, the recording electrode (which is intracerebral) can be very close to the AP or to a set of APs. In that case, since the electrode is close to the sink, potential attenuation at the recording point, even when it is proportional to the cube of the distance to the sink, can remain relatively low. Moreover, since intracerebral currents are not attenuated by the skull's bones, there is no need for as large a summation as for EEG in order for the electrode to record measurable activity. Therefore, when an afferent volley activates a large number of neurons, the resulting activity may be large enough to be measurable as local field potentials, even though only a small portion of the activity generated by the APs is actually summated; more so, if the electrode is near the generators.

3.2.1.3. *Field created by other neuronal activities*

There may also be some neurons for which particular APs do not depend on channels permeable to sodium, but rather on other ion channels, like, for example calcium. These channels permeable to calcium are essentially dendritic and, such as traditional APs, the APs they generate have large amplitudes. But unlike traditional APs, they are long lasting: ten to several tens of milliseconds [HEL 99]. They therefore accumulate easily. Although it is clear that they contribute to local field potentials, it is more difficult to understand their contribution to EEG, since there is not currently enough data about their activity *in vivo* [BUZ 12]. For the moment, we can only conclude that the possibility of calcium APs contributing to EEG is not ruled out.

In some neurons, when the opening of certain ion channels that depend on an intracellular ligand generates a net flow of ions, it generates primary currents that induce secondary extracellular currents. For example, calcium APs do not only depolarize the membrane, but they also increase intracellular calcium content. This increase in calcium concentration has an effect on potassium channels sensitive to intracellular calcium, which are located on the soma. Opening these channels allows an outflow of calcium that produces a primary hyperpolarizing current source [HOT 80] located at the cell body. The amplitude and the duration of these non-synaptic currents are of the same order of magnitude as those of PSP. Therefore, since these calcium-dependent potassium currents are located at the cell body, the position of the source most probably differs from the associated distributed sink's barycenter. The generated field will thus have a dipolar form and it may contribute to the EEG, in the same way as it does to PSP, provided that neurons activated in this manner are sufficiently many and sufficiently synchronous.

Some types of voltage-dependent channels, other than the sodium and potassium channels responsible for the APs, can confer electric resonance properties to some neurons [LLI 88]; that is to say that those neurons respond more effectively if the afferent volleys develop in a specific frequency range that represents their electric resonance frequency. Moreover, for sufficiently high depolarization levels, the activation of such channels can bring about self-sustained membrane potential oscillations in those same neurons. For example, it is their presence that allows thalamocortical neurons to generate periodic bursts of APs in relation to sleep spindles [STE 88]; such channels are also essential in the genesis of cortical oscillations of the gamma band

[LLI 07] and of slower EEG frequencies (0.5–1 Hz) during slow-wave sleep [LLI 06]. The contribution of these non-synaptic oscillatory activities to local field potentials is likely, but even though they are necessary for producing certain cortical rhythms as we noted above, their direct contribution to EEG has not yet been completely determined. It will depend on whether the currents generated by the channels on the dendritic and somatic membranes are more or less distributed, on the number of neurons involved and on the phase synchrony of those oscillations.

3.2.2. *Factors determining the value of the potential created by an ion current*

When positioned at a given point, in a given direction, a dipole is completely characterized by its moment. That moment is represented by the vector given by the segment connecting the sink and the source, oriented in the direction going from the sink to the source, and whose module is given by the product of the current intensity and the distance separating the sink from the source. The intensity of the current depends only on the channels' conductance, their number and the electrochemical gradient for the ions carrying the current. The distance depends on the synapse's position (or on the non-synaptic sources/sinks, such as the calcium-dependent potassium currents as mentioned above) and on several factors related to the neuron's shape.

Concerning the neuron's shape, we can mention the following non-exhaustive factors:

1) the dendrite's length will determine how far from its entry point the current can outflow;

2) the number, nature and branching points of that dendrite will determine the possible leakage areas for the exiting current;

3) the dendrite's diameter is also an important factor. Indeed, since the current follows the lines of least resistance, it tends to follow the longitudinal direction (parallel to the dendrite's axis) since the lipid membrane is far more resistive than the intracellular milieu. Therefore, the greater the diameter of the dendrite, the lower the longitudinal resistance; the more the current can follow that direction, the more it can propagate (and exit or enter) farther from its point of entry.

