A PRIMER ON EEG AND RELATED MEASURES OF BRAIN ACTIVITY

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1. Indirect and direct reflections of brain activity

Behavior results from activity in the central nervous system. To the extent that the brain is involved in such activity, the resulting behavior can be seen as an indirect reflection of brain activity. It is indirect because, firstly, there is a macroscopic delay between brain activity and the ensuing behavior; and secondly, it is not a physical reflection of brain activity, but a physiological one.

Brain activity involves electric fields and changes in electric fields. Therefore, one way to record direct reflections of brain activity is to use a device that is fit to measure a difference in electrical potential (e.g., a pair of electrodes and something to read off the signal). The electrodes can be positioned in, or on, or outside the brain. If the brain's electrical activity is recorded with electrodes, the recorded signal provides a physical reflection of brain activity; as physical as it would have been when the electrodes were used to record the potential distribution on a sphere with a battery within a conducting medium inside. The recorded signal is said to result from **volume conduction** of the electrical component of neural activity. With volume conduction there is only a microscopic delay between the brain activity and its reflection in the electrode-recorded signal. The amount of this delay is far below the millisecond level that characterizes the time scale of most neurophysiological activity.

Volume-conducted brain activity can be recorded by inserting electrodes into the head, or even into a single neuron. Obviously this is no routine with human subjects. A non-invasive alternative involves the measurement of volume-conducted brain activity through electrodes attached to the scalp. The potential difference recorded in this way, and its fluctuation with time, is usually called the Electro-Encephalogram (EEG).

Relative to some other direct measures of brain activity (discussed below), the EEG has a high **temporal resolution**: Changes in activity can be followed on a millisecond basis. In contrast to some other methods, the EEG has a poorer **spatial resolution**: It is less accurate in indicating where in the brain the activity is located. The remainder of this text is mainly devoted to EEG principles and methods. First however, we briefly address other, mostly indirect reflections of brain activity.

Indirect reflections of brain activity, like behavior, depend on intervening physiological
processes. For example, between a certain brain activity and the behavioral act many events occur: Synaptic transmission, the gradual build-up of post-synaptic potentials, action potentials, and so on. These events take time, resulting in a delay between the brain activity and the behavioral act that is easily measured on a millisecond basis. The final record of behavioral activity reflects multiple synaptic transmissions, muscle activity, and so on; it is not a volume-conducted reflection of the brain-electrical activity.

Of course, most devices used to record behavior (e.g., the closure of a micro-switch as the result of a button-press) can hardly be considered as appropriate to record volume-conducted activity. However, the qualification as indirect also holds for the measurement through volume conduction of many forms of physiological activity other than brain activity. For example, heart activity can be recorded with electrodes attached to the body, and it certainly depends on preceding brain activity to a substantial extent; yet, it is an indirect reflection of that brain activity. The same holds for many other forms of peripheral physiological activity which do not in themselves take place within the brain. Some of these forms will be discussed in section 1.5.

Modern neuro-imaging techniques are not based on volume conduction either and therefore are usually labeled as indirect. They more directly reflect processes such as regional cerebral blood flow, or regional ratios of oxygenated and de-oxygenated hemoglobin levels in the blood. As a consequence, there is a substantial time delay between these processes as they are recorded and the neural events that they indirectly reflect. In spite of this delay, the rendering of neural events that is inferred from such indirect reflections is often amazingly accurate. One example is Positron Emission Tomography (PET), which results in a record of the extent to which a given substance is present in various parts of the brain. The amount of substance present at a certain location in the brain depends on the amount of blood flow to that location. The amount of blood flow in turn is considered as depending on the amount of neural activity in that particular brain site. A big advantage of PET over techniques based on volume conduction is that the former provides a 3-dimensional display of the distribution of brain activity with very high spatial resolution, in the order of 4 to 8 mm. A relative disadvantage of PET is that its temporal resolution is very poor: Changes as a function of time can only be recorded on a time base of tens of seconds.

A more recent development is the introduction of functional Magnetical Resonance
Imaging (fMRI). This technique is used to detect changes in the spin of microscopic particles, which also depends on neural activity at the site of measurement. fMRI provides spatial resolution comparable to or better than that of PET, and a temporal resolution of a few seconds. Like PET, fMRI essentially measures blood flow. This implies a fundamental limit to the temporal resolution of fMRI, because a change in local blood flow related to local neural activity takes some seconds.

A further technology that is based on volume conduction of electrical brain activity is Magneto-Encephalography (MEG). MEG is based on the principle that each change in electrical activity involves a change in magnetic field as well. Both MEG and EEG provide very high temporal (in the order of a millisecond or less), and MEG has better spatial resolution, but its scope is almost completely limited to cortical sulci. The causes of this poor spatial resolution will be discussed in sections 1.3 and 1.4. Beforehand, it should be mentioned that there are conditions in which this drawback carries relatively little weight, as for example, when there is isolated activity in a limited part of the cortex. Furthermore, it is not always necessary to know much about the source of the recorded signal to come up with an interesting interpretation.

1.2 Recording and analyzing the EEG

Two electrodes and a signal display\(^1\) suffice to record the EEG. Often one electrode is placed as close to the brain as possible, whereas the other is attached to a site that is considered relatively "silent" with respect to brain activity, because its distance to the brain is relatively large. A popular site for such a "reference electrode" is the mastoid, the bony complex just behind the lower part of the ear. The recording covers an arbitrary amount of time. The signal that is obtained in this way is amplified, displayed, and in, current times, digitized most of the time for further analysis. A typical EEG is shown in Fig. 1. The on-going EEG is depicted as a function of time (x-axis); the amplitude of the difference in potential between the two electrodes is represented on the y-axis. The EEG can always be transformed so that its average value across

\(^1\) Actually much more is needed, e.g., conducting paste, a 3rd electrode (the "ground"), and an amplifying system.

