SUSTech
Southern University of Science and Technology

神经计算与控制实验室
Neural Computing & Control Lab

Brain Intelligence and Artificial Intelligence

人脑智能与机器智能

Lecture 17 - EEG source localization

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Lecture 17 – EEG source localization

- Definition of EEG source localization problem
- Problem characteristics of EEG source localization
- Numerical methods with mathematical constraints
  - Instantaneous solvers with sparse/non-sparse priors
  - Time block solvers
- Data-driven methods with anatomical and physiological constraints
  - Deep neural networks with simulated dataset biological constraints
  - Generative Model with meta-fMRI Priors

AI能做什么？

在CV和NLP领域：

1）分类

2）回归

3）生成：VAE, GAN, diffusion

4）重构：BERT, MAE

5）时序预测(自回归)：GPT

6）语言大模型：LLMs

7）多模态大模型：MLLMs

AI能为脑科学做什么？

在CV和NLP领域：	在脑科学领域：
1）分类 →	1）脑疾病分类与诊断…
2）回归 →	2）疾病程度回归、预后效果回归…
3）生成 →	3）神经数据增广、认知实验stimuli生成…
4）重构 →	4）EEG超分辨、sEEG补齐、fMRI时间插值
5）时序预测 →	5）预测神经活动、预测癫痫发作
6）语言大模型 →	6）脑电基础模型 (EEG foundation model)
7）多模态大模型 →	7）多模态神经信号基础模型

AI能为脑科学做什么？

在CV和NLP领域：

1）分类 → 1）脑疾病分类与诊断…

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5）时序预测 → 5）预测神经活动、预测癫痫发作

6）语言大模型 → 6）脑电基础模型 (EEG foundation model)

7）多模态大模型 → 7）多模态神经信号基础模型

在脑科学领域：（右列见上）

AI在神经信号处理中的**基本步骤**

1. 定义任务
2. 找到合适的数据集（至少2个）
3. 提出AI模型：模型结构、损失函数
4. 训练AI模型：数据驱动
5. 性能测试：各种metrics
6. 稳定性：多个datasets，跨被试或OOD数据的泛化
7. 可解释性分析：ablation解释AI模型的各个模块、表征分析

How do we know what is happening **inside** the brain through observations from **outside** of the brain?

EEG source-level analysis

- Forward problem (head model)
- Inverse problem (source reconstruction)

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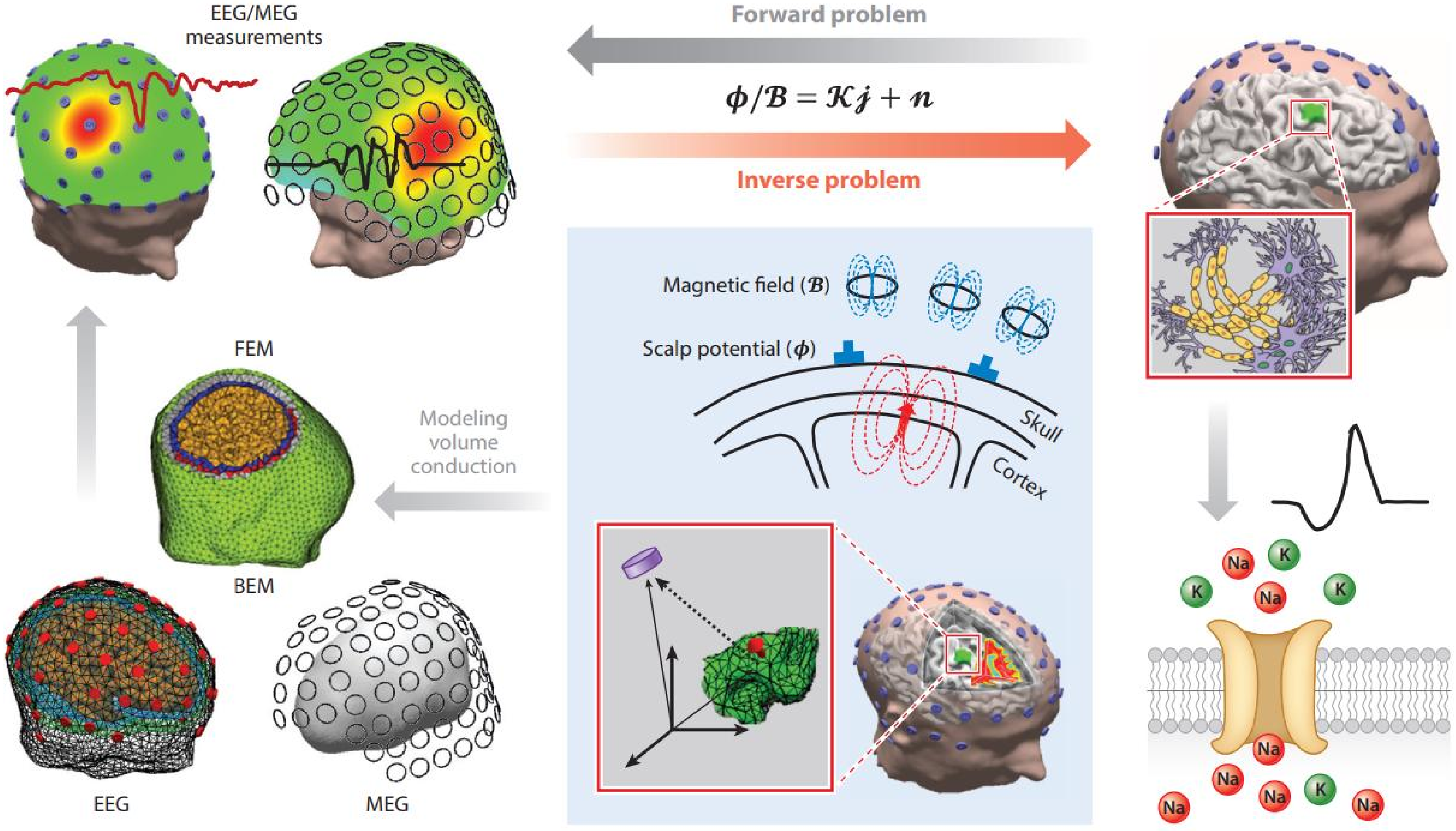
Brain signals at sensor / source level



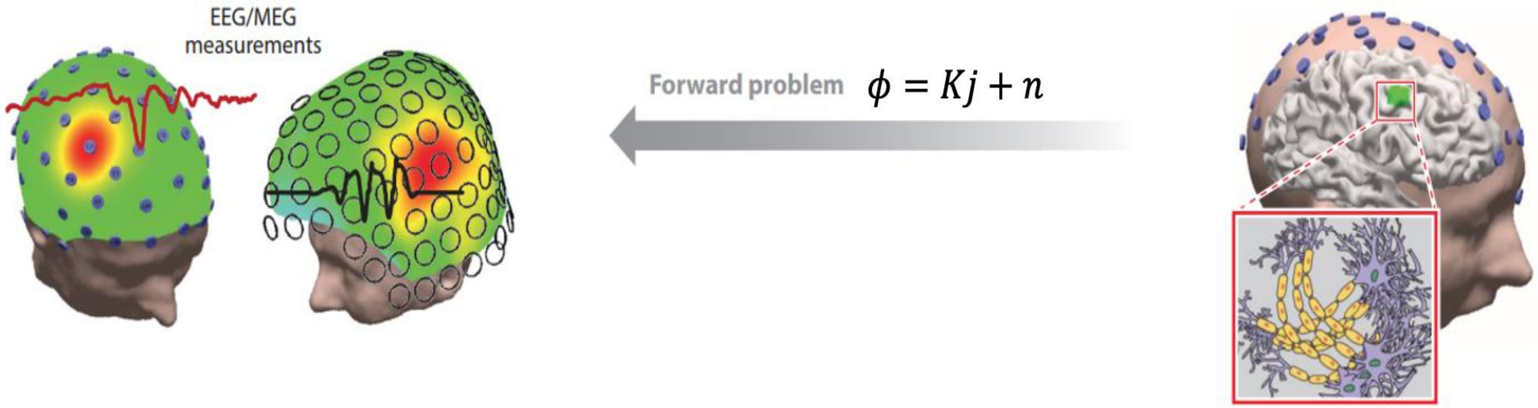
He et al., Annu. Rev. Biomed. Eng. (2018)

EEG Forward problem

In EEG/MEG source localization, this forward problem can be formulated as:

$$\phi = Kj + n_{\phi}$$

$\phi \in \mathbb{R}^{m \times T}$ containing measurements from **m** sensors
$j \in \mathbb{R}^{n \times T}$ denoting the unknown amplitudes of **n** current sources
$K \in \mathbb{R}^{\mathrm{m} \times n}$ is the lead-field matrix representing the mapping from currents to EEG/MEG signals



He et al., Annu. Rev. Biomed. Eng. (2018)

EEG Inverse problem

To reconstruct a mapping function: $\mathcal{K}_{\Theta}^{\dagger}: Scalp \rightarrow Source$ satisfying the **pseudo-inverse** property:

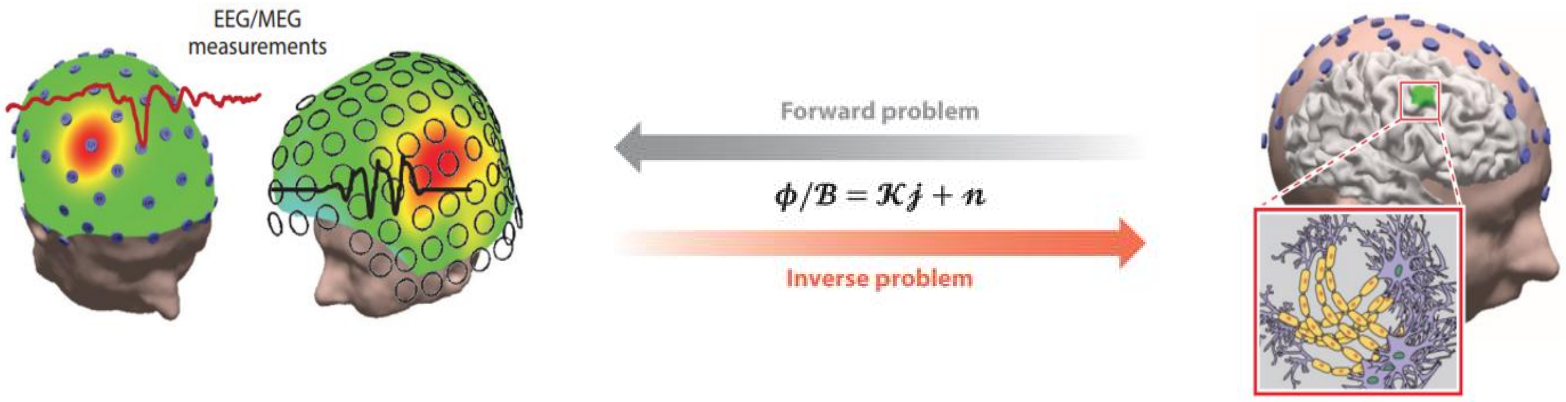
$$\mathcal{K}_{\Theta}^{\dagger}(\phi) \approx j_{true}$$

The corresponding loss function:

$$L = \arg\max_{j} P\,(\Phi | j, K) P(j)$$

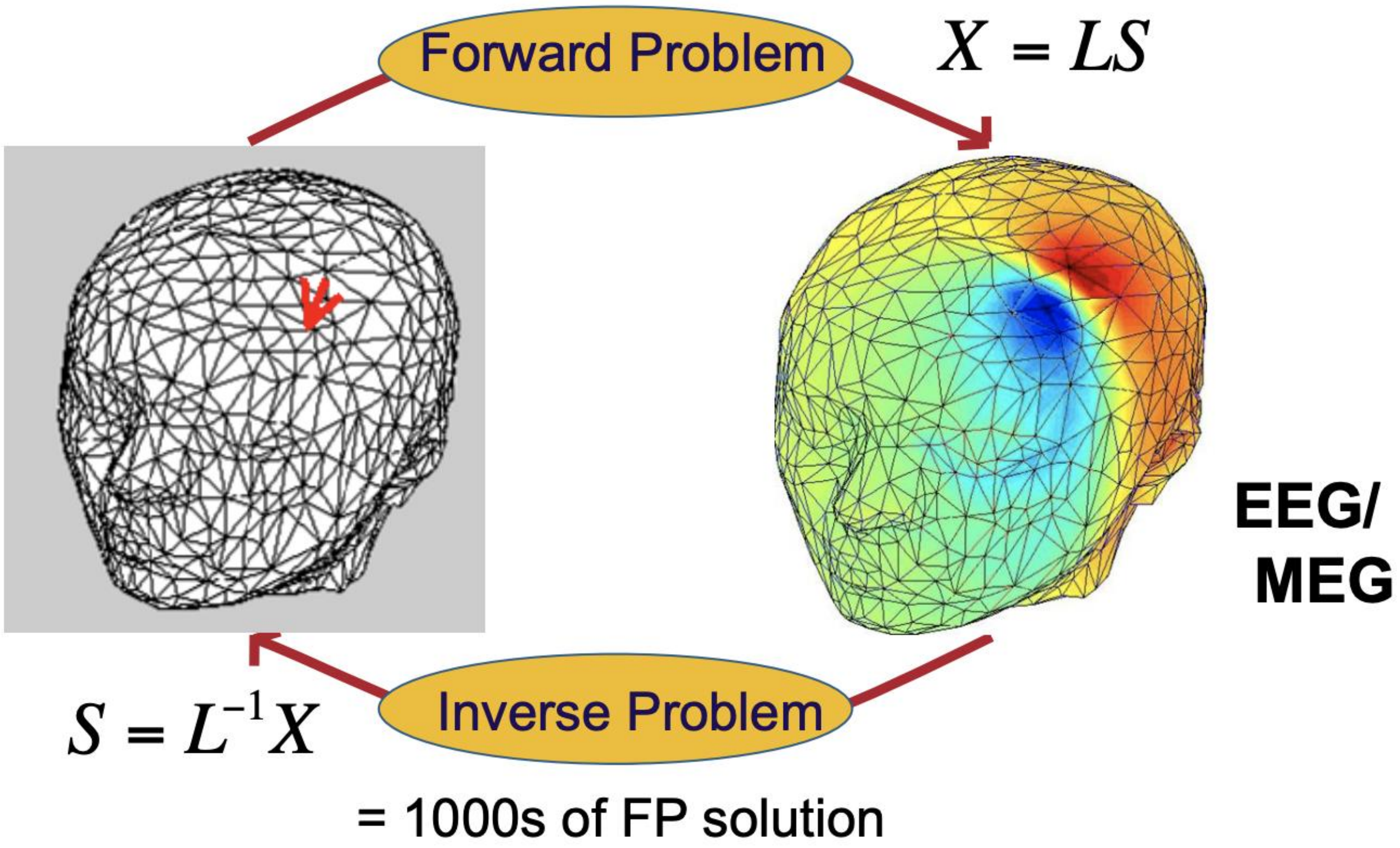
$$= \arg\max_{j} \frac{1}{2} \|\phi - Kj\|_{C}^{2} + R(j)$$

$R(j)$ is the penalty or regularization term, and C is noise covariance matrix.



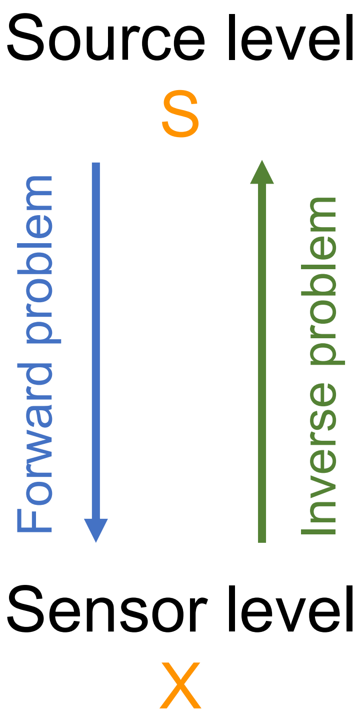
He et al., Annu. Rev. Biomed. Eng. (2018)

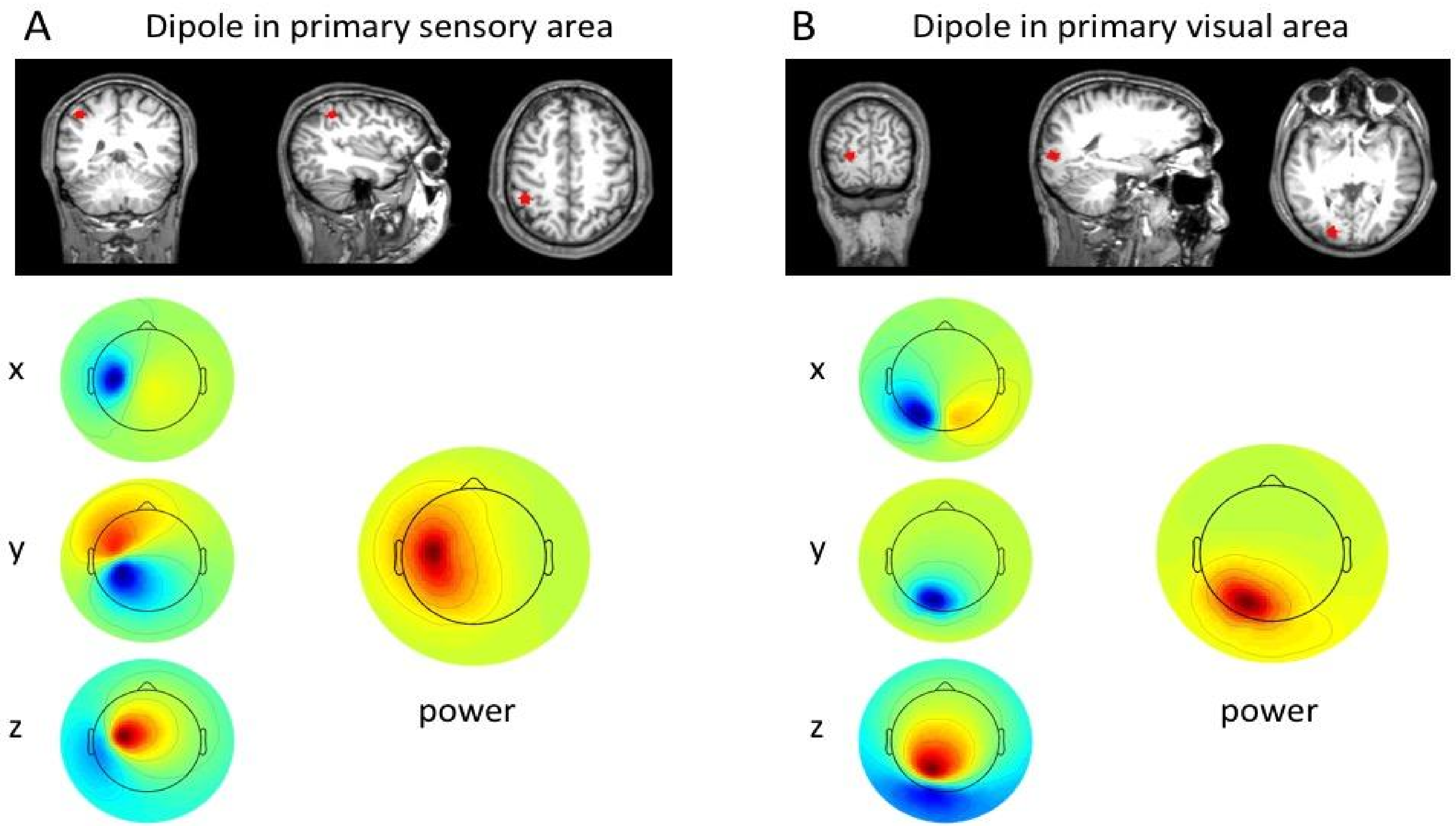
EEG Source Analysis



Forward Solution and Inverse Problem

Head model: bridging sensor/source levels





Forward Problem → Inverse Problem

$X = LS$ $\quad\quad$ $S = L^{-1}X$

Observations

Sensor Signal (X)

[M * T] dimension

&

Head model

Leadfield Matrix (L)

[M * 3N] dimension

→

Estimated source distribution

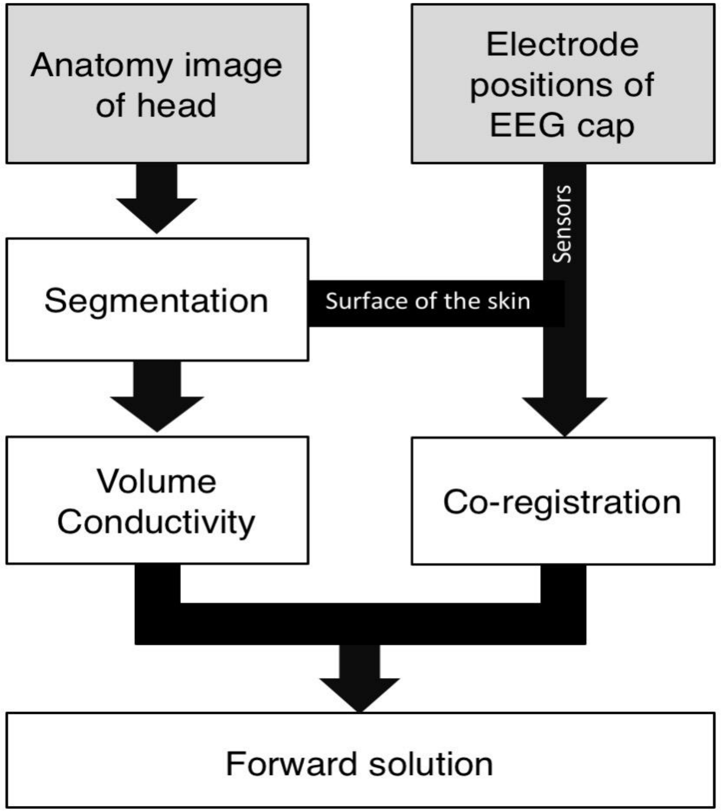
Source Signal (S)

[3N * T] dimension

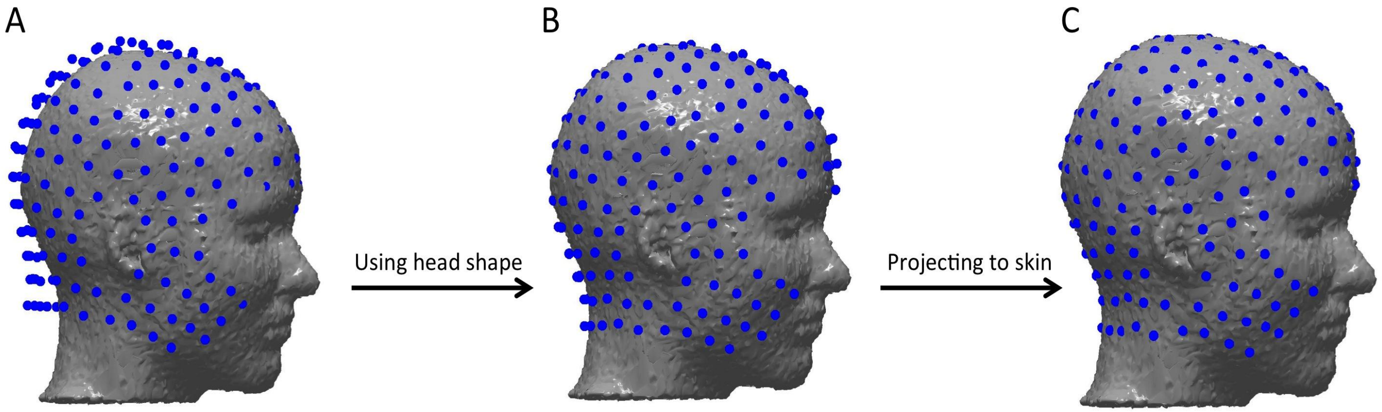
1, Solve forward problem, to obtain the leadfield matrix L.

The solution of the forward problem is the leadfield matrix L.

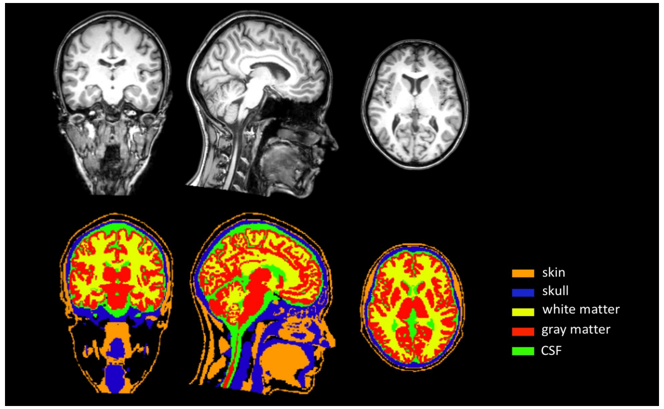
Pipeline for the solution of forward problem

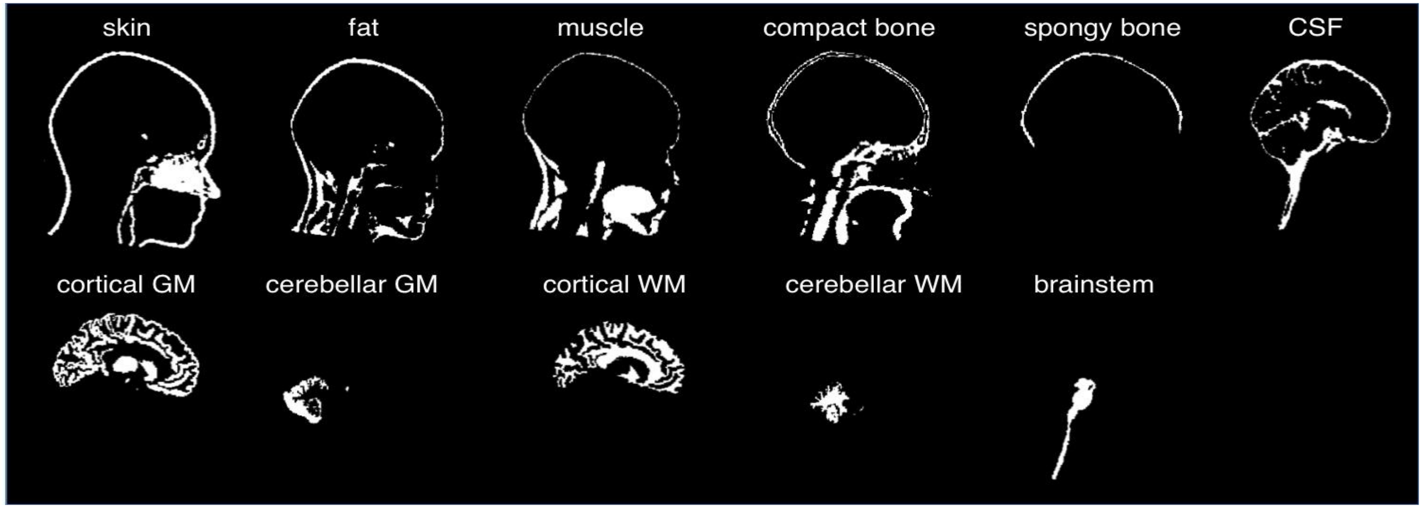


EEG Electrodes co-registration： 电极配准到头皮



Segmentation
图像分割





Head volume conductivity

A realistic head model requires the definition of multiple tissues of the head, each characterized by a specific conductivity value.

