Dipole

A 3 dimensional dipole is a vector in space with the direction from one start point (negative charge) location (***r0***) to one end point (positive charge) location (***r1***). 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 (***d***) is calculated by the difference between the location of end point and location of start point as shown in Fig. 1. That is: $\mathbf{d} = \boldsymbol{r1} - \boldsymbol{r0}$ (1)

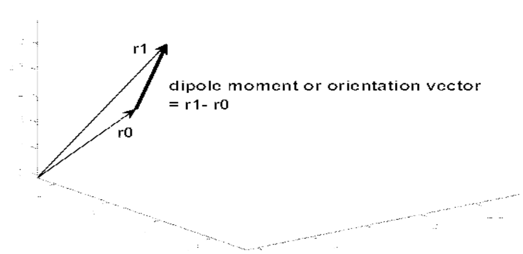

Fig. 1: dipole representation in 3 dimesional cartesian space

As we know from electric fields the direction is from negative charge to positive charge. So, ***r1*** can be replaced by $\boldsymbol{r}_+$ and $\boldsymbol{r}_0$ can be replaced by $\boldsymbol{r}_-$ and we have: $\boldsymbol{d} = \boldsymbol{r}_+ - \boldsymbol{r}_-$ (2)

The dipole moment (momentom) is: $\boldsymbol{p} = q\boldsymbol{d}$ (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. 2 [1].

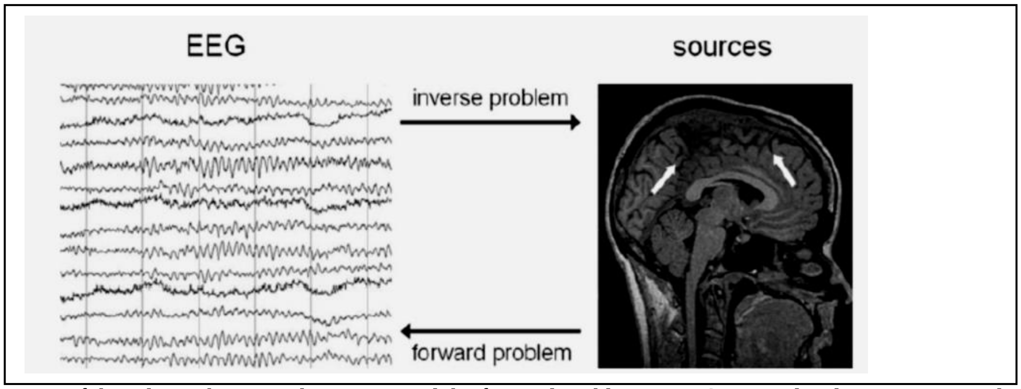

Fig. 2: Schematic of the relation between the inverse and the forward problem in EEG source localization. Potential sources are indicated by white arrows [1]

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. By default, each point on the cortex can generate in 3 perpendicular directions, 1 radial and 2 tangential **(why? Radial source is chosen to be along the vector perpendicular to the surface containing two tangential vectors, in other words we can define these three current sources in the direction of 3 perpendicular vectors in Cartesian coordinate),** as shown in Fig. 3. Orientation of activities of groups of neurons at each location of cortex can be detected by external stimuli to each part of cortex. The gain-orientation curve shows maximum value for stimuli with angle 90 with respect to cortical surface [2]. Hence, by knowing the normal activation with respect to surface, surface parts of brain most generate radial current sources and deep folds of the brain, for example the central sulcus (for deeper areas we need more information from diffusion tensor imaging), often generate tangential sources (add the citation. We can say this without the prove and we need to know why? With reference). An example of locations for radial and tangential sources is shown in Fig.4.

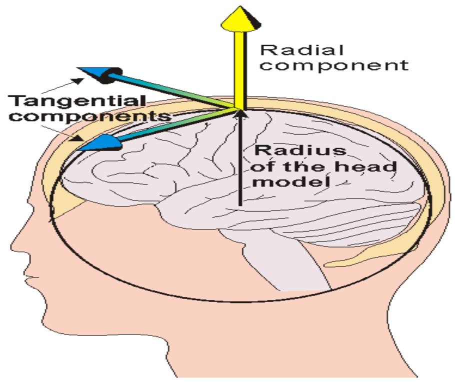

Fig. 3: showing radial and tangential components of a current source at a specified location of cortex

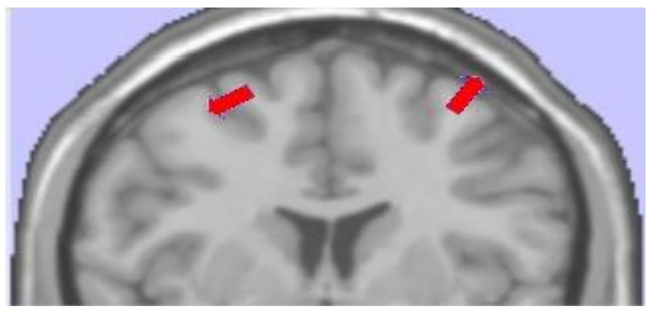

Fig. 4: An example of locations for radial and tangential sources, radial source (right dipole) is located on surface part of brain and tangential source (left dipole) is located on brain fold

the forward and inverse problem

The inverse problem doesn't have a unique solution, since there are multiple configurations of sources that generate the same potential distribution, but the forward problem has a unique solution from source to sensor. This means that given some sources, there is only one potential distribution on the scalp generated by these sources.

Maxwell's and Ohm's laws allow deriving a mathematical relation between the current sources and the potential distribution to help us solve the inverse problem [1].

The speed of electromagnetic waves resulting from potential changes in the brain is very high (10^5m/s). these potential changes can be detected almost instantaneously everywhere on the skull. Therefore it suffices to consider only the stationary (time-independent) Maxwell equations for the electric field **E** and the magnetic field **B**:

$\nabla.\boldsymbol{E} = \frac{\rho}{\epsilon_0},\ \nabla \times \boldsymbol{E} = 0,\ \nabla.\boldsymbol{B} = 0,\ \nabla \times \boldsymbol{B} = \mu_0 \boldsymbol{J}$ (4)

ρ is the charge density, ϵ_0 is the dielectric constant (permittivity) of the vacuum, and J the current density. **E**, **B**, **J** are vector valued functions defined for every point **r** in space. From second of 4 we have: $\boldsymbol{E} = -\nabla \boldsymbol{V}$ (5), Ohm's law states the current density **J** results from the primary current $\mathbf{J}^{\mathrm{P}}$ and a passive volume current proportional to the electric field **E:**

$\boldsymbol{J} = \boldsymbol{J}^{p} + \sigma\boldsymbol{E}$ (6)

By subtituting **E** according to 5 we have:

$\boldsymbol{J} = \boldsymbol{J}^{p} - \sigma\nabla\boldsymbol{V}$ (7)

σ is the conductivity of the medium (in the case EEG: brain, cerebrospinal fluid, skull and scalp) which depends on the position in space. For EEG, $\boldsymbol{J}^{p}$ is due to the activity of neurons in or very close to the neuron cell, whereas the volume current flows everywhere in the medium. The source of EEG is found by localizing the primary current.

