I. EEG_inverse_methods

$X(3num_{source} * 1)$: $dipole\ current\ source\ vector(to\ be\ detected\ in\ inverse\ problem)$

$L(num_{elec} * 3num_{source})$: **Lead-field matrix**

EEG($num_{elec} * 1$): EEG vector at each time sample

Optimization functions:

$Min\ \ F_\alpha(X) = \|LX - EEG\|^2 + \alpha\|WX\|^2$ **for METHODS: MNE, WMNE, LORETA →** $X = (L'L + \alpha\, W'W)^{-1}L'\ EEG$ [1][4]

$Min\ \ F_\alpha(X) = \|LX - EEG\|^2 + \alpha X'W_jX$ **for METHODS: LAURA→** $X = W_jL'(LW_j{}^{-1}L'\alpha I)^{-1}EEG$ **[2][4]**

Source detection: calculating the magnitude (modulus) of each source after X calculation, Magnitude ($\vec{a}$) = $\sqrt[2]{a_x^2 + a_y^2 + a_z^2}$

Source localization: Comparing magnitudes and selecting sources locations with magnitudes more than a threshold

Distance Error: The vector from one detected source (by algorithm) to one real source location is $\vec{a} = location_{source} - location_{real}$ **and the** $distance\ = \sqrt[2]{(a)_x^2 + a_y^2 + a_z^2}$

Usually real sources locations are concentrated: so distance from one detected source to all real source locations can be computed and the $minimum\_distance$ **is source distance to real region of source**

→ for each detected source location we consider if

$predefiend\_minimum\_range(mm) < minimum\_distance(mm) < predefined\_maximum\_range(mm)$

$Grid\_unit$ **(mm): the** $minimum\_distance$ **between two source points defined in a grid(mm)**

$Minimum\_distance\_in\_grid\_unit = minimum - distance(mm)/Grid\_unit(mm)$

➢

$$predefiend\_minimum\_range(mm)/Grid\_unit(mm) \quad < minimum\_distance(mm)/Grid\_unit(mm)$$

$$AND$$

$$minimum\_distance(mm)/Grid\_unit(mm) < predefined\_maximum\_range(mm)/Grid\_unit(mm)$$

We consider whether $minimum\_distance(mm)/Grid\_unit(mm)$ **for each detected source location is in range**

(0-1 $grid\_unit$), (1-2 $grid\_unit$), (2-3 $grid\_unit$), (3- $grid\_unit$)….

Hence, the percent of detected sources with error in each $grid\_unit$ range is calculated.

A Method with maximum percent of sources in minimum distance error range ($grid\_unit$) will have the best performance.

Max. Error in grid unit: The maximum distance among all $minimum\_distances\_in\_grid\_unit$ which is preferred to be minimum.

Table 1: methods and source localization outputs [1]

method	weight matrix (W)	Output dipole current sources (X)	Percent of sources with error range in grid unit (gridunit=1.3mm)	Max. Error in grid unit	speed
MNE **(Minimum norm estimate)**	**W=I (identity matrix)**	$X = (L'L + \alpha\, W'W)^{-1} L'\, EEG$	**(0-1 gridunit) 13.42%** **(1-2 gridunit) 47.49%** **(2-3 gridunit) 8.85%** **(3-4gridunit) 12.11%** **(4-5gridunit) 6.24%** **(5-6gridunit) 1.88%**	**5.48** **gridunit**	**-** **not evaluated**
WMNE **(weighted Minimum norm estimate)**	**W= B** $\mathbf{B} = \mathbf{diag}(\mathbf{norm}(\mathbf{columns}\ (\mathbf{L})))$ Diag(…): diagonal matrix with non zero components in diagonal, each component is norm of one column of L	$X = (L'L + \alpha\, W'W)^{-1} L'\, EEG$	**(0-1gridunit) 14.24%** **(1-2 gridunit) 47.33%** **(2-3 gridunit) 19.71%** **(3-4gridunit) 13.99%** **(4-5gridunit) 4.24%** **(5-6gridunit) 0.53%**	**5.2** **gridunit**	**-**
LORETA **(Low resolution electromagnetic tomography)**	**W=ΔB,** Δ: **laplacian operator** $\mathbf{B} = \mathbf{diag}(\mathbf{norm}(\mathbf{columns}\ (\mathbf{L})))$ Diag(…): diagonal matrix with non zero components in diagonal, each component is norm of one column of L **laplacian of $\mathbf{B_i}$ for each source location:** $\frac{1}{d}\left(6\mathbf{B_i} - \sum_{i=1}^{p} \mathrm{B_p}\right),$ $\forall$p under constraint $\lVert \mathrm{r_i} - \mathrm{r_p} \rVert = \mathrm{d}$ d: minimum distance between two gridpints	$X = (L'L + \alpha\, W'W)^{-1} L'\, EEG$	**(0-1gridunit) 20.52%** **(1-2 gridunit) 75.97%** **(2-3 gridunit) 3.47%** **(3-4gridunit) 0.04%**	**3.16** **gridunit**	**-**
LAURA **(local autoregressive averages)**	$\boldsymbol{W_j = (W_m A)'(W_m A)^\wedge I_3}$ **^:kronecker matrix product (each row-element in first matrix multiplied by all row-elements of other matrix)** $\boldsymbol{W_m}$ = diag(mean(norm(3_{columns}(L)))) Diag(…): diagonal matrix with non zero components in diagonal, each component is mean(average) of norm of 3 column of L $\boldsymbol{A}$: $\boldsymbol{distance\ matrix}$, **for hexahedral grid** $\boldsymbol{A_{ii}}$ **=26/num_nearestneighbours** $\boldsymbol{(\sum_{K=1:\mathrm{num\_nearestneighbours}} {d_{ki}}^{-3})}$ $\boldsymbol{A_{ki} = {d_{ki}}^{-3}}$ $\boldsymbol{A}$ **is defined based on Physiological constraints from forward problem (based poisson's equation)** **Reason:** $\boldsymbol{V_o(r) = \frac{d.(r - r_{dip})}{4\pi\sigma \lVert r - r_{dip} \rVert^3} = \frac{\lVert d \rVert \cos(\theta)}{4\pi\sigma \lVert r - r_{dip} \rVert^2}}$ **d=J** $\boldsymbol{dipole\ current}$, $\boldsymbol{J = \sigma E = \sigma(-\nabla V)}$, $\boldsymbol{\nabla}$: **gradient**	$\boldsymbol{X = W_j L' (L {W_j}^{-1} L' \alpha I)^{-1} EEG}$	**(0-1gridunit) 32.35%** **(1-2 gridunit) 63.24%** **(2-3 gridunit) 4.41%** **(3-4gridunit) -**	**2.45** **gridunit**	**-**

