Multiple source analysis of EEG and MEG

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M. Scherg, Sept. 2008

This presentation was held at the 3rd International Summer School in Biomedical Engineering on **Reconstruction of sources of electrophysiological signals** in Weimar / Ilmenau, Sept. 9, 2008.

Overview

- Focal epilepitc spikes activity:
  Single source localization – often not correct
- Basic principles of multiple source analysis:
  Simulated and real example data sets
- Somatosensory evoked potentials:
  Multiple sources provide separation of components
- Auditory evoked potentials:
  High resolution and separation by multiple sources
- Cognitive ERP:
  Multiple sources seeded from fMRI

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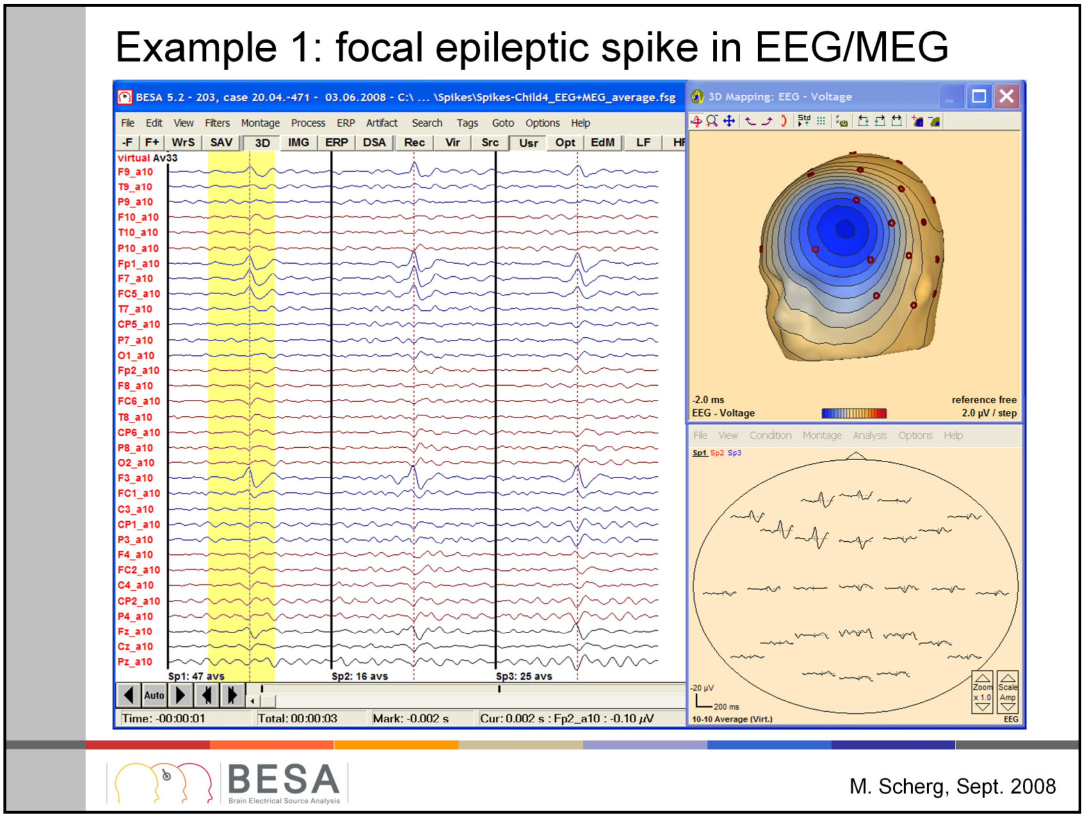
After a first example of an important clinical application of inverse multiple source modeling using EEG data, we will outline the basic principles and use other real data to demonstrate the enormous possibilities – and also the limits – of discrete multiple source modeling.



The analysis and localization of the onset zone of seizures and interictal spikes in patients with intractable epilepsy is one the key goals of EEG/MEG inverse modelling.

The following papers on review, source analysis and imaging of epilepsy data can be obtained as PDF file from the author (mscherg@besa.de):

Bast, T., Boppel, T., Rupp, A., Harting, I., Hoechstetter, K., Fauser, S., Schulze-Bonhage, A., Rating, D., Scherg, M. (2006). Noninvasive source localization of interictal EEG spikes: effects of signal-to-noise-ratio and averaging. J. Clin. Neurophysiol. 23: 487-497.

Bast T, Ramantani G, Boppel T, Metzke T, Ozkan O, Stippich C, Seitz A, Rupp A, Rating D, Scherg M. (2005). Source analysis of interictal spikes in polymicrogyria: Loss of relevant cortical fissures requires simultaneous EEG to avoid MEG misinterpretation. Neuroimage 25:1232-1241.

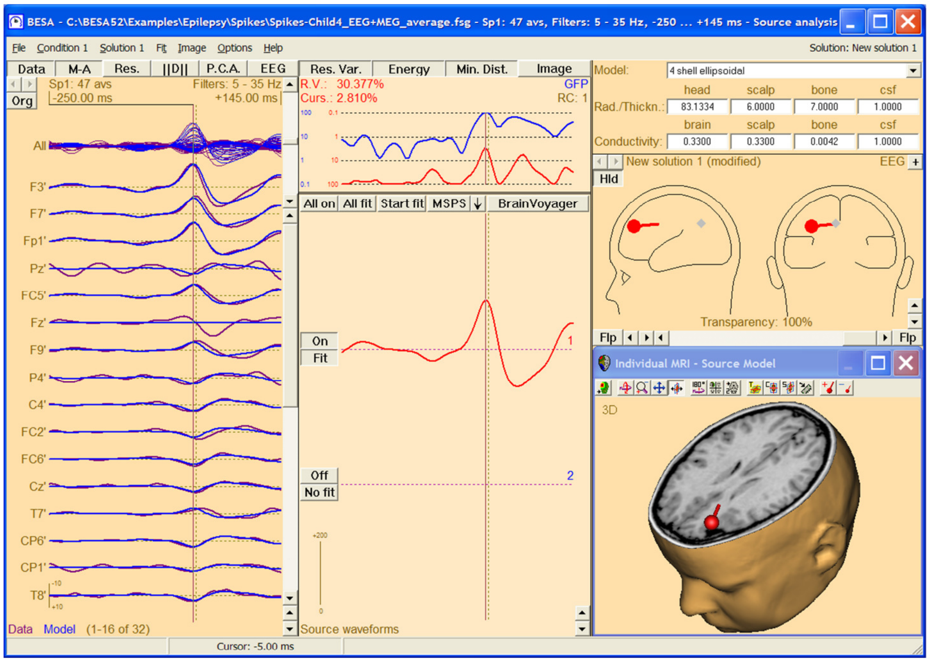
Scherg, M., Bast, T., Hoechstetter, K., Ille, N., Weckesser, D., Bornfleth, H., Berg, P. (2004). Brain source montages improve the non-invasive diagnosis in epilepsy. International Congress Series, 1270C: 15-19

Scherg, M., Bast, T. and Berg P. (1999). Multiple source analysis of interictal spikes: Goals, requirements and clinical value. J. Clin. Neurophysiol. 16: 214-222.

Scherg, M., Ille, N., Bornfleth, H., Berg, P. (2002). Advanced tools for digital EEG review: virtual source montages, whole-head mapping, correlation and phase analysis. J. Clin. Neurophysiol. 19: 91-112.

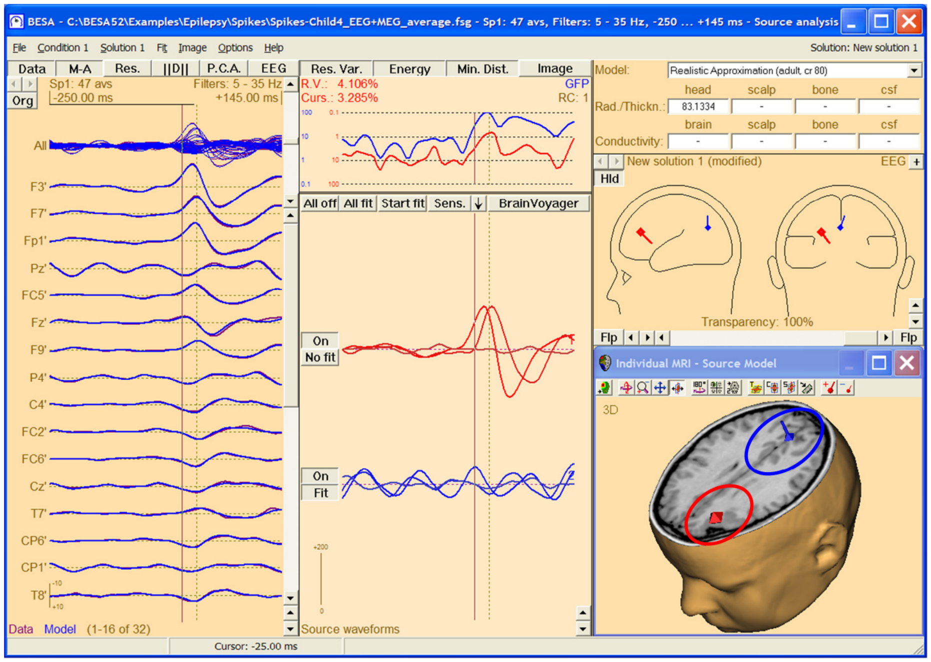
Ille, N., Berg, P., Scherg, M., (2002). Artifact correction of the ongoing EEG using spatial filters based on artifact and brain signal topographies. J. Clin. Neurophysiol. 19: 113-124.

Localization by a single dipole: what does this mean ?

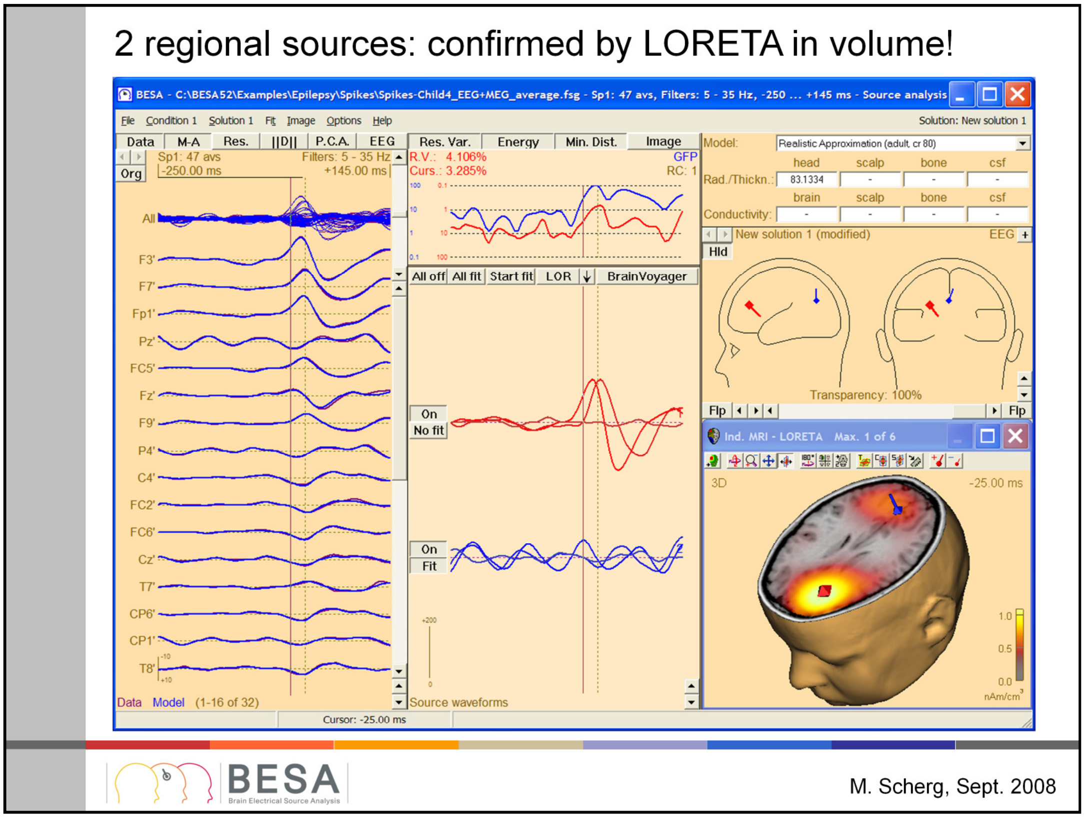


Accuracy of single dipole localization is highly dependent on EEG background. Even after averaging, this can lead to a mislocalization (higher than the lesion in this case).

Localization by 2 regional sources: much better model !



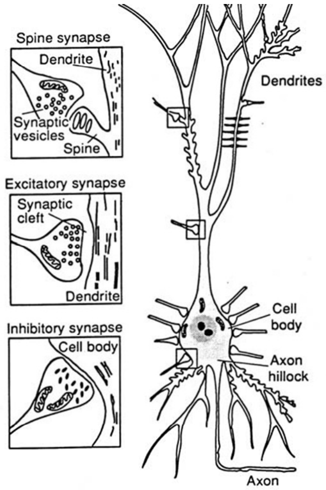
The EEG background (high amplitude alpha rhythm) can be modelled by a regional source in the parietal/occipital region in additional to the frontal regional source model the local spike propagation/rotation. Thereby, more precise localization in the boundary zone of the dysplastic lesion is achieved.

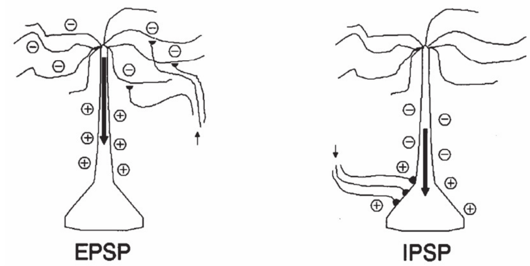


The inverse solution by multiple discrete sources is confirmed by a LORETA image that is calculated on a 7 mm grid covering the whole brain volume. No cortical constraint is imposed to assure unbiased estimation of a smoothed image.

Basic principles of discrete multiple source analysis

Currents in cortical columns: dipolar far fields





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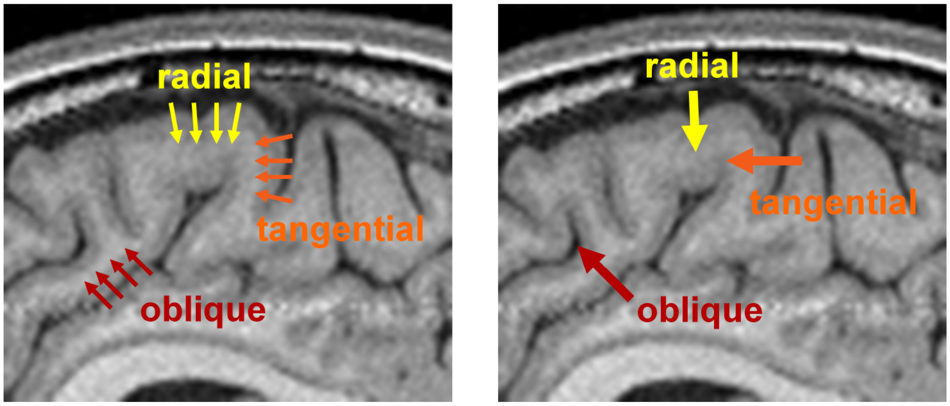
The dominant source of the EEG signals recorded at the scalp are volume return currents associated with the intracelluar currents generated by excitatory and inhibitory post-synaptic activity in cortical pyramidal cells (current loops are closed!). Pyramidal cells may have their apical dendrites both in superficial and deep cortical layers, but all are aligned in parallel across the cortical layers. Thus, net dipolar currents are orthogonal to the cortical surface and may flow in and out of the cortex.

