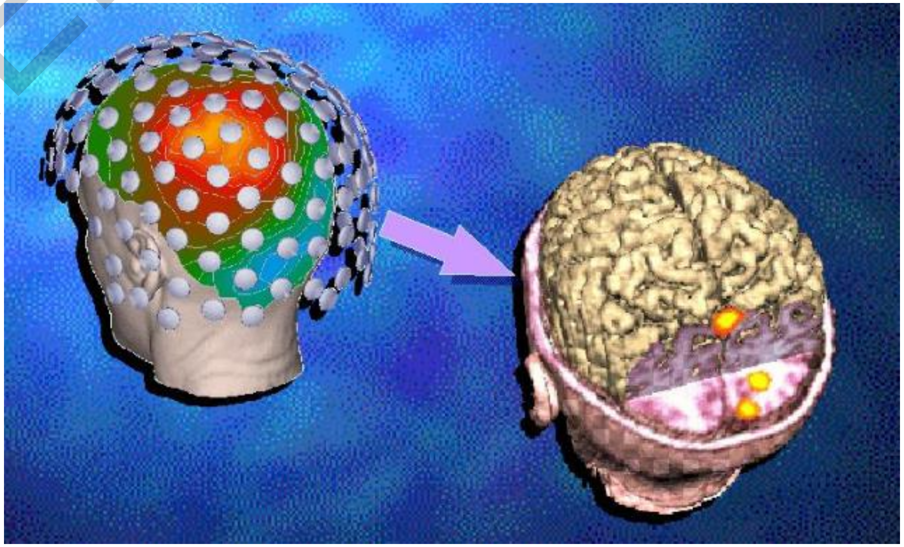
# Why EEG source localization

- EEG source localization methods may help to determine the regions of the brain where the spikes or any event are generated.
- Performing an accurate localization of EEG sources of interictal spikes is of particular interest to better understand their generation and propagation.



# Overview of the 3D source localization techniques

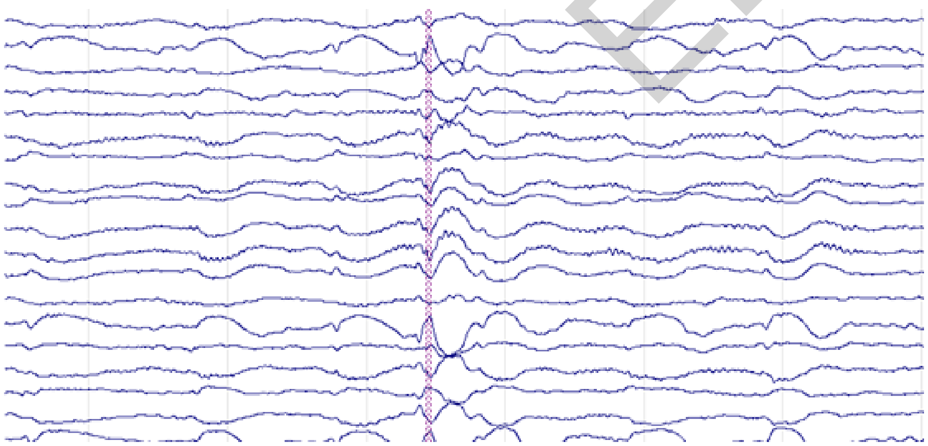
**Goals:**

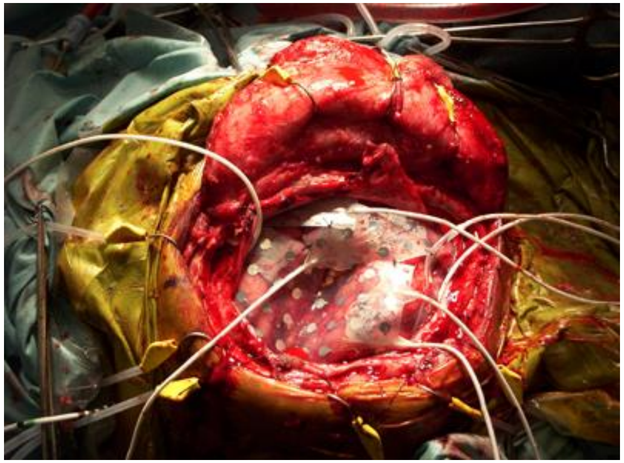
- More accurate source localization to improve post-surgical prognosis.
- Source localization based on non-invasive tests and scans instead of subdural EEG.

**Contributions:**

- A new framework for non-invasive source localization based on scalp EEG that:
  - Incorporates prior information from MRI and other sources.
  - Utilizes state-of-the-art patient specific head modeling (BEM model).
  - Tool for processing raw EEG data.

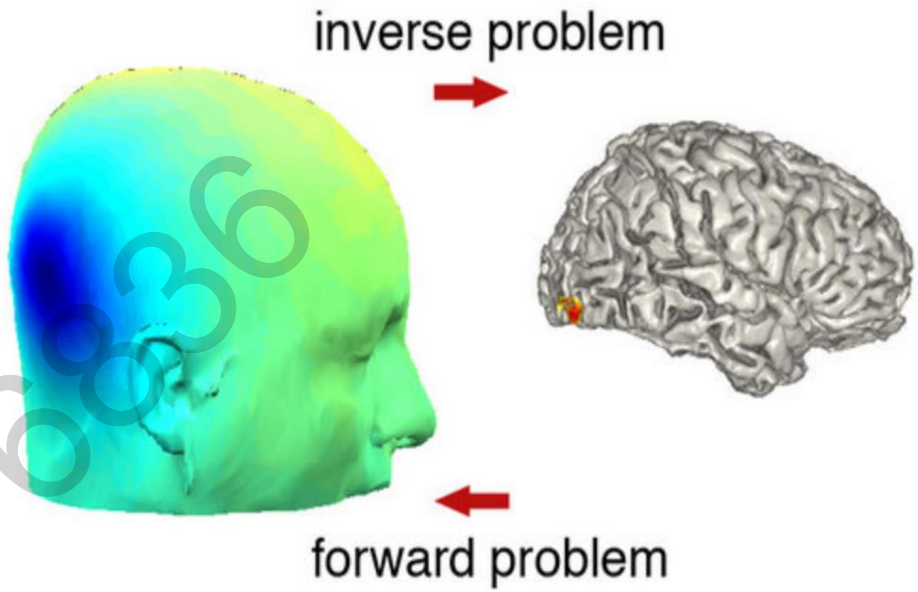






# Source Localization Problem

- EEG gives us voltage readings at electrodes on the scalp.
- From the Maxwell equations we get the state equation relating source currents in the head to voltages on the scalp:
  - **Forward problem**: Find voltages at electrodes given source configuration.
  - **Inverse problem**: Find source configuration given voltages at electrodes.




The inverse problem is highly ill-posed and must in practice be solved through iterative solution of the forward problem to search for a current configuration that best explains the voltages measured.

# Maxwell equations

- The propagation of EEG signals through the head is modeled using the theory of electromagnetism.
- EEG signals represent the electric waves and the head is modeled as a volume conductor.
- Maxwell's equations are used to describe the behavior of EEG signals.

$$\oint E \,.\, dA = \frac{Q_{inside}}{\varepsilon_0}$$

$$\oint B \,.\, dA = 0$$

$$\oint E \,.\, dl = -\int \frac{\partial B}{\partial t} \,.\, dA$$

$$\oint B \,.\, dl = \mu_0 I + \mu_0 \varepsilon_0 \int \frac{\partial E}{\partial t} \,.\, dA$$



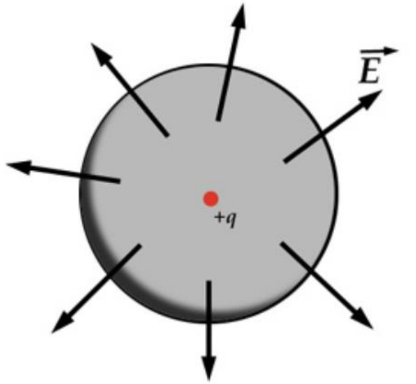
Maxwell's equations are the fundamental equations for all fields in Electricity and Magnetism.

Maxwell equations are a set of 4 equations that describe the relations between electricity and magnetism together with the Lorentz force.

# Maxwell equations

$$\oint E.dA = \frac{Q_{inside}}{\varepsilon_0}$$

Gauss' Law




Electric flux due to a single positive charge *+q*

The area <u>integral</u> of the Electric field (E) through a closed area (dA) is equal to the total charge inside of the area ($Q_{inside}$) divided by $\varepsilon_0$.

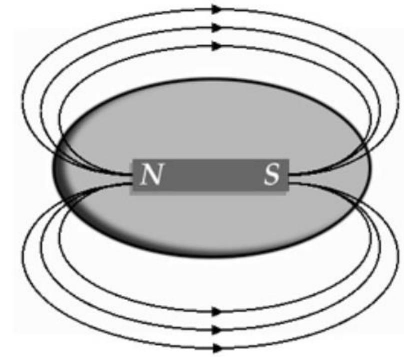
Electric field measure: *Newton/Coulombs=N/C*

**Note:** $\varepsilon_0$ is a constant called the Permittivity of Free Space. It is the <u>capacity of free space to permit the electric field lines</u>.

# Maxwell equations

$$\oint B \cdot dA = 0$$

Gauss' Law for Magnetism



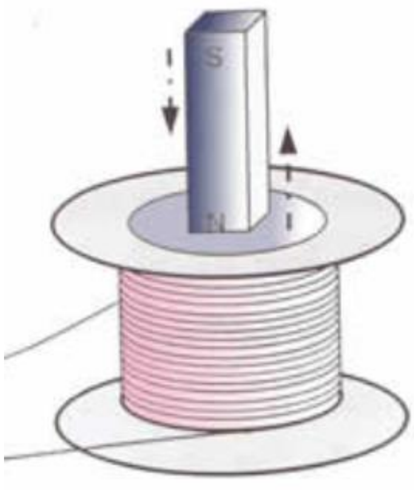

The integral of B (magnetic field) over a closed surface (dA) is zero.

This does not mean that zero magnetic field lines penetrate the surface, it means that for every magnetic field line that enters the volume enclosed by the surface, there must be a magnetic field line leaving that volume.

The magnetic flux emerges from *N* and ends at *S*. This means that what comes out of the Gaussian surface also goes into it.

Magnetic field lines are always closed loops. In this case Gauss's law refers to magnetic flux: the number of magnetic field lines passing through a closed surface

# Maxwell equations




### Faradays Law

$$\oint E.dl = -\int \frac{\partial B}{\partial t}.dA$$

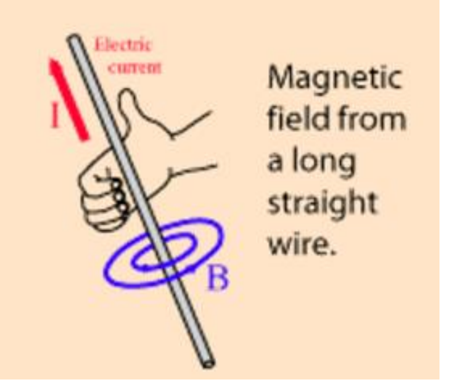
- The total E field (voltage induced) around a closed loop dl.
- $\partial B/\partial t$ is the rate of change of B, its how much B is changing ($\partial B$) in a given time ($\partial t$). And that is being integrated over an area dA.
- dA is the area inside the closed loop dl.
- The total E around a loop is equal to the minus of the changing B through the loop.

**Note:** What happens <u>if you have a constant B? ∂B is 0</u>. So $\partial B/\partial t$ is zero, which makes the integral 0. You can only induce an E field from a **changing** B field.

# Maxwell equations

**Amperes Law**

$$\oint B.dl = \mu_0 I + \mu_0 \varepsilon_0 \int \frac{\partial E}{\partial t}.dA$$



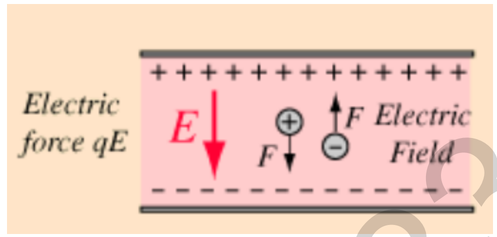

- Integral of B around a closed loop.
- Magnetic field around a loop is equal to the changing E field going through it times by $\mu_0\varepsilon_0$, plus $\mu_0 I$, which is the current going around the loop times by $\mu_0$.

**Note**: $\varepsilon_0$ is a constant called the Permittivity of Free Space
$\mu_0$ is the Permeability of Free Space equal to approximately
$1.257 \times 10^{-6}$ Henry per meter.

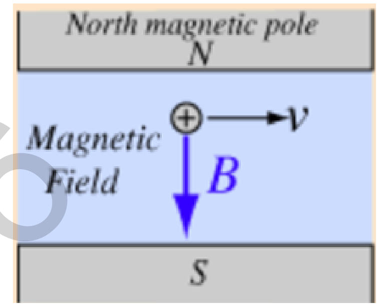
# Maxwell equations

**Lorentz force:** total electromagnetic force on a point charge *q.*

$$\mathbf{F}_{EM} = q\,(\,\mathbf{E} + \mathbf{v} \times \mathbf{B}\,)$$




Electric force




Magnetic force



- **F** is the force on a point charge due to electromagnetic fields.
- If a particle of charge *q* moves with velocity **v** in the presence of an electric field **E** and a magnetic field **B**, then it will experience a force.
    - The force is proportional to *q*, including the sign of *q*.
    - The force is proportional to **B**.
    - The force is proportional to **v**.