	$J\alpha\frac{1}{\|\hat{r}\|^3}$, $\hat{r}$=$(r-r_{dip})$, **in head volume J attenuates with power 3 of distance to source**				
EPIFOCUS	***T=L*W*** ***L:leadfield matrix*** **W= B** $\mathbf{B} = \mathbf{diag}(\mathbf{1/norm}(\mathbf{columns}\ (\mathbf{L})))$ Diag(...): diagonal matrix with non zero components in diagonal, each component is 1/norm of one column of L $$G = \begin{bmatrix} T_1{}^{\dagger} \\ T_2{}^{\dagger} \\ \dots \\ T_{np}{}^{\dagger} \end{bmatrix}$$ $T_i^{\dagger}$: *pseudo inverse of each three columns of T* $$T_1{}^{\dagger} = \left(T_1{}^{T} T_1\right)^{-1} T_1{}^{T}$$ **The idea for dividing by norm: reducing the condition number (explained in part II) of the inverse matrix, which leads better source reconstruction** **The total idea: based on subspace reconstructions of a matrix and lowering condition number**	***X=G*EEG***	**(0-1gridunit) 94.94%** **(1-2 gridunit 5.06%**	**1 gridunit**	**-**

- **LAURA has the minimum error, since using Physiological constraints from forward problem (based poisson's equation) for making Weight matrix (W) and is used because of low error in source detection [4].**
- **EPIFOCUS has best results for focal source reconstruction and is widely used in clinic [6].**

II. PROVE EEG_inverse_methods

- **Inverse localization problems based minimum norm regularization method[3][5]**

$$\boldsymbol{LX} = \boldsymbol{EEG} \; (1),$$

- forward problem is well-posed that means there is a unique solvable solution from sources to sensors based physical laws

$\boldsymbol{L}: \boldsymbol{N_{elec}} * \boldsymbol{3N_{source}}$ $leadfield\ matrix$,

$\boldsymbol{X}: \boldsymbol{3N_{source}} * \boldsymbol{T}$ $dipole\ current\ sources, \boldsymbol{T}: time\ samples$

$\boldsymbol{EEG}: \boldsymbol{N_{elec}} * \boldsymbol{T}$ data, generally noisy data

The inverse problem is:

$$\boldsymbol{X} = \boldsymbol{L}^{\dagger}\ \boldsymbol{EEG} \; (2)$$

Where, $\dagger = pseudo\ inverse,\ \ L^{\dagger} = (L'L)^{-1}L'$, $': transpose$

- Inverse problem is illposed that means there is not a unique solution for sources localization. Generally we don't know where are sources, so we define a set of distributed dipole sources, hence we use leadfields of many locations in $\boldsymbol{L}^{\dagger}$ and seek $\boldsymbol{X}$ which better minimizes ($\|LX - EEG\|^2$).
- In Eq. (2), any small change in EEG may cause a large change in $\boldsymbol{X}$, (reason: eigenvalues / singular values of $\boldsymbol{L}^{\dagger}$ are largest in the reverse mapping where they were smallest in the forward mapping, high Eigen value causes discontinuous change in X with a little change in EEG) [3]. hence discontinuity occurs in solution $\boldsymbol{X}$ which causes false source reconstruction. Eq. 2 is called an ill-posed exact solution for $\boldsymbol{X}$.
- **So, we seek for a best approximate well-posed solver for $\boldsymbol{X}$ to avoid discontinuity.**

