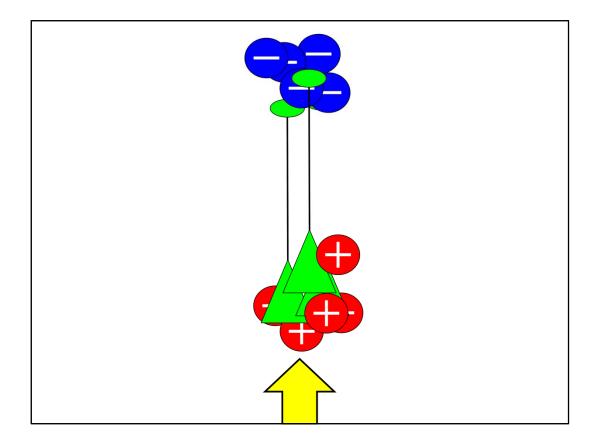
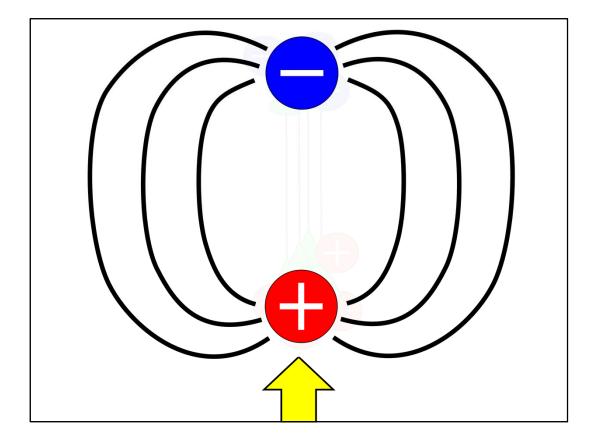


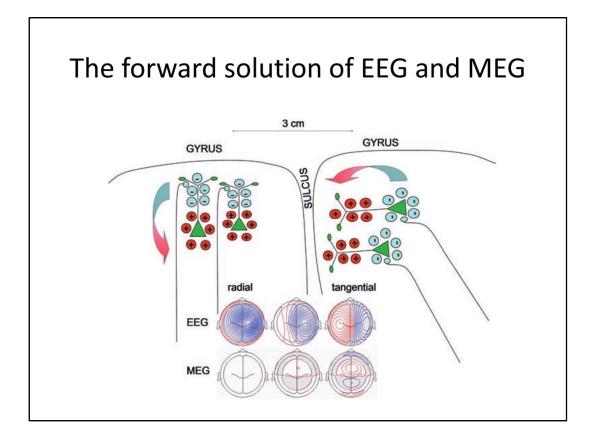
EEG and MEG field result from the superposition of many synchronously firing and parallely oriented neurons. Such bundles of active neurons can be approximated by a dipole.



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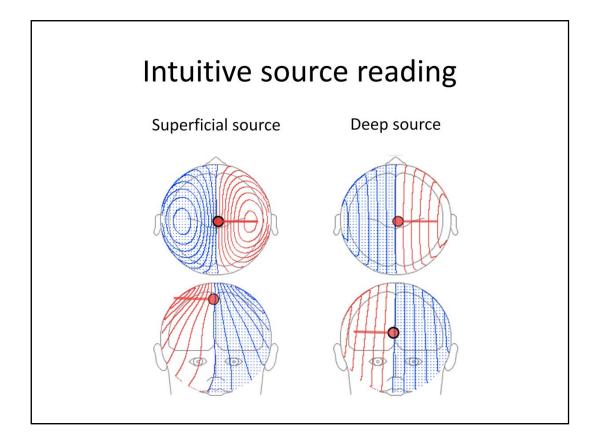


EEG and MEG field result from the superposition of many synchronously firing and parallely oriented neurons. Such bundles of active neurons can be approximated by a dipole.



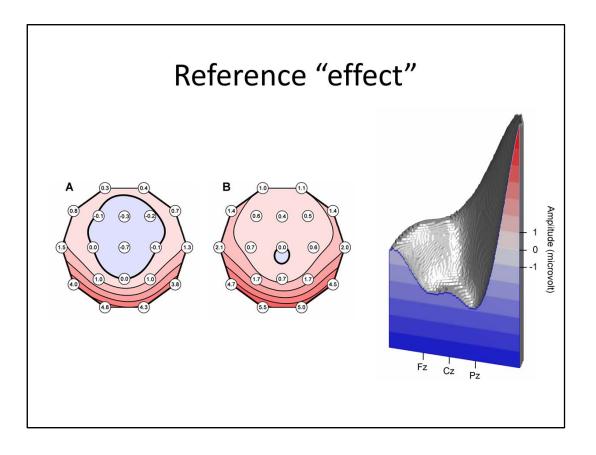
EEG and MEG have orthongal forward solutions