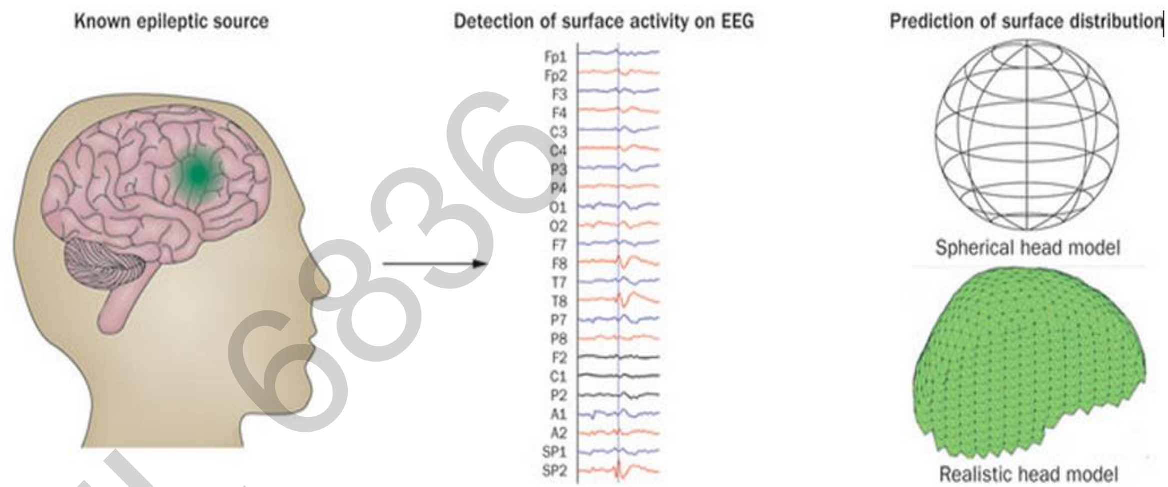
# Source Localization

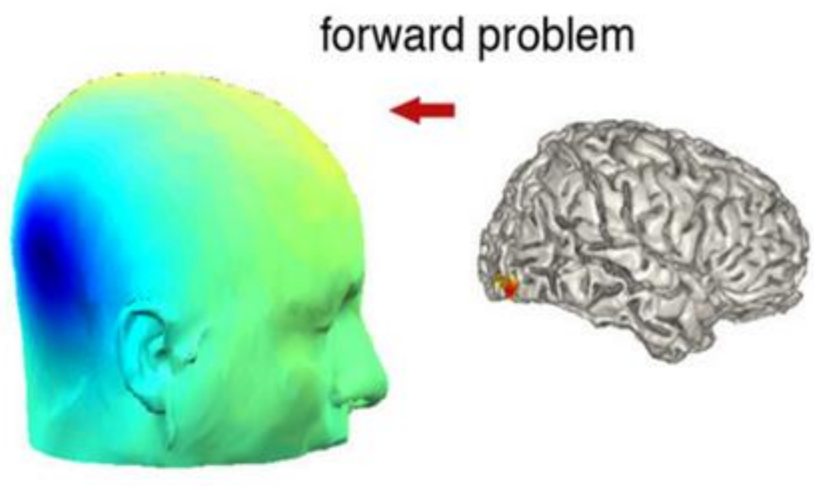
## Forward Problem

- Strength and location of a source inside a head are known. The functional data (EEG) that would be measured on the outside of the head are unknown.

- The problem has a unique solution.

- Computing the solution requires information on sensor locations.



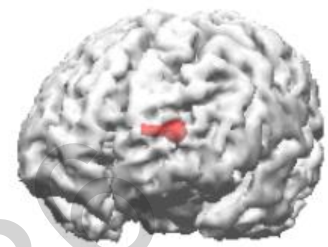



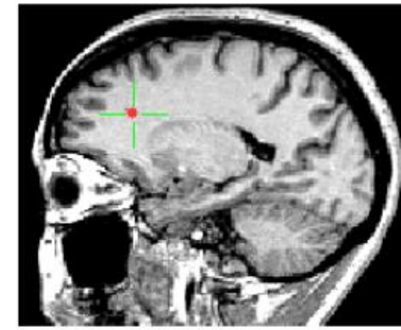
# Source Localization

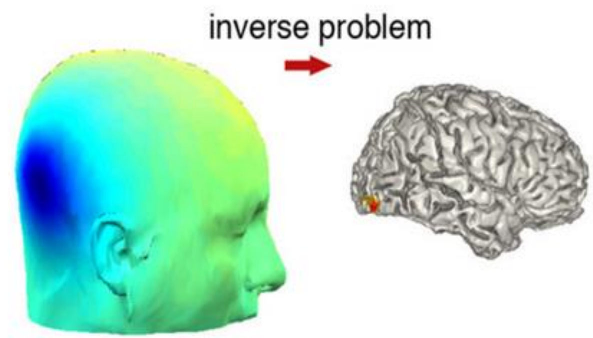
## Inverse problem

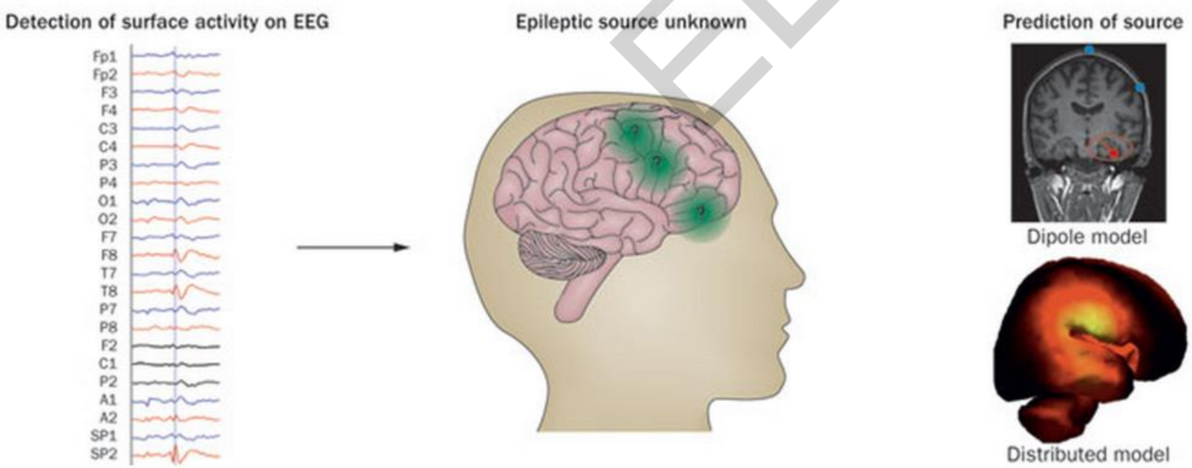
- <u>Signals on the outside of the head are known</u>, while the source or <u>sources in the head are unknown</u>.

- This problem <u>does not have a unique solution.</u> For each set of functional data, an infinite number of sources or combination of sources generating the data can be found.







# Modeling the Head

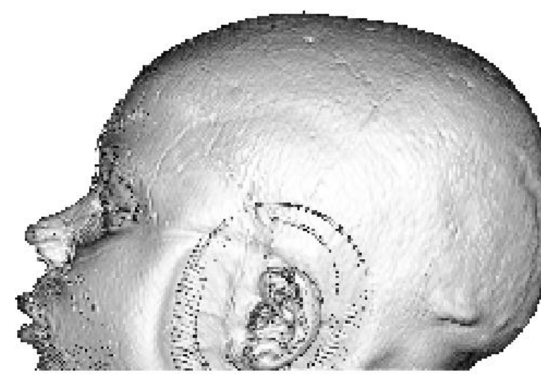
- The very complex shape of a human head with all its anatomical details is represented by a simplified model.

- Its parts such as the brain or the skull are represented by different compartments with each compartment being assigned an electrical conductivity.

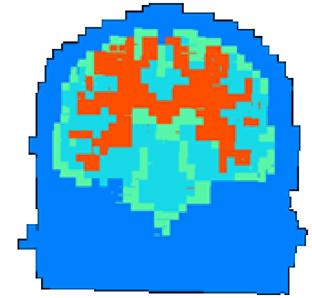
- The shape of these compartments is either spherical, or is derived from the actual shape of the head using anatomical data (Boundary Element Method (BEM) model).

- Skin, skull, and brain tissue assumes homogeneous conductivity:

  0.33 S/m (Siemens per meter)
  0.0042 S/m
  0.33 S/m



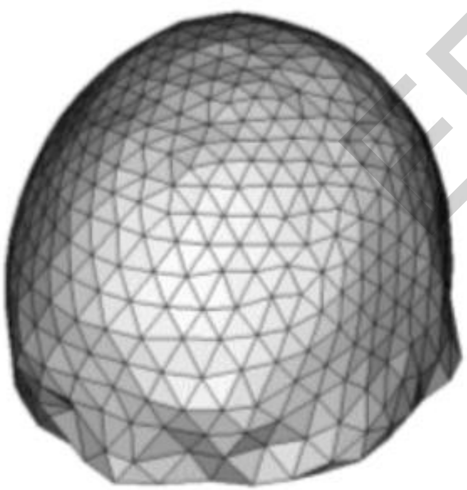
# Modeling the Head



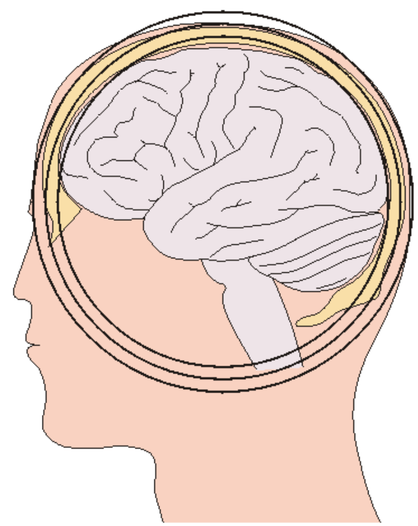
## Head Models

- In order to solve the forward problem we need a model of the head as a **volume conductor**.
- Current clinical practice uses simple multi-shell spherical head models.
- BEM allows realistic modeling of scalp and skull.



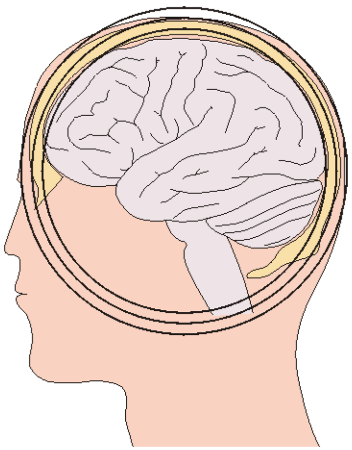


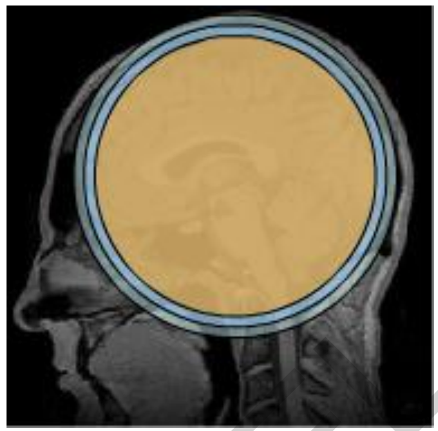
Scalp



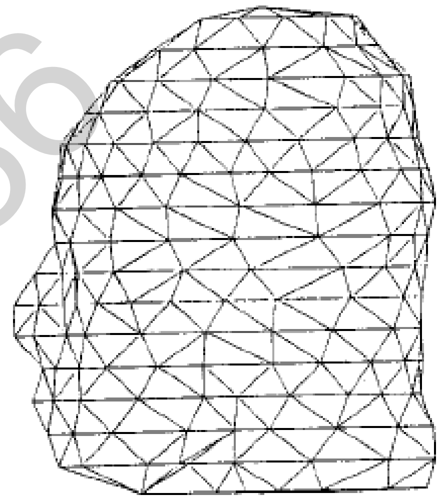
# Modeling the Head

**3-spheres Head Model**





**Realistic Head Model**



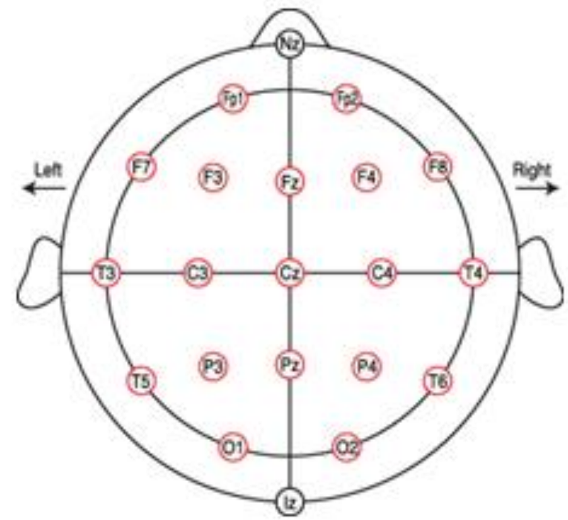


## Creating a Head Model

We define a BEM Realistic Head Model geometry using triangle meshes.

**Boundary Element Method** (**BEM)** models are superior in non-spherical parts of the head like temporal and frontal lobe or basal parts of the head, where spherical models exhibit systematic mislocalizations of up to 30 mm.

