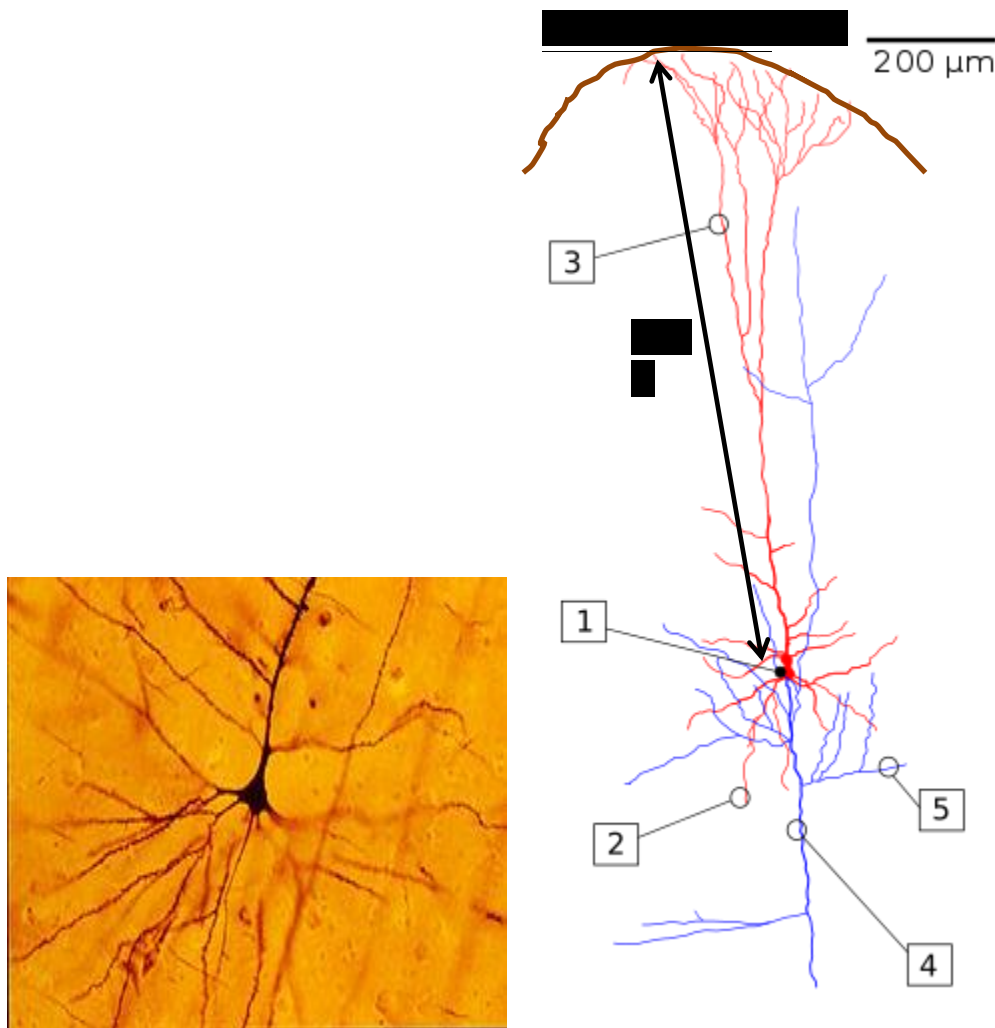


## Dipole

EEG source generators are supposed to be pyramidal shaped neurons extending to cerebral cortex (outer covering of gray matter), with parallel axes of their dendrites and a direction normal (perpendicular) to the arrival surface (cerebral cortex in Fig. 1).

These neurons are located in the outer layer of gray matter (cerebral cortex or neocortex). Cerebral cortex or neocortex has 2-4 mm width (depth) and is divided to 6 layers. The 3d and 5th layers of neocortex are the probable locations for 10-14 billion [pyramidal cells](#) (nearly at 0.9 mm and 1.5 mm depth). So, the apical dendrite (number 3 in Fig. 1) is able to reach the outer covering of gray matter (gray matter mesh which has been extracted from MRI).



**Fig1: Left:** Visualization of pyramidal neuron by light microscopy technique ; the apical dendrite extends vertically above soma [pyramidal cells](#)

**Right:** A reconstruction of a pyramidal cell. Soma and dendrites are labeled in red, axon arbor in blue. (1) Soma, (2) Basal dendrite, (3) Apical dendrite, (4) Axon, (5) Collateral axon.