However, the conductivity value is usually measured **in vitro** (体外的).

How to estimate the head conductivity **in vivo** (在活体的) is still a technical issue!

Conductivity values of different tissues

Tissue name	Conductivity (S/m)
Skin	0.4348
compact bone	0.0063
spongy bone	0.0400
CSF	1.5385
cortical gray matter	0.3333
cerebellar gray matter	0.2564
cortical white matter	0.1429
cerebellar white matter	0.1099
brainstem	0.1538
eyes	0.5000
muscle	0.1000
fat	0.0400

During the last two decades, researchers have tried to solve **Poisson's equation** in a realistically shaped head model obtained from 3D medical images, which requires **numerical methods**.

Warning: math heavy!!!

Poisson's equation $\nabla \cdot \mathbf{J} = I_m.$

Ohm's law $\mathbf{J} = \sigma \mathbf{E},$

$\mathbf{E} = -\nabla V.$

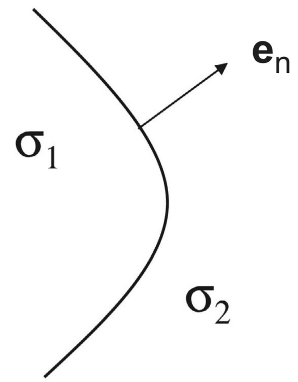
$$\sigma = \begin{bmatrix} \sigma_{11} & \sigma_{12} & \sigma_{13} \\ \sigma_{12} & \sigma_{22} & \sigma_{23} \\ \sigma_{13} & \sigma_{23} & \sigma_{33} \end{bmatrix}$$

- **J(x, y, z):** current density with the unit *A/m2*
- **Im**: the current source density with the unit *A/m3*
- **sigma**: position dependent conductivity tensor with units *A/*(*Vm*) = *S/m*
- **E**: the electric field with the unit *V/m*
- **V**: the scalar potential field with unit volt

$$\nabla \cdot (\sigma \nabla (V)) = -I_m$$

$$\boxed{\nabla \cdot (\sigma \nabla (V)) = -I\delta(\mathbf{r} - \mathbf{r}_2) + I\delta(\mathbf{r} - \mathbf{r}_1)}$$

$$\sigma_{11}\frac{\partial^2 V}{\partial x^2} + \sigma_{22}\frac{\partial^2 V}{\partial y^2} + \sigma_{33}\frac{\partial^2 V}{\partial z^2} + 2\left(\sigma_{12}\frac{\partial^2 V}{\partial x \partial y} + \sigma_{13}\frac{\partial^2 V}{\partial x \partial z} + \sigma_{23}\frac{\partial^2 V}{\partial y \partial z}\right)$$
$$+\left(\frac{\partial \sigma 11}{\partial x} + \frac{\partial \sigma 12}{\partial y} + \frac{\partial \sigma 13}{\partial z}\right)\frac{\partial V}{\partial x} + \left(\frac{\partial \sigma 12}{\partial x} + \frac{\partial \sigma 22}{\partial y} + \frac{\partial \sigma 23}{\partial z}\right)\frac{\partial V}{\partial y} + \left(\frac{\partial \sigma 13}{\partial x} + \frac{\partial \sigma 23}{\partial y} + \frac{\partial \sigma 33}{\partial z}\right)\frac{\partial V}{\partial z} =$$
$$-I\delta(x - x_2)\delta(y - y_2)\delta(z - z_2) + I\delta(x - x_1)\delta(y - y_1)\delta(z - z_1).$$



Boundary condition at two compartments

$$\mathbf{J}_1 \cdot \mathbf{e}_n = \mathbf{J}_2 \cdot \mathbf{e}_n,$$
$$(\sigma_1 \nabla V_1) \cdot \mathbf{e}_n = (\sigma_2 \nabla V_2) \cdot \mathbf{e}_n,$$

Boundary condition at the surface

$$\mathbf{J}_1 \cdot \mathbf{e}_n = 0,$$
$$(\sigma_1 \cdot \nabla V_1) \cdot \mathbf{e}_n = 0.$$

Hallez et al (2007) Review on solving the forward problem in EEG source analysis

Methods to solve forward problem,

- Boundary element method (BEM)
- Finite element method (FEM)
- Finite difference method (FDM)

Leadfield Matrix (L)

[M * 3N] dimension

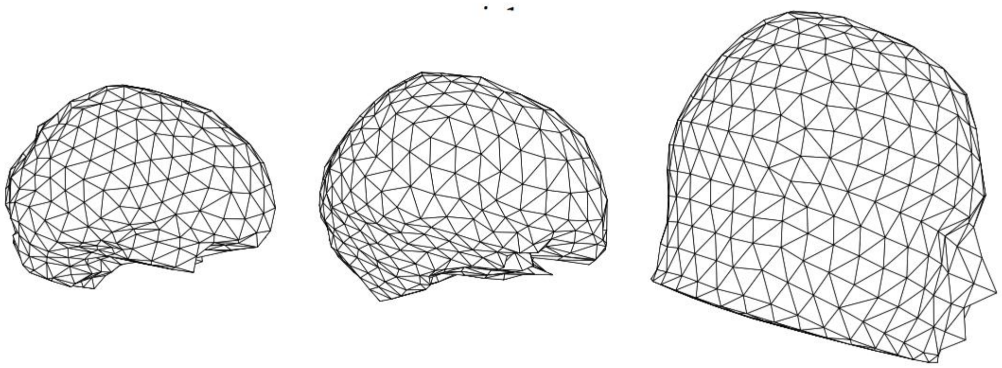


Figure 9
Example mesh of the human head used in BEM. Triangulated surfaces of the brain, skull and scalp compartment used in BEM. The surfaces indicate the different interfaces of the human head: air-scalp, scalp-skull and skull-brain.

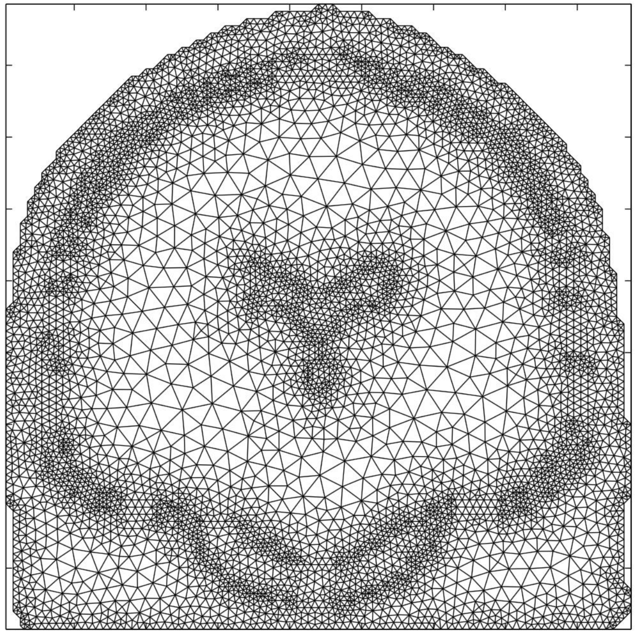


Figure 10
Example mesh in 2D used in FEM. A digitization of the 2D coronal slice of the head. The 2D elements are the triangles.

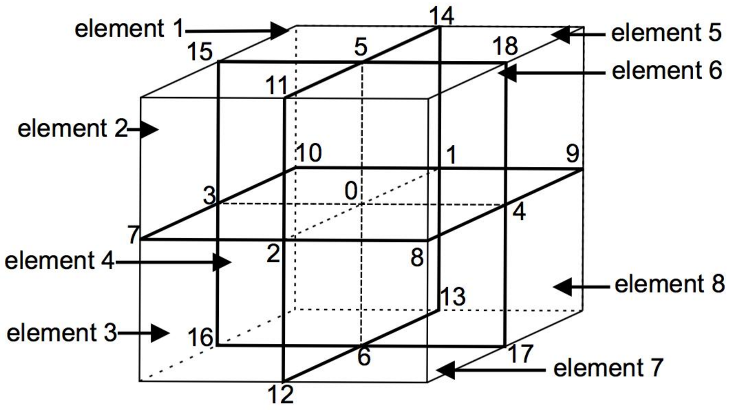


Figure 12
The computation stencil used in FDM if anistropic conductivities are incorporated. The potential at node 0 can be written as a linear combination of 18 neighbouring nodes in the FDM scheme. For each node we obtain an equation, which can be put into a linear system $Ax = b$.

Hallez et al (2007) Review on solving the forward problem in EEG source analysis

Forward Problem → Inverse Problem

X = LS   S = L^{-1}X

Observations		Head model		Estimated source distribution
Sensor Signal (X) [M * T] dimension	&	**Leadfield Matrix (L)** [M * 3N] dimension	→	**Source Signal (S)** [3N * T] dimension

2. Estimate source distribution
N>>M, Source localization is ill-posed.

The inverse problem refers to finding S given the known X.

objective function: $\underset{S}{\operatorname{argmin}} \|X - LS\|^2$

Some regularizations from prior knowledge on sources: sparsity, connectivity, …

$$\varphi = Kj + n_0 \quad (1)$$

Objective function: with additional regularization terms

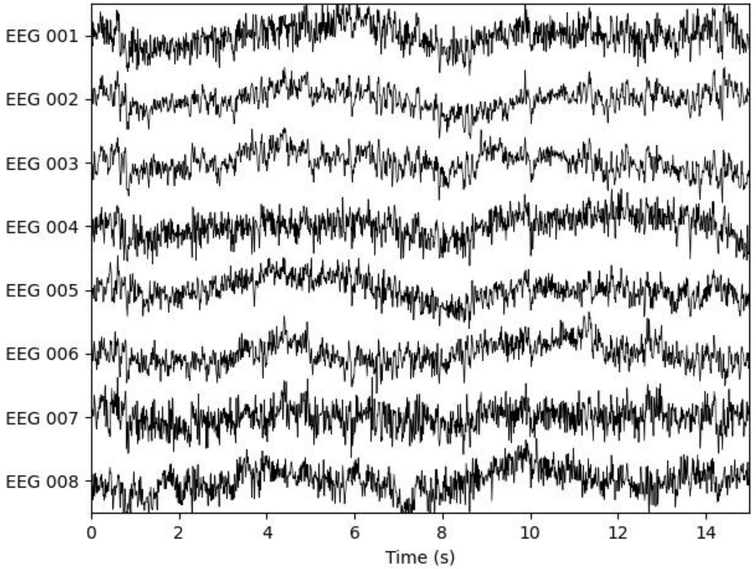
$$\begin{aligned} & j^{est} = \mathrm{argmin}_j \|Vj\|_1 + \alpha \|j\|_1 \\ & \text{subject to} \quad (\varphi - \mathrm{Kj})^T \Sigma^{-1} (\varphi - \mathrm{Kj}) \leq \beta \end{aligned} \quad (2)$$

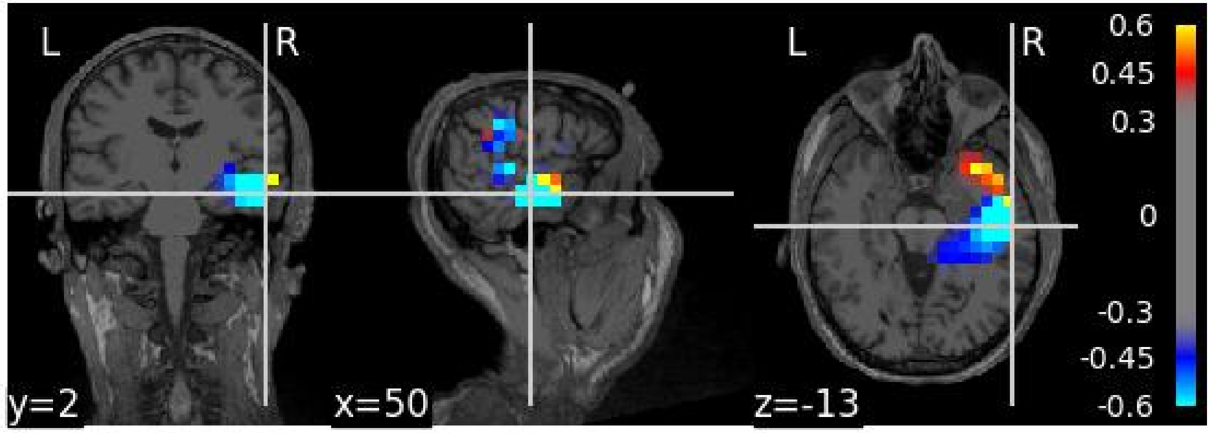
Iteratively reweighted edge sparsity minimization (IRES)

$$V = \begin{pmatrix} v_{11} & \cdots & v_{1n} \\ \vdots & \ddots & \vdots \\ v_{T1} & \cdots & v_{Tn} \end{pmatrix}$$
$$\begin{cases} v_{ij} = 1 \ \textit{and} \ v_{ik} = -1 & \text{if dipole } j \text{ and } k \text{ are neighbors over edge } i \\ v_{ij} = 0 & \text{otherwise} \end{cases} \quad (4)$$

Abbas Sohrabpour et al (2020) Nature communications

EEG Source Analysis





MNE, wMNE
Beamforming
LORETA, sLORETA, eLORETA
...

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The complex characteristics for EEG source problem

1. Ill-posedness
   - The number of unknown sources out numbers the number of measurements
2. Spatiotemporal sparsity
   - Locally clustered and globally sparse
3. Depth bias
   - Conduction attenuation
4. Spatial correlation
   - Synchronization of neighboring sources
5. Temporal correlation/common sparsity
   - Temporal basis: Event related potential, pathological wave shapes

Mannepalli, T., & Routray, A. (2021). Sparse algorithms for EEG source localization. *Medical & Biological Engineering & Computing*, *59*(11), 2325-2352.

The complex characteristics for EEG source problem

6. Anatomical constraints (Forward model)
    - Fixed orientations
    - Location of the dipoles (Gray matter)
7. Physiological constraints
    - Smoothness in dipole magnitude
    - Distant connection between cortical patches
8. Non-stationarity of the sources
    - Sources are not stationary with time.
9. Characteristics of noise
    - Baseline noise: signal from the brain from non-targeted stimuli (Background activity).

Mannepalli, T., & Routray, A. (2021). Sparse algorithms for EEG source localization. *Medical & Biological Engineering & Computing*, *59*(11), 2325-2352.

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Instantaneous solvers with non-sparse priors - MNE

Some of mentioned characteristics can be transformed into simple mathematical constraints, eg: Noise level represented by covariance matrix and scalp observation.

In Gaussian assumption, **Bayesian *maximum a posteriori* (MAP)** or a $\boldsymbol{L_2}$ **minimum-norm solution** is:

$$j^{MNE} = RK^T(KRK^T + \lambda^2 C)^{-1}\phi = W\phi$$

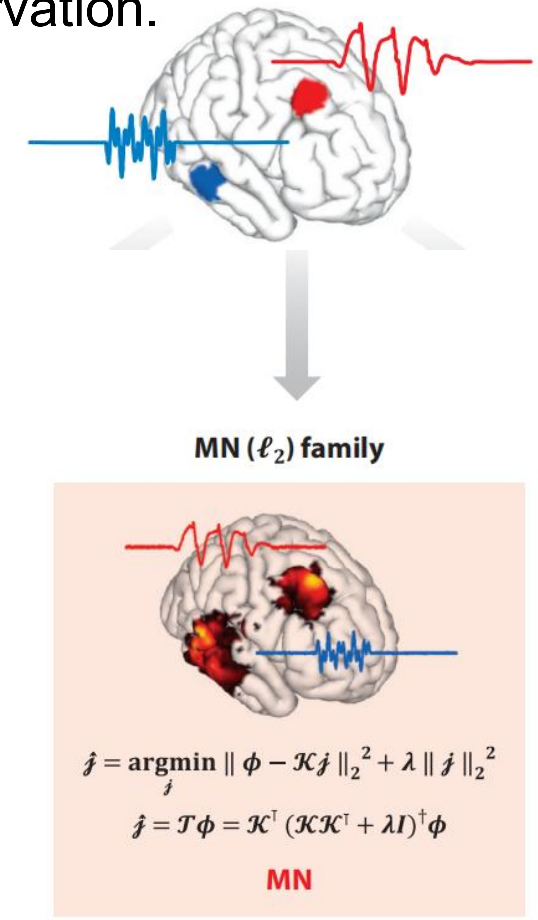
where C is a sensor noise covariance matrix,

and R is a source covariance matrix (here $R = I$).

This solution can be viewed as **the analytic solution** of an optimization problem where the objective function is:

$$j^{MNE} = \underset{j}{\operatorname{argmin}} \left\{ \|\phi - Kj\|_{C^{-1}}^2 + \lambda^2 \|j\|_{R^{-1}}^2 \right\}$$

Here, $\|A\|_{C^{-1}} = \sqrt{tr\{A^T C^{-1} A\}}$ denotes the Mahalanobis distance.



(He et al., 2018, Annu. Rev. Biomed. Eng.)

Instantaneous solvers with non-sparse priors – variants of MNE

- **Weighted minimum norm estimate (WMNE):**

To better deal with the *depth bias*, the source covariance matrix R can be modified:

$$R^{WMNE} = diag\left(K_i^2\right),\ K_i\ is\ the\ i^{th}\ column\ of\ K$$

where R_{ii}^{WMNE} is the weights of i's sources. Then, we derive:

$$j^{WMNE} = R^{WMNE} K^T (K R^{WMNE} K^T + \lambda^2 C)^{-1} \phi$$

- **Low-resolution impedance tomography (LORETA):**

Similarly, we can modify the source covariance matrix R with the *depth bias* and *neighborhood correlation* of sources:

$$R^{LORETA} = B diag\left(K_i^2\right),$$

where B is the discreate Laplacian operator. We set $B_{ij} > 0$, if source i and j are neighbors. Then, we derive:

$$j^{LORETA} = R^{LORETA} K^T (K R^{LORETA} K^T + \lambda^2 C)^{-1} \phi$$

Instantaneous solvers with sparse priors – l_p norm

The main issue with non-sparse solvers is their tendency to spread across the brain. Here, sparse prior is introduced by using l_p norm.

<u>*Objective function*</u> is given by:

$$j^{l_p} = \underset{j}{\operatorname{argmin}} \left\{ \|\phi - Kj\|_{C^{-1}}^2 + \lambda^2 \|j\|_p \right\}$$

Here $p < 2$. When $p = 1$, it employs the l_1 norm penalization (LASSO) which j follows a Laplacian. It also can be written as:

$$j^{l_p} = \underset{j}{\operatorname{argmin}} \left\{ \|j\|_p \right\}$$

$$s.t. \ \ \|\phi - Kj\|_{C^{-1}}^2 \leq \ \epsilon$$

which can be solved by an iterative solver.

Instantaneous solvers with sparse priors – IRES

IRES impose sparsity on the spatial gradient of sources (edge sparsity) which is particularly suitable for epileptic lesion localization.

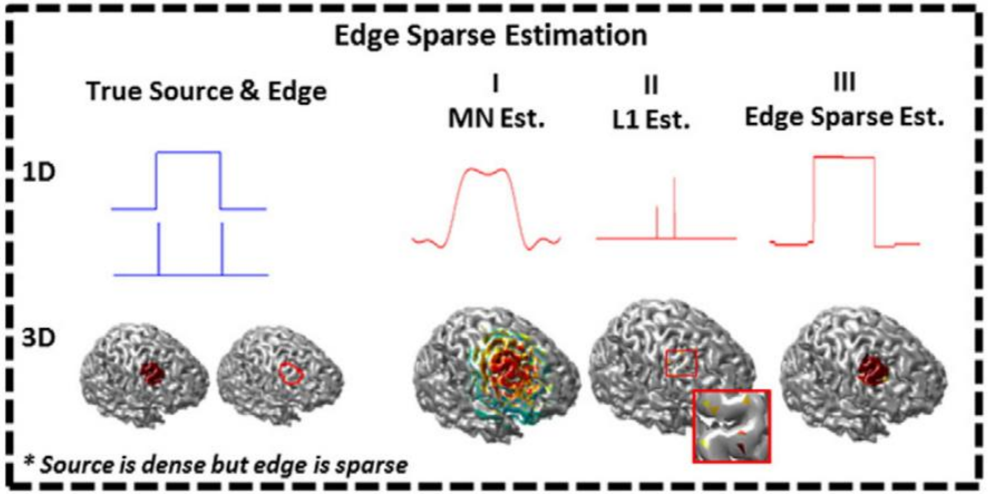
Objective function is:

$$j^{IRES} = \underset{j}{\operatorname{argmin}} \{\|Vj\|_1 + \|j\|_1\}$$
$$s.t.\ \ \|\phi - Kj\|_{C^{-1}}^2 \leq \epsilon$$

Here $\|Vj\|_1$ is the strength of spatial gradient, and V can be presented as:

$$V = \begin{pmatrix} V_{11} & \cdots & V_{1n} \\ \vdots & \ddots & \vdots \\ V_{T1} & \cdots & V_{Tn} \end{pmatrix}$$

where $V_{ij} = 1\ and\ V_{ik} = -1$, if dipole j and k are neighbors over edge i; $V_{ij} = 0$ *for others.*



(Sohrabpour et al., 2016, NeuroImage)

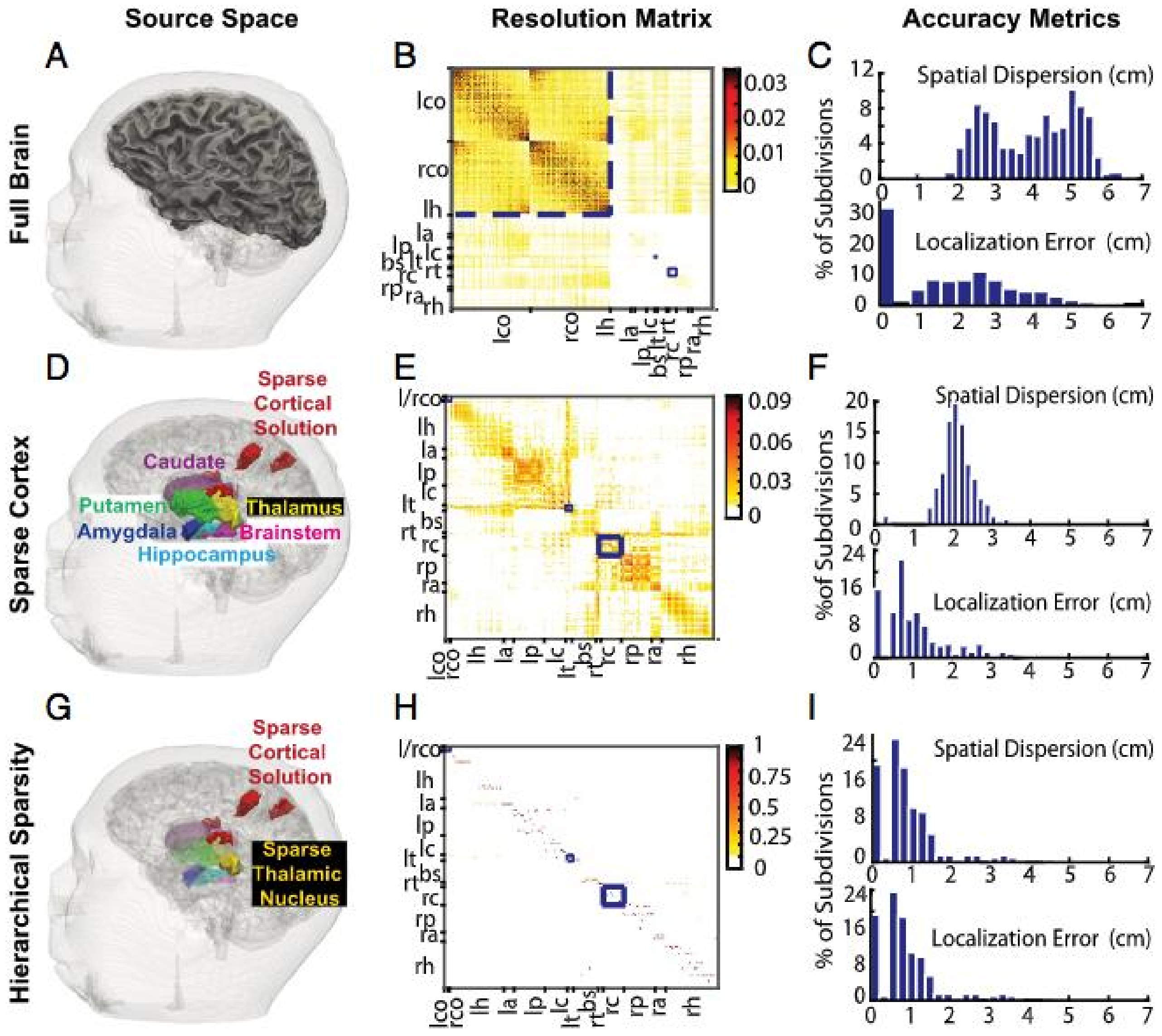
Sohrabpour, A., Lu, Y., Worrell, G., & He, B. (2016). Imaging brain source extent from EEG/MEG by means of an iteratively reweighted edge sparsity minimization (IRES) strategy. *NeuroImage*, *142*, 27–42.