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time is about zero; then the amplitude will vary between negative and positive values. The lower panel of Fig. 1 features clear rhythmic activity, known as the alpha rhythm, which is often observed when subjects are at rest (but awake).

![Low-amplitude, high-frequency dominated](image)

![Alpha dominated](image)

**Fig. 1.** Two typical EEG records. Lower panel: Rhythmic activity dominated by a cycle-period of about 0.1 s (alpha: 10 Hz). Upper panel: Low-amplitude, more random-like activity with more cycles of shorter period (i.e., higher frequencies). *Source information lost.*

It should be noted here that the freshly recorded EEG is never free of "artifacts", parts of the signal that do not reflect brain activity. Artifacts may include movements, or fluctuations in the signal stemming from muscle activity (see section 1.5), and especially the effects of eye movements and blinks. The latter entail potential shifts caused by ocular activity which are conducted from the region of the eyes to the EEG electrodes. These potential shifts may have amplitudes which may be as five times as high as those reflecting brain activity, depending on how close the EEG electrode was to the eyes. The ocular artifacts are dealt with by omitting trials with ocular activity from further analysis, or by methods in which a correction factor is computed and applied for each EEG electrode.

The alpha rhythm shown in the upper panels of Fig. 1 gives way to low-amplitude, fast activity when subjects engage in some mental activity (as shown in the upper panel). A typical way to have a subject engage in mental activity is to present a stimulus: A tone, a flash of light, or whatever. Further exemplary characteristics of the typical ‘resting-state’ EEG are illustrated in Boxes 1 and 3.

**Box 1: Characteristics and determinants of resting-state EEG**
Resting-state EEG is generally recorded over a period of 4 to a 8 minutes, with the subject sitting or lying down, often with eyes closed, and in the absence of dedicated external events. It can tell us interesting things about the state of the brain in various conditions. In the figure below, the traces in the first row each show 15-second recording of full EEG from an electrode over the frontal cortex from a single healthy individual.

The traces on the second row (‘theta’) are the result of a filtering operation on the full traces that only retains frequencies between 4 and 8 Hz (‘theta rhythm’). The traces on the third row (‘alpha’) are the result of a filter operation on the full traces that only retains frequencies between 8 and 12 Hz (‘alpha rhythm’). The left column represents data recorded in a control condition; the right column data recorded after inhaling 69 mg of delta-THC. The bottom panels contain corresponding ‘time-frequency plots’. These represent the strength of the contribution to the recorded signal (‘power’) separated for different oscillation frequencies as a function of time. Black is high power, white is low power. It can be seen that especially in the theta range there is reduction in strength from 0 mg to 69 mg. This reduction in theta power was significantly correlated across multiple individuals with a cannabis-induced reduction in efficiency of search in working memory. From Böcker et al., 2010.
In the late fifties it became clear that applying a stimulus had more effects on the EEG than only "alpha desynchronization", as the disappearance of the alpha rhythm is called. However, whatever more there was, was hard to discern, because it mixed with the on-going background EEG. For a better view the method of signal averaging was applied. This method is based on the idea that the background EEG has no fixed temporal relationship with the point in time at which the stimulus was presented. Signal averaging involves the repeated presentation of stimuli. The EEGs recorded during and after each stimulus presentation are subsequently subjected to (signal) averaging. For example, the same stimulus could be presented on a number of trials. On one trial the alpha rhythm might be in an ascending phase at the moment of stimulus presentation, going from negative to positive; on a second trial it might be in a descending phase (see box 2 for an extreme example of this sort). If sufficient trials are collected and EEG amplitudes at the moment of stimulus presentation are averaged across trials, the result will approximate zero. The same principle would hold for all points in time after stimulus onset. On the other hand, that part of the EEG that is specifically related to the presentation of the stimulus, is supposed to have a fixed temporal relation with it. If on each trial the stimulus causes an increase in negativity which peaks at about 100 ms after its presentation, averaging across trials of the amplitudes at 100 ms post-stimulus would still result in this same negative peak.

Perhaps the method of signal averaging is best illustrated when including the principle of digitization. Fig. 2a shows three EEG epochs. Suppose that for each of the three epochs a stimulus had been presented at the beginning of the trace. Fig. 2b shows how signal averaging goes about. For each of the three epochs (trials) samples are taken at fixed time intervals, resulting in a time series of sample values for each of the trials. Note that in this example digitization is rather coarse: Sample values take on only integer values, whereas the true amplitude takes on all kinds of intermediate values. Corresponding values in the 3 time series are summated (2c) and averaged (2d). The two lower panels show the summated and the averaged sample values, along with the "true" sum and the "true" average. Fig. 3 shows another example. In this experiment the subject had to respond with a button press to stimulus S2; S2 was always preceded by a warning stimulus S1. Recording on each trial commenced at 1 s before S1.

\footnote{Nowadays most analog-to digital converters in EEG research have at least a 12-bits resolution, implying that there are $2^{12} = 4096$ values to represent the analog signal, instead of the 7 values used in this example.}
and ended at 2 s after S2. The waveforms numbered 17 to 32 represent the EEG as recorded on 16 separate trials. The uppermost waveform shows the result of signal averaging. The most notable features are a slowly rising negativity, plotted upwards, between S1 and S2, which is usually identified as the so-called "Contingent Negative Variation" (CNV), and a prominent positive peak some hundreds of milliseconds after S2, which is usually identified as "P300". The CNV and the P300 are parts of what is called the (average) Event-Related Potential or ERP, "event" in this case referring to the presentation of the stimulus. The ERP is assumed to be elicited on each single trial, but to show up most clearly after averaging. Although the CNV and the P300 can be traced in some of the single-trial waveforms, it is clear that they are identified much more easily in the average waveform.