The neural source model most commonly used to represent electrical activity in the brain is a “current dipole”. It represents an infinitely small oriented source of current positioned at  $\mathbf{r}_0$  (Fig. 2). A 3 dimensional dipole is a vector in space with the direction from one start point (sink) location ( $\mathbf{r}_0$ ) to one end point (source) location ( $\mathbf{r}_1$ ). The locations are defined in (x,y,z) with respect to origin (0,0,0) in 3 dimensional space of cartesian coordinate system. The dipole orientation ( $\mathbf{d}$ ) is calculated by the difference between the location of end point and location of start point as shown in Fig. 1. That is:  $\mathbf{d} = \mathbf{r}_1 - \mathbf{r}_0$  (1)

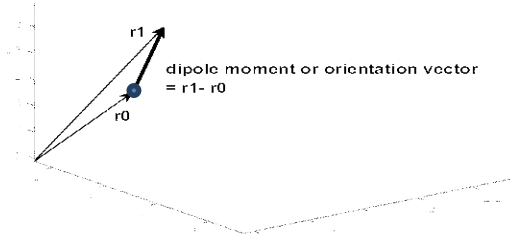


Fig. 2: dipole representation in 3 dimensional cartesian space

The direction of electric field in the intracellular environment of a neuron is from sink to source. So,  $\mathbf{r}_1$  can be replaced by  $\mathbf{r}_+$  and  $\mathbf{r}_0$  can be replaced by  $\mathbf{r}_-$  and we have:  $\mathbf{d} = \mathbf{r}_+ - \mathbf{r}_-$  (2)

The dipole moment (momentum) is:  $\mathbf{p} = q\mathbf{d}$  (3), Where  $q$  is the dipole electric (magnetic) charge. Since the scalp EEG is generated by groups of parallel orientated pyramidal neurons in the outer layer of cortex, we can model activities of neuronal current sources by dipoles for each part of the brain (cortical parts or deep parts). It is also called an equivalent current dipole (ECD). EEG inverse problem is the method of extracting source activities by estimating their probable location, orientation and intensity in each time instant. The forward problem is estimating the EEG potentials or sensor space potentials by predefining dipole sources in brain as shown in Fig. 3 [1].

If the neuronal current source at specified point of brain generates in the direction perpendicular to scalp it is called a radial source and if generates sources in the direction tangential to scalp it is called a tangential current source

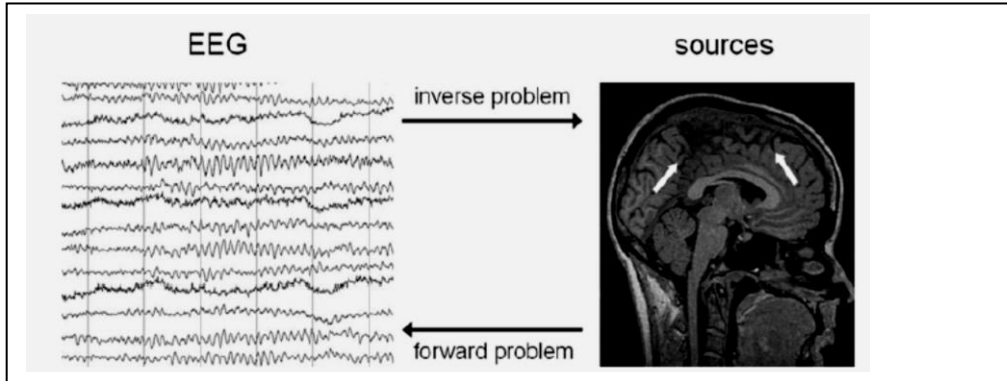


Fig. 3: Schematic of the relation between the inverse and the forward problem in EEG source localization. Potential sources are indicated by white arrows [1]

## Lead-field idea

Assume we have M channels EEG. For a desired source point on cortex with desired fixed orientation,  $\vec{e}_{d(3*1)}$ , we have:  $EEG_{M*t}(volt) = L_{M*1}(1/semens) \bullet d_{1*t}(amper)$  (1)

Lead-field ( $L_{M*1}$ ) is a vector with M coefficients.

$d_{1*t} \bullet \vec{e}_{d(3*1)}$  is the neural source momentum and  $d_{1*t}$  is amplitude of dipole current at time  $t$ .

- Lead-field gives the sensitivity of M electrodes (M coefficients) to activity of each point on cortex in the desired fixed orientation,  $\vec{e}_d$ .

Based on forward problem,  $L_{M*1}$  coefficients are proportional to

1. conductivities of volume conductor tissues ( $\sigma_i$ ) and
2. inner product of source momentum vector and vector connecting source location to each electrode location ( $d_{1*t} \bullet \vec{e}_{d(3*1)} \bullet (\vec{r} - \vec{r}_d)$ ). This is a result of forward problem by boundary element method (BEM) which was considered in detail in [dipole-concept-formulas.docx](#) (refer to formule. 32, 37, 41 and 45).