By taking divergence of 7:

$\nabla.\boldsymbol{J} = \nabla.\boldsymbol{J}^{p} - \nabla.(\sigma\nabla\boldsymbol{V})$ (8)

As we know in mathematics the divergence of rotation (curl) is zero, so we have:

$\nabla.\nabla\times\boldsymbol{B} = \nabla.\mu_0\boldsymbol{J} = \mu_0\,\nabla.\boldsymbol{J}$=0 (9)

By combining the last 2 equations:

$\nabla.J^{p} = \nabla.(\sigma\nabla\boldsymbol{V})$ (10)

This is the poisson equation for the primary current (the source) which can in principle be solved from the measured potential **V** (the EEG) when the conductivity of the medium (σ) is known.

In some cases an analytical solution exists, but mostly computers and numerical mathematical approaches are needed to find an approximate solution to the Poisson equation. An analytical solution to the Poisson equation exists for the case in which , conductivity is position independent and the medium is infinite (why? The condition to solve this kind of equation is to have an infinite space or infinite volume conductor) and isotropic [1]. So the scalp potential V regarding a source at location $\boldsymbol{r_0}$ is:

$V(\boldsymbol{r_0}) = \frac{-1}{4\pi\sigma}\iiint_{volume}\frac{\nabla.\boldsymbol{J}^{p}}{|\boldsymbol{r}-\boldsymbol{r_0}|}d\boldsymbol{r}.$ (11) (where is come from?)

r_0 is the source position to find the potential and r is general location in space and σ is the conductivity of homogeneous medium. Here, the volume integral represents a summation over all current sources in the volume. This is the mathematical view of forward problem, i.e. from current dipole sources to electrode or sensor voltages. This equation can't be calculated for head since the conductivity depends on position (different tissues of brain, scalp, skull have different conductivities) and also the inverse problem has many solutions (ill-posed), besides the volume or the head which is not infinite.

The current distribution of a dipole at position $\boldsymbol{r_Q}$ with strength $\boldsymbol{Q}$ is mathematically expressed as:

$\boldsymbol{J}_{dip}(r) = \boldsymbol{Q}\delta\,(\boldsymbol{r}-\boldsymbol{r_Q})$ (12, explain it?)

δ is dirac delta (تابع ضربه?) function which is zero everywhere except at $\boldsymbol{r} = \boldsymbol{r_Q}$. This can be replaced in 11 instead of the $1/|\boldsymbol{r}-\boldsymbol{r_0}|$.

$V_i(\boldsymbol{Q},\boldsymbol{r_Q}) = \int \boldsymbol{L_i}(\boldsymbol{r}).\boldsymbol{Q}\,.\,\delta(\boldsymbol{r}-\boldsymbol{r_Q})dv = \boldsymbol{Q}.\boldsymbol{L_i}(\boldsymbol{r_Q})$

The equation 11 can be solved by two assumptions: 1) using current dipoles 2) modelling head as a multiple sphere consisting scalp, skull, and brain tissues with different conductivities. The advantage is that for a spherical model, as shown in Fig. 5, the analytical solution for poisson equation for a dipole in a homogeneous space exists.

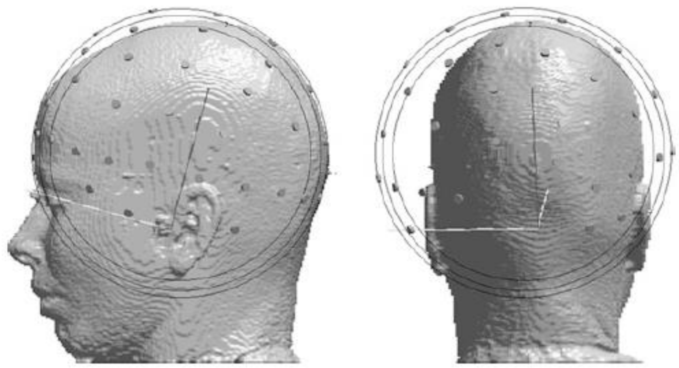

Fig. 5: Multilayer spherical model fitted to an anatomically correct head. Notice the good fit on top and bad fit at the sides and bottom

In reality the head tissues are not spherical. To solve the inverse problem, first of all the head different tissues are segmented and each segment surface is meshed by triangles like Fig. 6 to show boundaries. By using discrete points or vertices, the continuous volume integral to find the surface scalp potential, can be solved at each boundary, hence continuous surface integral. Since the poisson equation is linear this problem can be solved for each dipole and summed to solve for multiple dipoles active at the same time.?

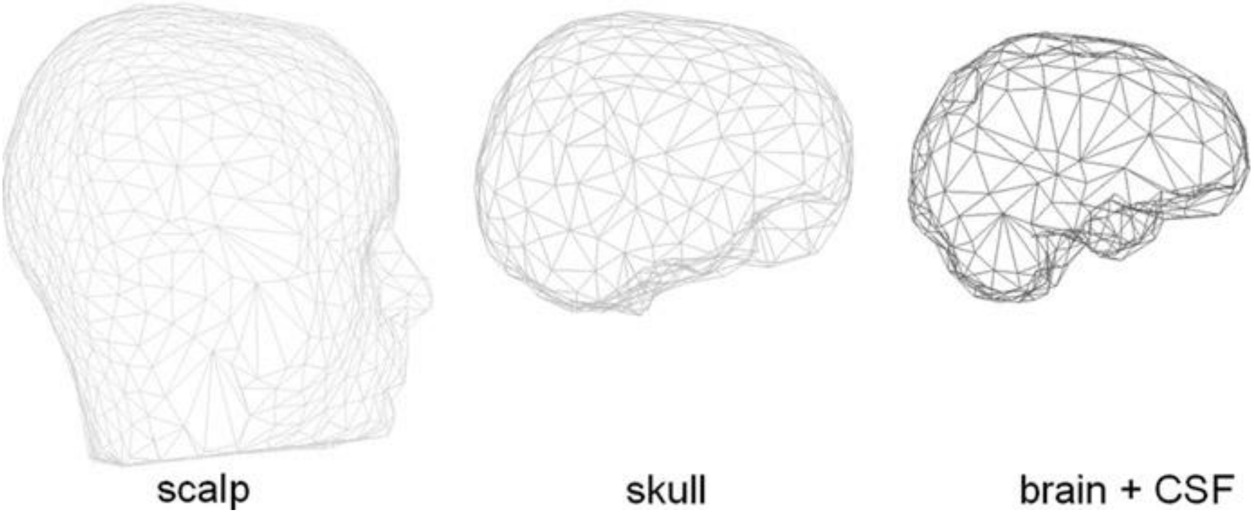

Fig. 6: Individual volume model for boundary element method as derived from the MRI. Each boundary is covered with triangles, which allows a rather accurate representation of the actual anatomy. From left to right: scalp, skull, brain, and cerebrospinal fluid

Triangulations are very useful because the potential on the scalp, which is expressed as a volume integral (Eq. 11), can also be expressed as an integral equation on each of the boundaries. This integral (the solution to the Poisson equation) is approximated numerically, when the number of points are limited by vertices. The potential is calculated only at each of the vertices. Since the number of points for the solution is now limited, the continuous surface integral can be translated into a large matrix equation that needs to be solved and there are multitude of methods available to do that. The approach of solving the surface integral is called a boundary element method (BEM). There are other methods such as finite element method (FEM) to solve the forward problem. FEM uses each small volume for forward model calculations and hence is more accurate than BEM.

