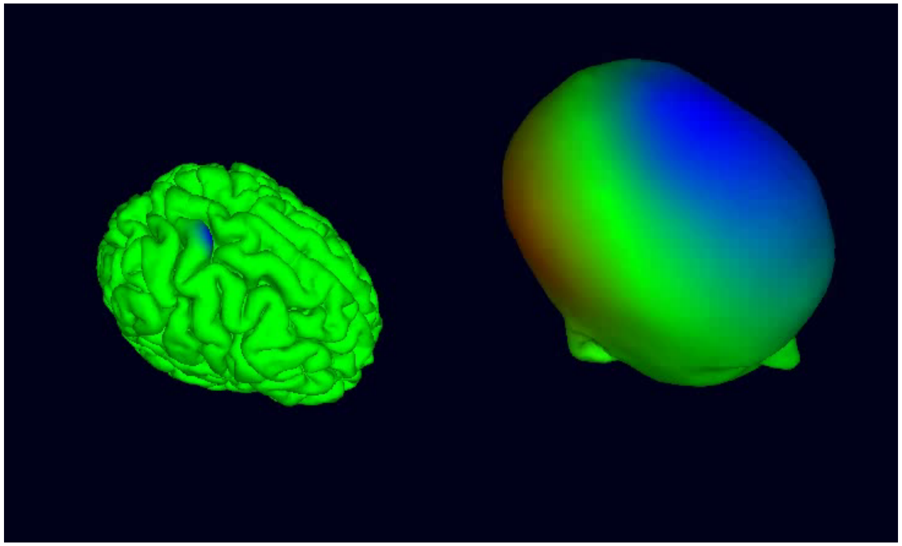


Forward and Inverse Problem of EEG

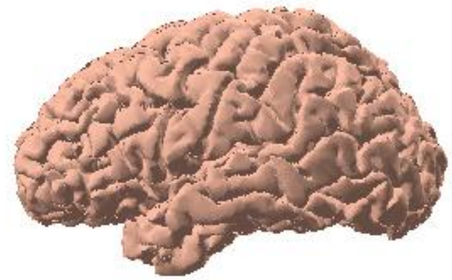
Zeynep AKALIN ACAR

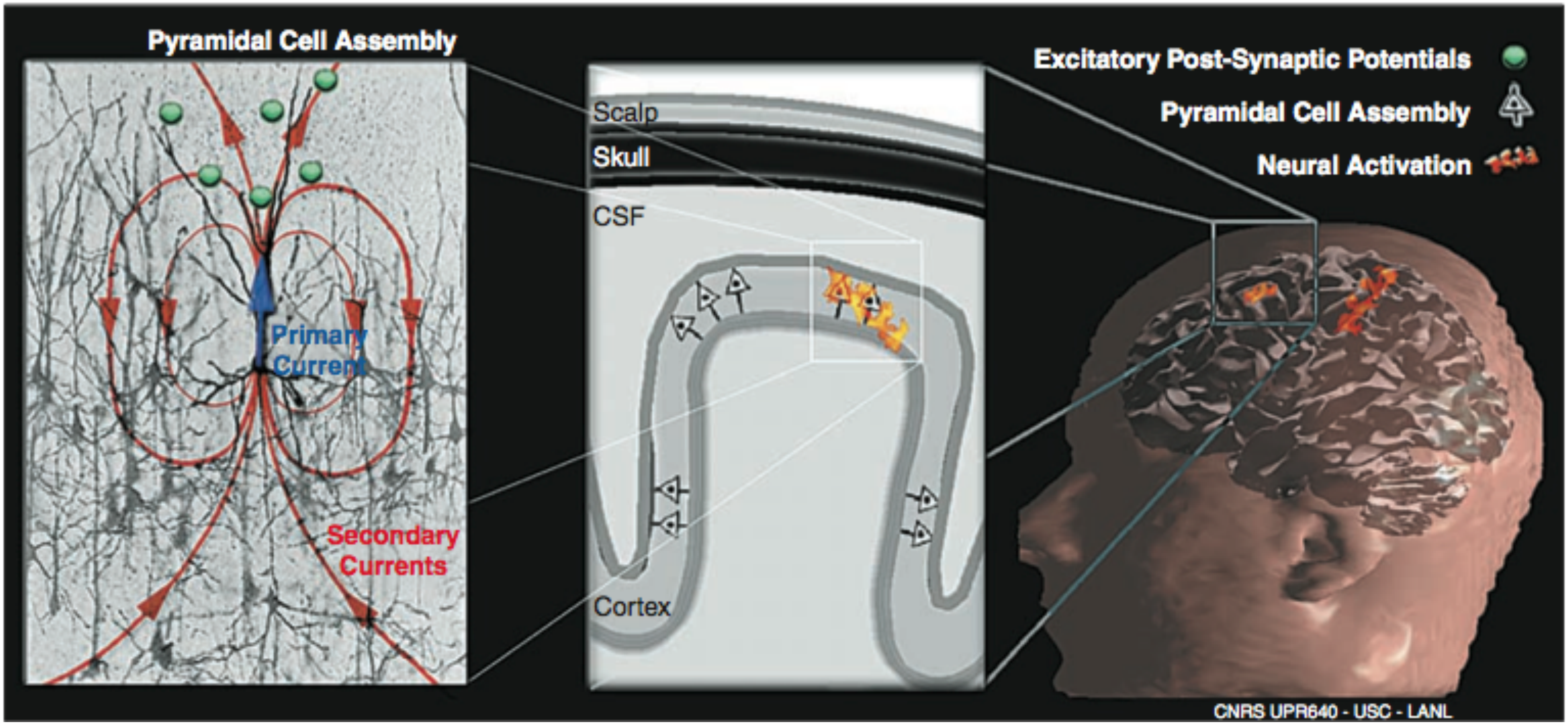
Swartz Center for Computational Neuroscience

November, 2012

Generators of EEG

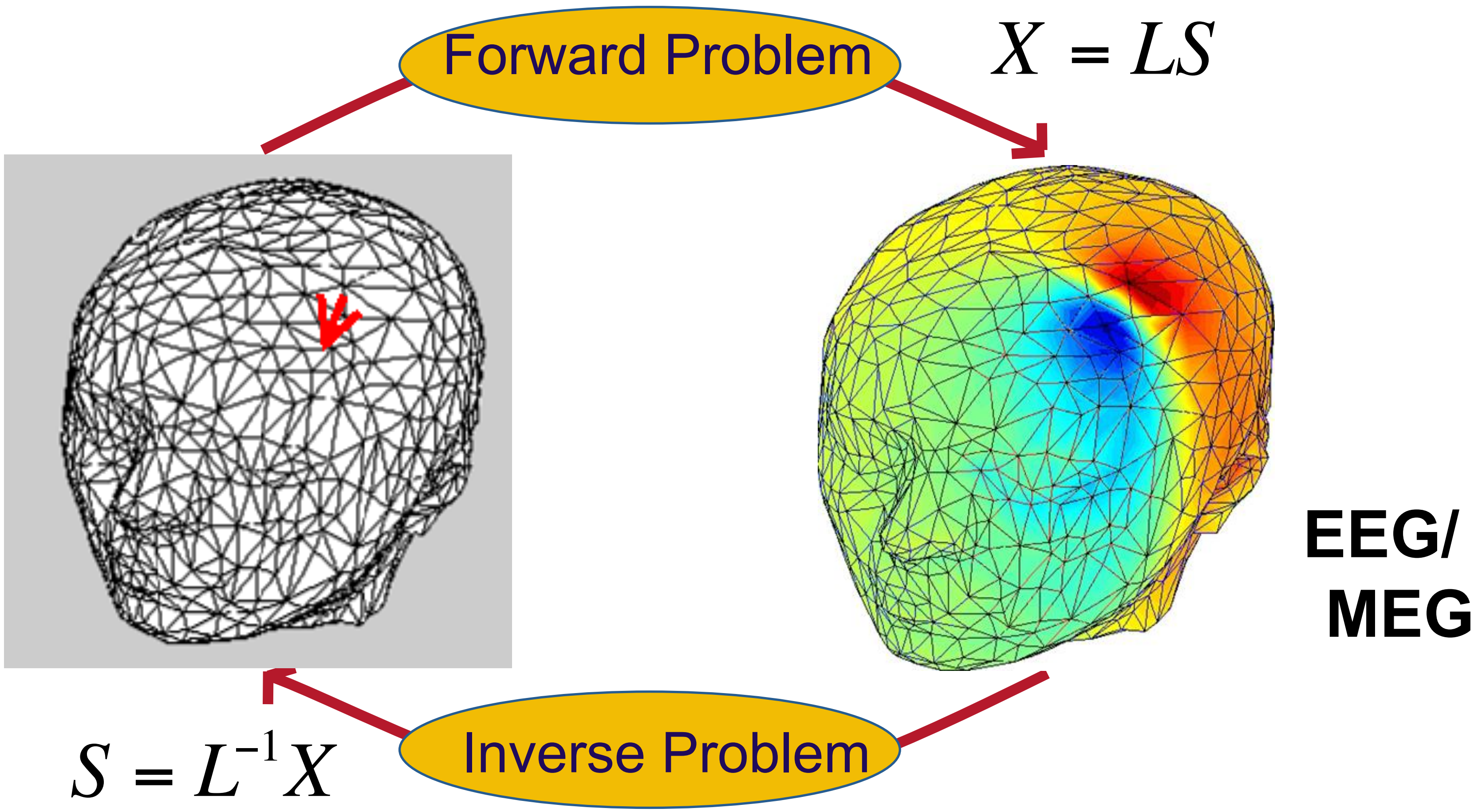
Cortical surface





Baillet et al, 2001

Forward and inverse problem



= 1000s of FP solution

Source localization is ill-posed

$$X = LS + n$$

X: scalp recorded potentials
S: current density vector
L: transfer matrix ‘the head volume conductor model’

The inverse problem refers to finding S given known X.

$$O(S) = \min \left\| X - LS \right\|^2$$

Infinite solutions!

Apply electrophysiological neuroanatomical constraints

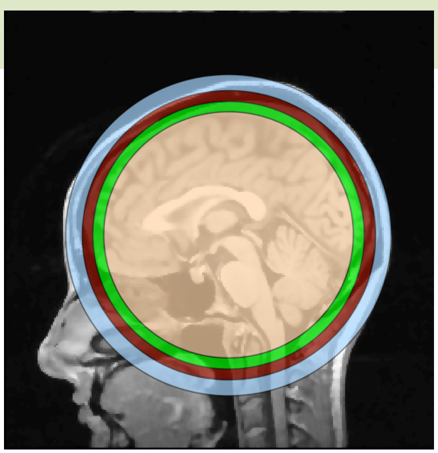
1. The electrical head model used,
2. The inverse solution itself

Head volume conductor model

Simple Head Models

- Single layer sphere, spheroid
- 3-4 layer sphere

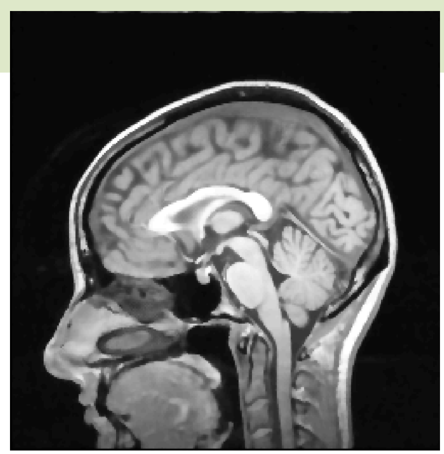
ANALYTICAL SOLVER
Simple, fast, but not accurate

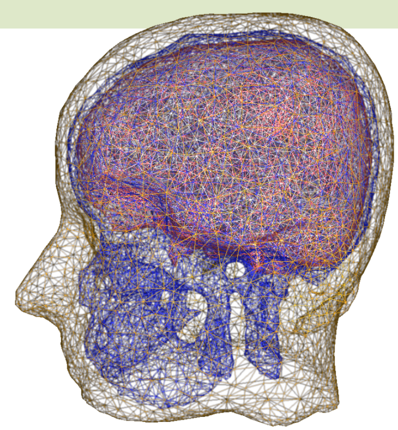


Realistic Head Models

- Boundary Element (BEM)
- Finite Element (FEM)
- Finite Difference (FDM)

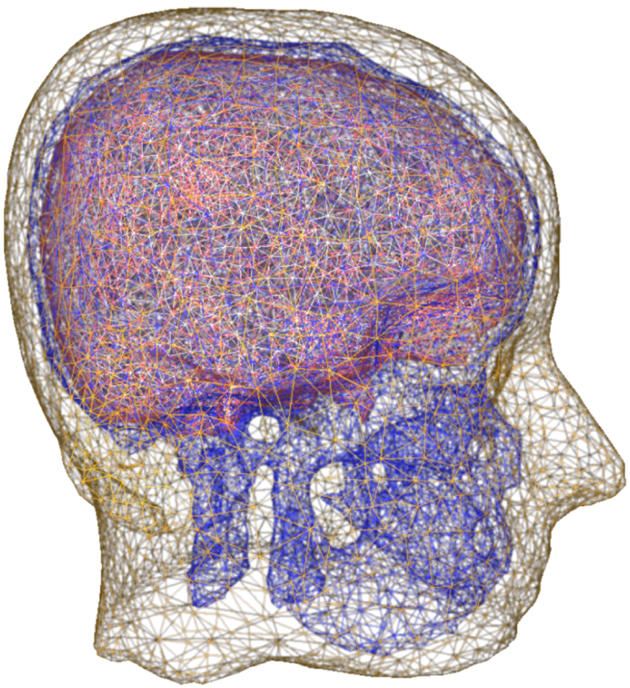
NUMERICAL SOLVER
Represents head shape better, but computationally complex





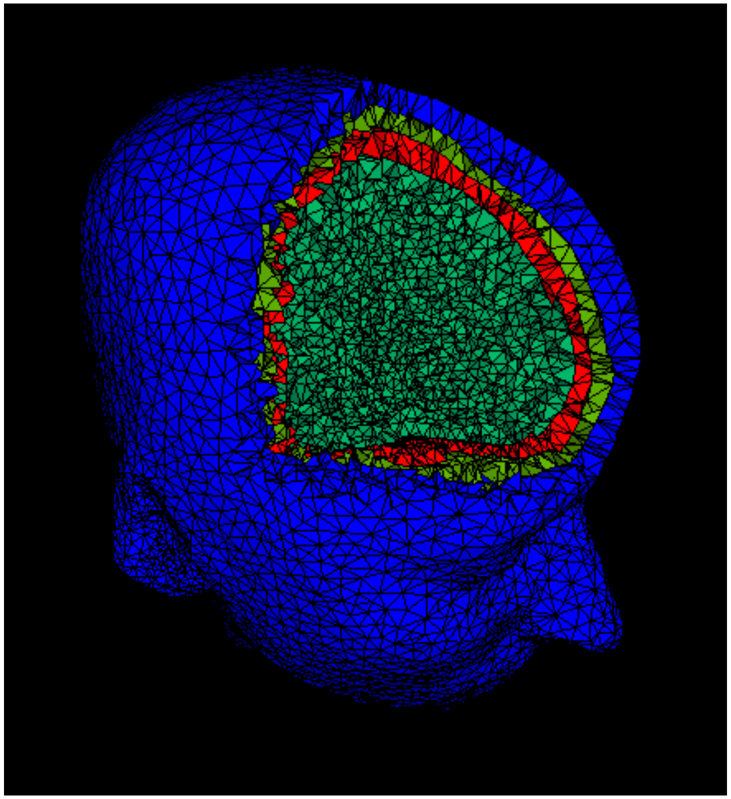
Numerical Head Models

BEM



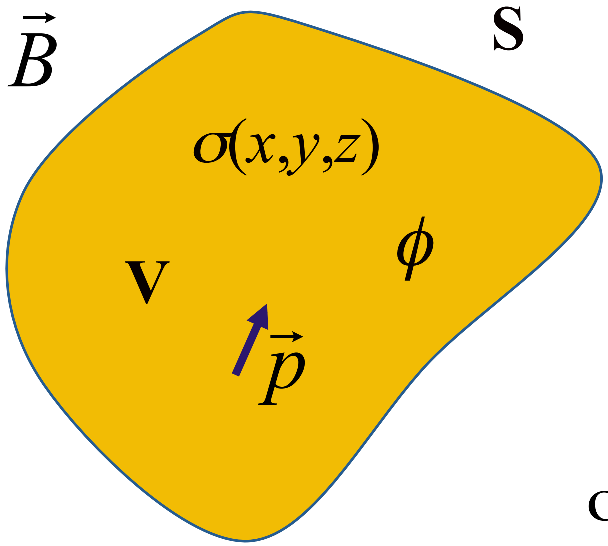
NFT BEM mesh

FEM



Generated using Tetgen
from NFT BEM mesh

Formulation of the FP



$$\nabla \cdot \left(\sigma \nabla \Phi\right) = -\nabla \cdot J^P \quad \text{inside } V$$

$$\sigma \frac{\partial \Phi}{\partial n} = 0 \qquad \text{on } S$$

$\sigma(x,y,z)$: conductivity distribution

$\vec{p}$: current source

Reference: Gulrajani, R., Bioelectricity and biomagnetism

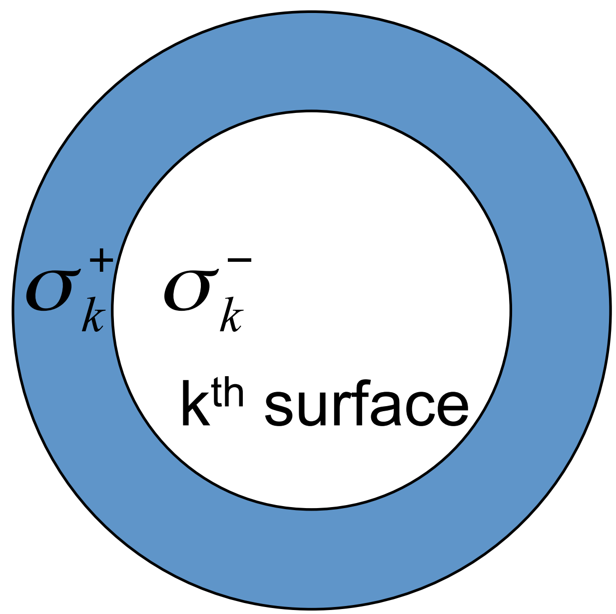
BEM Formulation

Integral equation for Potential Field:

$$\phi(\vec{r}) = \boxed{2g(\vec{r})} + \boxed{\frac{1}{2\pi}\sum_{k=1}^{n}\left(\frac{\sigma_k^- - \sigma_k^+}{\sigma_i^- + \sigma_i^+}\right)\int_{S_k}\phi(\vec{r}\,')\frac{\vec{R}}{R^3}\cdot d\vec{S}_k(\vec{r}\,')}$$

Primary sources

Secondary sources



BEM Formulation

Integrating the previous integral equation over all elements a set of equations are obtained.

In matrix notation for the potential field we obtain

$$\Phi_{M\times 1} = C_{M\times M}\Phi + g_{M\times 1} \qquad \Phi = [I - C]^{-1} g \qquad \Phi = \mathbf{A}^{-1} g$$

M: number of nodes

The expression for the magnetic field:

$$B_{n\times 1} = B_0 + \mathbf{H}_{n\times M}\Phi$$

n: number of magnetic sensors

Transfer matrix

Electrode potentials

$$\Phi_e = D\mathbf{A}^{-1}g$$

Φ_e mx1 vector of electrode potentials

D is an mxM sparse matrix to select m rows of $\mathbf{A}^{-1}$

Let the transfer matrix E be defined as:

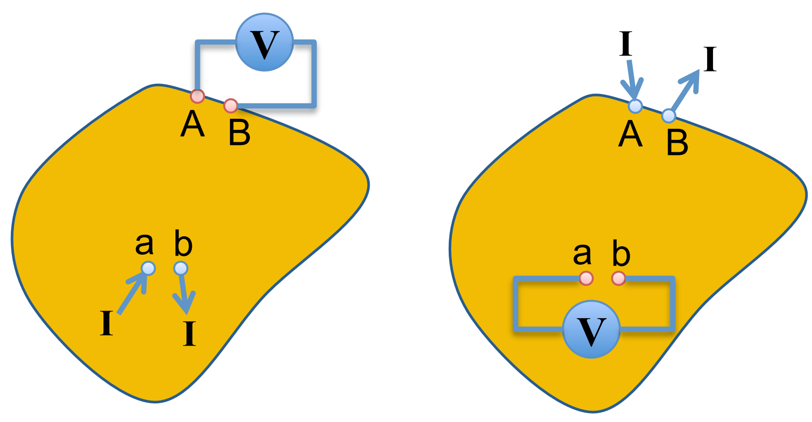
$$E = D\mathbf{A}^{-1}$$

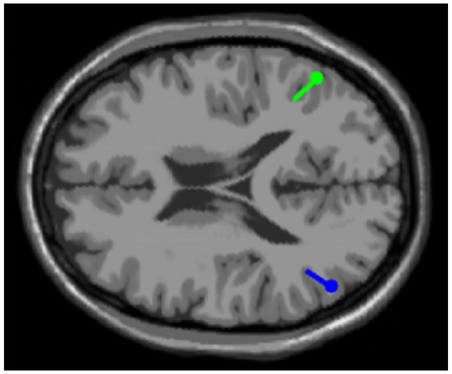
Taking the transpose of both sides, and multiplying by $\mathbf{A}^T$

$$A^T e_i = d_i$$

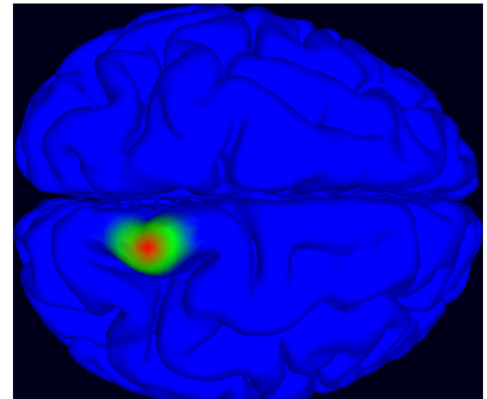
FEM transfer matrix

- FEM computes volume potentials
  - Solving the matrix for every source is slow
  - We only need potentials at electrode locations
- Use the reciprocal formulation:
  - Inject current at electrodes, solve volume potentials