Recalling [dipole-concept-formulas.docx](#) we have **two boundary conditions** for solving BEM in boundaries (Fig. 3):

$J_1 \cdot e_n = J_2 \cdot e_n$ , (25), called Neumann boundary condition

$(\sigma_1 \nabla V_1) \cdot e_n = (\sigma_2 \nabla V_2) \cdot e_n$ , called, the homogeneous Neumann boundary condition

$J$  is current density ( $A/m^2$ ) and  $e_n$  is the normal component. The air conductivity is very low, so no current is injected to air outside the human head. Therefore at the surface of scalp we have:

$$J_1 \cdot e_n = 0, (27)$$

$$(\sigma_1 \nabla V_1) \cdot e_n = 0$$

Eq. 25 and 26 are the Neumann boundary condition and the homogeneous Neumann boundary condition, respectively.

The other boundary condition in interfaces (except air), is that

$V_1 = V_2$ , (28), which means the potential can't have any discontinuity by crossing an interface.

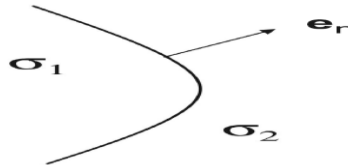


Fig.3 **The boundary between two compartments.** The boundary between two compartments with conductivity  $\sigma_1$  and  $\sigma_2$ . The normal vector  $e_n$  to the interface is also shown.

**And the forward problem mathematics for BEM is:**

$$V(\mathbf{r}) = \frac{2\sigma_0}{\sigma_r^- + \sigma_r^+} V_o(\mathbf{r}) + \frac{1}{2\pi} \sum_{k=1}^R \frac{\sigma_k^- - \sigma_k^+}{\sigma_r^- + \sigma_r^+} \sum_{j=1}^{N_{s_k}} \int_{\Delta_{s_{k,j}}} V(\mathbf{r}') \frac{\mathbf{r}' - \mathbf{r}}{\|\mathbf{r}' - \mathbf{r}\|^3} dS_k \quad (2)$$

$V_o(\mathbf{r}) = \frac{d \cdot (\mathbf{r} - \mathbf{r}_{dip})}{4\pi\sigma \|\mathbf{r} - \mathbf{r}_{dip}\|^3}$  (3), this is the first part of Eq. (2) and is the forward problem for an infinite homogeneous space with conductivity  $\sigma_0$ .

$\sigma_0$  corresponds to the medium in which the dipole source is located (the brain surface (cortex)).

$V_o(\mathbf{r})$  is the potential at  $\mathbf{r}$  for an infinite medium with conductivity  $\sigma_0$

$\sigma_j^-$  and  $\sigma_j^+$  are the conductivities of the, respectively, inner and outer compartments divided by the interface  $S_j$

$R$  is the number of interfaces in the volume which the integral is calculated on each interface surface.

$dS_k$  is a **vector oriented orthogonal to a surface** element and  $\|dS\|$  the area of that surface element.

The integral is over  $\Delta_{s_{k,j}}$ , the  $j$ -th triangle on the surface  $s_k$ .  $R$  is the number of interfaces in the volume.

Recalling Eq. (2), the unknown parameter is  $V(\mathbf{r}')$ , the potential on every triangle. To solve  $V(\mathbf{r}')$ , we write  $\mathbf{r} \rightarrow \mathbf{r}'$  and we have:

$$V(\mathbf{r}') = \frac{2\sigma_0}{\sigma_r^- + \sigma_r^+} V_o(\mathbf{r}') + \frac{1}{2\pi} \sum_{k=1}^R \frac{\sigma_k^- - \sigma_k^+}{\sigma_r^- + \sigma_r^+} \sum_{j=1}^{N_{s_k}} \int_{\Delta_{s_{k,j}}} V(\mathbf{r}') \frac{\mathbf{r}' - \mathbf{r}}{\|\mathbf{r}' - \mathbf{r}\|^3} dS_k \quad (2')$$

The integral is over  $\Delta_{s_{k,j}}$ , the  $j$ -th triangle on the surface  $s_k$ .  $R$  is the number of interfaces in the volume.

An exact solution of the integral is generally not possible, therefore an approximated solution  $\tilde{V}^k(\mathbf{r})$  on surface  $s_k$  may be defined as a linear combination of  $N_{s_k}$  simple basis functions,

$$\tilde{V}^k(\mathbf{r}) = \sum_{i=1}^{N_{s_k}} V_i^k h_i(\mathbf{r})$$

The coefficients  $V_i^k$  represent unknown potentials on surface  $s_k$  whose values are determined by constraining  $\tilde{V}^k(x)$  to satisfy eq. 2' at discrete points, also known as collocation points (typically the centroids of the surface elements and the unknown potentials  $V$  are the potentials at each triangle).