"Identification" hardly ever goes without quantification. There are several aspects of the ERP that researchers may be interested in. They may focus on the onset latency of a clearly discernable part of the ERP. For example, this might concern the point in time after S1 at which the CNV "starts" to develop. Such an onset latency may be measured in different subjects and in different experimental conditions (but not so easily for different trials). Another relevant parameter might be the average amplitude across a given stretch of time. For example, the CNV might be quantified by computing the average amplitude between 300 and 1000 ms after S1. A further popular way of quantification concerns clearly discernable peaks: Peak amplitude and peak latency. Especially the latter has found many applications with respect to the P300. In Fig. 3, the latency of the P300 peak could be measured with reference to the point in time at which S2 was presented, just as reaction times (RTs) are measured.

"Easy identification" has a more technical expression: It is said that the "signal-to-noise ratio" (SNR) is improved. "Noise" in this case mainly refers to the contribution of the on-going background EEG, although in general it may include any error of measurement, that is: Any part of the variation in amplitude that one is not interested in. The signal, of course, is what one is interested in: the CNV, the P300, etc. The improvement in SNR is especially noted when the data are quantified. For example, measuring the amplitude of a certain part of the CNV at the single-

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3 Strictly, "event-related potential” refers to the part of the specific effect of the stimulus on the EEG that can be deemed "psychological". In contrast, the term "evoked potential" is more common for that part of the effect that is due to physical stimulus parameters. The latter effects are also called "exogenous"; the "psychological" effects are also termed "endogenous".

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trial level would yield very unstable results because of the contribution of the noise. This instability becomes manifest if a single-trial amplitude is measured in each member of a group of subjects. The low SNR would result in relatively large variation of the estimated amplitude across subjects; this could render any meaningful phenomenon statistically insignificant.
Fig. 2. A: Three EEG epochs; negativity is plotted upwards. B: The result of coarse digitization for each of the 3 epochs (trials), resulting in 3 time series. Corresponding values in each of the 3 time series are summed and averaged. C, D: The results of B plotted as points, along with the “true” results of summation (C) and averaging (D). From Cooper et al., 1980.
Fig. 3. The top trace shows the average waveform based on signal-averaging of the single-trial waveforms numbered 17 to 32. S1 was a warning stimulus, S2 another stimulus to which the subject had to make a button press. Reaction times (RT) were also recorded (right column). From Näätänen, 1992.
Note, that "signal" can have two meanings: Either it refers to all of the recorded EEG, or it refers to that part of the EEG that one is interested in. Note further that signal-averaging implies an alignment of the single-trial waveforms or their corresponding sample series to a certain point in time, e.g., the moment of stimulus presentation. It is also possible to use a different point in time for alignment, e.g. the point in time at which the button-press is made (reaction time or RT). Averaging would then result in a waveform which represents the activity that is time-locked to RT, rather than to the moment of stimulus onset. Box 2 provides a further schematic illustration of the signal-averaging procedure.

Box 2: Signal averaging in an ideal hypothetical situation

The figure presents an idealized example of exact counter-phase between the background activity on trial 1 and that on trial 2. In that case only two trials are needed to average out the background activity completely. In practice the phase relations vary much more randomly from trial to trial, and many more trials are needed for sufficient reduction of the background activity (as a rule of thumb, n trials reduce the background activity by \( \sqrt{n} \)).

Trial 1 contains ERP + background activity 1. Trial 2 contains ERP + background activity 2 (counterphase, as illustrated in the combined plot in the lower right panel). The average is point by point and reveals the exact ERP. From Kenemans & Kähkönen, 2011.
Signal averaging improves the SNR; but then nothing is for free. Generally, a decrease in
"variance" (the consequence of "noise") causes costs in terms of an increase in what is called
"bias". "Bias" refers to a loss of information that is not only disadvantageous in itself, but also
may lead to wrong interpretations. Bias in the particular case of EEG-signal averaging may take
on two forms. In both cases the bias stems from the implicit assumption that the part of signal in
which we are interested does not change across the repeated measurements that are used for
averaging, whereas in reality it does.

Firstly, bias concerns the fact that the amplitude of the ERP varies across trials. It may be
that we consider this variation as unimportant. For example, the single-trial amplitude of the
P300 peak in Fig. 1.3 might vary considerably around a mean value of 20 µV. If in a group of
subjects the average P300 amplitude would vary between 15 and 25 µV, than the average value
of 20 µV would still be interpreted as significant. Things might get worse if the P300 was elicited
only on the first few trials of a sequence. If the complete sequence is included in the average the
resulting average amplitude might become very small, say 2 µV. If variation across subjects is
sufficiently large, then it becomes hard to demonstrate a significant P300 at all.

The second form of bias probably induces more problems. This concerns the fact that the
latencies of the various parts of the ERP may vary from trial to trial. For example, in Fig. 3, the
peak of the P300 might occur at 300 ms after stimulus onset on trial 17, but at 400 ms on trial 18.
This kind of "latency jitter" can result in an average P300 waveform that is much flatter and
broader than the "true" underlying single-trial waveforms are. Consequently, its peak amplitude,
as based on the average signal, will be underestimated. A further problem would concern the
estimation, as based on the average signal, of the latency of a certain part of the ERP. For
example, suppose that at the time of S1 there is essentially zero-activity. A little later, the CNV
sets on; on some trials it has an early onset, on others a later one. In the average waveform the
amplitudes will also be zero at the time of S1; but as soon as the earliest CNV from the sequence
of trials sets on, the average value will start to deviate from zero. If we estimate CNV onset from
the average waveform, the estimate will reflect mainly the trials with an early CNV onset.
Therefore, it will deviate from the estimate that would have been obtained if it would have been
possible to determine CNV onset for each single trial and then average across trials. As a result of
signal averaging the estimation of CNV onset will be "biased" by the early-CNV trials. It appears
then, that the latency of the average is not the average of the latencies (Callaway et al., 1984).