We can write Eq. (2) in the following form:

$\boldsymbol{L}'\ \boldsymbol{EEG} = \boldsymbol{L}'\boldsymbol{LX}$ (3) , $': \boldsymbol{transpose}$

condition number: a number which shows how much $\boldsymbol{X}$ changes with respect to changes in $\boldsymbol{EEG}$. Low condition number is desired.

condition number for coefficient of X in Eq. (3) is:

$K(\boldsymbol{L}'\boldsymbol{L}) = \|(\boldsymbol{L}'\boldsymbol{L})\|\|(\boldsymbol{L}'\boldsymbol{L})^{-1}\| = \max(\mathrm{eig}(\boldsymbol{L}'\boldsymbol{L}))/\min(\mathrm{eig}(\boldsymbol{L}'\boldsymbol{L}))$, eig: eigen value

‖ ‖ is norm 2 of a matrix, root of sum of square of matrix components

eig($\boldsymbol{L'L}$) is a vector containing eigen values of $\boldsymbol{L'L}$, $\boldsymbol{K(L') = K(L), K(L'\,L) = K(L)^2}$

$\boldsymbol{K(L'\,L)}$ is very high, the solution to minimize condition number, is to add with identity matrix with coefficient α, i.e. $\boldsymbol{L'\,L + \alpha\, I}$, called tikhonov regularization, So $\boldsymbol{L'\,EEG = (L'L + \alpha\, I)X}$ (4),

- **$\boldsymbol{X = (L'L + \alpha\, I)^{-1}L'\,EEG}$ (5), is the well-posed approximate regularized minimum norm inverse solution.**
- Why we say minimum norm? Eq. (5) is equivalent to the output for the following optimization problem: $\boldsymbol{Min\ \ F_\alpha(X) = \|LX - EEG\,\|^2 + \alpha\|X\|^2}$ (6), which $\boldsymbol{X}$ is achieved by derivative $F_\alpha(\boldsymbol{X})$ with respect to $\boldsymbol{X}$ and $F_\alpha(\boldsymbol{X}) = 0$. $\boldsymbol{F_\alpha(X) = (LX - EEG\,)(LX - EEG)' + \alpha XX'}$
  $\frac{\partial \boldsymbol{F_\alpha(X)}}{\partial X} = (L'L + L'L)X - 2L'EEG + 2\alpha X = 0, \rightarrow X = (L'L + \alpha\, I)^{-1}L'\,EEG$ as in Eq.(5). **https://en.wikipedia.org/wiki/Matrix_calculus**
- **General form of minimum norm optimization is $\boldsymbol{Min\ \ F_\alpha(X) = \|LX - EEG\,\|^2 + \alpha\|WX\|^2}$ (7)**

  $\boldsymbol{X = (L'L + \alpha\, W'W)^{-1}L'\,EEG}$ (8)

- **To demonstrate effect of regularization on condition number by singular value decomposition (SVD)** $\boldsymbol{X = (L'L + \alpha\, I)^{-1}L'\,EEG}$,

We write singular value decomposition (SVD) of L.

$\boldsymbol{L = U\delta V'}$ **with** $\boldsymbol{\delta = diagonal\ matrix\ of\ singular\ values\ \delta_{ii}}$

$\boldsymbol{X = VDU'\,EEG}$ **with**

$\boldsymbol{D = diagonal\ matrix\ with\ elements\ \frac{\delta_i}{{\delta_i}^2 + \alpha^2}}$ **, so, decreasing the elements, form $\boldsymbol{\delta_i\ to\ elements\ in\ D}$, means decreasing the Eigen values or condition number. Hence, continuous well-posed inverse problem solver is achieved.**

- **Writing general form:** $X = (L'L + \alpha\, W'W)^{-1}L'\,EEG$

writing in SVD form we have:

$\boldsymbol{X = VDU'\,EEG}$ **Writing x in other form:** $\boldsymbol{= \sum_{i=1}^{q} \frac{\delta_i}{\delta_i^2 + \alpha^2}\, U_i'EEG\, V_i}$ **,** $\boldsymbol{q = rank\ of\ l}$[1] **[3][5]**

$\boldsymbol{D = diagonal\ matrix\ with\ elements\ \frac{\delta_i}{{\delta_i}^2 + \alpha^2\ \ ^2}}$

- $^{\boldsymbol{2}}$ **is related to** $W'W$, if W is selected a diagonal matrix, the elements in W, reduces more the inverse matrix condition number (reduces Eigen values). Different W leads different methods. Enhancing W leads better spatial resolution in source localization results.

One choice of W: **diag(norm(columns (L)))** **(WMNE method)**

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[1] **rank: number of rows of a matrix that are independent of each other, each independent row is not a linear combination of other rows**

$Diag(\dots)$: **diagonal matrix with non zero components in diagonal, each component is norm of one column of L**

- Conceptual: each inverse matrix has attenuation for each source location, it may attenuate some locations more, hence missing some locations of source. Normalization compensates for this attenuation by enhancing the condition number as above [4].

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