Neuronal current flows perpendicular to the cortex and creates dipole fields



net current density * surface = equivalent dipole moment [nAm]

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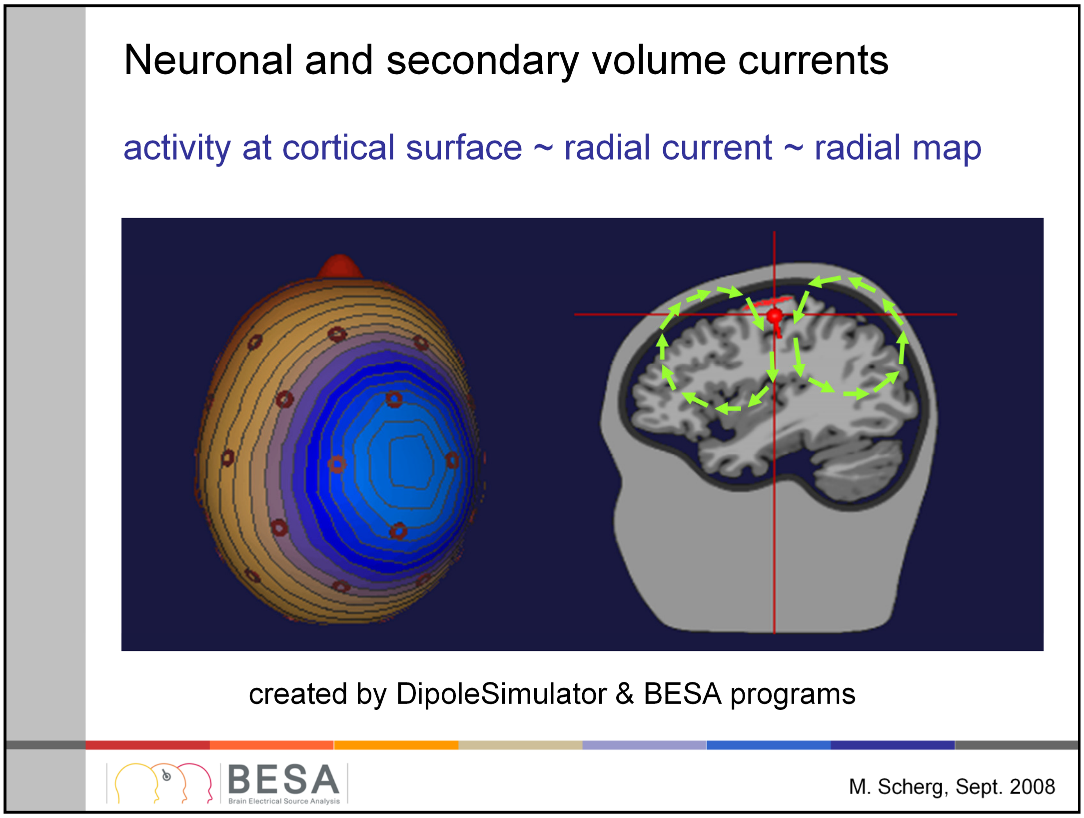
Neuronal current in the cortex flows predominantly perpendicular to the cortical surface for two reasons: First, the pyramidal cells in the cortical columns are aligned perpendicular to the cortical surface. Second, the dendritic trees that are parallel to the cortical surface have near-rotational symmetry and the electric fields of the related intracellular currents cancel to a large degree.

The intracellular current vectors of nearby cortical columns sum linearly and can be represented very accurately by an equivalent, compound dipole current vector. The magnitude, or strength, of the equivalent dipole is proportional to the number of activated neurons and therefore correlates with the area of activation and the mean dipole current density per square cm. Areas with up to 3 cm in diameter (!) can be very accurately (>99%) modeled by a single equivalent dipole.

Currents at the cortical convexity have a predominantly radial orientation, currents in cortical fissures have predominantly tangential orientation. Generally, a patch of activated cortex in a sensory, motor or spiking area will have an oblique orientation depending on the net orientation of the activated cortex.



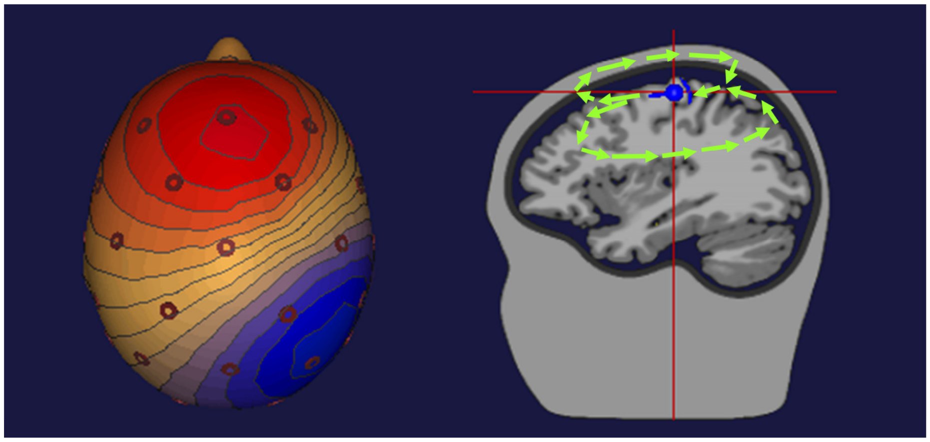
An ideal patch of superficial cortex creates a net radial current flow that can be very accurately modeled by an equivalent dipole near its center.

Current loops in a conductive medium like the head are closed. Therefore, the intracellular currents resulting from action and post-synaptic potentials are accompanied by secondary return currents in the head volume. Since the brain and scalp have a higher electrical conductivity as compared to the cranium, most currents return within the extracellular brain space. Only a very small fraction flows out through the poorly conducting cranium and along the scalp before returning to the brain.

The volume conduction results in a widespread, smeared voltage topography over the whole scalp with a negative maximum over the activated cortical sheet. A corresponding more widespread positivity appears on the other side of the head. By physics the integral of the voltage over the whole head is zero. Therefore, any negativity has a corresponding positivity somewhere else over the head. The displayed voltage map (topography) is typical for focal radial activities at the cortical surface. The map illustrates the limited spatial resolution of the EEG. The precise orientation of the map, and the underlying equivalent dipole, can only be determined, if inferior electrodes are present to help define the location of the positivity on the other side of the head.

Neuronal and secondary volume currents

activity in a fissure ~ tangential current ~ tangential map



created by DipoleSimulator & BESA programs

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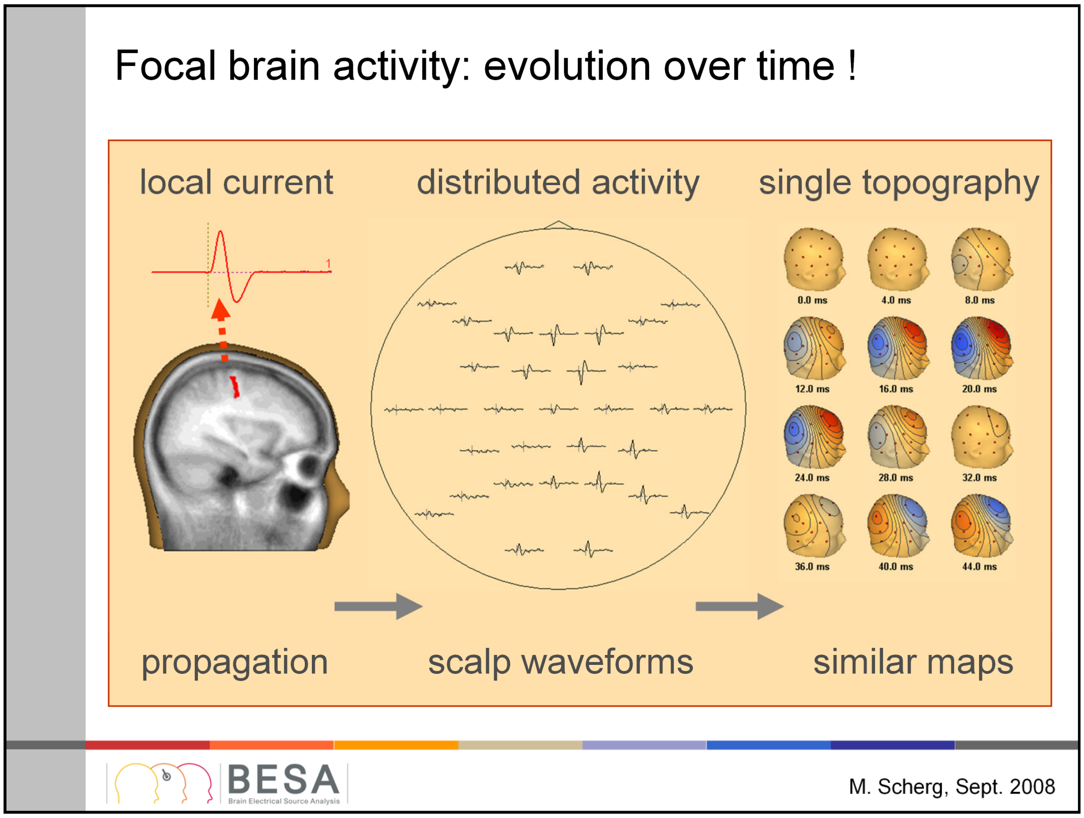
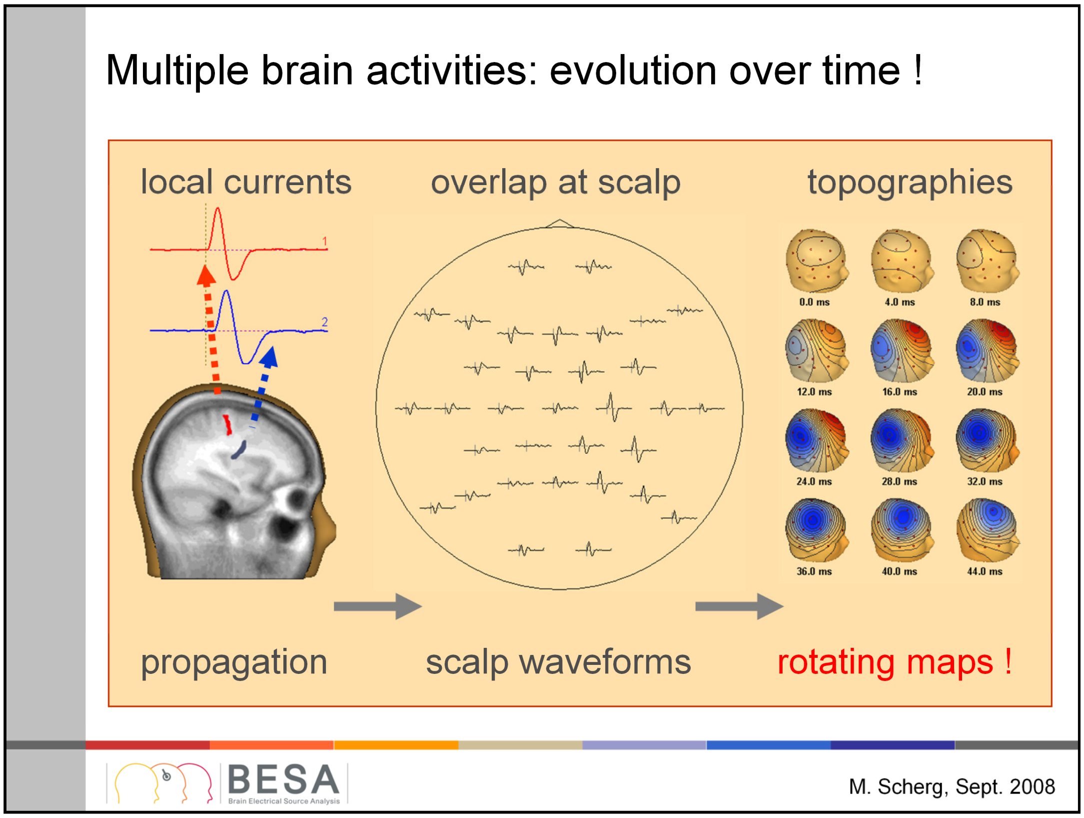
A cortical patch in a fissure generates a tangentially oriented dipole field. The return currents in the scalp create a dipole map with symmetric positive and negative poles aligned in the direction of the dipole. The voltage directly over the source is zero, but the gradients are maximal. The source is below the site of the densest equipotential lines. These lines and the whole shape of the topography carry more information on the location of the underlying generators than the colorful peaks.

The propagation of the volume currents to the scalp is described by the so-called **'head model'**. The head model, or forward model, predicts the voltage at any electrode due to an equivalent dipole with a given location and orientation within the brain.

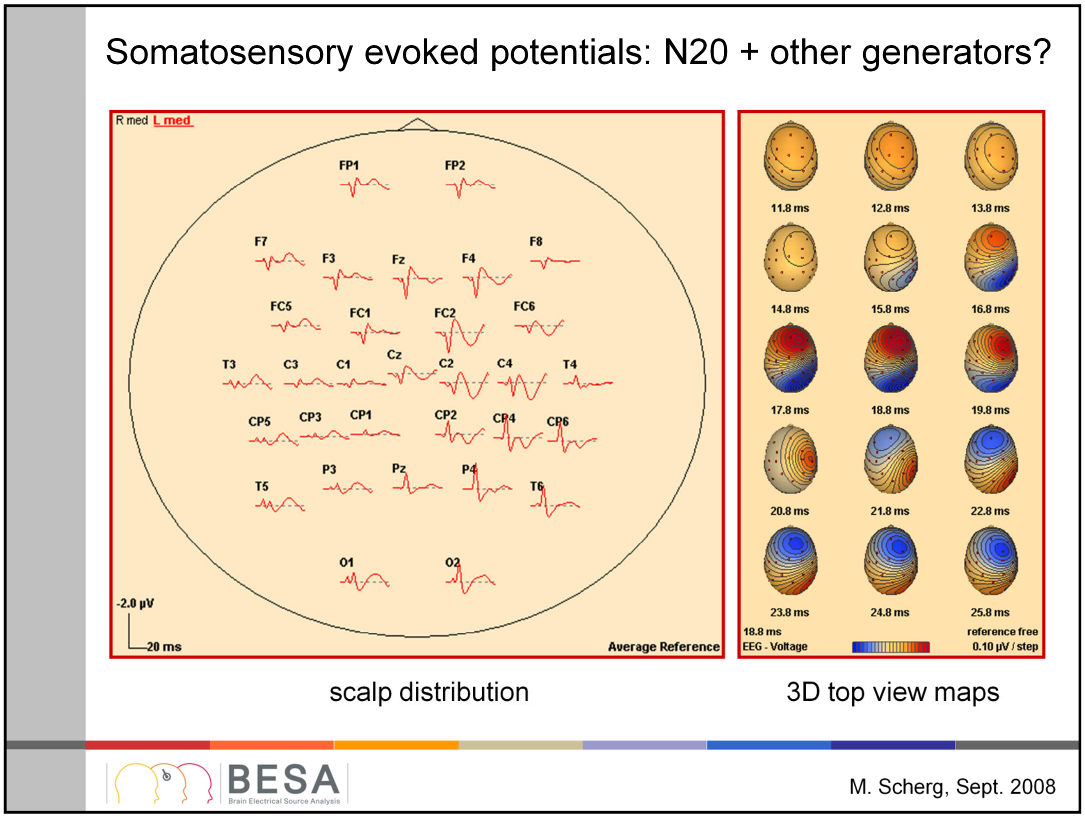


Using a simulated example, we will now learn how to discriminate the scalp waveforms and topographies due to a focal activity of one brain region and temporally overlapping activity of two brain regions.

An assumed activity in the right central sulcus produces a near-tangential dipole field with a positive peak over the mid-frontal (downward, e.g. at Fz and FC2=max.) and a negative more widespread peak over the right inferior parietal cortex (max. at P4). The patch is synchronously activated and there is no propagation. Accordingly, the net orientation remains the same. The waveforms at the different electrodes have different magnitudes but the same evolution over time. The topographic maps change only in magnitude but not in shape. Map polarity simply reverses in the second phase following the initial activity.



Now consider the situation of two brain regions separated by about 3 cm and activated within a few milliseconds. Each of the areas has a biphasic pattern with onset, peak, and polarity reversal. The two patches have different orientations. This is the main cause for their very different scalp topographies. Due to the time difference in activation their maps overlap with continuously changing magnitudes according to the instantaneous strength of the 2 compound currents. This results in an apparent rotation of the maps over time, and it becomes difficult to identify and separate the two sources by mere visual inspection.

