

This presentation was given during the Dianalund Summer School on EEG and Epilepsy, July 23, 2012.

The main purpose of tutorial talk is to give you a thorough understanding of the voltage topographies associated with focal epileptic spikes and to teach how to interpret 3D maps.

Disclosure:

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He has been heading the development of the software packages BESA Research and BESA Epilepsy.

Localization by polarity reversal and spike negativity?			
Fp1-F7 F7-T7 T7-P7 P7-01 Fp1-F3 F3-C3 C3-P3 P3-01		◆ Q 中 C J) 評 ※ G G I I G G G G G G G G G G G G G G G	
How is the EEG generated? Which factors determine scalp topography? Location of one (or more) focal activities?			
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Traditional EEG training teaches to look out for polarity reversals to identify the negative peak, e.g. of interictal spikes. Often, it is assumed that this peak identifies the region of origin.

However, this concept is too simplistic and may often lead to misinterpretation. Normally, the negative pole of a dipolar map is not exactly above the region of origin and may in fact be quite remote and even over the other hemisphere. Therefore, you should learn how to consider the whole topography including the positive pole to define the region of origin as you will see further on.



When using BESA Epilepsy or BESA Research in EEG review mode, you obtain a single 3D map when selecting a detected event or clicking on a spike peak or anywhere on the EEG traces. The 3D map automatically rotates to a viewpoint related to the center of the selected EEG topography.

The 3D maps allow for an approximate visual localization of focal brain activity, i.e. if the EEG activity originates only in one circumscribed brain region. Focal brain activity produces a dipolar voltage topography on the scalp with 2 poles, a negative and a positive pole. The size of the poles depends on the location **and** orientation of the active cortical region as we will learn below.

First, you need to check if the voltage map is dipolar: In the 3 maps above only the right map is dipolar, since there are 2 opposite poles. The negative pole over the left frontal scalp is more focal than the posterior positive pole.

Maps with midline foci must always be checked carefully if they are bilateral (middle). Then interpretation is complicated and often obsolete. Similarly, multiple poles in a map (left) reflect a complex overlap of activities in multiple regions that is not interpretable.



First, we want to understand how dipole maps arise from the human cortex and how they are related to focal activities.

We will especially point out the importance of the cortical orientation that influences the position of the negativity on the scalp even more than the location of the active focal region.



Epileptic spikes are associated with a depolarization of the apical dendrites of pyramidal cells in the superficial cortical layers. Current is entering into the intracellular space and flowing towards the cell body (current vector perpendicular to cortical surface into the cortex).

In the extracellular space secondary return currents close the current loops since the brain is a well conducting medium. A small portion of this return current flows through the skull and creates the minute voltage gradients in the scalp that are recorded in the EEG.



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.

If the spatial centers of sources and sinks are separated across the cortex they form a net dipole. For each cortical column the net dipole vector summates over all current sources and sinks across all layers. If the center of the sinks is closer to the surface as compared to the center of the sources, the current dipole vector points into the cortex (as in the case of a spike with strong superficial sinks).

Since the EEG is typically recorded with a time-constant to remove DC offset and slow drifts, the orientation of the current dipole fluctuates evenly between pointing inward and outward. Spikes, however, are prominent deviations from the baseline with the dipolar current pointing into the cortex, thus creating cortical surface negativities emerging from the EEG background.



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 4 cm in diameter (~ 12 cm² !) can be very accurately (>95%) modeled by a single equivalent dipole.

Currents at the cortical convexity have a predominantly radial orientation, currents in cortical fissures have a 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.



Current loops in a conductive medium like the head are closed. Therefore, the intracellular currents resulting from 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 nearby extracellular brain space. Only a very small fraction flows out through the poorly conducting cranium and along the scalp before returning to the brain.

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. The volume conduction results in a widespread, smeared voltage topography over the whole scalp with a negative maximum over the activated superficial cortical sheet. A corresponding more widespread positivity appears on the other side of the head. By physics, any negativity has a corresponding positivity somewhere else over the head, since the current loops are closed and the potential distribution over the whole head summates to zero.