The **basis functions,  $h_i(\mathbf{r})$** , defined with the approach of “constant-potential” at every triangular element.

$$h_i(\mathbf{r}) = \begin{cases} 1 & \mathbf{r} \in \Delta_i \\ 0 & \mathbf{r} \notin \Delta_i \end{cases}$$

$\Delta_i$  is the  $i$ th planar triangle on the tessellated surface.

The basis functions,  $h_i(\mathbf{r})$ , defined with the approach of “linear potential”, is defined by

$$h_i(\mathbf{r}) = \begin{cases} \frac{[\mathbf{r} \mathbf{r}_j \mathbf{r}_k]}{[\mathbf{r}_i \mathbf{r}_j \mathbf{r}_k]} & \mathbf{r} \in \Delta_{i(jk)} \\ 0 & \mathbf{r} \notin \Delta_{i(jk)} \end{cases}$$

$\mathbf{r}_i, \mathbf{r}_j, \mathbf{r}_k$  are the nodes of the triangle (positions of 3 nodes) and the triple scalar product is defined as  $[\mathbf{r}_i \mathbf{r}_j \mathbf{r}_k] = \det(\mathbf{r}_i, \mathbf{r}_j, \mathbf{r}_k)$ . The notation  $\Delta_{i(jk)}$  is used to indicate every triangle with nodes  $\mathbf{r}_i, \mathbf{r}_j, \mathbf{r}_k$ . The function  $h_i(\mathbf{r})$  attains a value of unity at the  $i$ th vertex and drops linearly to zeros at the opposite edge of all triangles to which  $\mathbf{r}_i$  is a vertex.

$$\text{So, } V(\mathbf{r}) = \frac{2\sigma_0}{\sigma_r^- + \sigma_r^+} V_o(\mathbf{r}) + \frac{1}{2\pi} \sum_{k=1}^R \frac{\sigma_k^- - \sigma_k^+}{\sigma_r^- + \sigma_r^+} \sum_{j=1}^{N_{s_k}} \sum_{i=1}^{N_{s_k}} V_i^k \int_{\Delta_{s_{k,j}}} h_i(\mathbf{r}) \frac{\mathbf{r}' - \mathbf{r}}{\|\mathbf{r}' - \mathbf{r}\|^3} dS_k \quad (2'')$$

Since,  $r$  can be any point on interfaces,  $V(r)$  can be any of  $V_i^k$ . This equation can be transformed into a set of linear equations:

$$\mathbf{V} = \mathbf{B}\mathbf{V} + \mathbf{V}_0, \mathbf{V} = (\mathbf{I} - \mathbf{B})^{-1}\mathbf{V}_0$$

Where  $V$  and  $V_0$  are column vectors denoting at every node the wanted potential value and the potential value in an infinite homogeneous medium due to a source, respectively.  $\mathbf{B}$  is a matrix generated from the integrals, which depends on the geometry of the surfaces and the conductivities of each region. Determination of the elements of the matrix  $\mathbf{B}$  is computationally intensive and there exist different approaches for their computation.

So,  $V(r)$  is proportional  $V_o(r)$ , and  $V_o(r) = \frac{\mathbf{d} \cdot (\mathbf{r} - \mathbf{r}_{dip})}{4\pi\sigma_0 \|\mathbf{r} - \mathbf{r}_{dip}\|^3}$ , So,  $V(r)$  is proportional  $\mathbf{d} = d\vec{e}_d$ , dipole moment. Again, recalling Eq. (2), as  $V_o(r)$  and  $V(r')$ , are proportional  $\mathbf{d} = d\vec{e}_d$ , dipole moment,  $V(r)$ , is proportional  $\mathbf{d} = d\vec{e}_d$ , dipole moment. So, the coefficient of  $\mathbf{d} = d\vec{e}_d$ , gives the Lead-field matrix or the EEG ( $V(r)$ ) produced by dipole (at  $\mathbf{r}_{dip}$ ) on each electrode (at  $\mathbf{r}$ ) in direction  $\vec{e}_d$ .

As a conclusion, dipole moment ( $\mathbf{d}_{1 \times t} * \vec{e}_d$ ), is used for Lead-field ( $L$ ) calculation.