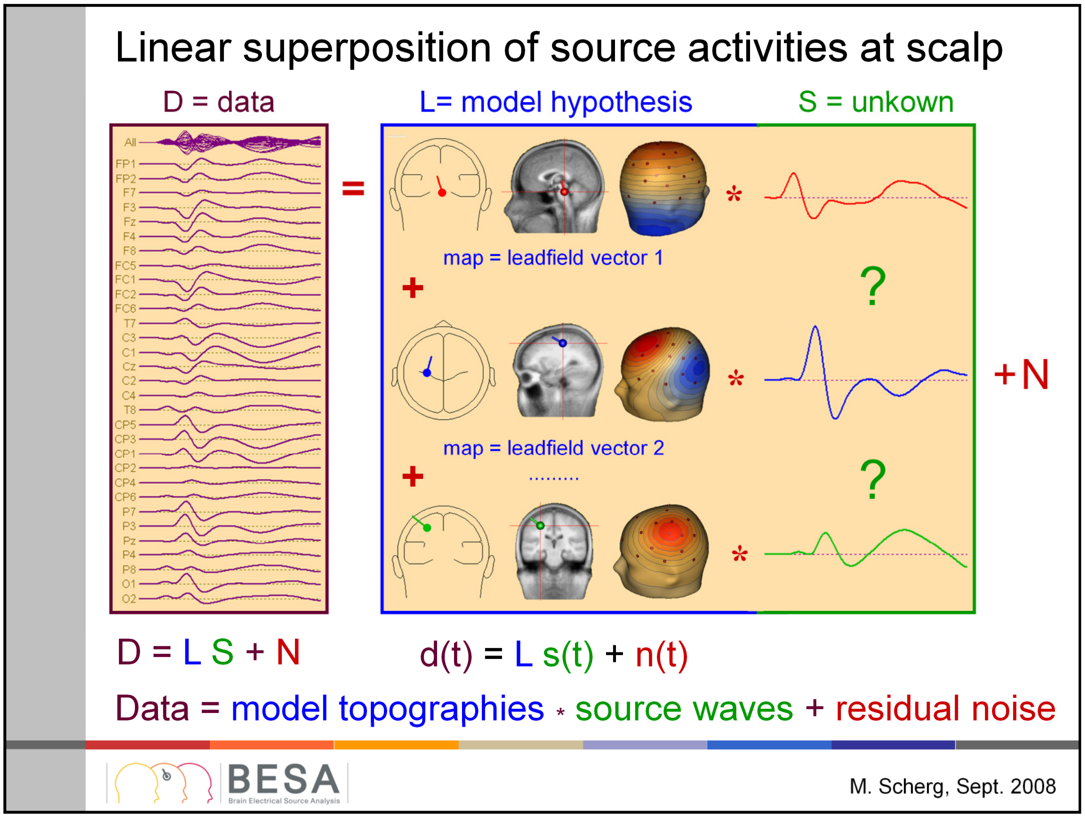


Constantly varying and widespread scalp topographies can originate in a small circumscribed region, as can be seen from left median nerve SEPs.

At the time of N20 (here at 18 ms), area 3b in the central sulcus is predominantly active and creates a near-tangential dipole field with near-zero potential directly over the post-central gyrus. 2 ms later, when the more superficial somtosensory areas 1 and 2 are activated, a radial positive pattern (P22) can be seen with maximum at C4.

Maps appear to rotate as a reflection of a constant change in relative strength and polarity of the source currents in the various primary sensorimotor areas all being in close vicinity but having different orientations of their cortical columns.

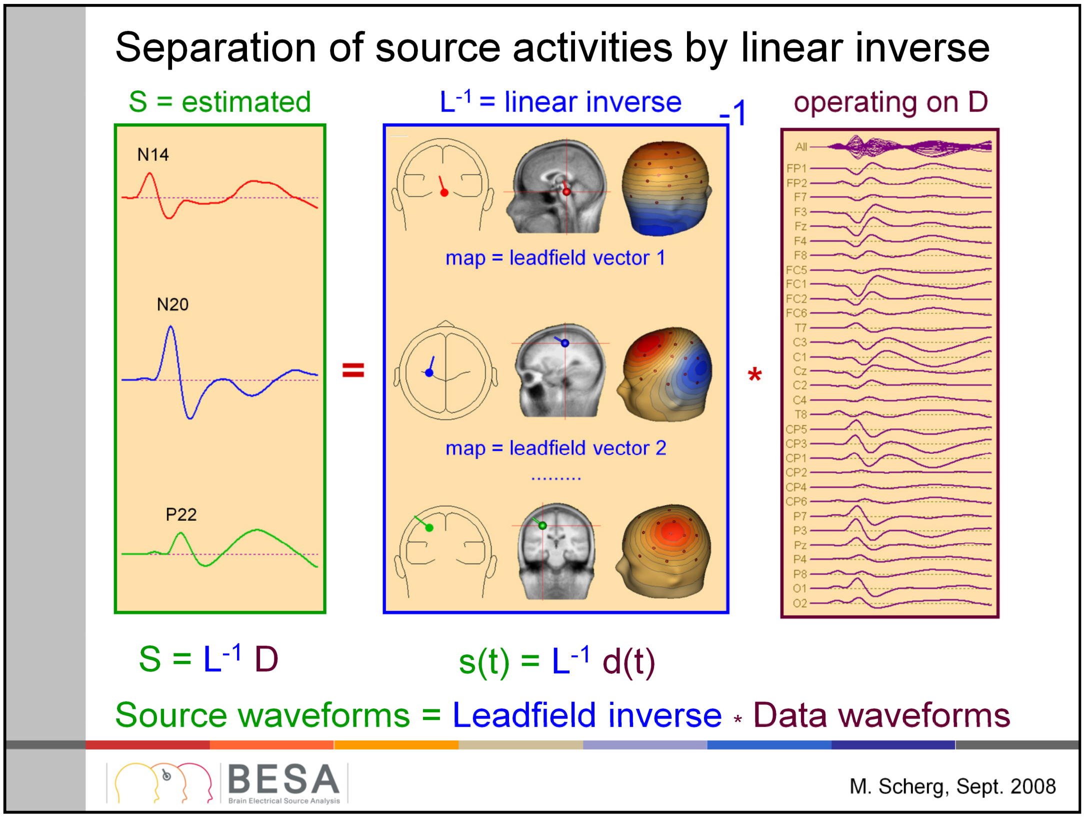
At most instances, the generator is not below the scalp negativity. The whole pattern and its evolution has to be understood!



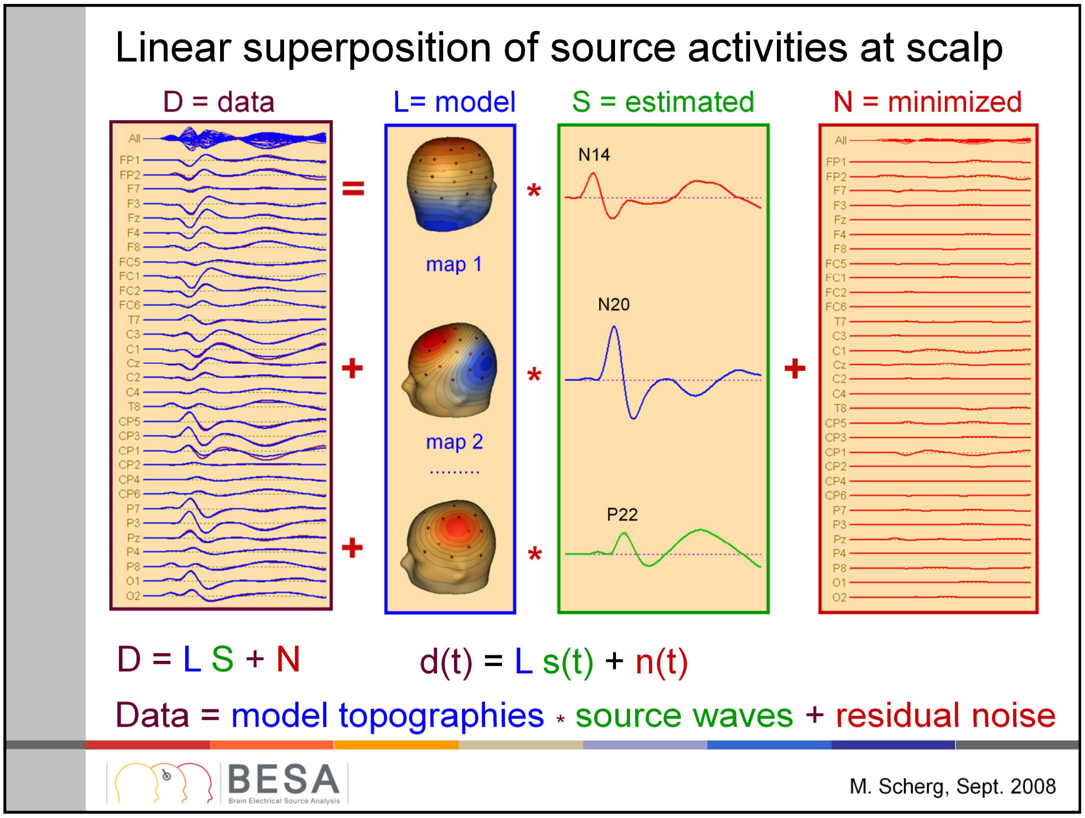
Using the laws of basic physics, we can now formulate the **principle of linear superposition**. This is illustrated here for 3 equivalent dipoles, that descibe the somatosensory evoked potential very accurately. The measured data D (in this figure EEG / SEP average references electrode signals) are the sum over the contributions of all sources (+). Each source is fixed to the region or cortical patch it represents, and changes its total current strength over time according to the local physiology. In 1986, this was named a source waveform (Scherg and von Cramon, Electroenceph. clin Neurophysiol. 65:344). A priori, this source activity S is unknown.

If we have a volume conductor model, for example a spherical head model, a boundary element model (BEM) or a finite element model (FEM), we can now predict the leadfields L, i.e. the magnitude of signal each source will contribute to each sensor. Because the model is an approximation, both in terms of the volume conductor and the simplification of using equivalent dipoles at the centers of activity, there is a residue (N). Ideally, if we have a good model, this residue should be small and consist only of sensor noise and brain background activity not related to the somatosensoy stimulus.

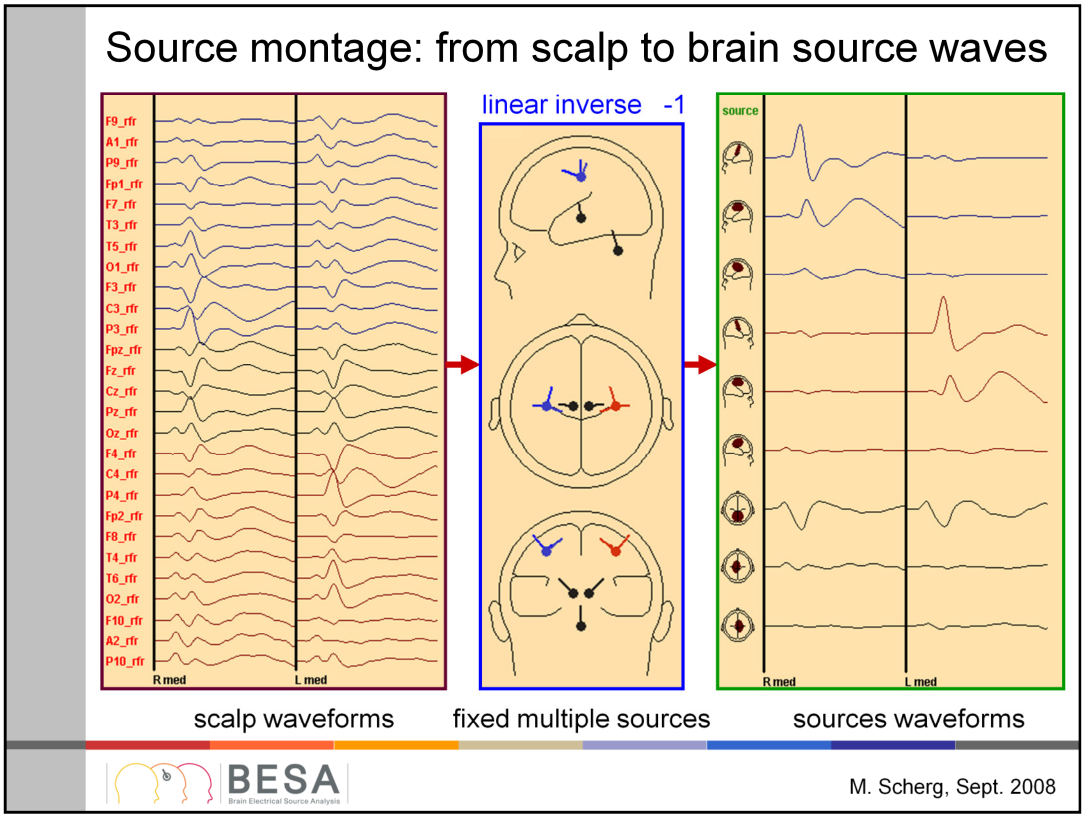
In discrete models, dipole sources can be fitted while this linear equation is calculated interactively to minimize the noise on the right. For the SEP, this can be achieved easily by a sequential strategy, first fitting a dipole to the N14 component (entrance of afferent volley into the brain volme through the foramen magnum), then fitting an additional dipole to the primary cortical N20 peak while holging the deep dipole at the level of the brainstem fixed. Finally, a 3rd dipole is fitted remaining P22 activity in the presence of the (fixed) dipoles modelling the N14 and N20 activities. During the fitting process, the the leadfields are recalculated according to the positions and orientations of the sources and the difference between the measured and predicted data is minimized.



As a consequence of the linear superposition at the scalp, we can now calculate a linear inverse to decompose and separate the measured scalp activity into the underlying equivalent source activities. The linear inverse operates onto the measured data and yields the estimated time course of the activity of each model source, i.e. its source waveform.



Finally, during each step of the fitting procedure, the estimated source wavefomrs S are projected back to the scalp using the leadfiled matrix L. Then, the model waveforms M (blue) can be subtracted from the measured data D to yield the residual noise matrix N. using a non-linear iterative procedure, the dipole positions and orientations can be optimized to minimize N. Thus, a model of 3 equivalent dipoles can be found that typically explains more the 98% of the variance in SEP data (provided sufficiently good SNR has been achieved by >= 2000 averages).



Here we see an example of a discrete multiple source model applied to recorded SEP data. On the left, averaged EEG responses to right and left median nerve stimulation are shown. Activities from the different brain regions overlap at the recorded electrodes, which makes it difficult to analyze the underlying brain processes in detail.

This is achieved by applying a multiple source model to the data. As shown in the middle panel, it consists of nine equivalent current dipoles: Three mutually orthogonal dipoles in the left somatosensory cortex (blue), three in the symmetrical location in the right hemisphere (red), one in the brain stem (black, 7th source), and one each in the left and right ascending pathway in the thalamus (black, 8th and 9th source).

The reconstructed time courses of these brain regions, the soure waveforms on the right side, illustrates the power of discrete source models in separating the activities of the different brain regions that overlap so severely on the scalp surface: In the response to right median nerve stimulation (the first of the two segments), clearly two large components in the left (contralateral) somatosensory cortex can be identified. They are preceeded in latency by activity in the brain stem (7th trace). Even the small activity in the left thalamus (8th trace) can be identified. The response to left median nerve stimulation (second segment) shows equivalent activities in the opposite hemisphere.

How do we determine a multiple source model?

- Goal: find equivalent sources for all active brain regions
- Question A (localization of peaks ?):
  - where localizes N20 (SEP) ?
  - where localizes N100 (AEP), etc.?
  - shall we consider peaks in the data as independent entities ?
- Question B (contribution to peaks !):
  - which activity is contributed to the scalp data by SI cortex ?
  - which activity is contributed by right and left auditory cortex ?
  - is there additional activity contributed from frontal, midline cortex etc., i.e. probing the whole brain ?

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Often it is inappropriate to assume that an observed peak in the EEG data corresponds to activity in a single brain region. Rather, generally multiple brain regions contribute to the observed EEG signal at any latency. Consequently, rather than fitting single sources to distinct EEG peaks, a fixed multiple source model should be applied to observed EEG data. The reconstructed source waveforms represent the activity of the modeled brain regions over time and thus illustrate the contribution of each brain region to the recorded data at each latency.

How do we determine a multiple source model?

There are different answers depending on your goals and knowledge of experiment and data:

- Place sources into all known regions using anatomy
- Fit single or multiple sources to data by some strategy
- Seed sources into maxima of images (fMRI / MEG etc.)
- Probe other brain regions
- ....

Discrete source analysis is hypothesis testing !

