M/EEG source analysis

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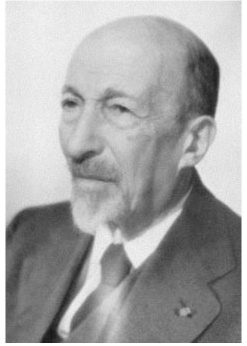
"Will it ever happen that mathematicians will know enough about the physiology of the brain, and neurophysiologists enough of mathematical discovery, for efficient cooperation to be possible"

Jacques Hadamard *(mathematician, 1865-1963)*



SPM for MEEG course – London – May 2016

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Ill-posed inverse problem
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Sensors

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ECD model
Imaging models
Setting priors
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Comparing models
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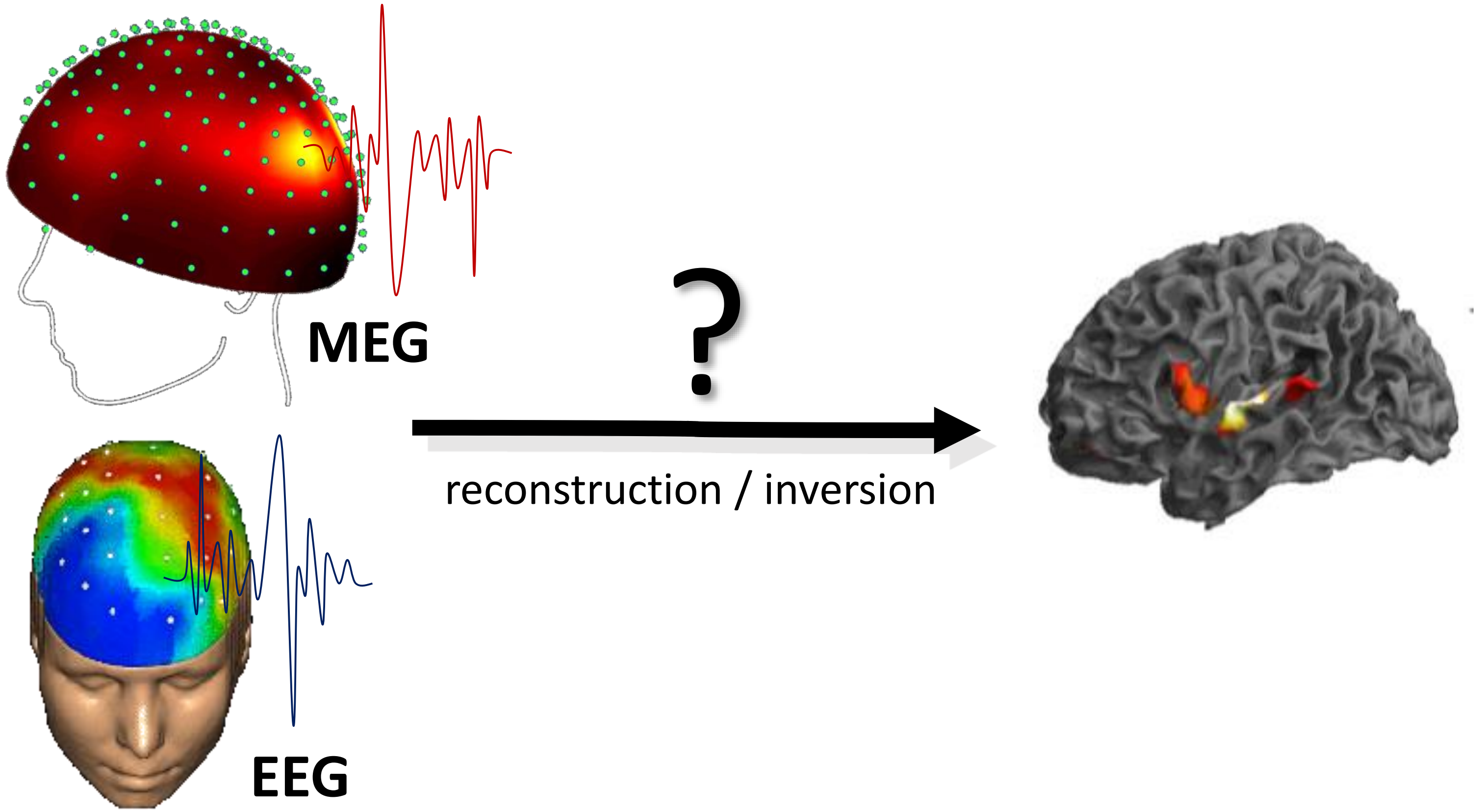
Example
MMN study
Group multimodal inference

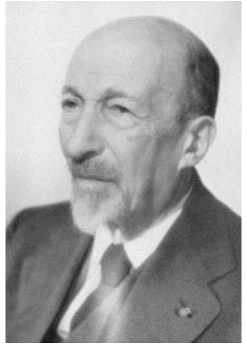
Introduction



<u>Well-posed inverse problem:</u>

- a solution exists ✔
- the solution is unique ✘
- the solution is stable ✘

Jacques Hadamard *(mathematician, 1865-1963)*



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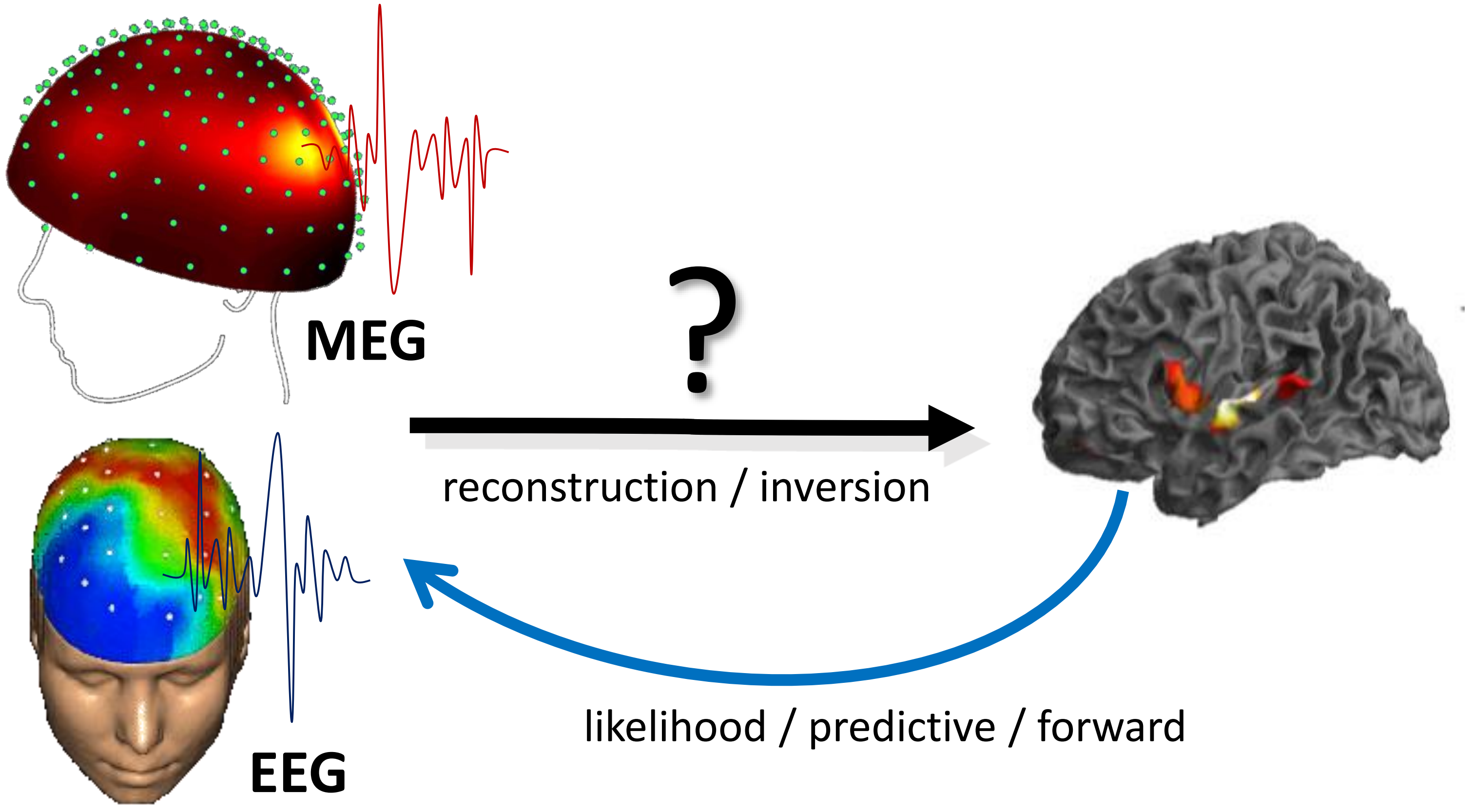