Instantaneous solvers with hierarchical sparse priors

Inverse Algorithm. Inputs: Data $\mathbf{Y}$, distributed gain matrix $\mathbf{G}_{\mathcal{B}}$, and target sparsity level L.
Notation: Denote the distributed cortical and subcortical source spaces as $\mathcal{B}_C$ and $\mathcal{B}_S \subset \mathcal{B}$, respectively. Denote $\mathcal{H}_r \subset \mathcal{B}_r$ as the set of L brain divisions whose estimated neural currents $\hat{\mathbf{X}}_{\mathcal{H}_r}$ best explain data $\mathbf{Y}$.

1. Do subspace pursuit on the distributed cortical source space $\mathcal{B}_C$: $[\mathcal{H}_C, \hat{\mathbf{X}}_{\mathcal{H}_C}] = \mathrm{SP}(\mathbf{Y}, \mathbf{G}_{\mathcal{B}_C}, L)$.
2. Construct $\mathcal{B}_{C,\mathrm{refined}} = \mathcal{H}_C \cup$ neighbors of $\mathcal{H}_C$ in a finer subdivision of cortical patches.
3. Repeat subspace pursuit on the coarse-to-fine hierarchy of cortical source spaces $\mathcal{B}_{C,\mathrm{refined}}$: $[\mathcal{H}_{C_{\mathrm{sp}}}, \hat{\mathbf{X}}_{\mathcal{H}_{C_{\mathrm{sp}}}}] = \mathrm{SP}(\mathbf{Y}, \mathbf{G}_{\mathcal{B}_{C,\mathrm{refined}}}, L)$.
4. Construct the composite space of sparse cortical sources and distributed subcortical sources: $\mathcal{B}_r = [\mathcal{H}_{C_{\mathrm{sp}}} \cup \mathcal{B}_S]$.
5. Repeat subspace pursuit on the composite sparse space $\mathcal{B}_r$: $[\mathcal{H}_r, \hat{\mathbf{X}}_{\mathcal{H}_r}] = \mathrm{SP}(\mathbf{Y}, \mathbf{G}_{\mathcal{B}_r}, \alpha L)$, where $\alpha > 1$.

Outputs: Cortical and subcortical source locations $\mathcal{H} = \mathcal{H}_r \subset [1, 2, \ldots, K]$; and the estimated time courses of neural currents at these locations $\hat{\mathbf{X}}_{\mathcal{H}} = \hat{\mathbf{X}}_{\mathcal{H}_r}$.



Krishnaswamy, et al. PNAS (2017)

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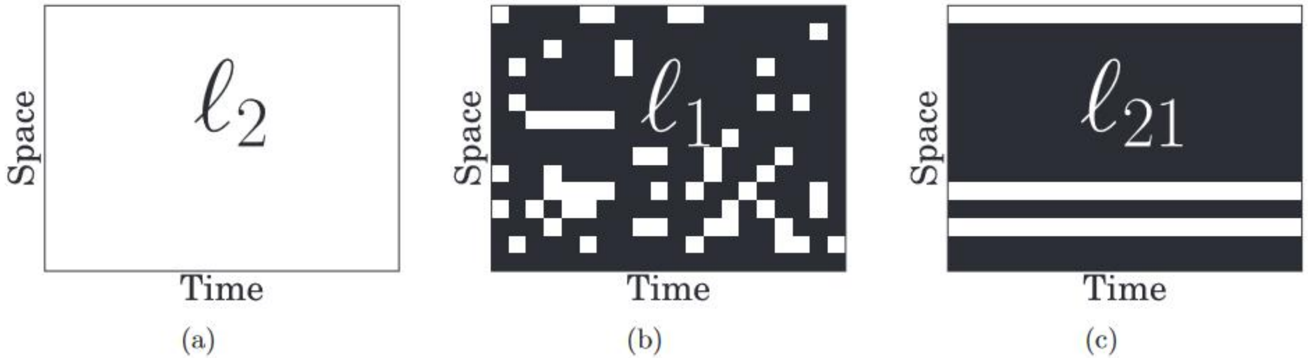
Time block solvers - MxNE

As these instantaneous solvers generally ignore that *sources are non-stationarity*, we can constrain the sparsity in spatial and smoothness in temporal simultaneously.

$$j^{MxNE} = \underset{j}{\operatorname{argmin}} \left\{ \|\phi - Kj\|_{C^{-1}}^2 + \lambda^2 \|j\|_{21} \right\}$$

Here $\|j\|_{21} = \sum_{t=1}^{T} \sqrt{\sum_{i=1}^{N} j_{it}^2}$.

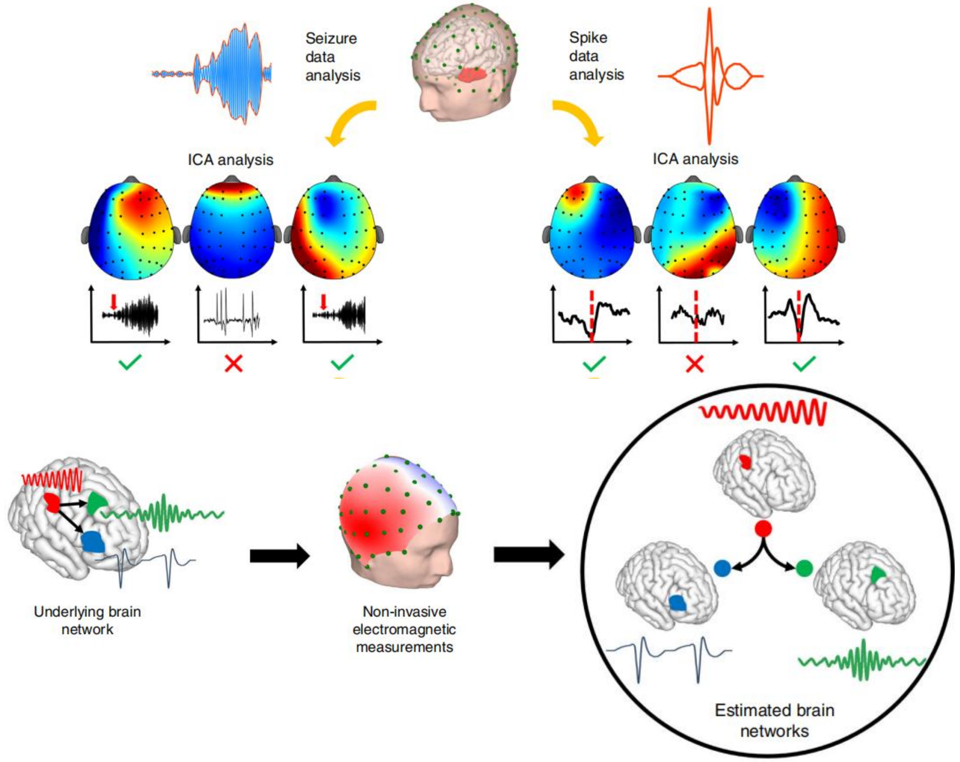


Gramfort et al. (2021), Phys. Med. Biol.

Time block solvers - epileptogenic brain sources

Data-driven priors from specific domain knowledge

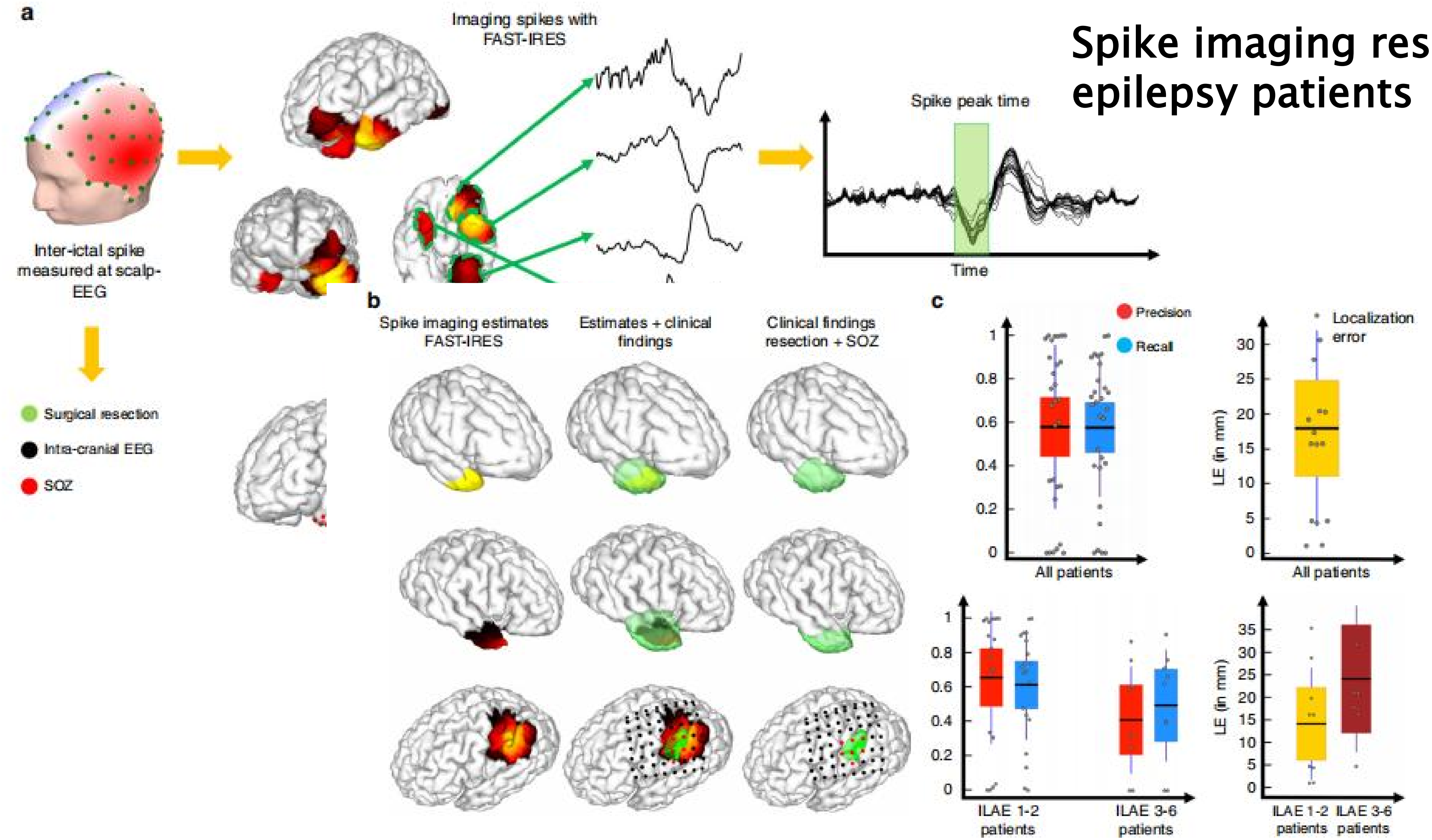
- Blind source separation (BSS) applied to extract interictal spikes and seizures from EEG recordings as the time basis function
- Spatial constraints that enforce the edge sparsity guarantee focally extended sources
- Constructing underlying brain network: the nodes and internodal connectivity (links) of these networks



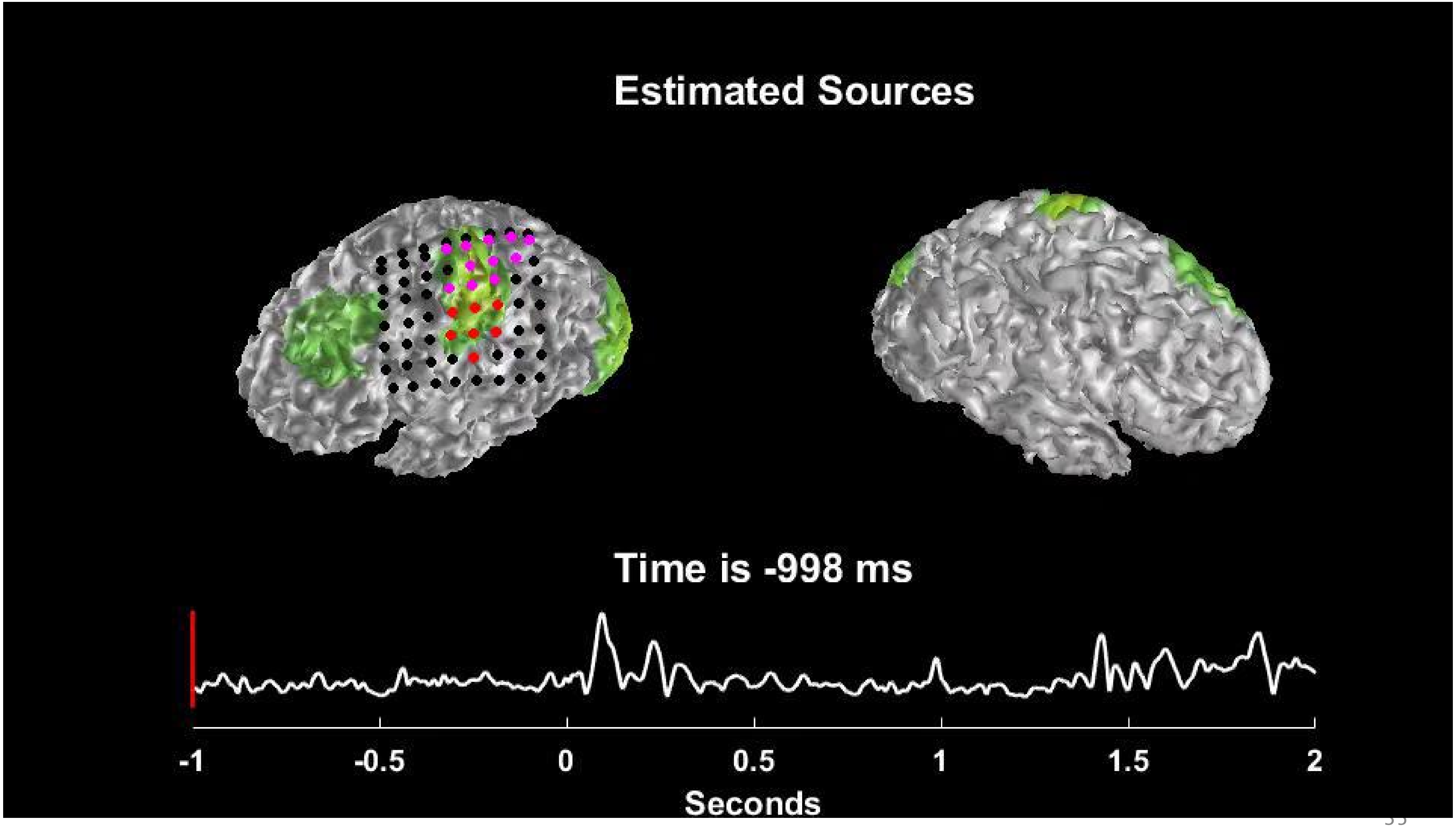
(Sohrabpour et al., 2020, Nat Commun)

Sohrabpour, A., Cai, Z., Ye, S., Brinkmann, B., Worrell, G., & He, B. (2020). Noninvasive electromagnetic source imaging of spatiotemporally distributed epileptogenic brain sources. *Nature communications*, *11*(1), 1-15.

Spike imaging results on epilepsy patients



Abbas Sohrabpour et al (2020) Nature communications


Estimated Sources
Time is -998 ms
-1
-0.5
0
0.5
1
1.5
2
Seconds

Limitations of Numerical methods with mathematical constraints

Drawbacks of exisiting numerical methods

1. Relying on designing mathematically simplified regular **terms** to deal with the ill-posed problem. However, it is hard to incorporate multiple physiological priors based on regularization terms.
2. For many algorithms, there is no analytic expression of the solution, and instead it requires optimization using **time-consuming** iterative algorithms
3. The **hetergenity** of EEG recordings makes it hard to find suitable parameters for each measurements.

→ Data-driven approach to improve source imaging

Research Questions

- Whether these data-driven models can learn priors from training data?
- How to naturally integrate data-driven model with multiple priors?

Outline

- Definition of EEG source localization problem
- Problem characteristics of EEG source localization problem
- Numerical methods with mathematical constraints
  - Instantaneous solvers with sparse/non-sparse priors
  - Time block solvers
- Data-driven methods with anatomical and physiological constraints
  - Deep neural networks with simulated dataset biological constraints
  - Generative Model with meta-fMRI Priors

Regularization in inverse problems

$$y \longrightarrow \boxed{\hat{\beta} = \arg\min_{\beta} \|y - X\beta\|_2^2 + r(\beta)} \longrightarrow \hat{\beta}$$

Classical: r(β) is a pre-defined smoothness-promoting regularizer (e.g. Tikhinov or ridge estimation)

Bayesian: r(β) = -log p(β)
Uses a prior distribution over space of β's
(e.g. sparsity, patch redundancy, total variation)

Learned: use training data to learn r(β)

- Deep CNN's for signal recovery
  Dong, Loy, He, Tang, 2014
  Mousavi and Baraniuk, 2017
  Jin, McCann, Froustey, Unser, 2017
  Ye, Han, Cha, 2018

  ConvDip
  Deepsif

- Compressed sensing with GANs
  Bora, Jalal, Price, Dimakis, 2017

  GANs with Deep Image Prior

- Unrolled algorithms for solving inverse problems

  - Deep proximal gradient descent nets
    Chen, Yu, Pock, 2015
    Mardani et al, 2018

    Unrolled optimization network

  - Deep ADMM nets
    Sun, Li, Xu, 2016
    Chang, Li, Poczos, Kumar, Sankaranarayanan, 2017

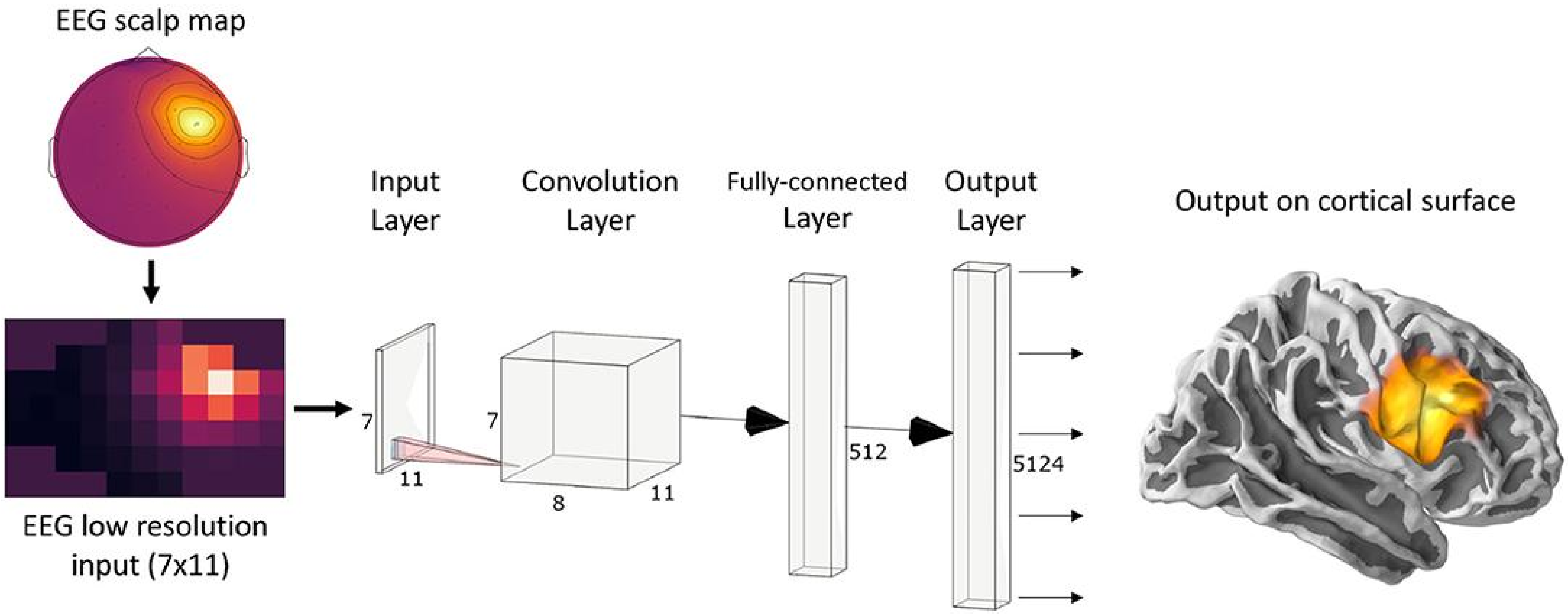
    ADMM-ESI

  - Deep half-quadratic splitting
    Zhang, Zuo, Gu, Zhang, 2017

  - Deep primal-dual nets
    Adler and Öktem, 2018

Convolutional Neural Network for ESI

Voxel-wise MSE is used to optimized the parameters in CNN.



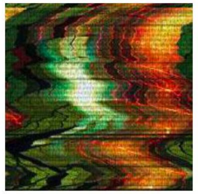
Hecker Lukas et al (2021) *Frontiers in Neuroscience*

GANs for inverse problems

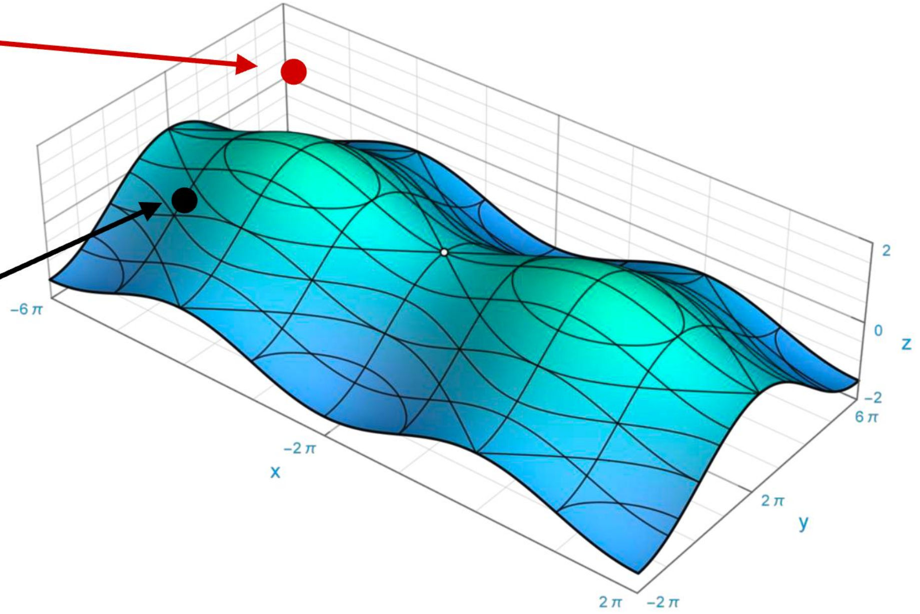
$$y \longrightarrow \boxed{\hat{\beta} = \arg\min_{\beta} \|y - X\beta\|_2^2 + r(\beta)} \longrightarrow \hat{\beta}$$

$$r(\beta) = \begin{cases} 0, & \beta \text{ on image manifold} \\ \infty, & \text{otherwise} \end{cases}$$