A cortical patch in a vertical fissure generates tangential currents. The small return currents through the scalp create a dipole map with symmetric positive and negative poles aligned in the direction of the dipole current. The voltage directly over the source is zero, but the voltage 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 3D maps resulting from a focal cortical activation are as much dependent on the location of the active cortex as on the orientation. Both poles of the dipolar map need to be considered to assess location and orientation:

The maps on the left and in the middle illustrate two idealized situations, tangential activity in a vertical fissure (going down at 90 degrees from the cortical convexity) and radial activity at the cortical convexity. In the tangential case (left) the 2 poles are of equal strength and symmetric. The focal source lies below the midpoint between both poles.

The purely radial spike (middle) has a prominent negative pole exactly over the active region while the positivity is widespread over the opposite side of the head.

Normally, the focal activity involves a cortical patch having an oblique net orientation (right). This is either due to varying contributions of superficial and fissural cortex or to the oblique orientation of an active fissure. The net orientation defines the dipole field and a small deviation from radial already results in a large shift of the location of the negative pole on the scalp.

Below, we will learn how to include the positive pole to improve our estimation of the source center over the consideration of the negative pole and polarity reversal alone.



The effect of the extent of the active cortex can be seen easily since dipole fields sum linearly. The equivalent dipole moment is proportional to the size of the spiking patch. If the area is small (2-4 cm²), the dipole moment is small and a spike from superficial cortex may just be visible (~30-60 μ V) in an EEG of low amplitude.

If the area is larger (9-12 cm²), the spike will be more conspicuous (~100-200 μ V).



The focal activity can still be well described by an equivalent dipole or regional source (see below), if orientation changes over the course of the spike as the relative amount of activated superficial and fissural cortex changes.

If the whole region spikes synchronously, one equivalent dipole with oblique orientation (see upper illustration) can still approximate the spike activity very well.

If the involvement of either superficial or fissural parts occurs with a delay due to propagation (see lower illustration), a regional source with a radial dipole and 2 tangential dipoles (one in the plane of the slice and the other perpendicular to it) are a more appropriate model and their time courses can be used to identify the onset zone.



Let us consider a situation with an activation that propagates locally over different aspects of the left central gyrus as shown above. For this, the proportion of active sulcal versus superficial cortex was varied in a more moderate way.

The first map involves only the posterior wall of the central sulcus (current direction is tangential and towards posterior), the second map involves both the upper part of the central sulcus and the crown of the post-central gyrus (oblique net dipole), the third map involves more the crown and, to a small extent, a downward fissure parallel to the midline that shifts the positive pole from right to left inferior (not illustrated above, cf. next slide).

In this simulation, the same location was assumed for each equivalent dipole to demonstrate the strong effect of the net cortical orientation:





In this simulation we consider a different type of local propagation in the left frontal cortex that involves more the fissures.

All maps have virtually the same center while the negativity is over the right frontal cortex (left), over the posterior midline (middle), and over posterior parietal cortex (right). However, the map center as defined by the shortest route between the negative and positive poles and their relative weights is just above C3 in all cases.

First, the spike current flows into the lateral wall of a fissure parallel to the midline. Next, the anterior wall of a lateral fissure gets involved as well and the net current orientation appears to rotate. Finally, only the anterior wall of the lateral fissure is involved. The tangential pattern appears with opposite polarity as compared to the previous example of the posterior wall of the central sulcus and a center that is slightly more anterior.



Using the presented simulations and real EEG spike examples, we can define some rules how to interpret 3D scalp maps to identify the equivalent center of a focal spiking region.



3D mapping can substantially improve spike review and understanding of the origin of spikes. Let us learn how to interpret dipolar voltage topographies:

First, consider a line connecting the negative and positive maxima on the scalp (thin arrows). This line follows the shortest route having the highest voltage gradient (~ narrowest distance between equipotential lines).

Second, find the region of highest gradients (near thick arrows).

Third, consider the relative strength of the negative and positive poles.