- The EEG is sensitive to radial and tangential sources
- The MEG is only sensitive to tangential sources
- The differences in conductivity of brain/bone/skull/skin affect only the EEG
- The MEG is less sensitive to deep sources than the EEG

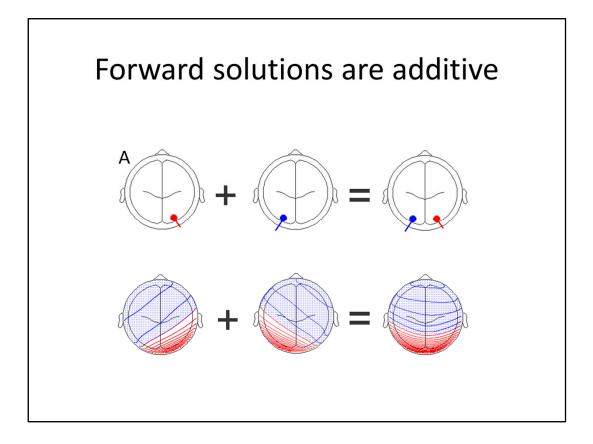


In EEG and MEG, the sources are between the positive and the negative pole In EEG and MEG, if there are strong gradients, one can assume active sources underneath

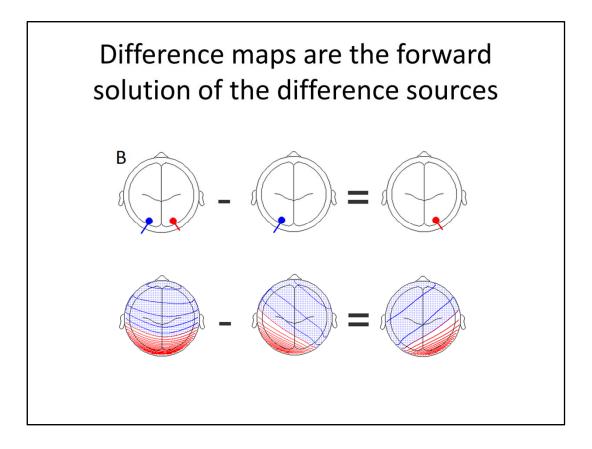
Deep sources make only low spatial frequencies



If you argue in terms of differences between two electrodes, there is no problem with the choice of the reference, because this difference does not change with the reference. It is analogous to the choice of the reference point when measuring height in geographic maps, wherever you place it, the landscape will not change, but the numbers attributed to a specific site will.



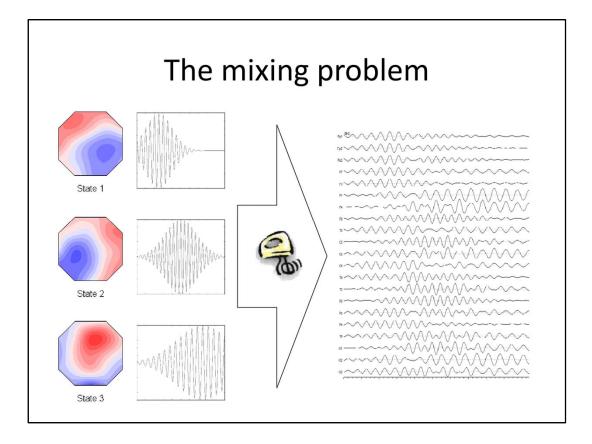
The field measured when two sources are active is the sum of the forward solutions of these two sources. The whole problem is linear.



If one computes a difference map, this map is the forward solution of all sources that differ between the two conditions that were compared. If you can prove that the difference map is larger then what you would expect under random conditions, you have a straight-forward argument that the difference of brain activity is real. This is the proper rationale for scalp-based statistical testing.

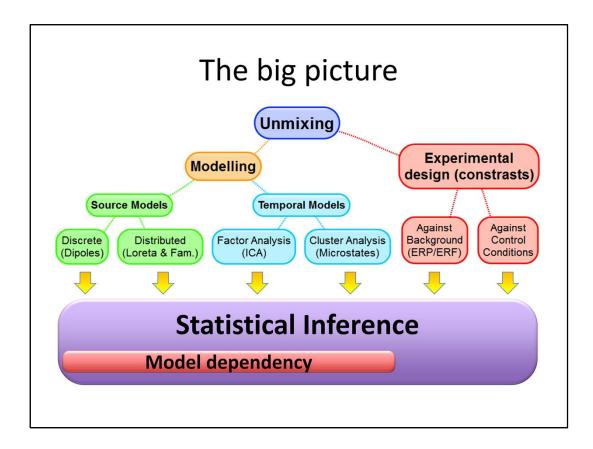
Spatial distributions as a starting point

- + Linear problem
- + Linear relation to sources
- + Reference independence
- + No model dependence
- + Intuitive reading
- Abstract result space (there is something)
- Not enough detail (there is an effect of....)