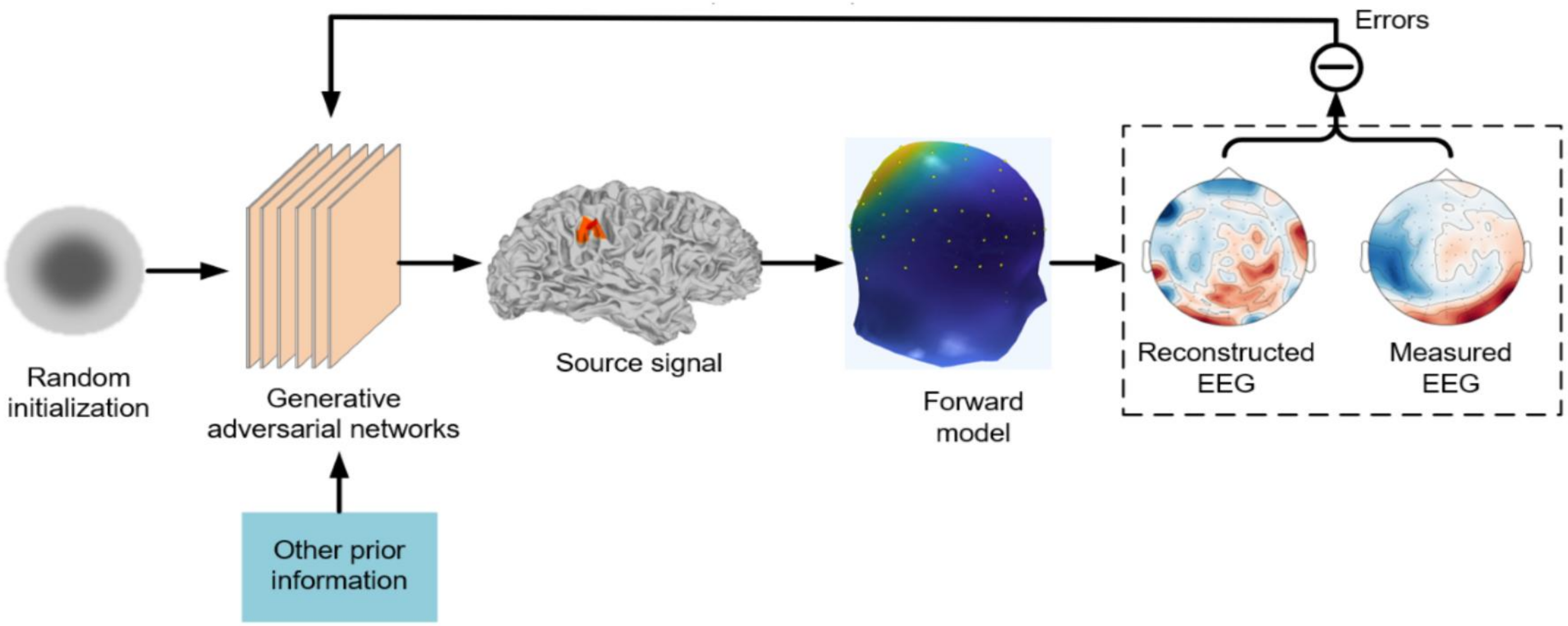
“Bad” image off manifold



“Good” image on manifold



GANs with Deep Image Prior for ESI

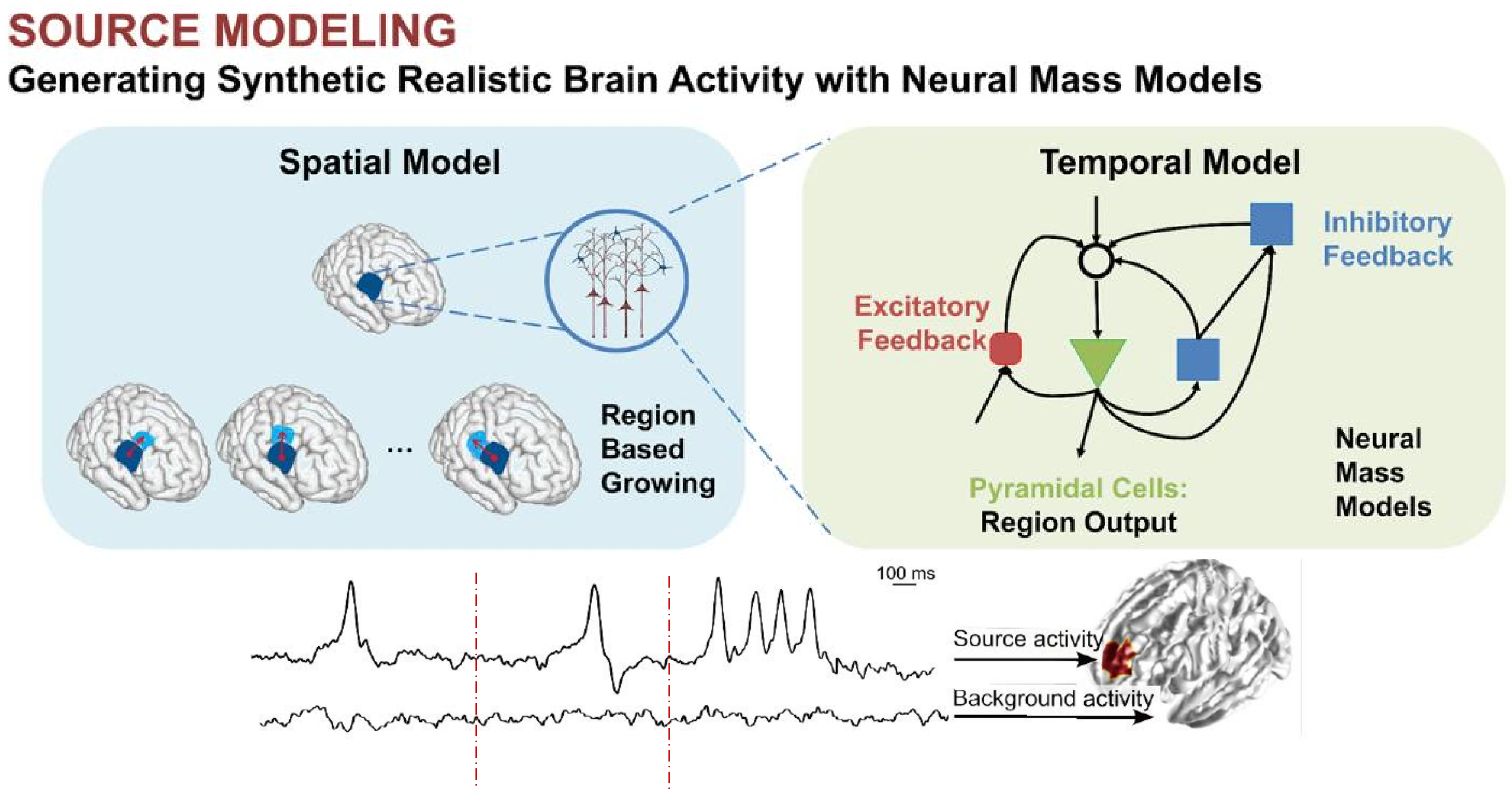


$$\underset{w}{\operatorname{argmin}} ||X - AG(z,w)||_2^2 + \lambda||(VG(z,w)||_1 + \beta||G(z,w)||_1$$

Where AG(z, w) is the reconstructed EEG signal and X is the real EEG signal λ and β are the hyperparameters for edge sparsity and l1 sparse on the source signal

Yaxin Guo and Meng Jiao et al (2022) *IEEE EMBC*

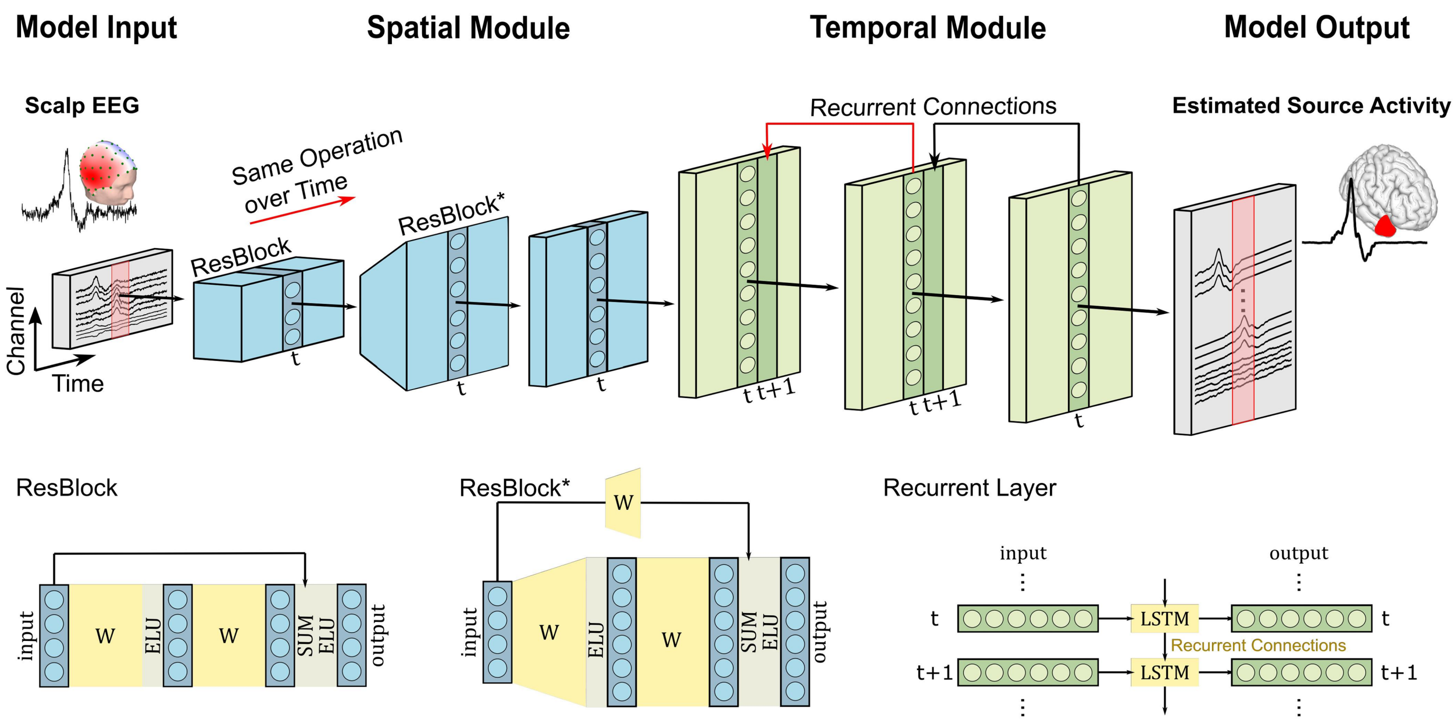
Neural Mass Models for simulating spike activity



Sun Rui et al (2022) *Proceedings of the National Academy of Sciences*

Deep neural networks constrained by neural mass models

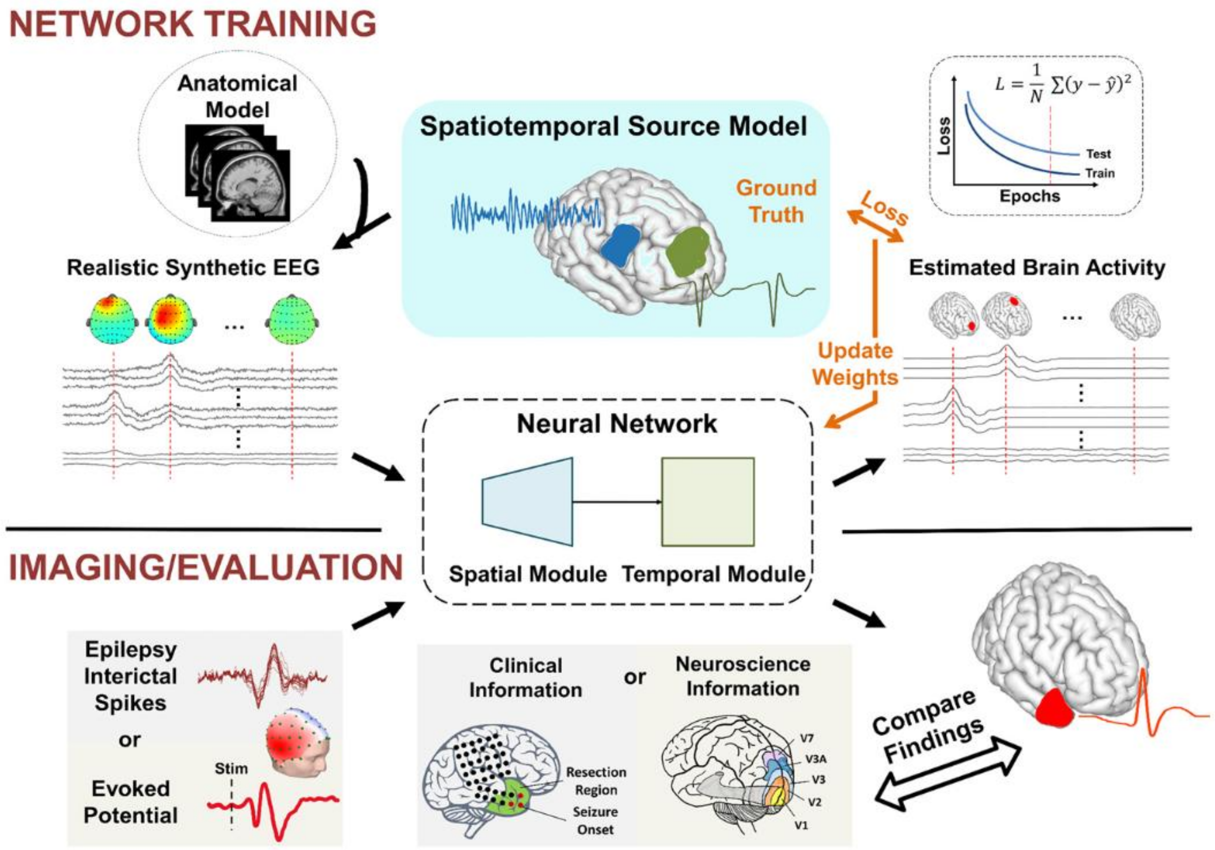
Using **Spatiotemporal Source Model** to localize the brain region that have spiking activity.



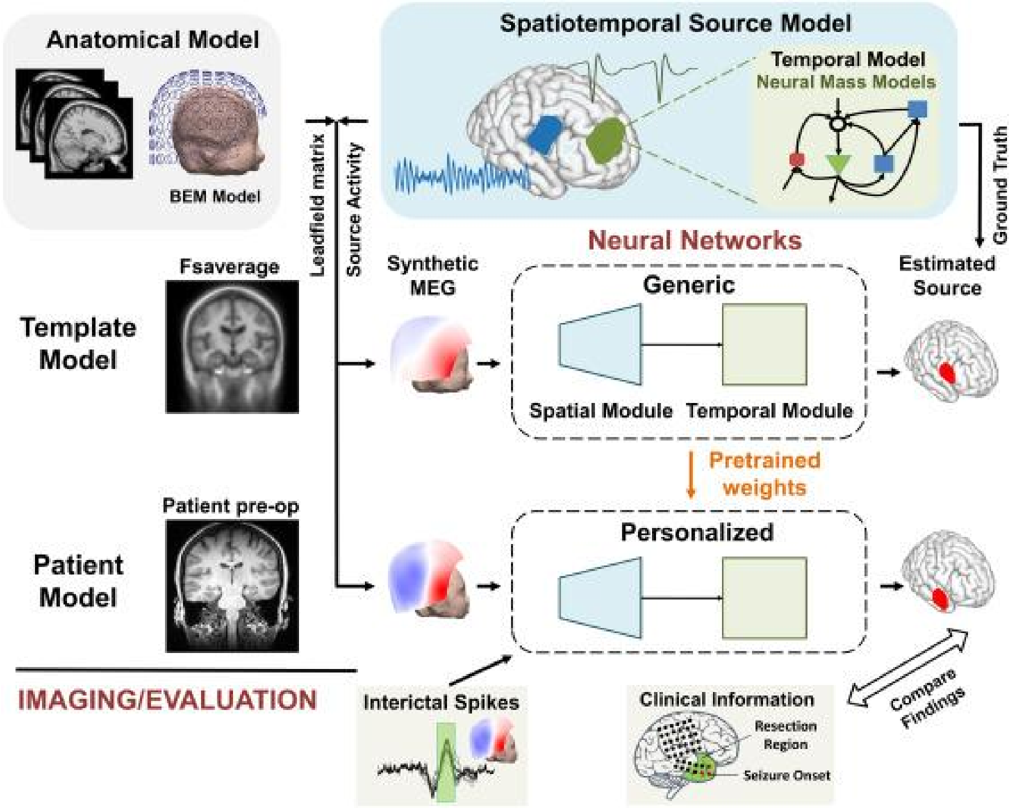
Sun Rui et al (2022) *Proceedings of the National Academy of Sciences*

Deep neural networks constrained by neural mass models

Using **pretrained** model for developing personalized model

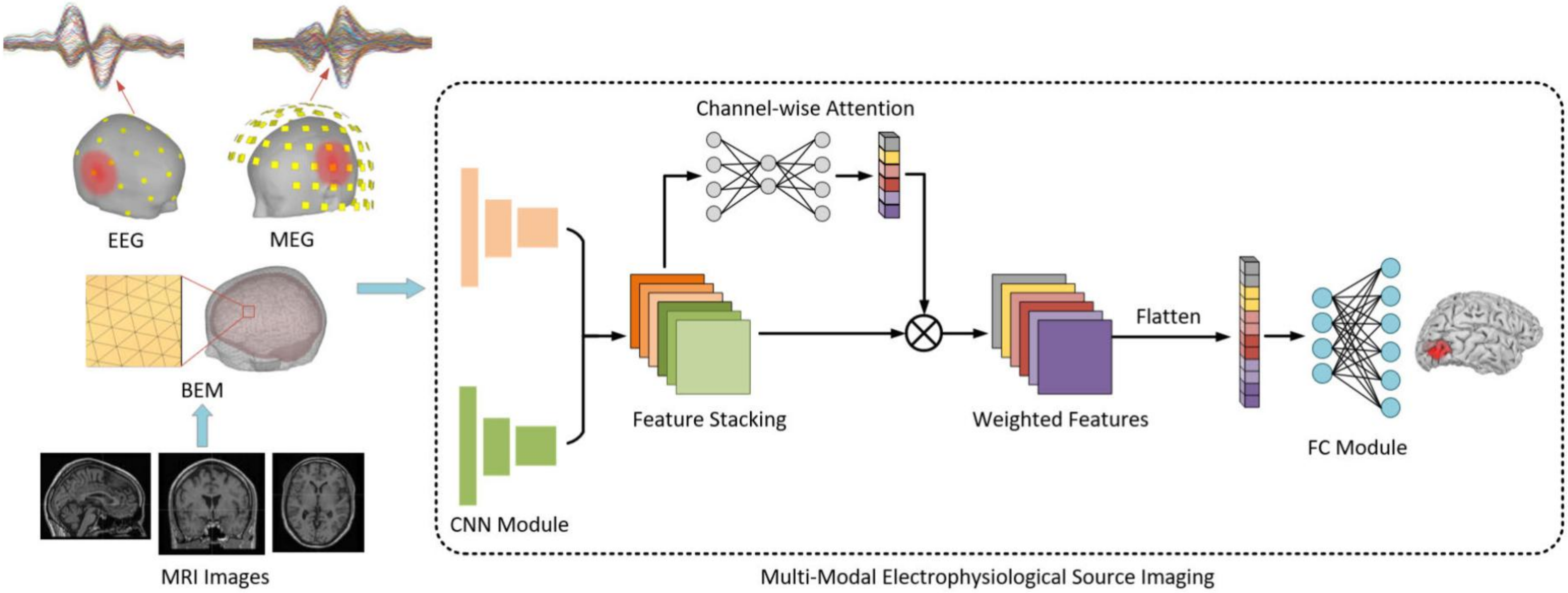


Sun Rui et al (2022) *Proceedings of the National Academy of Sciences*



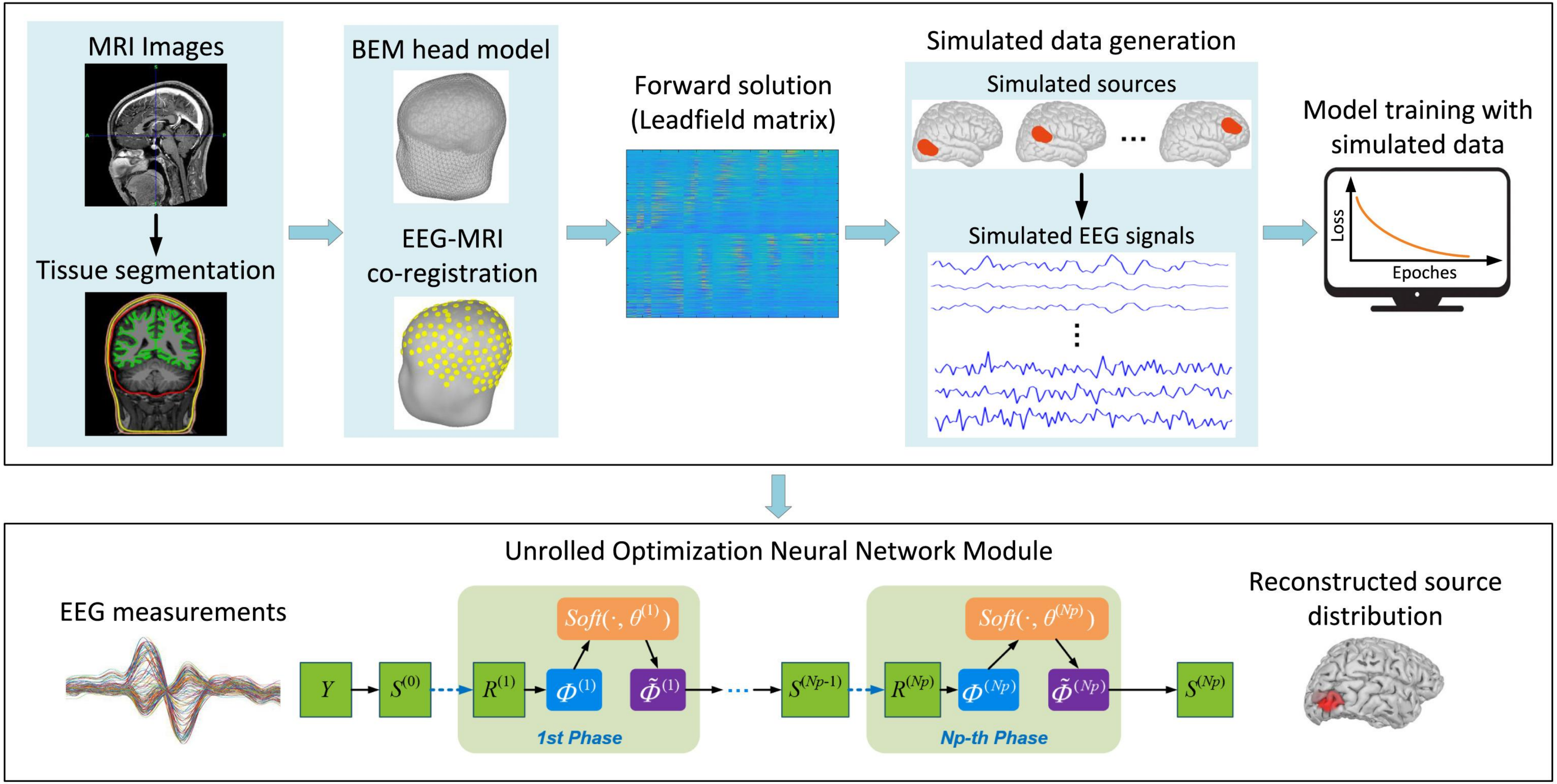
Sun Rui et al (2023) *NeuroImage*

ESI with Attention Neural Networks for EEG and MEG



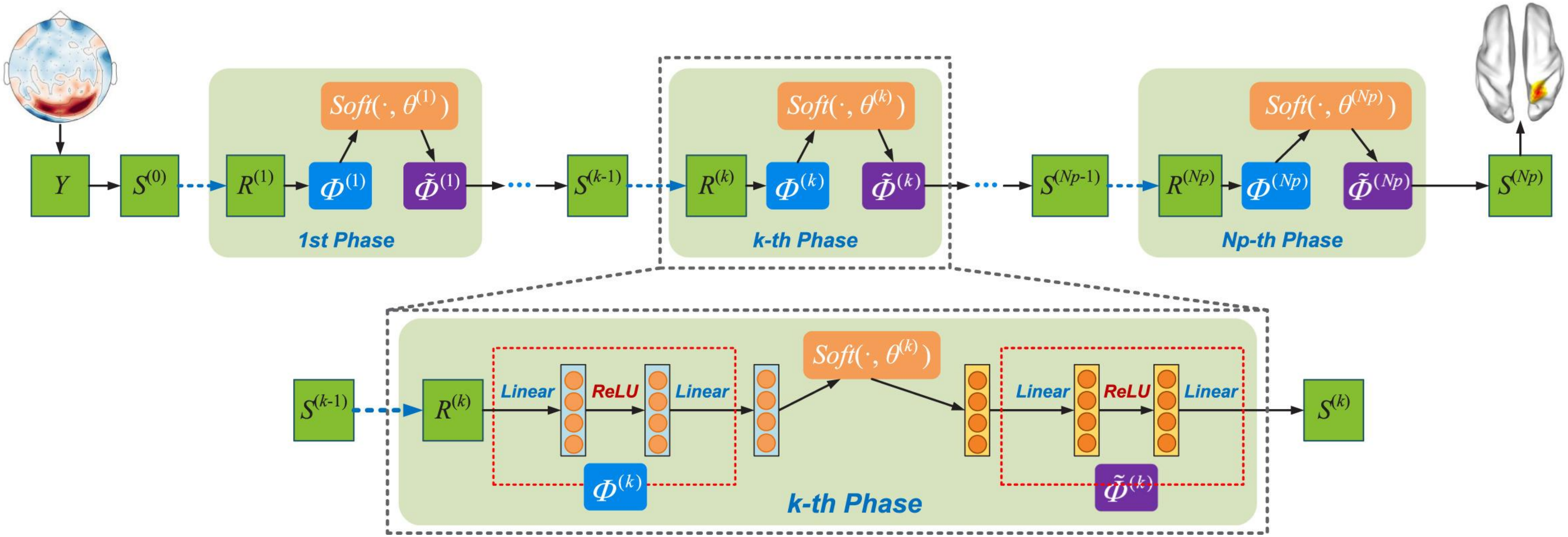
Meng Jiao et al (2024) *IEEE TNSRE*

Unrolled Optimization Neural Networks for ESI



Meng Jiao et al (2023) *NeuroImage*

Unrolled Optimization Neural Networks for ESI



Meng Jiao et al (2023) *NeuroImage*

Unrolled optimization methods

$$y \longrightarrow \boxed{\hat{\beta} = \arg\min_{\beta} \|y - X\beta\|_2^2 + r(\beta)} \longrightarrow \hat{\beta}$$

Initialize $\hat{\beta}^{(0)}$

$$\hat{\beta}^{(B)} = f_{X,r}(\hat{\beta}^{(B-1)})$$ iteration map parameterized by X,r

$$= f_{X,r}(f_{X,r}(f_{X,r}(\cdots f_{X,r}(\hat{\beta}^{(0)})\cdots)))$$ recurrent network

$$\hat{\beta}^{(0)} \longrightarrow \boxed{f_{X,r}} \xrightarrow{\hat{\beta}^{(1)}} \boxed{f_{X,r}} \xrightarrow{\hat{\beta}^{(2)}} \cdots \longrightarrow \boxed{f_{X,r}} \xrightarrow{\hat{\beta}^{(B)}}$$