Bayesian inference enables:

- to incorporate priors on the solution
- to account for uncertainty through probabilitic distributions
- to yield a unique and optimal solution given a likelihood model and priors over model parameters

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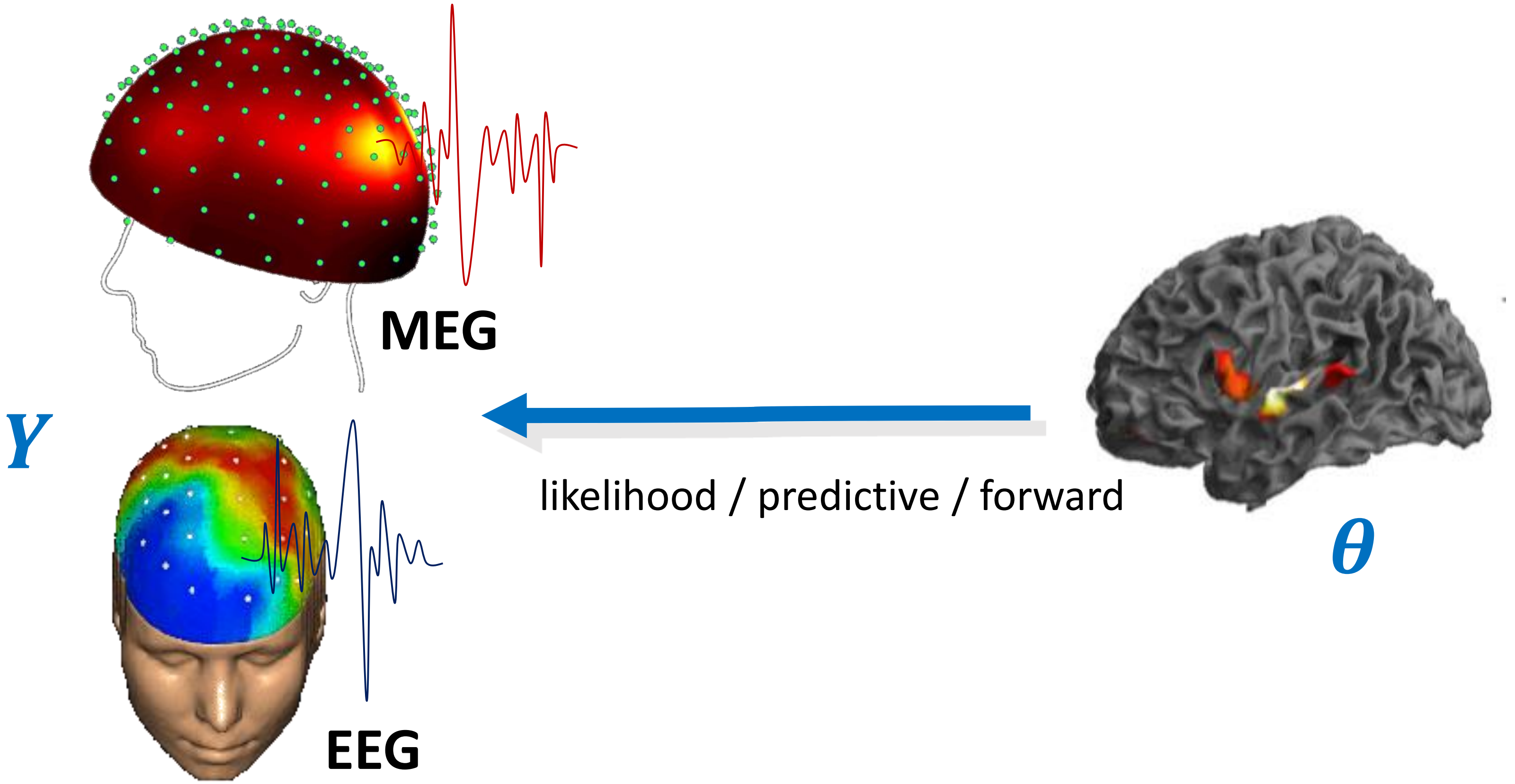
Generative models



A particular generative model is fully defined by:

- A **data** likelihood density function $p(Y|\theta)$

- A prior distribution over **source** parameters θ $p(\theta)$

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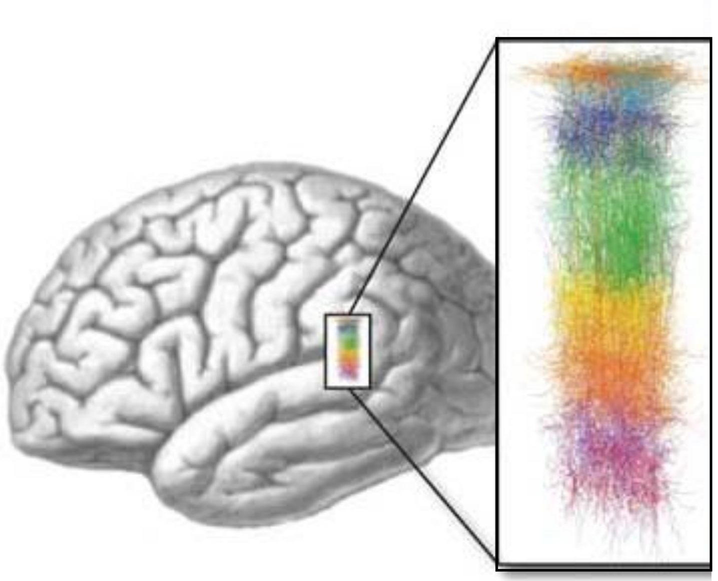
Sources

- Observable from scalp:
  the synchronous and additive activities of numorous neighbouring neurons



Cortical macro-column

Current dipole

$\boldsymbol{\theta}$:

- Dipole location (x, y, z)
- Dipole orientation (Ox, Oy, Oz)
- Dipole strength

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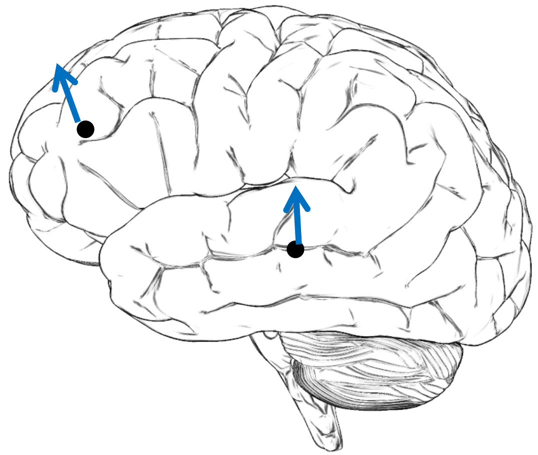
Sources

- **Equivalent Current Dipole (ECD)**
  - Only a few activated sources
  - Each source corresponds to a fairly large brain area
  - Each source activity is modelled by one current dipole