Further costs by the same principle are added when not only do we average across trials, but also across subjects. The resulting waveform is termed the grand average.

1.3 Neurophysiological basis of the EEG

Neural functioning involves the release of neuro-transmitter in the synapse. The neurotransmitter substance affects the properties of the post-synaptic membrane. This is reflected in post-synaptic potentials, either inhibitory (IPSP) or excitatory (EPSP). Gradual accumulation of the latter may eventually result in the nerve impulse, the action potential (Carlson, 1994). It is generally believed that the EEG is a volume-conducted reflection of the graded waxing and waning of post-synaptic potentials. These PSPs may last for hundreds of milliseconds, whereas action potentials last only a few. Therefore, it is thought unlikely that the latter contribute to the common EEG, especially to the extent that the EEG is dominated by relatively slow activity, like in the case of the alpha rhythm, the CNV and the P300.

From the site at which the PSP originates it induces changes in the potential distribution along the dendrite and the cell body. If the PSP entails negativity somewhere outside the cell membrane, it is immediately accompanied by positivity at an adjoining site along the dendrite. The negativity is usually called a "sink", the positivity a "source". This is shown schematically in Fig. 4. The small triangles represent cell bodies, the small circles pre-synaptic terminals, and the T-like forms (post-synaptic) dendrites. In the neuron at the left a negativity emerges after synaptic transmission at the cell body and is (volume-)conducted downwards. Simultaneously a positivity emerges somewhat upwards along the dendrite and is conducted in the opposite direction. The arrow indicates the current loop between the extra-cellular source and sink, which is closed inside the cell. Such a combination of an extra-cellular source and sink can be viewed as a dipole. A dipole is like a battery with 2 poles of opposite polarity.
Fig. 4. Schematic representation of the electrogenesis of the EEG as a function of time, recorded at different sides from the site of activity (upper and lower waveforms). In the first phase neural activity produces a sink in layer IV, which spreads downwards and concurs with a source upward. In the second phase the sink emerges in layer I and has a concurrent source downward. I, IV and VI represent hypothetical cortical layers. The arrows indicate current loops which close in the cell. From Wood & Allison, 1981.

The two waveforms in Fig. 4 reflect what can be recorded with electrodes at some distance from the site of neural activity. For example, suppose that the two neurons in fact represent one neuron
that is activated in two different ways, at two different points in time. Suppose further that the single neuron is located in the neo-cortex with its 6 layers. The upper waveform would be recorded from above the cortical surface; the lower waveform from below the cortex. First, an initial positivity is recorded from above the cortex; from below an initial negativity is recorded. Somewhat later in time the two waveforms reflect a negativity developing at the post-synaptic dendrite (the neuron as depicted to the right). This is reflected in negativity at one side of the dipole and positivity spreading to the other side.

Fig. 4 should not be taken to suggest that the polarity recorded on one side of the dipole can by itself tell us where the dipole is located. The polarity depends foremost on the orientation of the neuron and on the location of the synaptic connection, and on the nature of the PSP: Whether it involves a sink or a source outside the cell membrane. Information about the location can be obtained by inserting an array of electrodes (e.g., attached to a pin) throughout the depth of the cortex. Starting from above the recorded negativity (or positivity) would increase as we descend from electrode to electrode. Once we cross the depth at which the dipole is located, the polarity reverses and positivity (negativity) decreases steadily as we move on downwards.

Fig. 5 shows the manner in which a dipole field evolves in space, and the effect of distance between the site of the dipole and the recording electrode. Each concentric line connects points in space with equal amplitudes. Furthermore, with increasing distance from the dipole (+/-), these amplitudes decrease. In Fig. 5a an array of electrodes is positioned along line a. Waveform a represents the amplitude recorded at each of these electrodes; it is a representation of the potential distribution across points in space. It can be seen that as electrodes get closer to the site of the dipole the positive amplitude increases. It is said that waveform a represents the topography of the EEG that originates from the dipole field. Along line b electrodes are further removed from the dipole site. The resulting potential distribution has a much flatter appearance. What is not shown in Fig. 5 is that the maximum of the potential distribution b will be also proportionally smaller than the maximum of a. This reduction as well as the flatness reflect that for a dipole the volume-conducted potential decreases with the square of the distance between the dipole site and the electrode. Fig. 5b illustrates the effect of increasing distance between the electrodes and two active dipoles that are separated in space. Thus, waveform a in 5b is a combination of two waveforms, which are both like waveform a in 5a. The two corresponding
potential distributions (a and b) summate and are smeared (b). In addition to these distance effects, flatness (‘smearing’, or ‘blurring’) may be enhanced by bad conductors such as the skull.

Fig. 5. The effect of distance of the recording site on the potential distribution originating from a dipole field. Horizontal lines denote horizontally spaced arrays of electrodes. A: The potential distribution recorded close to the site of the dipole (a) is much more differentiated than the one recorded at a larger distance (b). B: Same for a situation in which 2 dipoles are active. From Wood & Allison, 1981.

There is another factor that determines the extent to which dipole activity can be recorded at a given electrode site. This factor is the amount of sinks or sources developing at approximately the same time in the same direction. The changes in potential distribution caused by activity of a single neuron are very small; to be able to notice something at the scalp the activity of one neuron must summate with that of tens of thousands of others. Furthermore such summation of activity should proceed in a special way. If for one of two neurons oriented in parallel a sink travels along it, and for the other a source in the same direction, the two will cancel and very little will be recorded at a distance. From a distance some structures in the brain, like the thalamus, look like a knot of neurons oriented in all possible directions. Therefore it is hard to record any thalamic

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activity outside the thalamus. This kind of global lack of recordable activity is said to reflect a "closed field".