Concerning the synapse's position, let us recall that if it is located on the distal end of a dendrite, the current leaks far more in the direction of the cell body, since there is little surface available on the distal side to allow a current leak; if the synapse is located on the proximal side, near the cell body, the current leaks far more in distal direction because there is, on that side, more surface available for current leakage. In both cases, if we consider the example of a sodium inflow, the distributed source's barycenter is an appreciable distance away from the sink and the field thereby created is very much like that created by a dipole current. Let us now consider an otherwise similar synapse located at the middle of the dendrite: the exiting current leaks as much on one side of the sink as on the other, and the barycenter of the distributed source is at the same place as the sink. Their distance being equal to zero, the dipolar term is equal to zero and the dipolar model is no longer valid. As in the case of an AP, the first non-zero term of the series, which describes the potential generated by such a synapse, is the quadrupole term, which becomes the dominant term compared to the following ones, which decrease even more sharply with distance. Just like that of APs, the activity generated by this kind of synapse contributes very little to EEG. All other things being equal, the more the synapses are positioned asymmetrically on the dendrite, far from the position (often close to the middle) at which the source's barycenter is at the same place as the sink, the greater the intensity of the field they generate.

3.3. The importance of geometry

3.3.1. *Spatial summation, closed fields and open fields*

We have seen above that in order to generate an electrical activity measurable with an EEG, the activities of several neurons must occur at the same time, which in turn allows them to summuate. This is a necessary condition, but it is not sufficient. We will now see that a spatial summation is also involved, and its effects at a distance depend on the geometry of the set of neurons activated in synchrony.

Let us assume that the simplest dipolar model, whose formula we provided above, applies. Each synaptic activity generates a current dipole that is characterized by its moment. The moment being a vector quantity, it is possible to account for the sum of several elementary synaptic activities with

a so-called “equivalent” dipole whose moment corresponds to the sum of moments for each elementary dipole.

Let us now consider a stellate neuron[8] receiving a synchronous afferent volley that activates several synapses on its several dendrites. A dipole current then appears on each dendrite. Let us assume that those dipoles have roughly the same moment and that the afferent volley is distributed throughout the set of dendrites in a roughly homogeneous manner. Since the dendrites of a stellate neuron radiate in may different directions away from the cell body, the equivalent dipole moment resulting from the sum of the elementary dipoles is equal to zero or almost zero [LOR 47] (Figure 3.2 on the right (a)). We will obtain the same result with one or several synapses arranged along the cell body, since the leak current will be distributed in a regular manner along the entire the dendritic tree. Therefore, due the geometry of such neurons, an afferent volley does not produce a perceptible field in the conditions where the dipolar model could be applied, that is, for observations carried out far from the neuron (as is always the case for surface EEGs), even if it generates strong local currents. These kinds of neurons are said to produce “closed fields”. Even if a population of several stellate neurons is activated synchronously as we have indicated, the fields they generate do not produce enough of a current to be detected at a distance, and for that reason they do not have a detectable influence on EEG either [LOR 47].

Let us now consider a structure containing neurons with asymmetries in their dendritic tree. If this structure receives an afferent volley, it can generate a resulting non-zero elementary dipole current at each neuron. However, if those neurons are not oriented in a predominant direction, that is to say that each neuron’s dendritic tree can point to any direction, the moments of dipoles generated by the activation of that structure’s neurons will also be oriented in all directions. If we assume that the moments of elementary dipoles generated by the activation of that structure’s neurons are more or less the same, the equivalent dipole – which is the sum of the elementary dipoles describing the activity of all of the structure’s activated neurons – will be close to zero. A cytoarchitectonic organization of this kind will also produce closed fields [LOR 47] (Figure 3.2 on the right (b)). As a result, the majority

8 These neurons have several dendrites that extend in many directions away from the cell body, accounting for their name.

of the cortical interneurons, since they tend not to be arranged in a given direction, barely contribute to EEG, even if they are strongly activated and generate intense local currents.

In order for the equivalent dipole corresponding to the synchronous activation of a large number of neurons to generate an intense field at a distance, it is necessary for those neurons to be arranged in a cytoarchitectonic organization that favors spatial summation of their activities [LOR 47] (Figure 3.2 on the right (c)). This is the case for pyramidal neurons in the cerebral cortex. In a given cortical area, the apical dendrites from those neurons are almost all parallel. If one afferent volley reaches those neurons, the moments of the generated elementary current dipoles will add up in an optimal manner because of their parallel distribution, and the module of the resulting equivalent dipole will be considerably large. The field generated at a distance is therefore sufficiently large to produce effects measurable by an EEG [LOP 82]. These kinds of fields are known as “open fields”. The most important part of an EEG recording is therefore produced by the cerebral cortex’s pyramidal neurons. Even though this fact may seem discouraging, it is important to note that those neurons are very numerous and that they represent the output pathway for cortical structures. EEG is thus sensitive to the entry (PSP) of output neurons of the cerebral cortex, which is of interest.