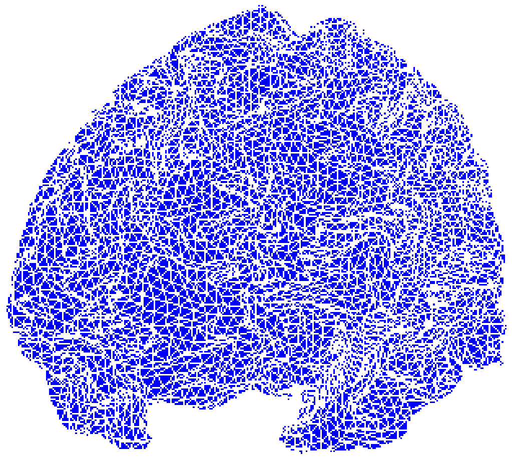
→ Only a few parameters θ to be estimated (location, orientation and strength)



e.g. early response to auditory stimulus

- **Distributed or imaging approach**
  - The whole brain/cortex may be active
  - The source space is discretized using a grid over the whole brain (voxels) or a cortical mesh (nodes)
  - Each voxel or node is the location of a dipolar source
  - Each dipole models the activity of a small brain region

→ Many parameters θ to be estimated (strength only)



e.g. MRI-derived cortical mesh

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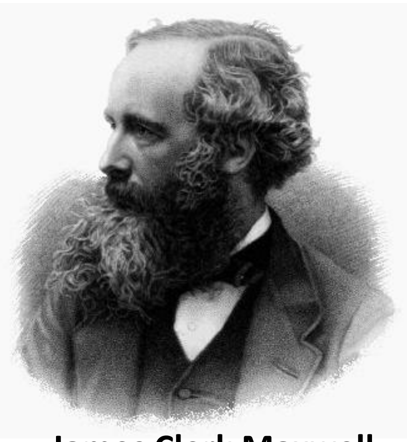
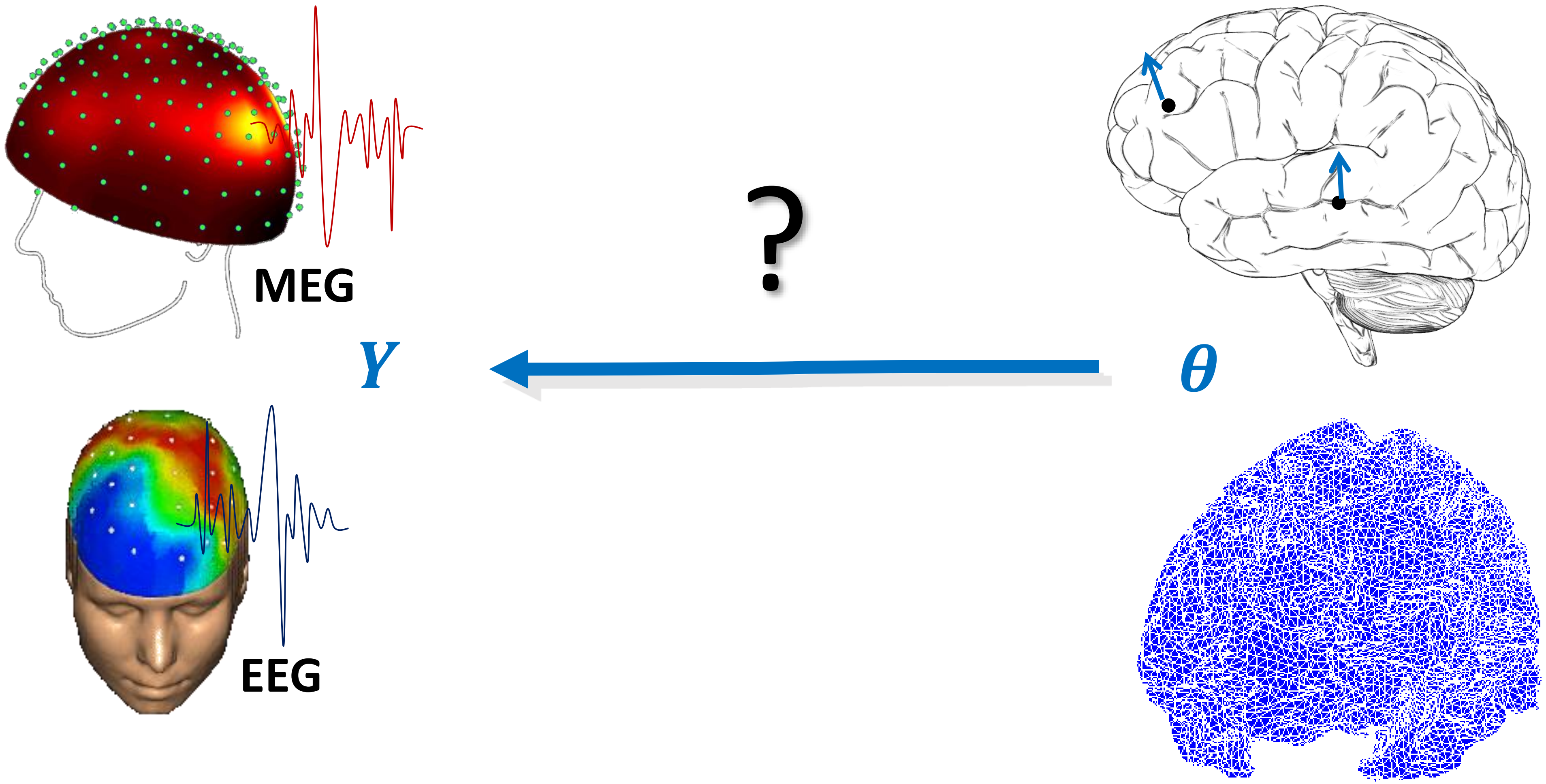
From sources to sensors



James Clerk Maxwell
(1831 - 1879)

- Predicting the sensor data $\boldsymbol{Y}$ from known source parameters $\boldsymbol{\theta}$:
  - requires solving the Maxwell's equations in a quasi-static regime
  - amounts to solving a well-posed forward problem
  - involves approximations



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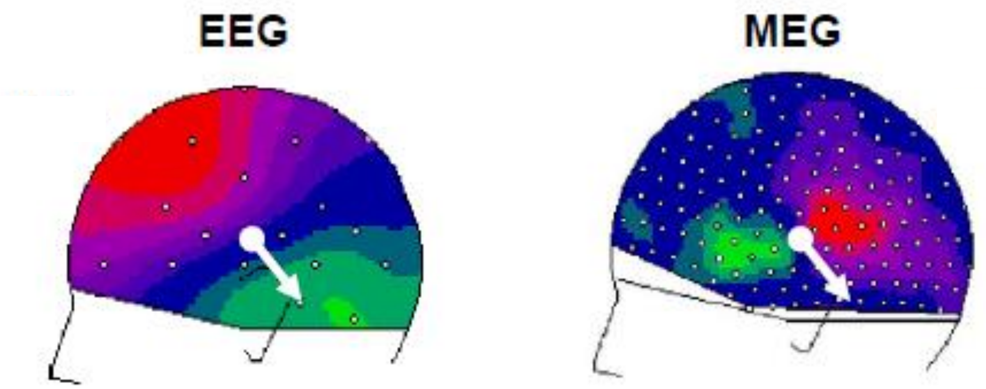
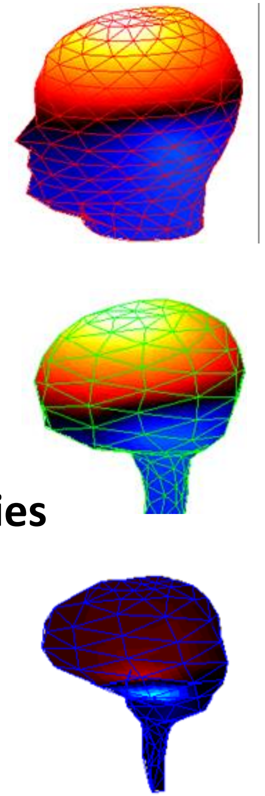
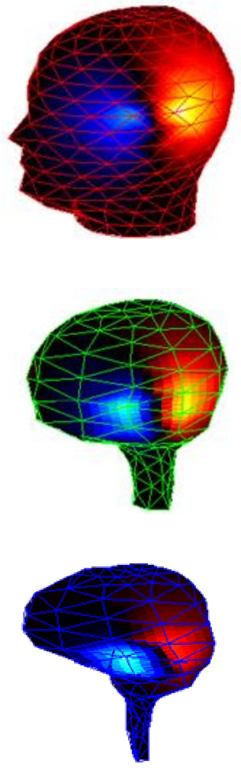
From sources to sensors