When, there is no prior information on dipole momentum,  $\mathbf{d}_{1 \times t} * \vec{e}_d$ :

1. As, we work in a coordinate system (cartesian), we can calculate Lead-field for each source point in 3 orthogonal Cartesian axes ( $\vec{e}_{dx}, \vec{e}_{dy}, \vec{e}_{dz}$ ), i.e.  $L_{M \times 3}$ , as shown in Fig. 4. In this figure, Lead-field is calculated for  $N$  dipoles hence,  $L_{M \times 3N}$ .  
Reason for this: Each desired orientation vector can be multiplied by orthogonal Cartesian vectors), so  $L_{M \times 1}$  is calculated next for each desired orientation by  
 $L_{M \times 1} = L_{M \times 3} * \vec{e}_d$ .

In order to fill Lead-field matrix like Fig. 1 right, for  $N$  desired source points and  $M = 5$  electrodes, each row of Lead-field matrix allocates one electrode and each 3 columns for each row, are the Lead-field coefficients by one dipole (at one location  $\mathbf{r}_{dip}$ ) with 3 general momentums ( $\vec{e}_{dx}, \vec{e}_{dy}, \vec{e}_{dz}$ ) and amplitude 1. The next 3 columns allocate to other dipoles, .... In Fig. 1, there are  $M=5$  electrodes and  $N$  dipoles, hence  $N \times 3$  columns.

2. As, source amplitude is unknown and variable in time, Lead-field can generally be calculated for amplitude 1. The real amplitude of source in time is calculated by EEG and Eq. (1).

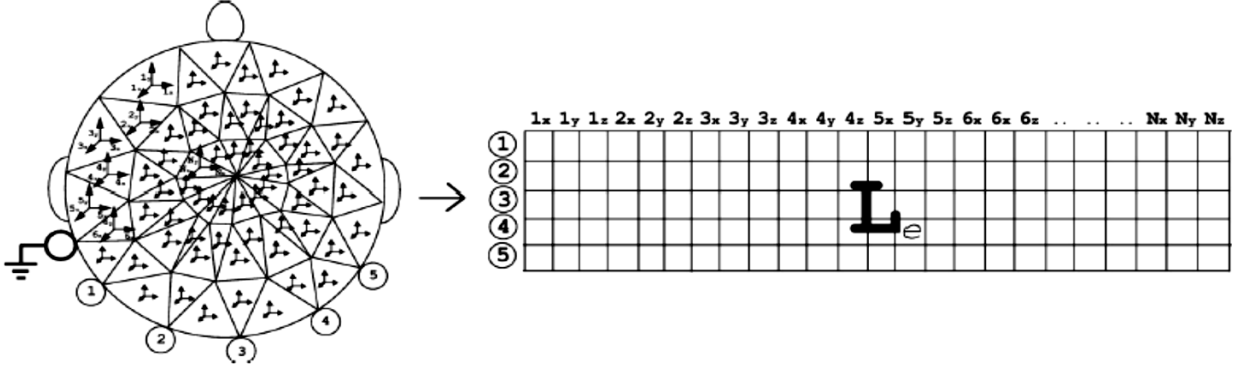


Fig. 4: Lead-field matrix for  $M = 5$  electrodes and  $N$  desired source points, each 3 columns are Lead-field for one source in 3 orthogonal axes in Cartesian coordinate system,  $L_{M*3}$ .

### After calculating Lead-field toward inverse problem

As we have EEG, for any desired source direction,  $\vec{e}_{d(3*1)}$ , source amplitude ( $d_{1*t}$ ) is calculated by: (2).

$$EEG_{M*t} = L_{M*3} * \vec{e}_{d(3*1)} * d_{1*t}, \text{ and } d_{1*t} = (L_{M*3} * \vec{e}_{d(3*1)})^\dagger * EEG_{M*t} \quad (2)$$

$\dagger$  is the Moore-Penrose pseudo-inverse.  $a^\dagger = (a^T a)^{-1} a^T$

### Inverse problem, find the optimum source direction and location, method: residual function mapping [1]

Assume  $EEG$  is real data and  $\widehat{EEG}$  is the output of forward problem by a desired source point with moment,  $\vec{d} = d\vec{e}_d$ , and Lead-field ( $L_{M*3}$ ):

$$\widehat{EEG} = L_{M*3} * \vec{d} \quad (3)$$

The optimum dipole source location is calculated by minimizing Eq. (4) [1]:

$$R = (\widehat{EEG} - EEG)^T (\widehat{EEG} - EEG) \quad (4)$$

That is minimizing the power of  $\widehat{EEG} - EEG$  in order to find best fit of  $\widehat{EEG}$  with real  $EEG$ .