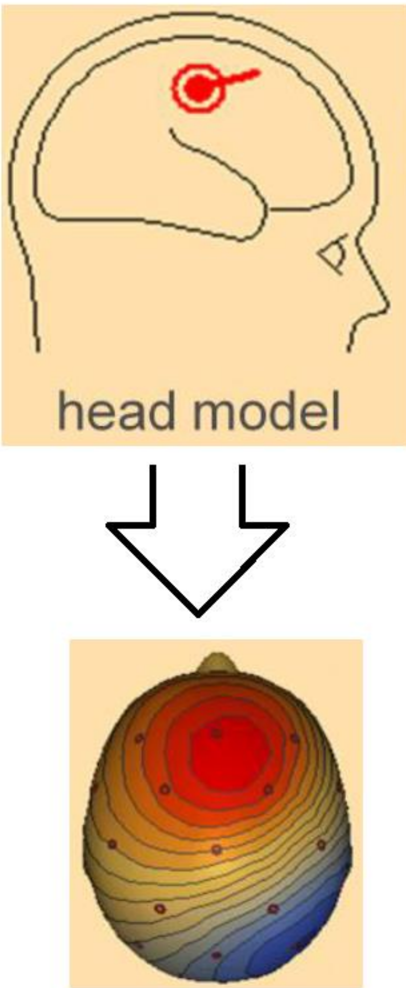
# Modeling the Electrodes




**Clinical Electrode Placement**

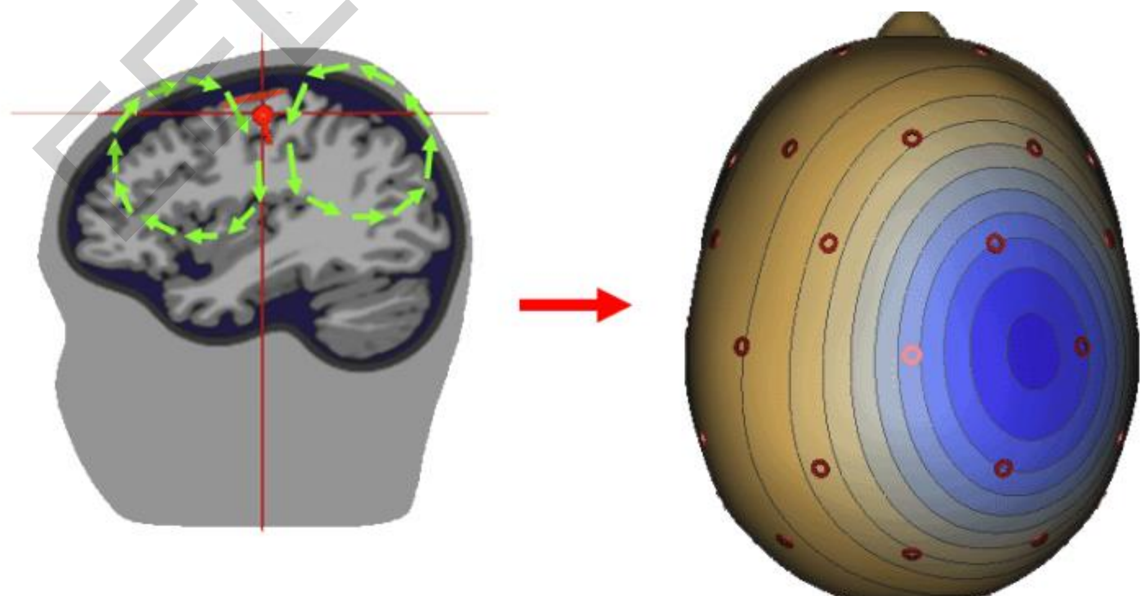
- There are several ways electrodes may be placed in an EEG acquisition.
- The most common method is the 10-20 system, requiring manual placement of 19-32 electrodes based on anatomical landmarks and relative distances.
- Better methods include electrode locations recorded with a 3D tracker.

# Dipolar fields

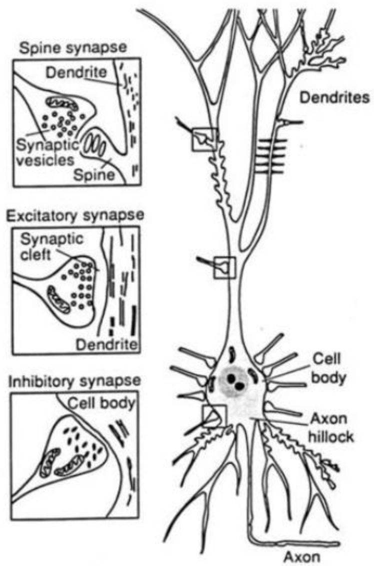


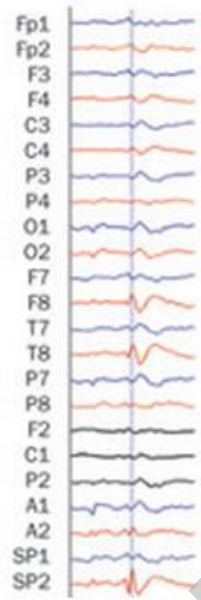

- An ideal patch of superficial cortex creates a net radial current flow that can be very accurately modeled by an equivalent single dipole (ECD) near its center.

- Focal brain activity produces a dipolar voltage topography on the scalp with 2 poles (positive and negative).

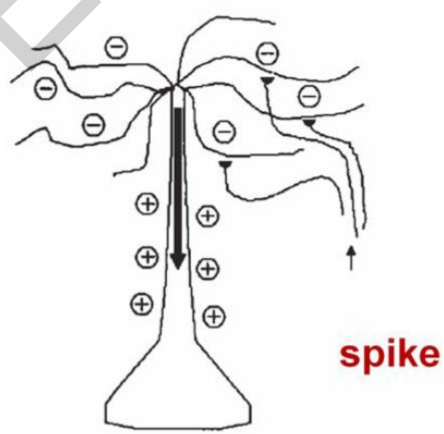


# Neuoronal Currents Create Dipolar Fields




- Epileptic spikes are associated with a depolarization of dendrites of pyramidal cells.
- Current vector perpendicular to cortical surface.
- Spike dipole is surface negative and perpendicular to cortical surface



# PCA decomposition

- PCA generates patterns and loadings that are orthogonal to each other.
- After the first factor is extracted (by fitting a regression line to a scatter plot), the second factor is extracted from the remaining variability, and so on until there is essentially no variance left.
- The resulting components are orthogonal to, or uncorrelated with each other ($1^{st}$ order decorrelation).

# ICA decomposition

- ICA generates patterns and loadings using a stricter criteria for statistical independence (requires that all second order and higher correlations are zero).

- The generality of ICA lies in the simple principle that different physical processes tend to generate statistically independent signals.

- Given that scalp-recorded EEG is the summation of signals from multiple sources, ICA computes individual signals that are statistically independent, and which are therefore likely to have been generated by different physiological processes.

- ICA has been asserted by some to be the preferred method for use with physiological signals.

## PCA and ICA decomposition

- The PCA is also used to estimate the number of mutually independent components to be found in the following ICA iteration. Components with a SNR in excess are appropriate for the ICA.

- The result of noise estimation affects the number of ICA components that are found.

- When you do ICA, a transformation for the subspace of the PCA results is calculated, such that the components are as independent from each other as possible.

# PCA and ICA decomposition

- The number of ICA components to be computed is generally based on the number of valid PCA components.

- Increasing the number of components will ultimately result in invalid ones.

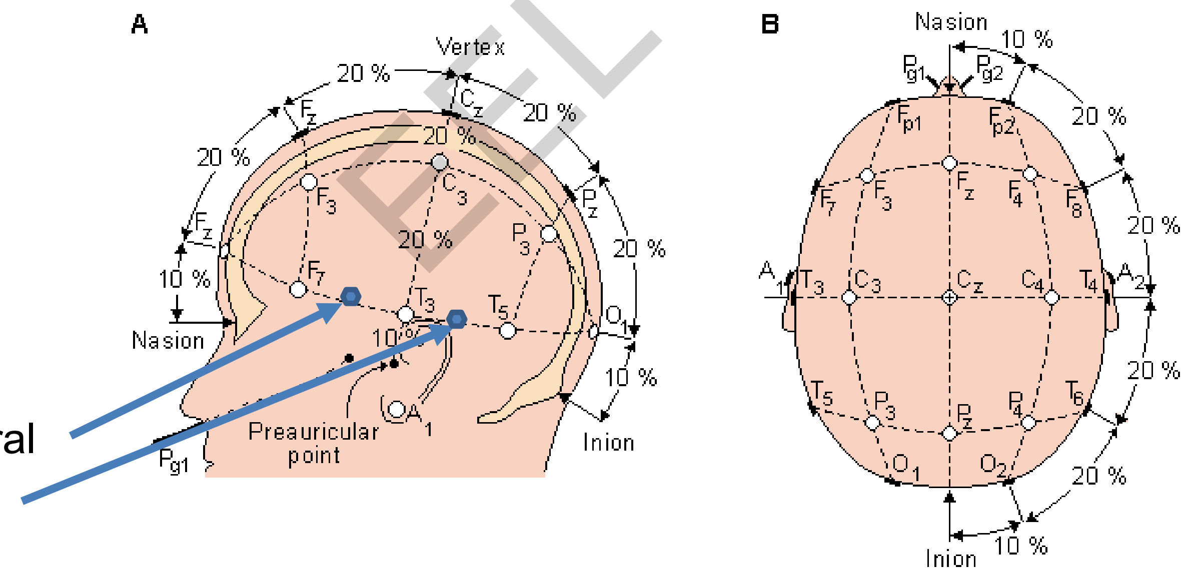
- With ICA, you can independently select components to be filtered.

- With PCA, since the extracted field patterns are orthogonal to each other, it is generally not appropriate to remove the leading or distinct non-noise components because this will have no effect on the trailing components. It is appropriate, however, to remove the trailing noise components.

# Recording Apparatus

EEG

- Standard 10-20 Montage with 4 extra temporal electrodes.
- Sampling frequency: 200Hz, 500Hz, 512hz, 1000Hz, 2000Hz



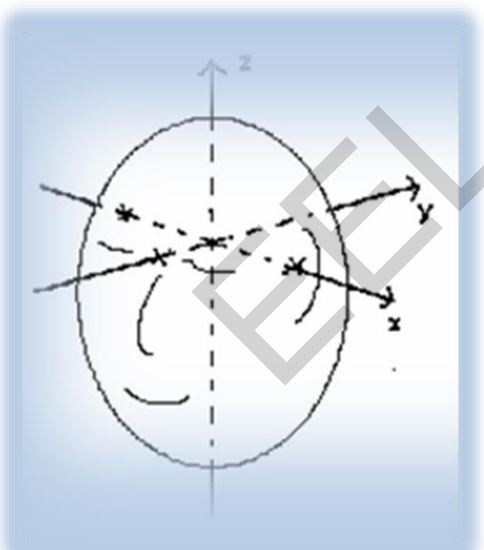

Extra temporal Electrodes

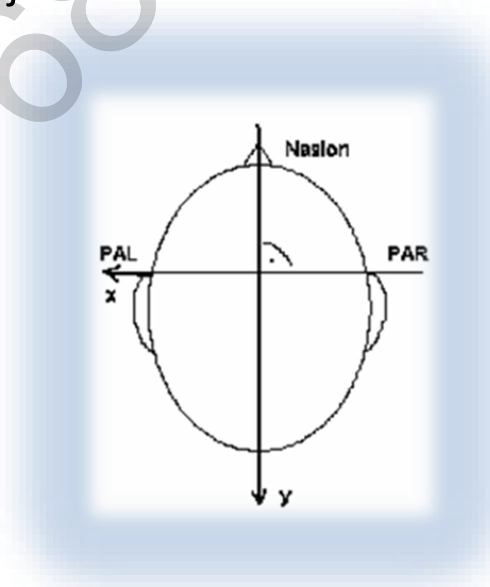
# Coordinate System

- Internal coordinate system to represent the location and orientation in the anatomical image used.

- The internal coordinate system could be based on: the PAN (pre-auricular and nasion) system, which uses the PAL (pre-auricular left point), PAR (pre- auricular right point) and the nasion of the subject obtained from the anatomical image data.

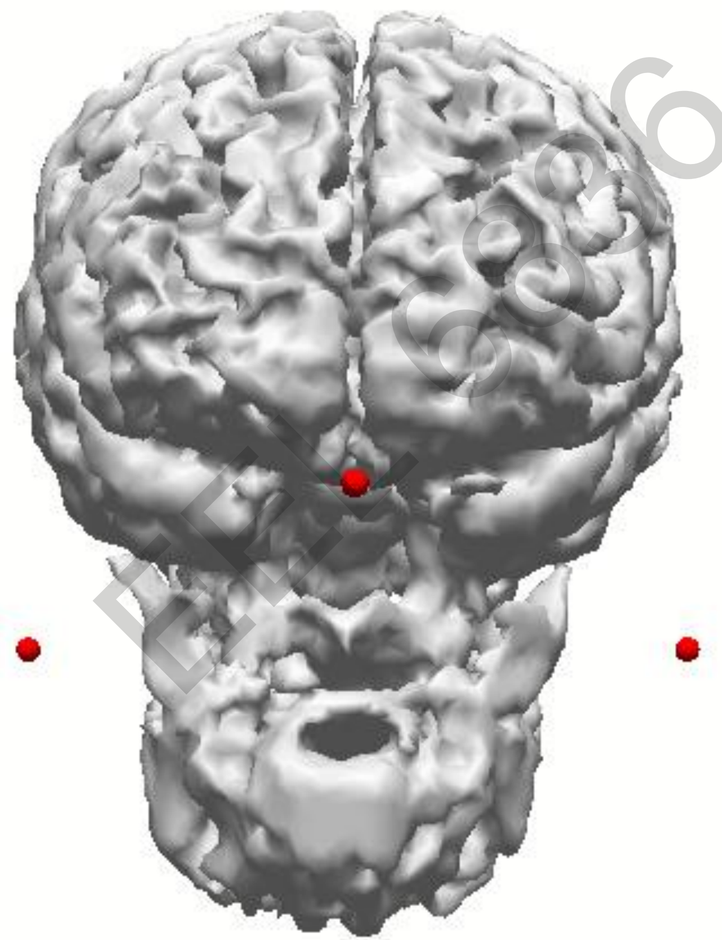


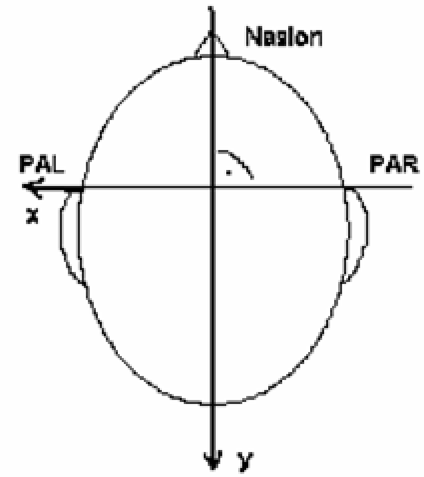


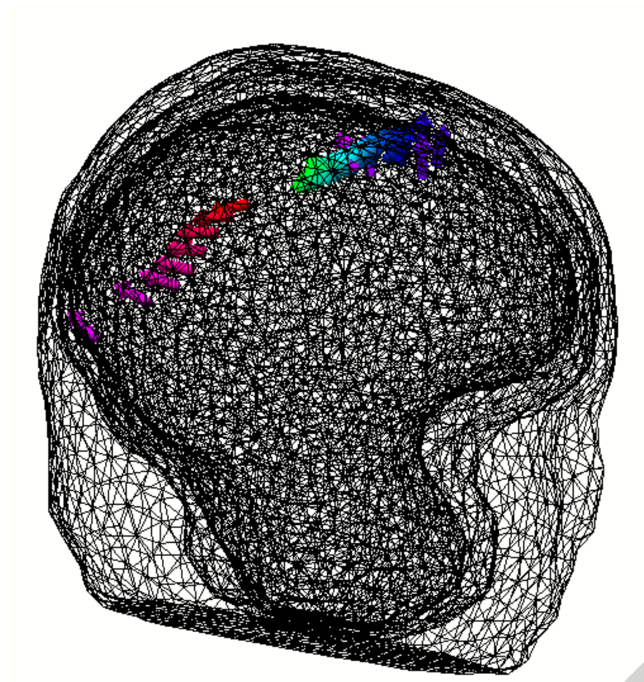

PAN(L,P,S): x axis going through PAL and PAR pointing left; y axis trough the back of head using the nasion and Z pointing upward.
Others: PAN(R,P,S); MINI/SPM99; etc.