- **EEG is sensitive to both radial and tangential sources**





- **MEG is barely sensitive to radial sources**

- **EEG is sensitive to conductivities**

- **MEG is barely sensitive to conductivities**

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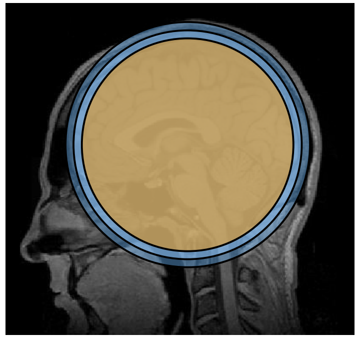
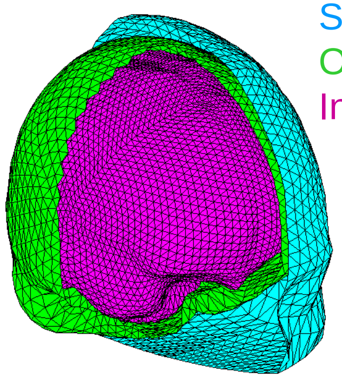
From sources to sensors

Simple Head Model



Concentric spheres

Realistic Head Model



Boundary element method (BEM)

Pros : Fast analytic solution | Realistic geometry

Cons : Heads are not spherical | Slow approximate numerical solutions

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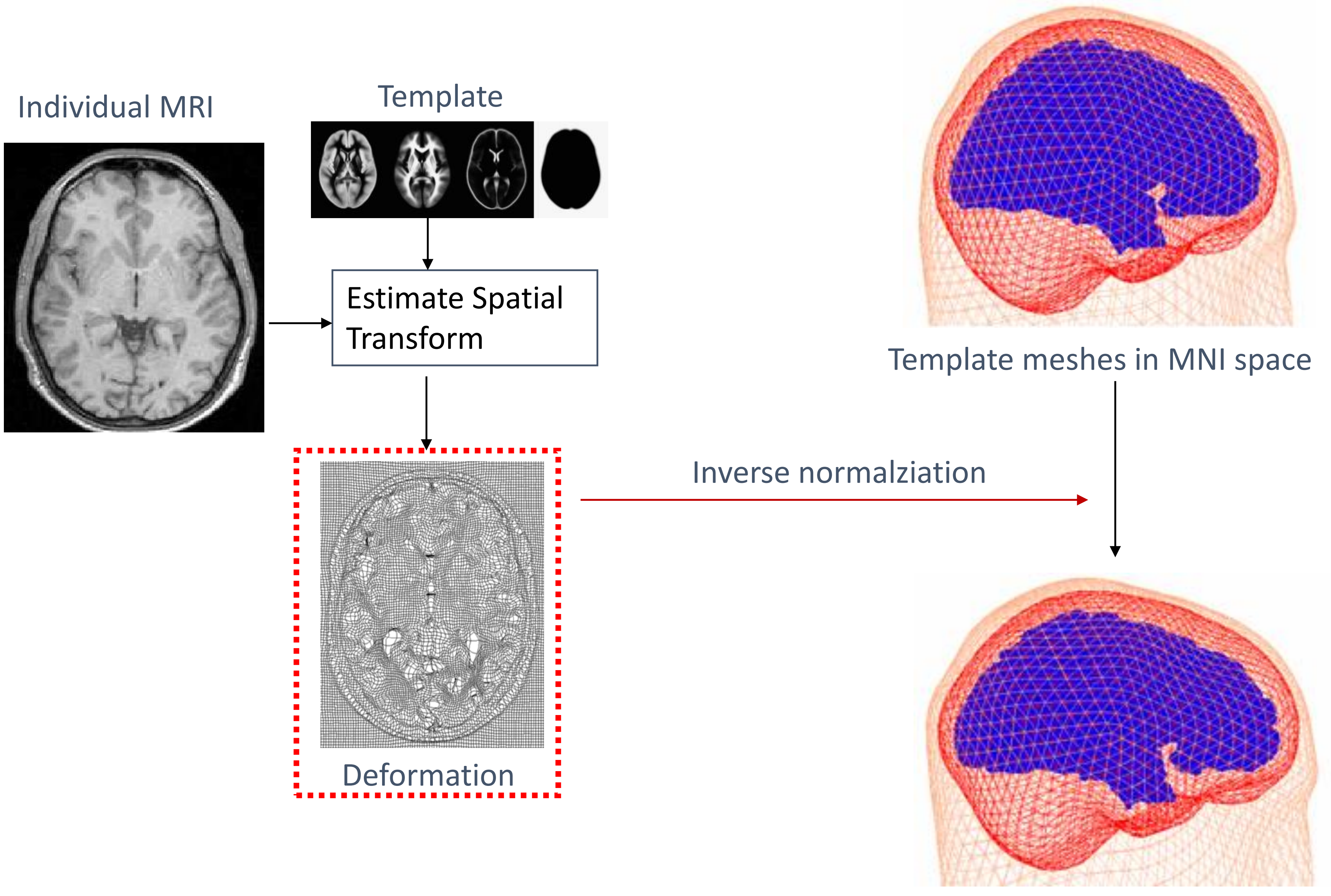
From sources to sensors

- <u>Automated extraction of individual meshes</u>



Canonical (individual) mesh

Mattout et al., Comp. Int & Neuro, 2007

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Sensors

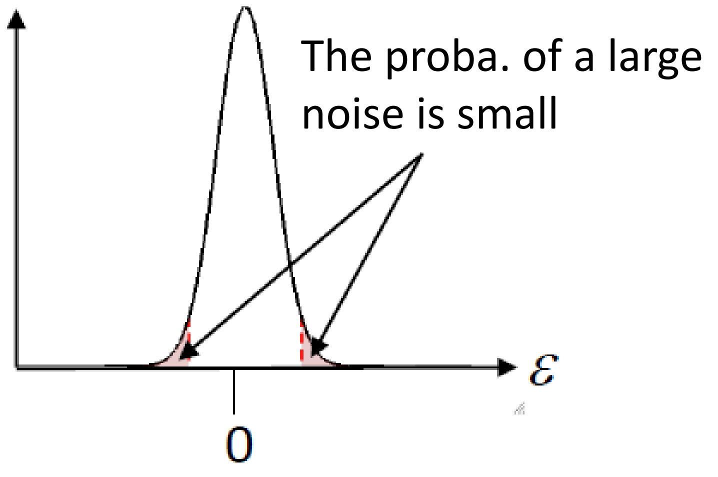
- Data features $\boldsymbol{Y}$ to be fitted/explained
  - Evoked response
  - Induced response
  - Steady-state response

- Accounting for noise $\boldsymbol{\varepsilon}$ in the data

$$\boldsymbol{Y} = \boldsymbol{g}(\boldsymbol{\theta}) + \boldsymbol{\varepsilon}$$

Gaussian noise

$$\boldsymbol{p}(\boldsymbol{\varepsilon}) = \boldsymbol{N}(\mathbf{0}, \boldsymbol{C}_{\boldsymbol{\varepsilon}})$$



Data likelihood

$$\boldsymbol{p}(\boldsymbol{Y}|\boldsymbol{\theta}) = \boldsymbol{N}(\boldsymbol{g}(\boldsymbol{\theta}), \boldsymbol{C}_{\boldsymbol{\varepsilon}})$$