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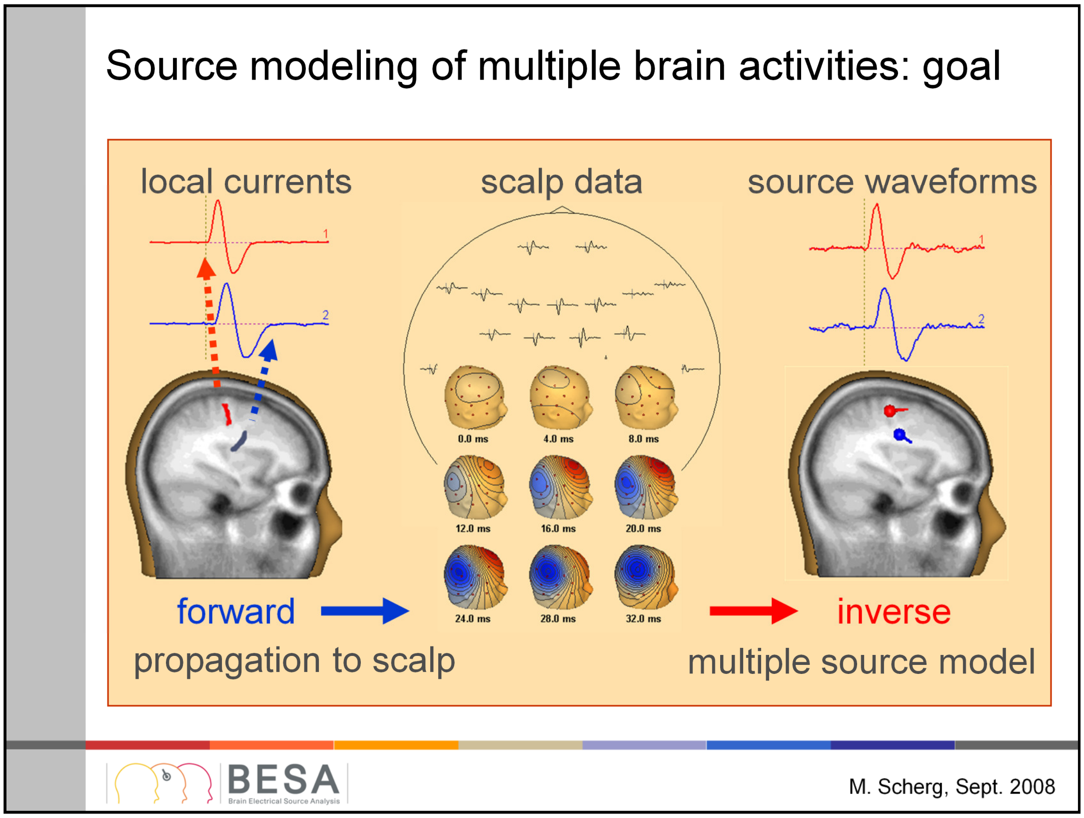
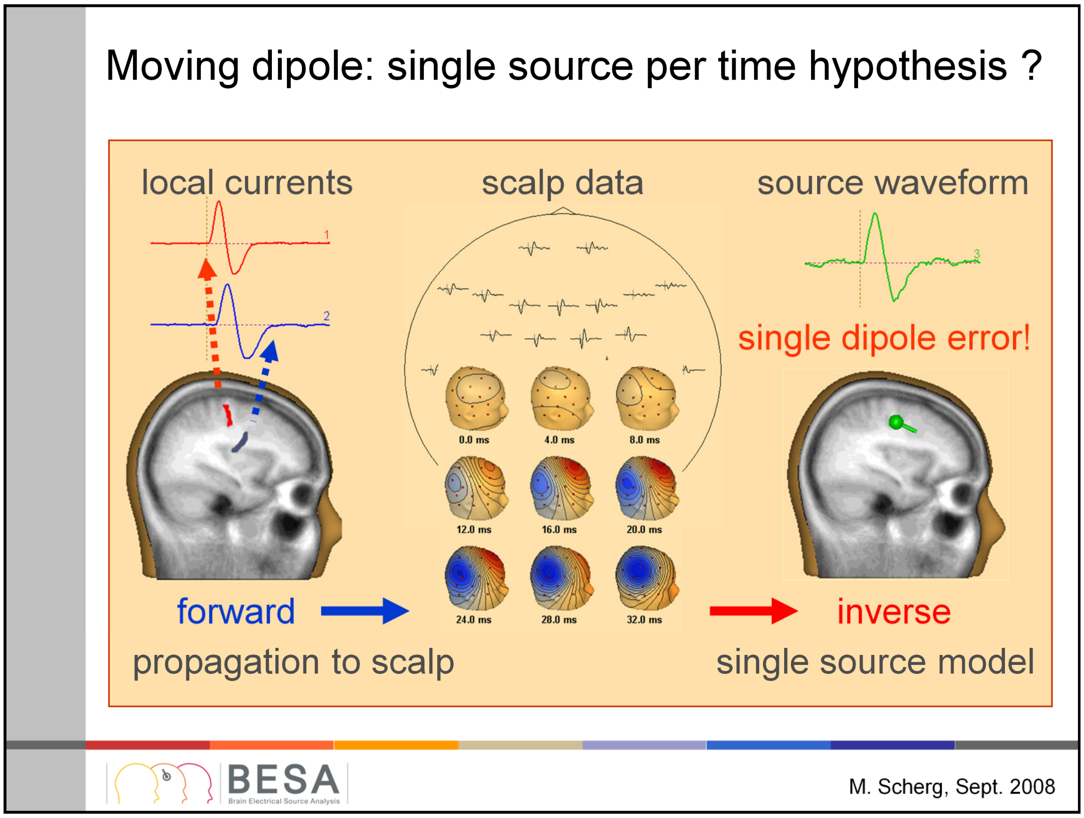
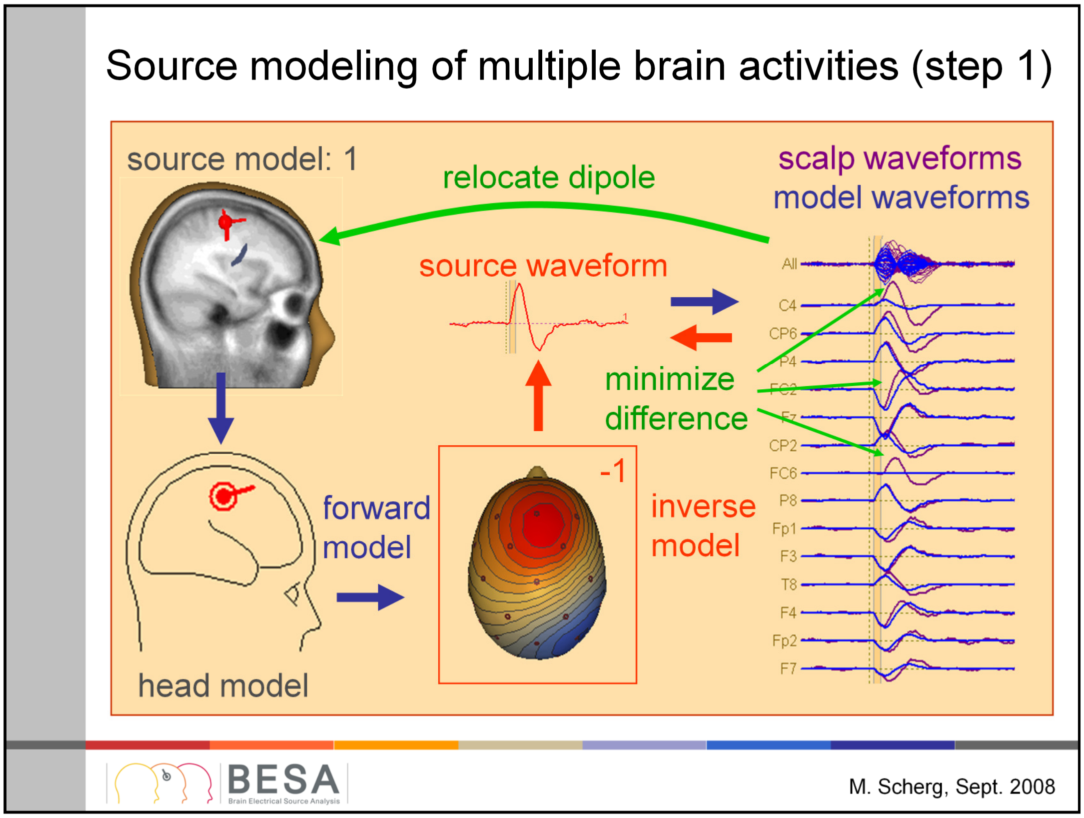


If we fit two dipoles to our simulated data set, they separate the two activities in their source waveforms provided that appropriate equivalent locations and orientations had been found.



If we fit only a single dipole at the 'peak activity' as determined by the electrode with the largest signal, we obtain an incorrect localization intermediate between both sources. The source waveform combines both underlying activities into a broader pattern which has a latency intermediate between the original activities. Therefore care must be taken to create a multiple source model that is appropriate for the current data set. How this can be achieved will be outlined in the next few slides.

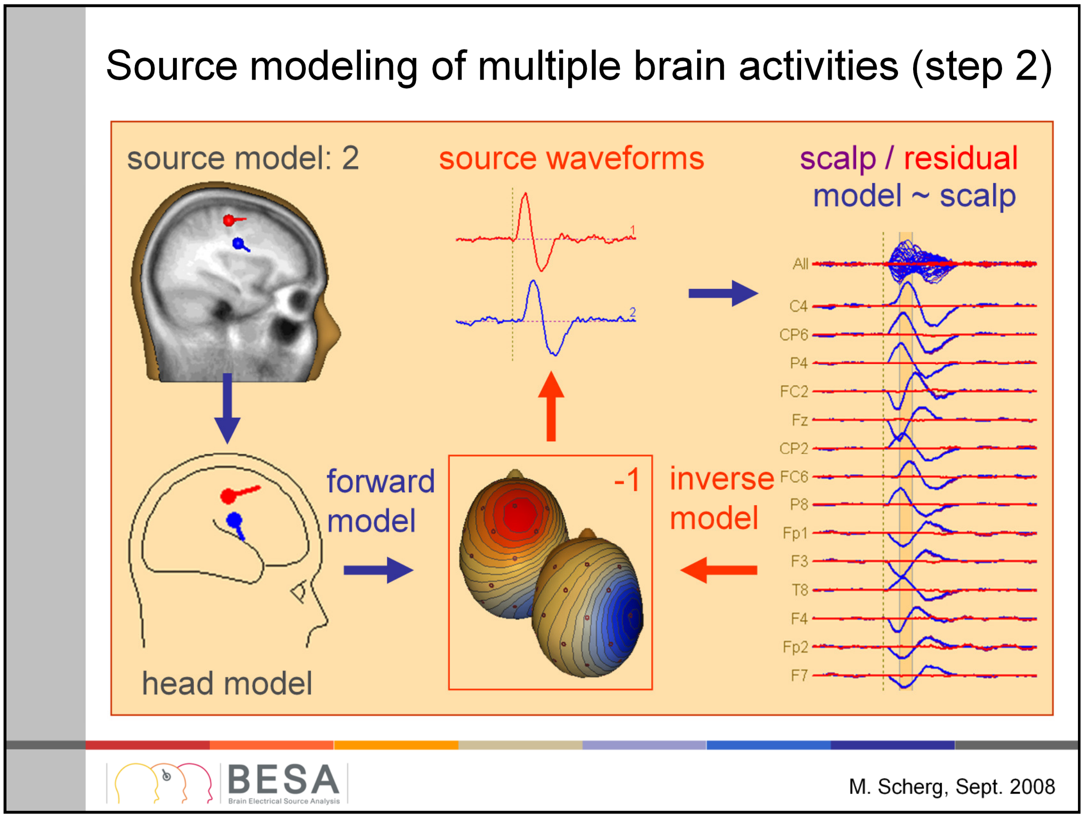


The fit procedure:

We assume that a single dipole will explain the early onset phase (i.e. initial source model hypothesis is a single equivalent dipole). Using the head model the forward model topography is estimated. The inverse of the topography matrix is applied to the data to estimate the source waveform. The source waveform is projected back to the scalp using the forward coefficients of the map to estimate the model signals (blue). Measured and modeled data are subtracted to estimate the residual waves. In an interactive process, dipole location and orientation is adjusted and the calculation process is repeated until the residual difference between scalp and model waveforms is minimized. The equivalent dipole locates in or near the active cortex if the hypothesis, head model, and data are sufficiently accurate.

Fitting strategy for multiple activities – step 1:

Use the 3D maps to define the fit interval from the time when a clear dipole field emerges until it starts changing. Performing a principal components analysis over this interval should show one dominant component. The percentage of variance it explains should decrease, if the interval is extended further. Fit the first dipole over this interval.

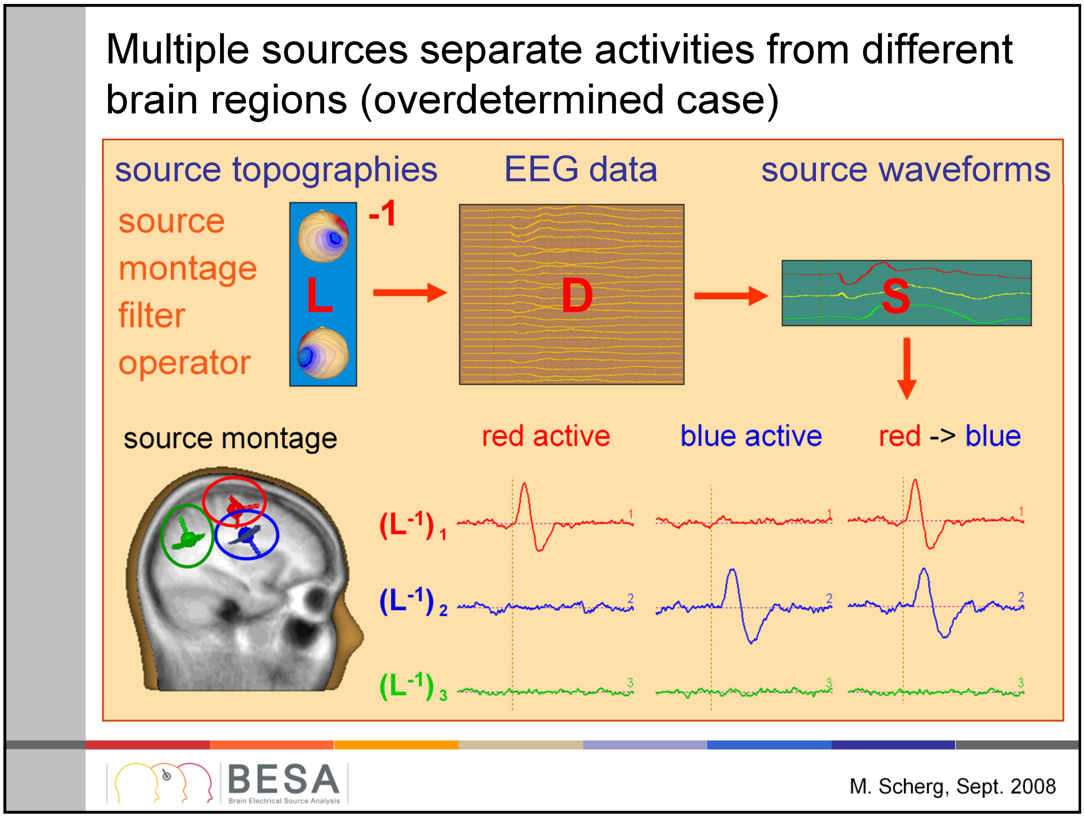


Fitting strategy for multiple sources – step 2:

Display the residual waves and maps. Perform a PCA on the residual waves and repeat the same procedure to mark the next onset interval in the residual data. Fit a second dipole to this interval while keeping the first dipole fixed in location and orientation.

In the simulated example with good signal-to-noise, this results in the separation of the underlying active areas and their source waveforms.

Finally, we should check the homologous brain region in the other hemisphere for a potential spread of activity using a probe source at the mirror location of dipoles 1 and 2.



The above example demonstrates the full separation of the source activities 1 & 2 in our simulation and illustrates the absence of activity in source area 3 since its source waveform shows only EEG background signal.