In a close-to-tangential map (left, origin only in sulcus), the equivalent location is approximately below the area of maximum gradient (thick arrow).

In a perfectly radial map (middle, origin only on cortical convexity or deep), the center location coincides with the peak of the negativity. Since all scalp fields are dipolar (by physics) there is a positive pole on the opposite side of the head. It is weaker since the posivity is more widespread.

A typical EEG spike map has one stronger and one weaker pole (right). The origin lies below the region of largest gradient along the line conneccting both poles, but may be shifted slightly towards the stonger pole if this is dominant (thick arrow).

In the presented simulation, the location of all 3 sources was kept identical to illustrate the predominant influence of source current orientation.

Download the free dipole simulator program from www.besa.de to gain a better understanding of the effects of orientation on EEG scalp topography.



How can we estimate the 'approximate source location' from these real temporal lobe spike maps? We follow the same principles as before:

First, consider a line connecting the negative and positive maxima on the scalp (thin arrows). This line follows the shortest route having the highest voltage gradient (~ narrowest distance between equipotential lines).

Second, find the region of highest gradients (near thick arrows).

Third, consider the relative strength of the negative and positive poles.

The left 3D map is a close-to-tangential map. The equivalent location is approximately below the area of maximum gradient (thick arrow). The vertical orientation is related to a current flow into the left temporal basal cortex (spike current flows into the cortex and, thus, produces cortex negativity).

The middle 3D map is also a close-to-tangential map. The negativity has rotated towards the left eye; the positivity is over the (left) posterior head. The center is more anterior, the current orientation points backward and upward. The only cancidate for such a pattern can be a spike source current at the left temporal polar cortical surface. Here, the basal surface is still somewhat active. If not, the negativity would have shifted more towards the left eye.

The right map shows the typical radial pattern of a left temporal-anterior spike originating at the lateral cortical convexity. Only this pattern leads to the typical polarity reversal in the longitudinal bipolar montage.

Without inferior electrodes or the whole head virtual montages and 3D mapping, such temporal-basal and polar spikes can be easily overlooked.



Here, we want to analyze spike onsets and peaks in the EEG of a patient with temporal lobe epilepsy. The average EEG spikes are shown using the temporal lobe source montage that will be explained further below.

Only the peak maps are shown to characterize the different detected spike types:

- Sp1: left basal EEG vertical map, the MEG shows the corresponding horizontal map, same center in left temporal lobe (92 averages)
- Sp2: left polar EEG oblique map with negative maximum over the eye, MEG map with reduced inferior negativity, pointing to the same more anterior center (49 averages)
- Sp3: right basal EEG vertical map, the MEG shows the corresponding horizontal map, same center in right temporal lobe (44 averages)
- Sp4: right polar EEG oblique map with negative maximum over the eye, corresponding orthogonal MEG map, pointing to the same more anterior center (49 averages)

In each hemipshere, 4 dipoles have been used to estimate the activity at the basal, polar, antero-lateral and postero-lateral aspects of the temporal lobe (left: traces 1-4, right: traces 5-8). The leading signal at the temporal base can be seen in the basal source channels (traces 1 & 4) in the averages Sp1 & Sp3; the leading signal at the temporal pole can be seen in the polar channels in the averages Sp2 & Sp4 below the basal channels (traces 2 & 5).



Next, we want to understand the effects of local spike propagation, i.e. within one lobe or region, and, later on, the effects of more widespread propagation, i.e. if the activities of multiple regions overlap at the spike peak.



Let us consider what kind of maps we might expect, if different aspects of the temporal lobe are activated, e.g. by an epileptic spike that typically involves more than 4-6 cm² of cortical surface to become visible in the scalp EEG.

Anatomically, each temporal lobe has 3 major surfaces, or aspects: basal, polar and lateral. Larger spikes in the EEG (> 50 uV) are likely to be oriented prependicular to the gross area they originate from. Therefore, we can expect the dipole fields to match the cortical surfaces that have a net vertical (basal), anterior-posterior (pole), or radial (lateral) orientation.