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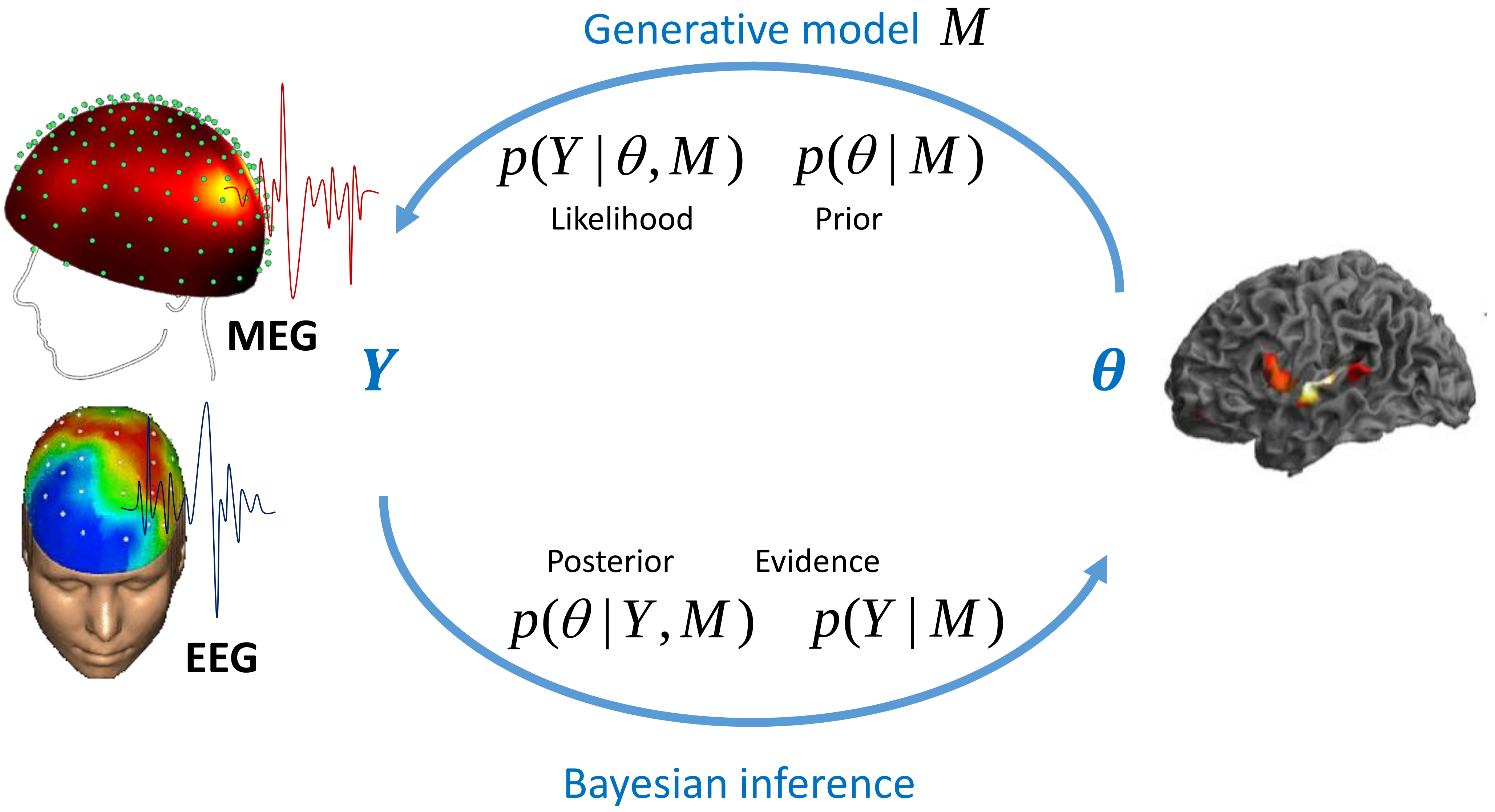
Bayesian inference

$$P(\theta|Y,M)=\frac{P(Y|\theta,M)P(\theta|M)}{P(Y|M)}$$



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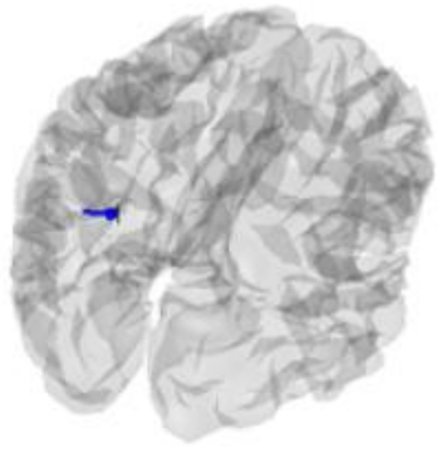
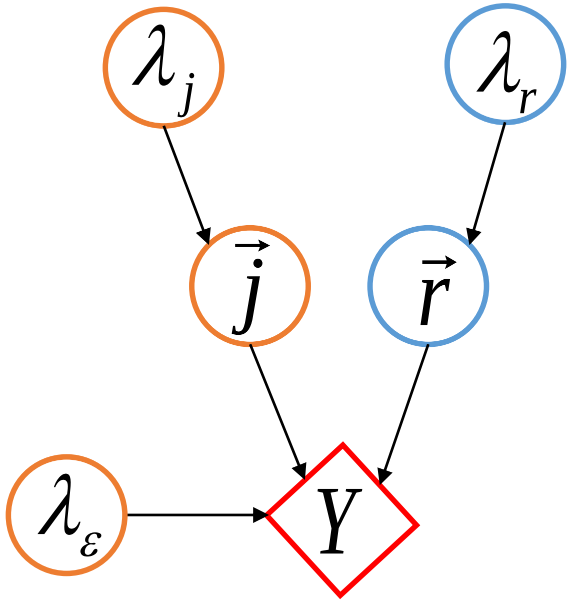
ECD model

- <u>A Bayesian model for Equivalent Current Dipole (ECD) solutions</u>
  - Enables to put priors on source parameters
  - Enables formal model comparison (e.g. on number of sources or initial conditions)





Kiebel et al., NeuroImage, 2008

ECD model

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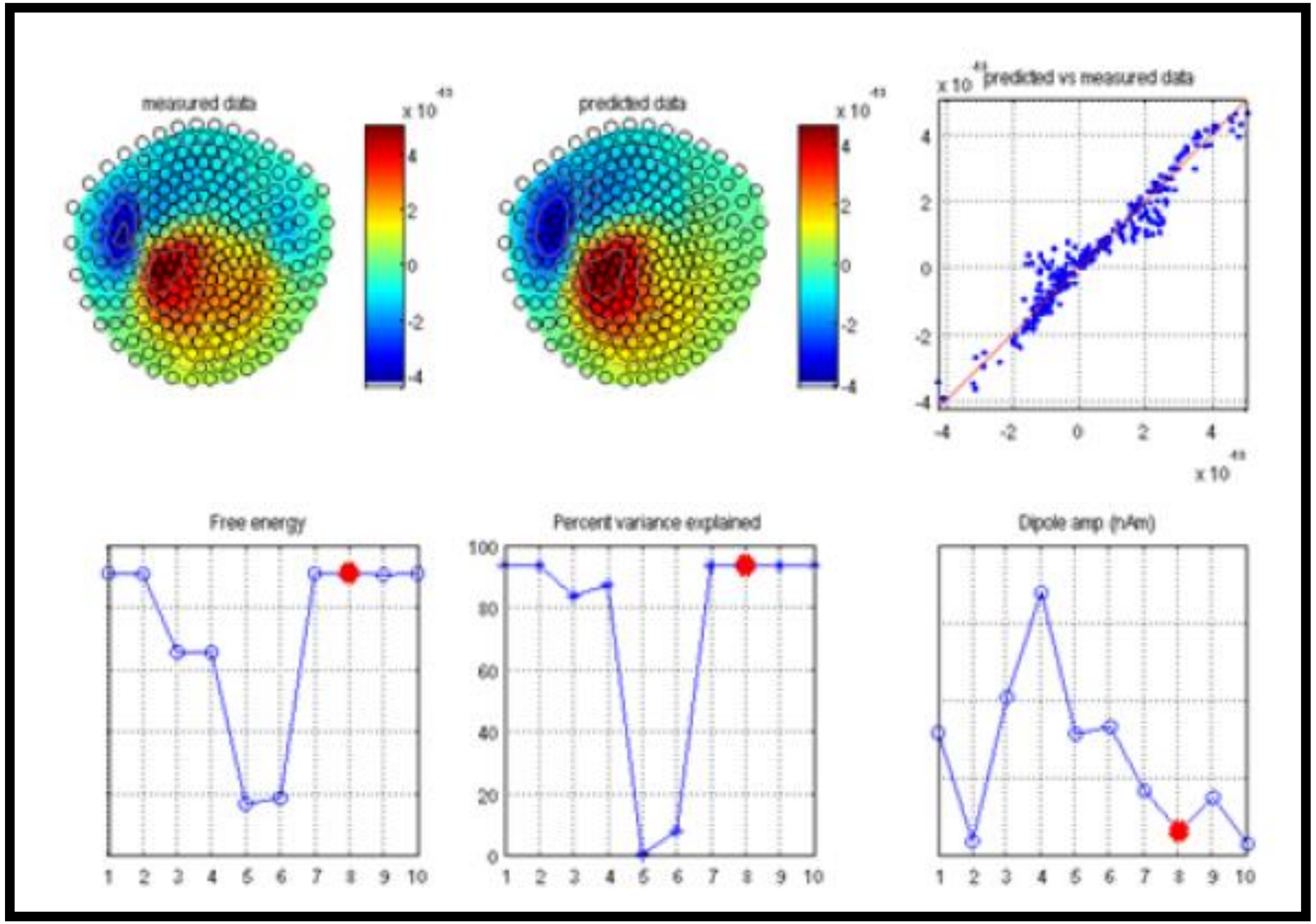