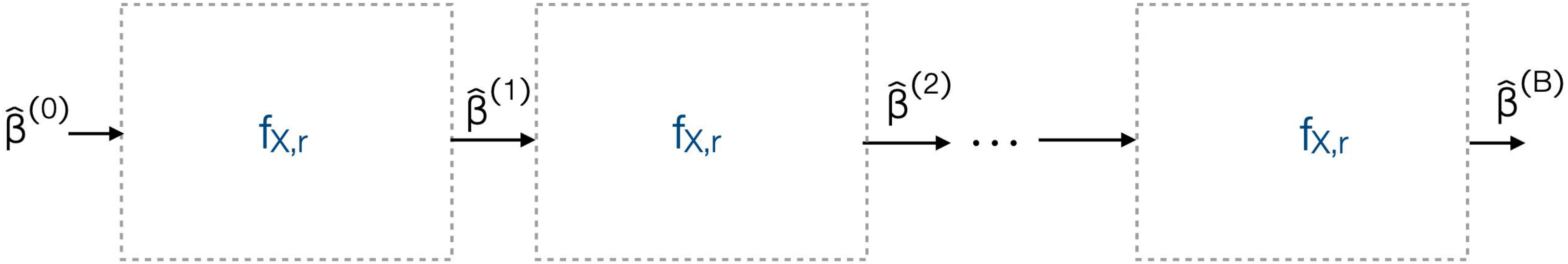
Unrolled optimization methods

$$y \longrightarrow \boxed{\hat{\beta} = \arg\min_{\beta} \|y - X\beta\|_2^2 + r(\beta)} \longrightarrow \hat{\beta}$$

Initialize $\hat{\beta}^{(0)}$

$$\hat{\beta}^{(B)} = f_{X,r}(\hat{\beta}^{(B-1)})$$ iteration map parameterized by X,r

$$= f_{X,r}(f_{X,r}(f_{X,r}(\cdots f_{X,r}(\hat{\beta}^{(0)})\cdots)))$$ recurrent network



learn r from training data

Gregor and LeCun, 2010

Deep learning solution for ill-posed inverse problem

Forward problem formulated as: $\phi = Kj + n$

To reconstruct a mapping function $\mathcal{K}_{\Theta}^{\dagger}: Scalp \rightarrow Source$, satisfying *the pseudo-inverse property*:

$$\mathcal{K}_{\Theta}^{\dagger}(\phi) \approx j_{true}$$

Unsupervised regularized objective function:

$$\min_{j \in X} \left[\mathcal{L}\left(\mathcal{K}(j), \phi\right) + \lambda S(j)\right]$$

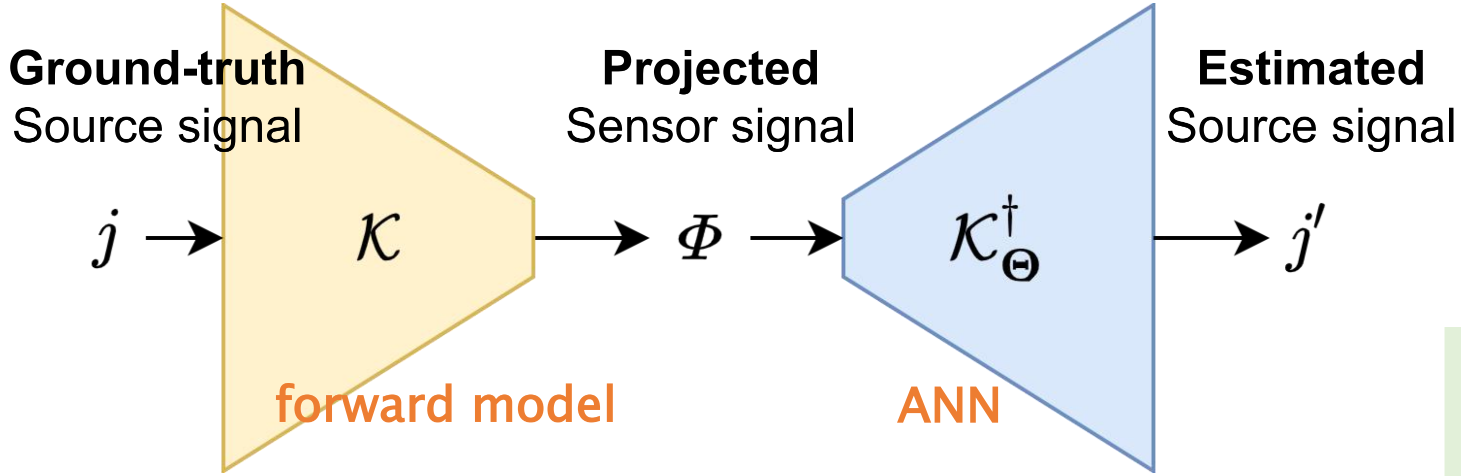
$\mathcal{L}\left(\mathcal{K}(j), \phi\right)$ denotes the **difference** between the original EEG and the projected EEG from the estimated sources using the forward model.
$\mathcal{K}$ is a linear operator here, and $S(j)$ is a regularization term, λ is hyperparameter with $\lambda \geq 0$
So, the **unsupervised** loss function is:

$$\mathcal{L}\left(\phi | \Theta\right) = \mathcal{L}(\mathcal{K}(\mathcal{K}_{\Theta}^{\dagger}(\phi)), \phi) + S(\mathcal{K}_{\Theta}^{\dagger}(\phi))$$

Supervised loss function is:

$$\mathcal{L}\left(\phi, j_{true} | \Theta\right) = \mathcal{L}(\mathcal{K}_{\Theta}^{\dagger}(\phi), j_{true}) + S(\mathcal{K}_{\Theta}^{\dagger}(\phi))$$

Source reconstruction by supervised learning



Forward operator $\mathcal{K}$: $K\ (i.e.,\ \ \phi = K(j + n_j) + n_\phi)$

Inverse operator $\mathcal{K}_{\Theta}^{\dagger}$: $ANN\ (i.e.,\ \ j = ANN(\phi))$

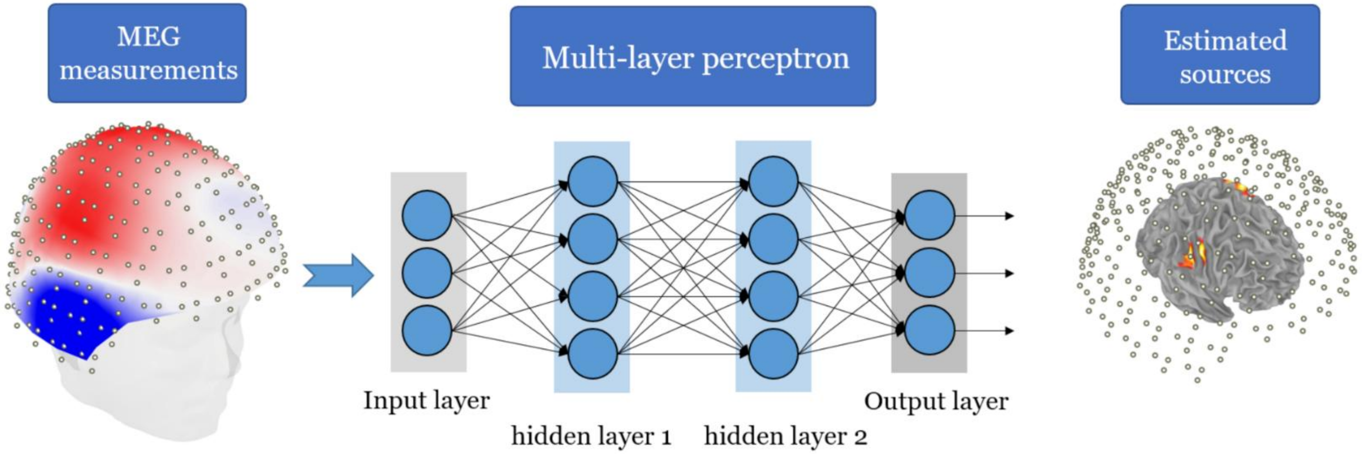
Loss function: $$j' = \underset{j}{argmin}\{\mathcal{L}(j,\ j_{ture}) + \lambda S(j)\}$$

Advantage:
- An end-to-end method, which can learn the target distribution directly

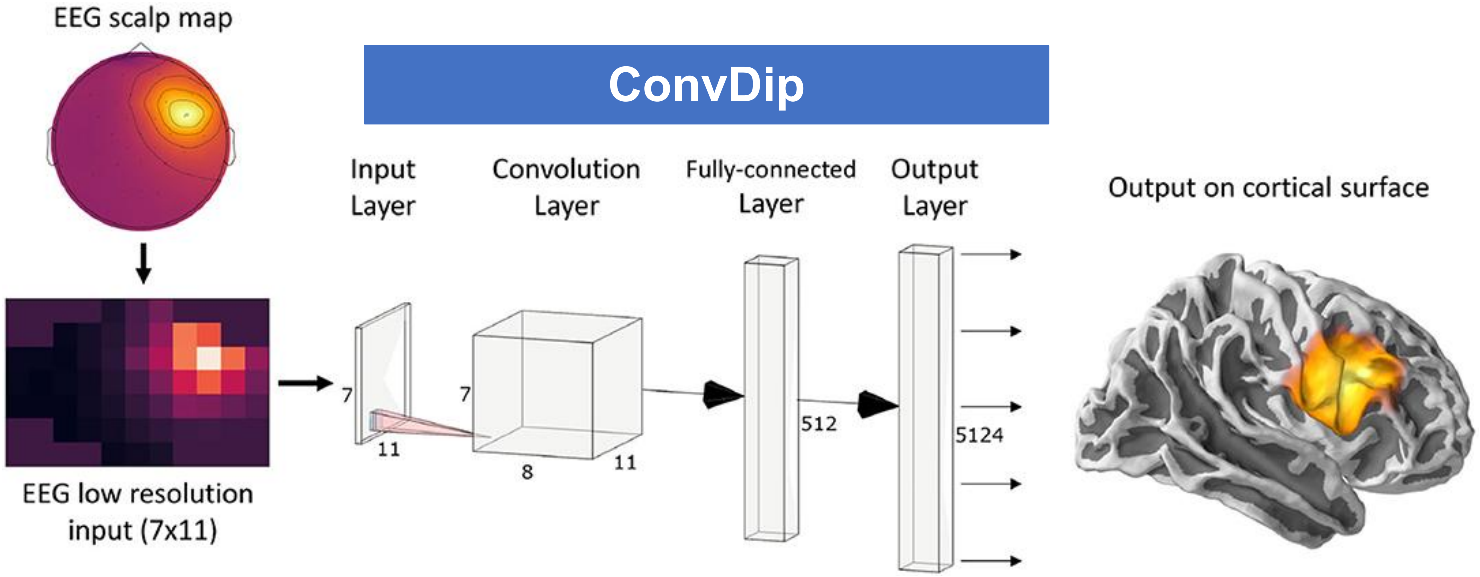
Disadvantage:
- Depends on the reliability of simulating datasets

Chen, et al, (2021) IJCNN

Basic Supervised network for EEG inverse problem

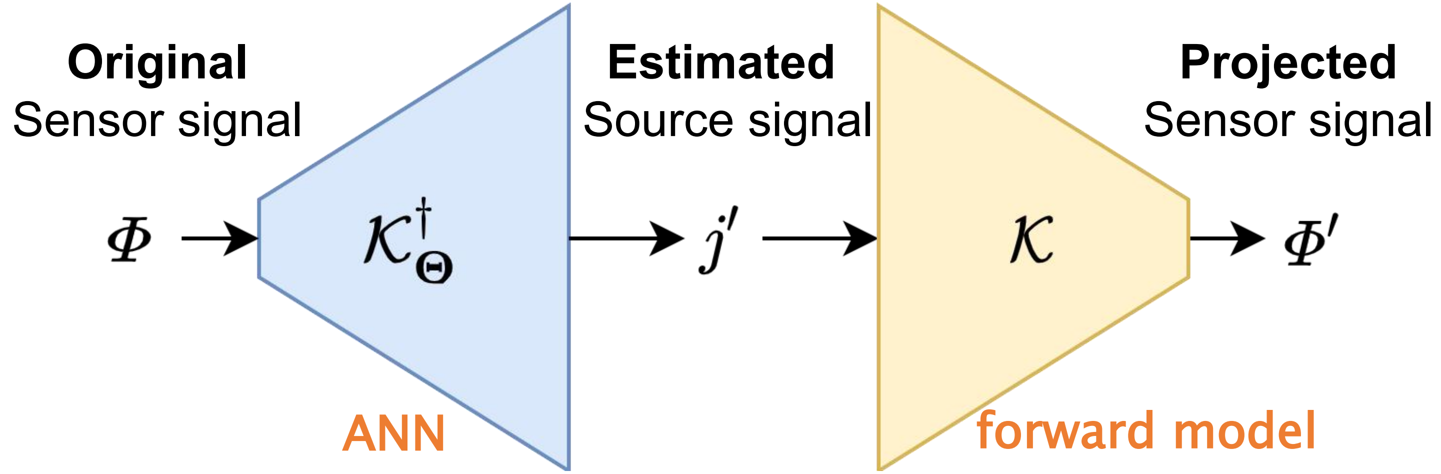


Pantazis, D., & Adler, A. (2021). MEG source localization via Deep Learning. *Sensors*, *21*(13), 4278.



Hecker, L., et al. (2021). ConvDip: A convolutional neural network for better EEG Source Imaging. *Frontiers in Neuroscience*, *15*, 533.

Source reconstruction by unsupervised learning



Forward operator $\mathcal{K}$: K $(i.e.\ \ \phi = K(j + n_j) + n_\phi)$

Inverse operator $\mathcal{K}_{\Theta}^{\dagger}$: ANN $(i.e.\ \ j = ANN(\phi))$

Loss function: $j' = \underset{j}{\operatorname{argmin}} \{\mathcal{L}(\phi,\ Kj) + \lambda S(j)\},\ \ j = \mathcal{K}_{\Theta}^{\dagger}(\phi)$

Chen, et al, (2021) IJCNN

Advantage:

- Data-driven and model-driven
- An framework that can cooperate with traditional numerical methods

Disadvantages:

- Sensitive to the noise
- Depends on the setting of priori (priori of source)

Solving by a learnable basis function

魏晨

楼可心

Presuppositions:

1) Activated EEG sources can be represented by a linear combination of independent basis functions in the source space

2) The brain state in each time can be expressed by a small set of basis functions (M is sparse.)

3) The basis functions have sparse edges (Ω is edge sparse.)

Loss function

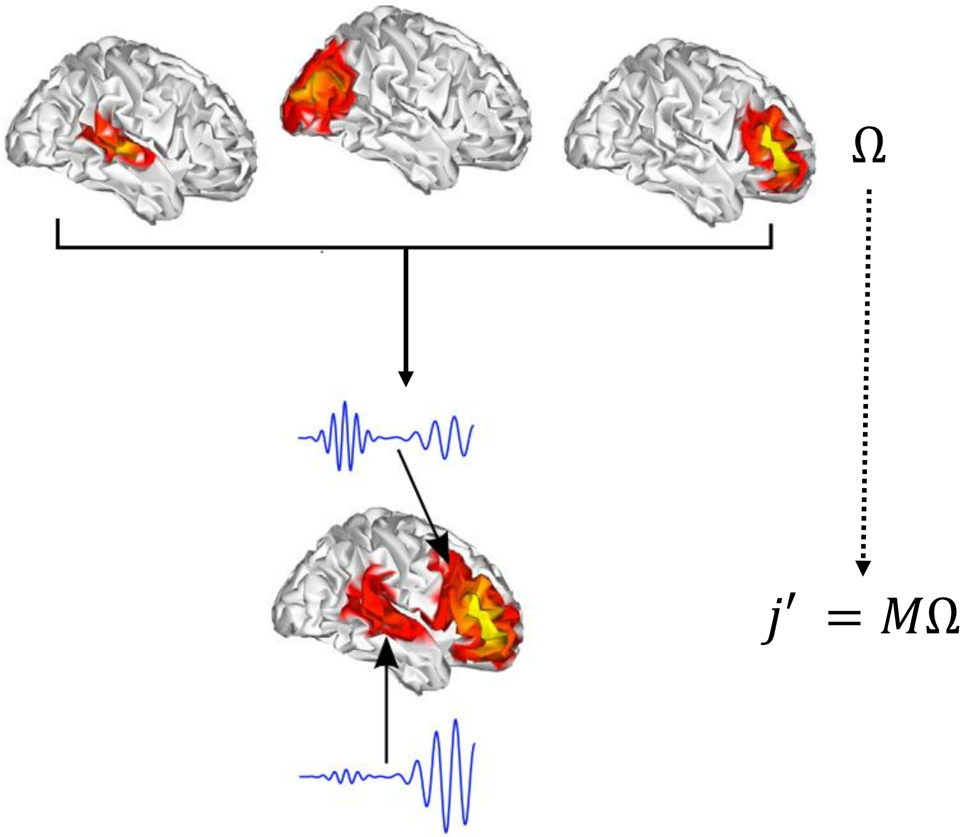
1) for supervised learning:

$$\mathcal{L}\,(\phi, j_{true}|\Theta) = \|j' - j_{true}\|_2^2 + S(M, \Omega)$$

2) for unsupervised learning:

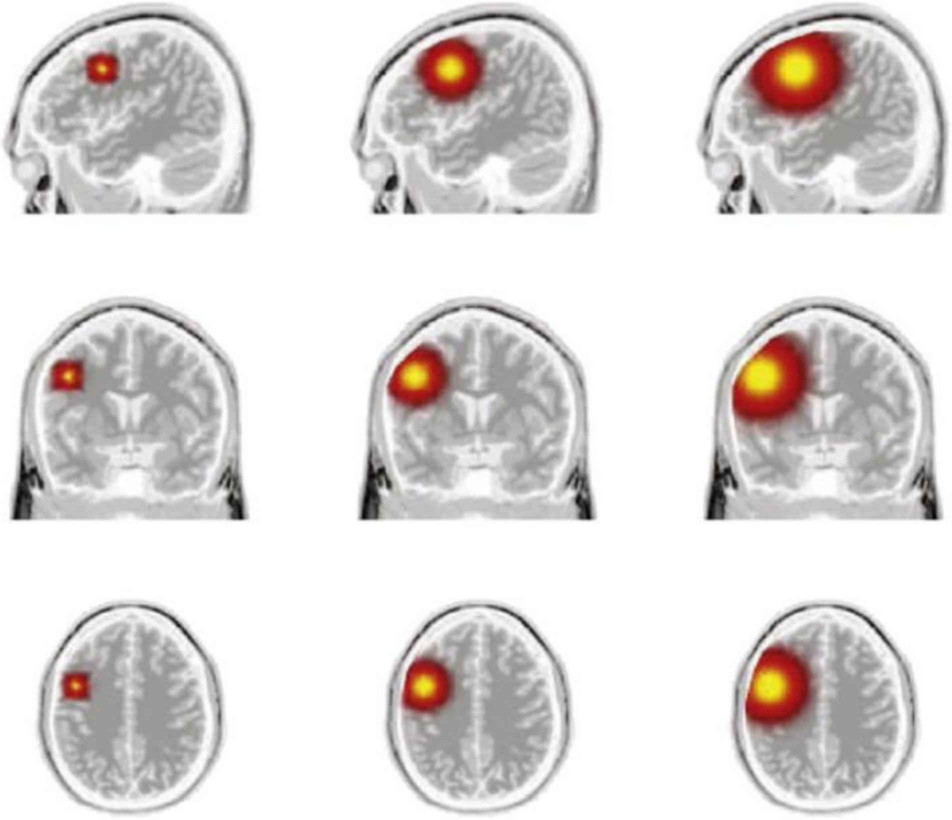
$$\mathcal{L}\,(\phi\,|\Theta, K) = \|Kj' - \phi\|_{C^{-1}}^2 + S(M, \Omega)$$

where $j' = M\Omega$;
M is the weight of the basis function represented by an ANN;
Ω is basis function, learnable from training data using gradient descent;
$S(M, \Omega)$ is the regularization term
C is the covariance matrix of sensor noise



Haufe et al., NeuroImage (2015)

Gaussian basis for synthetic source activities



Gaussian source basis:

$$\mu_n(x) = \omega_n(\sqrt{2\pi}\sigma_s)^{-3} \exp\left(-\frac{1}{2}\|x - x_n\|\sigma_s^2\right)$$

ω_n is the activity, sampled from Gaussian distribution
μ_n is the basis function centered at source x_n $(n = 1, \ldots, k)$
σ_s is the spatial standard deviation.

Synthetic source activities can be represented by:

$$j_{sim} = M\Omega + n_j$$

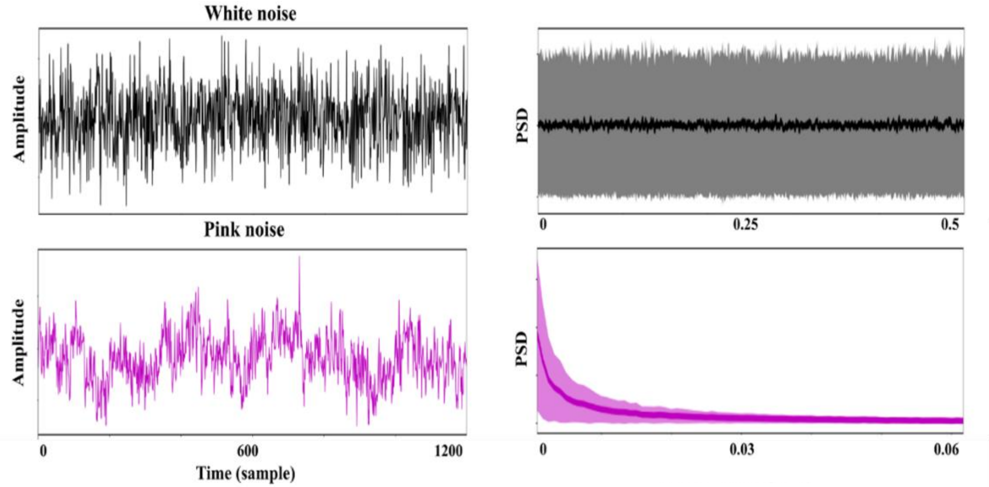
Ω is basis function, $\Omega = [\mu_1, \mu_1, \ldots, \mu_k]$;
M is the weight of the basis function;
n_j is the noise (Gaussian white noise and pink noise)

Simulating the source-sensor pairs

魏晨

楼可心

A **pipeline** to simulate EEG datasets
With empirical prior information



Noise

$n_j \sim N(0,\ \sigma_N^2 \boldsymbol{I}) \otimes filter$

Noise current $\boldsymbol{n_j}$

Liu et al., HBM (2017)

12-layer FEM
Head Model

Leadfiled matrix $\boldsymbol{K_0}$

$\boldsymbol{\Phi} = \boldsymbol{K}(\boldsymbol{J}+\boldsymbol{n_j}) + \boldsymbol{n_\Phi}$

$\boldsymbol{K} = \boldsymbol{K}_0$

$\boldsymbol{\Phi}$

Source current $\boldsymbol{J}$

Activation patterns

Sample
multi-Gaussian

Source
activity

Sensor
activity

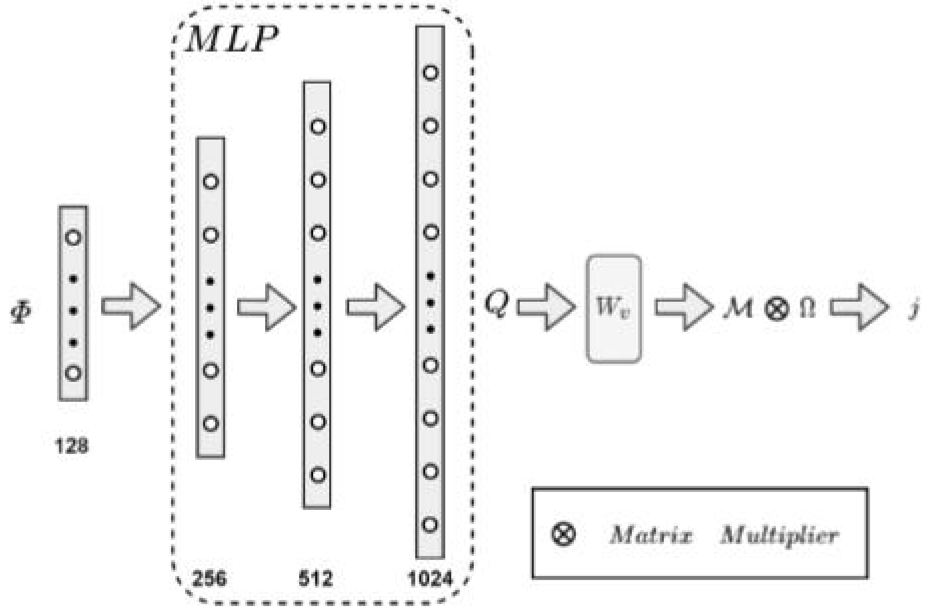
Synthetic dataset

Chen Wei et al. IJCNN 2021

Design ANN structure

Presupposition 1:

Activated EEG sources can be represented by a linear combination of independent basis functions in source space



The structure of the inverse operator (ANN)

As Presupposition 1, we define the activated source j as:

$$j = M\Omega$$

Ω is basis function, which can be optimized from the training data using gradient descent; M is the weight of the basis function:

$$Q = MLP(\phi)$$

$$M = W_v Q$$

where $Q \in \mathbb{R}^{1024}$ is the feature extracted through a Multi-Layer Perceptron (MLP) , which projects ϕ to Q, and M can be calculated by Q multiplies with coefficient matrixes $W_v \in \mathbb{R}^{3k\times1024}$.

Design regularization terms

Presupposition 2: The brain state in each time can be expressed by a small set of basis functions (M is sparse)

Presupposition 3: The basis functions have sparse edges (Ω is edge sparse)

Regularization terms:

$$S(M,\Omega) = S_1(M) + S_2(\Omega).$$

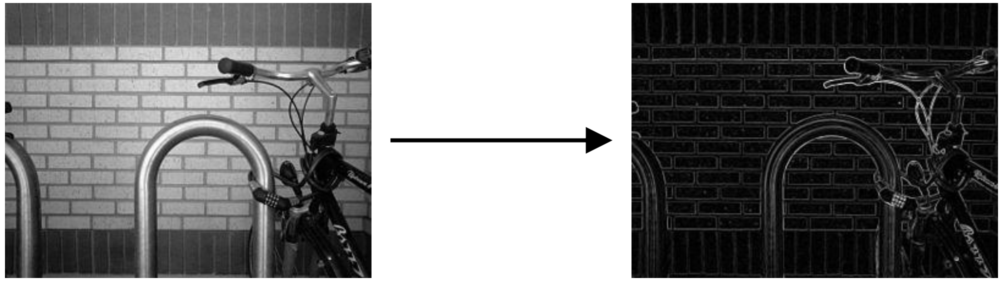
$$S_1(M) = \|M\|_1$$

$$S_2(\Omega) = \|Prewitt(\Omega)\|_1$$

$S_1(M)$ is to penalize the weight of basis function and constrains the number of activated basis;

$S_2(\Omega)$ is to penalize the basis function, making the edge of basis function sparser.