This was the forward problem. To solve the inverse problem, the forward problem is first calculated from prior information of sources (numbers, locations, orientations). The prior information about sources can be achieved from bold spots in fMRI or by pre knowledge of anatomical locations related to evoked potentials. Then the forward problem is applied and the error of the output model with respect to EEG is calculated. Then the proper changes in source parameters is applied and the forward problem is calculated again. This is the iterative approach and is shown in Fig. 7.

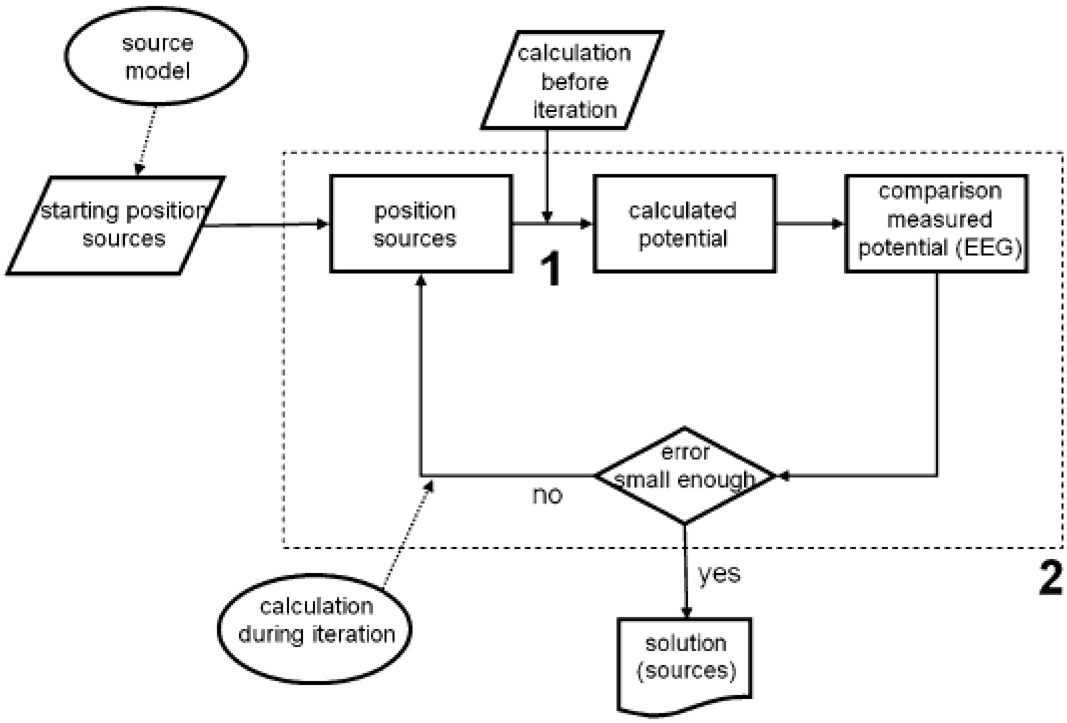

Fig. 7: Diagram of the iterative approach to solve the inverse problem. 1) Forward problem; 2) inverse problem

Repeated Calculation of the Forward Problem: The Lead Field Matrix

Instead of repeatedly solving a new matrix equation for the forward problem in a realistic head model, some calculations can be done once, before the process, which greatly reduces calculation time. As indicated before, the Poisson equation is linear. This allows writing the potential V_i at an electrode **i** as a linear combination of the primary current density $\boldsymbol{J^p}$:

$$V_i = \int \boldsymbol{L}_i(\boldsymbol{r}).\boldsymbol{J}^{\boldsymbol{p}}(\boldsymbol{r})dv \qquad (13)$$

$\boldsymbol{L_i}$ is the lead field operator which depends on the geometry and conductivities of the head model. $\boldsymbol{r}$ is the general location which can be solved for locations of source (s) in space.

For the dipole current source with strength (**Q**) at position ($\boldsymbol{r_Q}$) and from 11, 12 and 13 we have:

$$V_i(\boldsymbol{Q}, \boldsymbol{r_Q}) = \int \boldsymbol{L_i}(\boldsymbol{r}).\boldsymbol{Q}\,.\,\delta(\boldsymbol{r} - \boldsymbol{r_Q})dv = \boldsymbol{Q}.\boldsymbol{L_i}(\boldsymbol{r_Q}) \qquad (14)$$

So, the scalp potential at each dipole point location $\boldsymbol{r_Q}$ with strength $\boldsymbol{Q}$ is calculated. $\boldsymbol{L_i}$ is leadfield calculated for dipole at $\boldsymbol{r_Q}$ and the electrode with number or indices i or ith electrode.

The discretized version of the lead field operator, the lead field matrix, has as many rows as there are electrodes and as many columns as there are possible source locations. Thus, lead field matrix corresponds to the potential at recording sites (electrodes) due to one specific source location.

Applicability of reciprocity to anisotropic conductors

The reciprocity principle by von Helmholtz provides a good attitude to calculate the leadfield matrix in inhomogeneous space [3]. It is exactly the reciprocity principles in electric circuit, besides in this issue the orientation of the source is important. The reciprocity principle states that given a dipole with strength $\boldsymbol{Q}$ and the need to find the potential difference between two scalp points **A** and **B**, it is sufficient to know the electric field **E** (-gradient of potential) at the dipole location resulting from a current $\boldsymbol{I}$ placed between points A and B with 90 degree orientation with respect to scalp.

$$V_A - V_B = \frac{\boldsymbol{E.Q}}{\boldsymbol{-I}} \quad (15)$$

This can be used to easily calculate leadfield (**L**). comparing Eq. 14 and 15, $\boldsymbol{L_i}(\boldsymbol{r_Q}) = \frac{\boldsymbol{E}}{\boldsymbol{-I}}$ So, this method is used instead of forward problem for leadfiled calculation for any source location. This issue is shown in Fig. 8 for a dipole with strength P and with a predefined orientation. If we consider an orientation for a predefined dipole with an angle with respect to electric field, the nominator of Eq. 15 is defined as the dot product of the dipole moment and electric field as shown in Fig. 8 [3].