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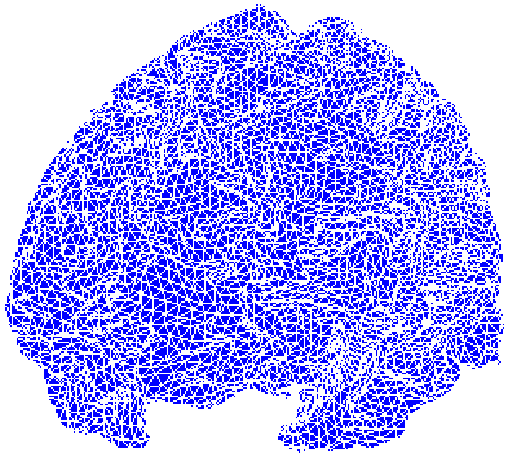
Imaging models

- <u>A Bayesian model for Distributed / Imaging solutions</u>
  - Many dipoles with fixed location and orientation
  - Dipole strength ? -> linear model

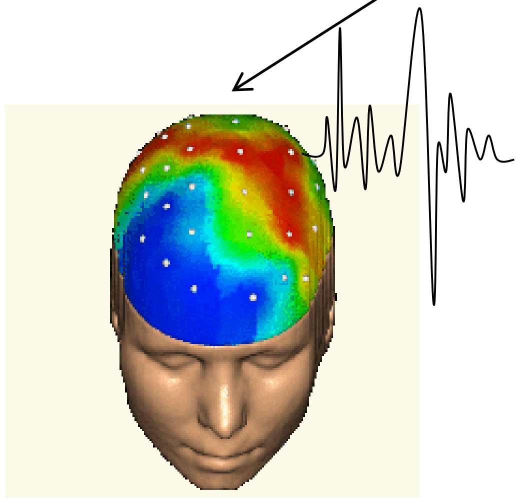


$$\boldsymbol{Y = K.\theta + \varepsilon}$$

noise

Unknown source dynamics: Nsources x Time

Forward operator or lead-field matrix: Nsens x Nsources



Evoked EEG response: Nsens x Time

$$\boldsymbol{p(Y|\theta) = N(\mathrm{K}.\theta, C_\varepsilon)}$$

Setting priors

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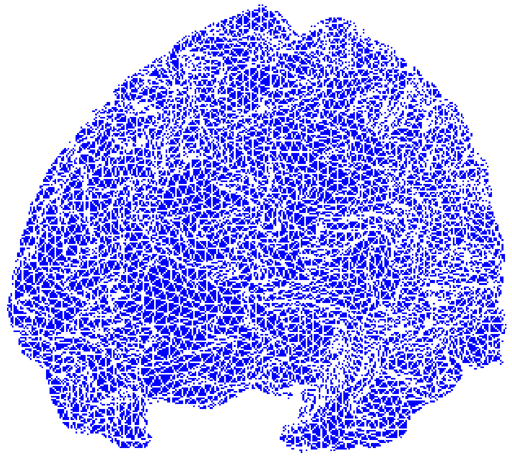
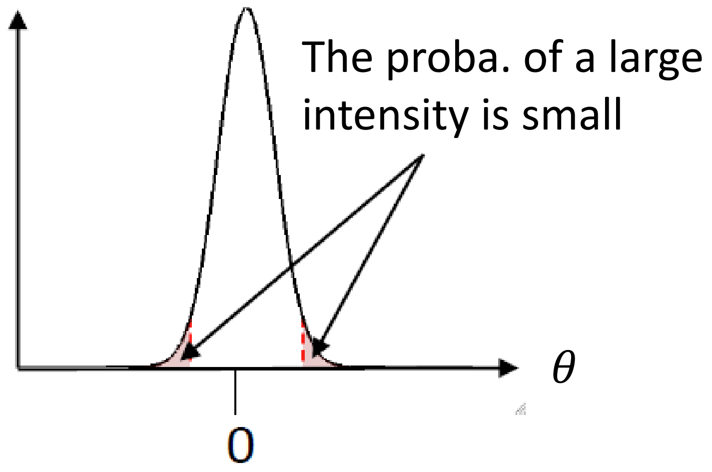
  - Many dipoles with fixed location and orientation
  - Dipole strength ? -> linear model





Prior over dipole strength

$$p(\theta) = N(0, C_\theta)$$

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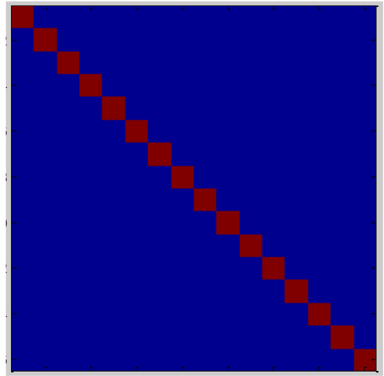
Setting priors

- Alternative priors correspond to alternative prior covariance matrices

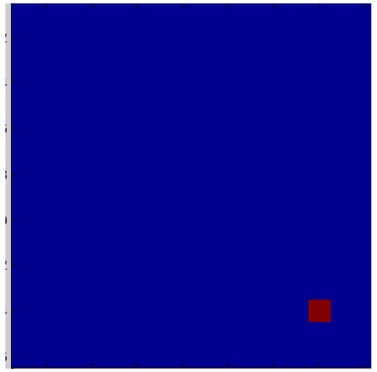
$$p(\boldsymbol{\theta}) = \boldsymbol{N}(0, \boldsymbol{C}_{\boldsymbol{\theta}})$$

Ndip x Ndip

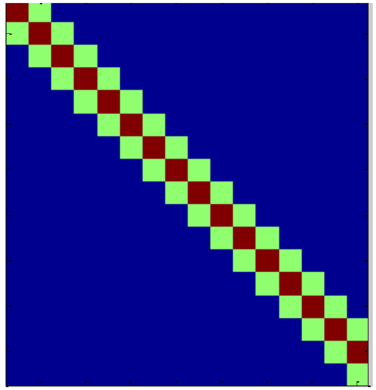
- Typical priors



i.i.d or Minimum norm



Single dipole



Smoothness (like LORETA)