Therefore, each temporal cortex can be modeled by 3 equivalent dipoles reflecting the basal, polar and lateral aspects, as illustrated above for the left temporal lobe. In addition, the large lateral region can be divided up and represented by an antero-lateral and a postero-lateral radial dipole.

The topographies that can be expected to be seen at the scalp are quite different with predominantly tantential patterns related to basal and polar activities and radial patterns to the lateral convexity.

To some extent, the vertical basal dipole will also pick up source currents in the supratemporal plane within the Sylvian fissure. Then, the spike polarity can help dissociate which side of the Sylvian fissure is discharging. Basal spikes have the opposite polarity to spikes that originate at the superior surface of the temporal pole.



Mapping of the spike peak of a patient with left temporal lobe epilepsy shows a left temporal-lateral negative peak. However, the temporal evolution of the serial maps starting 35 ms before the spike peak shows a rapidly changing topography from spike onset (-25 ms) to peak (0 ms) with an initial vertical dipole field during spike onset.

The initial negativity is below the temporal lobe and is picked up mainly by the inferior temporal electrodes. Using spherical spline interpolation the negative peak below the temporal lobe can be extrapolated with sufficient accuracy.

The negativity appears to rotate forward towards the temporal pole before changing into the radial pattern at spike peak. The rotation of the map from the initial vertical topography to a radial-lateral pattern indicates propagation from basal to polar and lateral resulting in quite some overlap at the spike peak.



Previously, we have seen various examples of the typcial dipolar maps resulting from activities at the basal, polar and lateral aspects of the temporal lobe.

Can we use these types of maps to disentangle spikes in the EEG such that we will see how much each pattern is contributing to a recorded spike?

The answer is yes.

By creating a model with multiple dipole sources in the right and left temporal lobe as well as in other brain regions we can construct a source montage to show the approximate contributions of each source to the recorded EEG.

As shown above, we can use 3 dipoles to represent the different aspects of the left anterior temporal lobe. Similarly we can use one equivalent center within the left temporal lobe and 3 current vectors in x,y,z direction to represent anny current in the surrounding volume with a good precision (regional source, below).



We can extend our model and add similar, symmetric sources (red) in the right temporal lobe in order to separate the contributions of the right and left hemispheres.

Our model will now try to separate the contributions of the right and left temporal lobe and divide them further up into basal, polar and lateral activites (using the dipole oriented appropriately). Alternatively, a regional source with 3 orthogonal waveform in each hemisphere can be used.



To separate activities from other brain regions and the temporal lobe, we further extend our model and add regional sources in frontal, central, parietal and midline regions.

Without going into further details, the resulting source montage represents a linear transformation of the EEG signals - recorded at standard electrodes - into approximate source waveforms of the included regions and the different aspects of both temporal lobes.



We can now use this temporal source montage and inspecet our previous example again to observe that spikes in the left temporal lobe (TL, Sp1 & Sp2) are predominanly reflected in the associated traces 1-4 while right TL spikes (Sp3 & Sp4) are visible in the right temporal traces 5-8. Cross-talk to the other regions is small.

Furthermore, the basal and polar traces show a clear dissociation in the onset and peak times of their source waveforms depending on spike type:

The basal spike is earlier and more prominent in Sp1 & Sp3, while the polar spike appears earlier and larger in Sp2 & Sp4.

Lateral activity (traces 3 & 7) is delayed and smaller in all cases.

When mapping the onset of each (averaged) spike type, the patterns are weaker (less cortex involved at onset) but similar to the displayed peak patterns.



We are now ready to look at more complicated cases with spikes propagating into several, separate brain regions. In such cases, the apparent spike peak may already presents severe overlap from multiple regions. This will mostly result in 3D map that are no longer dipolar and too complicated to be analyzed.

Thus, we will need to map spike onset instead of the peak with the aim to find a focal dipolar topography at the beginning. Often this will not be possible without averaging similar spikes to enhance the onset signal over a noisy background EEG.



Again, we will use a simulation that reflects to some degree what has be seen in cases with juvenile myoclonic epilepsy.