We use three-dimensional Prewitt operator as the edge extractor of the 3D source image.



Two-dimensional Prewitt operator as an edge extractor

P. Dhankhar and N. Sahu (2013)

Training details for synthetic data

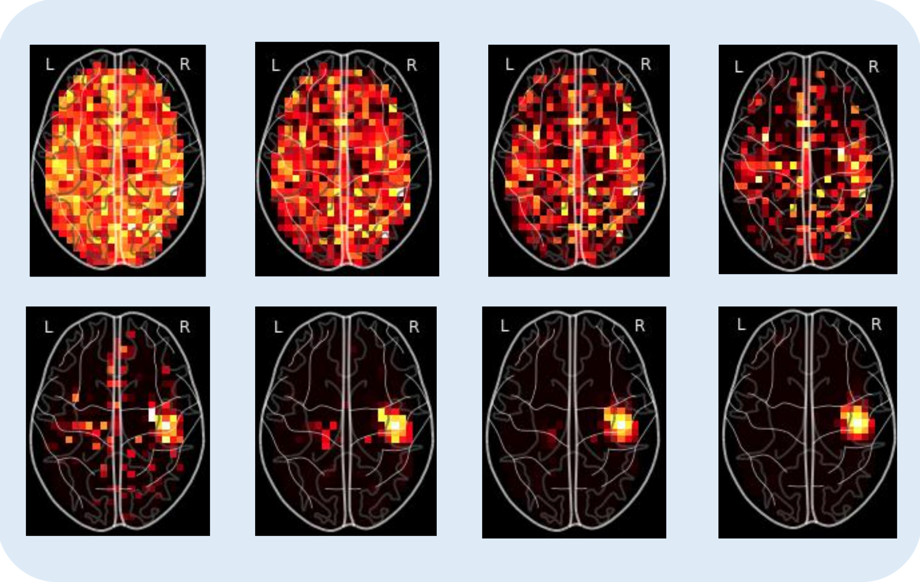
loss function:

$$\mathcal{L}\,(\phi, j_{true}|\Theta) = \|\, W_v MLP(\phi)\Omega - j_{true}\|_2^2$$

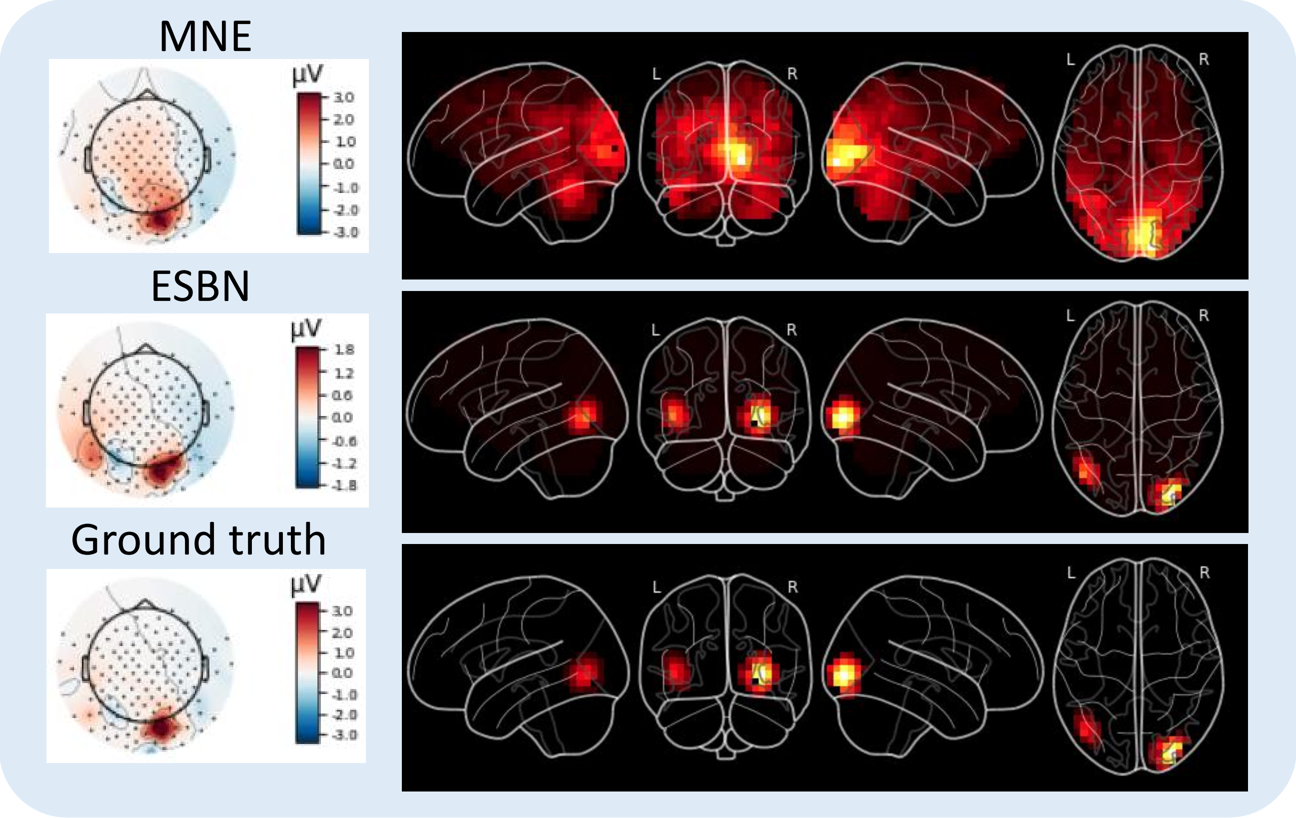
$$+\,\lambda_1\|M\|_1 + \lambda_2\|Prewitt(\Omega)\|_1 + \lambda_3\sum_{i,j}\frac{\Omega_i\Omega_j}{\|\Omega_i\|_2\|\Omega_j\|_2}$$

where λ_1=0.1, λ_2=0.00001, λ_3=0.01

Basis function evolves during training



Source localization results for different method



Results on synthetic data

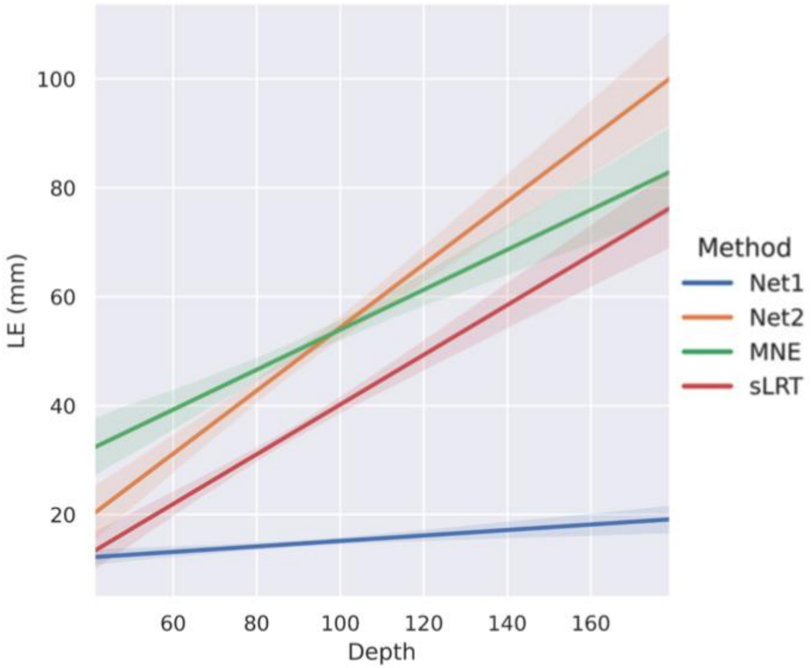
Evaluation of methods on synthetic data

Methods	LE	SD	AUC
ESBN Supervised *	**14.98(10.63)**	**21.96(8.02)**	**0.91(0.11)**
MNE	49.04(31.36)	64.34(13.82)	0.81(0.17)
dSPM	35.42(12.98)	48.48(7.87)	0.88(0.11)
sLORETA	34.84(23.95)	66.39(11.44)	0.89(0.11)
eLORETA	38.58(26.35)	67.37(11.25)	0.88(0.12)

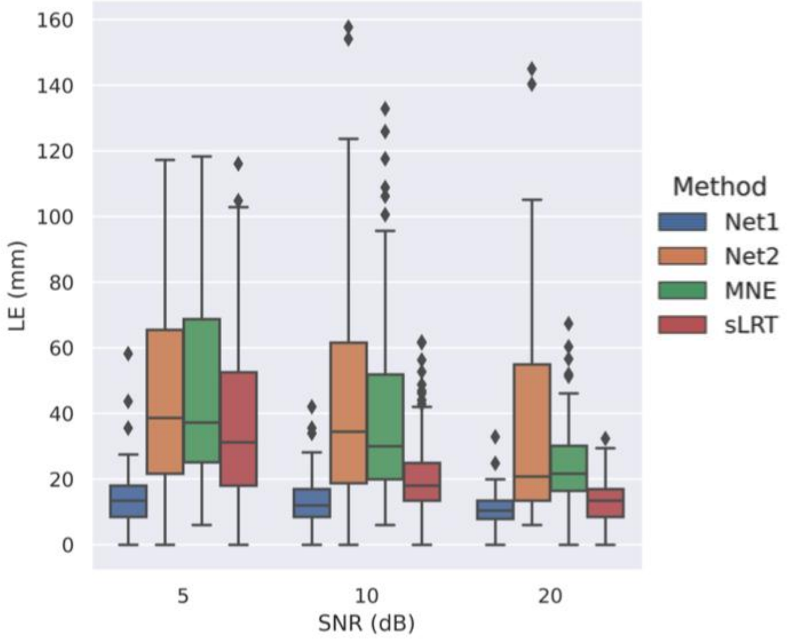
* *Abbrev.*:
LE, Localization Error
SD, Spatial Dispersion
AUC, Area Under Curve

J. G. Samuelsson et al.
NeuroImage (2021)

Localization error for sources with different depths



Localization error for signals with different SNRs



Training details for real data

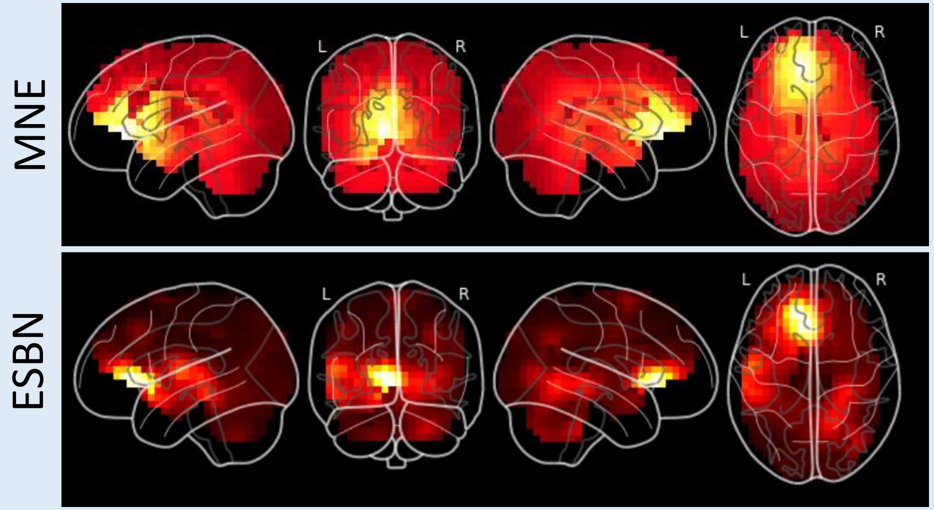
Loss function:

$$\mathcal{L}\,(\phi\,|\Theta, K) = \|K\,W_v MLP(\phi)\Omega - \phi\|_{C^{-1}}^2$$

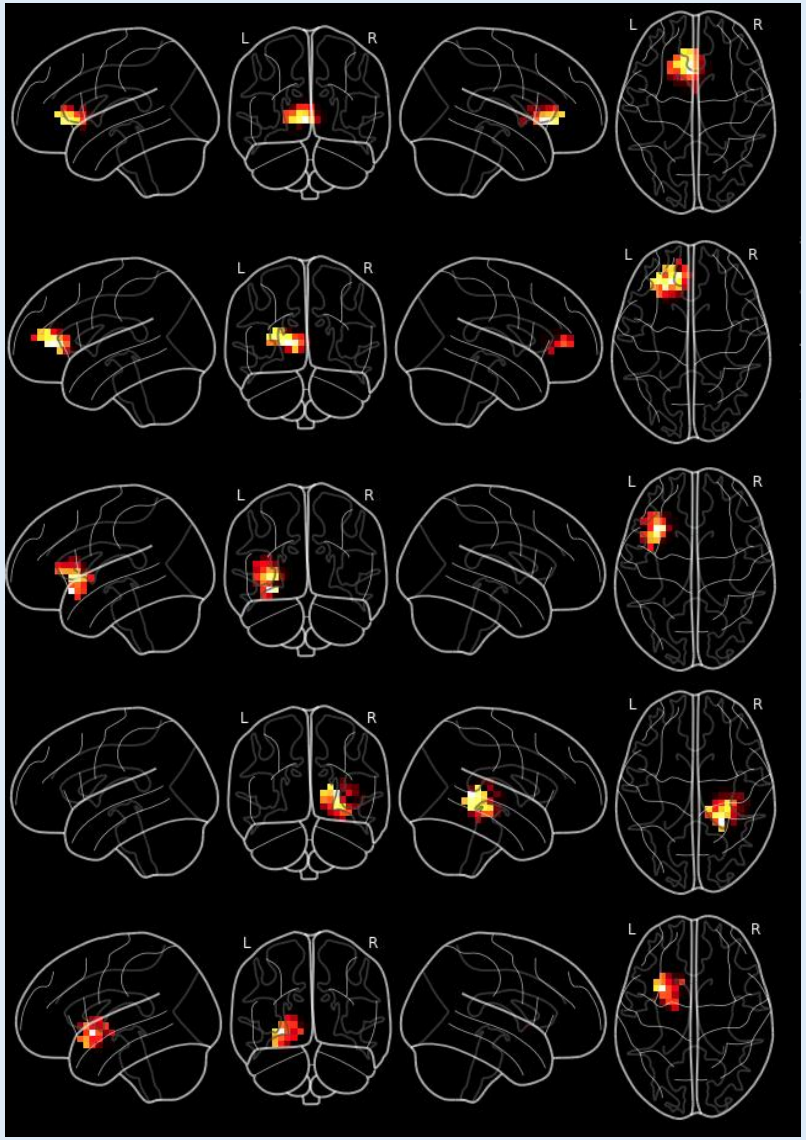
$$+\,\lambda_1\|M\|_1 + \lambda_2\|Prewitt(\Omega)\|_1 + \lambda_3\sum_{i,j}\frac{\Omega_i\Omega_j}{\|\Omega_i\|_2\|\Omega_j\|_2}$$

where λ_1=1, λ_2=0.0001, λ_3=0.1

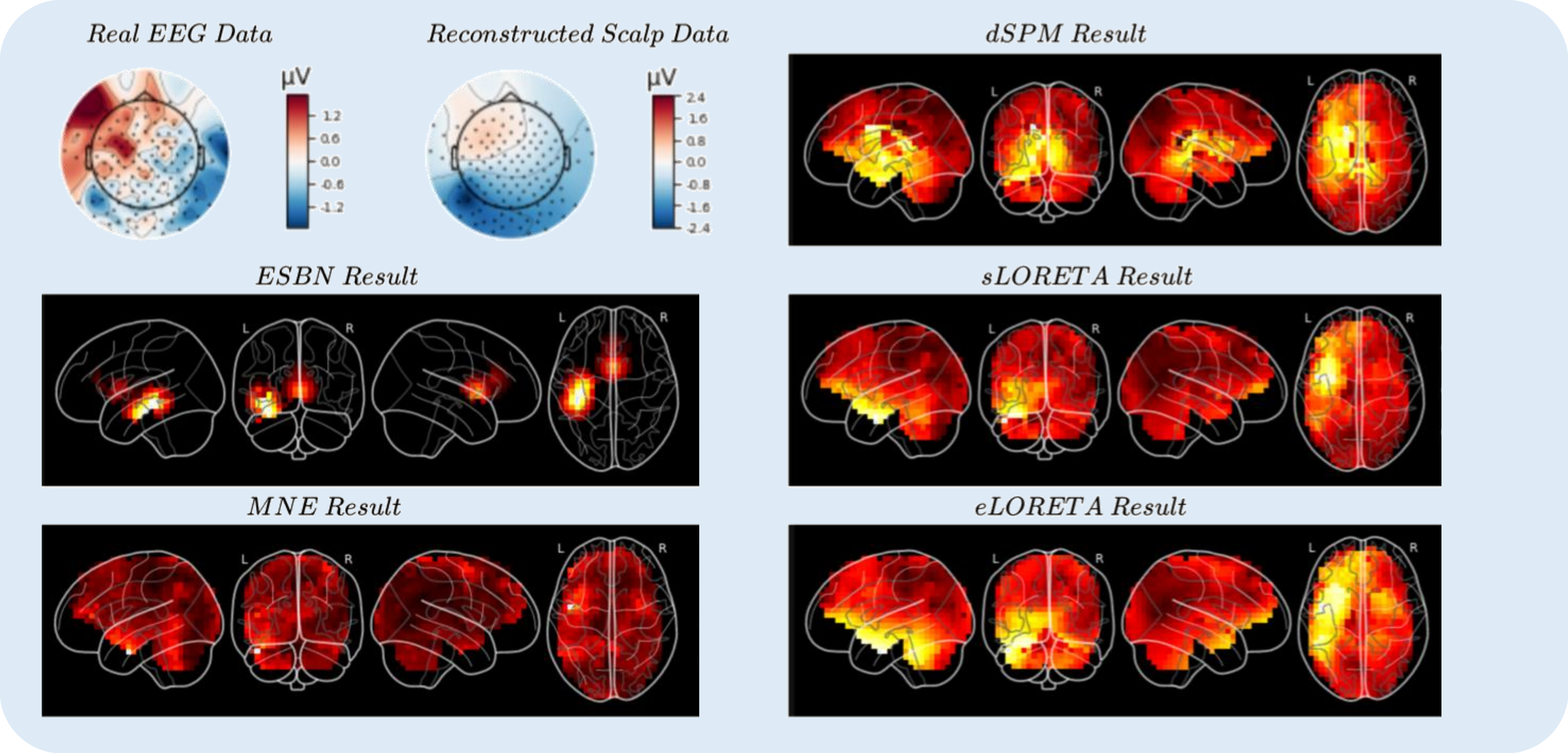
Average result of MNE source localization



The most frequent basis functions



Results on real data

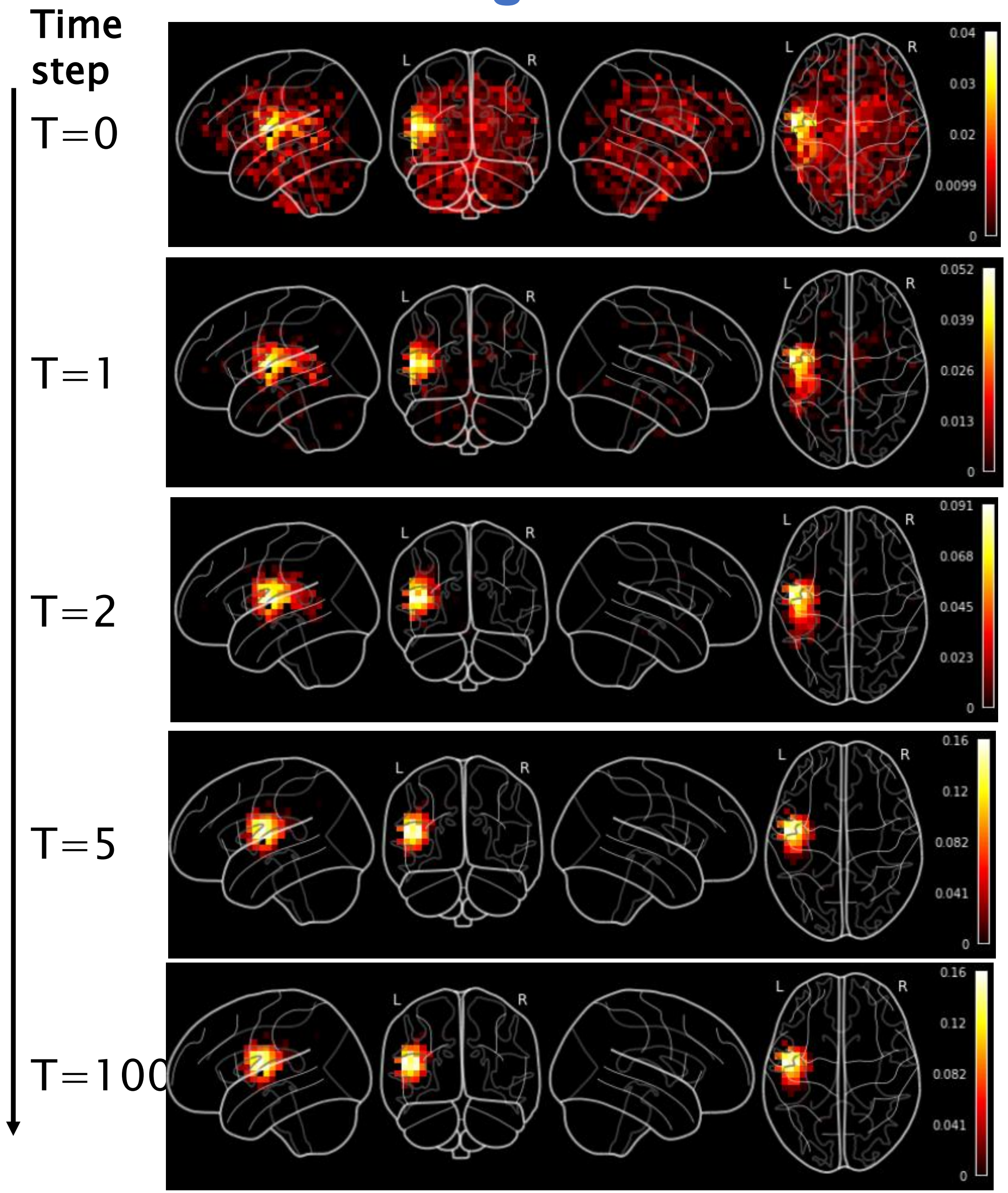


- The framework of ESBN allows for bidirectional flow of information:
  1) generate EEG data from EEG source
  2) reconstruct EEG source from EEG data.
- ESBN has an end-to-end supervised version based on synthetic data and an unsupervised version to fine tune the model based on real EEG data for better generalization
- Learn the basis prior from training data
- Robust under different source depths, SNR and source direction conditions
- Better performance than numerical algorithms with less time consumption

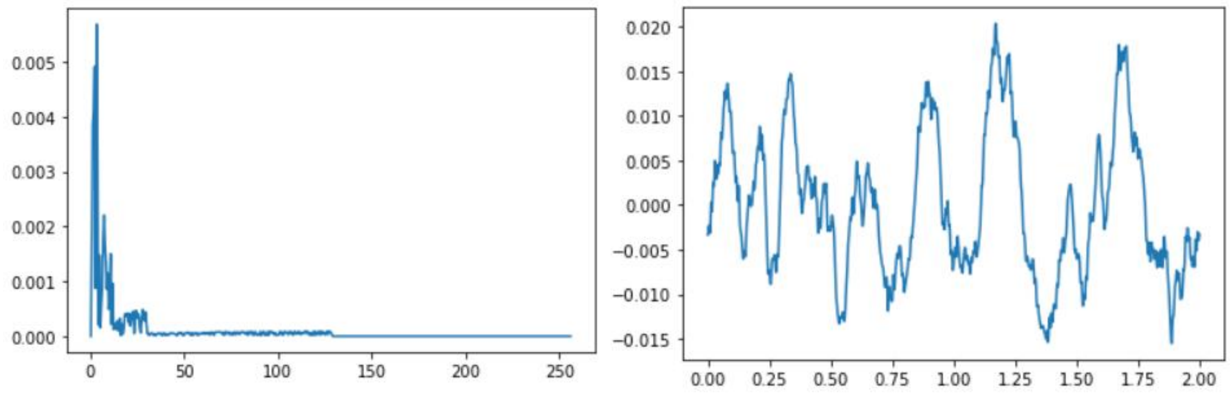
Next step:

- incorporate temporal information for robustness and source dynamics
- Incorporate information from other modal neural data, eg., invasive