In contrast to structures like the thalamus, the neo-cortex is largely made up of massive stretches of neural fibers oriented in parallel, which may result in "open fields". Furthermore, in many
conditions these parallel pathways are activated in the same way, so that the configurations of sources and sinks summate across individual neurons without considerable cancellation. And of course cortical tissue is close to where we generally put our recording electrodes. Thus, the major part of the EEG is thought to reflect cortical activity, although there are some notable exceptions like the activity in auditory pathways in the brain stem, that can be picked up from the scalp under special conditions. Generally the stretches of cortical neurons are oriented perpendicularly ("radially") to the cortical surface (like in Fig. 4, if the upper waveform were recorded at the cortical surface). However, the cortical surface itself is not arranged neatly in parallel to the skull. In contrast, it is highly twisted and folded in gyri and sulci. Therefore, in a given stretch of cortical tissue, the surface may be oriented perpendicularly to the skull (and the neurons in parallel to it), resulting in so-called "tangential" orientations of the neural pathways and the corresponding dipole fields. Fig. 6a shows varying dipole-field orientations in adjacent small patches of cortex. Depending on the distance of the recording electrode and on the strength of the cortical activity a more or less average orientation may dominate the recorded potential distribution (Fig. 6b and c). In this way Fig. 6 demonstrates a further important principle: A set of dipoles at different locations and with different orientations can be modelled by a single dipole; the orientation and the location of this single dipole represent the averages for these parameters across the whole set. The single dipole is termed the equivalent dipole.

Event-related changes in the EEG can also take the form of a change of amplitude in specific frequency band. One example can be found with regard to the so-called "40-Hz" or "gamma" rhythm. Tones like the one that elicited the ERPs in Fig. 3, also elicit a small but significant burst of fast rhythmic activity, with an onset latency of about 50 ms post-stimulus (Fig. 7). A similar rhythmicity has been reported many times in recent years with respect to action potentials in visual-cortical areas of the cat brain. That is, neurons may produce a series of action potentials at a regular rate of 40 or more per second, in response to a stimulus. More importantly, the rhythmic bursts of different neurons appear to become mutually synchronized after stimulus presentation. While each of the individual neurons may react to a certain aspect of the stimulus, their mutual synchronization could reflect that it is still one and the same stimulus that they react to. Because of the synchronization, the rhythmic burst of action potentials in parallel neurons might be recordable at quite some distance. Therefore, it is possible that the gamma rhythm
recorded in man in fact reflects such bursts of action potentials, directly or indirectly.

![Waveform](image)

**Fig. 7.** Forty-Hz responses elicited by an 1100-Hz tone, at 2 different electrode sites (left and right panel, respectively). Time is presented on the x-axis, amplitude on the y-axis. S represents moment of stimulus onset. From Näätänen, 1992.

1.4 Topographical analysis and source localization

Fig. 8 shows the results of hypothetical dipole configurations on scalp-recorded potential distributions (McCarthy & Wood, 1985). An array of electrodes is positioned along a curved line; hence, the values on the x-axis represent angular degrees, rather than a linear dimension. Note first that all EEG values contained in one potential distribution represent recordings made at the same point in time. Note further that the term "source" is used differently from the way it was used in connection to "sink". Here, it denotes what was previously termed the equivalent dipole, with its location, its orientation, and its strength. Unfortunately, both ways to use the concept of "source" are very common.

Fig. 8a represents the same situation as Fig. 5a does. The two potential distributions reflect a dipole field that is, on average, oriented radially to the electrode array, the site of maximum activity being closest to the middle of the array. At this point the recorded signal is of maximum positivity, which gradually falls off to zero along both sides of the array. Two experimental conditions were simulated: One (x) in which dipole activity is relatively strong, and one (o) in which it is relatively weak. It is important to note that such a combination of potential distributions is consistent with the interpretation that in both conditions the same equivalent
dipole is active; what differs between conditions is the strength (the "moment") of that equivalent dipole. Note that "same" refers to the fact that the equivalent dipoles in the two conditions have the same location and the same orientation.

Fig. 8. Potential distributions recorded in different simulated experimental conditions. The x-axis represents a curvi-linearly spaced

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elected array; the y-axis amplitude. Distance from the source increases from the middle electrode to the edges of the array. A: The potential distributions reflect activity of the same radially oriented source with different moments. B: The potential distributions reflect activity of the same tangentially oriented source with different moments. C: The potential distributions reflect activities of 2 different radially oriented sources. From McCarthy & Wood, 1985.

A similar situation is shown in Fig. 8b. Here the two potential distributions reflect an equivalent-dipole field that is oriented tangentially (parallel) to the electrode array. In that case the amplitude at the electrode that is closest to the location of the equivalent dipole approximates zero; again, this holds for the amplitude of the middle electrode. The negative amplitudes at one side of the array and the positive ones at the other reflect the evolving sinks and sources to both sides of the location of the equivalent dipole. Fig. 1.8c represents the situation in which the equivalent dipole differs in location between the two conditions. In that case, the maxima of the two potential distributions are observed at different electrode positions.