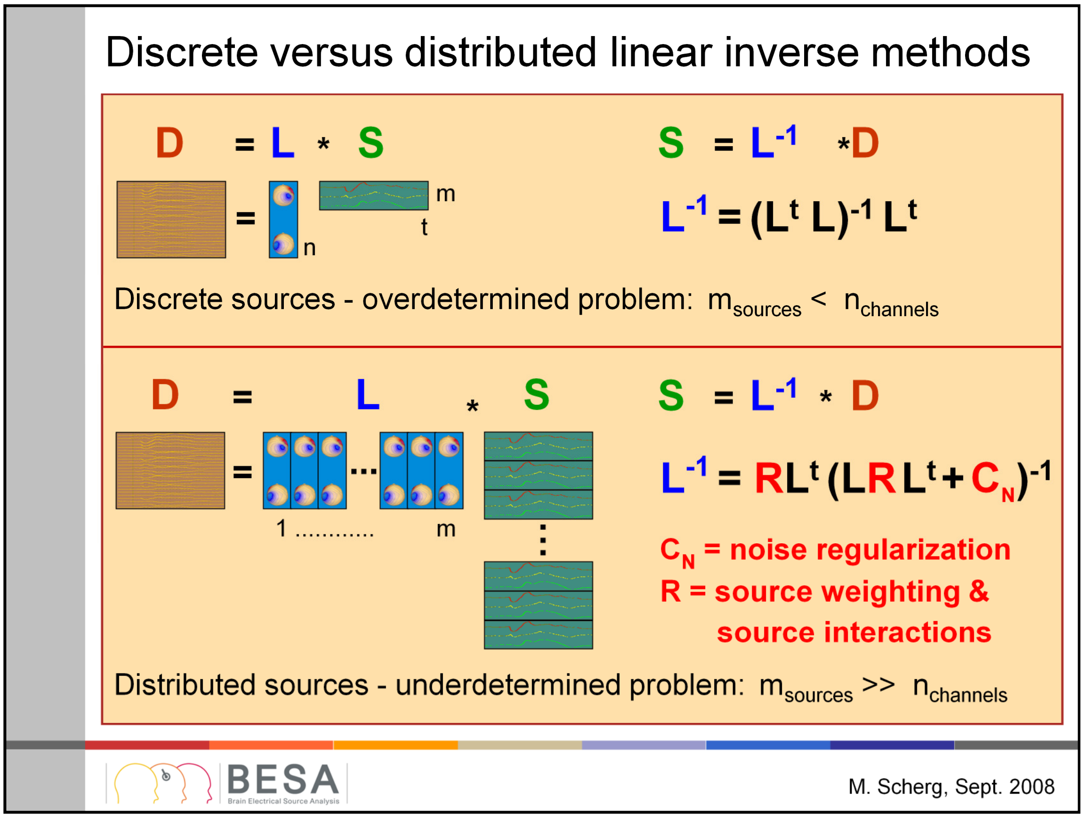
Thus, multiple sources can mutually contrast and separate the activities of the brain areas that they represent.

The displayed circles on the left illustrate that separation of the activity from several brain areas is principally possible, if they are sufficiently remote from each other (> 3 cm). However, precise localization within each region is not possible in typical data because of the EEG background noise.

In the **overdetermined** case, i.e. if there are less sources than measured channels, the linear inverse multiple source operator is constructed to **fully separate the different source activities**. The vector operator for source 1 will fully recover source activity 1, but not see and suppress any contribution from sources 2, 3... and vice versa. This sharp separation has a drawback, if some of the sources have a high spatial correlation in the sensor space. Then the inverse operator will have large entries and the noise will be amplified accordingly. However, this problem is easily handled by modest regularization (BESA default = 1%) when calculating the inverse of the topography matrix.

Discrete multiple source modeling (principle)

- Each source should represent one active brain area
- The inverse separates and mutually constrasts the activities of all the modeled areas:
  - source waveform 1 images 100% of activity 1
  - source waveform 2 images 100% of activity 2
  - etc.…
  - source waveform 1 images 0% of activities 2,3,4…
  - source waveform 2 images 0% of activities 1,3,4…
  - etc… (ideally 0%, in reality ~ 5-20%)
- Activity from unmodeled regions spreads over all source wavefoms depending on spatial correlation



In practice, discrete and distributed inverses can be distinguished. In both cases, the the basic assumption is that the data D is constructed by the superposition of the contributions of multiple dipolar sources (D=L*S). But whereas in the discrete case, the number of dipoles is smaller than the number of recorded sensors, a distributed model consists of many more dipoles than recorded sensors, i.e. The leadfield matrix L has more columns than rows.

As a consequence, the mathematical form of the inverse operator that computes the source waveforms S from the data differs between the two approaches. In the distributed case, many different source current configurations S exist that all explain the recorded data (underdetermined problem). Therefore, generally side constraints are added explicitly by means of the matrix R that incorporates prior assumptions of source weighting and source interaction. It is this matrix R that represents the difference between methods like minimum norm, LAURA, LORETA. In addition, the inverse operator is generally regularized (matrix C_N).

An intrinsic negative property of distributed source models is that there is spatial blurring: Activity of a given brain region generally appears spread out to neighboring sources of the distributed model. As a consequence, the source waveform of each dipole shows substantial contributions of other brain regions in the distributed case.

Decide on source model depending on goals

- Source models:
  - discrete dipoles (m < n, overdetermined – difficult !)
  - discrete regional souces (m < n, overdetermined – easier !)
  - distributed sources in brain volume (m ≫ n, underdetermined)
  - distributed sources at the cortex, i.e. gray-white matter boundary (m ≫ n, underdetermined)
- Once a model is defined and fixed, a linear inverse can be calculated for each of these source models
- We will first discuss these options using auditory evoked potentials (AEP)

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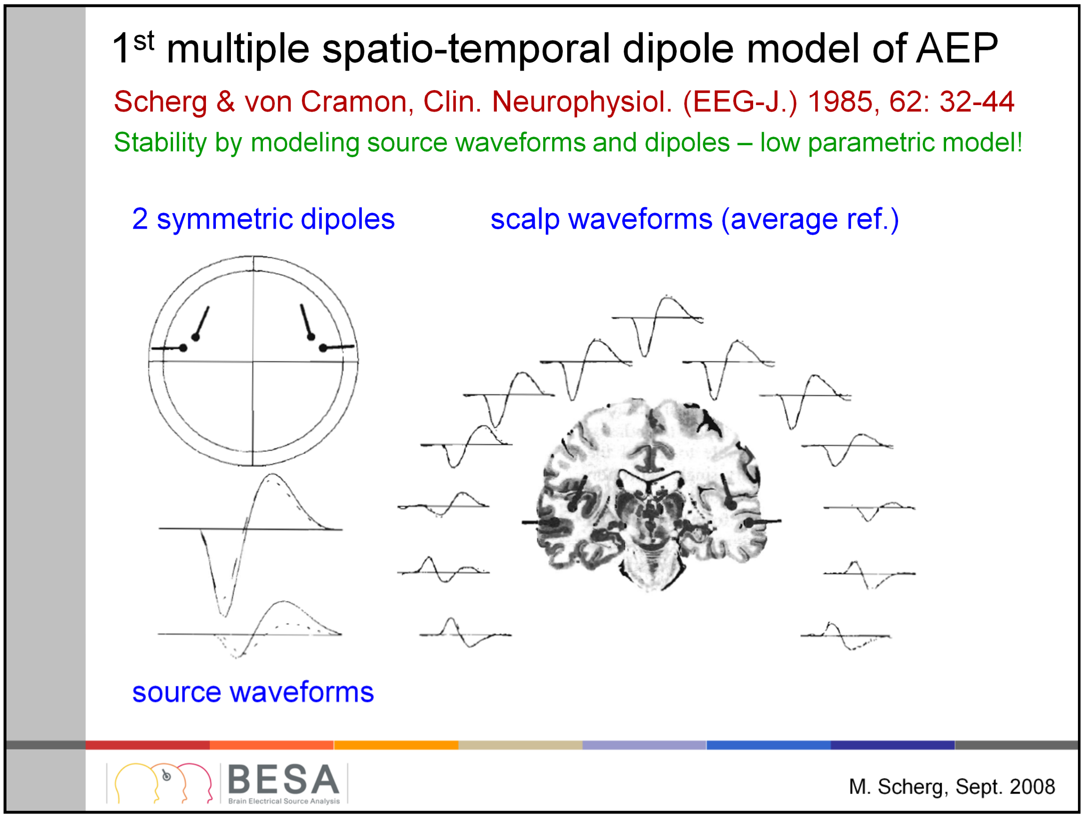

In 1985, the first spatio-temporal dipole model of the late AEP was published.

This model consisted of 2 pairs of dipoles with symmetric location and independent orientations in the coronal plane. Their source waveforms were modeled by biphasic spline functions. Thus, a spatio-temporal model with very few parameters was obtained. This resulted in a very stable model and allowed to separate the tangential N100 and radial N150 components in both hemispheres despite their strong temporal overlap. Thus, the source waveforms revealed different activities in the superior temporal plane (N100) and at the lateral surface of the supra-temporal gyyrus (N150).

Definition of discrete multiple source models

Scherg & von Cramon, Clin. Neurophysiol. (EEG-J.) 1985, 62: 32-44

Model has an anatomical, physiological and neuropsychological basis !

According to the mechanisms of far-field generation outlined above, a spatio-temporal dipole model (STDM) was conceived on the basis of the following assumptions.

(1) The neural substrate generating the surface EP can be defined as consisting of a limited number of neural subsets (generators), such that each is localized within a small volume as compared to head size.

(2) The external far field of each neural subset adds linearly to the scalp potential according to the laws of electrostatics (spatio-temporal superposition).

(3) The spatial properties, i.e., the scalp potential distribution associated with each generator, can be approximated by the field of an equivalent dipole located within or in close proximity to the neural substrate. Location and orientation of each dipole are stationary, as is the spatial organization of the underlying neural structure.

(4) The temporal properties of each generator are reflected in the magnitude of the equivalent dipole, which is assumed to be a continuous function of time described by an onset latency and several peaks following. The temporal course of dipole magnitude is thought to depict the compound discharge processes of the underlying structure.

Given these assumptions, both prediction and analysis of surface potential wave forms can be accomplished, considering:

(a) The forward problem: given a certain hypothesis on location, orientation and temporal course of compound activity of one or more (n) generators, the potential wave forms on the scalp can be predicted by superimposing the dipolar fields of all generators according to:

$$u_k(t) = \sum_{i=1}^{n} m_i(t) \cdot d(\vec{r}_i, \zeta_i, \alpha_i; \vec{e}_k)$$

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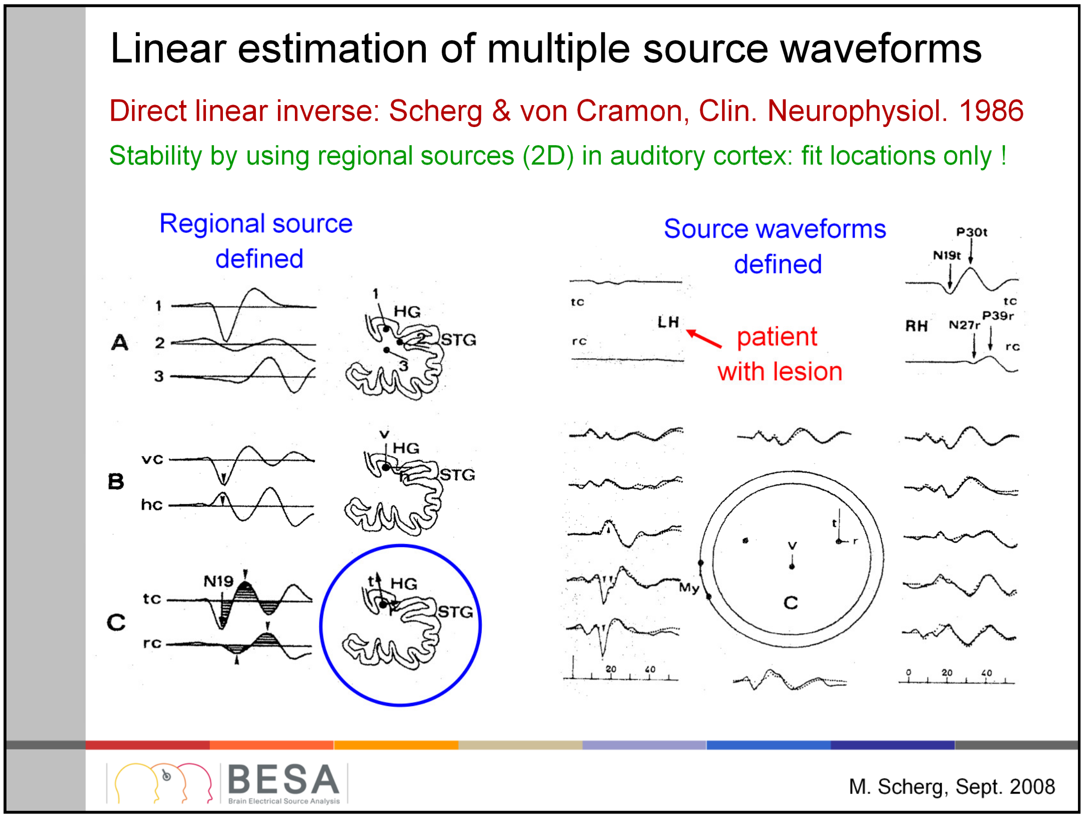
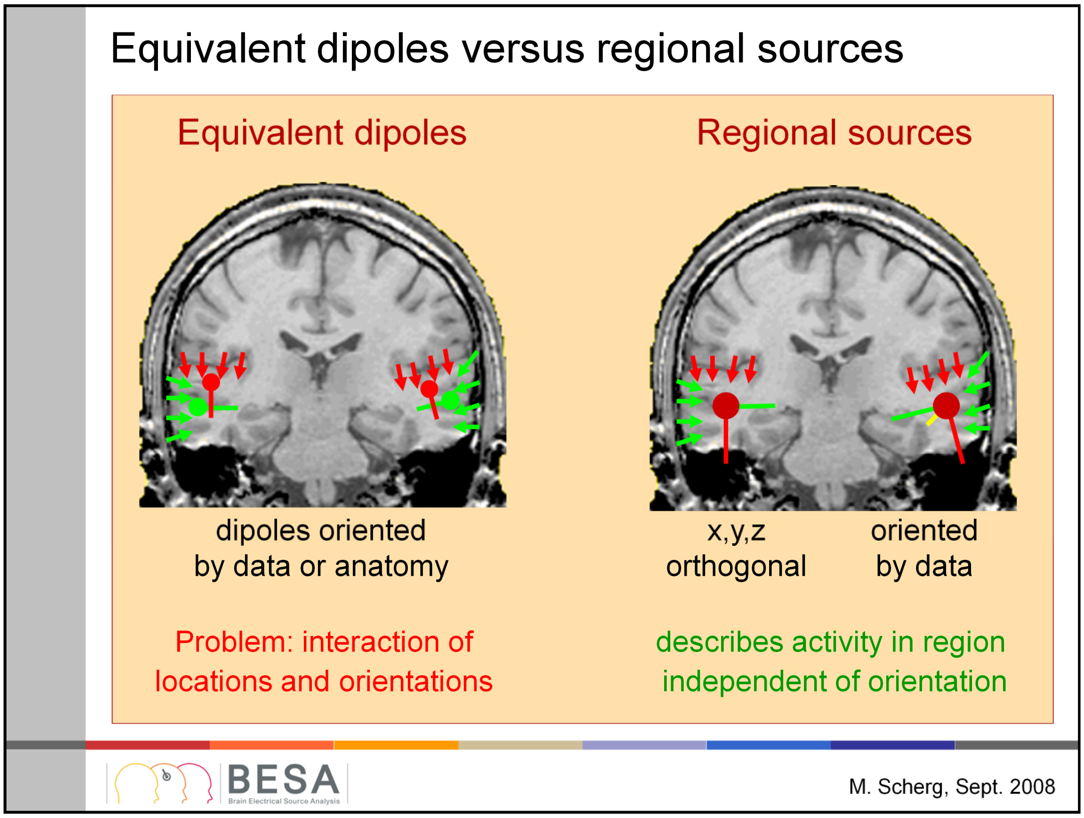
Spatio-temporal dipole modeling has a solid anatomical, physiological and neuropsychological basis. Current research on dynamic causal modeling (DCM) begins to fill the gap on how to model the temporal evolution of the source activities based on physiological and anatomical knowledge (Kiefer et. al. Neuroimage 2006, 30:1273-1284).