Even though cortical pyramidal neurons are the main EEG generators, they are not the only ones. Other cortical neurons also have predominant orientations and may therefore also generate open fields. In the same manner, some groups of subcortical neurons, since they are characterized by asymmetric dendritic arborizations and since they have predominant orientations, can also generate activities measurable by EEG [LOR 47].

Let us come back to the cortical pyramidal neurons. The cerebral cortex is folded; it contains sulci and fissures (that is deep sulci). If the two banks of a sulcus are activated at the same time, the moments of the equivalent dipoles accounting for their activities are oriented in opposite directions. If their modules are of comparable sizes, they tend to cancel each other out and the activity of the two banks of the sulcus does not contribute significantly to the EEG.

3.3.2. *Effect of synapse position on the polarity of EEG*

Let us consider a structure located on a part of the cortex parallel to the surface of the scalp (gyrus). Its activation generates a current dipole perpendicular to the scalp (this is known as a "radial" dipole). Let us suppose that the activation of this area results from an excitatory afferent volley reaching the outermost layers of the cortex, that is to say the distal region of pyramidal neurons' apical dendrites (like in the neuron in Figure 3.1 on the left). The negative pole of the elementary current dipoles will be superficial and the negative pole of the equivalent dipole will be oriented toward the scalp. An EEG electrode placed above this structure will therefore record a negative deflection. If, on the other hand, the afferent volley is inhibitory, it will produce point current sources at the synapses and distributed sinks along the rest of the dendrites and cell bodies. The generated dipole's orientation will be the opposite of that in the previous example, and its positive pole will be oriented toward the scalp. An electrode placed above this structure will record a positive deflection.

Let us now suppose that the activation of this same cortical area results from an excitatory afferent volley in the deep layers, close to the neuron's soma (like the neuron in Figure 3.1 on the right). The negative pole being deep, it is the positive pole that will be directed toward the scalp and an electrode placed above it will record a positive deflection, as in the case of a superficial inhibition. In the same way, the effect of a deep inhibitory volley will be recorded by an EEG electrode as a negative deflection, such as a superficial excitatory volley.

Therefore, without specific previous knowledge regarding the generators responsible for variations in the measured potential, it is not possible to decide whether a negative wave recorded on an EEG corresponds to a superficial excitation or to a deep inhibition; nor to know if a positive wave represents a superficial inhibition or a deep excitation. However, it is certain that if a negative wave is recorded in an experimental condition and a positive wave in another condition, both in the same latency range, the negative and positive waves do indeed represent two different physiological phenomena.

3.3.3. *Effect of active areas' position*

The maximum value and the form of potentials recorded by EEG electrodes depend on the generators' position.

Let us take the expression for the potential generated by the activation of a synapse in the simplest scenario, which is the case described by the formula [3.1] above. We can see there that potential decreases proportionally with the square of the distance between the point where measurement is taken and the generator. This explains why the cortical generators contribute most to activities captured by EEG, since they are closest to the surface. This being said, there are also deep cortical generators, like the insula, the medial temporal cortex or the calcarine sulcus, whose contribution to EEG recordings is much attenuated due to their distance from the surface. This makes it quite difficult to study them with EEG. Moreover, the same formula shows that the potential generated by a dipole also depends on its orientation with respect to the recording point; indeed, it is proportional to the cosine of the angle formed by the dipole and the segment connecting its midpoint and the point where measurement is made. Since $\cos(0) = 1$ and $\cos(\pi) = -1$, the potential is greatest (in absolute value) right above the dipole if it is radial; that is to say, if it accounts for the activation of one part of the cortex located on a gyrus. Let us now consider the activation of a portion of the cortex located on the bank of a sulcus. The equivalent dipole that accounts for it is still perpendicular to the cortical surface but it is no longer right above the scalp: it is inclined in such a way that it is parallel to the scalp's surface (this is called a tangential dipole). The expression of the potential created by such a dipole shows, in a counterintuitive manner, that an electrode placed directly above the activated structure records nothing. Indeed, the angle formed by the dipole and the segment joining its midpoint and the point where measurement is taken is a right angle; since $\cos(\pi/2) = 0$, the potential measured by an electrode perpendicular to the generator is equal to zero. For a tangential dipole, the maximum and minimum potentials are located at a distance from the point right above the dipole, along the line that, on the surface, is parallel to the dipole's direction. Indeed, a distance away from the point right above the dipole, the angle diverges from $\pi/2$, which increases or decreases the value of measured potential. But, since measurements are carried out on the surface, opening the angle is accompanied by a distancing from the generator. The maximum potential amplitude generated by a tangential dipole is therefore lower than the maximum amplitude generated by a radial dipole

with the same moment. We must also add that since tangential dipoles are located in sulci or fissures, they are usually deeper than radial dipoles.