## Coordinate System Landmarks



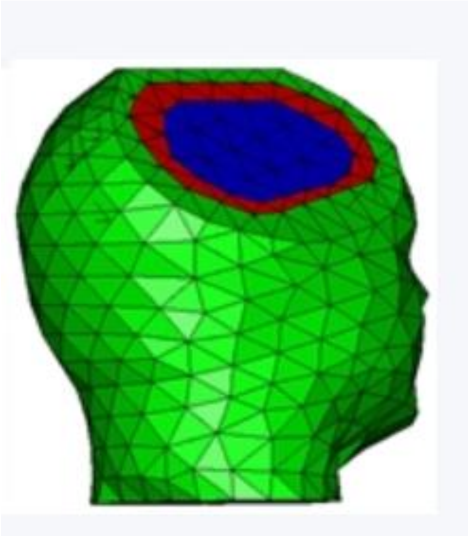


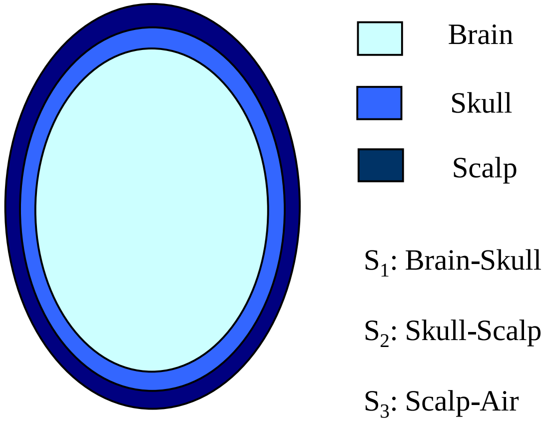
# BEM Model



Boundary Element Model –BEM head

- Based on 2D triangulation of surfaces.
- Constructed by segmentation and mesh generation of an individual subject 3D Brain MRI image.



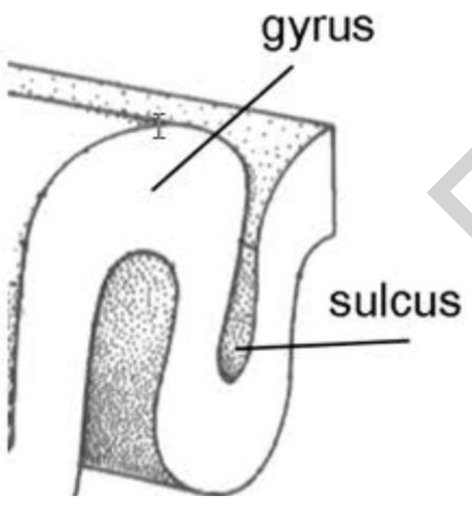


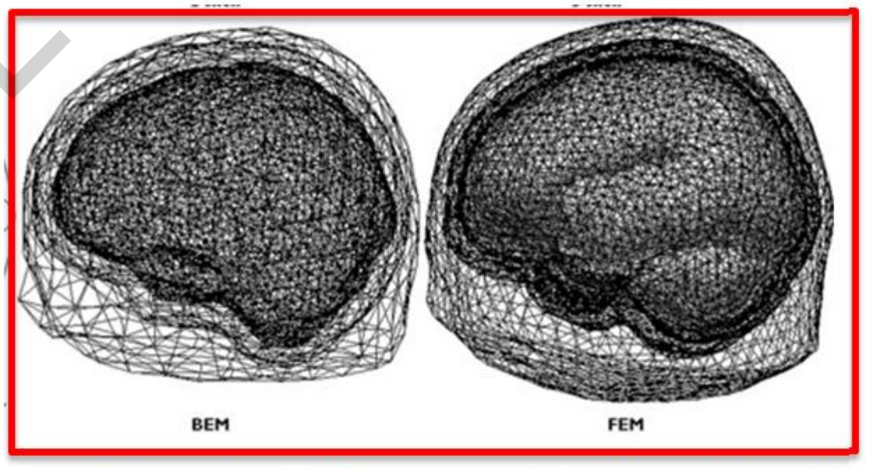

BEM gives a more realistic shape of brain compartments by using closed triangle meshes.

# BEM model

- **BEM** approach is able to improve the source reconstruction in comparison with spherical models, particularly in basal brain areas, including the temporal lobe, because it gathers a more realistic shape of brain compartments. It takes less time than FEM model.

- The **FEM** model allows better accuracy than the BEM because it allows a better representation of the cortical structures, such as sulci and gyri in the brain, in a three-dimensional head model.




Realistic shape – (BEM isotropic, FEM anisotropic)

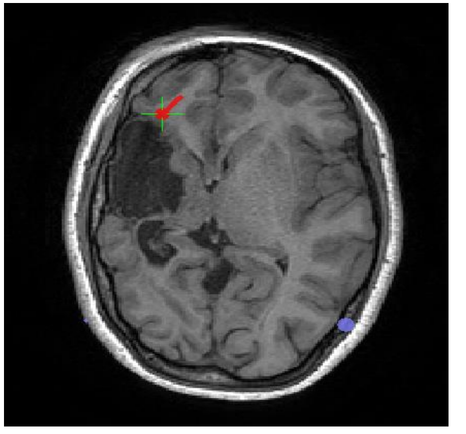
FEM (Finite Element Method) and BEM (Boundary Element Method)

# Source Localization Goal

1) To help <u>localize the cortical area generating the earliest part of the epileptiform discharge</u>.

2) To study the <u>propagation</u>.

3) To assess the <u>extension</u> of the irritative zone.

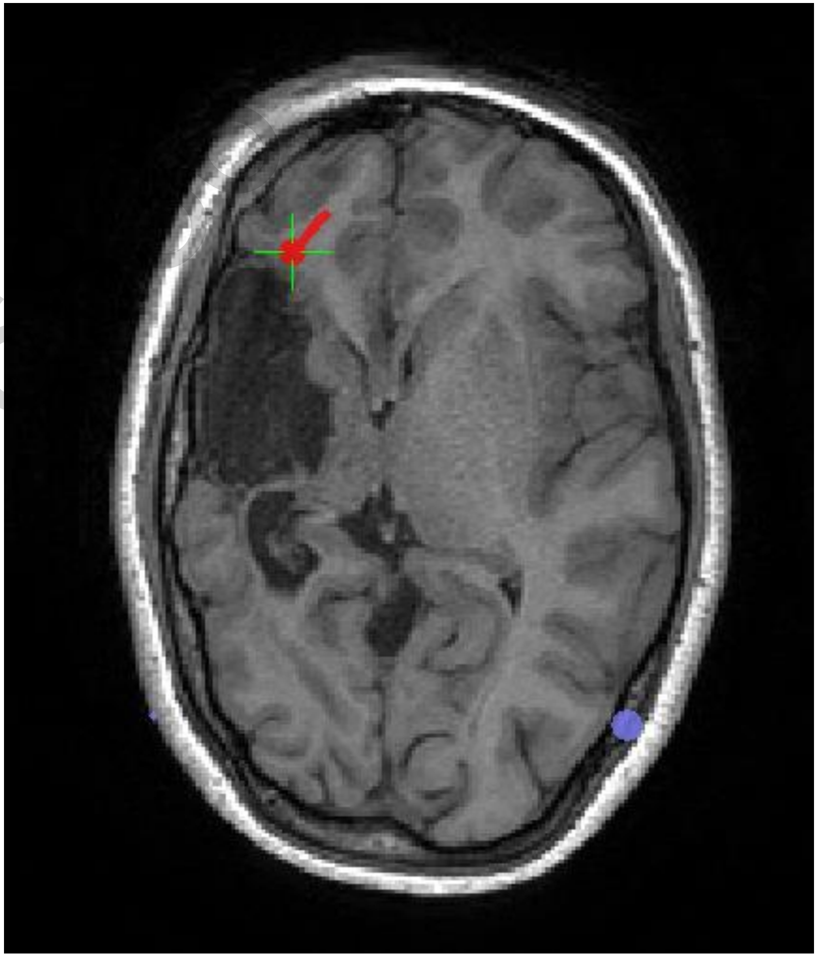


# Source Reconstruction

- The purpose of the source reconstruction is <u>to determine the anatomical location as well as the nature of the electrical sources that explains the EEG data.</u>

- <u>Source reconstruction requires the solution for an inverse problem</u>, where the EEG data outside the head is given while the <u>source or sources in the head are to be determined</u>.

- The <u>simplest solution is the **dipole**</u>.



# The Forward/Inverse Problems

- **Forward problem:** Find **K** that translates dipoles **J** to Scalp potentials **Φ.**
- **Inverse problem:** Find function ***F*** that transforms Scalp potentials **Φ** to dipoles **J**.

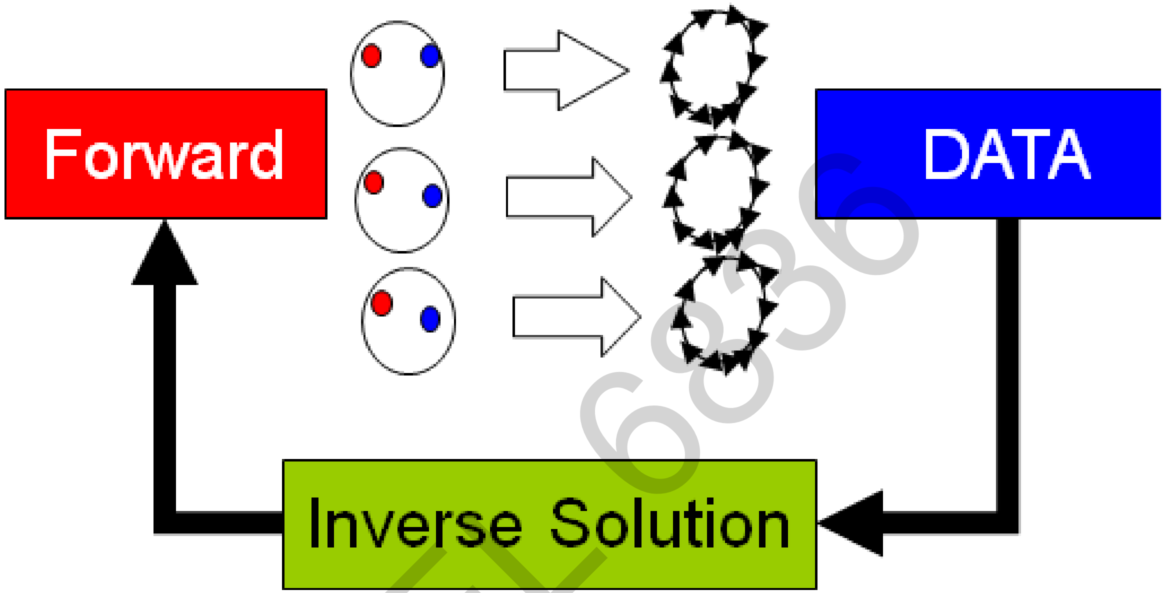
$$\vec{\Phi}(t) = K \cdot \vec{J}(t)$$

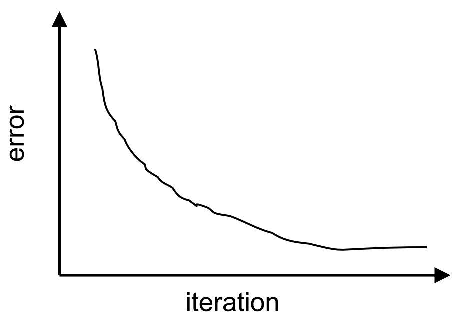
$$\hat{\vec{J}}(t) = F\left(\vec{\Phi}(t)\right)$$

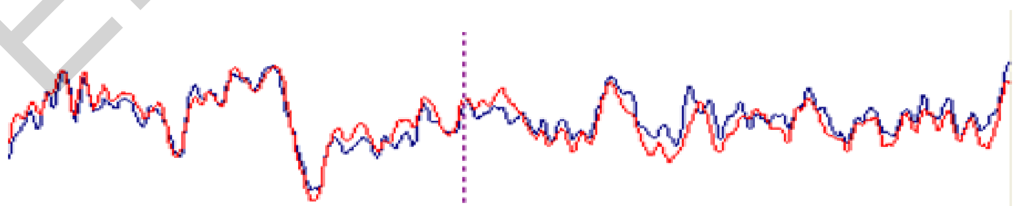


$$\begin{bmatrix} \vec{\Phi} \end{bmatrix} = \begin{bmatrix} \quad & K & \quad \end{bmatrix} \begin{bmatrix} \vec{J} \end{bmatrix}$$

# Inverse Problem



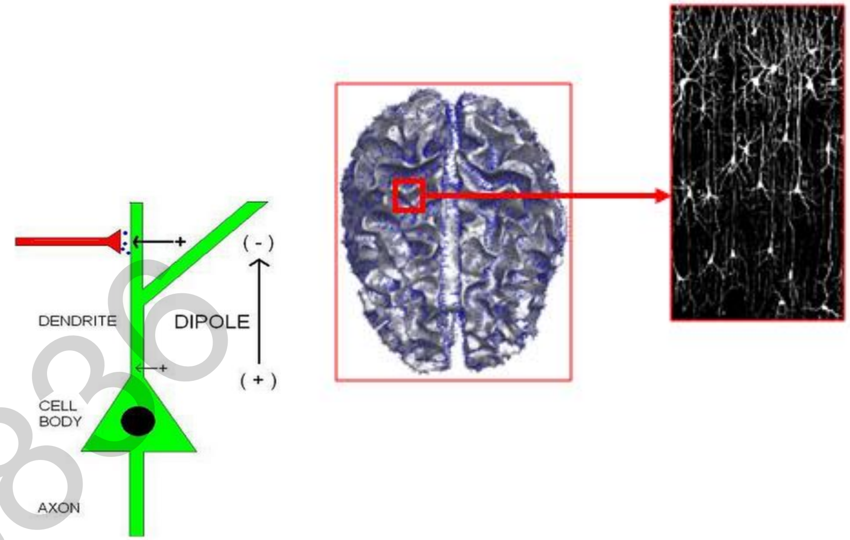



Iterative process until solution stops getting better (error stabilises)

# Dipole Solution

**Electric Dipole:**

A system of two equal and opposite charges separated by a certain distance

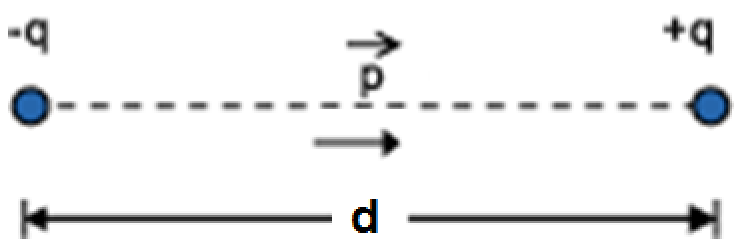



**Dipole moment** - a measure of the strength of electric dipole.

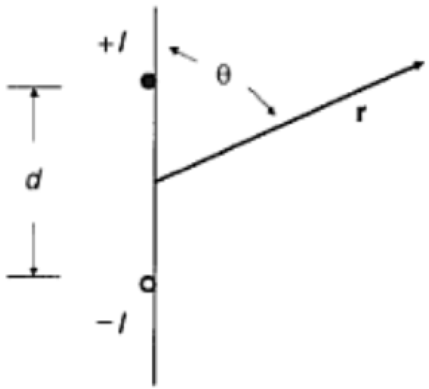
**Magnitude of dipole moment** - product of the magnitude of either charge and the separation between them.