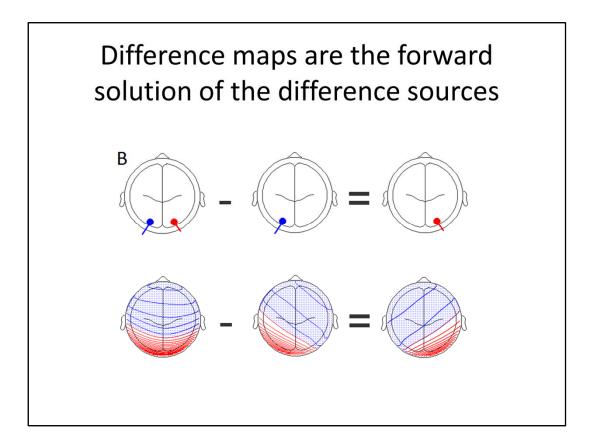
EEG and MEG fields extend over the entire scalp, so even the activity of a very focal source is measurable on most locations on the scalp. In the presence of several sources, this implies that at almost any location, the signals that we measure is composed by contributions from several sources. We end up with an un-mixing problem that by itself has no unique solution.

One source affects many sensors One sensor is affected by many sources

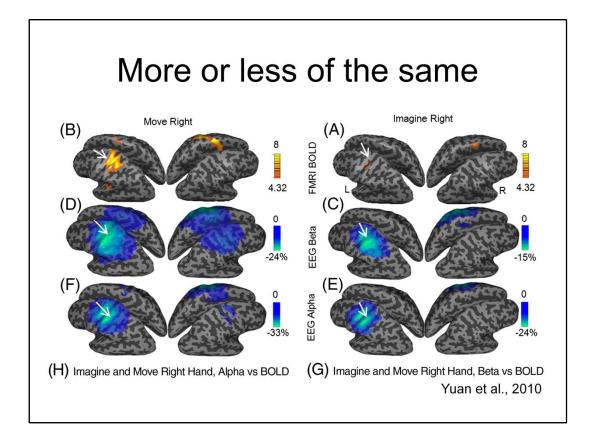


To unmix the data, you have to have a model

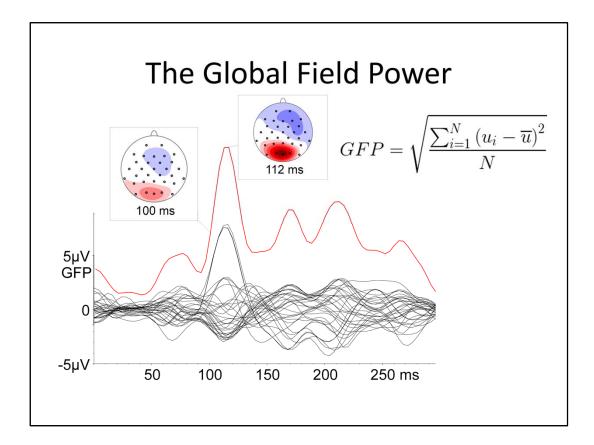
- You can choose a functional model where you manipulate something in your experiment that you think is related to brain processing, like memory. You then contrast the resulting data and obtain the forward solution of all sources assumingly associated with that function
- You can choose a data model by assuming that your data has a certain distribution in time or space
 - In time, there is the ICA model and the microstate model
 - In space, there are the inverse solutions
- Statistics can be done on any model. I however think it is a wise choice to obtain the hard statistical evidence based on data that does not depend on to many a-priori parameters.



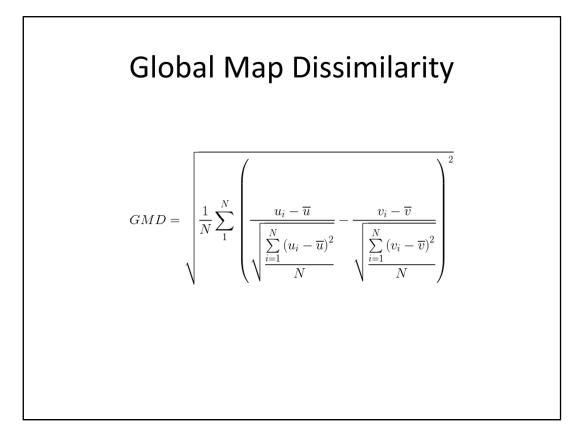
We go into the scalp-based rationale for statistics