Activity in the auditory cortex can be modeled in different ways. A: A model consisting of three dipoles, each representing a different patch of the auditory cortex. Alternatively, these dipoles can be replaced by a regional source consisting of three mutually orthogonal dipoles at a common equivalent location (only two orientations are shown in Fig. B). The regional source can be rotated so that the first dipole component models all primary activity at a given latency (N19 in Fig. C). This provides an adequate model and a separation of distinct processes in the auditory cortex.

On the right, an example of such a source model is shown in a patient with a lesion in the left hemisphere. Source analysis reveals an almost complete loss of brain activity in the affected brain region.

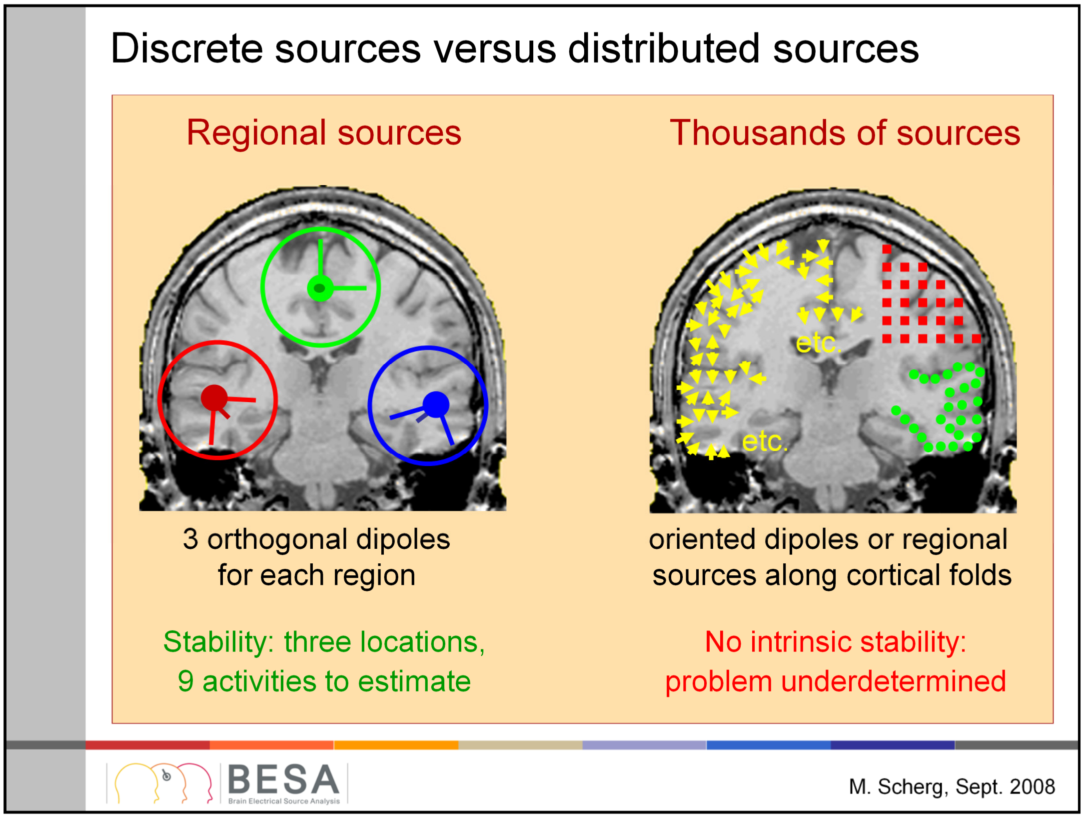


Currents at the cortical convexity have a predominantly radial orientation, currents in cortical fissures have predominantly tangential orientation. Generally, a patch of activated cortex in a sensory, motor or spiking area will have an oblique orientation depending on the net orientation of the activated cortex.

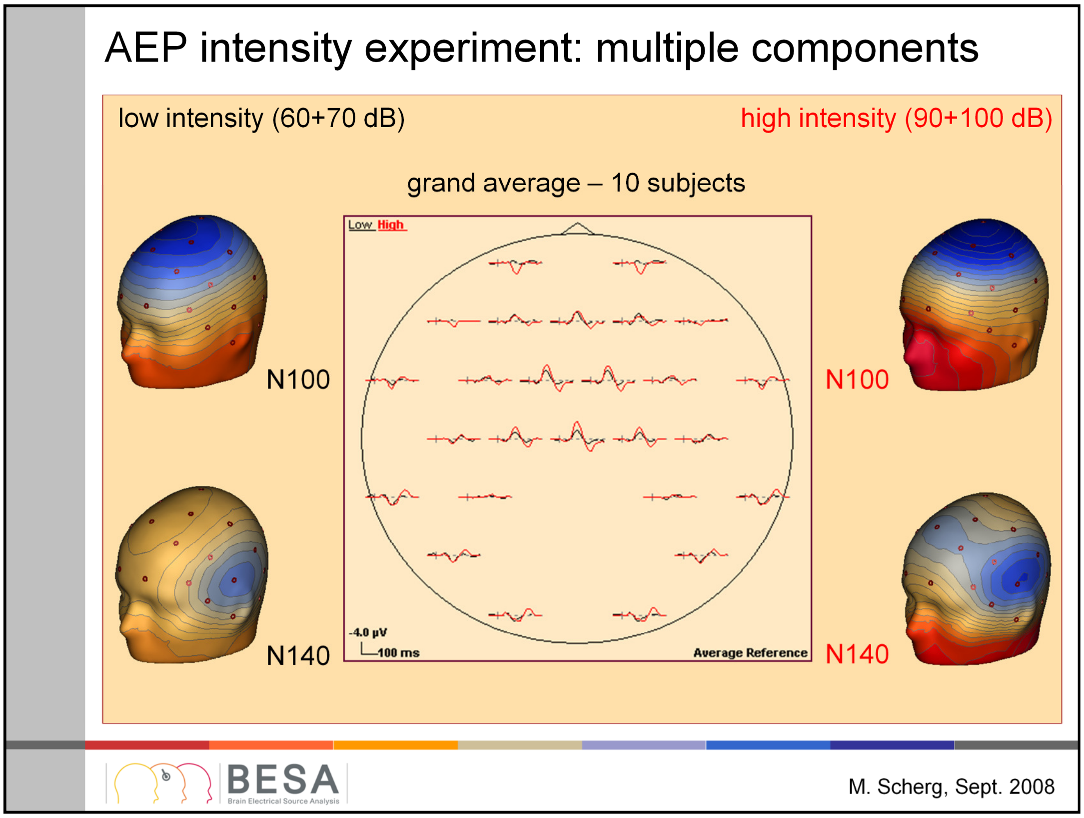
In the auditory cortex the dominant surfaces are the supra-temporal plane, i.e. the upper surface of the supratemporal gyrus lying in the Sylvian fissure. This surface creates predominantly tangential dipole fields, often oriented towards the frontal scalp.

As opposed to that, the lateral surface generates a predominantly radial dipole field, with the largest activity generated at the scalp directly above the active brain area.

In a discrete source model, these two aspects of the temporal lobe can be modeled with two dipoles at the corresponding equivalent locations and with the corresponding orientation. However, an independent fit of these two pairs of dipoles to recorded data will fail in most cases due to interaction due to the closeness of the two generators. A more stable alternative is to model the two aspects of the temporal lobe with a single regional source (consisting of three mutually orthogonal dipoles) in this brain region. Regional sources provide more stable fits than dipoles and can account for any activity in an extended brain region, independent of the current orientations. In the example of an AEP, a regional source can model both the (tangentially oriented) N100 and the (radially oriented) N140 component.

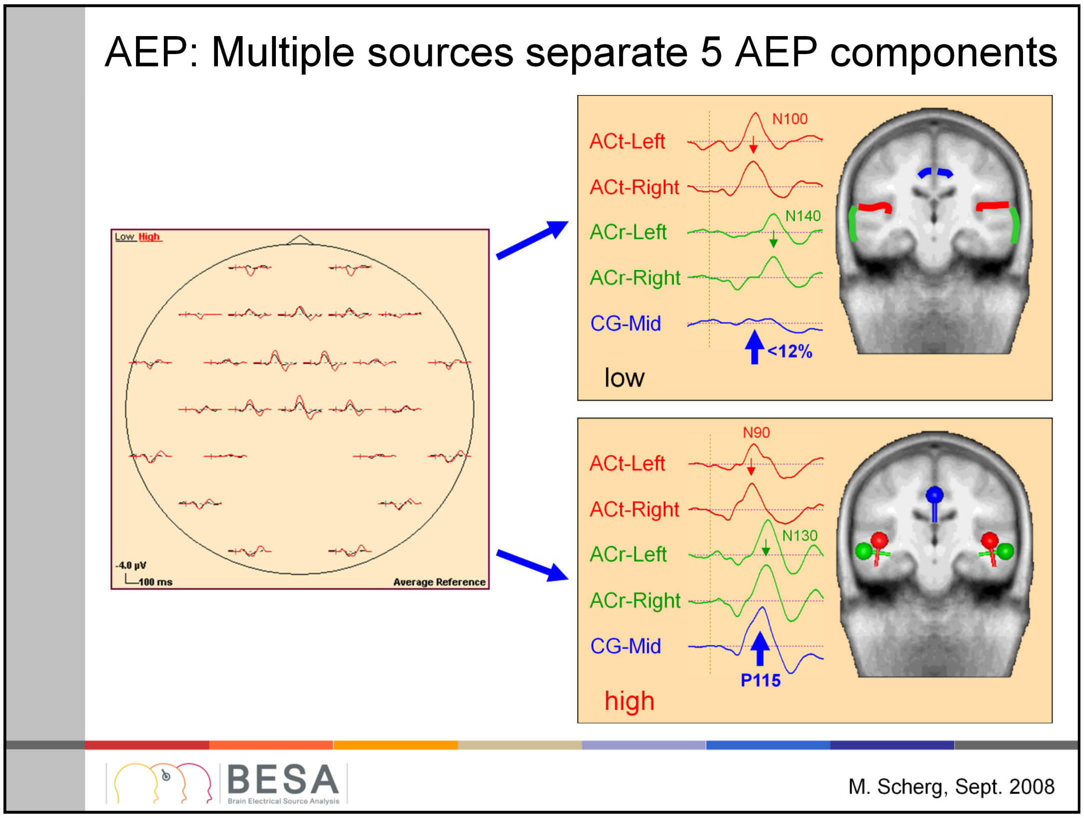


In a distributed source model (right), thousands of dipoles or regional sources are placed along the cortical folds in order to simultaneously model the whole brain. This prevents the need to fit a source model, but requires additional constraints on the source activities, because the problem is underdetermined.



This slide and the following two illustrate these facts by means of a grand average AEP data set. High and low intensity auditory stimuli were presented to the subjects, and the brain responses were averaged time-locked to the stimulus in both cases. The superposition of the two averages (middle panel) and the comparison of the scalp maps at the 100 and 140 ms demonstrate differences between the brain responses.

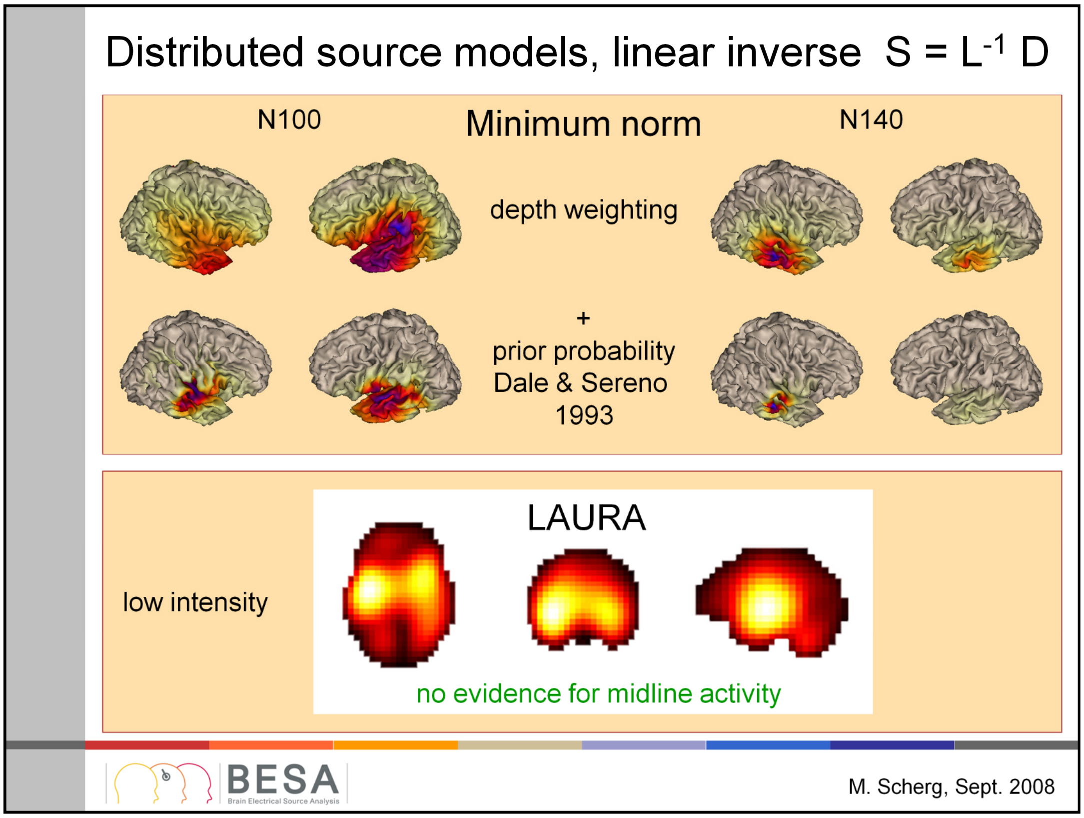
In the following, discrete and distributed source analysis is demonstrated on this data set in order to analyze these differences in brain source space.



A discrete dipole model is applied. Tangential dipoles (ACt) in the left and right auditory cortex model the N100 response. The N140 is represented in the radially oriented dipoles (ACr) in both hemispheres. In the high intensity condition, a midline cingulate source (CG) is required that reveals additional activity in that brain region around 115 ms.

The discrete model adequately models and mutually separates the activities in the different brain regions. The separation manifests itself in the clearly distinct peak latencies of the different components – an important criterion to judge the quality of a given source model.

A comparison of the reconstructed source waveforms allows to determine which brain regions show a response that is sensitive to stimulus intensity: Whereas the N100 amplitude does not change significantly between the two conditions, the N140 component increases in amplitude at high stimulus intensities. The effect is even more striking in the cingulate source, which exhibits hardly any activity in response to low intensity auditory tones.



This slide shows the application of distributed source models (minimum norm [top] and LAURA [bottom]) to the low intensity condition. Common to both methods is the substantial blurring of focal brain activity that is characteristic for all distributed source imaging methods.