Inverse Problem

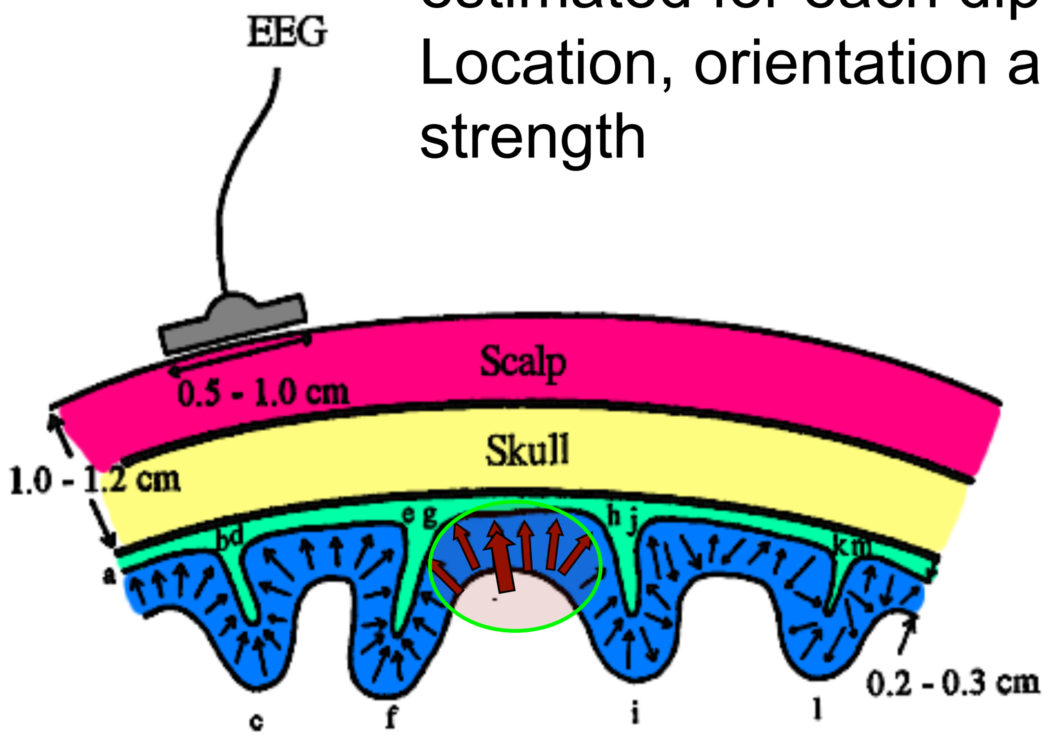


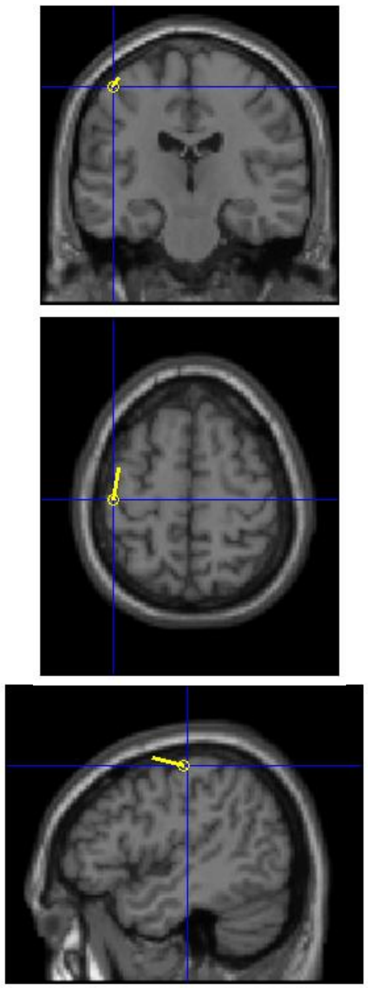
Equivalent dipole Methods	Linear distributed Methods
Overdetermined	Underdetermined
Searches for parameters of a number of dipoles	Searches for activation in given locations.
Nonlinear optimization techniques	Linear optimization techniques
May converge to local minima	Needs additional constraints
Non-linear least squares, beamforming, MUSIC, simulated annealing, genetic algorithms, etc.	Bayesian methods, MNE, LORETA, LAURA, etc.

Equivalent current dipole (ECD)

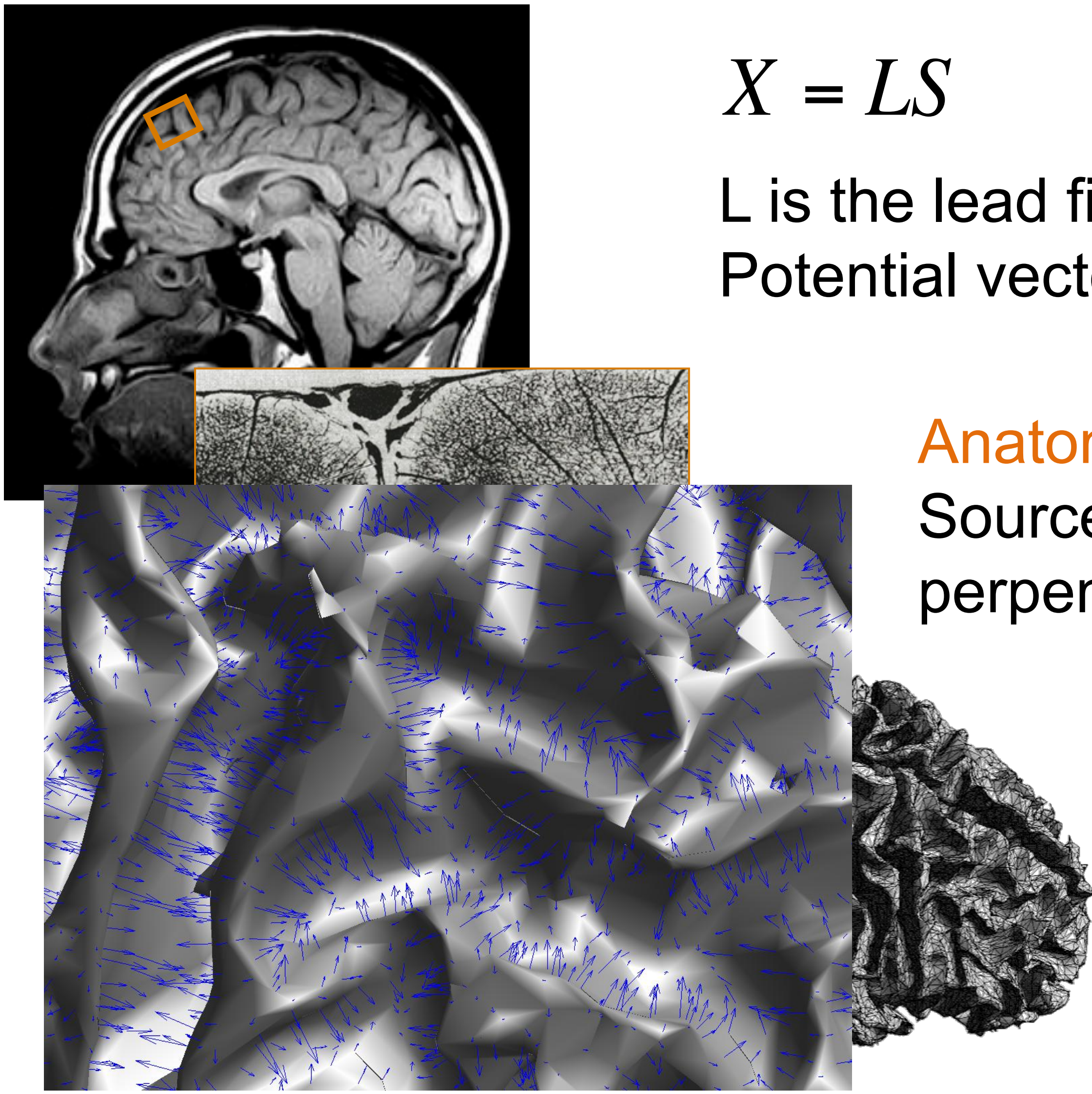
$$O(S) = \min\|X - LS\|^2$$

6 parameters are estimated for each dipole: Location, orientation and strength





Linear distributed methods



$$X = LS$$

L is the lead field matrix:
Potential vectors of all possible solutions

Anatomical constraint:
Sources are on the cortex
perpendicular to the cortex

Multi-scale patch-basis source localization with Sparse Bayesian Learning

$$D_{ij} = \text{geodesic\_distance}(i,j)$$

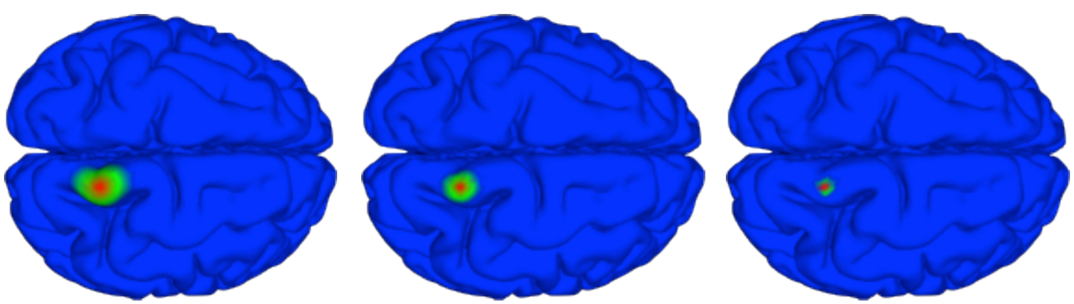
$$D_{ij} = Inf \quad \text{if } D_{ij} > scale$$

$$W_{ij}^{(k)} = gauss(D_{ij},\sigma_k) = \frac{1}{\sqrt{2\pi\sigma_k^2}}\exp\left(-\frac{D_{ij}^2}{2\sigma_k^2}\right)$$

$$\sigma_k = scale/3$$

Three truncated Gaussian patches of different scales (radii)

radius	10 mm	6 mm	3 mm
σ_k	3.33 mm	2 mm	1 mm



Akalin Acar, et al (2008a,2009) IEEE EMBC
Ramirez, et al, HBM, 2007

Forward Model

$$X = LS$$

$$L := [m \times v]$$ Lead field matrix

$$\tilde{L} = \left[LW^{(1)} \cdots LW^{(3)}\right]_{m\times 3v}$$

ICA Mdel

$$X = A\hat{S}$$

$$\hat{S}_q := [1 \times T]$$ q^{th} IC activation

ICA+SBL Inverse Model

$$A_q = \tilde{L}\tilde{M}_q + \dot{U}_q$$

$$\tilde{L}^{-1} = \text{SBL}(A_q,\tilde{L})$$

$$\tilde{M}_q = \left[\tilde{L}^{-1}A_q\right]_{3v\times 1}$$

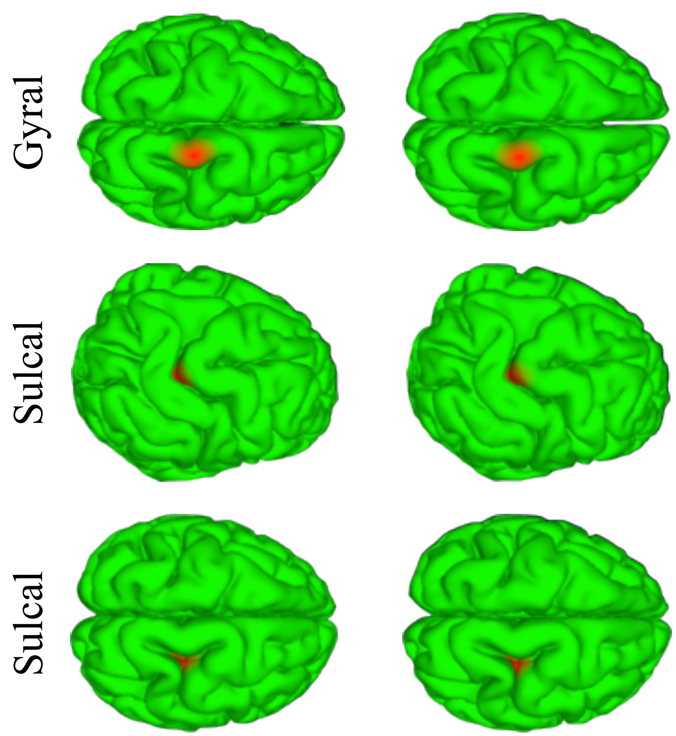
$$M_q = \text{reshape}(\tilde{M}_q, v \times 3)$$

$$M_q = \sum_{i=1}^{3}\tilde{M}_q(:,i)$$

$$P_q = M_q\hat{S}_q$$ [v x T] cortical surface potentials for q^{th} IC

SBL Simulation Study with MNI model (SNR=50)

Three examples:	
original	reconstructed

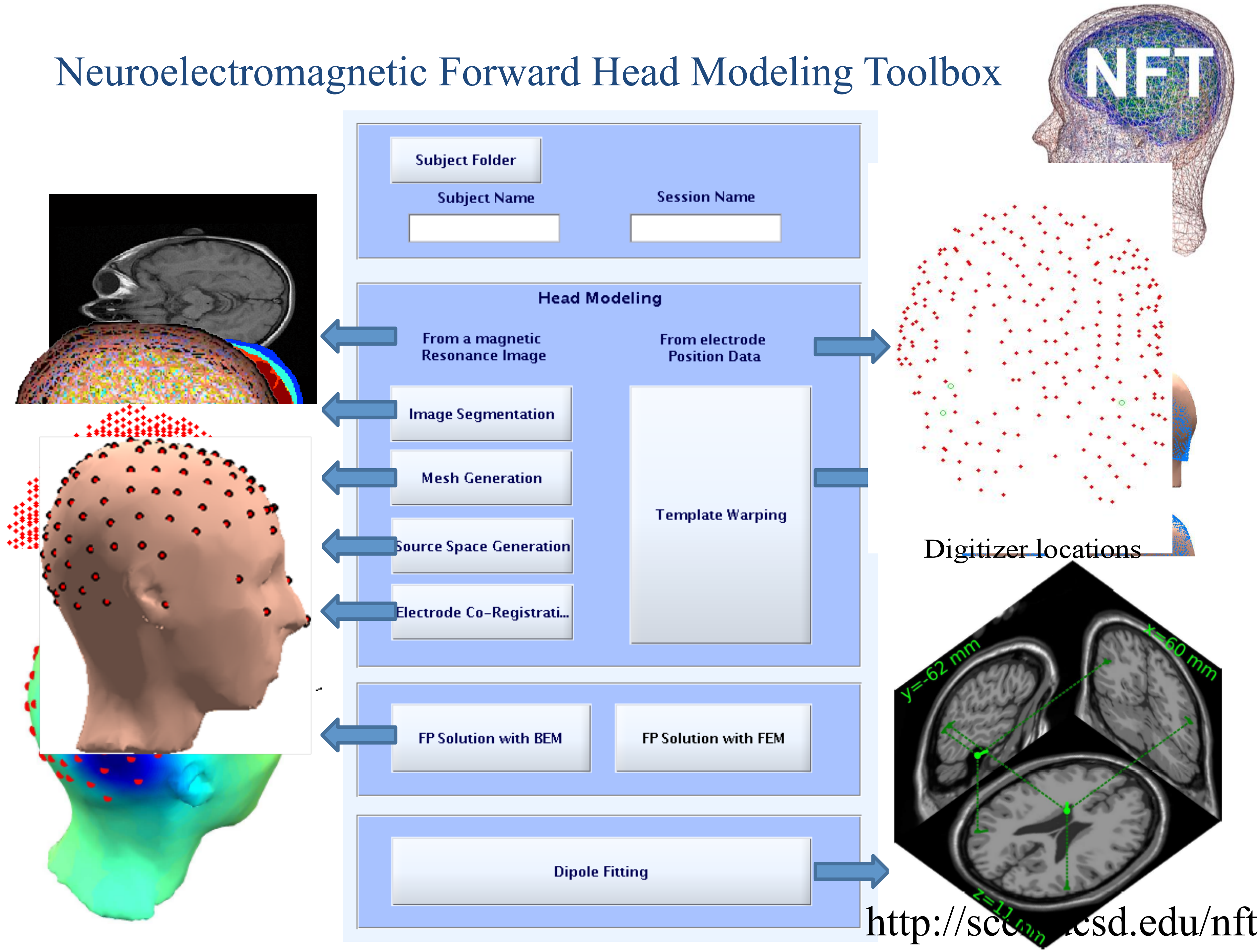


Akalin Acar, et al (2009) IEEE EMBC

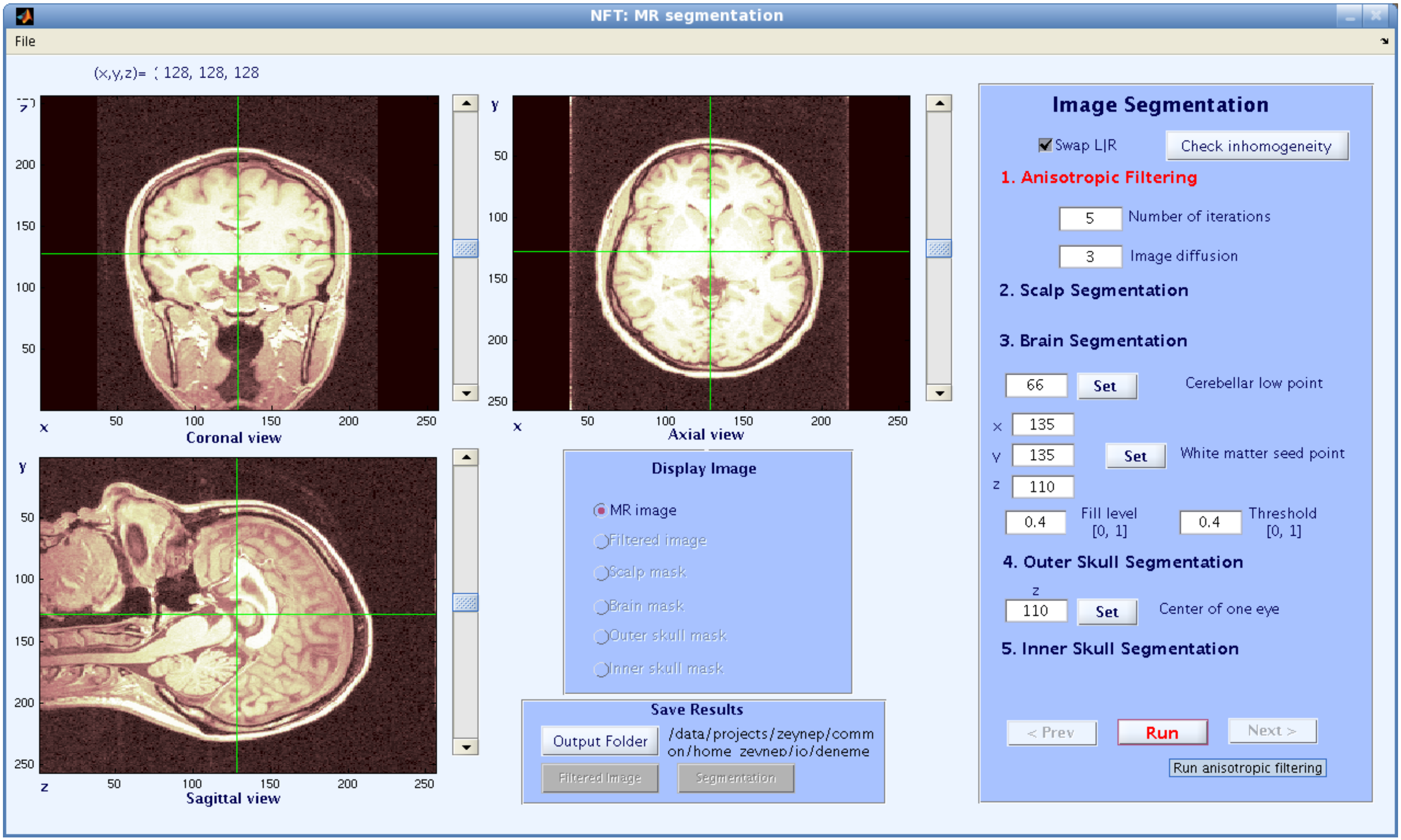
Source (x 15)		Max. dis. (mm)	Energy dif.	DF (%)
Type	Scale (mm)			
Gyral	10	0	1.5	103.8
Sulcul	10	1.01	29.8	101.4
Sulcul	5	2.12	4.1	37.6
Dual	10	11.6	29.3	89.2
Gyral	5	1.01	4.7	41.3
Sulcul	12	1.8	10.6	125.5

Term	Definition
max displacement	geodesic distance between original and reconstructed patch centers
energy difference	|original energy - reconstructed energy|
degree of focalization (DF)	reconstructed energy / original energy

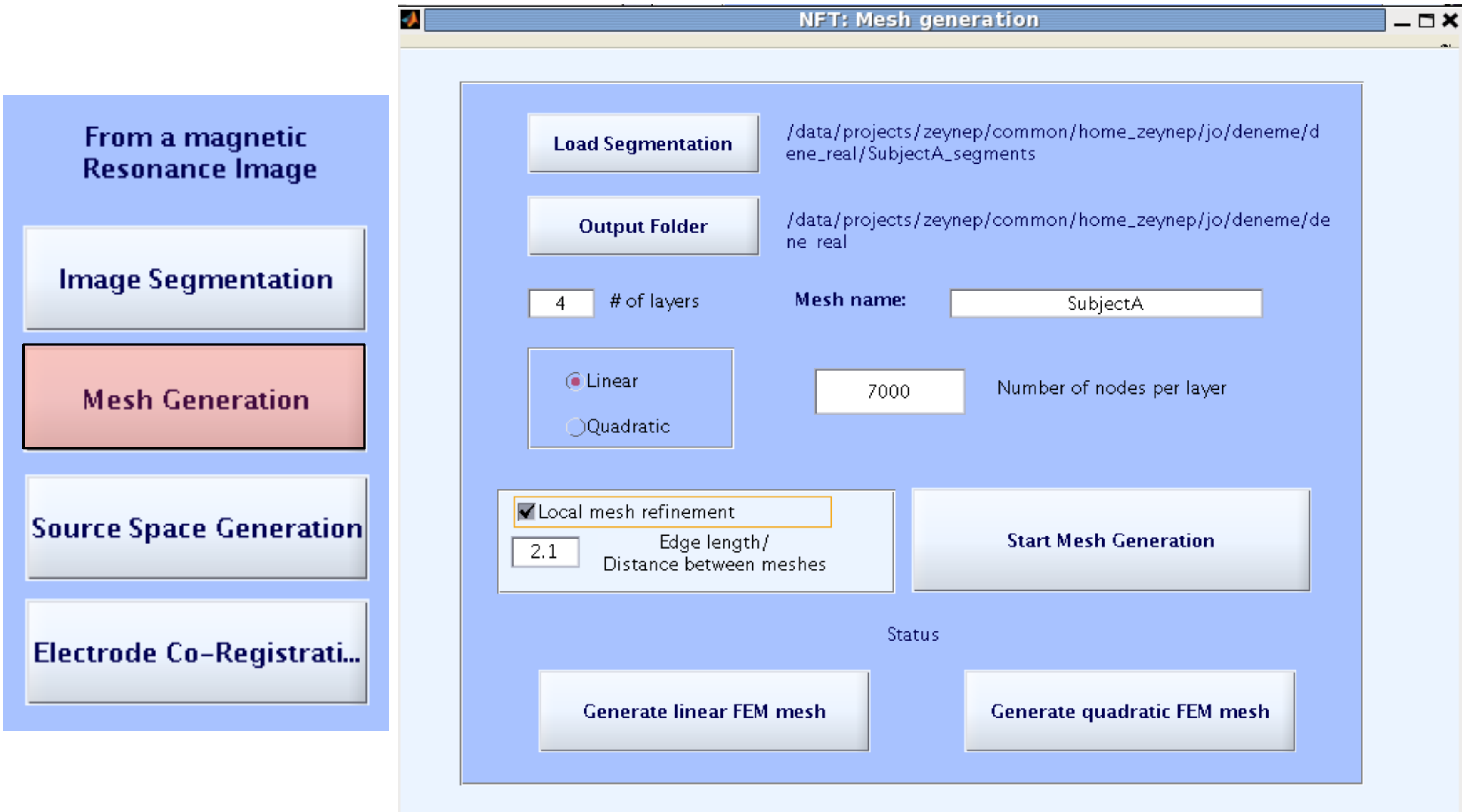
Neuroelectromagnetic Forward Head Modeling Toolbox