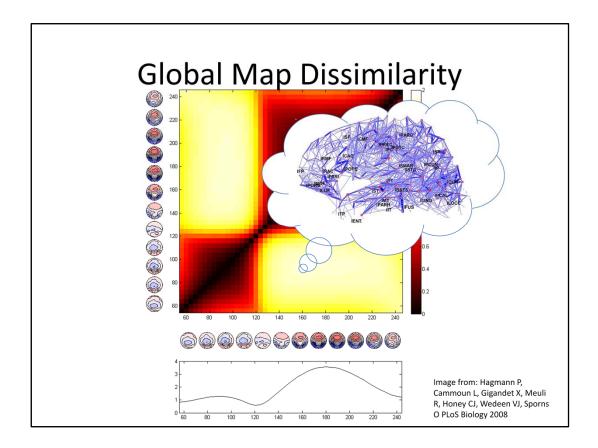
Same shape, but different strenght means more or less of the same



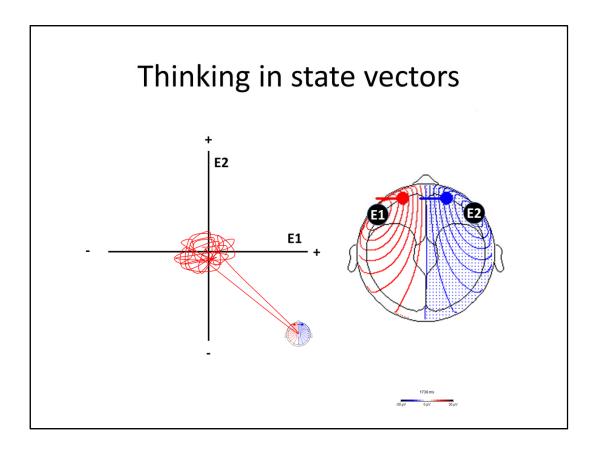
A quantifier that is independent of topography is the Global Field Power



A GFP independent quantifier of topographic difference is the Global map dissimilarity. Global the global map dissimilarity matrix obtained when comparing different time points of spontaneous and evoked activity clearly point at network-type patterns of activity.



A GFP independent quantifier of topographic difference is the Global map dissimilarity. Global the global map dissimilarity matrix obtained when comparing different time points of spontaneous and evoked activity clearly point at network-type patterns of activity.



N-Channel EEG and MEG data can be seen as an n-dimensional state-space, where each moment in time is vector.

- The length of a vector is equivalent to the Global Field Power
- The length of the difference between two normalized vectors is equivalent to the map dissimilarity
- 'Educated' rotations of the coordinate system let you extract meaningful features.

Summary

- Sources translate and mix linearly to the scalp
- The unmixing needs an educated choice of apriori information (modelling)
 - About the design of the experiment, or
 - About the distribution of activity in space or time
- Various well established models are available and yield replicable information in specific conceptual and/or physiological domains

Basic Principles of EEG and MEG Analysis

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1 Introduction

This text intends to give a general introduction to the basic physics of EEG and MEG. We will see how intracerebral electromagnetic activity of single and multiple sources is represented by EEG / MEG scalp measurements. We will learn what we measure on the scalp if the activity of several generators changes with time. It will become apparent that the problem that we usually face is that we want to isolate some processes in the brain based on the measures on the scalp. While there is no unique solution to the problem, there are a series of well established and validated procedures that yield meaningful and unambiguous conclusions.

2 From Brain-Space to Scalp-Space and back

To start with, we are interested in the electric activity of neurons. A single neuron, when active, produces an intracellular electric field (that must be measured inside the neuron) and an extracellular field. The extracellular field of neighbouring neurons sum up to the so-called **local field potential**. Depending on the geometry of the involved neurons, this local field is so called closed or open (Fig. 1).

Only open local fields produce potential differences that may be recorded on the scalp. Open local fields have a position and a direction of the flow of electric current. In EEG / MEG this is typically represented by a so-called **dipole**, or dipole source. A dipole is defined by its location (the dipole position) and a vector that represents the strength and orientation of the flow of electric current (the dipole orientation). In the three-dimensional brain space, a single dipole is therefore described by 6 parameters, 3 for the position, and 3 for the orientation. However, in many analyses, the dipole orientation is neglected and only dipole position and strength are considered relevant.

2.1 From a Single Dipole in the Brain to a Scalp Field

The physics that relate the activity of a given dipole source in the brain to a measurable electric and/or magnetic field on the scalp is well known. It is defined by the geometry and, in the case of EEG, the volume conduction properties of the tissues of the head (brain, liquor, skull, scalp, hair, electrode paste, etc.). These properties are incorporated in the so-called **leadfield**, a matrix that relates intra–cerebral activity to scalp electric and/or magnetic fields [7]. The relation is very simple; for a given single source in the brain with a given position on the scalp, the potential difference measured between two defined sites on the scalp is linearly related (i.e. proportional) to the activity of the source. The factor that needs to be applied to compute the scalp potential differences from the source activity is defined by the lead-field and can be positive and negative. Accordingly, if one describes a scalp field obtained from some source, one often speaks about the positive and negative pole. The leadfield has been shown to be a spatial smoothing function, which implies that even single, point-like bipolar sources (i.e. a single dipole) in the brain produce a bipolar field extending over the entire scalp surface.