The simulated red spike starts in the mesial wall of the right cingulate gyrus. Due to the cortical surface negativity the initial map shows a paradoxical lateralization of the negativity to the left (yet the map center is correctly on the right).

We have further assumed fast propagation to the superior frontal gyri via fibre connections. I.e. the ipsilateral right superficial frontal cortex (blue) is spiking about 10 ms later, followed by the contralateral, left frontal cortex (green) with another short delay (~ 5 ms).



If we inspect the peak map at the scalp when all 3 regions are involved, we observe a wide-spread negativity over the frontal cortex that appears bilateral. This is a typical pattern when both hemispheres are involved.

The almost synchronous onset of the left and right supercical activities leads to severe overlap. The peak map is blurred and exhibits a bilateral pattern that cannot be lateralized nor localized.

Polarity reversals are seen at the peak on both sides in the 4th segment that is related to this situation, but the larger amplitude over the left in the longitudinal bipolar channels must not misinterpreted as lateralizing sign.

In fact, it was the continuing right mesial activity that enhanced the peak negativity over the left (see next slide).



If we map the onset (simulated EEG background noise was moderate) and use the same scale as for the peak, we see a pattern that is hard to interpret.

In any case, the center seems close to the midline, the current flow appears transversal, but, the map center is hard to lateralize due to the EEG background blurring the onset signal.

Yet, if we were sure that this was a spike, we could postulate the right hemisphere as the origin by considering polarity: the negativity over the left scalp corresponds to a negativity at the spiking mesial surface of the right frontal cortex deep in the interhemispheric cleft. Thus, spike polarity in combination with the near-tangential dipolar pattern can help to dissociate which side (of a sulcus) is involved.



If we assume only ipsilateral propagation (same onset in red source, propagation only to blue source), the predominantly radial peak map would show a clear lateralization to the right. In the related 3rd segment, the associated polarity reversal at the spike peak can be seen only over the right. Polarity reversal during the onset is weaker, earlier and over the wrong hemisphere (cf. Map in previous slide).

The typical rapid propagation of frontal spikes to both hemispheres, however, makes lateralization often impossible. Hence, analysis of the spike onset phase is required.



Thus, as a rule, we should consider to map spike onset whenever possible.

Propagation may only be local. In this case, we can still identify the region of origin using the peak map, if the origin is not too close to the midline.

However, propagation may have occurred from a more remote onset region. Therefore, we should attempt to map spike onset as well.

In the following, we want to look at some real data sets to underline this suggestion.



The single spikes of this patient show a polarity reversal between F7-T7 and T7-P7 similar to typical temporal lobe spikes. The corresponding radial map at the spike peak has a maximum negativity over the temporal lobe.

Spike onset is unclear and varies between the single spikes. The single spike map during onset reflects mostly EEG background activity.

After averaging, the tangential topography during spike onset becomes apparent. The onset pattern shows a negativity over the frontal cortex and a more superior horizontally oriented, oblique dipolar pattern.

But, when just considering the spike peak, this seems to reflect a left temporal lobe spike. Is this correct?



As shown in the previous example, averaging is mandatory to map spike onset adequately. This was also the case in the following examples.

The procedure for averaging and mapping of onset as realized, e.g. in the BESA Research program, is briefly explained above.



Is this radial spike peak coming from the lateral surface of the left temporal lobe?

How can we estimate the 'approximate source location' from the maps?

Again, consider a line connecting the negative and positive maxima on the scalp (red arrows). This line follows the shortest connection having the highest voltage gradient (~ narrowest distance between equipotential lines).

Then, find the region of highest gradients and consider the relative strengths of the positive and neagtive poles

The onset map is close-to-tangential (upper row), the equivalent location is approximately below the area of maximum gradient (green arrow).

The peak map appears radial (lower row), but the center location is shifted slightly from the negative peak towards the positive pole along the region of largest gradient. The positive pole is not on the other side of the head, but superior!