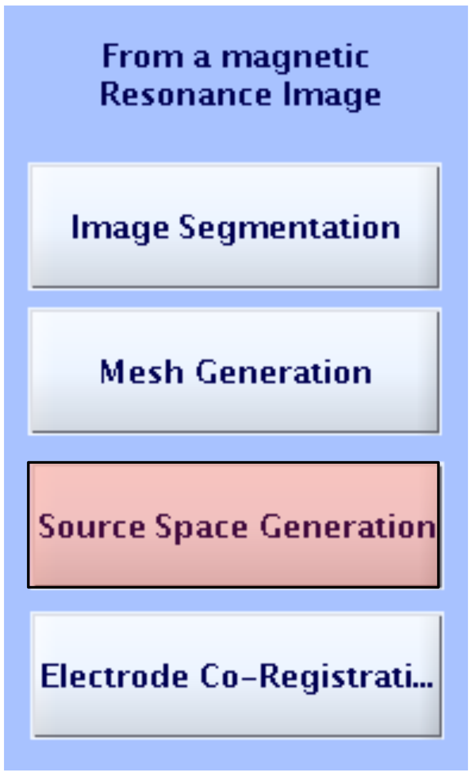
NFT - Segmentation

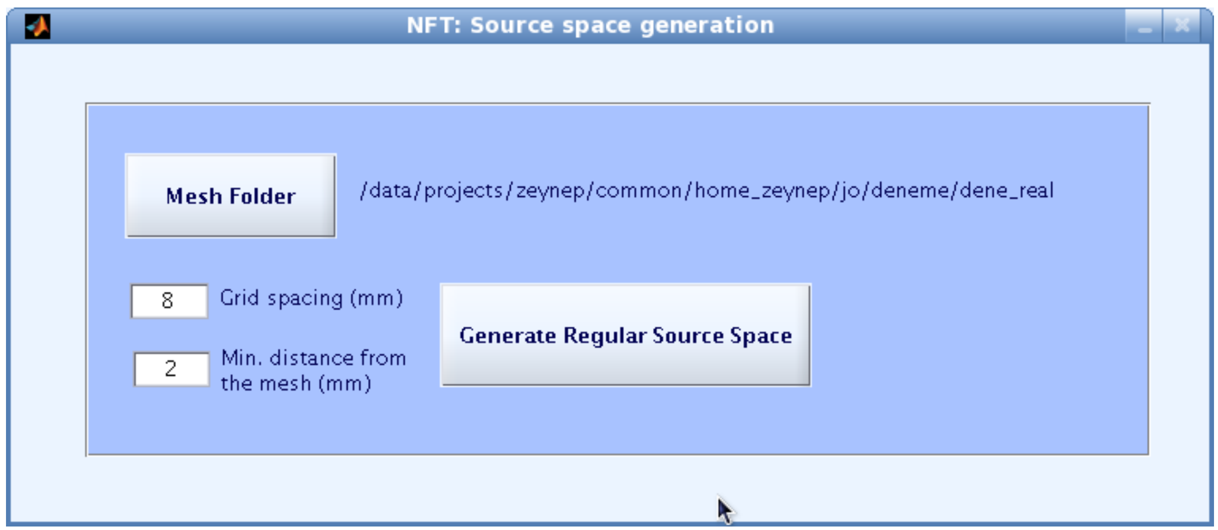


NFT – Mesh generation



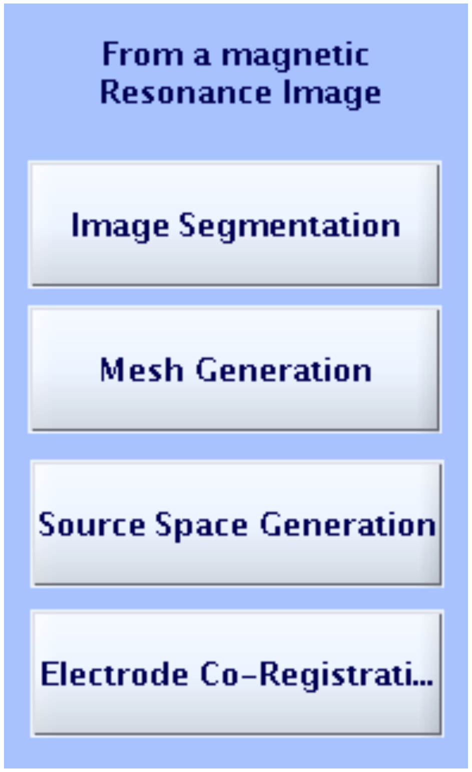
NFT – source space generation

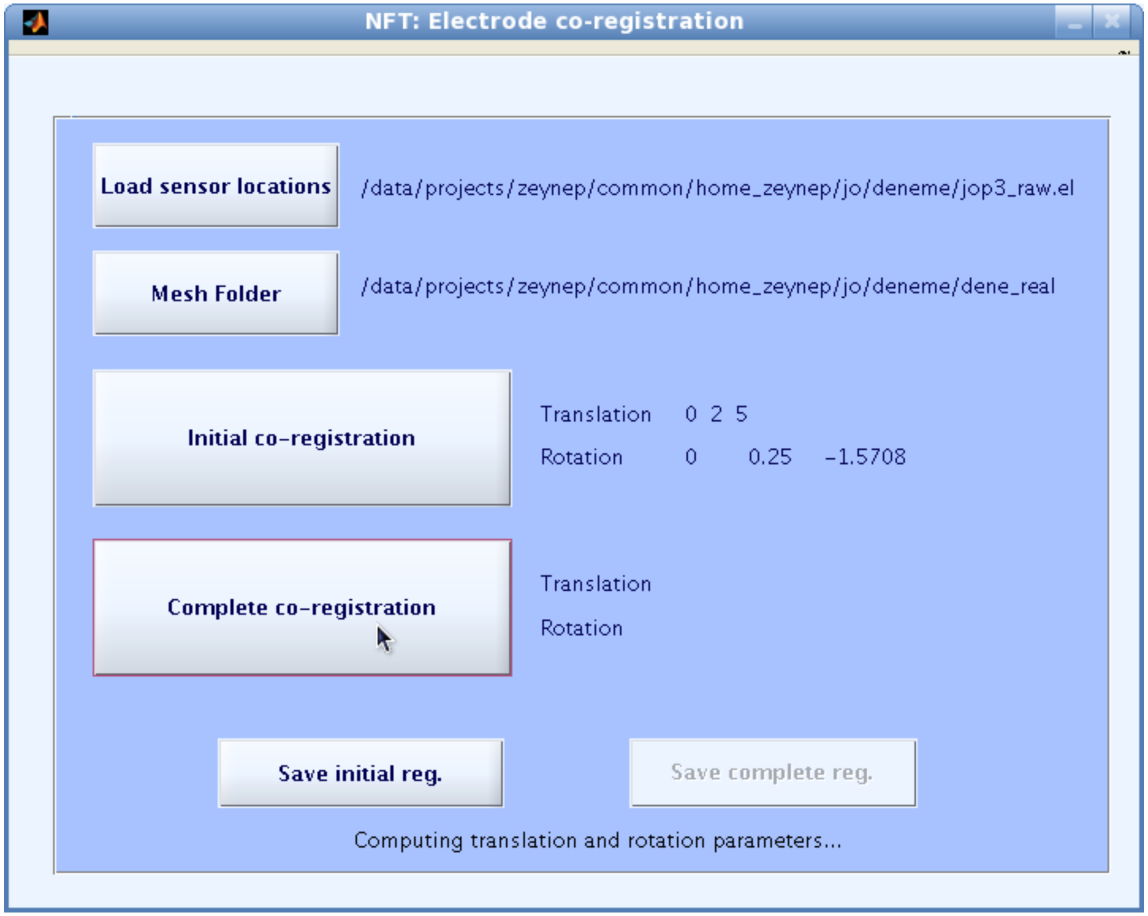




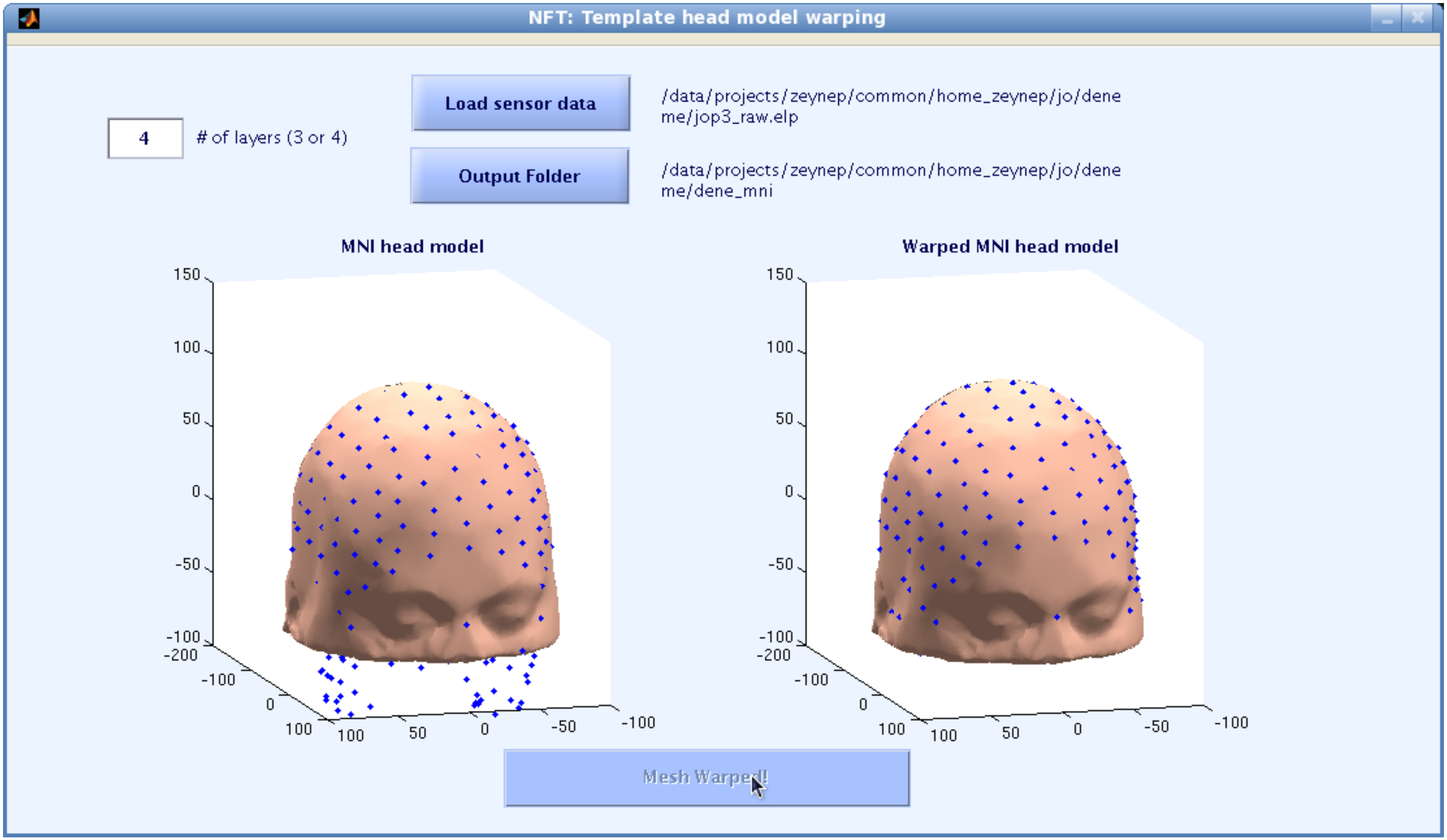
Generates a simple source space:
Regular Grid inside the brain
With a given spacing and distance to the mesh

NFT – electrode co-registration





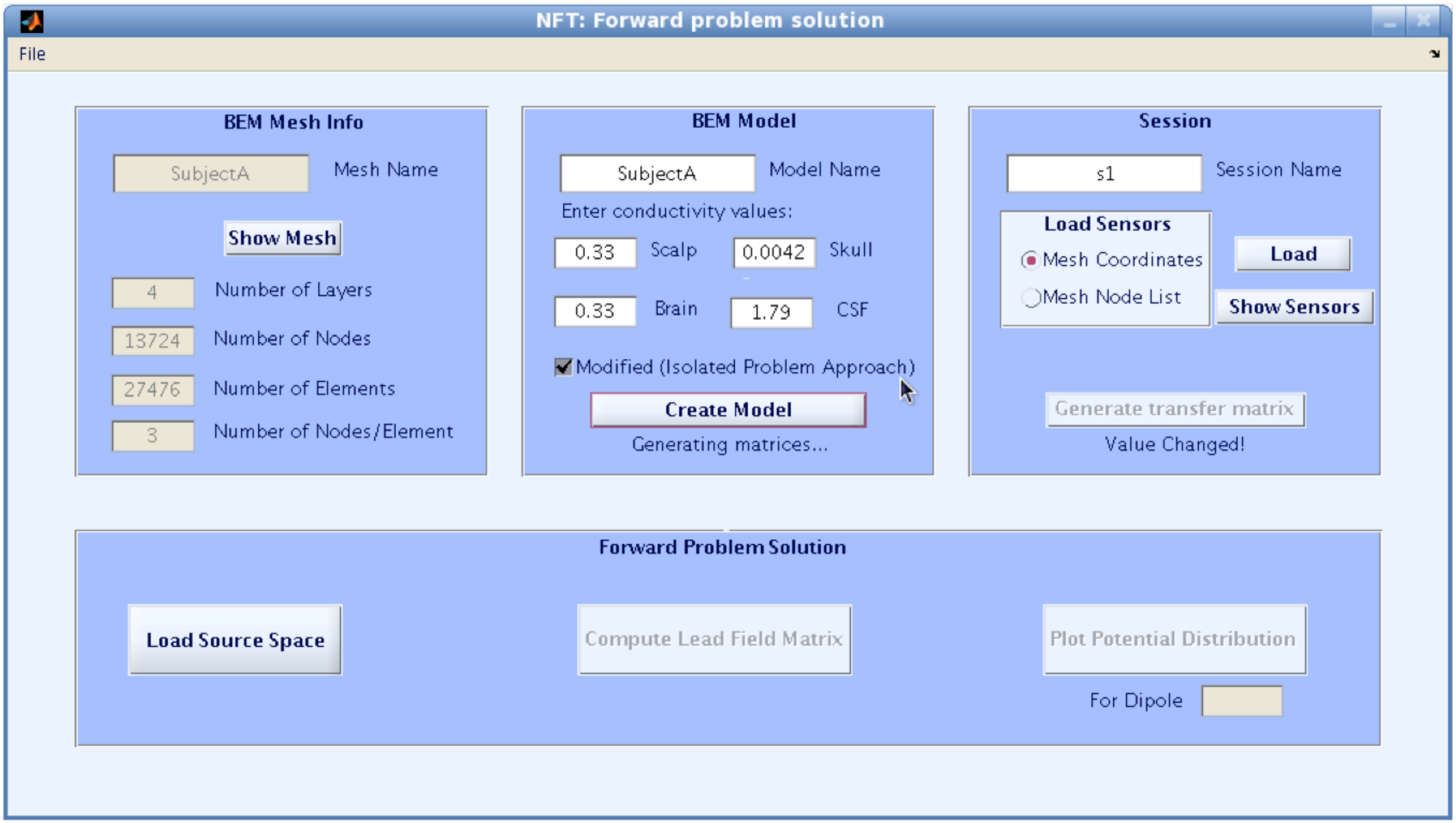
NFT – Template warping



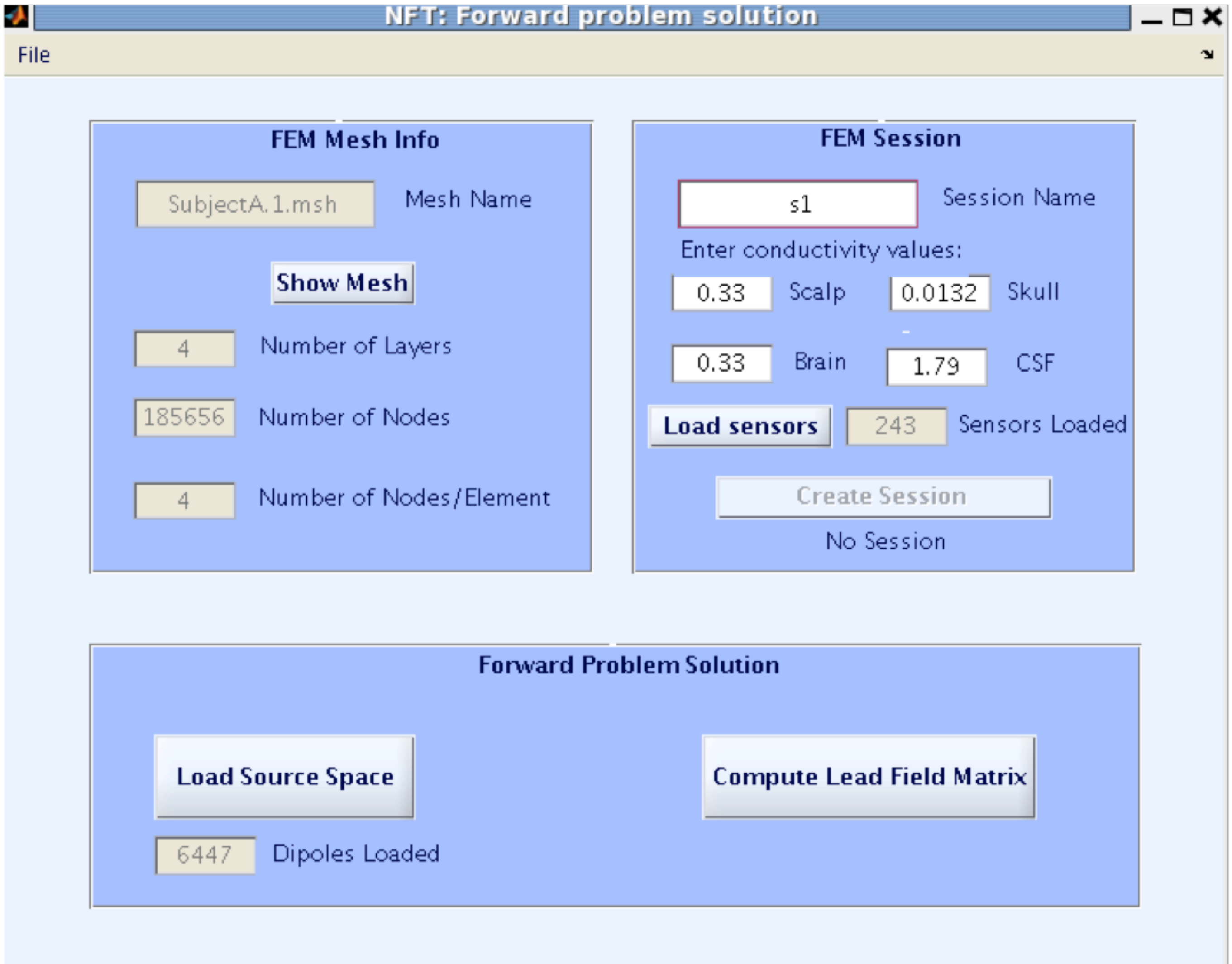
NFT – Forward problem solver

- MATLAB interface to numerical solvers
- Boundary Element Method or Finite Element Method
  - EEG Only (for now)
  - Interfaces to the Matrix generator executable written in C++
- Other computation done in MATLAB
- Generated matrices are stored on disk for future use.