3.4. The influence of conductive media

3.4.1. *Influence of glial cells*

Just like that of neurons, the membrane of glial cells (GC) is electrically charged. Their resting potential depends on the existence of a transmembrane transport of potassium, on the one hand, and on the existence of selective leak channels for potassium, on the other hand. As with neurons, their membrane potential can vary, but those variations are very slow. Given that there are at least as many GCs as neurons in humans, it is worthwhile considering their contribution to slow EEG variations, but answering that question is not easy. Variations of GC membrane potentials depend, as for neurons, on transmembrane ion currents. Unlike synapses, these ion currents are not as concentrated around a single point, although they can be fairly localized. These primary currents therefore produce secondary currents in the extracellular space and, for that reason, they contribute to slow variations in local field potentials [AMZ 00]. In the retina and the cerebellum, there are GCs with regularly organized, long extensions. If such glial arrangements exist into adulthood in the cortex, they could contribute to slow variations in EEG [SOM 75]. Moreover, intracellular compartments of adjacent GCs are connected by permeable gap junctions [GUT 81]. If incoming potassium currents located in a GC population cross their membranes, intracellular diffusion currents can propagate to neighboring cells through the gap junctions and generate distributed current sources, especially if the membrane's resistance to current leaks is high (note that GCs' resistance is rather low). Furthermore, the population's geometry will also determine whether sources' barycenter and sink coincide or not and, thereby, if variations in the GCs membrane's potential significantly contribute to slow EEG variations. It seems to us that it is difficult to answer this question at present.

However, when neurons are intensely activated, they tend to release potassium in the extracellular milieu. GCs have potassium channels and can absorb a part of the excess extracellular potassium. These potassium displacements are accompanied by water displacements that involve a

swelling of the GCs and a reduction of the extracellular compartment's volume [AMZ 00]. GCs can therefore modify the composition and the volume of the extracellular space, which modifies its conductance. And yet, we have seen in the expression of the potential created by a dipole that it is inversely proportional to the medium's conductivity. Through their action on the extracellular medium, GCs can therefore bring about variations in potential, even at a distance, but those effects are not directly due to their membrane potential; they are more indirect via the effect of variations in the conductivity of the extracellular medium on the field generated by neural activity [BIR 90].

3.4.2. *Influence of skull bones*

We have up to now omitted the fact that the formula [3.1] provided above refers to a homogeneous medium. But the media through which currents flow before reaching an EEG electrode are not homogeneous at all. Currents must flow through the brain tissue, cerebrospinal fluid, the meninges and, most importantly, the bone before they can reach the scalp. They therefore encounter different types of electrical diopters, especially when they flow through the bone, which is extremely resistant. This does not contradict what we have presented thus far, but it does add some further effects.

Before reaching the scalp, currents will come up against the resistant wall formed by the bone and will tend to follow the paths of least resistance. They are thus more prone to take parallel than perpendicular directions to the bone. This produces a diffusion of currents when they cross the bone and this diffusion causes a spread of potential distributions toward the surface of the scalp, thus "blurring" the image of the distribution. This flow, which is introduced by diffusion, produces a mixing effect: activities coming from generators activated at the same time, even when they are far from one another, can partially or totally be combined, producing a sort of "spatial averaging". This averaging represents an important challenge to the interpretation of EEG phenomena.

For example, let us imagine that two different generators are activated in the same latency range. They run the risk of producing a single wave because their effects are combined in the surface. This uniqueness can make it look like a unique physiological phenomenon has been recorded and thus lead to a false interpretation of the data, even without thinking about the generators'

locations. “Disentangling” the respective contributions of different generators to recorded surface activities is an important challenge for physiologists, but this question is beyond the scope of this chapter.

3.5. Conclusions

We have just seen that even though EEG only records a part of electrical brain activity, it is very sensitive to dendritic activity from an essential class of neurons in the cerebral cortex: pyramidal neurons. These represent the majority of neurons and a subset of them is responsible for the majority of cortical outputs, either toward other cortical areas or toward subcortical structures. The information provided by EEG recordings is therefore of great interest for medicine and neuroscience research.

The primary cellular mechanisms that produce currents captured by EEG are due to the opening of ion channels. Analogous mechanisms are responsible for the activity of other excitable tissues, such as striated skeletal muscle (electromyogram or EMG) or heart muscle (electrocardiogram or ECG). ECG and EMG activities are much larger than EEG and can contaminate recordings; they therefore constitute an important source of biological artifacts, which should be reduced or eliminated as much as possible in order to reliably measure EEG activity in the framework of brain–computer interfaces.

3.6. Bibliography

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