Basic principles of multiple source analysis

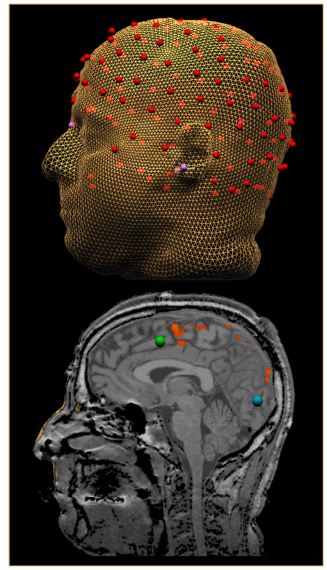
- Brain ⟶ Scalp: Forward solution = source & head model
- Scalp ⟶ Brain: Inverse solution = linear inverse
- Understand the goals of the experiment / limits of data
- As a result of this, define appropriate constraints for the model of brain activity:
  - circumscribed regions -> discrete, overdetermined model
  - hypothesis testing based on anatomy / physiology (MRI/fMRI)
  - distributed sources -> undertermined, needs constraints, e.g.
    - ➢ spatial smoothness (LORETA, LAURA), only spatial
    - ➢ a priori probability based on data (Bayes statistical methods)

BESA Brain Electrical Source Analysis

M. Scherg, Sept. 2008

AEP: Simple auditory reaction time experiment

- Subject hears a brief tone binaurally and presses a key as fast as possible
- Temporally overlapping activities in auditory & motor cortex, SMA and cerebellum must be expected (RT~150 ms)
- 128-channel EEG recording, EGI-System with Geodesic net and 3D digitization
- Averaging of about 250 responses relative to tone onset and key press
- Independent recording of event-related fMRI (3T)



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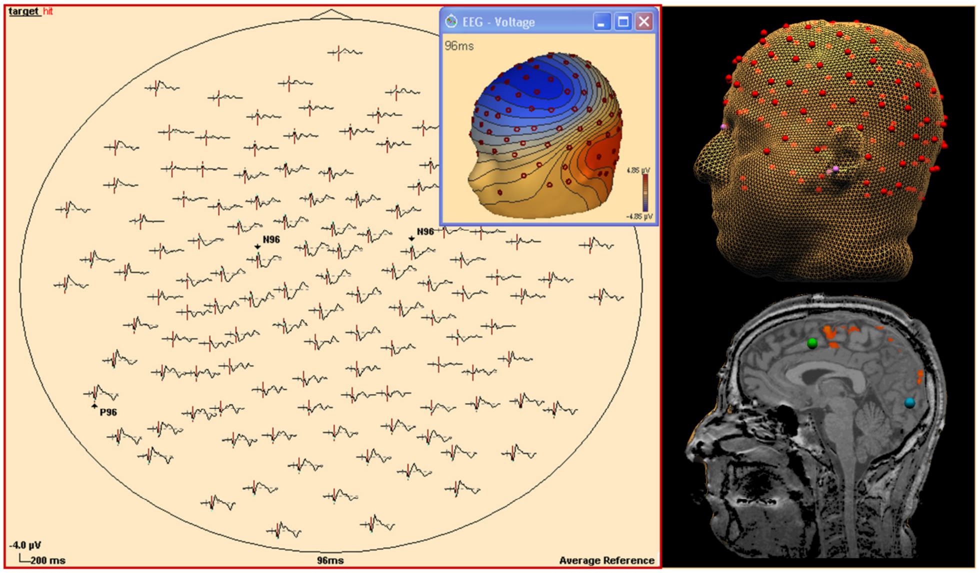
In the following we will demonstrate the capabilities of discrete source modeling using example data from an auditory reaction time experiment.

AEP: RT experiment => Fit / probe likely regions



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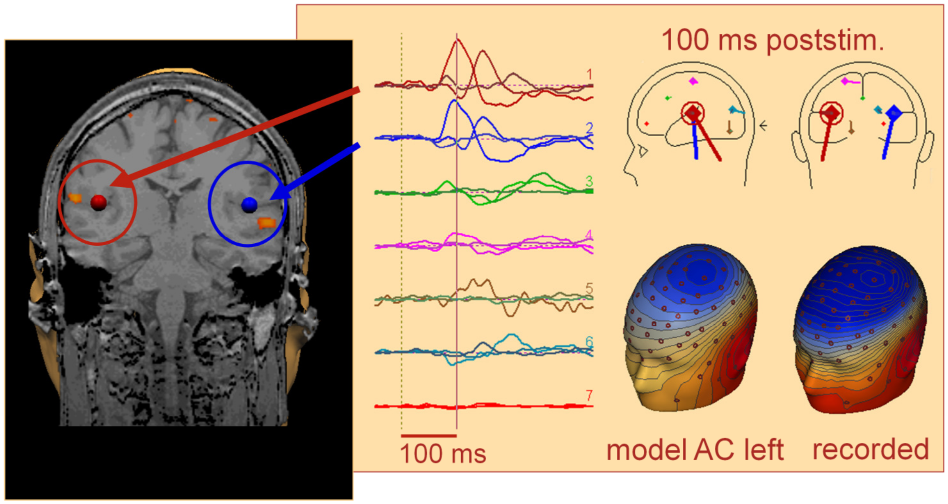
We will apply source analysis to disentangle the activities of the involved brain regions that overlap substantially on the scalp surface. To construct a source model, we have the option to fit sources based on the recorded EEG data alone (high signal-to-noise ratio required), or to seed them at locations that we hypothesize to be active, based on the obtained fMRI BOLD clusters.

N100 – Auditory Cortex right + left



Source activities and localization from EEG

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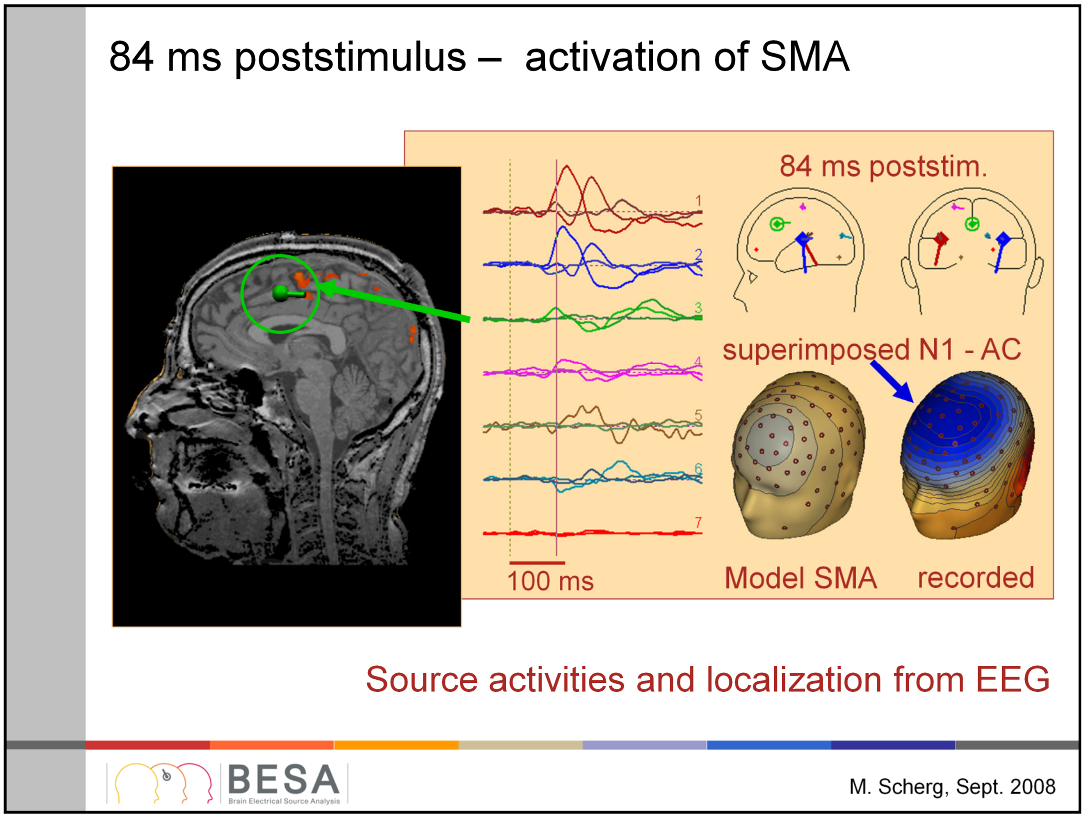
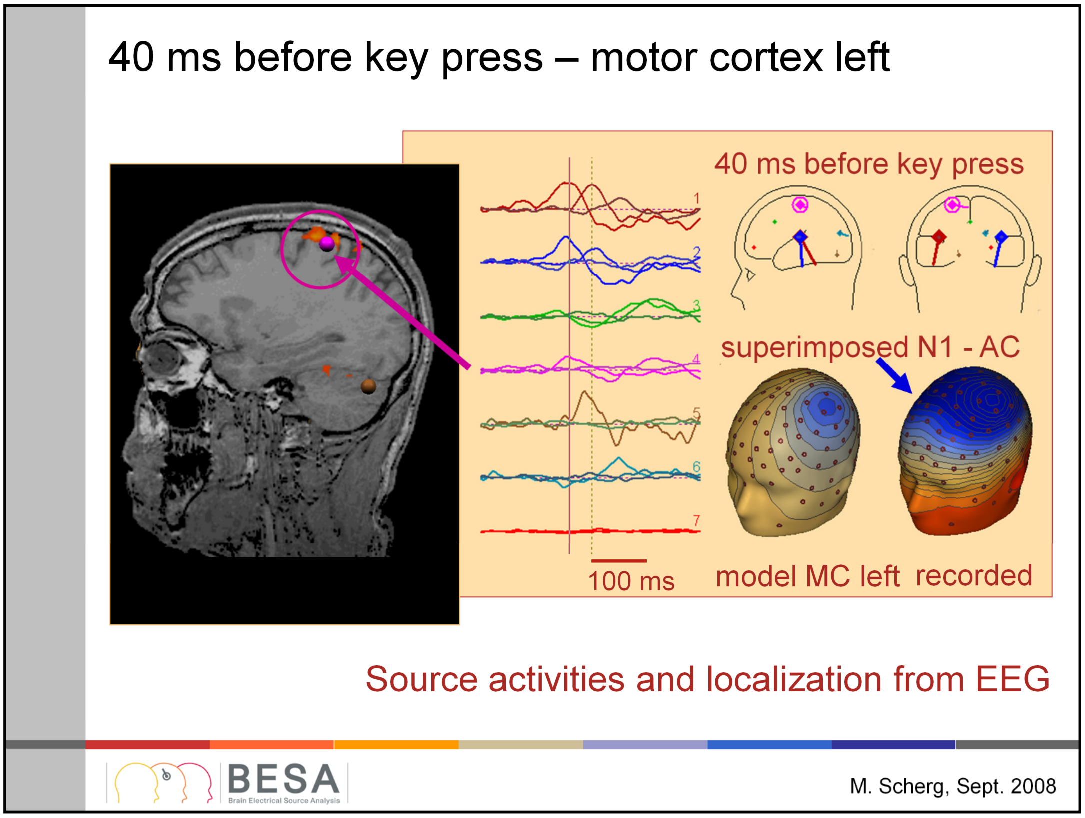
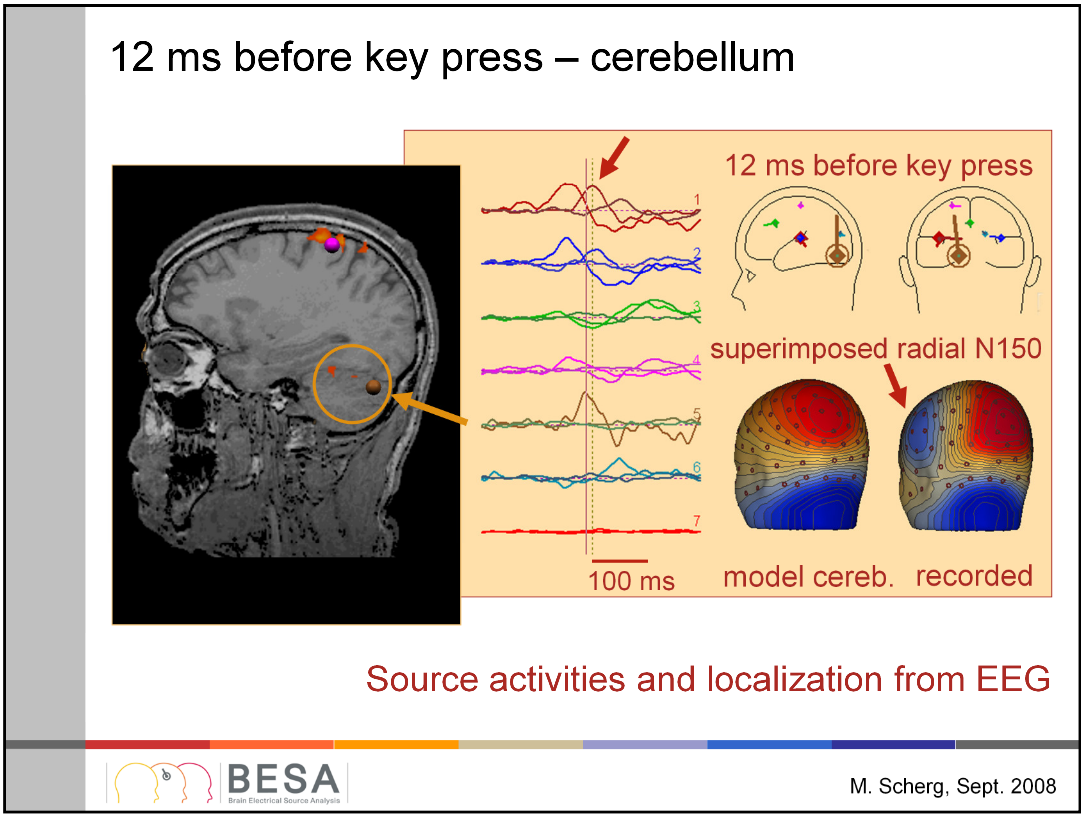
Source fitting results in bilateral regional sources in the region of the auditory cortex. They model both the vertical current flow accounting for the N100 component, and the radially oriented N150.



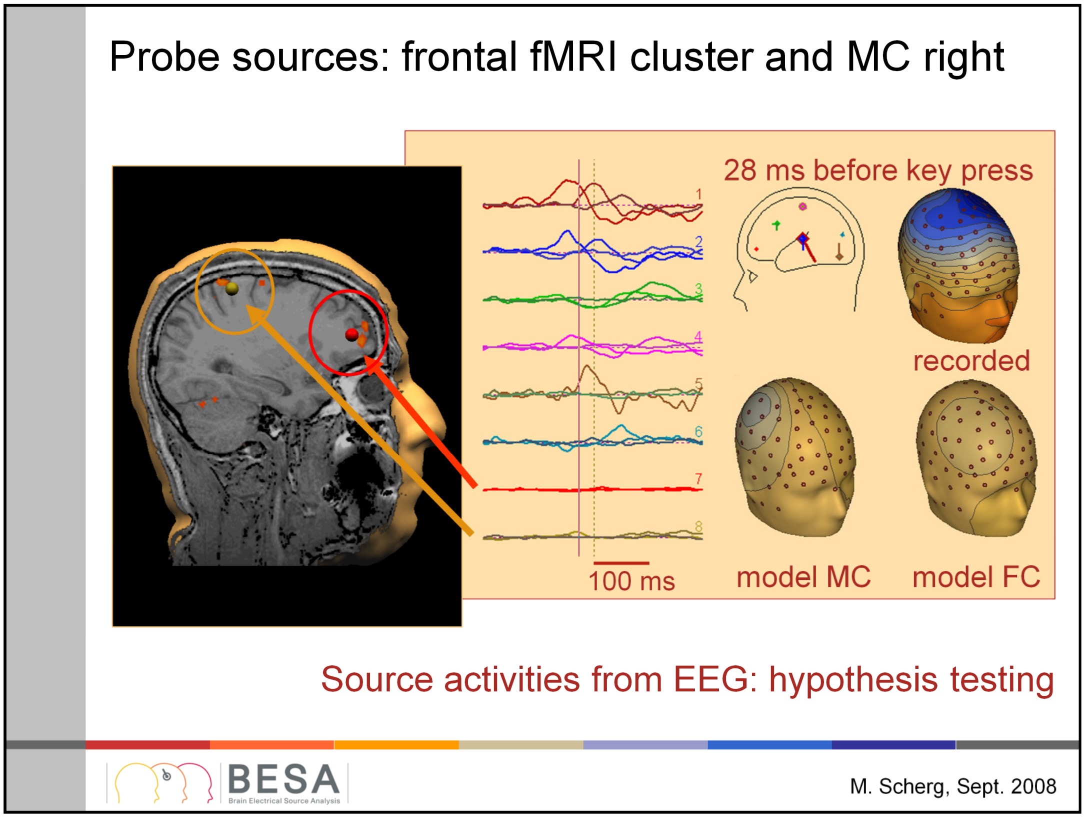
At 84 ms poststimulus, SMA region shows peak activation, indicating the initiation of the key press.