Scalp fields are visualized by so called scalp-field **maps**. Similar to maps of a threedimensional landscape, these scalp field maps code the potential at a given position with a color-code, and may contain iso-potential lines (lines connecting points with the same potential) as the contour lines in the maps of a landscape. Scalp field maps are conventionally shown as seen from above, with the nose up. Fig. 2 illustrates the mapping of a typical scalp electric field.

There is a very useful program called Dipole Simulator available on freely here on the internet (http://www.besa.de/updates/tools/) where the user can insert and move one or more dipoles in the brain and study the resulting scalp fields. In the following text, several such simulations are shown and discussed. In the first example (Fig. 3A), the scalp field of a single dipole is shown. Although the dipole is quite close to the scalp surface, its scalp field extends over the entire head. The activity of such a single dipole thus affects almost all electrodes, although not equally strong and with different polarity (positive vs negative). The maximal activity lies almost above the dipole.

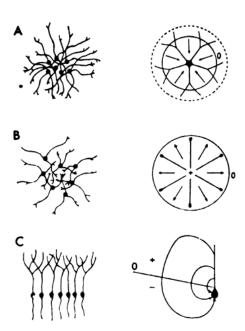


Figure 1: Examples of closed, open, and open-closed fields. Left: The populations are drawn. Right: Neurons representing the simultaneously activated pools are shown together with the arrows representing the lines of flow of current at the instant when the impulses have evaded the cell bodies. The zero isopotential lines (0) are also indicated. A: All neurons have dendrites oriented radially outward. The isopotential lines are circles; the currents flow entirely within the nucleus, resulting in closed field (all points outside the nucleus remain at zero potential). B: Several neurons, all having a single dendrite oriented radially inward. The currents result in a closed field. C: Neurons with a single long dendrite. This permits the spread of current in the volume of the brain and thus results in an open field. (From [4])

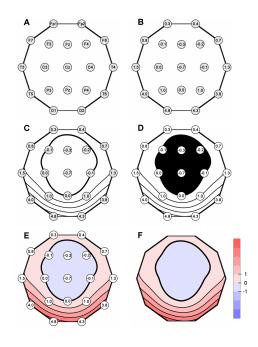


Figure 2: Construction of a scalp field map. (A) Scheme of the electrode positions projected on a two-dimensional plane. The head is seen from above, nose up. (B) Scheme of the electrode positions with the values (in microvolts) at time point 100 msec. (C) Values with isopotential lines at -1, 0 (bold line), 1, 2, 3 and 4 microvolts, measured against the electrode Pz. (D) Same as (C) but negative areas are shown in black with white isopotential lines. (E) Same as (D) but with blue areas indicating negative, and red areas indicating positive values. The color intensity is proportional to the voltage differences from zero. (F) Same as (E) but with an additional color scale and the numbers removed. (From [6])

The next example (Fig. 3B) shows the effect of a dipole located at the same position, but now with an orientation that is tangential to the scalp surface. Note that the scalp field has changed completely and that there is nearly no voltage above the source. The locations of the most positive and most negative electrodes are remote from the location of the source. The example shows that the orientation of the sources has a massive effect on the scalp measurements, and that the locations of maximal or minimal scalp amplitude are not necessarily identical to the location of the sources.

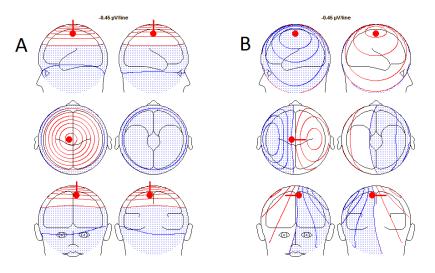


Figure 3: A: A single dipole close to the electrode position Cz, with an orientation perpendicular to the scalp. On the left part, the head is seen from left (upper left graph), right (upper right graph), top (middle left graph), bottom (middle right graph), front (lower left graph) and back (lower right graph). Positive values are shown in read, negative values are shown in blue and with dots. B: A single dipole at the same position as in A, but the orientation of the dipole has been changes by 90 degrees. The scalp field has drastically changed.

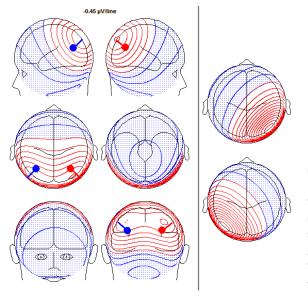
2.2 More than one Dipole

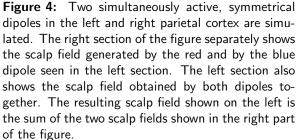
In a living brain, many sources are active simultaneously. What happens to the scalp electric field in this case? In other words, how does the activity of several dipoles interact on the scalp?