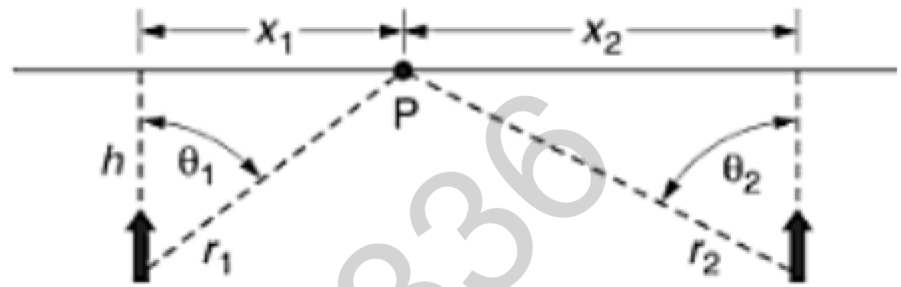
Direction of dipole moment – it points from negative towards positive charge

P = q (d) SI unit C m



# Dipole Current Source





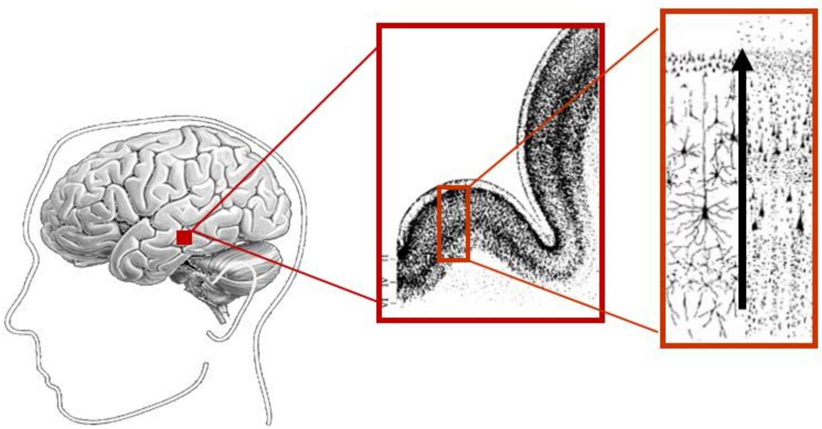

A current dipole has a current source +I and current sink –I separated by a distance d.

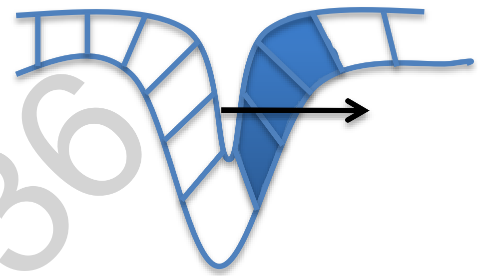
The collection of sources and sinks produces a dipolar potential at distances r, large compared to d.

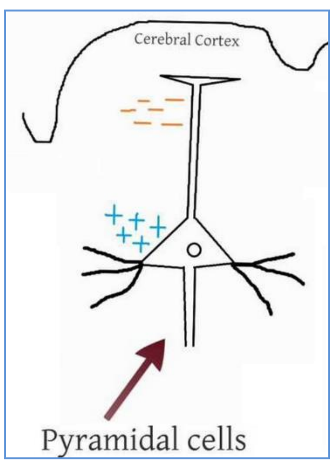
Current spreads throughout the two poles of the dipole.

Volume conduction: the transmission of electrical current from its source through the conductors (brain tissue) towards measurements (EEG scalp electrodes).

# Dipole



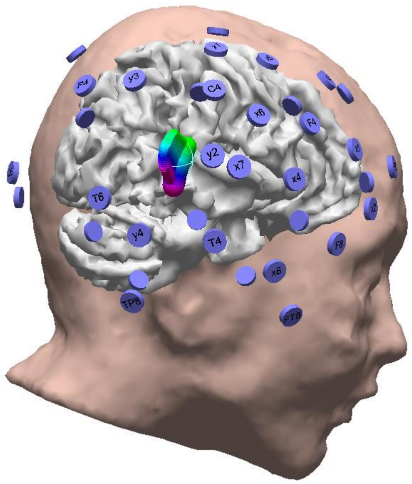





- ✓ EEG generators are electrical dipoles.
- ✓ A current dipole represents an extended brain area.
- ✓ Many tiny dipoles result in an equivalent current dipole.
- ✓ The dipole results in a topography at the scalp.
- ✓ Characterized by P<u>osition, Direction, and Strength</u>.

# Dipole Solution

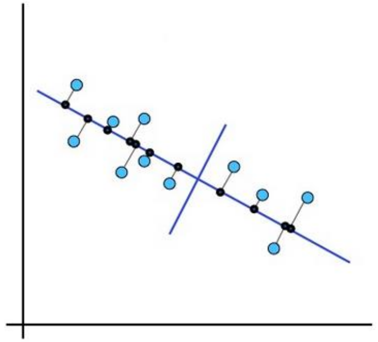
The simplest dipole model is the **single equivalent current dipole (ECD)**. Its components are determined for a given time point so as to minimize the deviation between measured (input EEG) and forward calculated (estimated EEG) data.

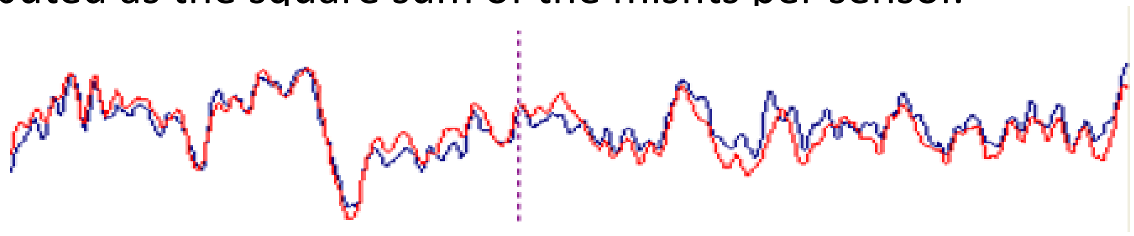


For a valid dipole, you would expect to see, during the approximate same time course, a strong dipole, low residual or unexplained standard deviation and a good signal to noise ratio (SNR).



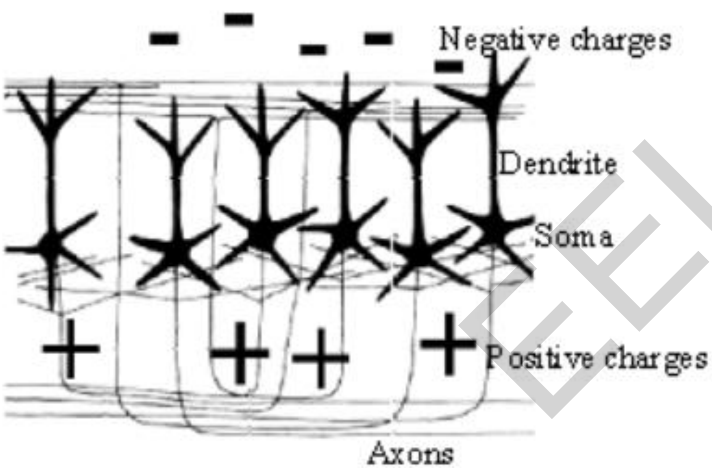
To find the optimal source model parameters, the variance (the squared deviation between measured data and forward calculated data is taken into account (and normally minimized). It is computed as the square sum of the misfits per sensor.

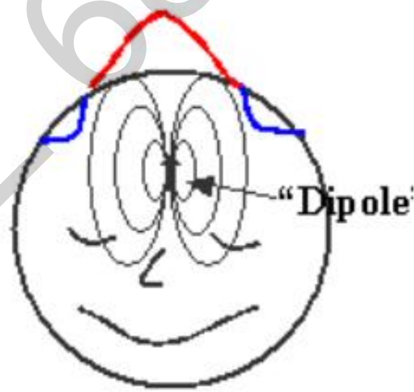


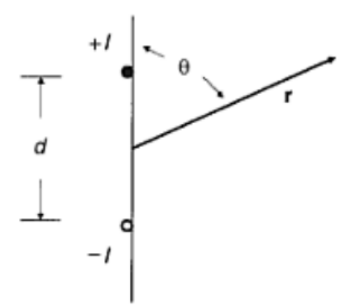


# ERPs: Spikes

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).



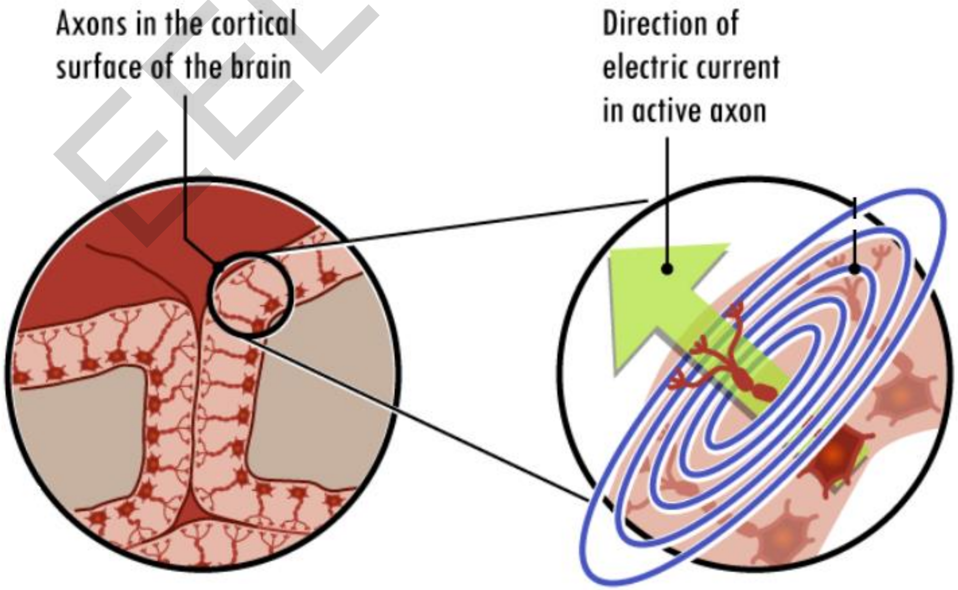



**Note:** source +I and current sink –I

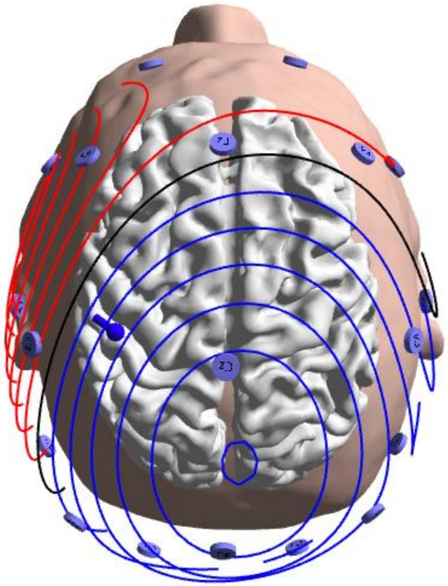
# ECD

Equivalent current dipole (ECD) is specified by:

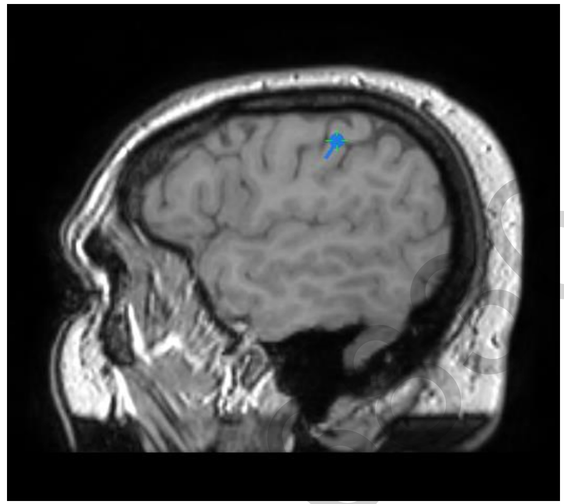
- **Location** (the equivalent center of the modeled gray matter patch).
- **Orientation** (the net direction of the modeled postsynaptic neuronal current, perpendicular to the surface of the modeled gray matter patch).
- **Strength or Amplitude**, reflecting the modeled net postsynaptic current flow. It can be thought of as the product of the total postsynaptic current flow (in nA) and the length (meter) over which this current is flowing.