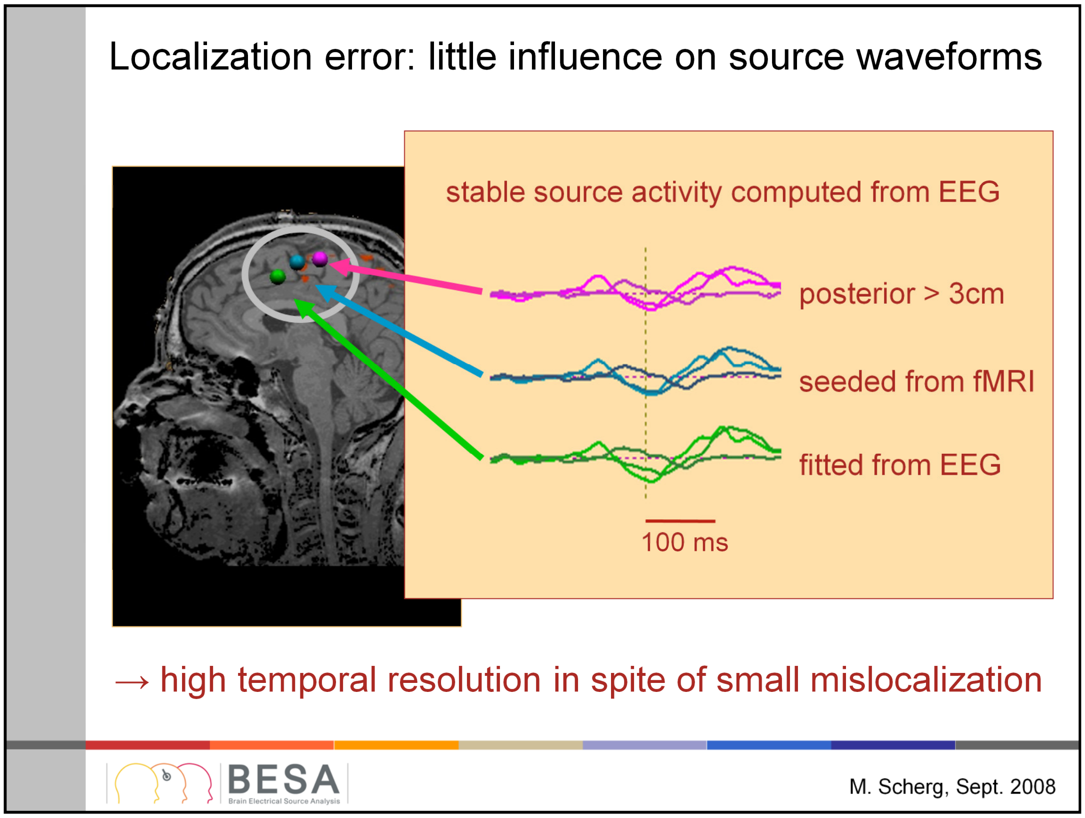
40 ms before the key press, the motor cortex becomes activated.



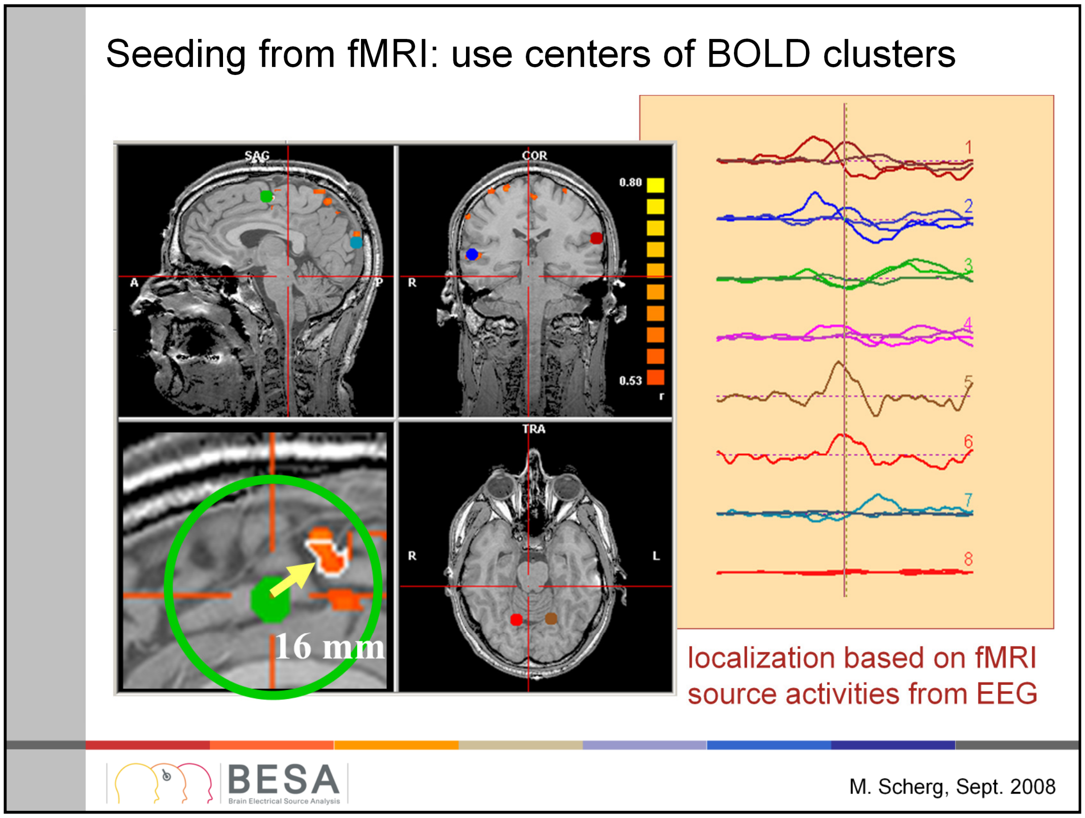
12 ms before the key press, activation of the cerebellum is observed. The corresponding scalp voltage pattern is completely buried within the large voltage distribution of the N150 component and therefore cannot be identified by visual inspection of the voltage maps.



Probe sources added in additional fMRI clusters in the frontal cortex and the right motor cortex indicate that these regions are nearly silent in the EEG recording. Only a small coactivation of the ipsilateral motor region can be seen shortly after the activation of the contralateral motor area before button press.



This fact is illustrated here. Source waveform topography is rather insensitive to small variations in source location.



fMRI bold clusters can be used to seed dipoles into the EEG head model. This method combines the capabilities of fMRI to localize sources and of EEG to analyze the temporal evolution of the corresponding activities. While fitted and seeded source locations may differ on the order of 1-2 cm, the resulting changes in source waveforms are small.

The philosophy of BESA

Fitting / Probing: Place or fit sources into the brain at all regions contributing to the data to create a linear inverse operator that separates these activities.

Hypothesis testing: Use as much knowledge as available from anatomy and other imaging modalities to define the likely regions of brain activation.

Source waveforms: The discrete sources image the temporal evolution of brain activity and reduce the data to few, robust source waveforms.

Reliability: Use different methods (Maps, Min. Norm, MSA, Beamformer, Probes). Finally, use bootstrap statistics to analyze significance of peaks in source waveforms.

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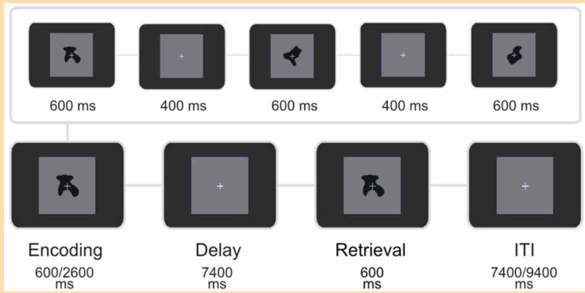
How have other groups used this philosophy?

- Gallinat et al. Neuroimage 2002: AEP – temporal and frontal generators
- Gutschalk et al. Neuroimage 2002: AEF – periodicity & intensity sources
- Frishkoff et al. Cogn. Brain Res. 2004: N400 - multiple sources analysis
- Vanni et al. Neuroimage 2004: Sequential activation of V1-V5 in visual cortex. fMRI + EEG, seeded multiple sources.
- Bledowski et al. J. Neurosci 2004: P300 – fMRI + EEG
- Bledowski et al. J. Neurosci 2006: Memory – fMRI + EEG

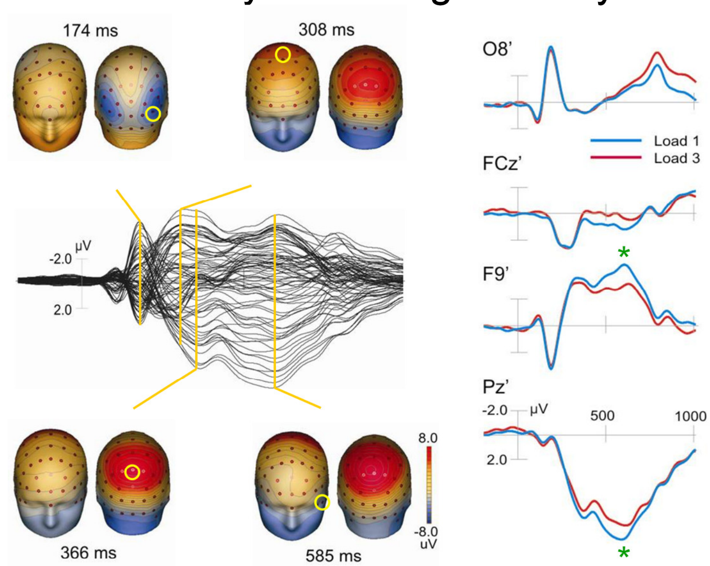
Load 3

Load 1



ERP: Mental chronometry – working memory

Bledowski et al.
J. Neurosci. 2006



- 18 subjects (9 males, 9 females, mean age 27.2)
- separate EEG and fMRI sessions (counterbalanced order)

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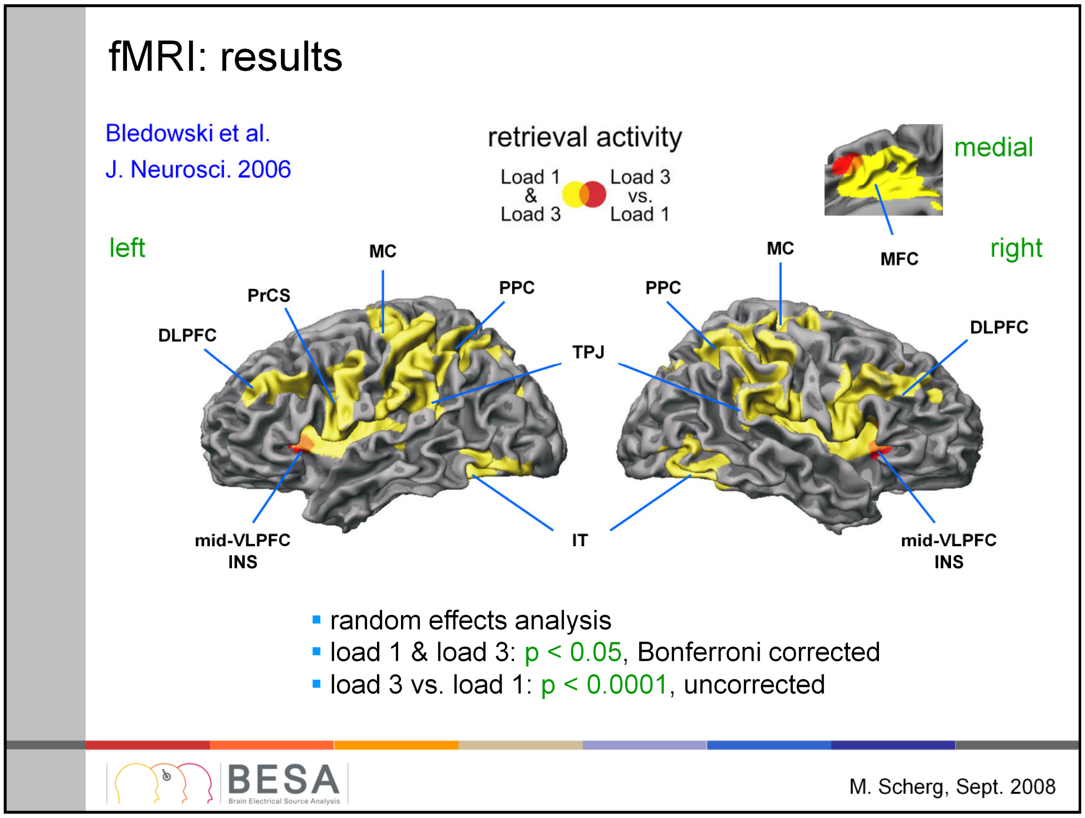
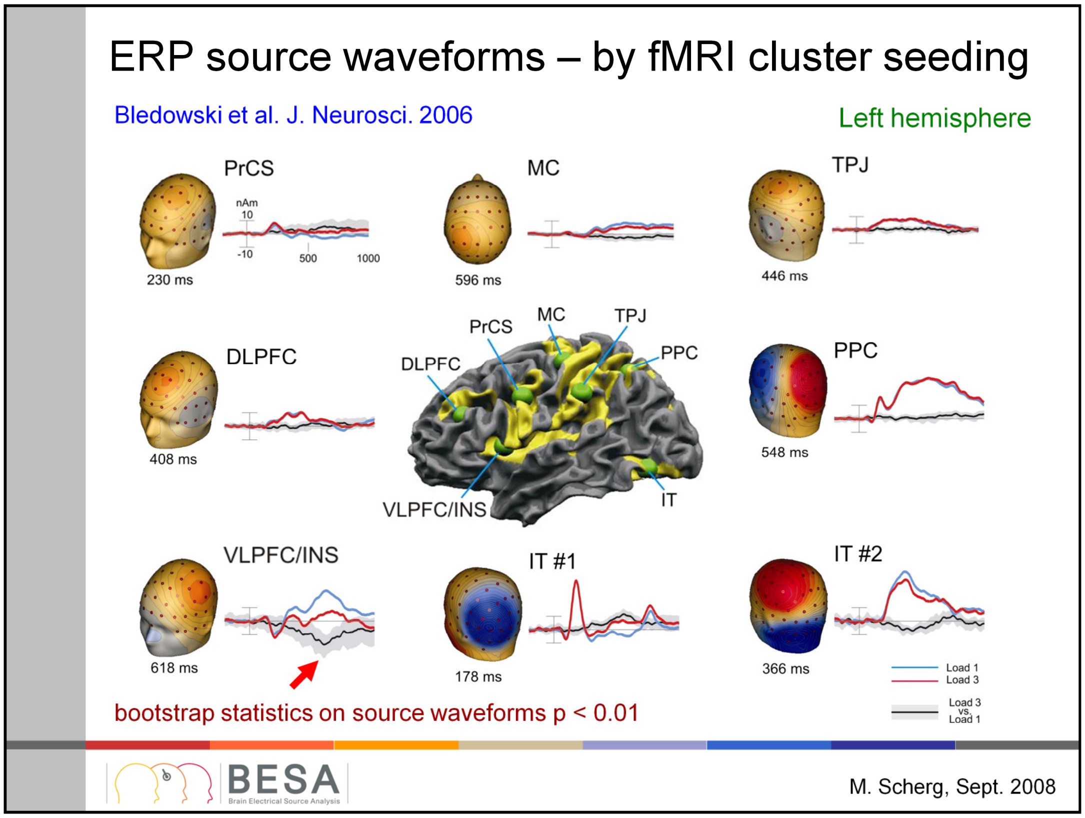
The example on this page and the following is taken from the publication of Bledowski et al.: Mental Chronometry of Working Memory Retrieval: A Combined Functional Magnetic Resonance Imaging and Event-Related Potentials Approach, J Neuroscience 26, 821.829 (2006). A combination of functional magnetic resonance imaging and event-related potentials was used to decompose the processing stages (mental chronometry) of working memory retrieval. In the averaged EEG data, significant differences in the responses to low and high memory load are observed e.g. in electrodes F9 and Pz. However, source analysis is required in order to determine which brain region(s) are responsible for the observed difference.



In the fMRI, the mid-frontal cortex (MFC) and the ventrolateral prefrontal cortical areas (VLPFC) show significant differences in the response to the two conditions. However, fMRI cannot indicate the accurate time course of the activities of these brain regions. Therefore, a discrete multiple source model is seeded, with sources placed in the brain areas that exhibit substantial fMRI activity.



The reconstructed source activities (here only the left-hemispheric sources are shown) allow for a more detailed analysis of the differences in the brain responses between the two conditions. The result confirms the fMRI result of significant differences in the VLPFC area. In addition, the EEG source waveform provides the latency information that was missing in the fMRI image.

Summary and outlook

- Discrete multiple source models provide a profound separation of the activities in different brain region
- Distributed source models show more smoothing and less separation of the different brain activities
- Multiple source probe scan images are helpful in validating a multiple regional source model
- Source montages allow for direct imaging of raw, i.e. single trial EEG scalp data into brain source space
- Time-frequency analysis on this basis separates induced and evoked oscillatory activities of the different brain regions
- Source coherence can reveal connectivities between the analyzed brain regions if their coupling exhibits oscillations with good SNR.

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For more information on source modeling and the BESA software please refer to our homepage at www.besa.de. At this site further tutorials, lectures and demo movies are available.