The principles illustrated in Fig. 8 have a very general and therefore far-reaching implication. They define a criterion on which to decide whether or not in different conditions different brain processes are active. A brain process then, is characterized by the location and the orientation of the corresponding equivalent dipole\footnote{It should be noted that there may still be some ambiguity involved in this definition. Theoretically, the same group of neurons may be active in two conditions, but the orientation of the corresponding equivalent dipole may be exactly opposite in one condition compared to the other. In that case the resulting potential distributions would have the same absolute values as in, e.g., Fig. 8a, but for one condition the signs would be reversed (i.e., positivity becomes negativity). This could happen if in one condition the group of neurons was inhibited, involving IPSPs, whereas it was excited, involving EPSPs, in the other.}. It is not distinguished from other brain processes by its strength (moment); one and the same brain process may be active in different conditions to different extents. This situation is illustrated in 8a and b; in contrast, the potential distributions in 8c would lead to the conclusion that two different processes were active in the two conditions. So, inferences can be made as to whether an experimental manipulation activates a brain process different from that in the control condition. This inference may rest solely on the observed characteristics of the potential distributions in the different conditions. It can be made without any reference to the actual, absolute values of the parameters that define the brain process (i.e., the location and orientation of the corresponding equivalent dipole). It suffices to show that these parameters differ (or do not differ) between conditions; and this can be inferred directly from the observed potential distributions.

\footnote{It should be noted that there may still be some ambiguity involved in this definition. Theoretically, the same group of neurons may be active in two conditions, but the orientation of the corresponding equivalent dipole may be exactly opposite in one condition compared to the other. In that case the resulting potential distributions would have the same absolute values as in, e.g., Fig. 8a, but for one condition the signs would be reversed (i.e., positivity becomes negativity). This could happen if in one condition the group of neurons was inhibited, involving IPSPs, whereas it was excited, involving EPSPs, in the other.}

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Directly inferring from the observed potential distributions could proceed as follows. In Fig. 8a the mean of the potential distributions has a maximum for the same electrode location as the difference between the two has. In other words, the "basic" distribution (as reflected in the mean) has the same pattern as the distribution of the experimental effect (as reflected in the difference). One could say that there is "spatial correspondence", "spatial" referring to the electrode space, between the basic distribution and the experimental effect. Spatial correspondence holds for 8b, and it does not hold for 1.8c. If there is spatial correspondence we conclude that there was only one brain process; if there is no spatial correspondence we conclude that there was more than one brain process.

Whenever researchers ask themselves whether their behavioral data reflect the operation of one or of more separable psychological functions, the spatial-correspondence principle can be applied. For example, consider one condition in which a subject has to compare a briefly presented digit to a number of digits that have been specified earlier ("memory search"). In a second condition she has to compare a number of digits that are presented briefly and simultaneously to a single digit specified earlier ("display search"). Both conditions obviously involve access to some kind of memory to compare items amongst each other; but to what extent can the memory and comparison operations in the 2 conditions be considered as identical functions? It has turned out that adding items to the memory set that had to be searched has an effect on the ERP to the test item that is maximal above the frontal cortex. For the display set however, this maximum was found more posteriorly. According to the principle of spatial correspondence then, the two functions involve different brain processes (Wijers, 1989).

Thus far, we have discussed topographical analysis on a fairly limited scale. It is of course possible to extend our electrode space, which would allow for a more detailed and extended topographical analysis. Fig. 9 depicts an electrode montage that has been used as a standard since the 1950s. It is called the 10/20 system because it is based on partitioning the circumference of the head in tenths (10%) or fifths (20%) of the distances between nasion and inion (anterior-posterior dimension) and between the 2 pre-auricular points (left-right). "F" stands for frontal, "C" for central", "P" for parietal, "O" for occipital, and "T" for temporal electrode sites; for example, the Fz electrode is positioned somewhere above the frontal cortex. Even affixes denote the right hemisphere; odd ones the left hemisphere; the affix "z" refers to locations on the
anterior-posterior midline. The electrode labels as defined within the 10/20 system do not carry any intrinsic meaning; they just conveniently convey information on where on the head a given EEG was recorded without further necessary specification of the absolute or relative distances.

In many studies only a limited amount of electrode sites is used, most often the 4 midline sites Fz, Cz, Pz, and Oz. Recall that the EEG is always recorded as a potential difference between 2 electrodes. In most cases the same "reference" electrode is used for each of the "active" electrodes; a popular site for the reference electrode is the mastoid, which is considered to be relatively far removed from the brain activity of interest. Recently, a new standard system has been introduced. Essentially this system entails extending the 10/20 system to a 10/10 system, in which additional positions have been defined in gaps between adjacent 10/20 sites that covered 20% of the circumference of the head.

Fig. 9. The 10/20 and 10/10 systems for electrode positions. Adjacent electrodes are separated either 10 or 20% of the circumference between nasion and inion or between the 2 pre-auricular points (just anterior to the mastoids A1 and A2, on the other
side of the ears. T3, T4, T5, T6: 10/20 nomenclature replaced by the 10/10 labels T7, T8, P7, P8, respectively. From http://www.skiltopo.com/skil3/10-10.jpg.

Box 3 demonstrates the application of topographical analysis to resting-state EEG parameters, with respect including power fluctuations as a function of space and time, and how that can be used to predict human behavior, in some cases up to 20 seconds in advance.

Box 3: Resting-state EEG topography and timing predict behavior

In one experiment (Mazaheri et al., 2009), subjects had to respond with button press to each equally probably presented digit out of the range 1-9 except to 5. Figure B3A depicts the difference in alpha power during the one second *before* the ‘5’ stimulus was presented between false-alarm button presses to ‘5’ and correct rejections. Red means more alpha power for false alarms than for correct withhold. The black dots represent sensor locations for which the difference in alpha power between false alarm and correct withhold was significant at p < 0.008. Figure B3B represents power as a function of frequency for false alarm versus correct withhold, as calculated for each of, and averaged across, the black dots. Note that this was actually an MEG, not an EEG study.
In another experiment (O’Connell et al., 2009), EEG alpha power was used to predict whether an infrequent target interspersed within a stream of non-target visual patterns would be detected or not. The predictive capacity was apparent already at 20 seconds before the presentation of the target. Figure B3C shows time-varying alpha power, where the x-axis denotes seconds, the target appearing at \( x = 0 \), and the y-axis alpha amplitude (square root of power).