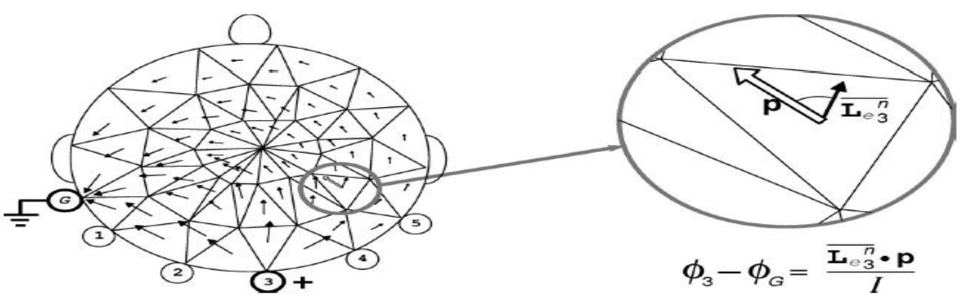

Fig. 8: Depiction of the reciprocity-based method. A unit current is applied between electrodes ‘‘3’’ and ‘‘G.’’ The reciprocity principle states that the voltage difference between 3 and G due to a dipole source p placed in element e^n will be equal to the dot product of p and the electric field in e^n.

paper [3] tells about computing the stiffness matrix (relating head properties (geometry and conductivity)) and a finite element method (FEM) for leadfield calculation based the mensioned reciprocity principle but it wasn’t clear in paper [3] and should be studied more in 4 reference papers of [3] . FEM means calculating the forward problem on each small volume of head to arrive the scalp potential by particle potentials. This method also conssists of boundary element method (BEM) which has the calculations only on surface of boundaries. So, FEM has much more calculations which is under study....

Matrix form of EEG forward problem

In the following the reciprocity and matrix formulation of EEG (forward model) based leadfield is reviewed. The leadfield matrix allows for the computation of the potential distribution on the sensors from a current source (e.g. synchronously firing neurons) placed inside the brain. The EEG based dipole and leadfield matrix (L) can be written as:

$\emptyset = L.j + n$ (16)

$\emptyset$ is the recorded scalp (sensor) potentail, j is the neural source represented as a current dipole with orientation j, and n represents the noise in the system. The potential at each sensor caused by a dipole in a source element is the dot product of the dipole orientation vector (j^N) and the leadfield vector (L^N) for the element. Reciprocity explains that the roles of the dipole and sensor can be reversed, compared to the direct forward method. A full leadfield matrix can be created by applying current between each sensor and a ground (potentially zero) electrode, and storing the electric field induced in each element of the head model. Current dipoles or equivalent current dipoles, which simulate the active patches of cortex, can have three dimensional orientations (in x,y,z direction) in general. The reciprocity principle states that inorder to identify the voltage ($\emptyset$) difference between any two points resulting from a single unit current dipole (j), it is sufficient to know the electric field (E) at the dipole location produced by injecting a known current (I) through two points (A, B):

$\emptyset_A - \emptyset_B = \frac{E.j}{I}$ (17)

This equation is proved in [7]. For M electrodes (sensors), we can put the leadfield information, L for all N source(s) location(s) in a matrix called leadfield matrix:

$$\begin{bmatrix} L_1^{1,x} & L_1^{1,y} & L_1^{1,z} & \dots & L_1^{N,x} & L_1^{N,y} & L_1^{N,z} \\ L_2^{1,x} & L_2^{1,y} & L_2^{1,z} & \dots & L_2^{N,x} & L_2^{N,y} & L_2^{N,z} \\ \dots & \dots & \dots & \dots & \dots & \dots & \dots \\ L_M^{1,x} & L_M^{1,y} & L_M^{1,z} & \dots & L_M^{N,x} & L_M^{N,y} & L_M^{N,z} \end{bmatrix} \begin{bmatrix} j^{1,x} \\ j^{1,y} \\ j^{1z} \\ \dots \\ j^{N,x} \\ j^{N,y} \\ j^{N,z} \end{bmatrix} = \begin{bmatrix} \emptyset_1 \\ \emptyset_2 \\ \dots \\ \emptyset_M \end{bmatrix} \quad (18)$$

So, the dipole current source strength (in 3 directions of Cartesian coordinate) is acquired by Eq. 18 with the knowledge of leadfield and scalp potentials. If number of sensors (electrodes) is M, only M-1 iterations are needed to find the leadfield for each point of brain based reciprocity. This is the advantage of reciprocity which is shown graphically in Fig. 9. But if using the direct forward model for leadfield calculations, there are thousands of iterations to create a leadfield from a dense array of sources.

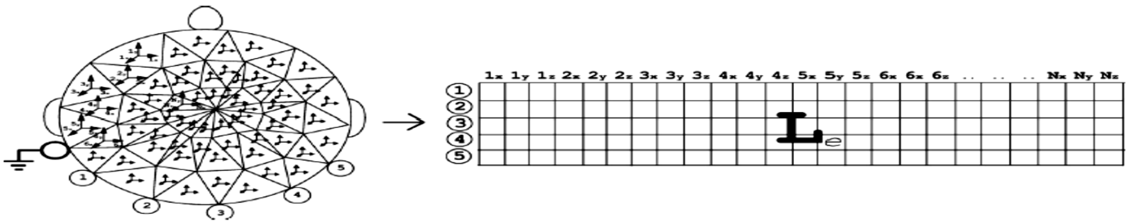

Fig. 9 Depiction of the leadfield matrix. Each orthogonal dipole in each element corresponds to a column of L, and each electrode corresponds to a row of L. That is, each entry of L corresponds to the potential measured at a particular electrode due to a particular source.

The concept of reciprocity gives a good attitude to realize the lead filed matrix and also reduces the computation time, since instead of defining current sources on cortex and solving the poisson's equation to compute the scalp voltage differences between every electrode pair (forward problem), we can put a current source and a current sink (or reference zero potential) between any electrode pair and solve the forward problem from sensor space to source space. Each dipole is a current source from a negative charge to a positive charge, so has a potential difference (gradient) which is equal electric field at dipole position ($\boldsymbol{E} = -\nabla \boldsymbol{V}$). So, the parameter E in Eq. 17 can be proved because potential difference (gradient) is equal electric field.

optimum dipole source orientation

The following is to find the optimum dipole source orientation based leadfield matrix equation [4]:

Assume we have computed leadfield for each desired dipole position in 3 directions (x, y, z), one may select a dipole and want to find the optimal orientation of the predefined dipole. In other words find the best fit of real EEG with the EEG acquired by the predefined current dipole activity. This is also called residual function mapping [4]. First the scalp potential ($\emptyset$) is measured and the scalp potential due to a predefined dipole (j) is also calculated:

$Lj = \widehat{\emptyset}$ (19)

The optimal location of a single dipole can be found by minimization of the residual function (R):

$R = \left(\widehat{\emptyset} - \emptyset\right)^T (\widehat{\emptyset} - \emptyset)$ (20)

T means transpose of mattrix. If $\widehat{\emptyset}$ is set to the measure potential ($\emptyset$), the best moment of this dipole is given by:

$j = L^{\dagger}\emptyset$ (21)

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

The residual regarding the optimal orientation is:

$R = \widehat{\emptyset}^T [I - LL^{\dagger}]\, \widehat{\emptyset}$ (22)

Suppose we have done these computations (optimum orientation and residual) for a lot of dipole source locations. The location of the global minimum of the residual function reflects the best guess for the position of dipole within the mesh (a way for dipole source localization based lead field).

After understanding the dipole and the mathematics of forward problem, it is needed to make the real head model, We need head model to define the source and sensor locations and to analytically find a relation between current sources and electrode voltages, i.e. to solve the head forward model (obtaining the lead field matrix).