By setting  $\widehat{EEG}$  to  $EEG$ , the **best moment** for each dipole location will be [1]:

$$\vec{d} = (L^\dagger) * EEG \quad (5)$$

$L^\dagger = (L^T L)^{-1} L^T$  is the Moore-Penrose pseudo-inverse of the Lead-field matrix.

This was a base idea of optimum source orientation (for each desired location,  $r_{dip}$ ).

After finding optimum orientation for each source, the **residual regarding the optimal orientation** is [1]:

$$\mathbf{R} = \widehat{\mathbf{EEG}}^T [\mathbf{I} - \mathbf{LL}^\dagger] \widehat{\mathbf{EEG}} \quad (6)$$

For each dipole source location,  $\mathbf{r}_{dip}$ , **best source moment and residual regarding the optimal orientation** is gathered. The probable source location, is the location with minimum  $R$ , residual, which can be color mapped on cortex. Hence this method is called **residual function mapping** and the location corresponding minimum value of  $R$  is the source location in this method.

## Inverse problem, other methods:

There are some methods like minimum norm estimate[2,5], ELECTRA (source local field potentials (LFPs) estimator) and Laura (source current density estimator) [2], Loreta [3] and etc. for inverse problem (source extraction and localisation).

### Minimum norm estimate (MNE)

$$\text{As we know } \mathbf{EEG} = \mathbf{L} \vec{\mathbf{d}}, \vec{\mathbf{d}} = d \vec{\mathbf{e}}_d \quad (7)$$

The general solution of **inverse problem (current estimation)** is achieved by [4] [5]

$$\text{Min } (\mathbf{L} \vec{\mathbf{d}} - \mathbf{EEG})^t \mathbf{w}_d (\mathbf{L} \vec{\mathbf{d}} - \mathbf{EEG}) + \lambda^2 (\vec{\mathbf{d}} - \vec{\mathbf{d}}_p)^t \mathbf{w}_j (\vec{\mathbf{d}} - \vec{\mathbf{d}}_p) \quad (8)$$

$\mathbf{w}_d$  and  $\mathbf{w}_j$  are symmetric (semi) positive definite<sup>1</sup> matrices representing the (pseudo) metrics associated with the measurement space (EEG) and source space.

Vector  $\vec{\mathbf{d}}_p$  denotes any available a priori value of the unknown, e.g., from other varieties of brain functional images.

The regularization parameter is denoted by  $\lambda$  independently of the rank of  $\mathbf{L}$ ,

The solution to Eq. (8) is unique if and only if the null spaces of  $\mathbf{w}_j$  and  $\mathbf{L}^t \mathbf{w}_d \mathbf{L}$  intersect trivially, that is,  $\text{Ker}^2(\mathbf{w}_j) \cap \text{Ker}(\mathbf{L}^t \mathbf{w}_d \mathbf{L}) = \{0\}$ . In this case the estimated solution vector  $\vec{\mathbf{d}}$

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<sup>1</sup> a [symmetric](#)  $n \times n$  [real matrix](#) is said to be **positive definite** if the scalar  $\mathbf{Z}^T \mathbf{M} \mathbf{Z}$  is positive for every non-zero column [vector](#) of  $n$  real numbers.

can be obtained using the change of variable  $\vec{d} = \vec{d}_p + \mathbf{h}$  and solving the resulting problem for  $\mathbf{h}$ , that is:

$$\vec{d} = \vec{d}_p + [L^t W_d L + \lambda^2 W_j]^{-1} L^t W_d [EEG - L \vec{d}_p] \quad (9)$$

If and only if matrices  $W_j$  and  $W_d$  are positive definite, Eq. (9) is equivalent to

$$\vec{d} = \vec{d}_p + W_j^{-1} L^t [L W_j^{-1} L^t + \lambda^2 W_d^{-1}]^{-1} [EEG - L \vec{d}_p] \quad (10)$$

In the case of null a priori estimates of the current distribution ( $\vec{d}_p = 0$ ), the general solution can be written as

$$\vec{d} = G EEG \text{ with } G = W_j^{-1} L^t W_d L (L^t W_d L W_j^{-1} L^t W_d L)^{-1} L^t W_d \quad (11)$$

If  $L W_j^{-1} L^t$  is invertible we can take the limit of expression 11 (with respect to  $\lambda$ ) to obtain a simpler expression, that is:

$$G = W_j^{-1} L^t (L W_j^{-1} L^t)^{-1} L^t W_d, {}^t \text{is transpose and } \vec{d} = W_j^{-1} L^t (L W_j^{-1} L^t)^{-1} L^t W_d EEG, \quad (12)$$

$\vec{d}$  is current vector, output of inverse problem by MNE which gives the amplitude of source in 3 x, y, z directions.