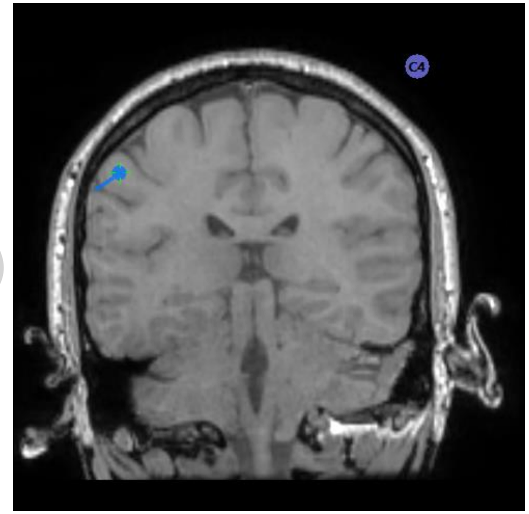


# Dipole Solution

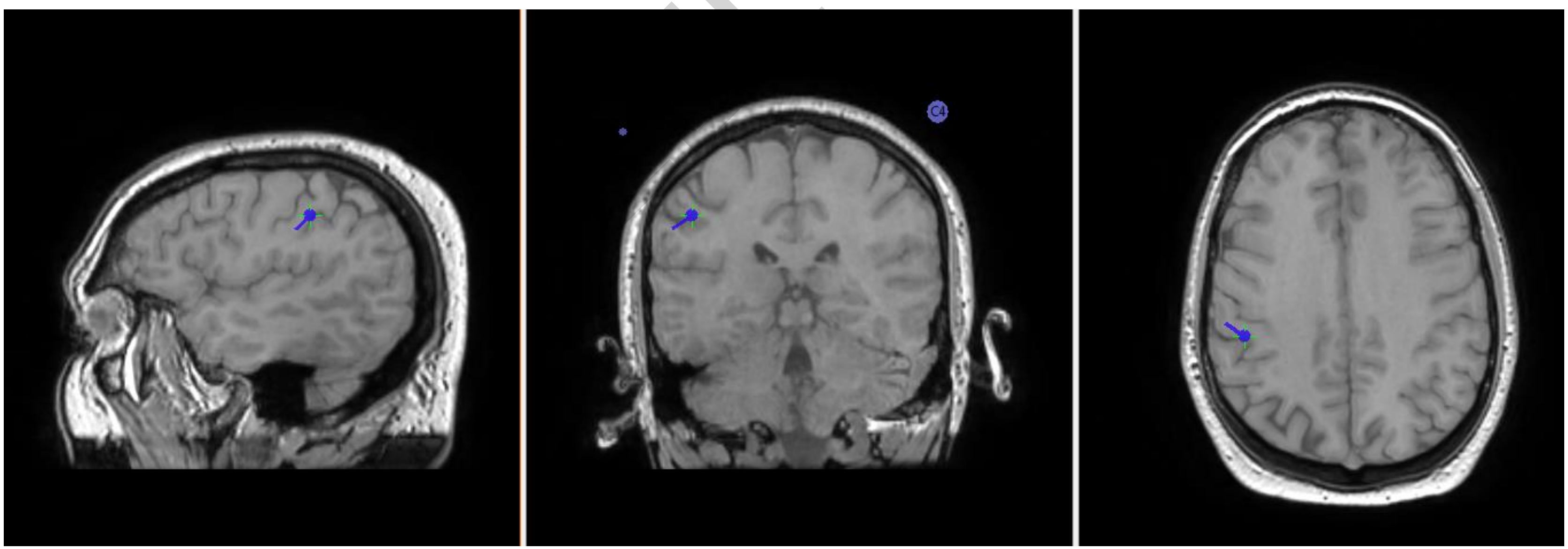


EEG time: 8015.6 ms (-52.1, 12.7, 85.2) mm

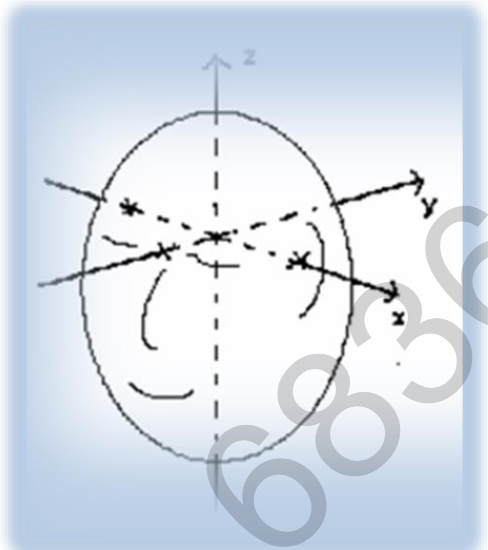





EEG time: 8011.7 ms (-46.1, 11.1, 80.1) mm,

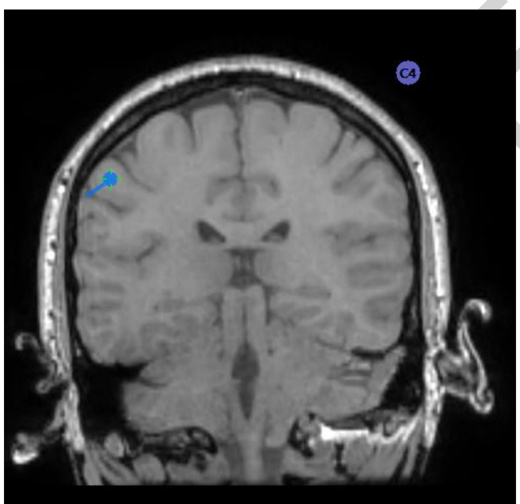


# Dipole Solution



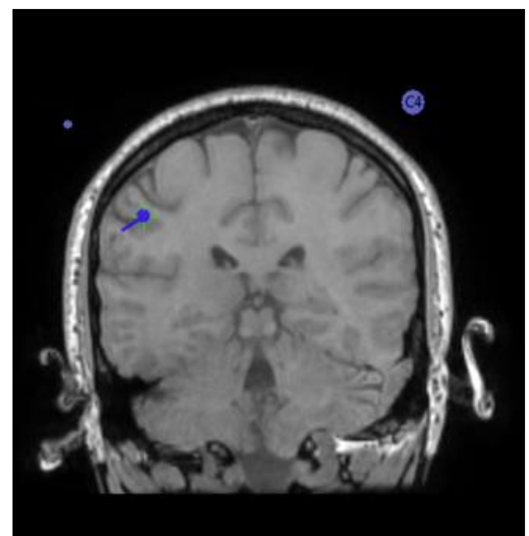

SNR: 6758.7,
explained signal: 78.6%

8015.6 ms
X,Y,Z: (-52.1, 12.7, 85.2) mm




SNR: 6992.4,
explained signal: 77.8%

8011.7 ms
X,Y,Z:(-46.1, 11.1, 80.1) mm,

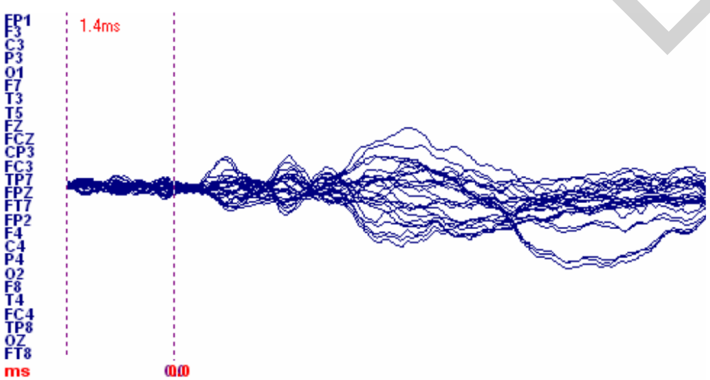


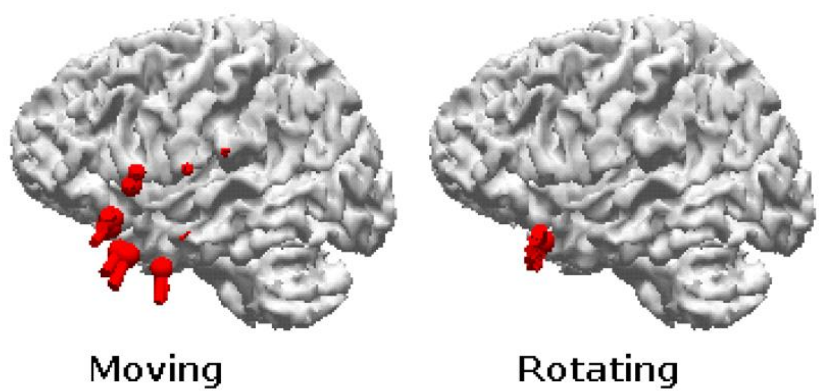
# Dipole Solution

- The **<u>Dipole Strength</u>**, **<u>Residual Deviation</u>**, and **MGFP** <u>functions are useful in helping you determine if the dipole solution is a valid one.</u>
- <u>Dipole Strength shows the strength</u> and time range of the dipole(s).
- The <u>Residual Deviation</u> function displays the <u>residual standard deviation</u> through the time range.

**Note:** Mean global field power

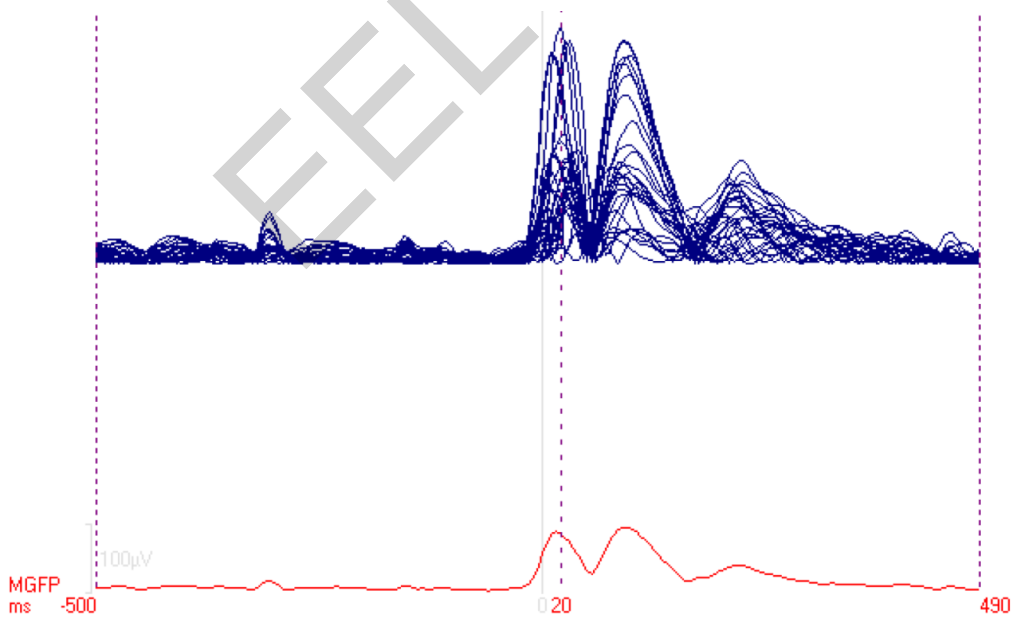




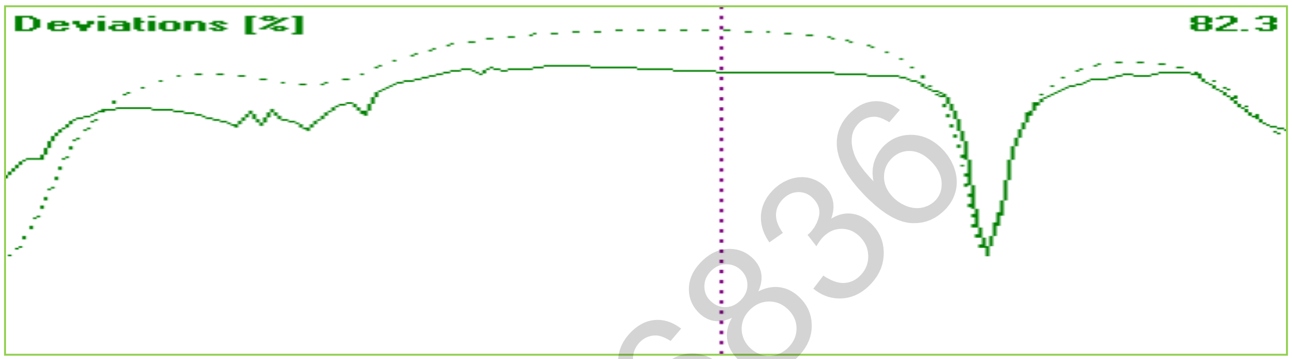



# Dipole Solution

- MGFP is a composite measure that indicates the strength of the signal against the noise background.
- For a valid dipole, you would expect to see, during the approximate same time course, a strong dipole, low residual or unexplained standard deviation, and a good signal to noise ratio



# Source location






The Residual Deviation (D) is a measure for the fit quality (how well the source model explains the measured data). D is the root mean square of the difference between measured EEG (Ri) and calculated EEG signals (Fi):

D = Sqrt [ 1 / n * Sum ((Ri - Fi) * (Ri - Fi))] / MGFP
= Sqrt [Sum ((Ri - Fi) * (Ri - Fi)) / Sum (Ri * Ri)]

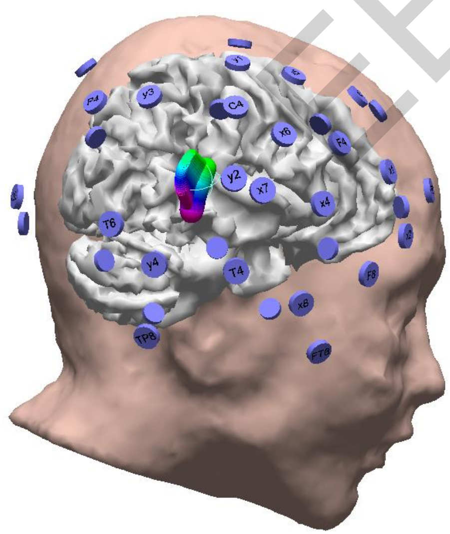
,which is normalized for the measured field (MGFP).