Fig. 10a shows a hypothetical potential distribution that has been derived from an EEG recorded at 32 scalp sites. The potential distribution is represented by a so-called "iso-potential contour map". In such a map, sites with equal potentials are connected through lines, yielding a contour for that potential; the difference between the potentials associated with two adjacent contour lines is the same for each pair of adjacent contour lines (cf. Fig. 5a). If the change in amplitude across electrode space is fast, adjacent contour lines are densely packed; if it is slow they are more widely separated. Referring to Fig. 8a, the amplitude change across electrode sites is slow around the peak in the middle and at the edges of the electrode array; it is fast in the intermediate sections. The map in Fig. 10a reveals a positive maximum in the left-posterior area, which gradually falls off in every direction.

In fact, this map was produced by simulating the potential distribution from a radial source close to the scalp somewhere in the left-posterior region. In Fig. 10b the dot represents the
location of the source, and the line originating from it the orientation. Note, that the term "source" is now used as the equivalent of "equivalent dipole". In this simulation, the location and the orientation of the source were specified, as well as the conductive properties of the media between the source and the various recording electrodes. These parameters completely determine the corresponding potential distribution; it is said that the result of such a "forward" computation is unique- if the parameters do not vary, the resulting potential distribution is also constant. The same holds for any number of arbitrary sources; for example, Fig. 10c shows the topographical map corresponding to a configuration of 2 active sources as shown in Fig. 10d (cf. Fig. 5b!).
Given the relevant parameters for the source configuration and the conducting media, the forward problem can always be solved. In experimental practice however, we are confronted not with a forward problem, but with an "inverse problem". That is, we start with a topographical
map (our data), without any knowledge of the underlying source configuration. The inverse problem is much more complex than the forward problem. This is because a single potential distribution can reflect an infinite number of source configurations. This was already alluded to in Fig. 6, in which a multitude of dipoles was modeled by one single equivalent dipole. For example, suppose that a true dipole configuration consisted of a radial source in frontal cortex together with a radial source in occipital cortex. To be able to solve the inverse problem for the observed potential distribution, we would have to know that there were in fact two sources; and this we cannot know in advance. Suppose that we guess that only one source had been active, and stick to this guess. We would then proceed to move this single dipole through the head with varying orientations. For each attempt we compute the forward solution, and compare the resulting model potential distribution with the observed one. After an arbitrary number of attempts we stop and choose the model dipole that gave the best fit between observed and model potential distributions. The most likely estimated location for that single dipole would be somewhere in the middle of the head.

The above example illustrates how the inverse problem is addressed in general, and the uncertainties that remain for each possible solution. For a given potential distribution we may start with a single-dipole model. For an arbitrary, often very large number of possible combinations of location and orientation the forward solutions are derived. For each forward solution the fit to the observed potential distribution is calculated; the lack of fit is expressed as the so-called "residual variance". In general, computer algorithms are used that are reasonably smart in finding the set of dipole parameters that yields minimum residual variance; but of course there is always the possibility that we have missed an even better one. Given the optimal inverse solution for a 1-dipole-model, we proceed to a 2-dipole model, maybe even to a third and further. In general the effect of adding more dipoles to the model is evaluated with respect to the decrease in residual variance observed when comparing the optimal solution for an x-dipole model to the optimal solution for an (x+1)-dipole model. If, according to some arbitrary criterion, the decrease in residual variance is not significant, it is concluded that the x-dipole model does just as well as the (x+1)-dipole model and we may just as well stick to the former.

Often, additional criteria for accepting a model are applied. Brain activity is often bilateral, that is, present at homologous sites in the two hemispheres; this condition can be included
in the estimation procedure. Furthermore, a candidate dipole source should have a plausible location (e.g., not in the skull), and the estimate of the location should not depend on where the iterative search procedure starts. If the latter requirement is not met, this suggests that the part of the potential distribution that the candidate dipole should explain can be considered as noise. Yet other considerations are based on other sources of knowledge, for example evidence from single-cell recordings, or from functional MRI or PET (e.g., Mangun et al., 2000). Such additional considerations may limit the amount of a priori possibilities that has to be searched through, especially with respect to source locations and the number of sources, or, in other words, constrain the (dipole-)source-localization procedure.

There are alternatives to the method of equivalent dipoles. These alternatives are generally referred to as “distributed-source models”. Instead of assuming a limited number of equivalent dipoles, in this method a dipole is modeled for every cortical voxel, the orientation being determined by anatomical information, as in figure 6. For each of these ten thousands of dipoles then, its contribution to the scalp topography is estimated (multiple forward solutions). This computational problem is under-determined, meaning that the solution cannot be calculated, because the number of model parameters to estimate (e.g., 10 000 dipole strengths) is far higher than the number of observations (e.g., 32, 64 or 128 sensor values). Therefore, additional assumptions have to be included in the model, specifying additional assumed properties of the dipoles, such as that their strengths vary smoothly form one dipole to its neighbors. This yields an additional set of equations that eventually allow for solving this enormous forward problem. Equivalent and distributed source models may have complementary value, because the assumptions underlying the two methods are quite different. If they nevertheless yield comparable results then these results can be considered as being mutually confirmatory. An example of such mutually confirmatory analysis is worked out in Box 4.

Box 4: Equivalent-dipole and distributed-source analysis compared

The example data (Massar et al., 2012) concern the so-called Feedback-Related Negativity (FRN), an ERP that is elicited by stimuli that provide negative feedback on an individual’s task performance. For various good reasons it was thought that this ERP originates in the Anterior
Cingulate cortex (ACC). The analysis presented below attempted to confirm this hypothesis. Figure B4A depicts the scalp topography (isopotential contour lines) for the FRN, at 238 ms post-stimulus.