The answer is rather simple: with several dipoles simultaneously active, the measured scalp field becomes the sum of the scalp fields produced by those dipoles. This is illustrated in Fig. 4, where two simultaneously active, symmetrical dipoles in the left and right parietal cortex are simulated.

2.3 Understanding Difference Maps

In the previous section, we have learned that if two sources are simultaneously active, the resulting scalp field produced by those two sources is equal to the sum of the scalp fields produced by each source alone: EEG and MEG forward solutions are additive (Fig. 5A). As a consequence, this means that we also have a simple interpretation of the subtraction of two maps: If we subtract map Y from map X and call the result map Z, i.e. if we





compute (Z = X - Y), map Z is the forward solution of all those sources that distinguish map X from map Y (Fig. 5B). Those sources that were identical in map X and map Y (let's call the map produced by those sources K) do not affect map Z. (In mathematical terms: Z = (X + K) - (Y + K) = X - Y.) Thus, if we can prove the existence of a difference map obtained by comparing two conditions, we have an excellent evidence that the two conditions differed in terms of the involved sources. More specifically, this map difference can be due to differences in location, orientation or strength of the active sources. We can furthermore directly interpret the field of the difference map, e.g. using inverse solutions (see below).

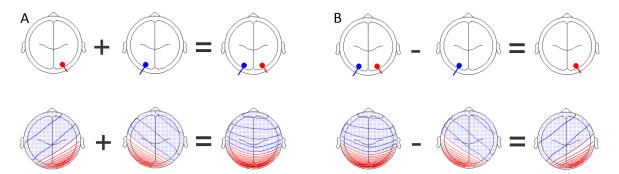


Figure 5: Addititivity (A) and subtractivity (B) of EEG maps. The upper row shows the location of the sources, the lower row the resulting EEG scalp field maps.

2.4 The Inverse Problem, and some Source Localization for Pedestrians

So far, we have only considered the question how the scalp electric field is defined for a given set of dipoles. This is called the **forward-problem**. However, in real life, we have measured the scalp electric field, but are actually interested in the sources that have caused the observed field. Due to the mixing explained above, and due to the fact that the scalp fields of several dipoles may cancel out, this so called **inverse problem** of the cannot be solved uniquely, neither for EEG nor for MEG. This means that for a given scalp field, we can find an endless number of configurations of dipoles that would produce our scalp field. This implies that the researcher has to use additional rules to select among this infinitive number of valid inverse solutions. This is however beyond the scope of this introduction.

Nevertheless, the projection of electric dipoles sources to a scalp electromagnetic field has some properties that often allow a rough estimate of the location of the predominant sources based on a visual inspection of the scalp field. Two aspects are particularly helpful here:

- In EEG, dipoles lay between positive and negative poles of the field. However, since the electrode grid does not cover the entire head, one or both poles of a dipole might lie outside the electrode grid and are therefore not well represented. This may easily yield false conclusions, both if the data is visually inspected, and if explicit inverse solutions are being used. It is therefore advisable to extend the electrode grid such that it covers as much as the scalp as reasonably possible. MEG maps have also positive and negative poles, but these poles are orthogonal to those of the EEG.
- Dipoles close to the scalp make strong gradients close to their location. Scalp field gradients describe the potential difference of nearby scalp positions. When looking at a scalp field with contour-lines, strong dipoles can be assumed where the field-lines are dense.

Two examples where the dominant sources can reasonably be inferred are shown in Fig. 6.

2.5 The Reference

We have learned above that active sources produce specific potential differences on the scalp. Accordingly, these potential differences must be recorded as differences of various scalp sites against another site, the so called reference. How does the choice of reference affect the data we obtain, and how does it affect the scalp maps we construct form this data? The problem is very similar to the measurement and display of the height profile of a geographic landscape, where height is referred to as a difference against a reference level (e.g. the level of the sea) which is somewhat arbitrarily defined to be zero. If we would have changed the reference level common for all our height measurements, all values would change, however, the differences among those measurements would have remain the same. This is equivalent to the observation that the shape of the landscape does not change if we change the reference point that we use to measure height at different positions in that landscape. In complete analogy, changing the reference thus does not affect the shape of the obtained map, it merely changes by which potential difference values a given site is labeled. Thus, the shape of brain electromagnetic fields is reference independent, it represents the same potential differences against any reference we might chose. And thus, any conclusion derived from EEG or MEG data that can be shown to be a consequence of one or several processes producing a potential difference between two defined sites can be said to be a conclusion that is reference independent. This is the case for all analysis that compare the shape of scalp potential maps.