NFT - Forward Problem Solver (BEM)



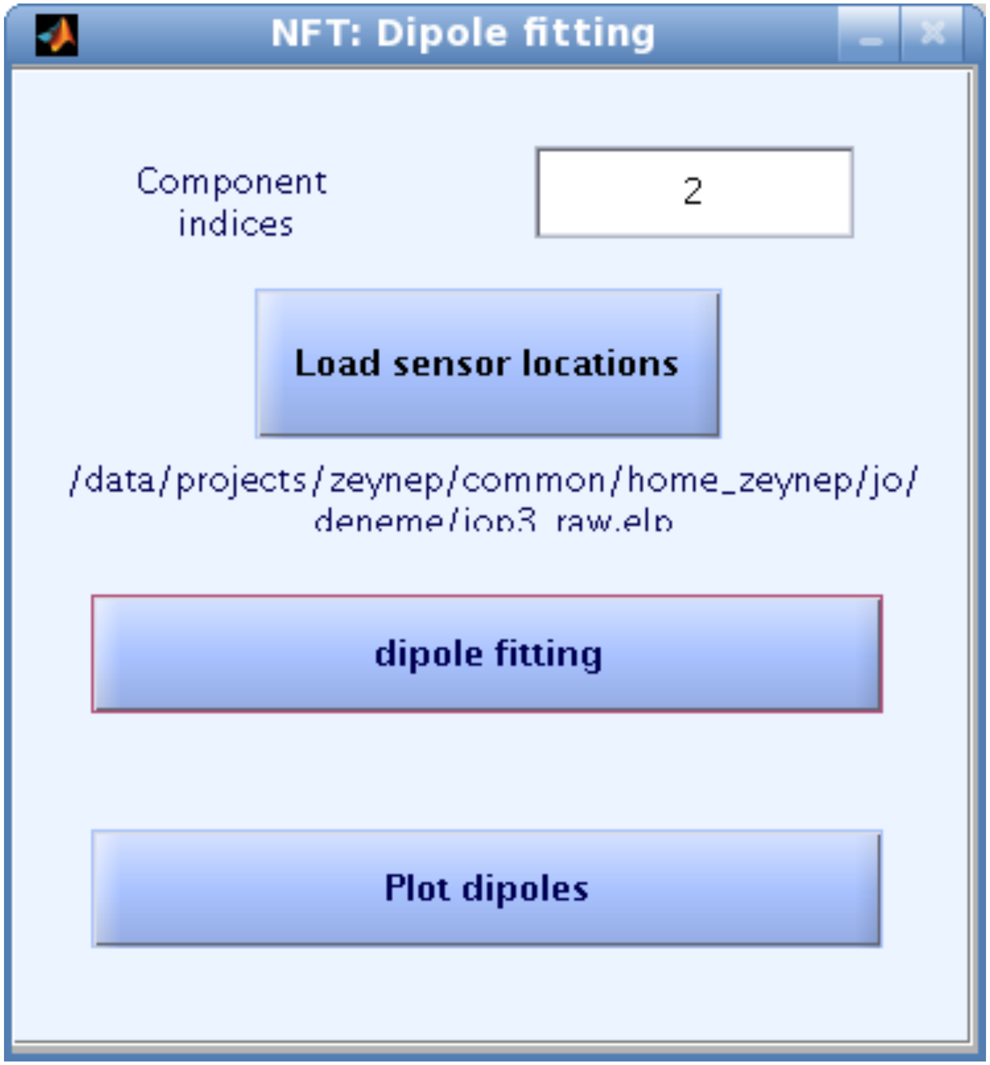
NFT – Forward Problem Solver (FEM)

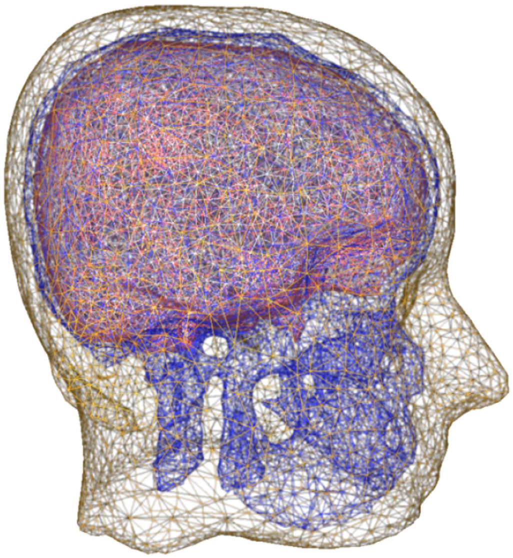
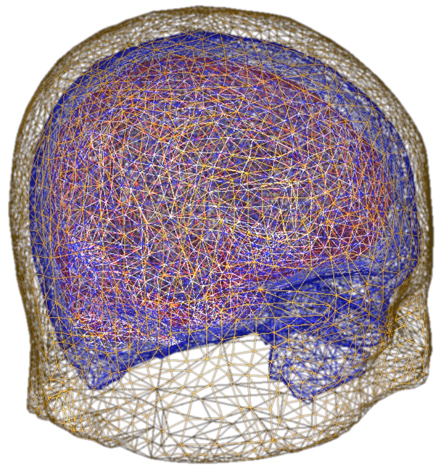
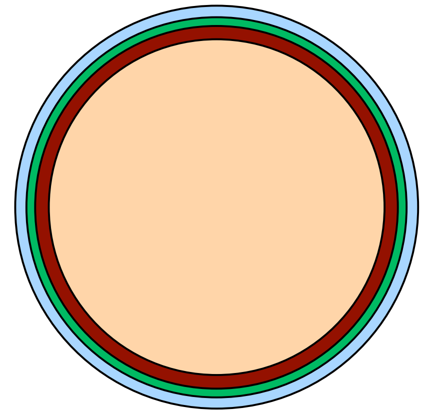


NFT – Dipole fitting

- Requires EEGLAB integration to access Component indices.
- Uses FieldTrip in EEGLAB for dipole fitting.

http://www.sccn.ucsd.edu/nft



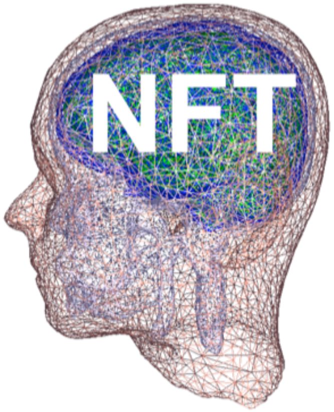




Effects of Forward Model Errors on EEG Source Localization

MODELING ERRORS

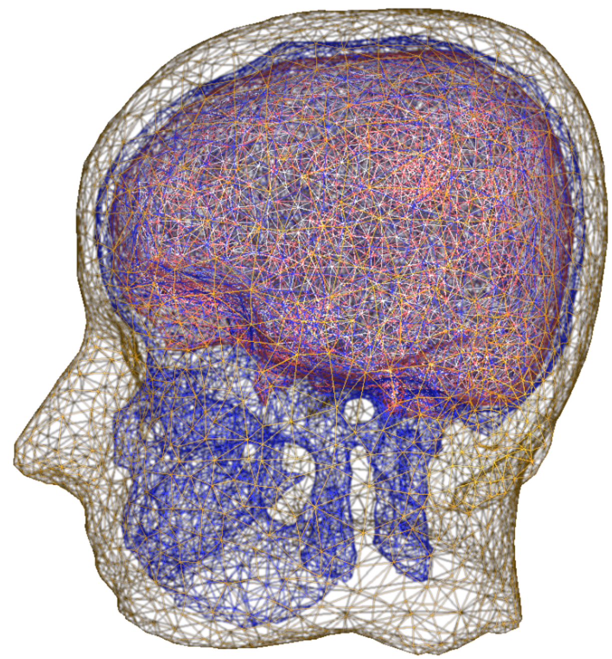
Head Model Generation

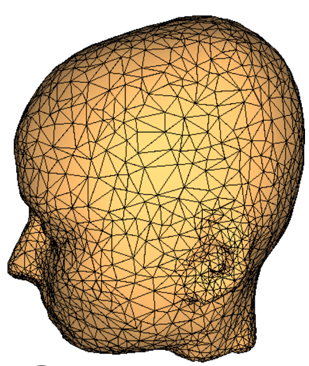
- Reference Head Model
  - From whole head T1 weighted MR of subject
  - 4-layer realistic BEM model
- MNI Head model
  - From the MNI head
  - 3-layer and 4-layer template BEM model
- Warped MNI Head Model
  - Warp MNI template to EEG sensors
- Spherical Head model
  - 3-layer concentric spheres
  - Fitted to EEG sensor locations



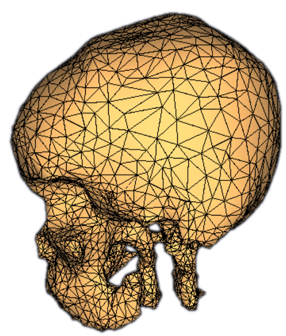
The Reference Head Model

- 18541 nodes
- 37090 elements
  - 6928 Scalp
  - 6914 Skull
  - 11764 CSF
  - 11484 Brain

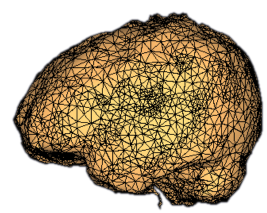




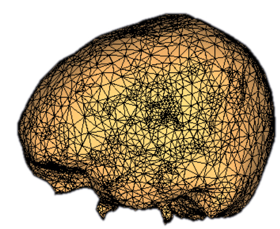
Scalp



Skull

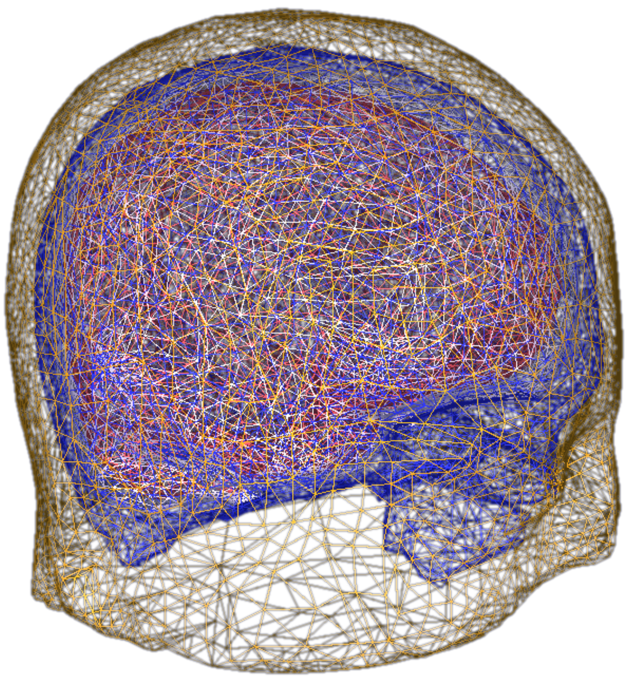


CSF

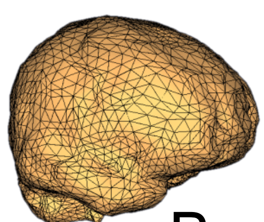


Brain

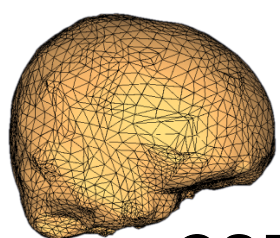
The MNI Head Model



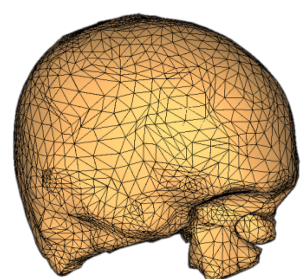
- 4-layer
  - 16856 nodes
  - 33696 elements
- 3-layer
  - 12730 nodes
  - 25448 elements



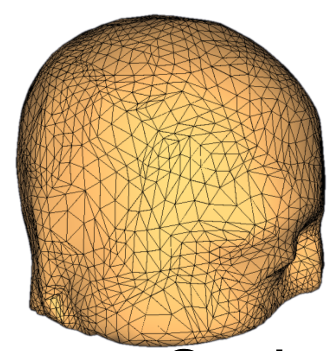
Brain



CSF

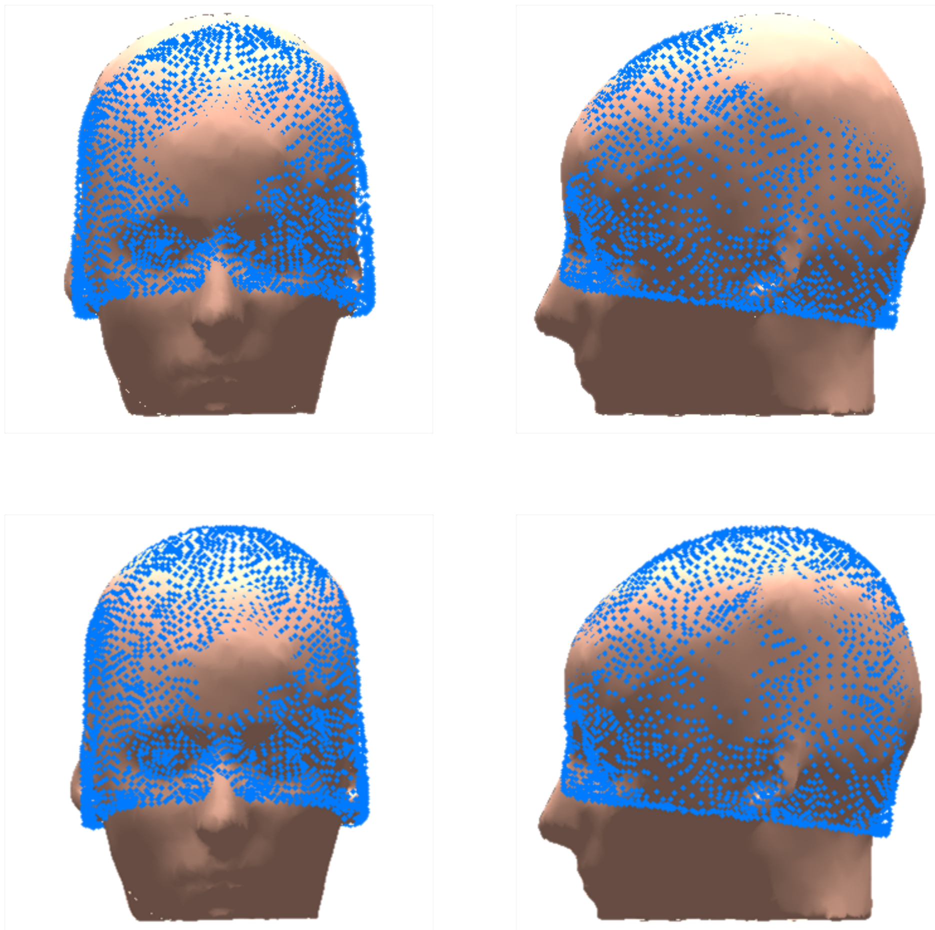


Skull



Scalp

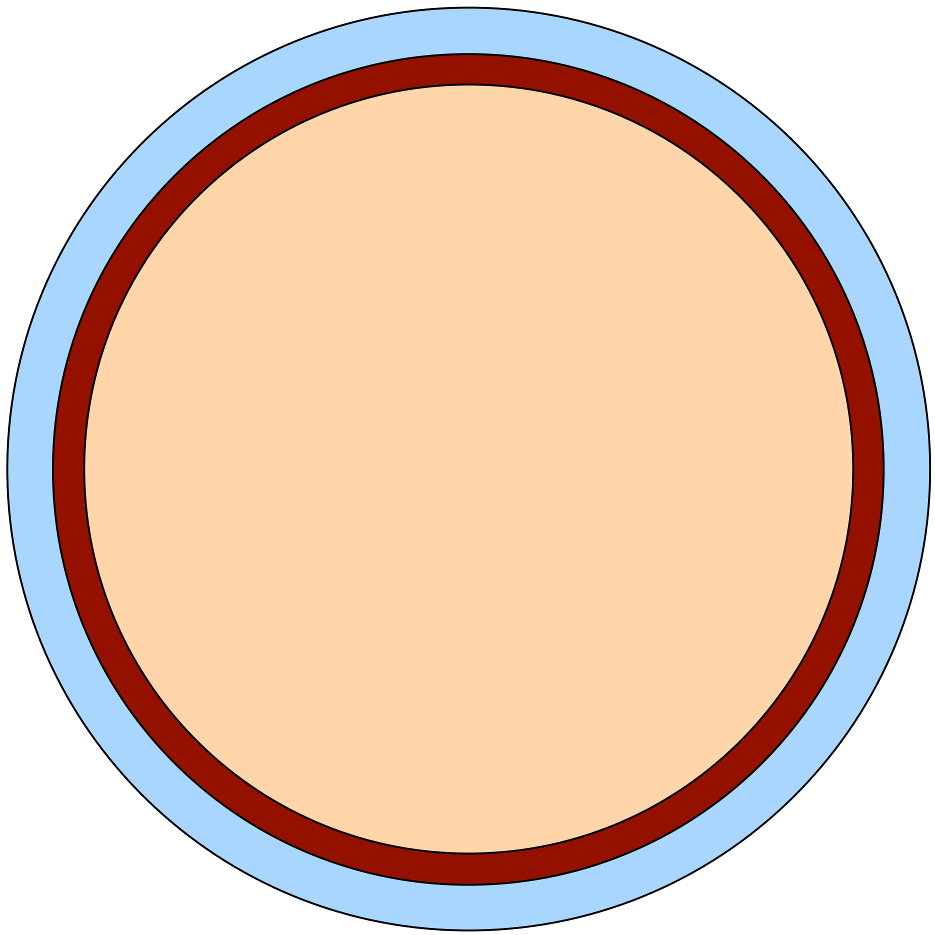
The Warped MNI Head Model



Registered MNI template

Warped MNI mesh

The Spherical Head Model

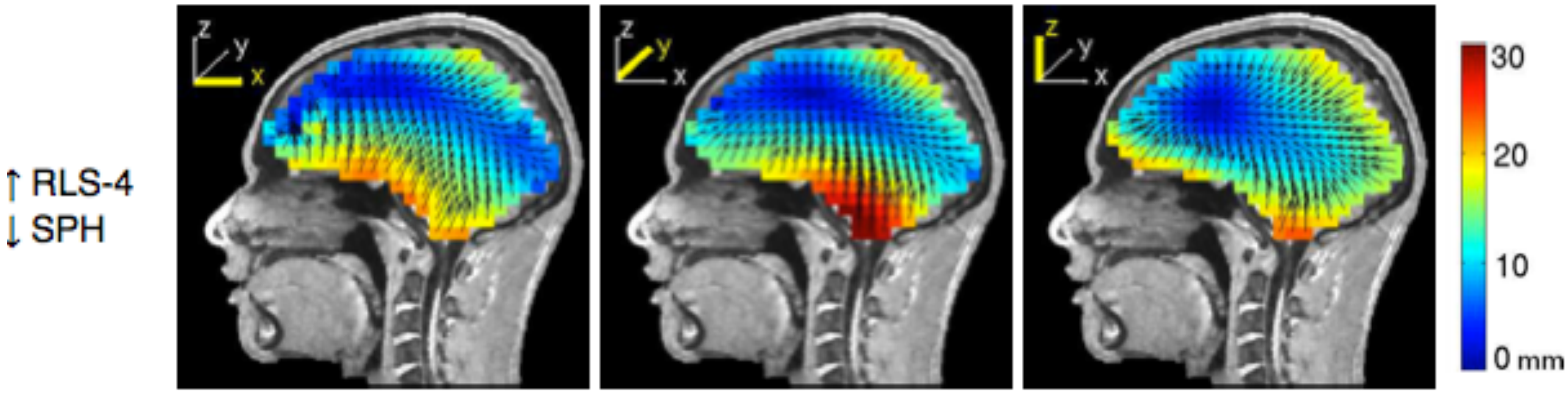


3-Layer model
Outer layer is fitted to electrode positions

Head Modeling Errors

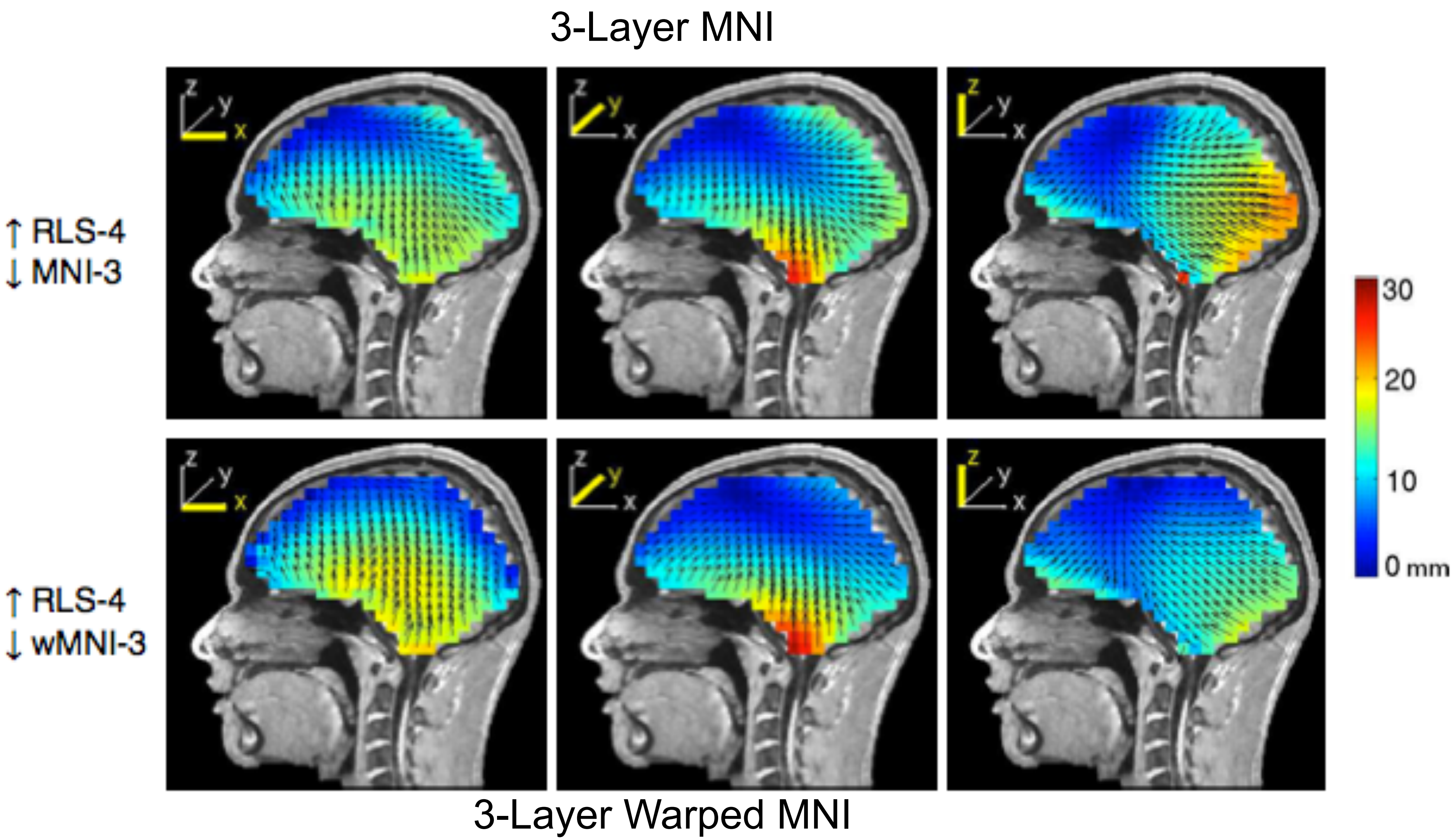
- Solve FP with reference model
  - 3D grid inside the brain.
  - 3 Orthogonal dipoles at each point
  - ~7000 dipoles total
  - 4 subjects
- Localize using other head models
  - Single dipole search.
- Plot location and orientation errors