Figure B4A.

Figure B4B.
Figure B4C. Yellow represents maximum activation, red less but still significant activation.

Figure B4B shows the equivalent-dipole solution that left 2.8% residual variance in amplitude across the 64 sensors (BESA 3.0 method). Figure B4C shows the results of the sLORETA (standardized low resolution brain electromagnetic tomography) technique, a typical distributed-source-modeling method. The results from both procedures are consistent with a bilateral, very much medial, slightly anterior source just dorsal to the corpus callosum, in or in the immediate vicinity of the ACC.

1.5 Indirect reflections of brain activity

This primer ends with a brief discussion of more or less celebrated measures of indirect reflections of brain activity. The foremost indirect reflection of brain activity is, of course, behavior. In the kind of experiments that are discussed in the chapters to follow behavior is limited mostly to pressing a button, or, in some cases, squeezing a dynamo-meter up to some specified criterion. Two parameters of behavioral performance are of major interest: Its speed and its accuracy. Speed is usually measured with reference to the timing of the onset of a stimulus, which has to be responded to in a certain way, depending on the task. It is expressed as reaction time or RT: The duration of the interval between stimulus onset and the point in time at which the criterion response is actually made (e.g., a button is pressed). Accuracy is usually expressed as the proportion of trials in a given condition on which an incorrect response was made. Correctness of the response depends on the nature of the task. In some tasks subjects have to choose between different buttons, using different hands or fingers, depending on the information
conveyed by the stimulus (choice-RT tasks). In other tasks subjects have to overtly respond to one particular stimulus and ignore others (go/ no-go tasks).

Trials with incorrect responses are usually omitted from the analysis of RT results. For example, the analysis of RTs is used to infer that a given manipulation has caused a certain brain process to take longer. More specifically, it is inferred that it took longer for the brain process to proceed adequately, given stimulus information and the choice between different responses. In case of an incorrect response, one cannot be sure that the brain process of interest had been completed or even initiated at all; it cannot be excluded that such an incomplete or even non-existent process was the very cause of the error. Therefore, error trials are excluded from the analysis of RT results. For the same reason they are also excluded from the analysis of physiological data. For example, recall that ERPs are derived from signal-averaging across multiple trials; error trials are simply not included in the average. Note that sometimes the ERP elicited on error trials may be of interest in itself.

Button presses and squeeze movements depend on muscular activity. Muscular activity involves a neurally induced change in potential distribution that can be recorded on the skin in the vicinity of the muscle. The resulting signal is termed the Electro-Myogram or EMG. The EMG can be recorded for any kind of muscle; for example, different facial expressions go with different patterns of EMG activity across the various facial muscles. As mentioned (section 1.2), EMG is also a potential artifact in EEG recording. In the kind of tasks that were discussed above, EMGs have sometimes been recorded from the muscles in the lower arm or the hand that govern the overt response. These EMG records are essentially flat at the moment of stimulus onset. Some 50 to 100 ms before the overt response is recorded, the EMG reveals a sudden upswing of activity which appears random-like and fast, much like the desynchronized EEG shown in Fig. 1.1. In general such "EMG onsets" are easy to detect in single-trial records: The EMG has a good signal-to-noise ratio. In the present context, such EMG records are of course particularly interesting when they provide information that could not be derived from overt-performance measures. For example, the EMG might indicate that the subject prepares a response with one hand, without this preparation being actually followed by an overt response with that hand.

Another form of behavior that is of interest concerns ocular activity. In visual tasks, both brain activity and behavior depend strongly on the position of the stimulus relative to the eye, or,
more specifically, to the retina and the fovea. Sometimes it is necessary to have a direct measure of ocular activity as an intervening factor for brain processes and behavioral performance. A common way to obtain such a measure is to record the changes in potential distribution across the head that accompany ocular activity. Such a record is called the Electro-Oculogram or EOG. As mentioned (1.2), the EOG is a major potential artifact in EEG recording. Often, the EEG is corrected for EOG by calculating and applying a correction factor. This calculation is based on EOG recordings by electrodes attached as closely as possible to the eyes. Such EOG records can also be used to derive whether and how a subject has moved her eyes, e.g., in response to a sudden change in luminance somewhere in the visual field. Eye movements can also be recorded, and probably a little more accurately, with the aid of infra-red reflection techniques. With these techniques, invisible infra-red light is directed at the eye, and its reflection is recorded so as to derive changes in eye position.

A widely applied indirect psychophysiological measure of brain activity is the Skin Conductance Response (SCR). Skin conductance is usually recorded from regions of the body with a high incidence of sweat glands, e.g. the hand; the conductance however, is only partially related to the amount of sweating. Conductance is usually recorded by applying a constant current between 2 electrodes positioned closely to each other in the palm of the hand or on a finger. Fluctuations in the voltage necessary to maintain a constant current are used to derive the fluctuations in conductivity. Skin conductance reflects the activity of the sweat glands which are exclusively sympathetically innervated; thus, skin conductance can be seen as a reflection of sympathetic activity. Reliable changes in basic skin conductance (i.e., SCRs) are especially elicited by stimuli that appear significant to the subject, e.g., as a result of prior conditioning, or because the stimulus is new or unexpected. On average, an SCR takes more than 1 s since stimulus-onset to evolve, reaching a peak after a few seconds. Traditionally the SCR has been the major component of lie-detection procedures. Although recent developments indicate that ERP measures might significantly contribute to these procedures, there are some advantages to the use of the SCR that will be hard to neglect: It is cheap and also very reliable, featuring an SNR that allows for single-trial analysis.
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