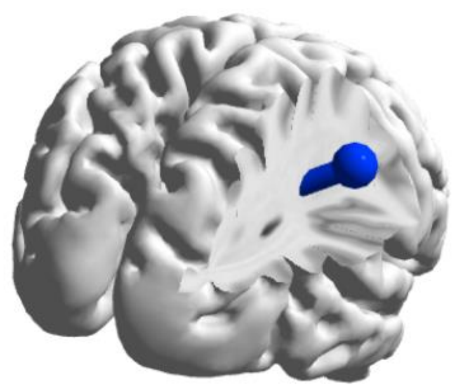
# Dipole source

- In source analysis, each active brain region is modeled by one **equivalent dipole source**. Each source is fixed to the cortical patch or region it represents, and changes its total current strength over time according to the local physiology.

- If we have a volume conductor model, for example a spherical head model, a boundary element model (BEM), we can now predict the lead fields, i.e. the magnitude of the signal each source will contribute to each sensor.

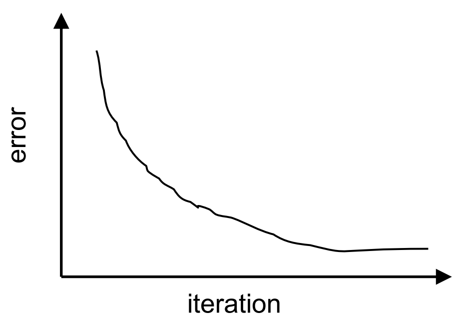
- Because the model is an approximation, both in terms of the volume conductor and the simplification of using equivalent dipoles at the centers of activity, there is a residual. Ideally, if we have a good model, this residue should be small and consist only of sensor noise and brain background activity not related to the stimulus.

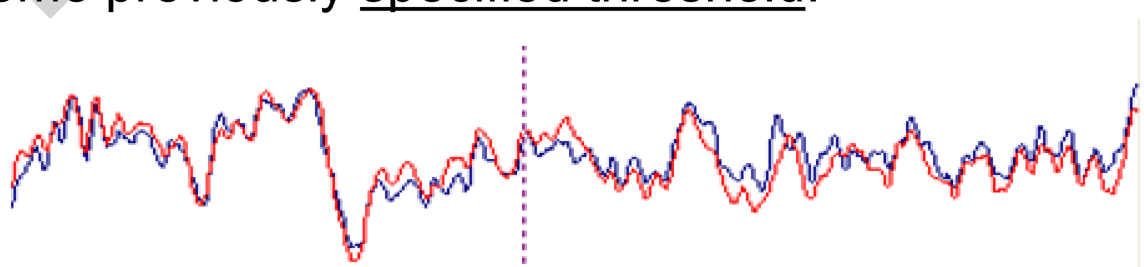




# Source location

- EEG source localization is a problem which does not have a **unique inverse solution.**
- The **Least-Squares solution** (LS) introduces additional constraints so that a single solution may be determined. It is an iterative optimization procedure that minimizes the squared difference between the measured potentials, $\mathbf{M}_{\mathbf{meas}}$ and potentials generated by the estimated dipole, $\mathbf{M}_{\mathbf{calculated}}$
- The squared difference between the calculated and measured data is calculated and the new dipole location is updated in such a way that it minimizes the previously calculated error.
- These steps are repeated until dipole location is determined for which the error is less than some previously specified threshold.

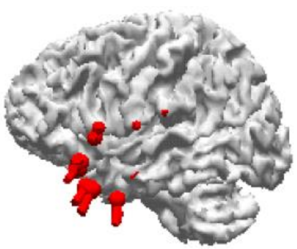


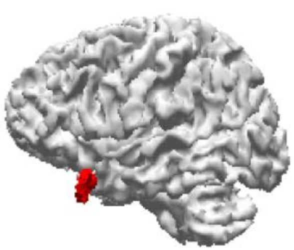
# Source solutions

**Source solutions:**

1) Rotating dipole solution.
2) Moving dipole solution.
3) CDR (Current Density Reconstruction)


Moving

**Moving Dipole:** For each instance in the selected EEG time range, an independent fit of the dipole will be performed. Every dipole will have a variable location and magnitude during source localization period. Moving dipoles help us in getting a first overview of the activity to be reconstructed.


Rotating

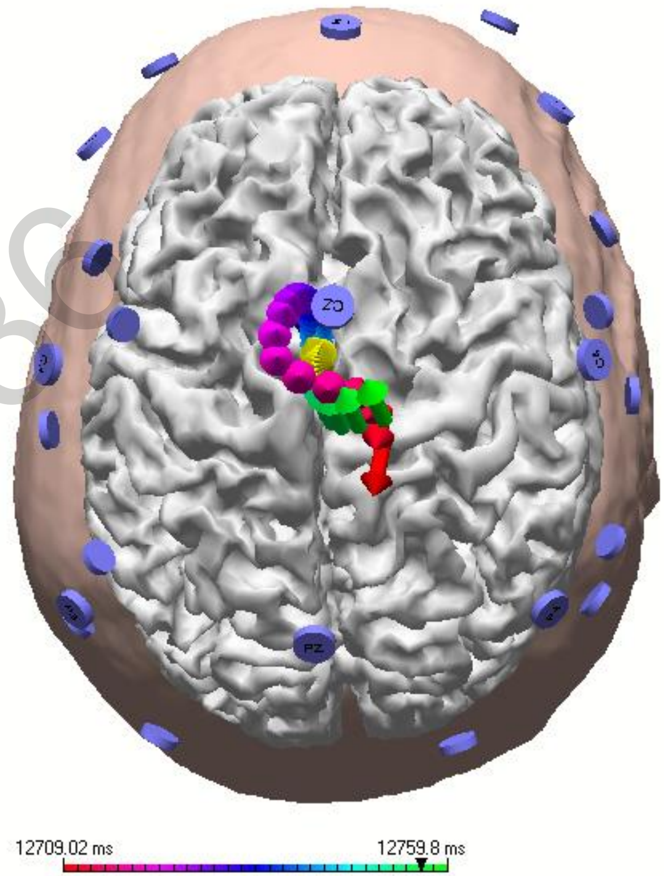
**Rotating Dipole:** At each latency in the selected EEG time range, independent dipole components will be determined. This results in fixed dipole positions, but free dipole orientations.

# Moving dipole

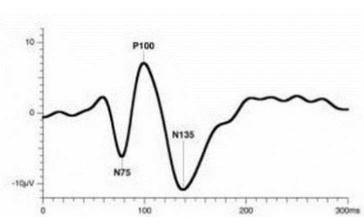
- The single dipole location is performed over a time period that is for the number of consecutive EEG time samples (if 256Hz- every 4 ms).

- A dipole location is obtained for each of these samples. If this result is sequentially presented, the actual propagation of the source can be obtained.

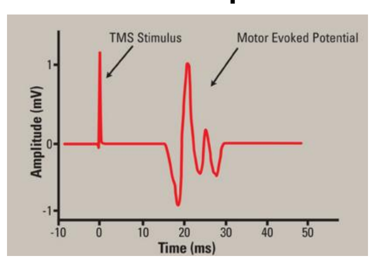
- This type of solution represents the moving dipole solution.



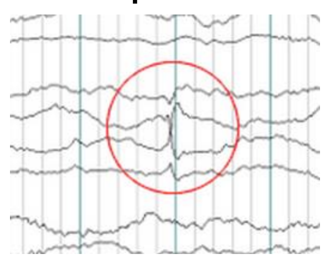

ERP



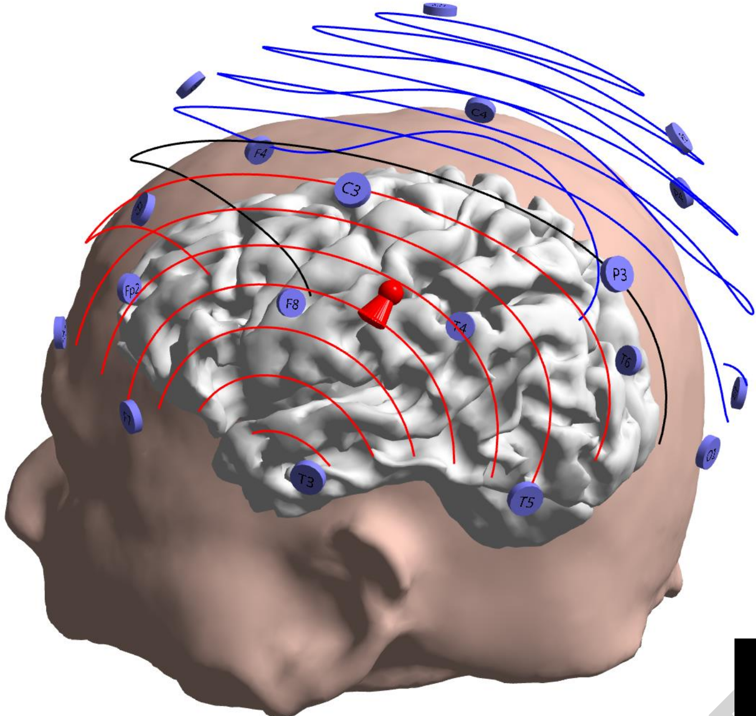

TMS evoked potential

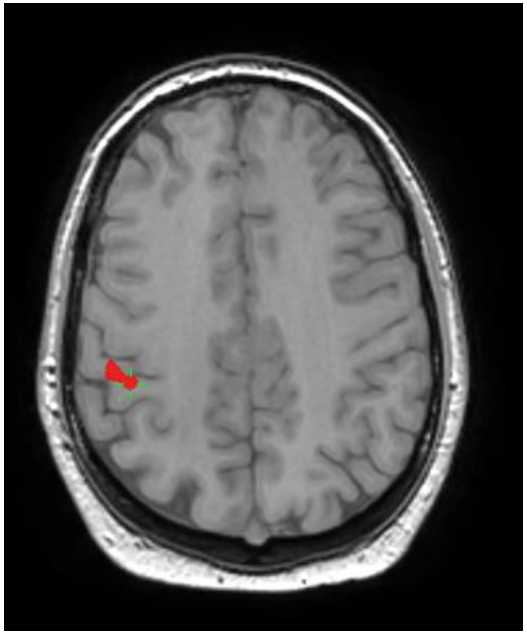


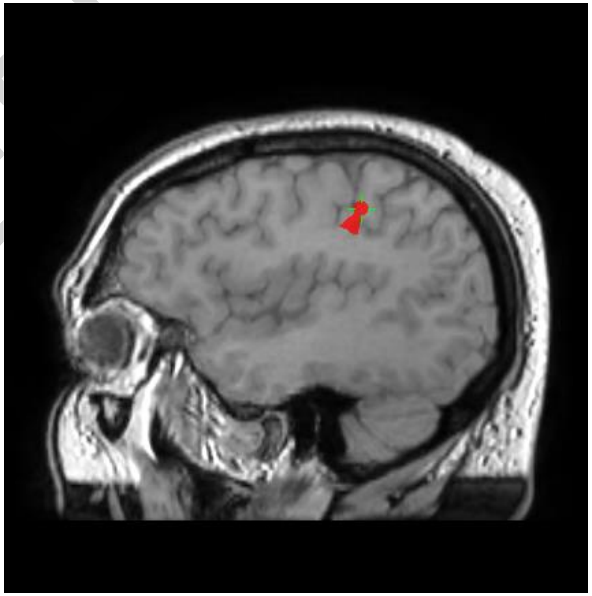

Spike



# Rotating Dipole





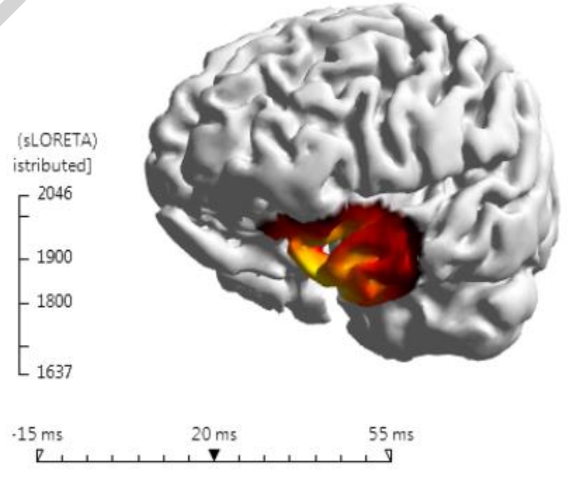
A dipole orientation is obtained for each of the EEG samples. If this result is accurate, <u>the actual location of the source can be estimated.</u>

# Source solutions

**Current Density:** It is defined as dipole moment per volume. Each dipole represents the current density in a given volume. This solution may help to assess the extension of the epileptogenic lesion. It assumes simultaneous activity at a large number of possible source locations.

Low-resolution electromagnetic tomography (**LORETA**) is an inverse solution technique that estimates the distribution of electrical neuronal activity in 3-dimensional space. This model makes assumptions about the nature of the sources, typically sources are assumed to be of similar strength as their neighbors.



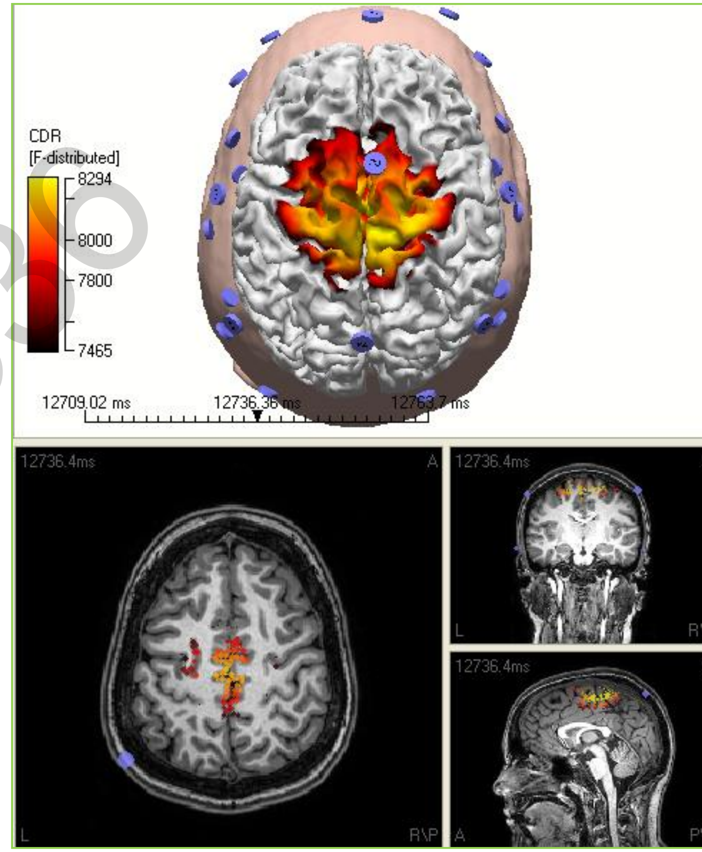


# CDR

- CDR is just a representation of all dipoles in the entire cortex.