Spherical Model Location Errors

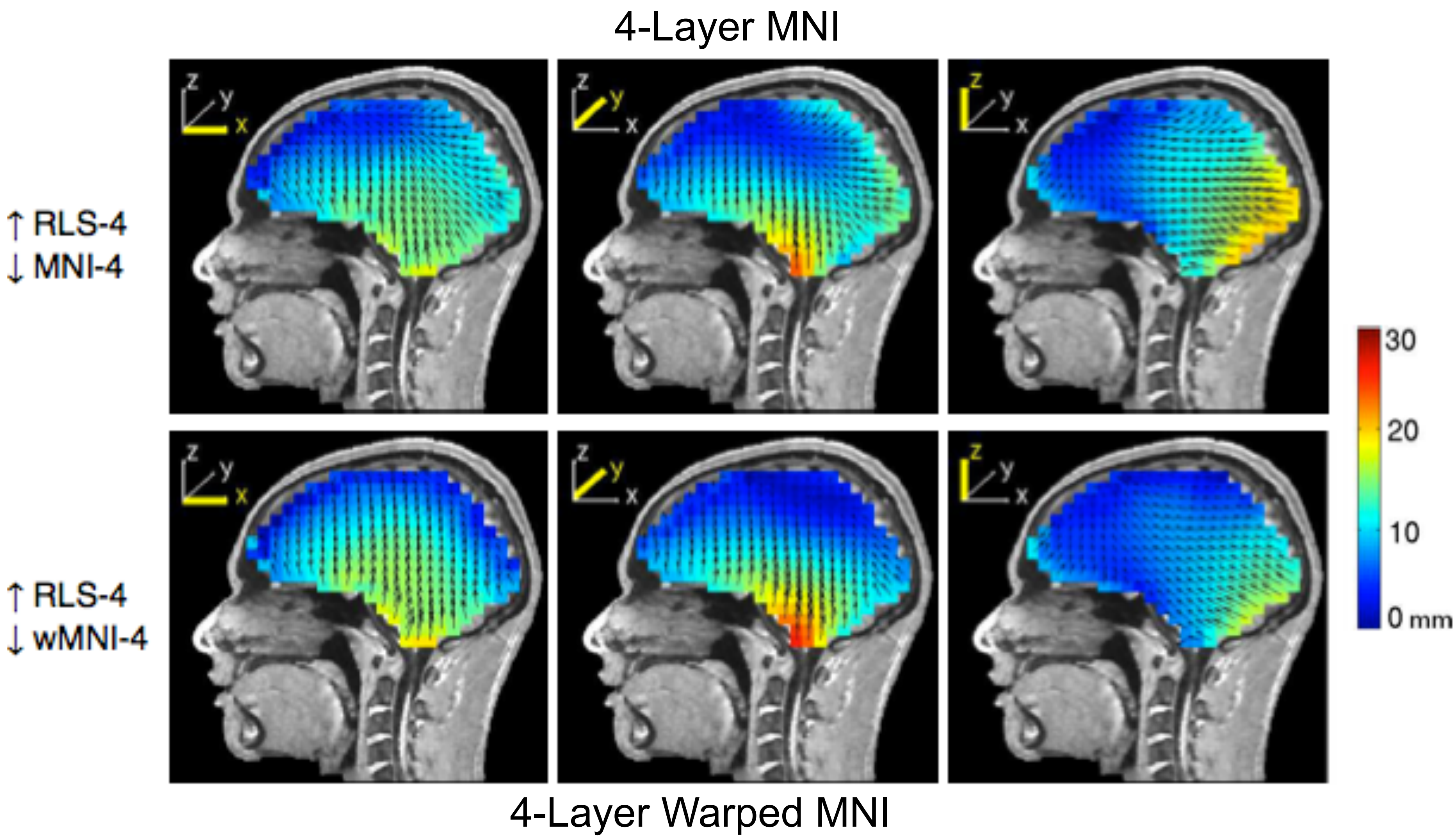


Localization errors may go up to 4 cm when spherical head models are used for source localization.
The errors are largest in the inferior regions where the spherical models diverged most from the 4-layer realistic model.

3-Layer MNI Location Errors



4-Layer MNI Location Errors



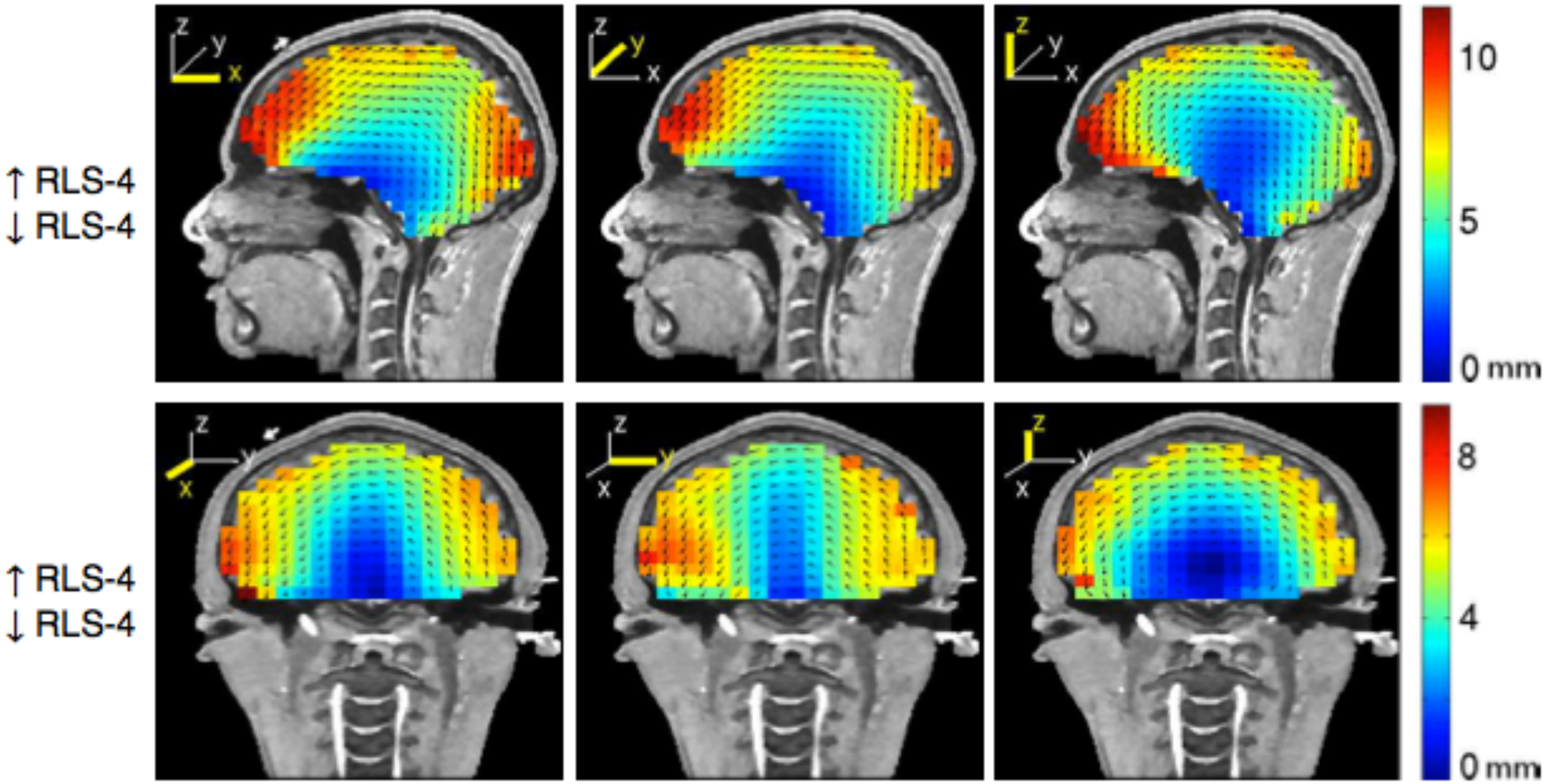
Observations

- Spherical Model
  - Location errors up to 3.5 cm. Cortical areas up to 1.5 cm.
- 3-Layer MNI
  - Large errors where models do not agree.
  - Higher around chin and the neck regions.
- 4-Layer MNI
  - Similar to 3-Layer MNI.
  - Smaller in magnitude.

Electrode co-registration errors

- Solve FP with reference model
- Shift all electrodes and re-register
  - 5° backwards
  - 5° left
- Localize using shifted electrodes
- Plot location and orientation errors

Location Errors with 5° electrode shift

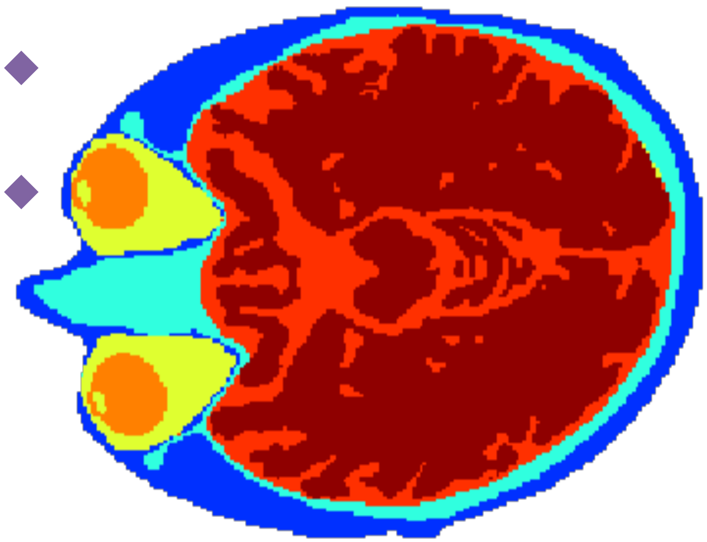


Observations

- Errors increase close to the surface near electrode locations.
- Changing or incorrectly registering electrodes may cause 5-10 mm localization error.

Head tissue conductivities

- Scalp : 0.33 S/m
- Skull: 0.0032 S/m (0.08-0.0073 S/m)
- CSF: 1.79 S/m
- Brain: 0.33 S/m

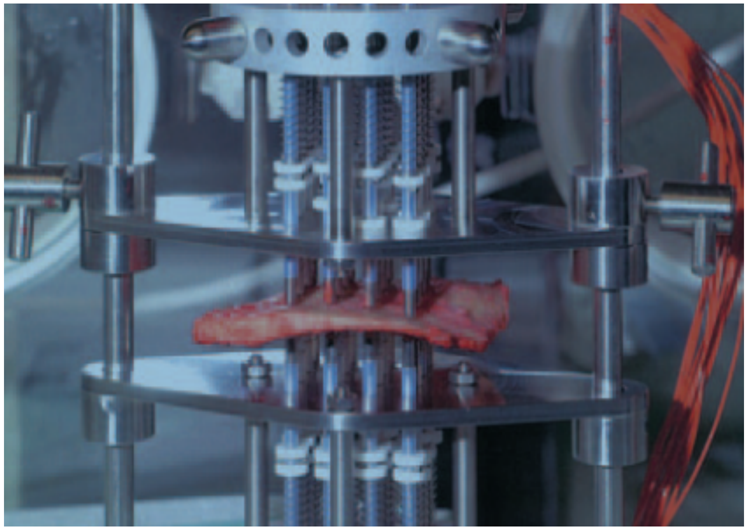


Skull conductivity measurement

Measurement of skull conductivity

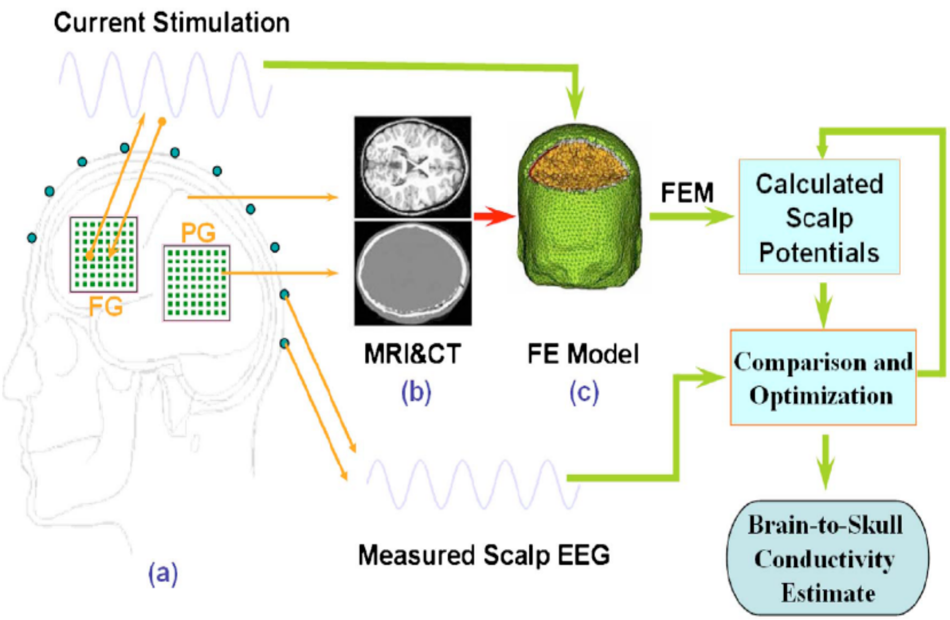
MREIT
Magnetic stimulation
Current injection

In vivo



Hoekama *et al*, 2003

In vitro



He *et al*, 2005

Skull conductivity

Brain to skull ratio		
Rush and Driscoll	1968	80
Cohen and Cuffin	1983	80
Oostendorp et al	2000	15
Lai et al	2005	25

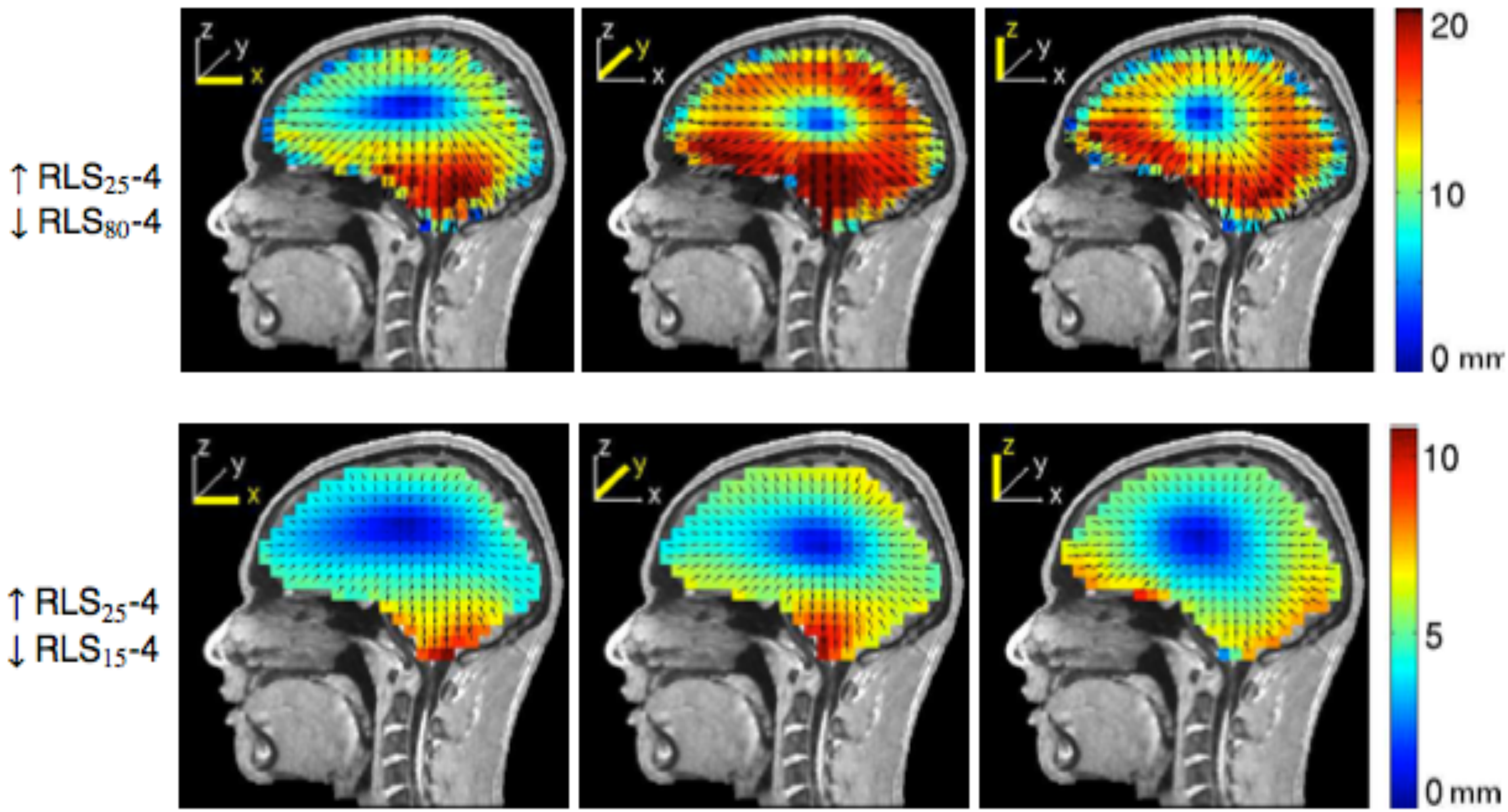
Measurement	Age	σ (mS/m)	ratio
Agar-agar phantom	–	43.6	7.5
Patient 1	11	80.1	4
Patient 2	25	71.2	4.6
Patient 3	36	53.7	6.2
Patient 4	46	34.4	9.7
Patient 5	50	32.0	10.3
Post mortem skull	68	21.4	15.7

Hoekama

Effect of Skull Conductivity

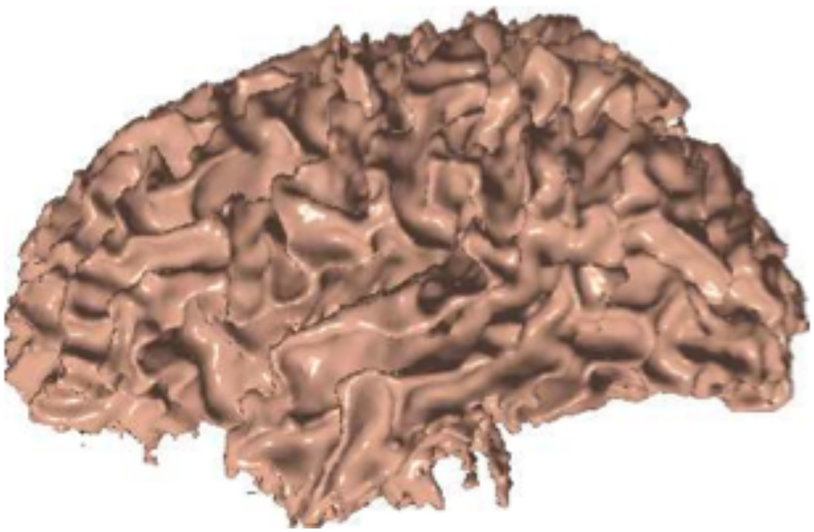
- Solve FP with reference model
  - Brain-to-Skull ratio: 25
- Generate test models
  - Same geometry
  - Brain-to-Skull ratio: 80 and 15
- Localize using test model
- Plot location and orientation errors