The equivalent centers of both maps are similar and point to a circumscribed region of origin in the rolandic cortex above the Sylvian fissure. Polarity indicates that the tangential rolandic spike is likely to arise from the anterior wall of the post-cental gyrus (~face area) with ensuing propagation to the surface of the gyrus (radial map), since the tangential onset current is flowing backwards into the posterior wall of the central suclus.

Onset and peak maps in this case were quite different. Looking at the negative peak in the EEG over O2, one might get the impression that the spike onset is in the right hemisphere. However, this is a typical case of the so-called 'paradoxical lateralization'. Again, just follow the rules of interpreting an EEG map by considering the corresponding positivity and the steepest gradients. You can observe immediately that the map center of the EEG spike onset is in the left mesial occipital cortex, consistent with the left MEG center.

At the spike peak, a clear lateralization to the left posterior temporal region can be seen with a relatively similar center between T7 and P7 in both EEG and MEG while the EEG negativity appears lower and more posterior (between P7 and P9). In addition, the MEG map is not a simple dipolar map but exhibits a 2nd, weaker dipolar pattern that seems to reflect the polarity reversal of the onset pattern.

This, in fact, can be seen from the dipole soure waveforms when using a model with separate onset and peak dipoles.

This example of a right temporal spike demonstrates the activation of yet another surface in the polar temporal region and a considerable propagation. Here, we analyzed 4 spikes averaged from a sharp transient in the MEG.

Note that the initial EEG dipole map at -30 ms shows a frontal negativity. When considering the accompanying inferior positivity and the gradients of the equipotential lines, it becomes evident that the underlying center is more inferior and corresponds to an oblique equivalent dipole pointing down and inwards.

The initial downward component is confirmed by the MEG map at -30 ms.

15 ms before the peak we observe a typical right temporal polar pattern, while superficial lateral activity with partly posterior orientation dominates at the peak (0 ms). Again, the polar current is confirmed by the MEG maps.

Thus, we might conclude that the spikes are initiated at the superior and lateral surface of the right temporal pole within the Sylvian fissure. This interpretation is supported by the small downward spike in the right temporal basal source waveform. This signal is constructed using a vertical dipole in the right basal temporal region within a multiple source model covering the other aspects of the right temporal brain region, the corresponding regions on the left and all other brain regions by regional sources. Thus, the basal source waveform will pick up spikes in the supratemporal plane as well, but with inverse, downward polarity.

After this short initial superior spike, the typical propagation to the polar and further on to lateral regions was seen in the right temporal polar and lateral source waveforms.

This slide illustrates that the interpretation of the 3D EEG maps was confirmed by source imaging and dipole localization – using orientation as key information as well. The 3D maps by themselves already allowed for the correct interpretation of onset and propagation:

Based on the rules of finding an equivalent center in a (predominantly) dipolar map, the downward activity at -30 ms was identifiable in both the EEG and MEG maps. Considering the fact that epileptic spikes are cortical surface negative, the only candiate for the origin of a downward-posterior current can be the upper surface of the temporal lobe within the Sylvian fissure. The anterior location and the subsequent propagation to the inferior and lateral part of the temporal pole suggest the upper surface of the temporal pole as origin.

The polar maps at -15 ms are quite typical for temporal-polar spikes and easy to interpret. The stronger negativity and oblique, backward orientation of the EEG polar map indicates anterior, inferior and lateral involvement of the polar region.

In contrast to the EEG, the MEG is dominated by the polar and basal activity and blind to the radial part. At the peak, the MEG map was more complicated and not clearly dipolar. The strong radial dipole of the lateral anterior temporal surface is only seen in the EEG. Where the MEG localizes, will strongly depend on which fissural aspects generate the predominant signals within a relatively widespread spiking zone involving the lateral and inferior cortical convexity.

MEG localization appeared a little more confined, but far from being able to identify precisely which part of the anterior temporal lobe was spiking. Here as well, the orientation was needed to dissociate the superior surface of the temporal tip from the basal polar surface.

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More lectures and tutorials showing the analysis of epileptic spikes and seizures can be found along with recommended electrode settings on:

www.besa.de