For any arbitrary inverse matrix  $G$  there are at least a pair of metrics  $w_d$  and  $w_j$  that, when optimized in the sense of Eq. (8), produce the desired inverse (current vector). For example, the minimum norm solution is obtained when both metrics are the identity matrix.

Eq. (12) can repeat for all dipole source locations and currents are estimated. The square of currents at each time instant can be color mapped on brain and source localization is done.

### Example of source localization by MNE

In 2013, Kanamori et.al. [6] applied MNE on MEG to detect the onset of inter-ictal epileptic discharges and compared their results to detections by invasive electrocorticography (ECoG) and showed MNE useful as a means for presurgical evaluation. A view of inter-ictal source localization by MNE is shown in Fig. 5.

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<sup>2</sup> **Kernel:** a vector  $v$  is in the **kernel of a matrix  $A$**  if and only if  $Av=0$ .)



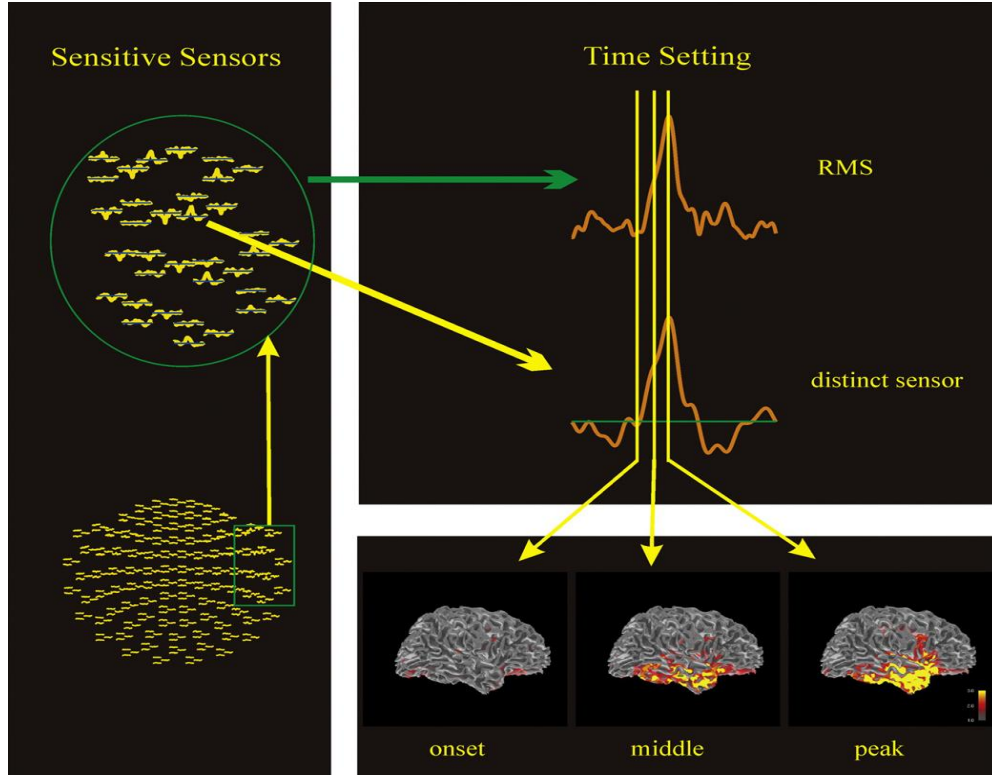


Fig. 5: Procedures for MEG pre-surgical analysis. i) examined RMS waveforms constructed from recordings of manually selected sensors around spikes; ii) selected one MEG sensor as a “distinct sensor” being closest to the RMS waveforms; iii) time setting at onset, middle and peak times of epileptic activity on distinct sensor; and iv) analysis of MEG spikes with MNE method. The distributions of current sources are shown on the cortical surfaces in a red/yellow color[6]

For evaluating MNE results, source localization by invasive electrocorticography (ECoG) is shown in Fig. 6.