Skull conductivity mis-estimation

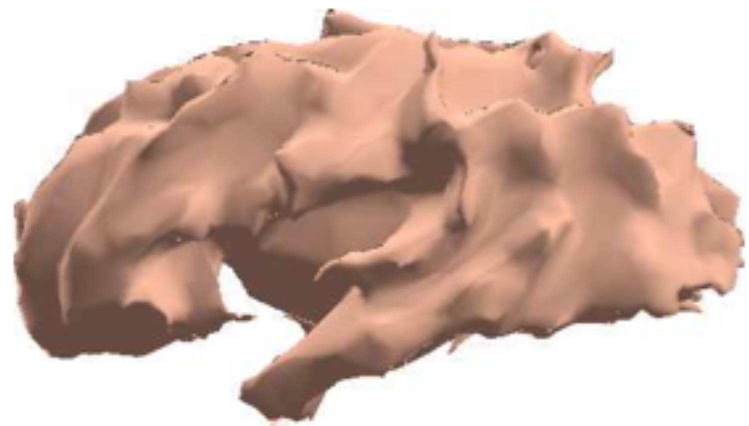


Effect of white matter

White matter conductivity: 0.14 S/m

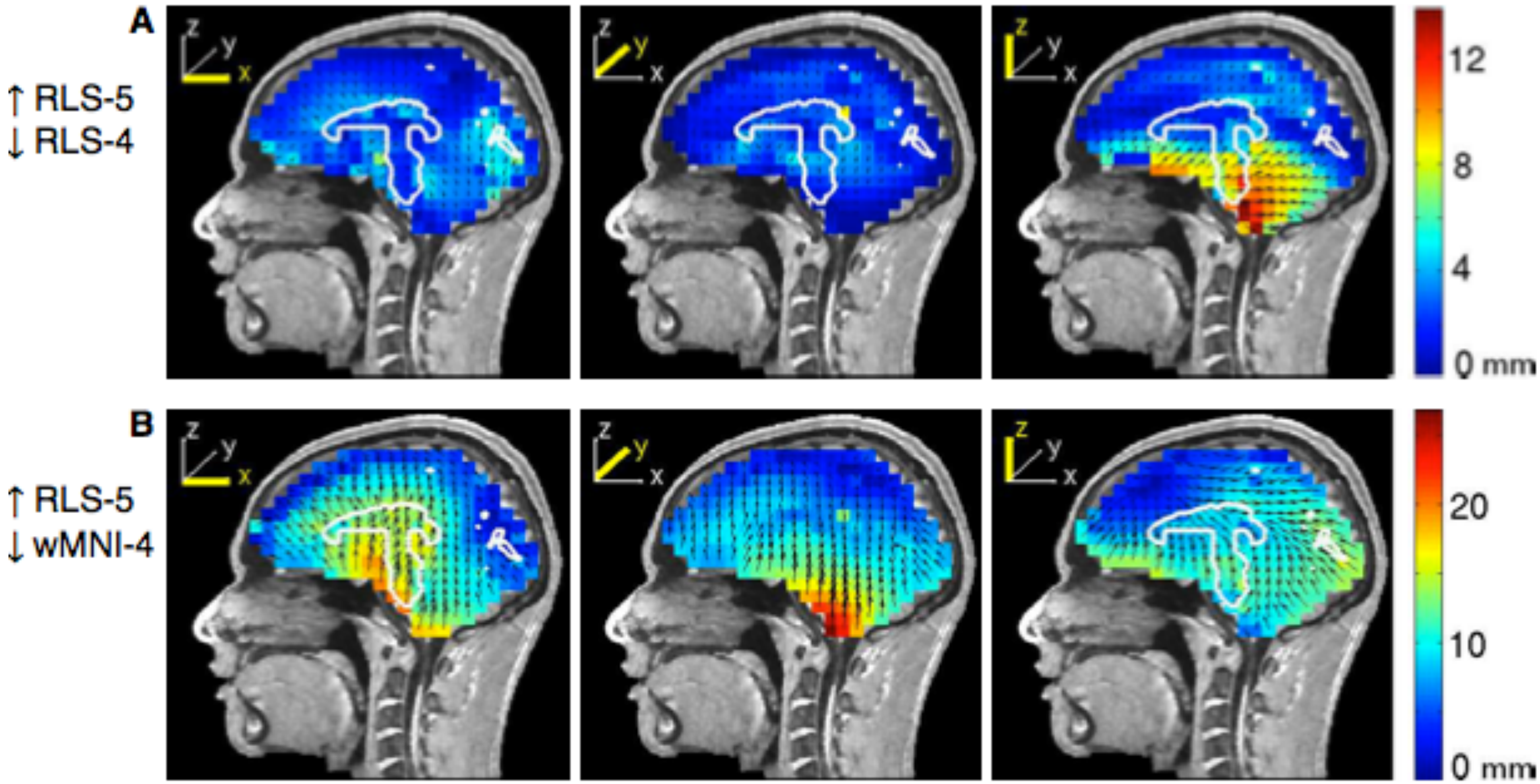


White matter surface obtained using Freesurfer

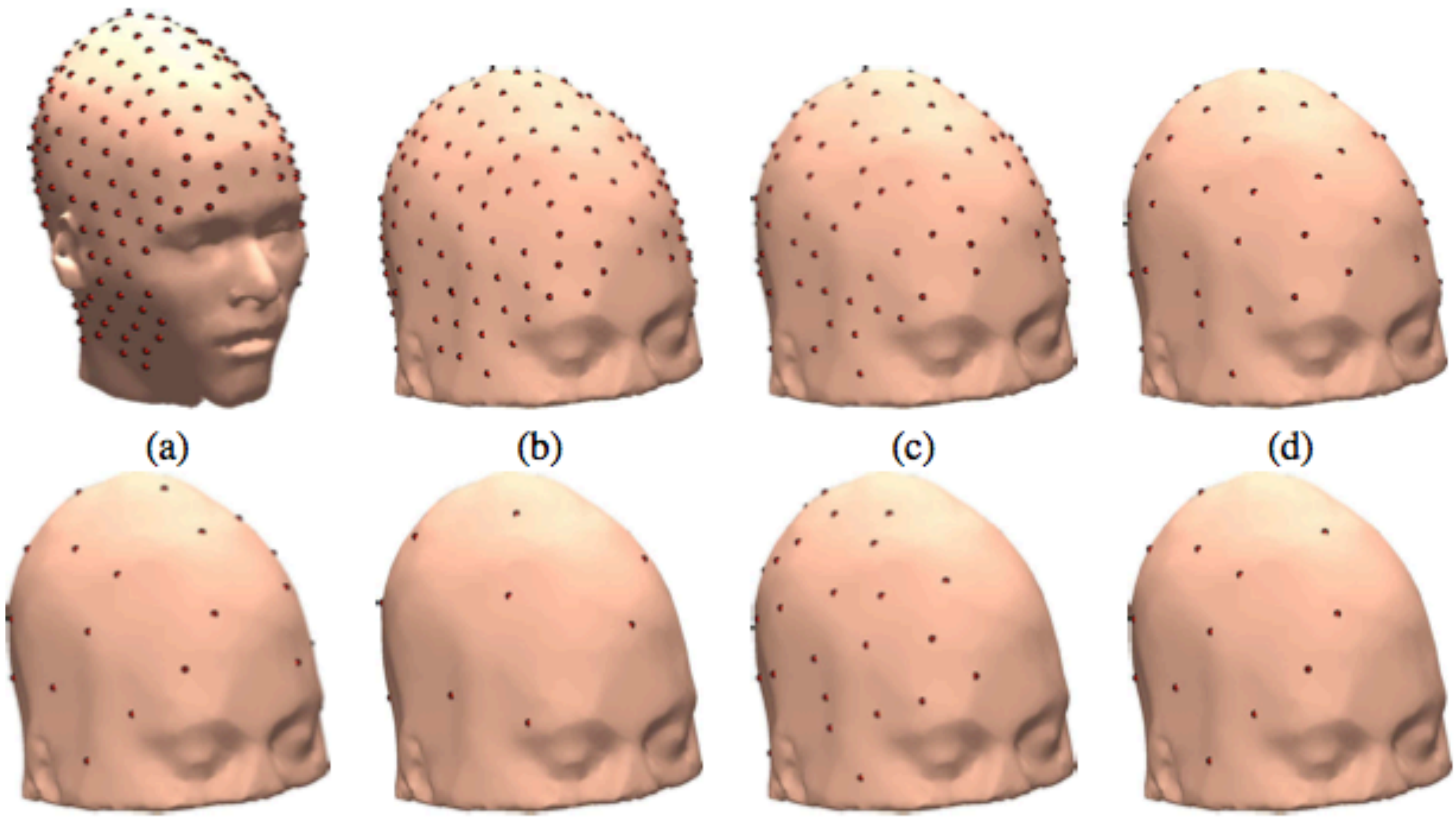


Simplified WM BEM model

Effect of white matter



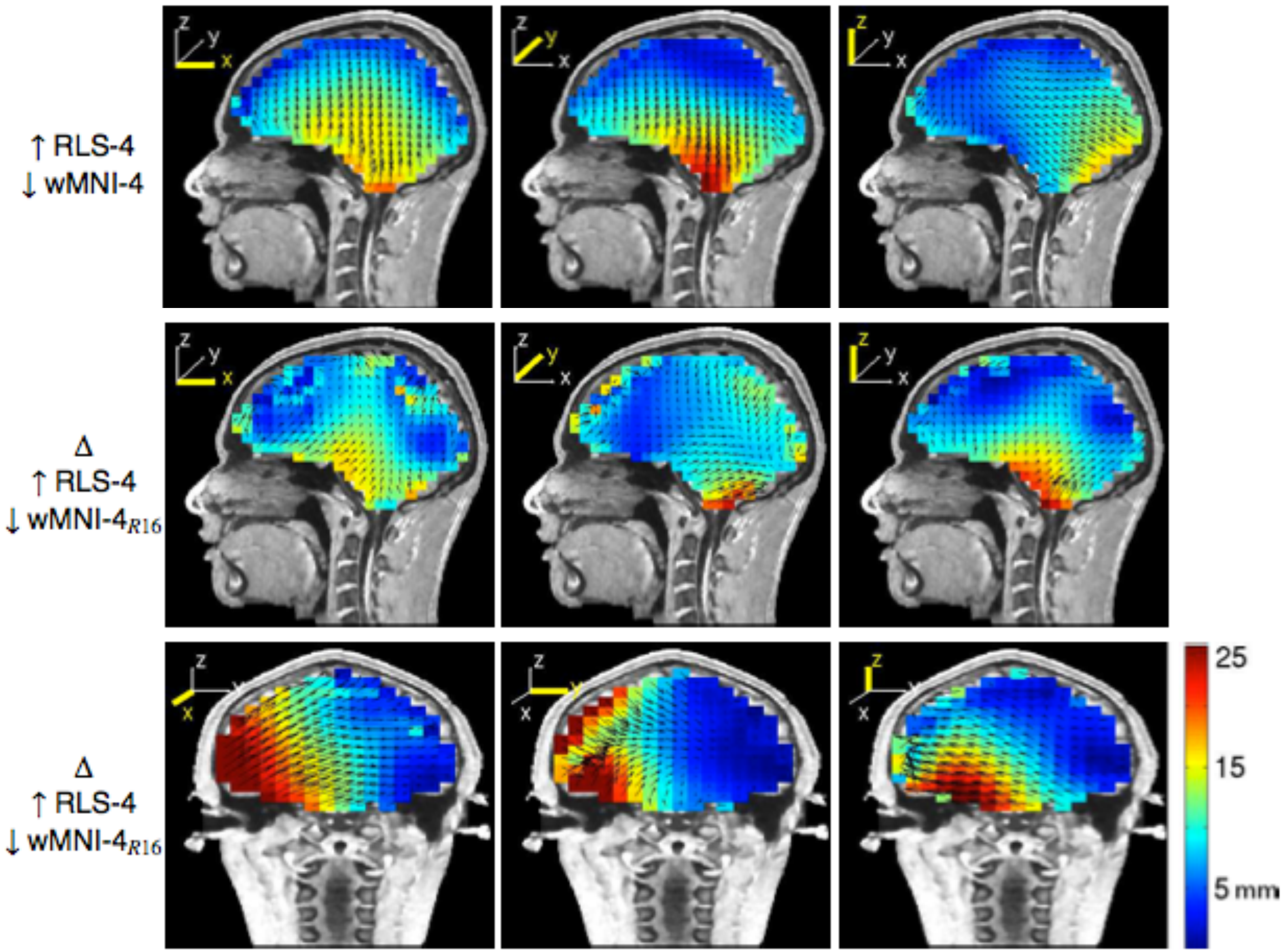
Number of electrodes and coverage



(a) (b) (c) (d)

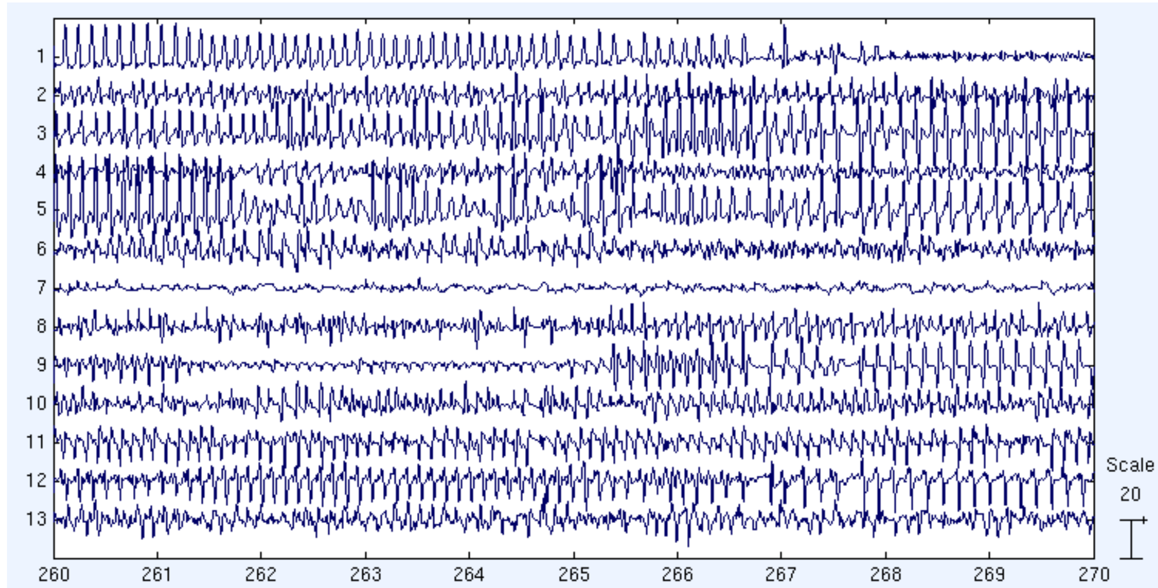
(e) (f) (g) (h)

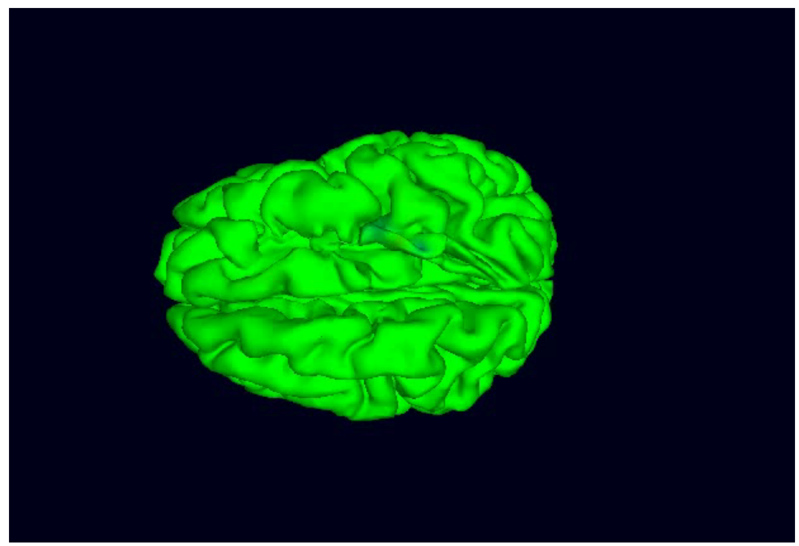
Location errors



Summary

- If we have MRI of the subject:
  - Subject specific head model
  - Distributed source localization
- If we don't have MRIs
  - Warped 4-layer MNI model
  - Dipole source localization
- Skull conductivity estimation is as important as the head model used.
- WM modeling does not have much effect on source localization.

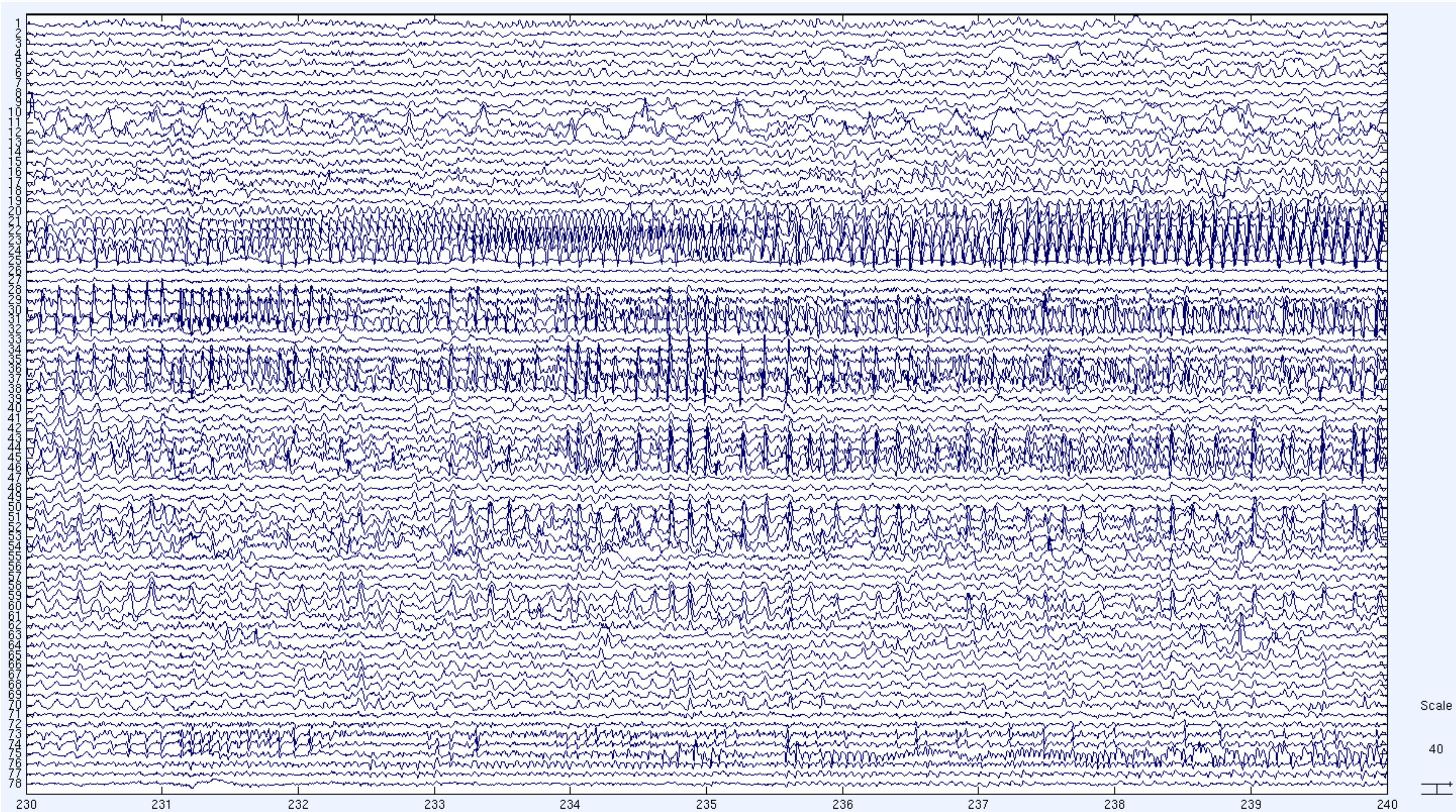




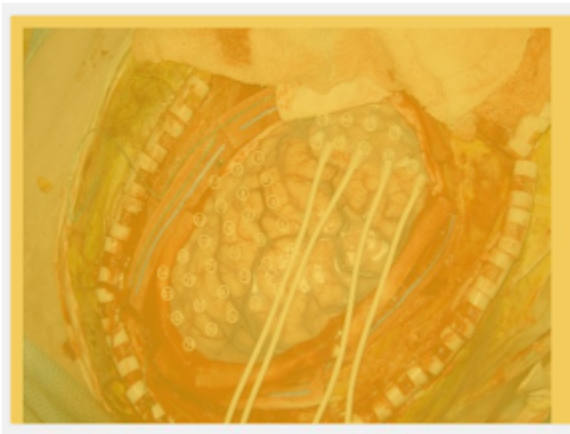
Epilepsy Head Modeling

CASE STUDY

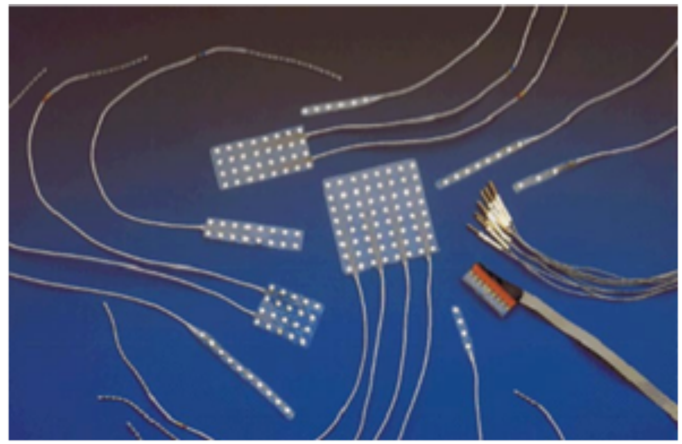
Epilepsy



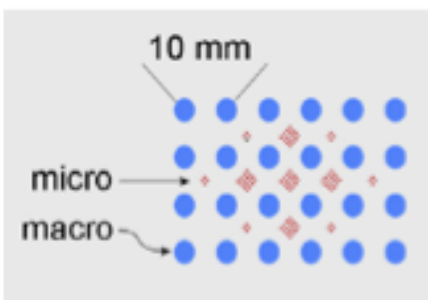
Electrocorticography



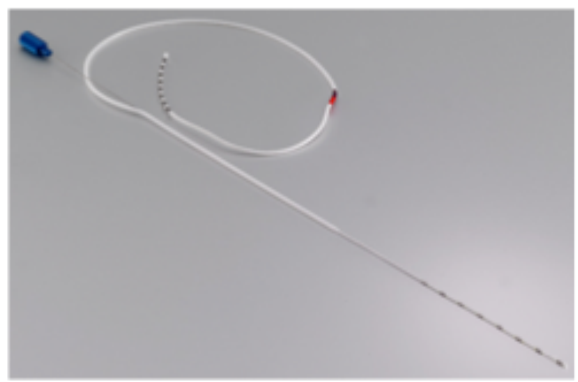
ECoG recording



ECoG grid and strips

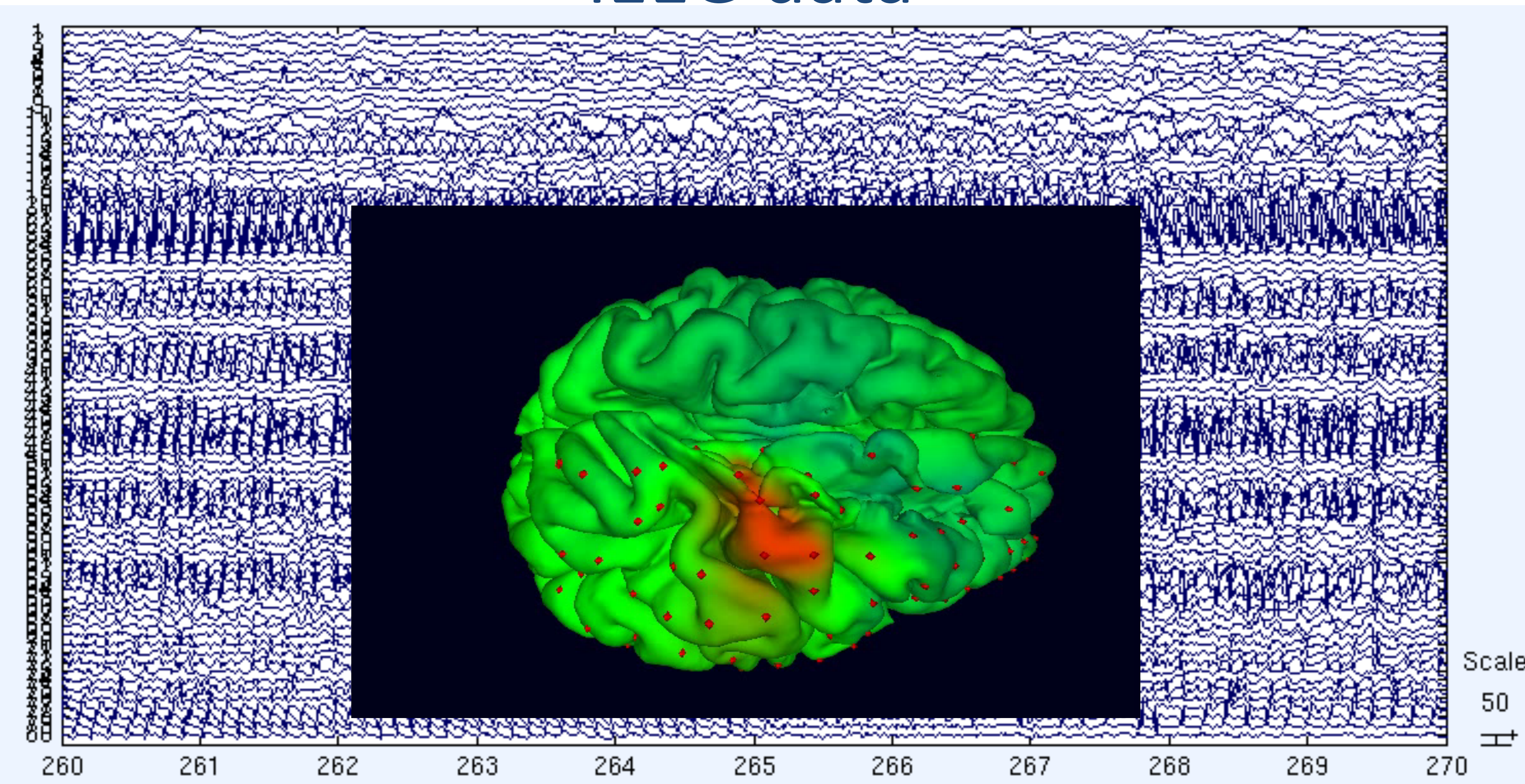


Macro and micro Electrodes (Mayo Clinic)