Using RNN to stabilize source localization for time series signal



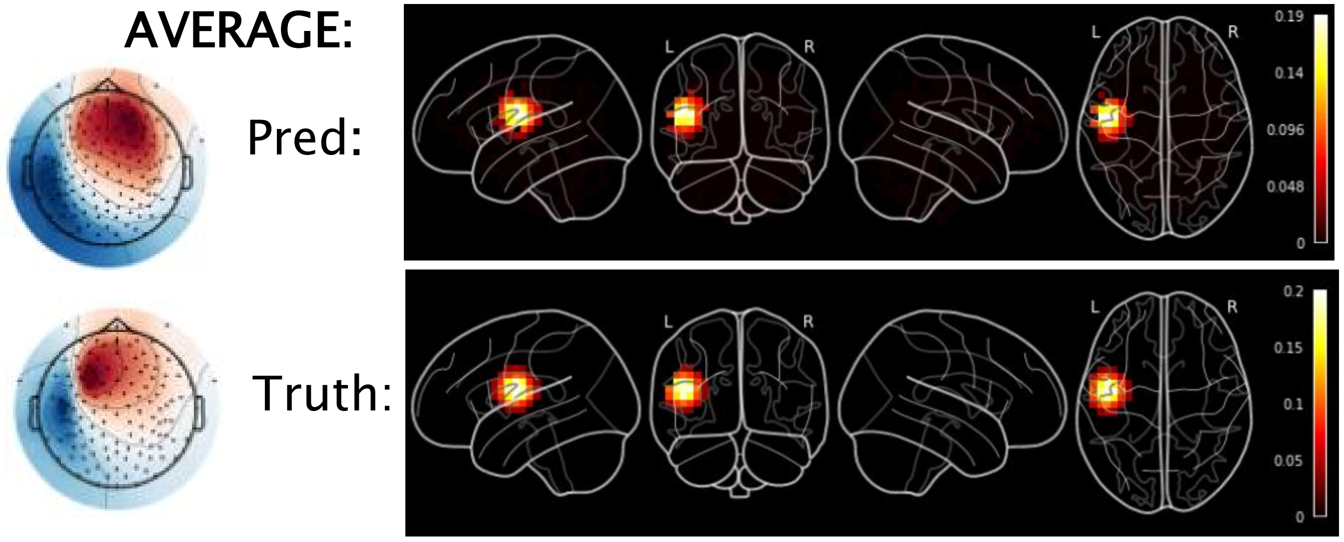
Source Simulation



Frequency domain

Time domain

AVERAGE:



Chen et al (unpublished data)

Dependency between sources

$$x_1(t) = \Phi(t) + n_1(t)$$
$$x_2(t) = i * x_1(t-a) + j * x_2(t-b) + k * x_1(t-c) + n_2(t)$$
$$x_3(t) = p * x_1(t-\mathrm{d}) + q * x_3(t-\mathrm{e}) + n_3(t)$$

$$x_1(t) = \Phi(t) + n_1(t),$$
$$x_2(t) = 0.35x_1(t-0.100) + 0.25 * x_2(t-0.0075) + 0.1x_2(t-0.0125) + n_2(t),$$
$$x_3(t) = 0.60x_1(t-0.200) + 0.10 * x_3(t-0.0125) + n_3(t)$$

S.A.H. Hosseini et al. Clinical Neurophysiology (20

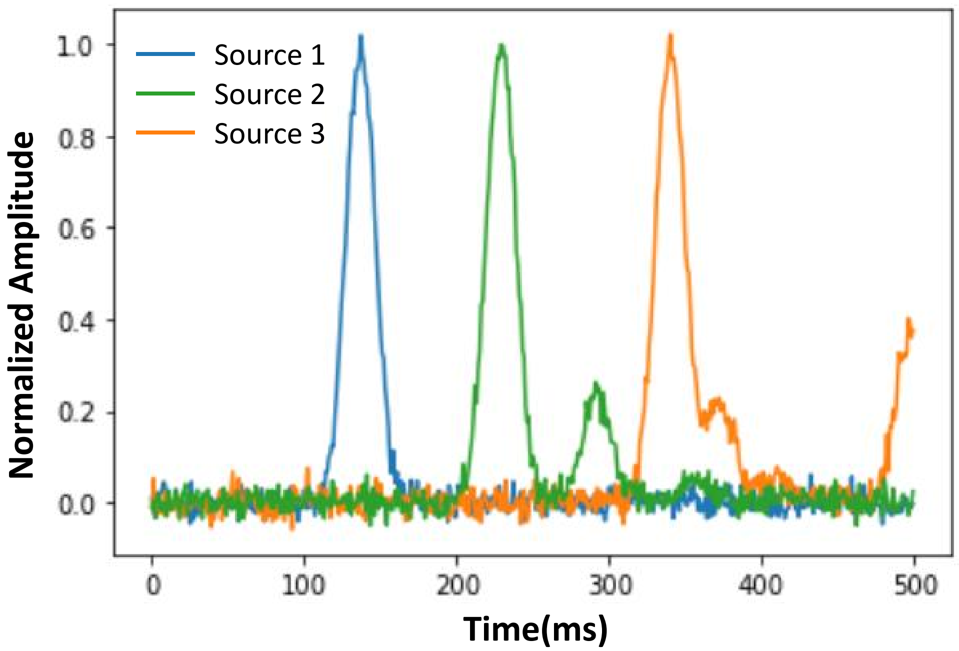
t timepoint

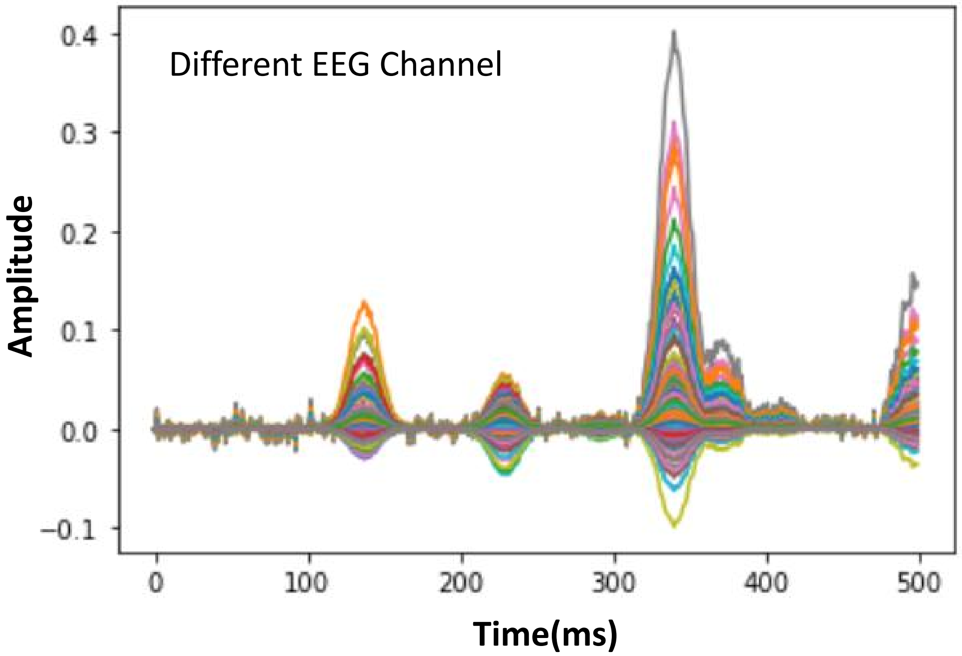
$\Phi(t)$ Gaussian waveform

$n_2(t)$ Gaussian white noise

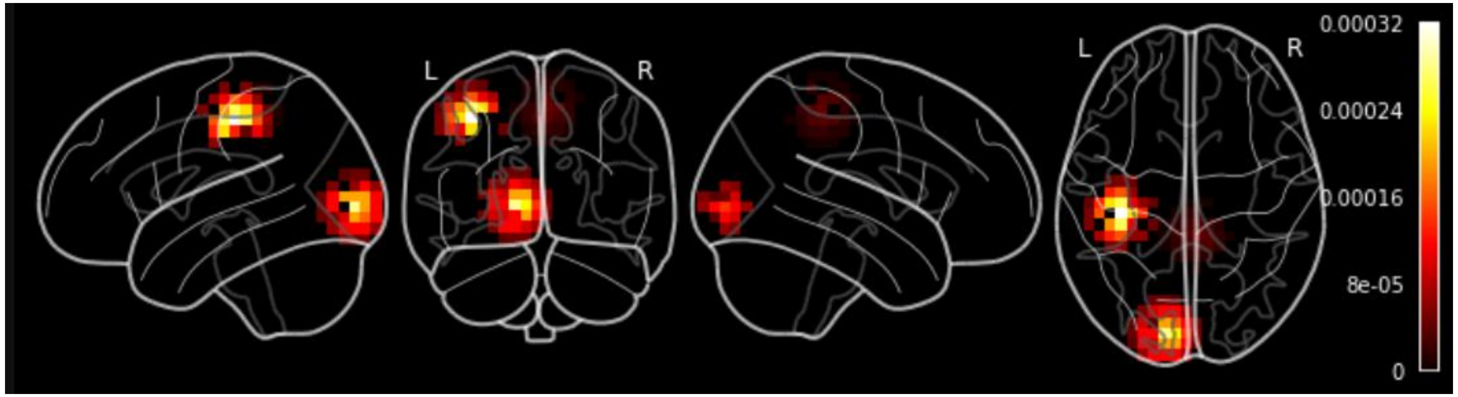
$i, \mathrm{j}, \mathrm{k}, \mathrm{p}, \mathrm{q}$ dependency ration sampled from uniform distribution

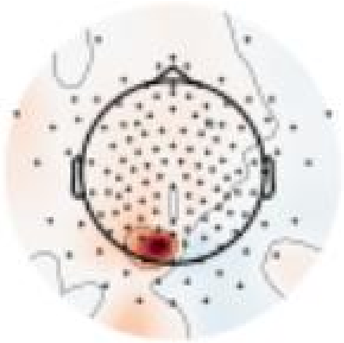
$a,\ b,\ c,\ d,\ e$ time delay, sampled from uniform distribution

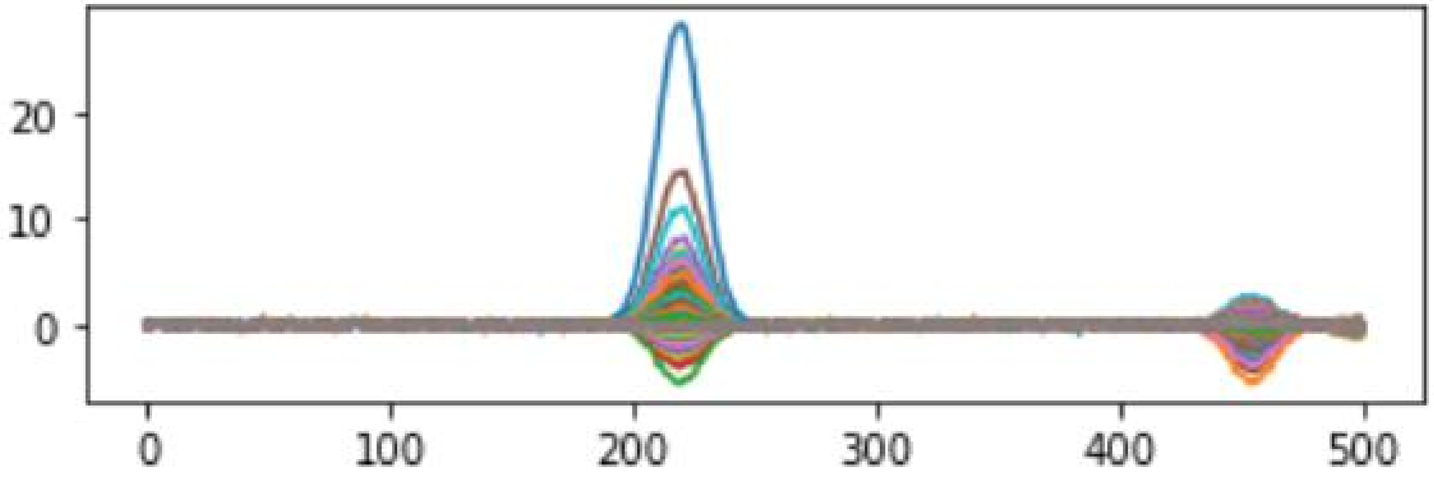




Combine temporal time series with spatial gaussian source basis



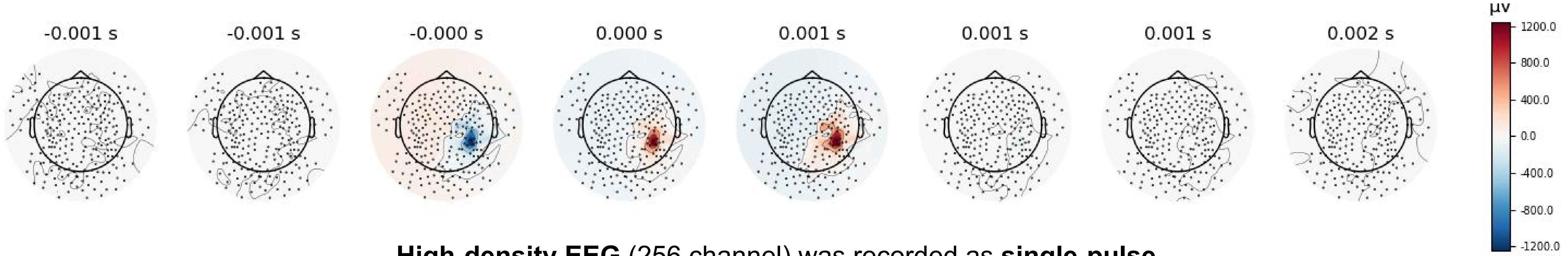




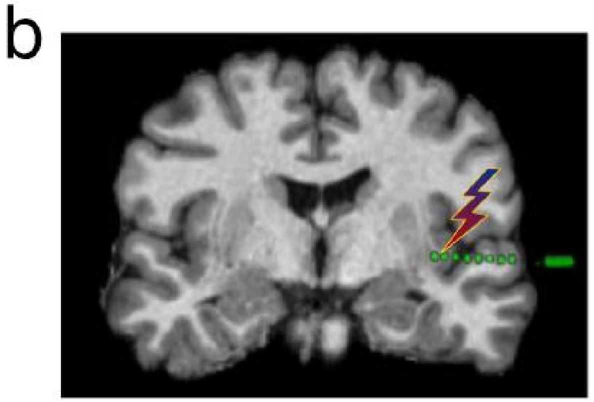
Combine other modal data: EEG + sEEG

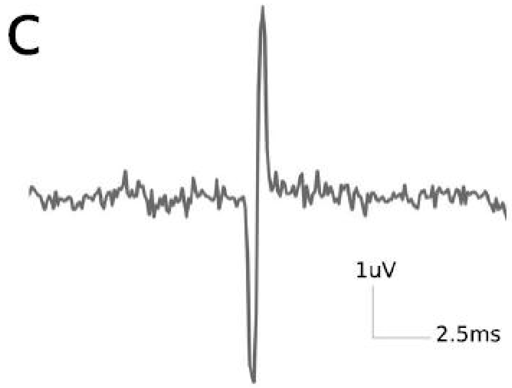
the Localize-MI dataset

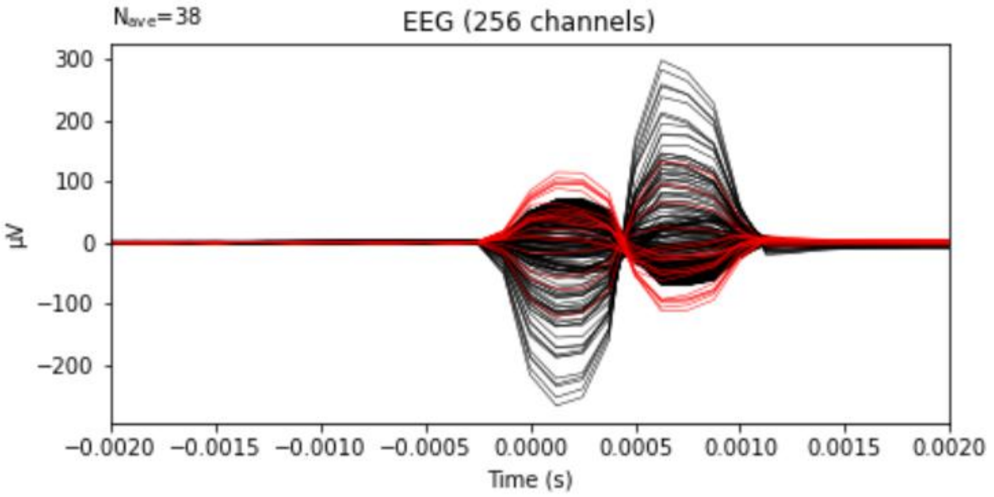
Trial-averaged EEG topography for Stim SEEG-HDEEG



High-density EEG (256 channel) was recorded as **single-pulse biphasic** currents were delivered on SEEG electrodes.





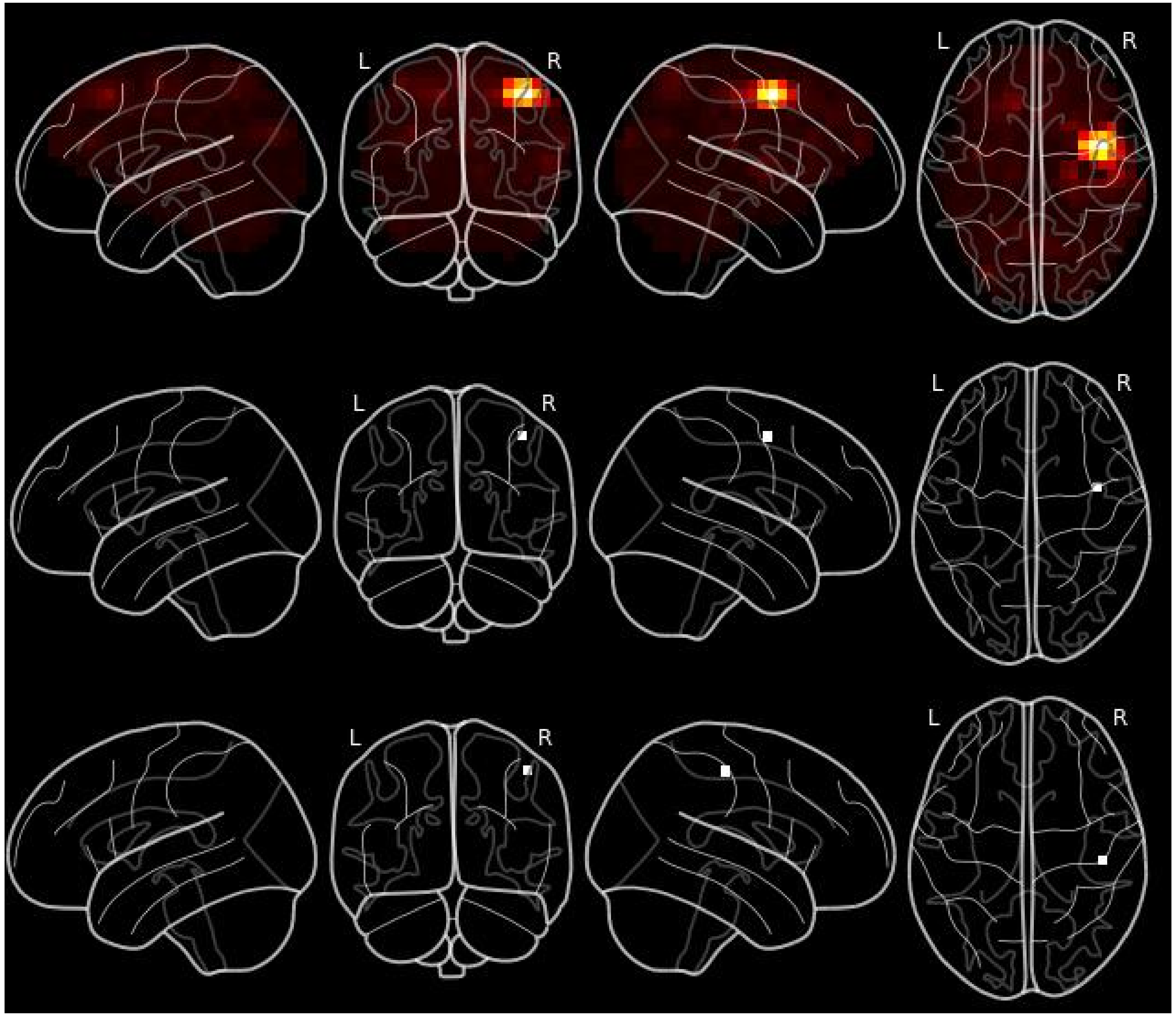


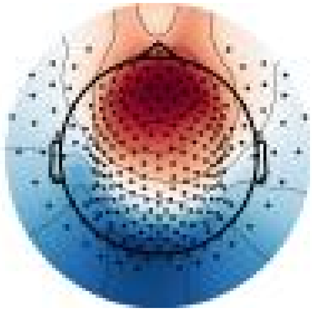
(Mikulan et al, Scientific Data 2020)

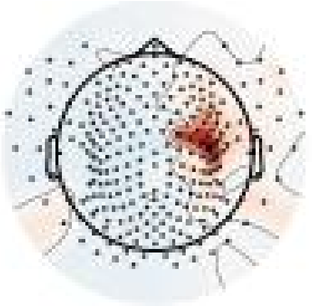
Network result

Peak source

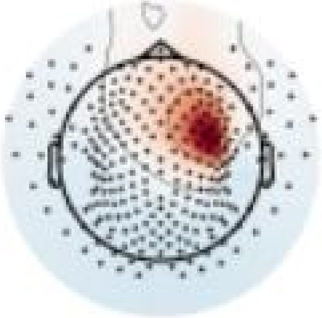
Real stim site



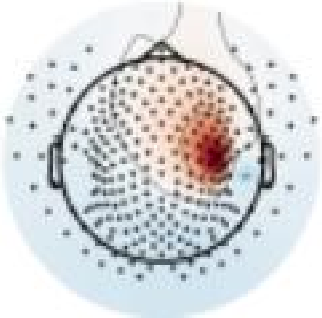




Reconstructed EEG



Peak source EEG

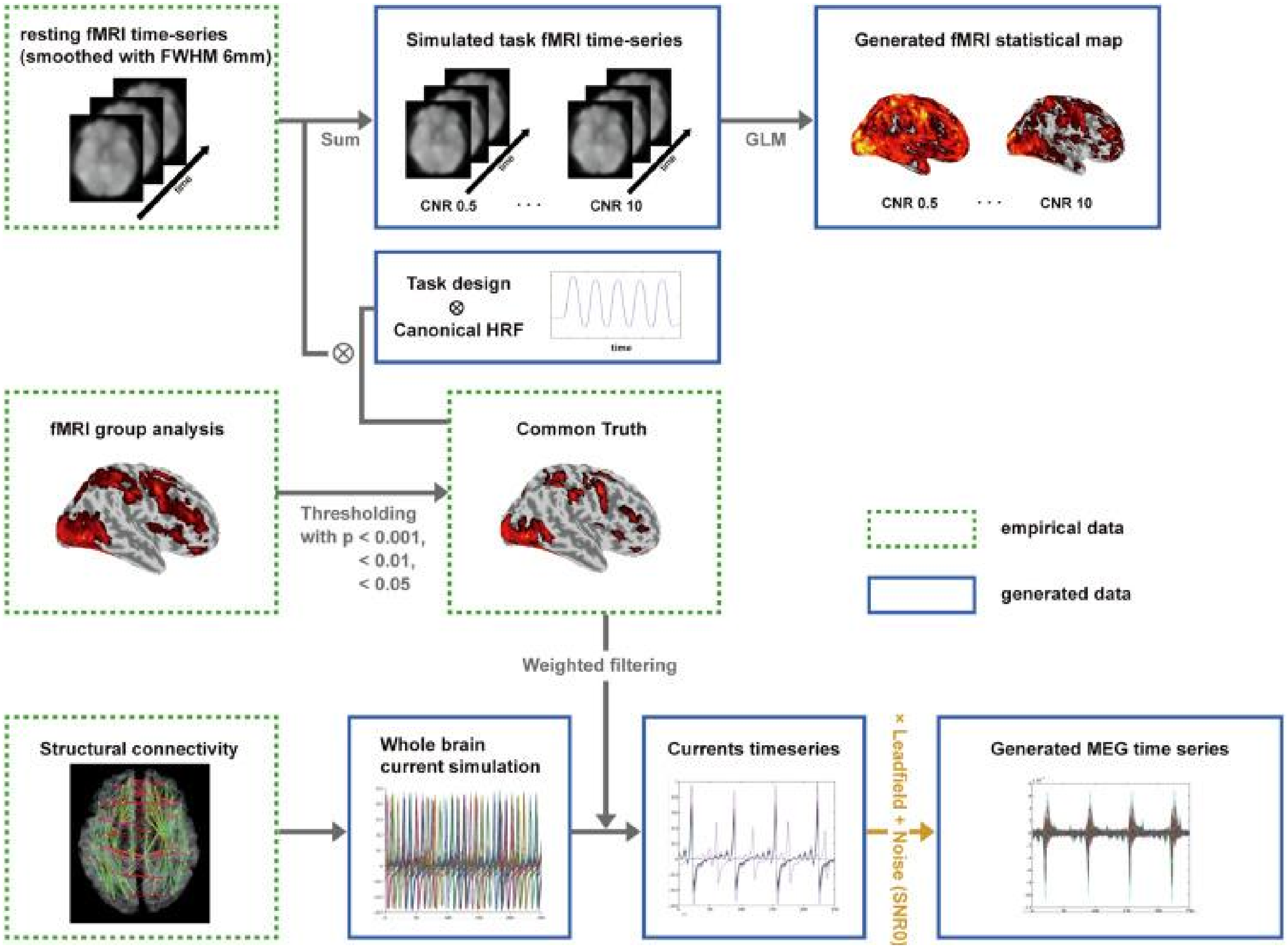


Stim source EEG

Outline

- Definition of EEG source localization problem
- Problem characteristics of EEG source localization problem
- Numerical methods with mathematical constraints
  - Instantaneous solvers with sparse/non-sparse priors
  - Time block solvers
- Data-driven methods with anatomical and physiological constraints
  - Deep neural networks with simulated dataset biological constraints
  - Generative Model with meta-fMRI Priors

Meta-fMRI Priors for Source Imaging



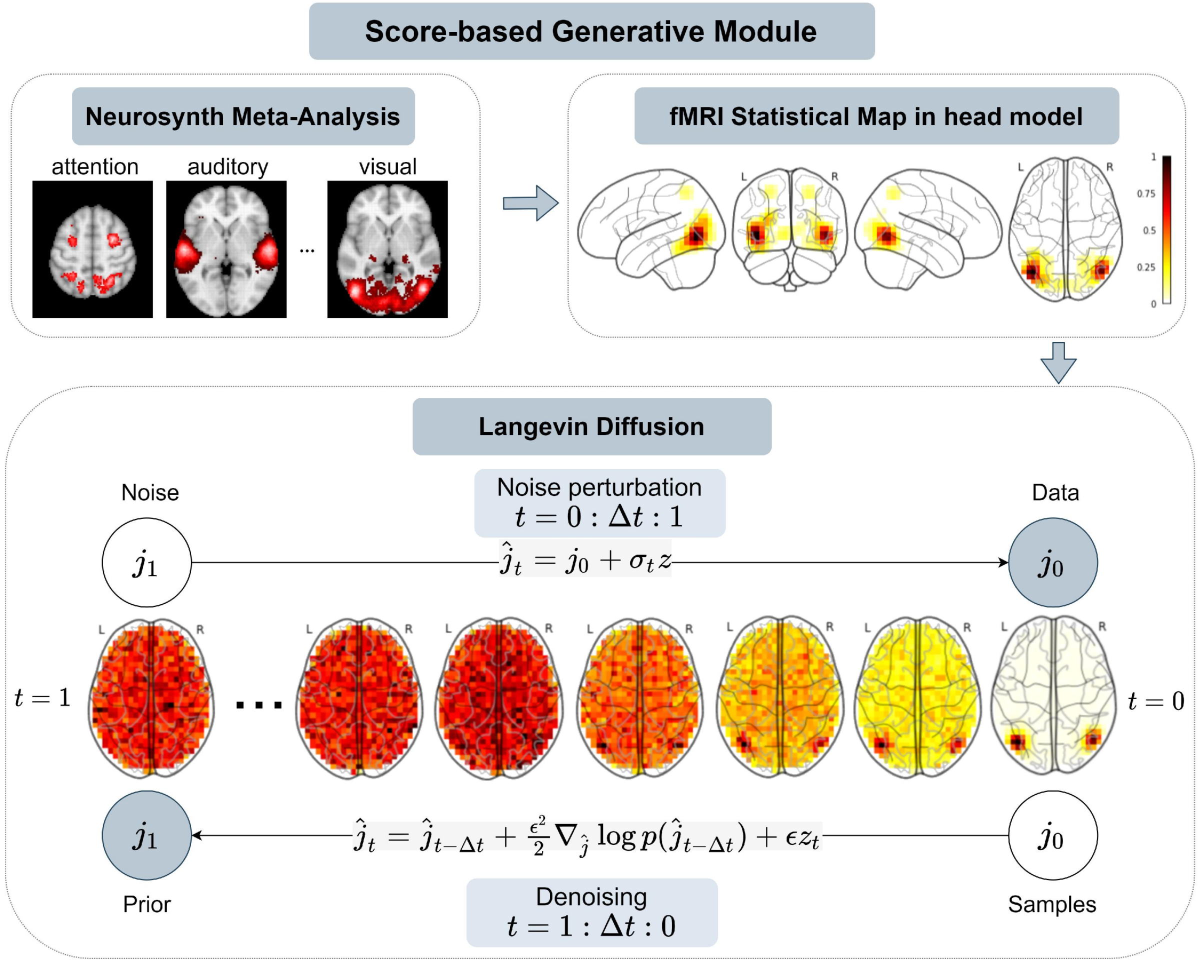
Suzuki, K., & Yamashita, O. (2021). MEG current source reconstruction using a meta-analysis fMRI prior. *NeuroImage*, *236*, 118034.