- It is going to calculate a dipole moment per voxel (volume) like a picture, so instead of having a single dipole solution (like the dipole), a lot of dipoles are calculated per volume representing the whole image with dipoles assuming that there is no a single focus like the single dipole moment assumes.

- The strength of the dipole is going to be calculated for each voxel (volume) and the orientation is going to be assumed perpendicular to the surface of the cortex.



# Quality of Single Dipole Solutions

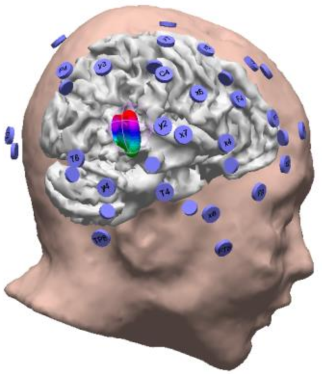
- In the case of single dipole solutions, only dipole components that reproduce a significant EEG data are reconstructed and also sometimes since this is an inverse problem solution, trying to identify dipole parameters that best explain the scalp potentials, it can get trapped in a local minima and stop the iteration process.

- Also depending on the location of the source, the single dipole model could be misleading.

- Equivalent current dipole algorithms are a simplification since they rely on the assumption that synchronously activated cortical areas are well represented by their centers of mass.

- They require a priori knowledge of the number of active sources.



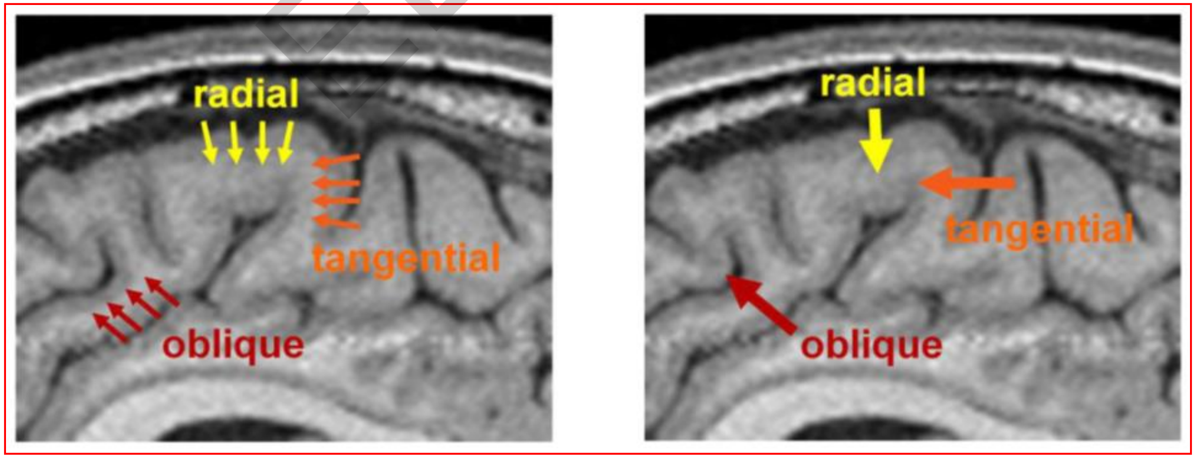


# Dipole orientation

- 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.

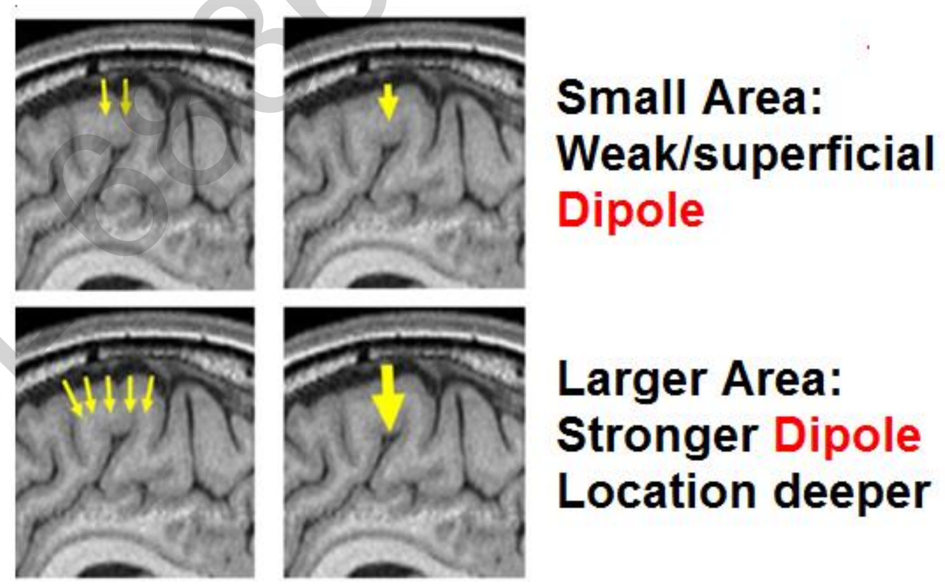
- Currents at the cortical convexity have a predominantly radial orientation, currents in cortical fissures have a predominantly tangential orientation. Generally, a patch of activated cortex in a sensory, motor or spiking area will have an oblique orientation depending on the net orientation of the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





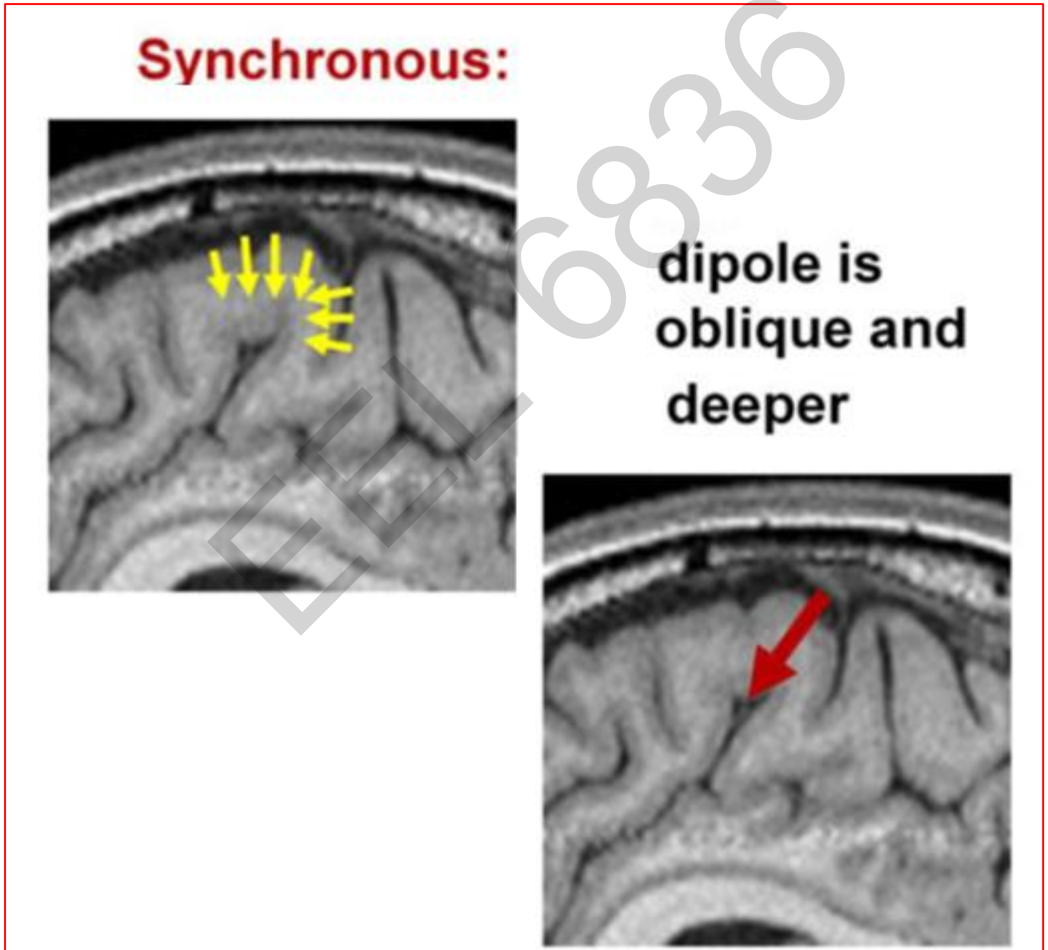
# Dipole Orientation

- 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 (2-6 $cm^2$), the dipole moment is small and a spike from superficial cortex may just be visible (~30-60 µV) in an EEG of low amplitude.
- If the area is larger (9-12 $cm^2$), the spike will be more conspicuous (~100-200 µV).



# Dipole Orientation

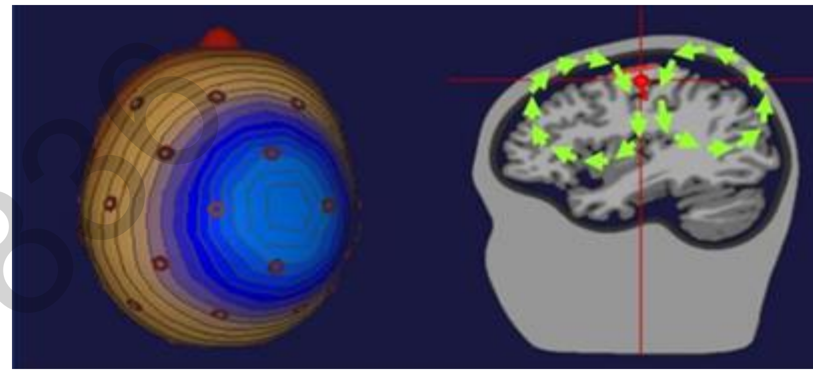
If the whole region spikes synchronously, one equivalent dipole with <u>oblique orientation can still approximate the spike activity very well</u>.



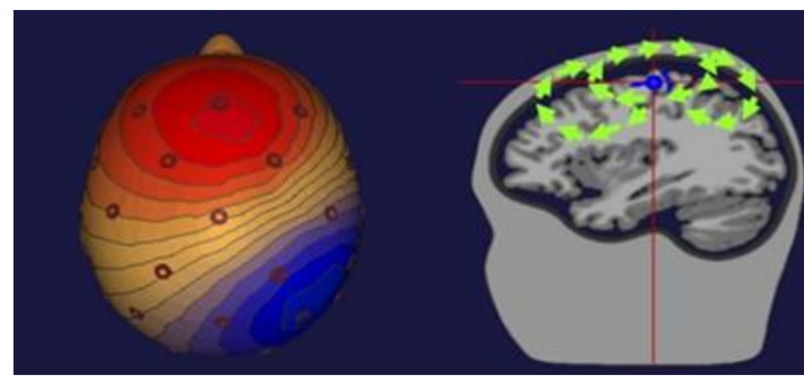
# Brain Activity

- The 3D maps allow for an approximate visual localization of focal brain activity if the EEG activity originates only in one circumscribed brain region.
- Focal brain activity produces 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.
- First, you need to check if the voltage map is dipolar. There are 2 opposite poles.
- Spikes dipoles are negative and surface perpendicular.

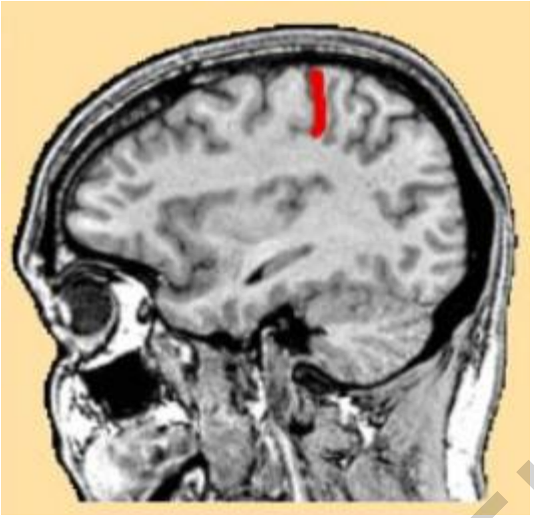
Radial orientation (cortical surface)



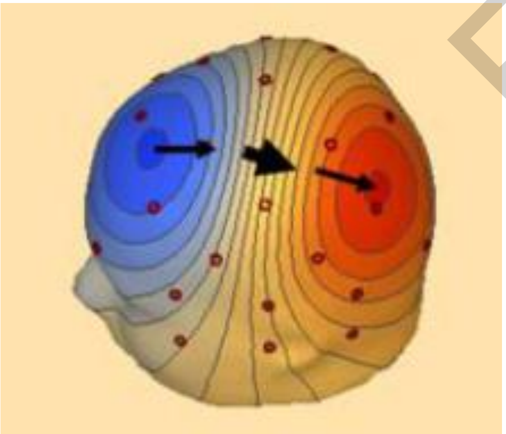
Tangential orientation (sulcal surface)



# Focal activity



Both poles of the dipolar map need to be considered to asses location and orientation.



- This is a tangential case where the 2 poles are of equal strength and symmetric.

- <u>Focal source lies below the midpoint between both poles</u>

# Advantages of 3D Source

- When there is not an obvious structural lesion, localization by EEG is really critical.

- Source analysis of the spikes provides more localization information than traditional visual inspection of EEG traces.

- The accuracy of localization is increased, which is very critical for planning surgery or intracanial electrode implantation.