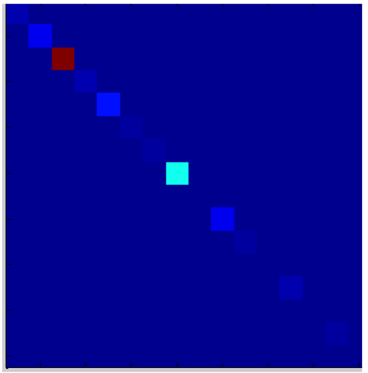
Setting priors

- Alternative priors correspond to alternative prior covariance matrices

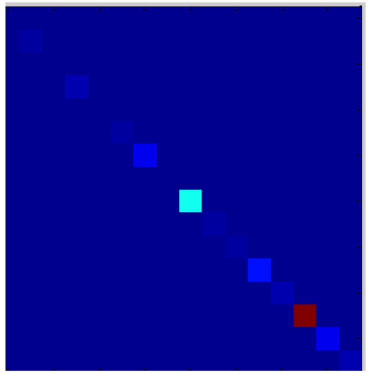
$$\boldsymbol{p}(\boldsymbol{\theta}) = \boldsymbol{N}(0, \boldsymbol{C}_{\boldsymbol{\theta}})$$

Ndip x Ndip

- More advanced priors



fMRI based



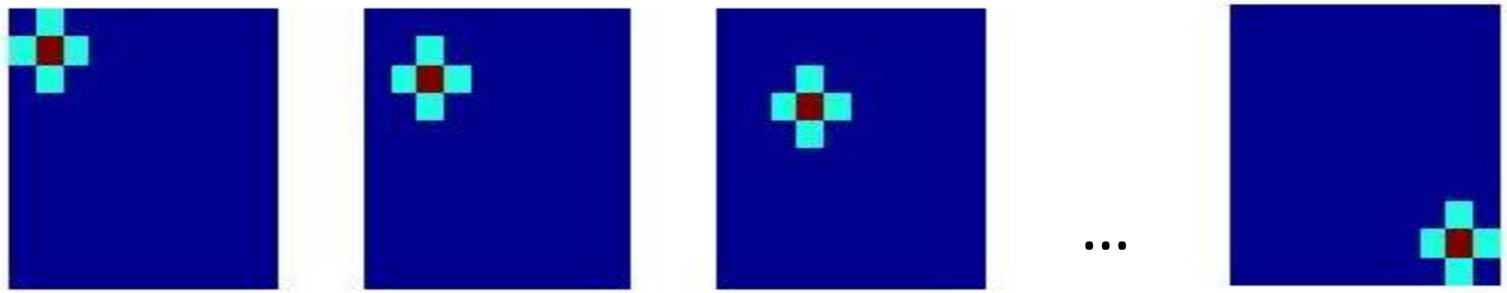
Data or Lead-field based
e.g. (Beamformer or MSP)

Henson et al., Hum. Brain Map., 2010

Mattout et al., NeuroImage, 2005

Empirical Bayes

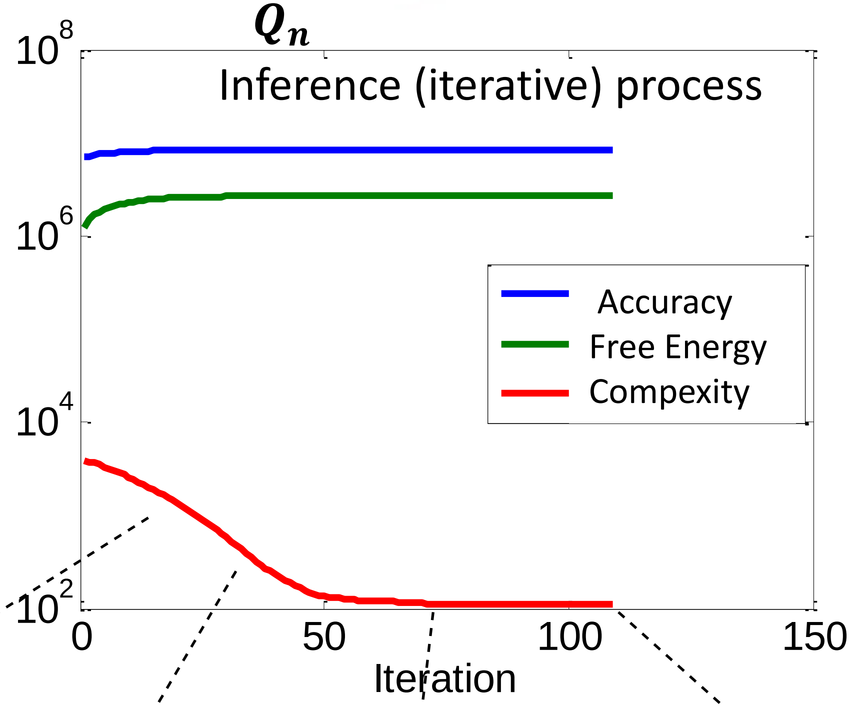
- Multivariate Sparse Priors (MSP)



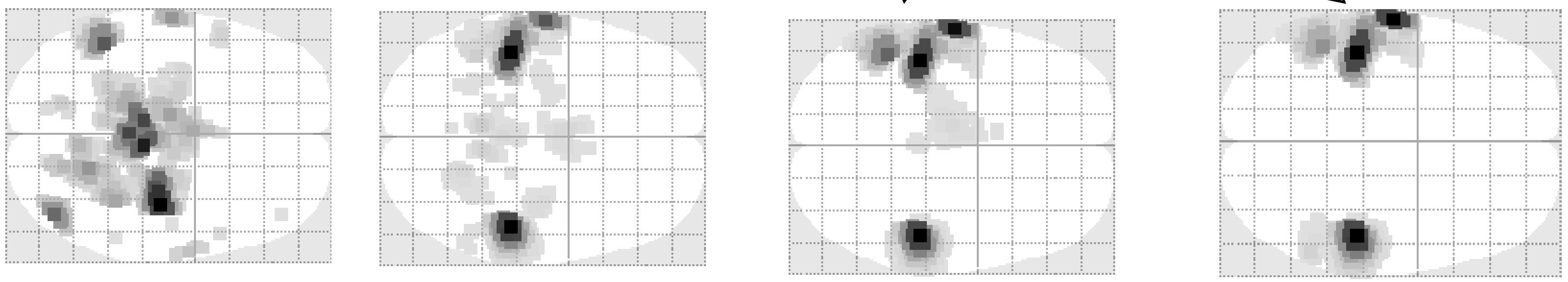
Q_1 Q_2 Q_3 … Q_n

Model (Hyper)parameters

$$C_\theta = \lambda_1 . Q_1 + \lambda_2 . Q_2 + \lambda_3 . Q_3 + \cdots + \lambda_n . Q_n$$



Philips et al., NeuroImage, 2005
Mattout et al., NeuroImage, 2006
Friston et al., NeuroImage, 2008
Lopez et al., NeuroImage, 2014



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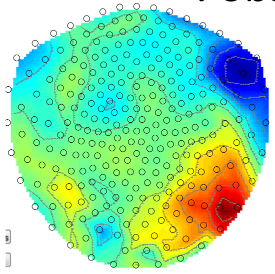
Comparing models