Score-based generative modeling: outline

Flexible models	Improved generation	Probability evaluation
• Bypass the normalizing constant • Principled statistical methods	• Higher sample quality than GANs • Controllable generation	• Accurate probability evaluation • Better estimation of data probabilities
[**Song** et al. UAI 2019 oral]	[**Song** & Ermon. NeurIPS 2019 oral] [**Song** & Ermon. NeurIPS 2020] [**Song** et al. ICLR 2021 oral] (Outstanding Paper Award) [**Song** et al. ICLR 2022]	[**Song** et al. ICLR 2021 oral] [**Song** et al. NeurIPS 2021 spotlight]

Courtesy on 宋飏，https://www.youtube.com/watch?v=nv-WTeKRLl0

Score-based generative model to learn source distributions



Algorithm 1 Unconditional Sampling

Require: N

$\hat{j}_t^g = \sigma_1 z_0, z_0 \sim N(0, I), \Delta t \leftarrow \frac{1}{N}$

for $i = N - 1$ to 0 **do**

  $t \leftarrow \frac{i+1}{N}$

  $\nabla_{\hat{j}} \log p(\hat{j}_{t-\Delta t}) \leftarrow s_\theta(\hat{j}_t, t)$

  $z \sim N(0, I)$

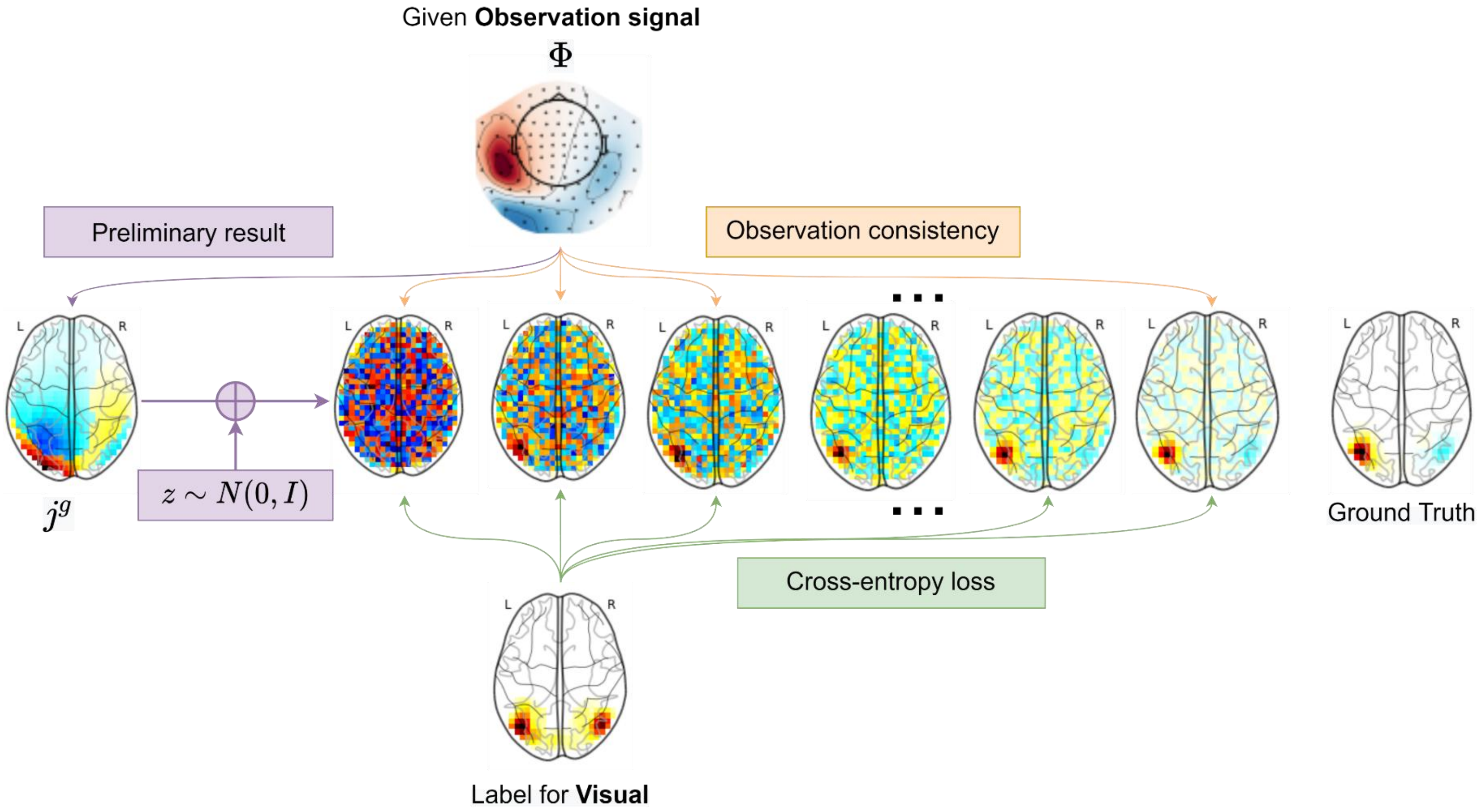
  $\hat{j}_t = \hat{j}_{t-\Delta t} + \frac{\epsilon^2}{2} \nabla_{\hat{j}} \log p(\hat{j}_{t-\Delta t}) + \epsilon z$

end for

return $\hat{j}_0$

Chen and Lou et al, (unpublished)

Deep generative model to integrate with multiple priors



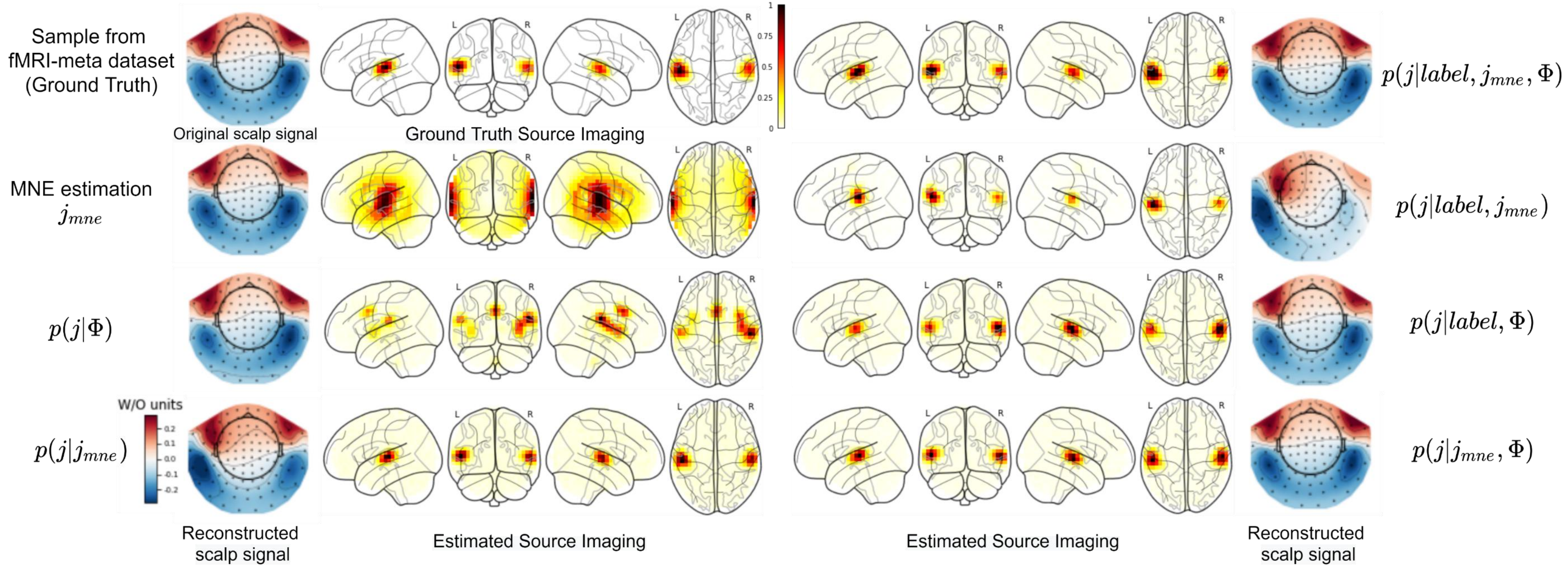
Algorithm 2 Iterative Reconstruction Module

Require: N, Φ, $\lambda(SVD)$, $c(label)$, j^g, $t_0(precondition)$

$\hat{j}^g_{t_0} = j + \sigma_{t_0} z_0, z_0 \sim N(0, I), \Delta t \leftarrow \frac{t_0}{N}$
for $i = N - 1$ to 0 **do**
  $t \leftarrow t_0 \frac{i+1}{N}$
  $\hat{j}_{t-\Delta t} \leftarrow h(\hat{j}_t, \Phi, \lambda)$
  $\nabla_{\hat{j}} \log p(\hat{j}_{t-\Delta t}|c) \leftarrow s_\theta(\hat{j}_t, t) + \log p(c|\hat{j}_{t-\Delta t})$
  $z \sim N(0, I)$
  $\hat{j}_t = \hat{j}_{t-\Delta t} + \frac{\epsilon^2}{2} \nabla_{\hat{j}} \log p(\hat{j}_{t-\Delta t}|c) + \epsilon z$
end for
return $\hat{j}_0$

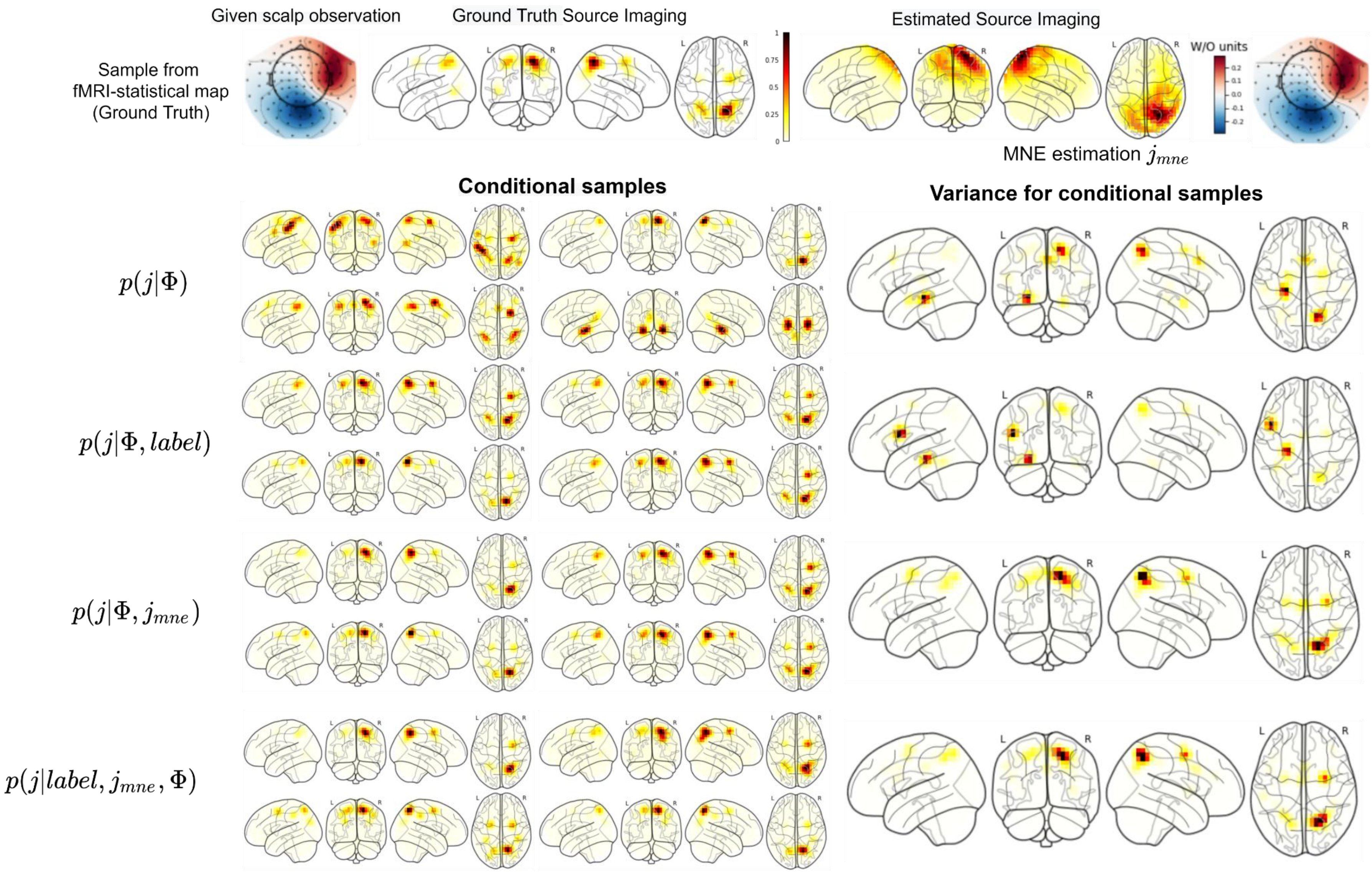
Chen and Lou et al, (unpublished)

Results on synthetic data

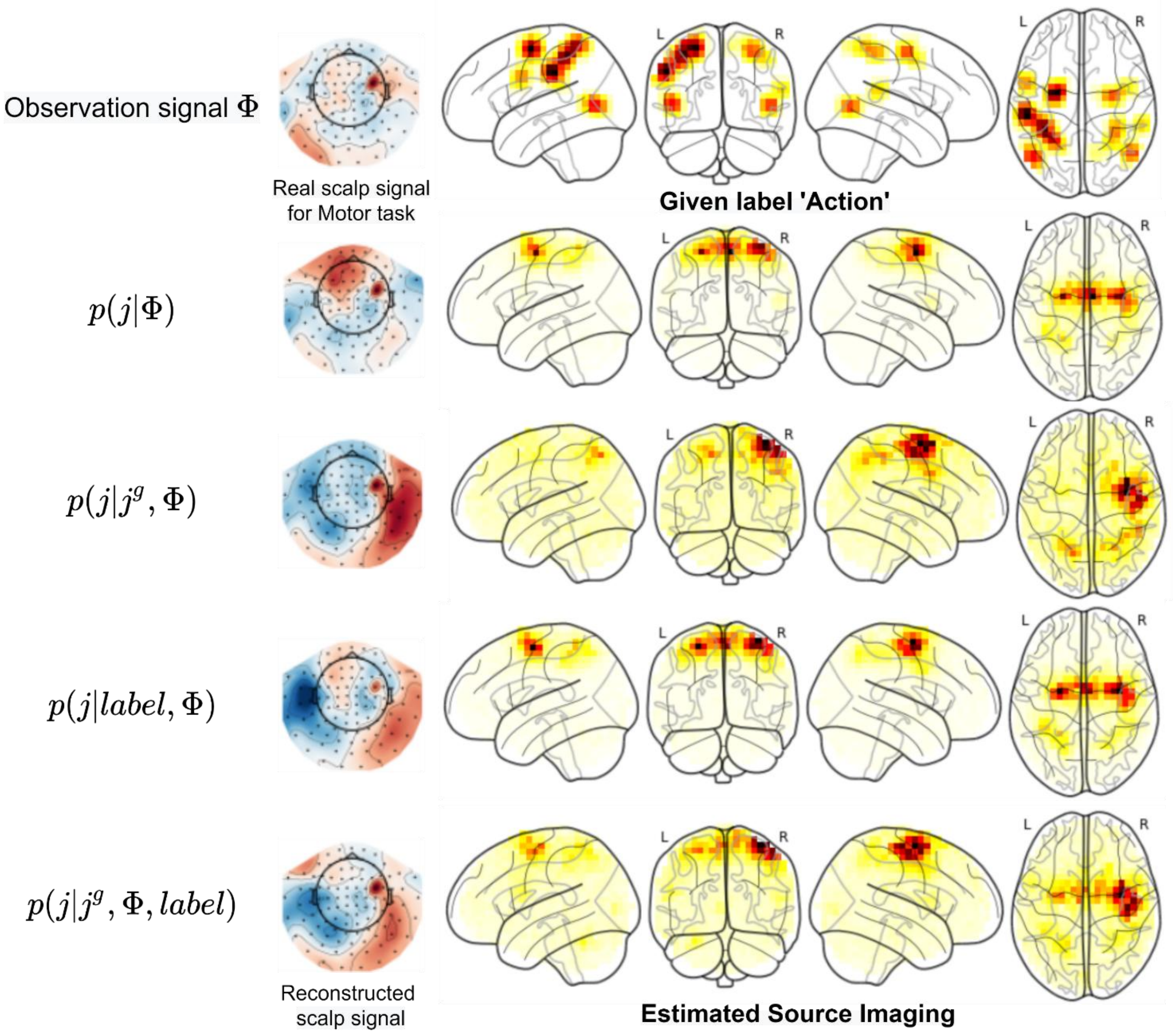


Chen and Lou et al, (unpublished)

The variance distribution of generated samples with different priors



Results on real EEG dataset



Summary

- **Numerical methods with mathematical constraints**

  Well designed model for specific tasks
- **Data-driven methods with anatomical and physiological constraints**

  Multiple priors with learnable data distribution

Future directions

Data perspective:

- Learn the prior knowledge in specific domains, eg., epilepsy and cognitive tasks.
- Introduce prior knowledge from other neuroimaging modalities, eg., fMRI, sEEG, ECoG.
- Extend the range of prior knowledge from spatial information to spatiotemporal informatio

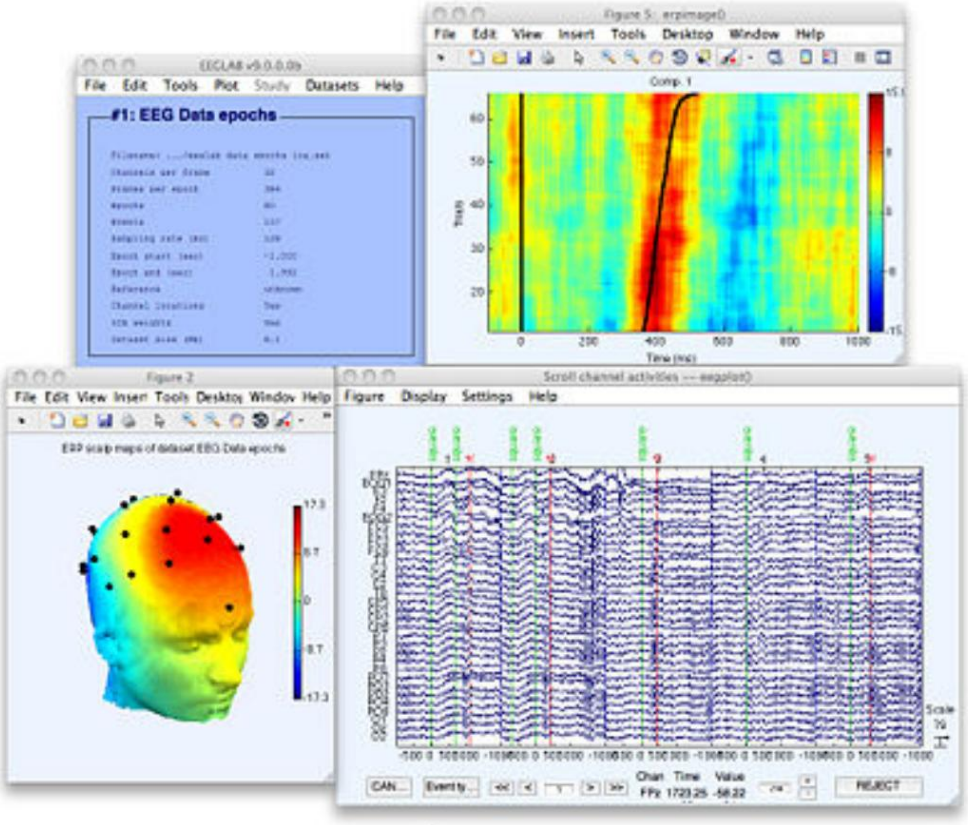
Model perspective:

- Improve the robustness of inverse solution to data noise, forward model noise, and other n
- Generalize specific inverse model to new tasks
- Learn model parameters in an adaptive way

Toolbox for EEG analysis

EEGlab (mathlab)

Official webpage https://sccn.ucsd.edu/eeglab/index.php
Tutorial https://www.bilibili.com/video/BV1mJ411s7vH

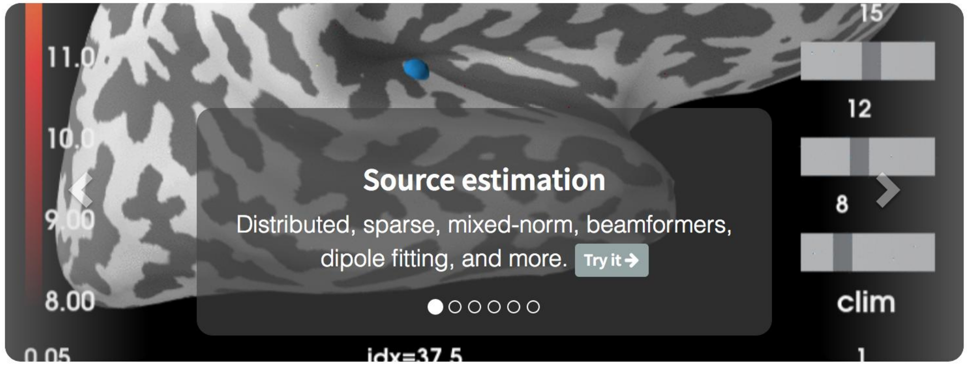


MNE-python

Official webpage https://mne.tools/stable/index.html
Tutorial https://www.bilibili.com/video/BV1YK411T7H

MEG + EEG ANALYSIS & VISUALIZATION

Open-source Python package for exploring, visualizing, and analyzing human neurophysiological data: MEG, EEG, sEEG, ECoG, NIRS, and more.



EEG Analysis Tool: MNE

Open-source Python package for exploring, visualizing, and analyzing human neurophysiological data: MEG, EEG, sEEG, ECoG, NIRS, and more.

EEG Analysis Tool: MNE

What can MNE do?

Source Estimation
Distributed, sparse, mixed-norm, beamformers, dipole fitting, and more.

Machine Learning
Advanced decoding models including time generalization.

Encoding Models
Receptive field estimation with optional smoothness priors.

Statistics
Parametric and non-parametric, permutation tests and clustering.

Connectivity
All-to-all spectral and effective connectivity measures.

Data Visualization
Explore your data from multiple perspectives.

EEG Applications

In disease diagnosis (e.g., epilepsy, depression, ADHD…)