To create a head model, T1 weighted structural MRI is acquired and segmented in to scalp, skull, gray matter, white matter, cerebrospinal fluid (CSF). So, a mesh (hexahedral or tetrahedral) containing nodes for mentioned layers (scalp, skull …) is created. Also, the electrode positions on scalp mesh is defined to solve the potential for specified electrode locations. In other words some scalp mesh nodes that have the least euclidean distance to electrode locations (electrode placement according to standard 10-20 or 10-10 electrode locations) are selected as electrode locations.
To solve the forward problem (poisson's equation (Eq. 10 and 11)), there are some methods such as boundary element methods (BEM), finite element method (FEM). The BEM solves the forward problem integral (Eq.11) on surface of each boundary (for example, scalp, skull, grey matter) but FEM defines tetrahedrals (hexahedrals) to fill the whole head space with and solves eq.11 for each small tetrahedrals (hexahedral) volume.
There are softwares such as openMEEG [5] and simbio [6] written to solve the forward problem for BEM and FEM respectively. A software also written for FEM based reciprocity proposed by [4].
The following is mathematics for solving forward problem.

Preliminaries for Boundary Element Method (BEM) [7]

Suppose we represent the activity of pyramidal cells in one position by a dipole current source in Cartesian space like fig. 10.

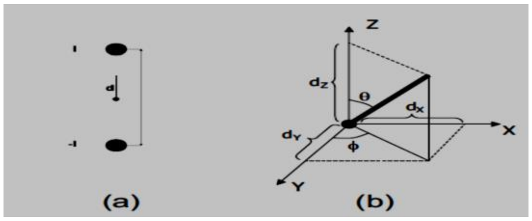

Fig. 10 **The dipole parameters**. (a) The dipole parameters for a given current source and current sink configuration. (b) The dipole as a vector consisting of 6 parameters. 3 parameters are needed for the location of the dipole (in 3 dimensions (x, y, z)). 3 other parameters are needed for the vector components of the dipole (orientation in 3 dimension (x, y, z)). These vector components can also be transformed into spherical components: an azimuth, elevation and magnitude of the dipole.

The dipole current is represented by a current source (inject (-I)) and sink (remove (I)), as shown in fig. 10 a. The dipole position ($\boldsymbol{r}_{dip}$) is defined in half of the distance between two monopoles (sink and source).

The dipole moment is a unit vector (e_d) in a direction from source to sink with magnitude of $d = \|\boldsymbol{d}\| = I.p$ with p the distance between two mono poles. It is suggested to define a small distance (unit). The dipole moment is defined by 3 components along the unit vectors (e_x, e_y, e_z) in Cartesian space as

$\boldsymbol{d} = d_x e_x + d_y e_y + d_z e_z$. (23)

Due to a dipole at position $\boldsymbol{r}_{dip}$ and moment $\boldsymbol{d}$, and according to poisson's equation (Eq. 10), the scalp potential at an arbitrary scalp point $\boldsymbol{r}$, is

$v(r, r_{dip}, d) = d_x V(r, r_{dip}, e_x) + d_y V(r, r_{dip}, e_y) + d_z V(r, r_{dip}, e_z)$ (24)

There are also some continuous boundary conditions in boundaries between head tissues:

Suppose we have a current crossing perpendicular ($\boldsymbol{e_n}$) to the boundary between two tissues (different conductivities) which is shown in fig. 11. At boundary we have:

$J_1 . e_n = J_2 . e_n$, (25)

$(\sigma_1 \nabla V_1). e_n = (\sigma_2 \nabla V_2). e_n$,

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:

$J_1 . e_n = 0$, (27)

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

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)

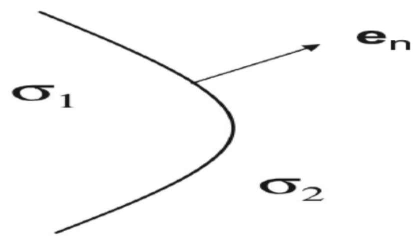

Fig. 11 **The boundary between two compartments.** The boundary between two compartments with conductivity σ1 and σ2. The normal vector $\boldsymbol{e_n}$ to the interface is also shown.

The EEG or scalp potential is defined by $g(\boldsymbol{r}, \boldsymbol{r}_{dip}, \boldsymbol{d})$ at electrode position $\boldsymbol{r}$ due to a dipole at position $\boldsymbol{r}_{dip}$ with moment $\boldsymbol{d} = d\boldsymbol{e_d}$ (with magnitude d and orientation $\boldsymbol{e_d}$).
For different configurations of N electrodes and p dipoles (with location $\boldsymbol{r}_{dip}$ and momentum $\boldsymbol{d}$) the electrode potentials in each time instant would be [7]:

$$V = \begin{bmatrix} V(r_1) \\ \vdots \\ V(r_N) \end{bmatrix} = \begin{bmatrix} g(\boldsymbol{r_1}, \boldsymbol{r}_{dip_1}, \boldsymbol{e_{d_1}}) & \dots & g(\boldsymbol{r_1}, \boldsymbol{r}_{dip_p}, \boldsymbol{e_{d_p}}) \\ \vdots & \ddots & \vdots \\ g(\boldsymbol{r_N}, \boldsymbol{r}_{dip_1}, \boldsymbol{e_{d_1}}) & \dots & g(\boldsymbol{r_N}, \boldsymbol{r}_{dip_p}, \boldsymbol{e_{d_p}}) \end{bmatrix} \begin{bmatrix} d_1 \\ \vdots \\ d_P \end{bmatrix} = \boldsymbol{G}(\{\boldsymbol{r_j}, \boldsymbol{r}_{dip_i}, \boldsymbol{e_{d_i}}\}) \begin{bmatrix} d_1 \\ \vdots \\ d_P \end{bmatrix} \text{ (29)}$$

$j = 1, \dots, N$
$\mathrm{i} = 1, \dots, \mathrm{p}$
V is the vector of data measured at electrodes at a time instant, $\boldsymbol{G}$ is the gain matrix and vector $d_1, \dots, d_P$ contains the dipoles' magnitudes (currents) at a specified time instant.
For *N* electrodes, *p* dipoles and *T* discrete time samples we have:

$$\boldsymbol{V} = \boldsymbol{G}(\{\boldsymbol{r_j}, \boldsymbol{r}_{dip_i}, \boldsymbol{e_{d_i}}\}) \begin{bmatrix} d_{1,1} & \dots & d_{1,T} \\ \vdots & \ddots & \vdots \\ d_{p,1} & \dots & d_{p,T} \end{bmatrix} = \boldsymbol{G}(\{\boldsymbol{r_j}, \boldsymbol{r}_{dip_i}, \boldsymbol{e_{d_i}}\})\boldsymbol{D} \text{ (30)}$$

So, each column of matrix $\boldsymbol{V}$ is EEG at one time instant and each column of matrix $\boldsymbol{D}$ contains the dipoles' magnitudes at one time instant.
Generally a noise or perturbation matrix is added:
$\boldsymbol{V} = \boldsymbol{GD} + \boldsymbol{n}$ (31)
The potential field generated by a current dipole with moment $\boldsymbol{d} = d\boldsymbol{e_d}$ at position $\boldsymbol{r}_{dip}$ in an infinite homogeneous and isotropic (isotropic means same value of conductivity with change in direction in tissue) conductor with conductivity σ is:

$$V(\boldsymbol{r}, \boldsymbol{r}_{dip}, \boldsymbol{d}) = \frac{\boldsymbol{d}.(\boldsymbol{r} - \boldsymbol{r_{dip}})}{4\pi\sigma\|\boldsymbol{r} - \boldsymbol{r_{dip}}\|^3} \text{ (32)}$$

Where, $\boldsymbol{r}$ is the position on which the voltage is calculated.
For a dipole located at origin of coordinate and oriented along the z axis of the cartesian coordinate

$$V(\boldsymbol{r}, 0, d\boldsymbol{e}_z) = \frac{d.cos\theta}{4\pi\sigma r^2} \text{ (33)}$$

θ is the angle between the z axis and $\boldsymbol{r}$ and $r = \|\boldsymbol{r}\|$.