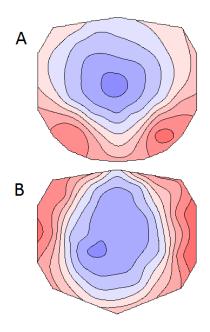


Figure 6: A: A typical scalp field map evoked around 100 ms after a visual stimulus. There are two occipital positive poles and a single, large negative one. In addition the isopotential field lines are densest bilateralally over occipito-temporal regions. This indicates the presence of two dominant sources in the left and right occipito-temporal cortex. The positive pole of those sources points toward lateral occipital electrodes, the negative poles of both sources point to the center of the scalp. B: A typical scalp field map evoked around 100 ms after an auditory stimulus. The gradients and the positive and negative poles point to bilateral tangential sources in the anterior temporal lobes.

2.6 Dynamics in Time

We have learned in the previous sections that the activity of a given source translates to a measurable potential on the scalp by a simple scaling factor that can be positive or negative. If the source has some dynamics over time, those dynamics translate to the scalp in the same way, the source dynamics is merely multiplied by a factor defined by the leadfield to yield the dynamics on the scalp. This is illustrated in Fig. 7.

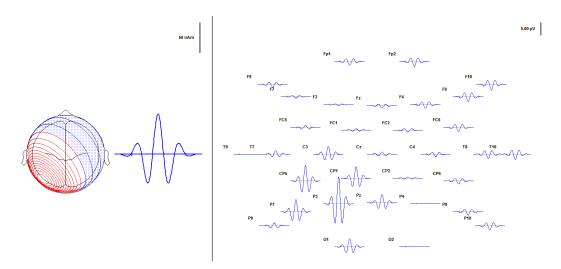


Figure 7: Left: the scalp field of a source, and the dynamics of that source. Right: The signal recorded at different, topographically arranged electrode positions. Note that depending on the polarity of the scalp field at a given electrode, the signal may be reversed.

3 The Unmixing Problem

What we measure with EEG and MEG is thus always a mixture: given that the scalp field of a single dipole extends over the entire scalp, and given that the scalp fields of different generators simply add up, each single electrode measures a mixture of activity resulting from several different sources, and many different electrodes measure the signals from the same sources. Univariate, single electrode analysis is therefore not specific to the activity of a circumscribed source, and the activity of a circumscribed source is poorly represented in a single electrode. See also Fig. 8 for illustration and try to find an electrode that gives an unconfounded representation of only one of the three processes shown. It is impossible.

One of the core problems of EEG and MEG is thus to find ways to unmix the recorded signals and separate the different processes that contributed to the data. There several conceptually different approaches to obtain solutions to this problem, as shown in Fig. 9. All of these approaches contain assumptions, either about the relation between an assumed mental process and the measurable brain processes, or about the distribution of brain activity in time or space. To conclude this introduction, the different branches are briefly discussed:

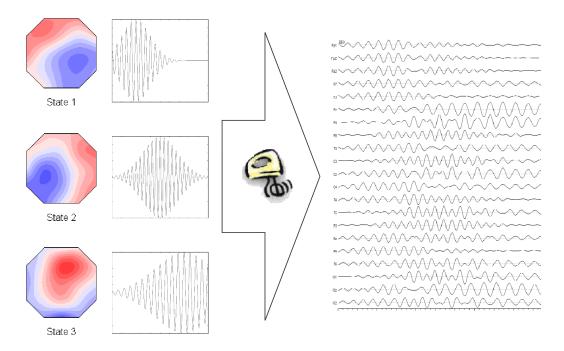


Figure 8: The mixing problem: On the left, we see three topographies and three corresponding temporal patterns of activity. Assuming these three processes were active (i.e. each topography would be modulated with the corresponding temporal pattern), the data on the right side would be obtained.

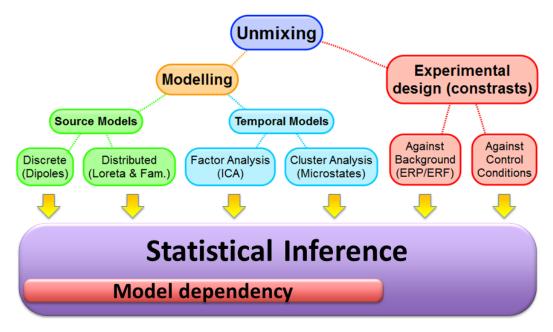


Figure 9: Outline of the the different families of EEG/MEG unmixing approaches.

3.1 Experimental Inference

Experimental inference attempts to un-mix the recorded EEG signals experimentally. By assuming that the measured data consists of a superposition of signals associated with an experimental event or condition that supposedly invariably activated a defined set of brain regions, and signals unrelated to the condition, the contrasts computed in the data as a function of the experimental condition will directly isolate the sources associated with the condition. There are two major types of cases, and for each type there exist powerful randomization tests to provide the necessary statistical evidence:

3.1.1 Identification of event related electromagnetic potentials against background activity by averaging

This is the standard situation for all event related analysis that separates brain electromagnetic activity with a consistent temporal association to a repeating event from activity that has no such association. Note that The presence of event related electromagnetic fields can be tested statistically using randomization techniques such as the Topographic Consistency Test [2].