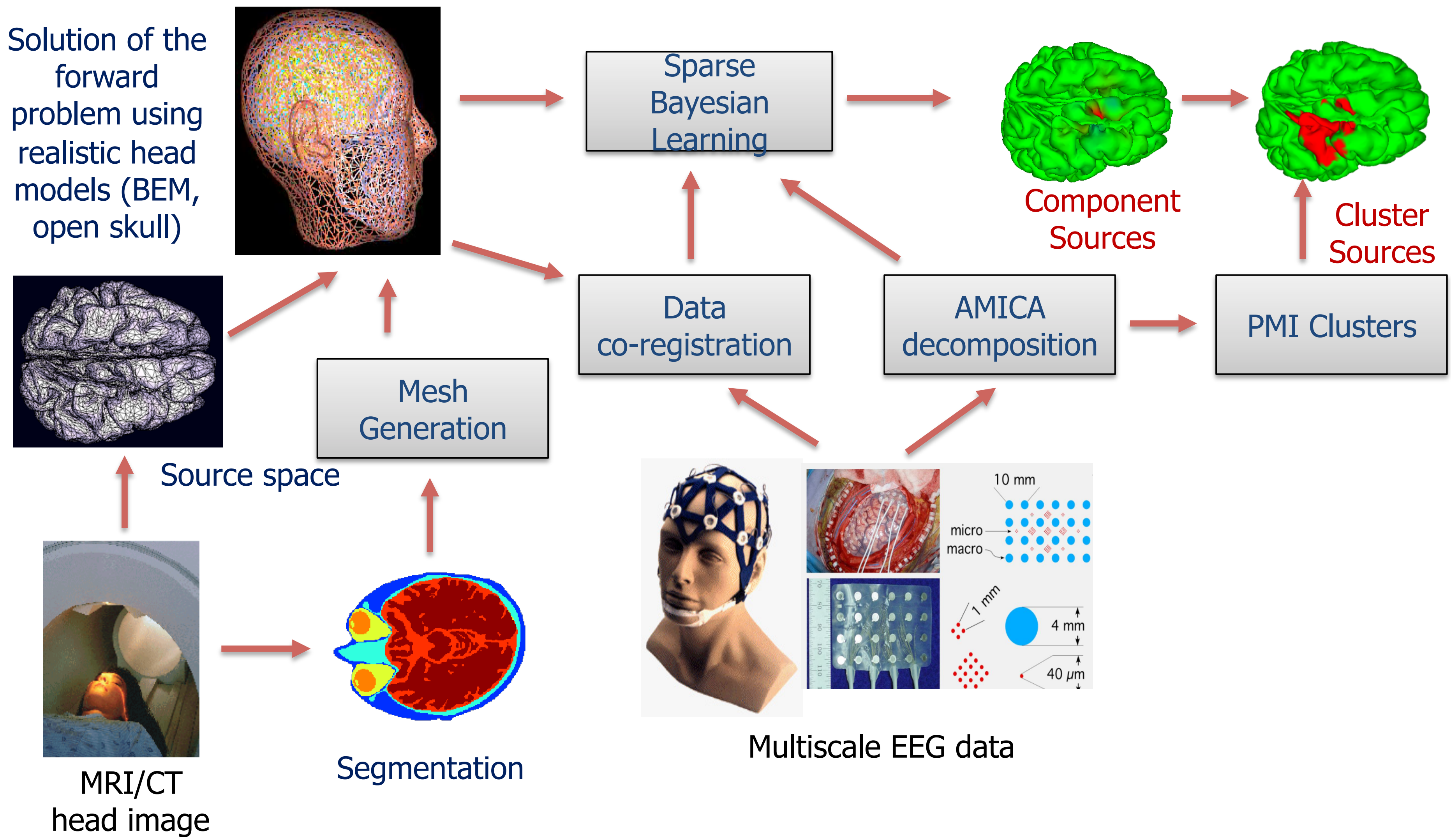


Depth electrodes

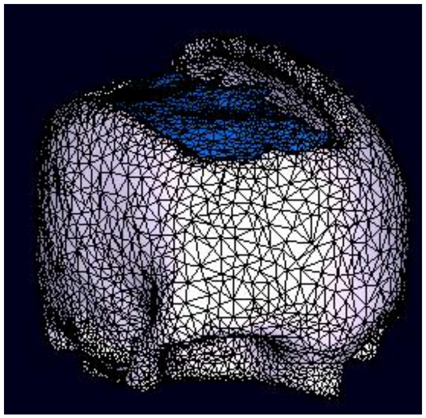
iEEG data

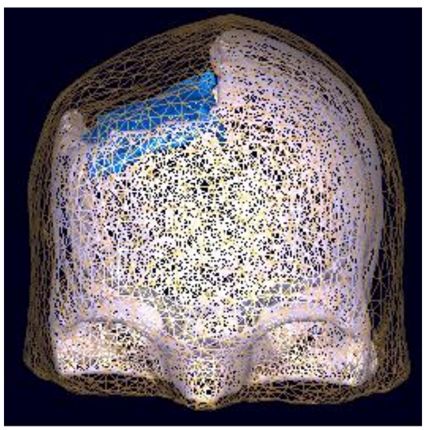


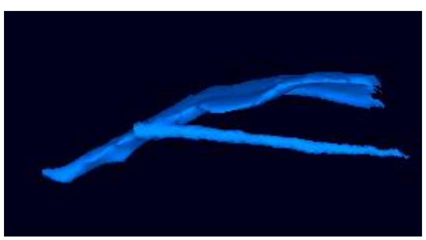
Project Summary

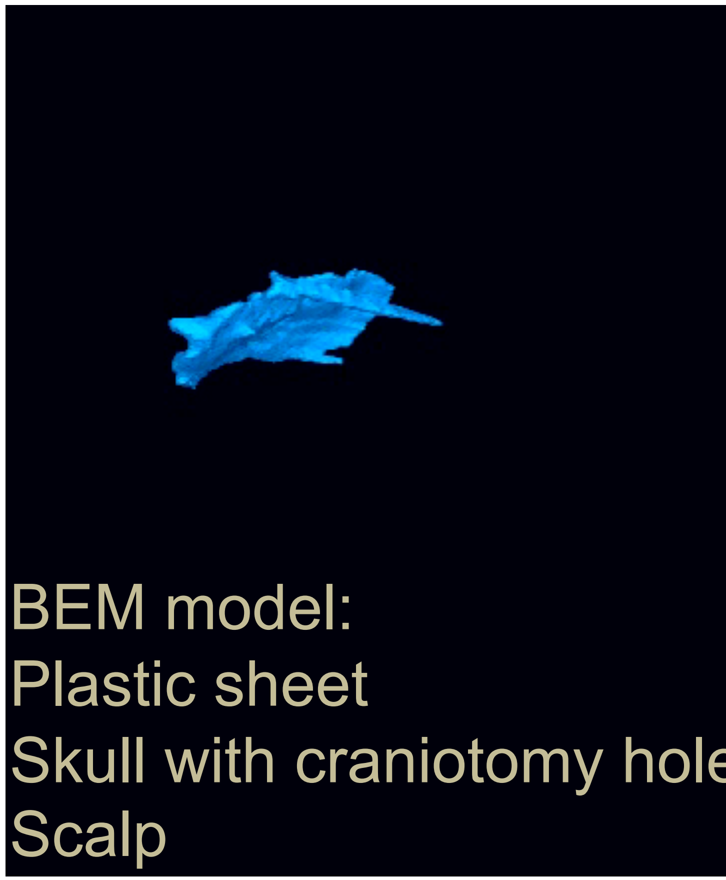


Forward modeling

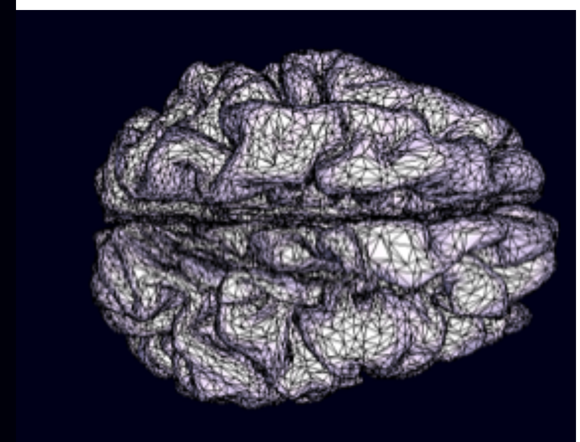






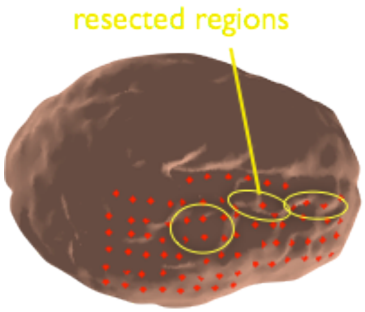


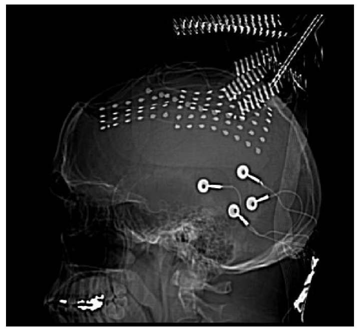
Cortex (Freesurfer)



80 000 source vertices

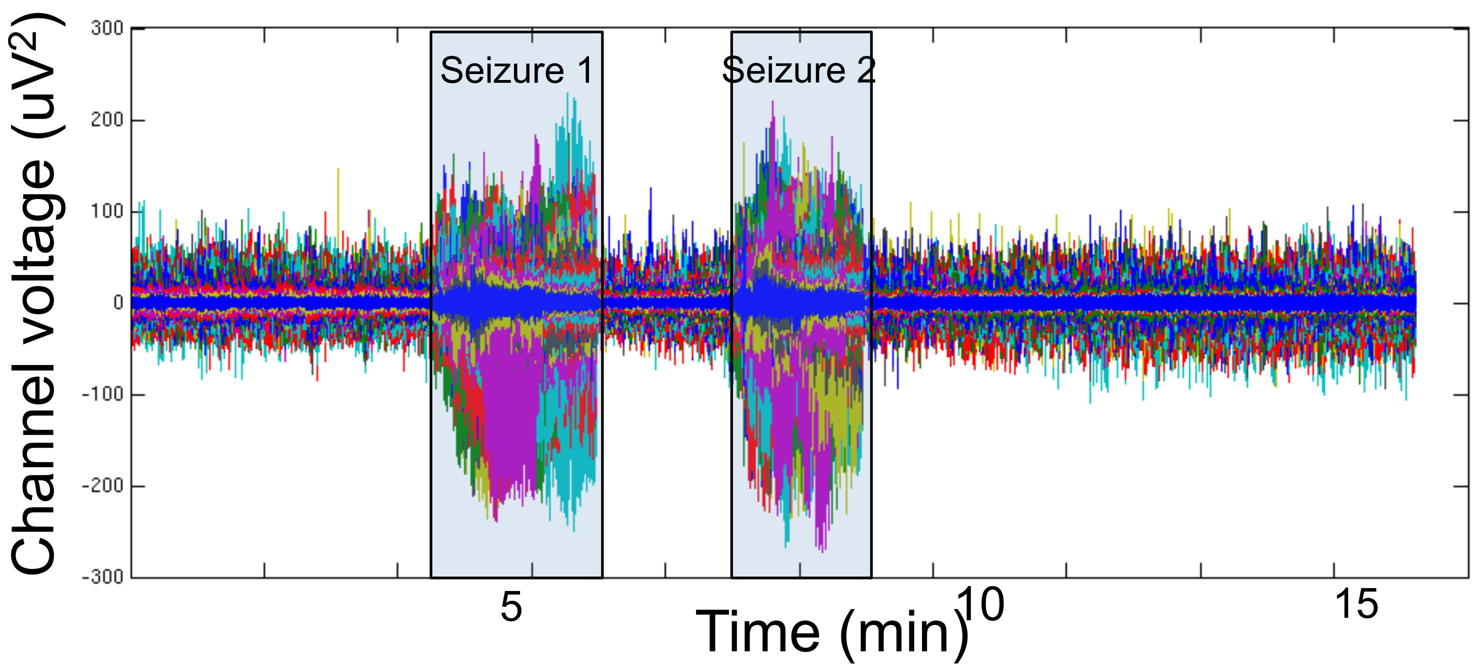
Analyzing Epilepsy Recordings



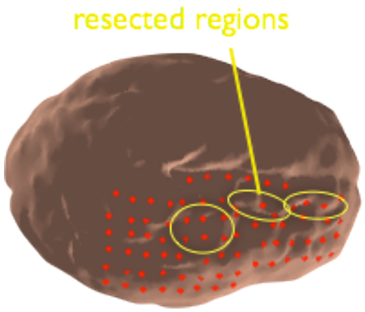


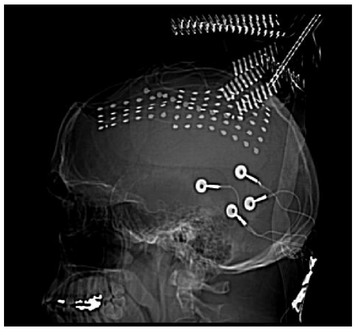
- Pre-Surgical Evaluation
- Rest Data
- 78 ECoG (subdural EEG) electrodes
- 29 scalp electrodes
- Surgical Outcome: Positive (seizure free)
- Provided by Dr. Greg Worrell, Mayo Clinic

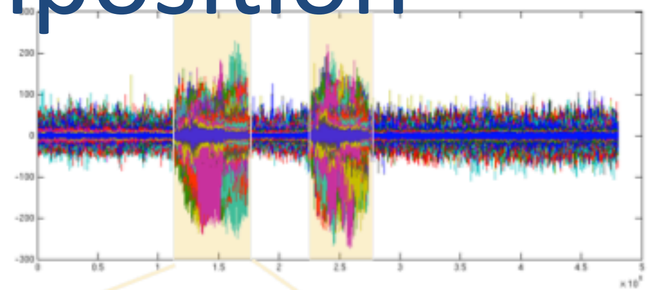
16 min of data, 2 seizures



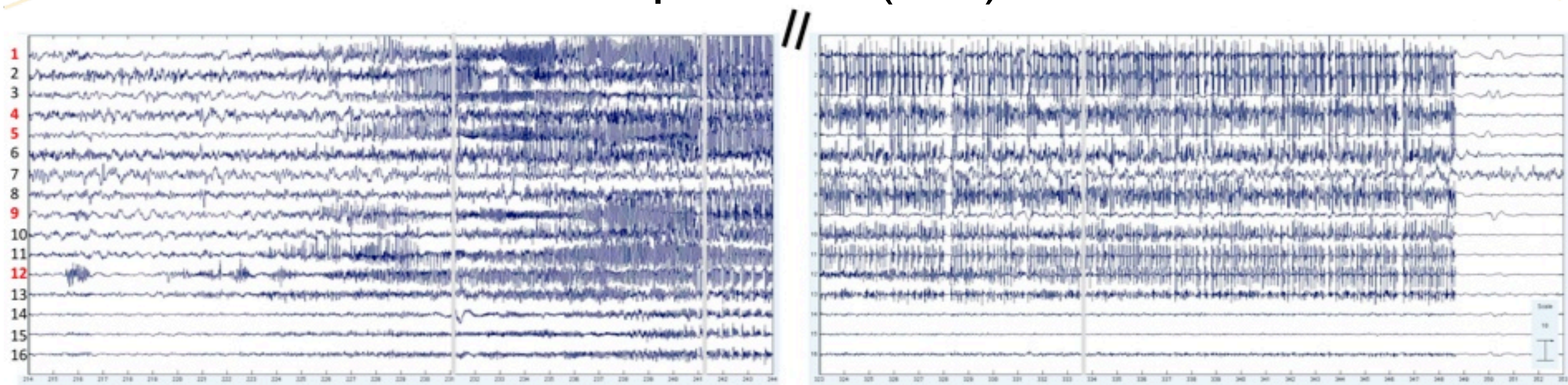
ICA decomposition





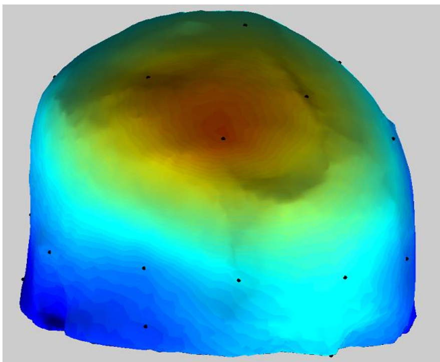


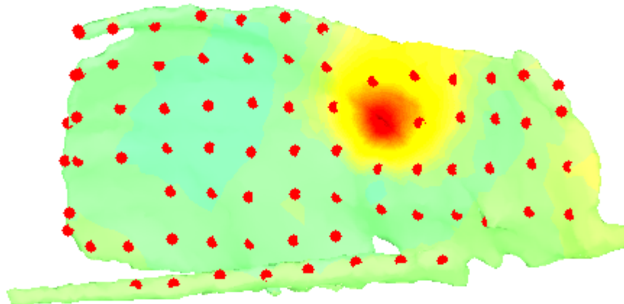
Extended Infomax ICA Decomposition
16 seizure components (ICs) selected