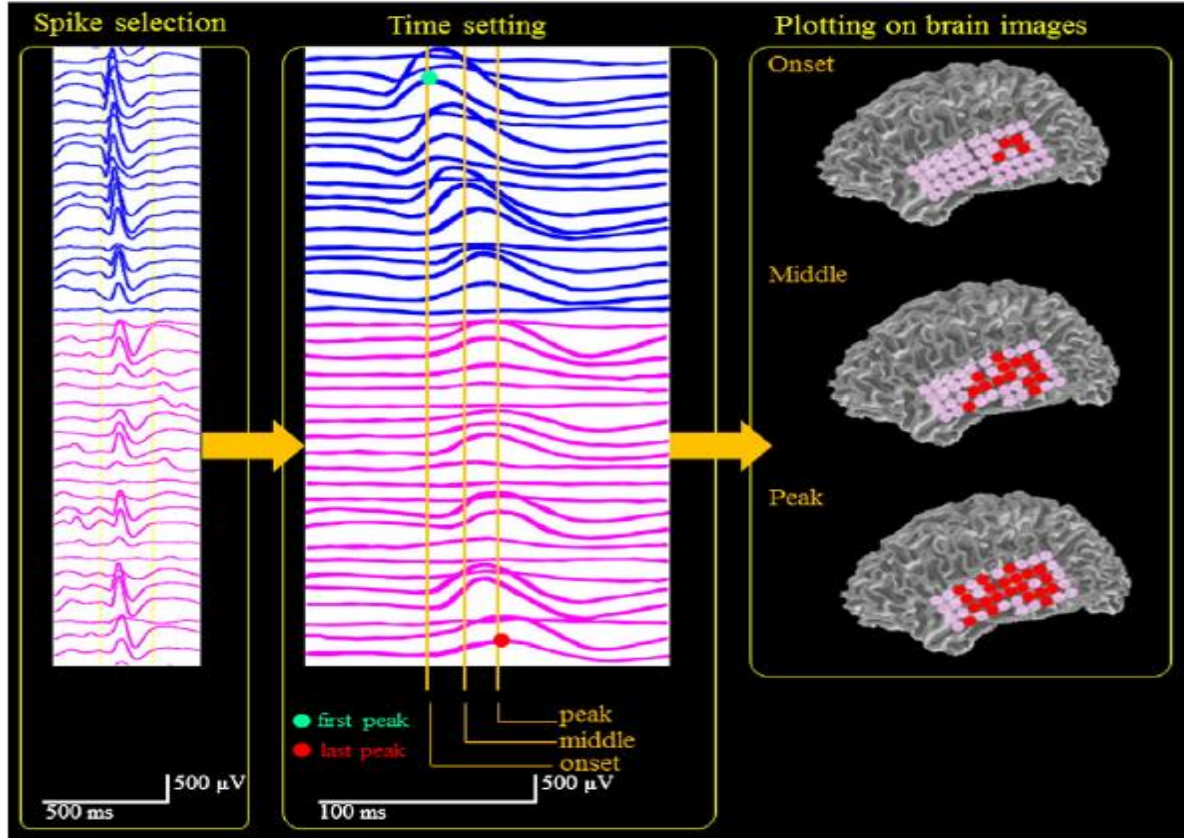


Fig. 6: Three step procedure for ECoG analysis. Three steps were adopted: i) picking up the interictal spikes from ECoG recorded in each case; ii) time setting of onset, middle and peak times for epileptic activity; and iii) displaying the activated electrodes at each time. subdural grid electrodes are all pink and red dots indicate the distribution of spikes.[6]

## **ELECTRA (source local field potentials (LFPs) estimator) and Laura (source current density estimator)**

These two methods mimic biophysical behavior of irrotational fields (neural currents which have fixed direction) and decaying trend of strength of potential and fields with the distance to their generation site to improve general constraint and solution of inverse problem. ...

## **References**

1. [Ziegler E, Chellappa SL, Gaggioni G, Ly JQ, Vandewalle G, André E, Geuzaine C, Phillips C. A finite-element reciprocity solution for EEG forward modeling with realistic individual head models. \*NeuroImage\*. 2014 Dec 1;103:542-51.](#)
2. Grave de Peralta Menendez R, Murray MM, Michel CM, et al. Electrical neuroimaging based on biophysical constraints. *Neuroimage* 2004;21(2):527-39 doi: 10.1016/j.neuroimage.2003.09.051.
3. Pascual-Marqui RD, Michel CM, Lehmann D. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *International Journal of psychophysiology*. 1994 Oct 1;18(1):49-65.
4. Grave de Peralta Menendez, R., Gonzalez Andino, S.L., 1998. A critical analysis of linear inverse solutions. *IEEE Trans. Biomed. Eng.* 4, 440– 448.
5. Hämäläinen MS, Ilmoniemi RJ. Interpreting magnetic fields of the brain: minimum norm estimates. *Medical & biological engineering & computing*. 1994 Jan 1;32(1):35-42.
6. Kanamori Y, Shigeto H, Hironaga N, Hagiwara K, Uehara T, Chatani H, Sakata A, Hashiguchi K, Morioka T, Tobimatsu S, Kira JI. Minimum norm estimates in MEG can delineate the onset of interictal epileptic discharges: a comparison with ECoG findings. *NeuroImage: Clinical*. 2013 Jan 1;2:663-9.