From eq. 32, it is also clear that potential V added with an arbitrary constant is also the solution of poisson's equation. So, a reference potential must be chosen. One can choose the reference electrode to be zero or opt for average reference

The spherical head model

The first volume conductor models of the human head consisted of a homogeneous sphere [8]. However it was soon noticed that the skull tissue had a conductivity which was significantly lower than the conductivity of scalp and brain tissue. Therefore the volume conductor model of the head needed further refinement and a three shell concentric spherical head model was introduced. In this model, the inner sphere represents the brain, the intermediate layer represents the skull and the outer layer is scalp. For this geometry a semi-analytical solution of Poisson's equation exists. The derivation is based on [9, 10]. Consider a dipole located on the z-axis and a scalp point P, located in the xz-plane, as illustrated in figure 12. The dipole components located in the xz-plane i.e. d_r the radial component and d_t the tangential component, are also shown in figure 12. Typical radius for scalp, skull, and brain are chosen. The component orthogonal to the xz-plane, does not contribute to the potential at scalp point P due to the fact that the zero potential plane of this component traverses P.

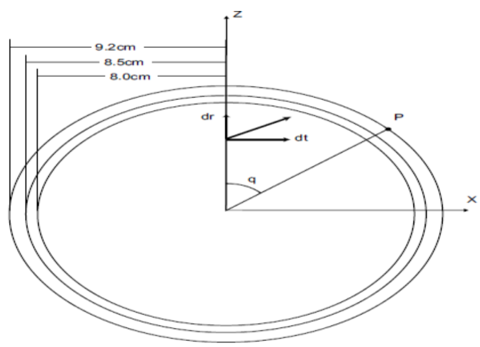

Fig. 12 **The three-shell concentric spherical head model**. The dipole is located on the z-axis and the potential is measured at scalp point P located in the xz-plane.

The potential V at scalp point P for the proposed dipole is given by [7]:

$$V = \frac{1}{4\pi S R^2}\sum_{i=1}^{\infty}\frac{X(2i+1)^3}{g_i(i+1)i}b^{i-1}[id_r P_i(cos\theta) + d_t P_i^1(cos\theta)], \quad (34)$$

$$g_i = [(i+1)X + i]\left[\frac{iX}{i+1} + 1\right] + (1-X)[(i+1)X + i]\left(f_1^{i_1} - f_2^{i_1}\right) - i(1-X)^2\left({f_1}/{f_2}\right)^{i_1}, \quad (35)$$

d_r is the radial component, (3 × 1-vector in meters),
d_t is the tangential component, (3 × 1-vector in meters),
R is the radius of the outer shell (meters),
S is the conductivity of scalp and brain tissue (Siemens/meter),
X is the ratio between the skull and soft tissue conductivity (unitless),
b is the relative distance of the dipole from the centre (unitless),
θ is the polar angle of the surface point see figure 12 (radians),
$P_i(.)$ is the Legendre polynomial,
$P_i^1(.)$is the associated Legendre polynomial,
i is an index,
i_1 equals $2i + 1$,
r_1 is the radius of the inner shell (in meters),
r_2 is the radius of the middle shell (in meters),
f_1 equals ${r_1}/{R}$ (unitless) and
f_2 equals ${r_2}/{R}$ (unitless)

The infinite series of equation (34) is often truncated to first 40 phrases (the reason: If the first 40 terms are used, the maximum scalp potential obtained with the truncated series, deviates less than 0.1% from the case where 100 terms are applied, for dipoles with a radial position smaller than 95% of the maximum brain radius).
This was a solution for spherical head model. But in real situation, the layers of head are not spherical and we need to use MRI for each subject and construct the volume conductor layers (scalp, skull, gray matter…) by the method of segmentation. Segmentation means each layer (scalp, skull, gray matter…) can be visualized by a triangulated mesh, which nodes of mesh are the locations for solving the poisson's equation. The 3 layer segmented parts of head (scalp, skull, brain) is shown in fig. 13.

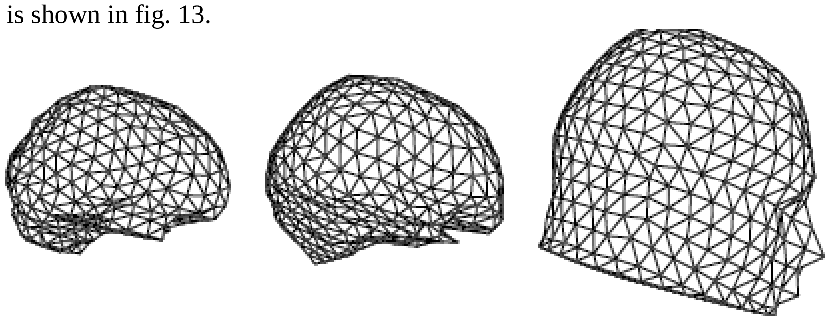

Fig. 13 **Example mesh of the human head used in BEM**. Triangulated surfaces of the brain, skull and scalp compartment used in BEM. The surfaces indicate the different interfaces of the human head: air-scalp, scalp-skull and skull-brain.

The boundary element method (BEM)

The boundary element method (BEM) is a numerical technique for calculating the surface potentials generated by current sources located in a piecewise homogeneous volume conductor. Although it restricts us to use only isotropic conductivities (conductivity doesn't change with direction in each segmented part (for example gray matter)), it is still widely used because of its low computational needs. As the name implies, this method is capable of providing a solution to a volume problem by calculating the potential values at the interfaces and boundary of the volume induced by a given current source (e.g. a dipole). The interfaces separate regions of differing conductivity within the volume, while the boundary is the outer surface separating the non-conducting air with the conducting volume. In practice, a head model is built from surfaces, each encapsulating a particular tissue. Typically, head models consist of 3 surfaces (boundary): brain-skull interface, skull-scalp interface and the outer surface. The regions between the interfaces are assumed to be homogeneous (constant conductivity) and isotropic conducting (conductivity doesn't change with direction in each segmented part or surface). To obtain a solution in such a piecewise homogenous volume, each interface is tesselated with small boundary elements.
The integral equations describing the potential $V(\mathbf{r})$ at any point $\mathbf{r}$ in a piecewise volume conductor V were described in [11-13]:

$$V(\boldsymbol{r}) = \frac{2\sigma_0}{\sigma_k^- + \sigma_k^+} V_0(\boldsymbol{r}) + \frac{1}{2\pi} \sum_{j=1}^{R} \frac{\sigma_j^- - \sigma_j^+}{\sigma_k^- + \sigma_k^+} \int_{\boldsymbol{r}' \in S_j} V(\boldsymbol{r}') \frac{\boldsymbol{r}' - \boldsymbol{r}}{\|\boldsymbol{r}' - \boldsymbol{r}\|^3} dS_j \quad (36)$$