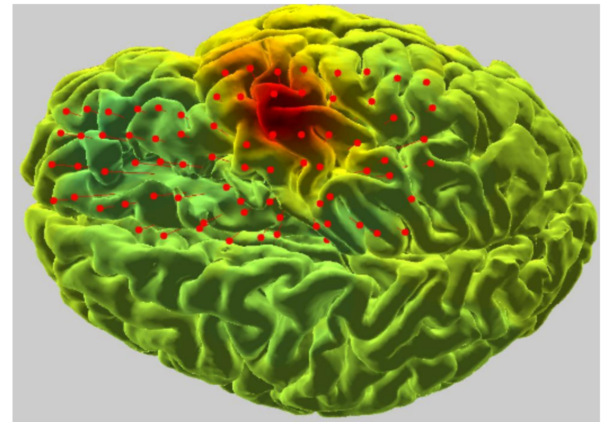


Independent Components

IC 1





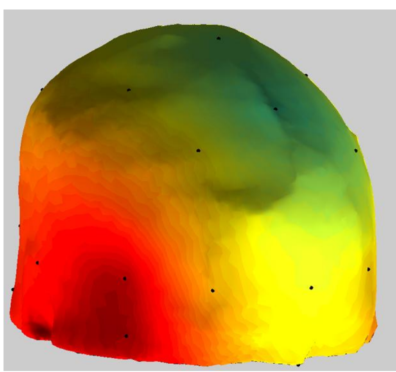


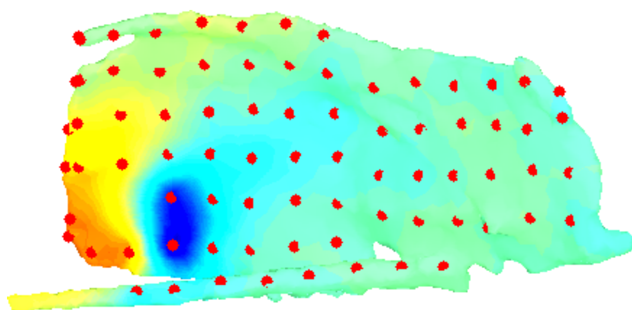
Potentials on scalp

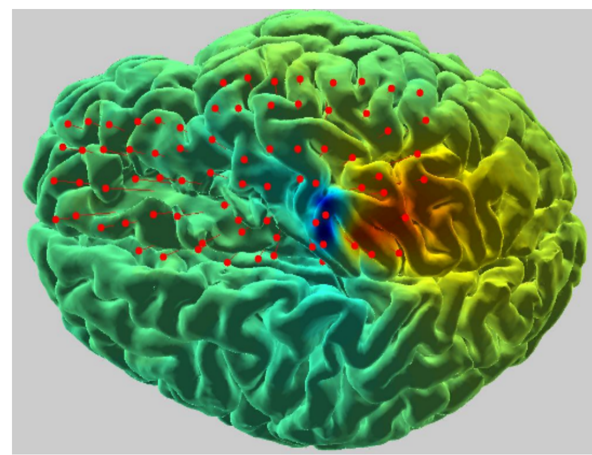
Potentials on plastic sheet

On the brain surface

IC 2



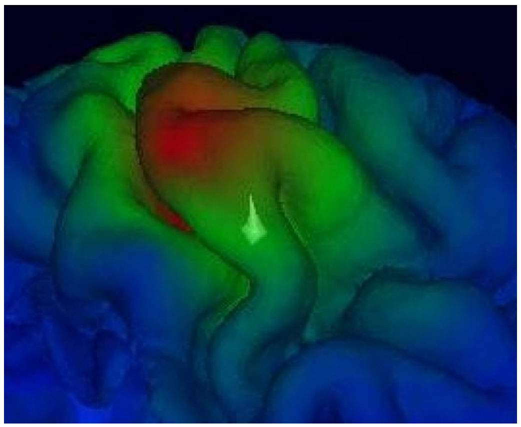




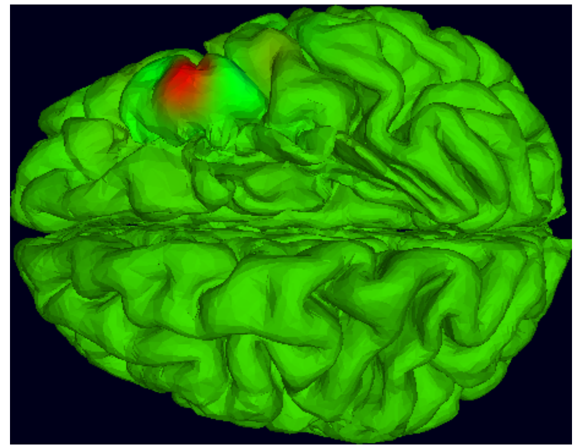
Source Localization Results

Dipole source localization | **Distributed source localization - SBL**

IC 1

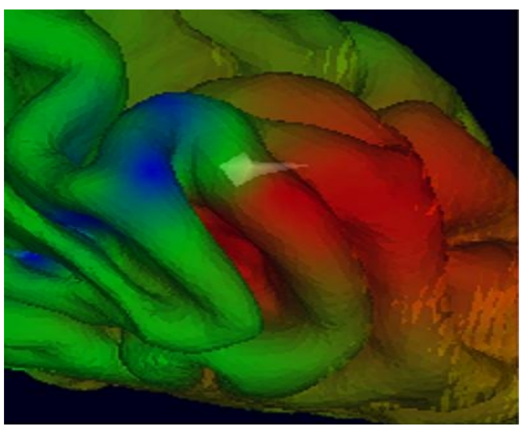


Radial source

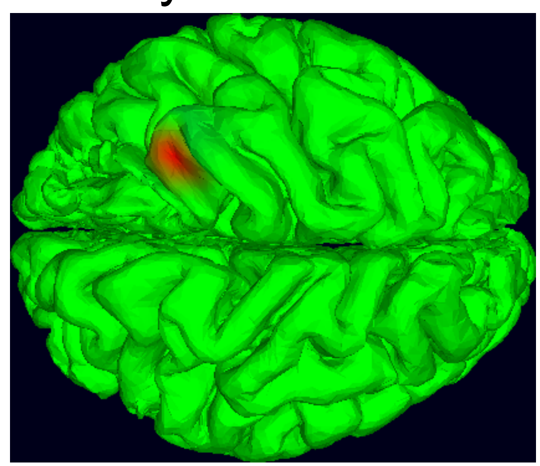


Gyral source

IC 2

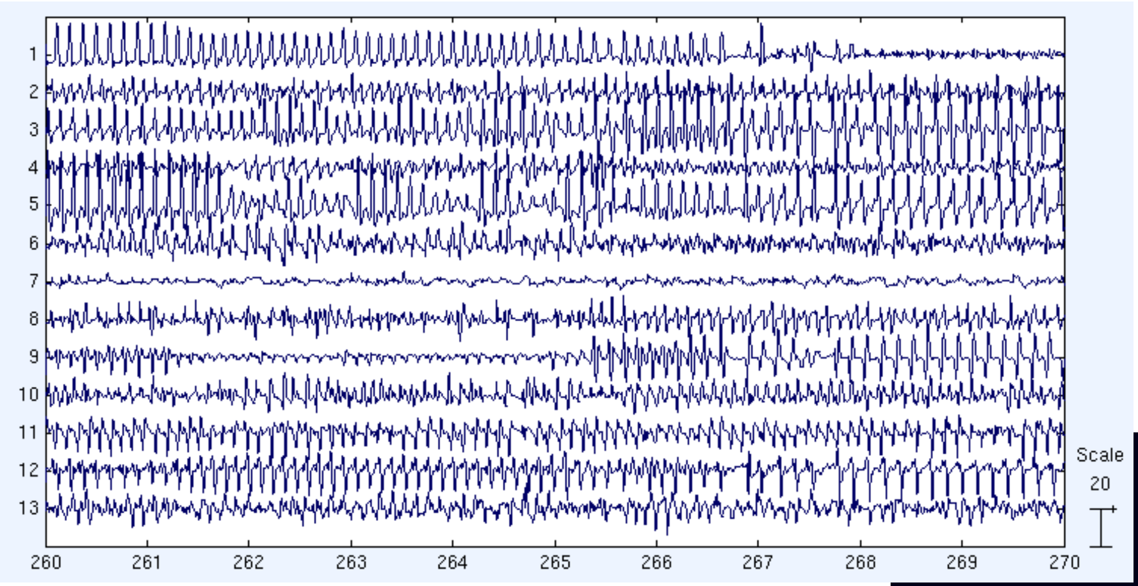


Tangential source

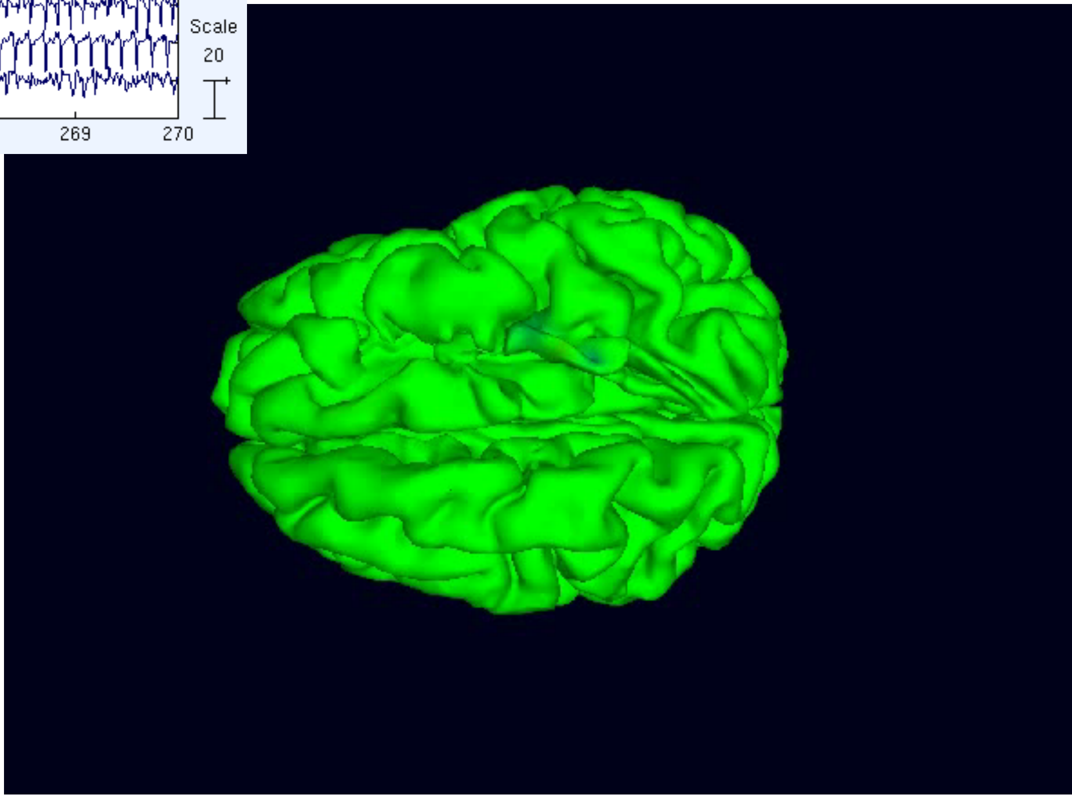


Sulcal source

Cortical activity of seizure components



Activations of 13 seizure components



Cortical activity of Seizure components

$$Movie(t) = \sum_{i=1}^{13} S_i \times Act_i(t)$$

Thank you…

Swartz Center for Computational Neuroscience

Algebraic formulation of the FP

Scalp potentials for N electrodes and p dipoles:

$$V(r) = \sum_i^p g(r, r_{dip}, d_i) = \sum_i^p g(r, r_{dip}, e_{d_i}) d_i$$

$$V = \begin{bmatrix} V(r_1) \\ \vdots \\ V(r_N) \end{bmatrix} = \begin{bmatrix} g(r_1, r_{dip}, e_{d1}) & \cdots & g(r_1, r_{dip}, e_{dp}) \\ \vdots & \ddots & \vdots \\ g(r_N, r_{dip}, e_{d1}) & \cdots & g(r_N, r_{dip}, e_{dp}) \end{bmatrix} \begin{bmatrix} d_1 \\ \vdots \\ d_p \end{bmatrix} = G(\{r_j, r_{dip_i}, e_{d_i}\}) \begin{bmatrix} d_1 \\ \vdots \\ d_p \end{bmatrix}$$

For N electrodes and p dipoles and T discrete time samples:

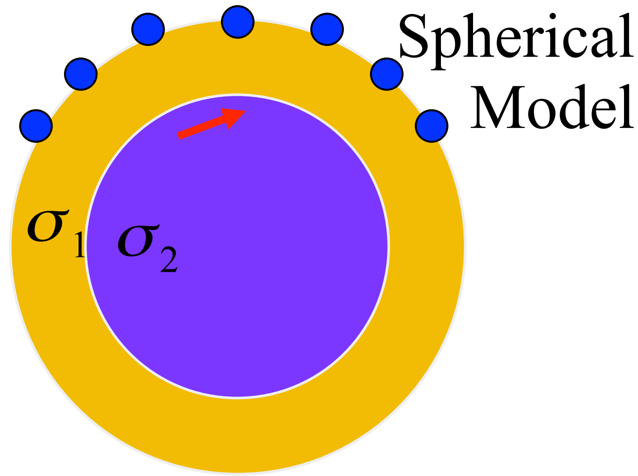
$$V = \begin{bmatrix} V(r_1, 1) & \cdots & V(r_1, T) \\ \vdots & \ddots & \vdots \\ V(r_N, 1) & \cdots & V(r_N, T) \end{bmatrix} = G(\{r_j, r_{dip_i}, e_{d_i}\}) \begin{bmatrix} d_{1,1} & \cdots & d_{1,T} \\ \vdots & \ddots & \vdots \\ d_{p,1} & \cdots & d_{p,T} \end{bmatrix}$$

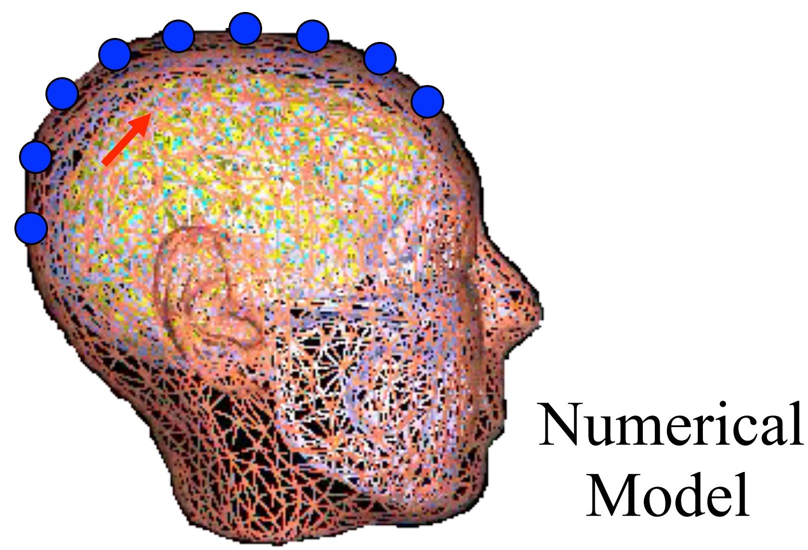
$$V = GD + n$$

To Solve the Forward Problem

WE NEED

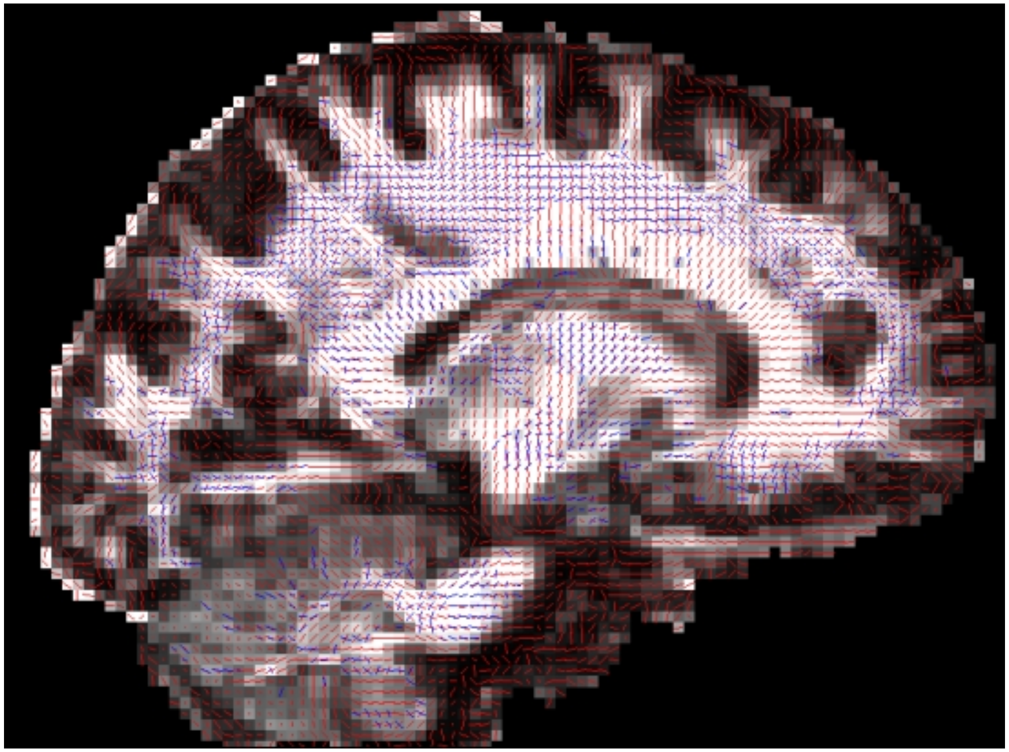
- Head Model
  - Conductivity values
  - Geometry
- Source distribution
  - Magnitude
  - Location
  - Direction
- Field Locations
- Solver



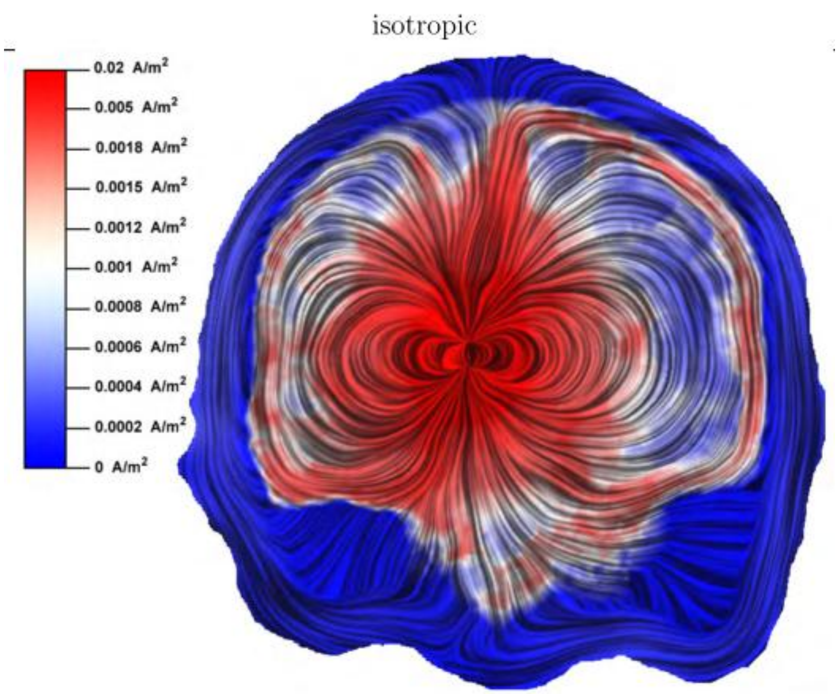


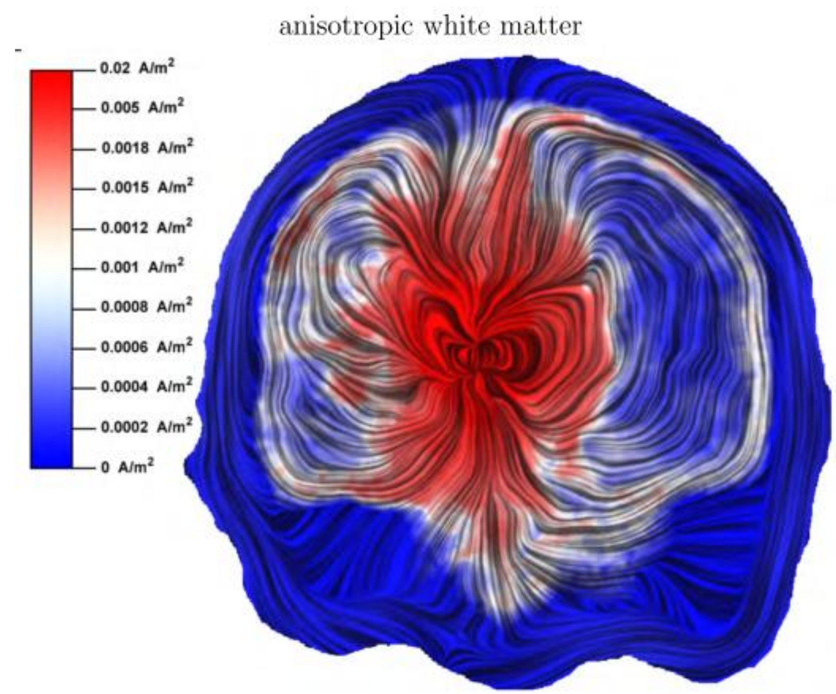
Anisotropy

- Directional conductivity for skull and WM.
- WM anisotropy can be obtained from diffusion tensor imaging (DTI).
- WM anisotropy ratio = 9:1
- Skull ratio = 10:1



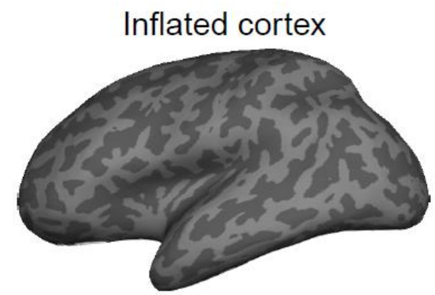
Anisotropy

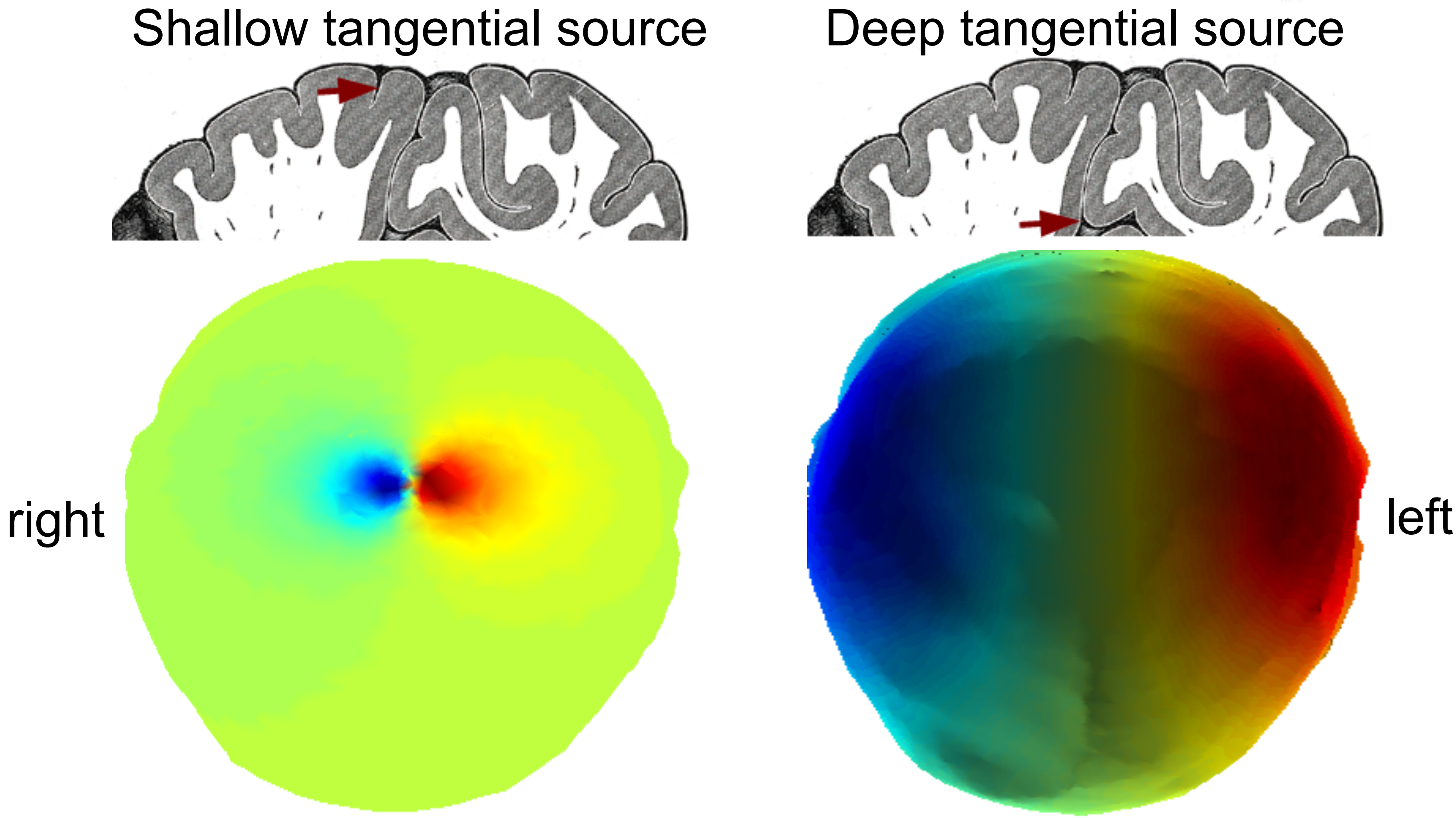




Return currents for a left thalamic source on a coronal cut
Wolters et al, 2006

Potential fields on the scalp





top view of head

Potential fields on the scalp