3.1.2 Identification of electromagnetic potentials specific to certain conditions:

Given the additivity of brain electromagnetic signals (2.2, p. 4), difference maps obtained from two or more condition isolate those sources that are related to the difference between conditions. Again, for testing the statistical significance of difference maps, randomization tests that are specific for brain electromagnetic scalp fields are available [9], including intuitive software solutions [1]. Note that the association with (and the resulting contrasts between) specific conditions and the scalp electromagnetic potentials can be assumed to be in time, in time-frequency or in frequency domain.

3.2 Modelling

The unmixing of EEG and MEG data can also be made unique by adding additional assumptions about some distribution of the underlying ingredients. This implies modelling, where the models are chosen such that they maximize their compatibility both with the a-priori assumptions and with the given data. There are two big families of assumptions, one makes specific assumptions about the distribution of the different constituents of the mixture across time, and one assumes specific distributions of the sources of the signals in brain space.

3.2.1 Temporal Models

Temporal models assume that the measured data consists of a combination of a typically relatively low number of processes that have a stable source configuration, and vary according to a certain distribution across time. The most commonly used models of this type are Independent Component Analysis (ICA, [5]) and Microstates [3].

• Independent Component Analysis (ICA)

The a-priori assumption when using the ICA is that the EEG/MEG is composed of a series of components (each consisting of synchronously active brain regions), and that

the temporal dynamics of these components are mutually independent. An ICA analysis yields, for each factor, it's dynamics over time, and it's relative weight at each sensor. The ICA is frequently use to identify spatio-temporally defined brain-oscillations such as spindles, and it is also very helpful to eliminate artefacts such as eye-blinks or scanpulse effects.

• Cluster Analysis (Microstates)

Microstate analysis assumes that the EEG/MEG is composed of a temporal sequence of brain states, each being stable for a brief period of time, and not overlapping with the temporally adjacent microstates [3]. Microstate analysis is typically used to extract precise information about the timing of stimulus evoked of spontaneously occurring brain states.

Both the ICA and microstate analysis have a common and interesting background: They both assume that the EEG data is composed of a small set of fixed topographies that vary across time only in intensity. If we (reasonably) assume that these fixed topographies are produced by more than one point-source, this strongly suggests that the sources contributing to a given, fixed topography have common temporal dynamics. Common temporal dynamics among distributed sources are on the other side a strong candidate for a binding mechanism in distributed networks [10].

3.2.2 Spatial Models: Inverse Solutions

Inverse solutions make specific assumptions about the spatial distribution of the sources that produced a measured scalp electro-magnetic field and "choose", among an infinite number of possible source configurations that explain the measured data, the one that is most compatible with the assumed spatial distribution. There are two families of inverse solutions: Discrete and distributed inverse solutions. They are briefly reviewed below.

• Discrete Inverse Solutions (Dipoles)

Discrete inverse solutions assume that the observed data originated from a typically very small, a-priori defined number of sources with a point distribution, and noise. The position of these point sources may be free, or may be constrained by addition a-priori information. Given appropriate head-models, discrete inverse solution may have a very high localization accuracy, given that there is indeed a very small number of focal "hotspots" of brain activity, and the number of sources has been chosen adequately. If these assumptions are not justified, discrete inverse solutions may however yield rather misleading results.

• Distributed Inverse Solutions

Distributed inverse solutions assume that all elements of a typically very large solution space contribute to the observed scalp electromagnetic field, and that in addition, the distribution of the activity of these elements maximized an a-priori assumption. Such an assumption is e.g. that the total amount of assumed activity is as small as possible (minimal norm inverse solutions) or that is spatially smooth (e.g. in sLORETA). Distributed inverse solutions are typically more adequate in more diffuse source configuration, but yield only a blurred estimate of the active sources, and have low spatial resolution.

4 Conclusion

Aim of the above text was to outline the nature of the lawful relationship between neuronal activity in the brain and the electromagnetic potentials as they can be measured non-non-invasivly in on the scalp. Despite this lawfulness, the data does not 'speak' directly to the observer in a comprehensible way; a given set of measurements may be explained by different underlying processes. We therefore have to introduce additional information in the form of particular models that establish rationales to interpret the measured data under a particular perspective. Fortunately, there are several such models available that have received overwhelming confirmation by other and independent clinical, experimental and neuropysiological evidence. The above text should help the reader to make adequate choices of the appropriate analysis model, and how these models bridge the gap between the data and its interpretation.

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