σ_0 corresponds to the medium in which the dipole source is located (the brain).
$V_0(\boldsymbol{r})$ is the potential at $\boldsymbol{r}$ for an infinite medium with conductivity σ_0
σ_j^- and σ_j^+ are the conductivities of the, respectively, inner and outer compartments divided by the interface S_j
dS is a vector oriented orthogonal to a surface element and $\|dS\|$ the area of that surface element.
R is the number of interfaces in the volume which the integral is calculated on each interface surface.
Each interface S_k is digitized in N_{s_k} triangles (fig. 13) and in each triangle centre the potentials are calculated using eq. 36.
The integral over the surface S_k is transformed into a summation of integrals over tringles on that surface.
So, the potential values on surface S_k can be written as

$$V(\boldsymbol{r}) = \frac{2\sigma_0}{\sigma_r^- + \sigma_r^+} V_0(\boldsymbol{r}) + \frac{1}{2\pi} \sum_{k=1}^{R} \frac{\sigma_k^- - \sigma_k^+}{\sigma_r^- + \sigma_r^+} \sum_{j=1}^{N_{s_k}} \int_{\Delta_{s_{k,j}}} V(r') \frac{\boldsymbol{r}' - \boldsymbol{r}}{\|\boldsymbol{r}' - \boldsymbol{r}\|^3} dS_k \ (37)$$

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 $\tilde{V}^k(\boldsymbol{r})$ on surface s_k may be defined as a linear combination of N_{s_k}simple basis functions,

$$\widetilde{V^k}\ (\mathrm{r}) = \sum_{i=1}^{N_{s_k}} V_i^k h_i(\boldsymbol{r}) \quad (38)$$

The coefficients V_i^k represent unknown potentials on surface s_k whose values are determined by constraining $\tilde{V}(x)$ to satisfy eq. 37 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, $h_i(r)$, defined with the approach of "constant-potential" at every triangular element.

$$h_i(r) = \begin{cases} 1 & \boldsymbol{r} \in \Delta_i \\ 0 & \boldsymbol{r} \notin \Delta_i \end{cases} \quad (39)$$

Δ_i is the ith planar triangle on the tessellated surface.
The basis functions, $h_i(r)$, defined with the approach of "linear potential", is defined by

$$h_i(r) = \begin{cases} \frac{[r\, r_j r_k]}{[r_i r_j r_k]} & \boldsymbol{r} \in \Delta_{i(jk)} \\ 0 & \boldsymbol{r} \notin \Delta_{i(jk)} \end{cases} \quad (40)$$

$\boldsymbol{r_i}, \boldsymbol{r_j}, \boldsymbol{r_k}$ are the nodes of the triangle (positions of 3 nodes) and the triple scalar product is defined as $[\boldsymbol{r_i r_j r_k}] = \det(\boldsymbol{r_i}, \boldsymbol{r_j}, \boldsymbol{r_k})$. The notation $\Delta_{i(jk)}$ is used to indicate every triangle with nodes $\boldsymbol{r_i}, \boldsymbol{r_j}, \boldsymbol{r_k}$. The function $h_i(\boldsymbol{r})$ attains a value of unity at the *i*th vertex and drops linearly to zeros at the opposite edge of all triangles to which $\boldsymbol{r_i}$ is a vertex.
So, eq. 37 can be rewritten as

$$\boldsymbol{V}(r) = \frac{2\sigma_0}{\sigma_r^- + \sigma_r^+} V_0(\boldsymbol{r}) + \frac{1}{2\pi} \sum_{k=1}^{R} \frac{\sigma_k^- - \sigma_k^+}{\sigma_r^- + \sigma_r^+} \sum_{j=1}^{N_{s_k}} \sum_{i=1}^{N_{s_k}} V_i^k \int_{\Delta_{s_{k,j}}} h_i(\boldsymbol{r}) \frac{\boldsymbol{r' - r}}{\|\boldsymbol{r' - r}\|^3} dS_k \quad (41)$$

This equation can be transformed into a set of linear equations:

$$\boldsymbol{V} = \boldsymbol{BV} + \boldsymbol{V_0} \quad (42)$$

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. $\boldsymbol{B}$ 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 **B** is computationally intensive and there exist different approaches for their computation.
Barnard et al. [14] showed that eq. 42 has no unique solution. The proposed solution was to replace $\boldsymbol{B}$ by

$$\boldsymbol{C} = \boldsymbol{B} - \frac{\boldsymbol{1}}{\boldsymbol{N}} \boldsymbol{e}\boldsymbol{e}^{\boldsymbol{T}} \quad (43)$$

$\boldsymbol{e}$ is a vector with all its N (total number of unknowns) components equal one. So, we have

$$\boldsymbol{V} = \boldsymbol{CV} + \boldsymbol{V_0} \quad (44)$$

The eq. 44 has a unique solution which is the solution to the eq. 42. If I is the identity matrix (a M*M square matrix with value 1 in diagonal and zeros elsewhere), and $\boldsymbol{A} = \mathbf{I} - \mathbf{C}$, then eq. 44 can be written as

$$\boldsymbol{V} = \boldsymbol{A}^{-1} \boldsymbol{V_0} \quad (45)$$

This equation can be solved using direct or iterative solvers.
$\boldsymbol{V_0}$ is calculated from eq. 32, ($V(\boldsymbol{r}, \boldsymbol{r}_{dip}, \boldsymbol{d}) = \frac{\boldsymbol{d}.(r - \boldsymbol{r_{dip}})}{4\pi\sigma \|r - \boldsymbol{r_{dip}}\|^3}$), so $\boldsymbol{V_0}$ is proportional to dipole current source moment ($\boldsymbol{d} = d\boldsymbol{e_d}$ (with magnitude (or current) d and orientation $\boldsymbol{e_d}(\boldsymbol{x}, \boldsymbol{y}, \boldsymbol{z})$).) .
So, the scalp potential , $\boldsymbol{V}$**,** is proportional to dipole moment and the ratio ($\boldsymbol{A}^{-\boldsymbol{1}}$) is called the lead filed matrix.

Finite element method (FEM)

Finite element method (FEM) solves the forward problem for the whole volume by filling the whole head space using tetrahedrals as is shown in fig. 14. Recalling the boundary conditions, eq. 27-28, FEM solves the poisson's equation for whole head volume which also concludes boundaries (scalp, skull, gray matter) which was used in BEM.

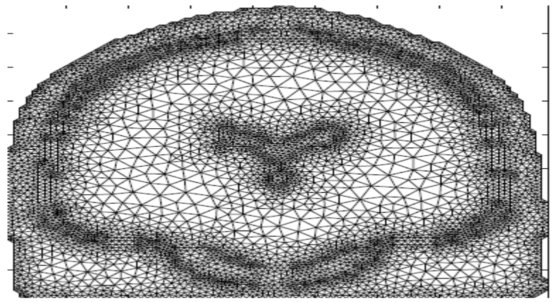

Fig. 14. **Example mesh in 2D used in FEM**. A digitization of the 2D coronal slice of the head. The 2D elements are the triangles. If shown 3D it was a tetrahedral.

The difference between the two methods for solving the forward problem is shown in table 1.

Table 1. A comparison of the two methods for solving Poisson's equation in a realistic head model is presented

	BEM	FEM
Position of computational points	surface	volume
Free choice of computational points	yes	yes
System matrix	full	sparse
Solvers	direct	iterative
Number of compartments	small	large
Requires tesselation	yes	yes
Handles anisotropy	no	yes

Implementation

One way for the implementation of forward problem with boundary element method (BEM) is to use the MATLAB software package OpenMEEG [5]. The geometrical model of surface meshes (fig.6 and fig.13) representing tissue interfaces must be provided to OpenMEEG, since OpenMEEG does not perform any segmentation or meshing. OpenMEEG computes the electric potential and the normal dipole current on each interface between two homogeneous tissues, due to electric sources within the brain. EEG sensors are electrodes, modeled in OpenMEEG as discrete positions on the scalp at which the potential can be measured (infinite impedance assumption for electrodes). On these sensors, OpenMEEG computes the EEG leadfield, representing the linear relationship between source amplitude (for fixed desired position and orientation) and sensor values. In fact, the linear eq.8 is going to be solved in OpenMEEG, due to the assumption that the air has low conductivity hence there is no current on the air-scalp interface ($\boldsymbol{J} = \boldsymbol{0}$ in eq.8). The outputs of the OpenMEEG calculations with the mentioned inputs (source space and electrode space definition and head model (surface mesh or segmeneted parts) will be the leadfield matrix, which is the output of solving linear relation from source space dipole current normal to each vertex on interface ($\sigma \frac{\partial v}{\partial n} \vec{n}$, σ is conductivity and $\vec{n}$ is the normal vector on each vertex of the interface) to sensor space potential (v). The conductivities of the 3 homogeneous volumes are set to 1, 1/80 (skull) and 1 (semens/m). The link for downloading the necessaries for implementing OpenMEEG is OpenMEEGlink.

There are also other software projects have the ability to solve the M/EEG forward problems. MNE, BrainStorm [15], EEGLAB (via the NFT Toolbox) [16], Fieldtrip for FEM and BEM[17] [18], Simbio (for FEM method) [6], NEUROFEM for BEM and FEM [19][20][21] and SPM, which shares with Fieldtrip the same M/EEG forward solvers.

Inverse problem

The first step to solve the inverse problem is lead field calculation for any source location. The inverse problem methods are divided in to groups:

1) spatio-temporal source tracking with an iterative approach based on prior information of sources (location and orientation) [22]: in this case first some locations and directions are selected for dipoles, then the leadfield transfer matrix is calculated. So, by the selected desired source locations it is possible to calculate EEG (forward model). If we have the real EEG data, we can calculate the error of data from model and the real EEG data. There are some methods [22] to update the predefined source features (locations and orientations) and again computing forward model and error with respect to real EEG data and repeat to achieve the minimum error. These methods are called iterative approaches. As the forward model is written as linear equation matrix form, so the number of electrodes (N) should be more than or equal number of sources (M) to be able to solve this problem. Hence, we have a limitation in number of dipole sources (M<=N). There are solutions based subspace and Principle Component Analysis (PCA) to solve the inverse problem [22]. These methods are solved in three common spatio-temporal dipole models: i) unconstrained (moving or rotating) dipoles, ii) dipoles with a fixed location (rotating or regional), iii) dipoles with a fixed orientation and location

2) The second groups of methods are optimization methods to find the best weight matrix ($\boldsymbol{w_d}$) for EEG based on leadfield matrix, in order to extract the accurate source signals for each desired location on the brain. These are based on minimization of the difference power between EEG ($\boldsymbol{d}$) and the synthetic EEG by model, i.e.

$\min(\boldsymbol{Lj}-\boldsymbol{d})^t\boldsymbol{w_d}(\boldsymbol{Lj}-\boldsymbol{d})$, where $\boldsymbol{L}$ is the leadfield, $\boldsymbol{j}$ is the current moment, $\boldsymbol{d}$ is EEG, and $\boldsymbol{w_d}$ is the weight matrix**.** $\boldsymbol{w_d}$ **should be find to minimize the cost function.**

There are methods called electric source imaging [23], which extract the best weight matrix for EEG in order to get the minimum difference power between real EEG and EEG by synthetic sources. These methods can extract magnitude of source current, which is always positive or source potential field (potentials generated by a source placed in a voxel as we know the relation between current source and electric field $j = \sigma E = \sigma \nabla V$), so potential field can be positive and negative. By potential fields or magnitude of currents it is possible to make a color mapping of source activities over the brain, hence source localization. There are some methods like ELECTRA (source local field potentials (LFPs) estimator) and Laura (source current density estimator) [23], Loreta [24] for this problem. These methods don't have any limitation on number of dipole current sources, hence it is possible to extract source signals from each location on the brain and then find the best source location from the whole sources. Eq. 19-22 in this document gives an idea for optimum source orientation detection and source localization. The source current estimation and mapping of source local filed potentials are shown in fig. 15. It is possible to localize the source activity by color mapping.

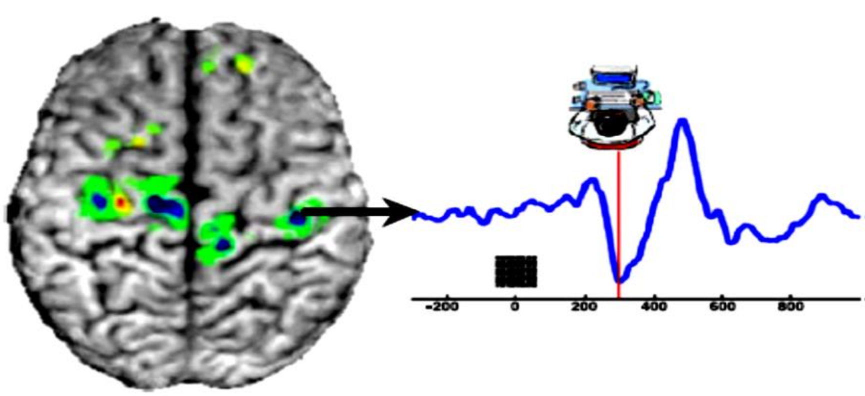

Fig. 15 mapping the source activities by allocating color to each source activity (potential fields or amplitude of currents), a view of current source extraction from a specified brain location is also shown.

The paper "Comparison of Algorithms for the Localization of Focal Sources: Evaluation with Simulated Data and Analysis of Experimental Data" [25] compares methods of inverse problem with the application of focal source localization.

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