- Comparing priors using log-evidence (free energy) $F \cong p(Y|M)$

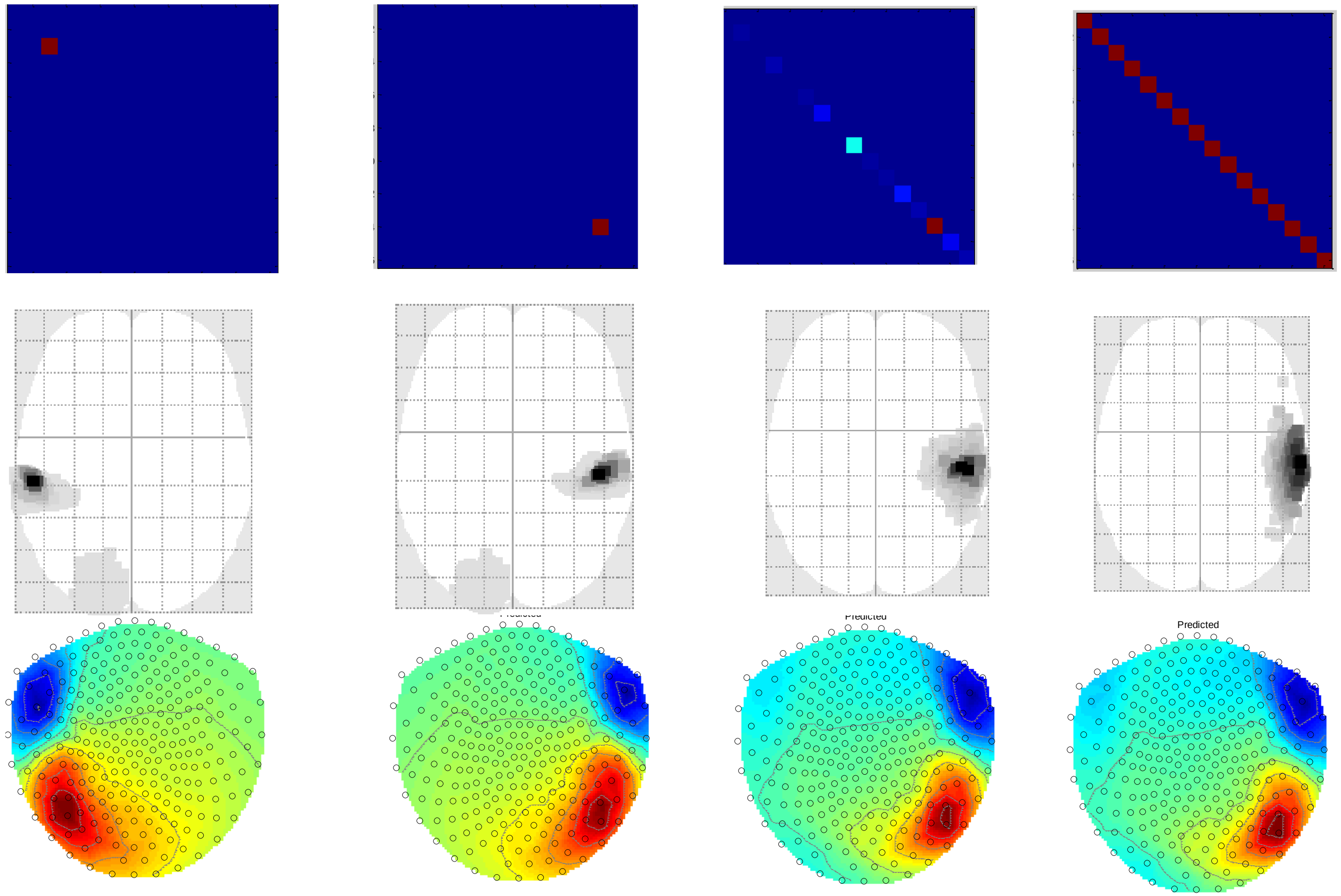
Y : observed data



Alternative priors

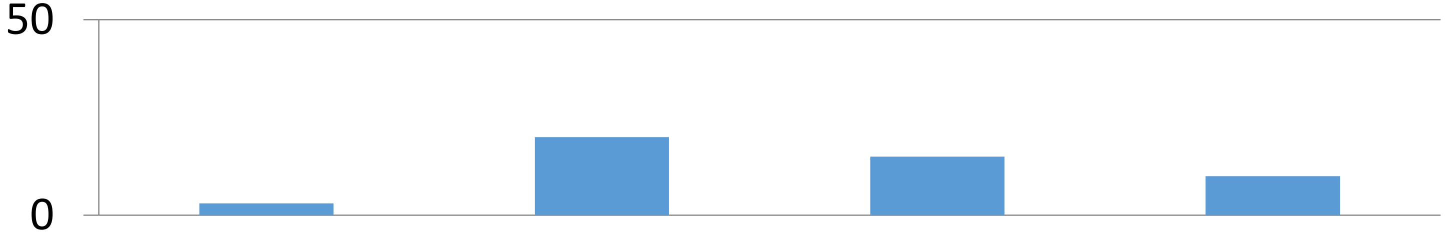
$\hat{\theta}$: estimated source intensities

$\hat{Y}$: predicted data



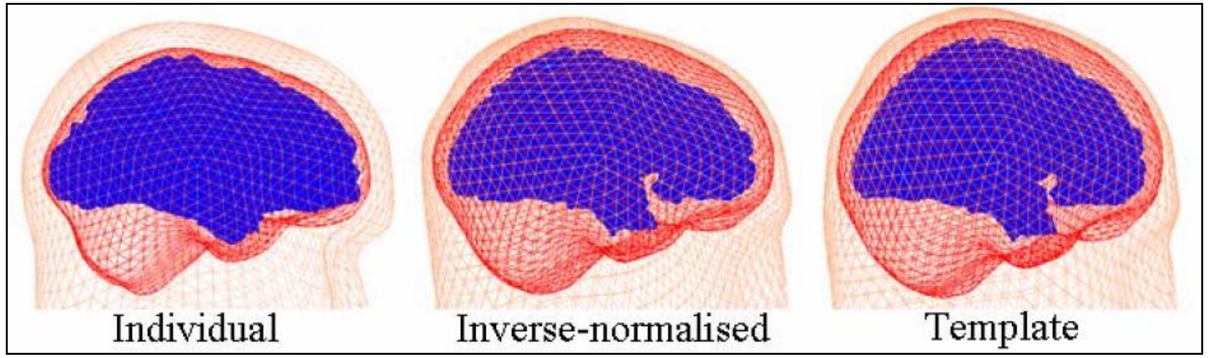
Explained variance 11 % 96% 97% 98%

Free-energy



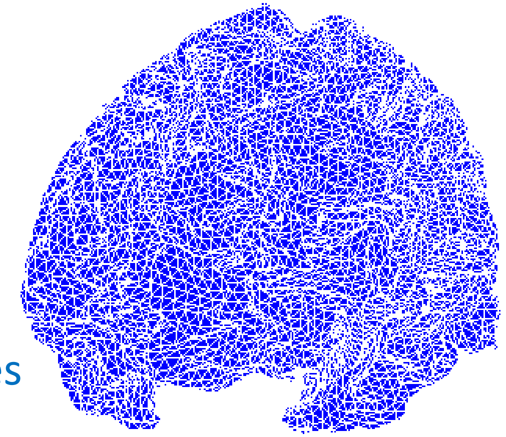
Comparing models

- <u>Any assumption (part of model M) can be formally tested on real data using Bayesian model comparison</u>



Anatomy

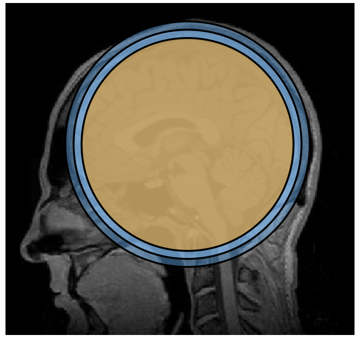
Mattout et al., NeuroImage, 2007



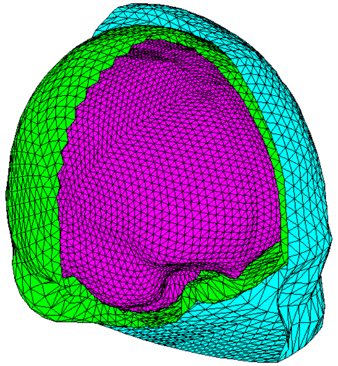
Sources

Mesh resolution (High / Low)
Dipole oreintation (fixed / free)

Biophysics



Spherical head model



Realistic surfacic model (BEM)

Henson et al., NeuroImage, 2007
Henson et al., NeuroImage, 2009

- **No evidence in favor of individual vs. Inverse-norm mesh**
- **Evidence in favor of BEM head model**
- **Evidence in favor of high + fixed vs. low + free**

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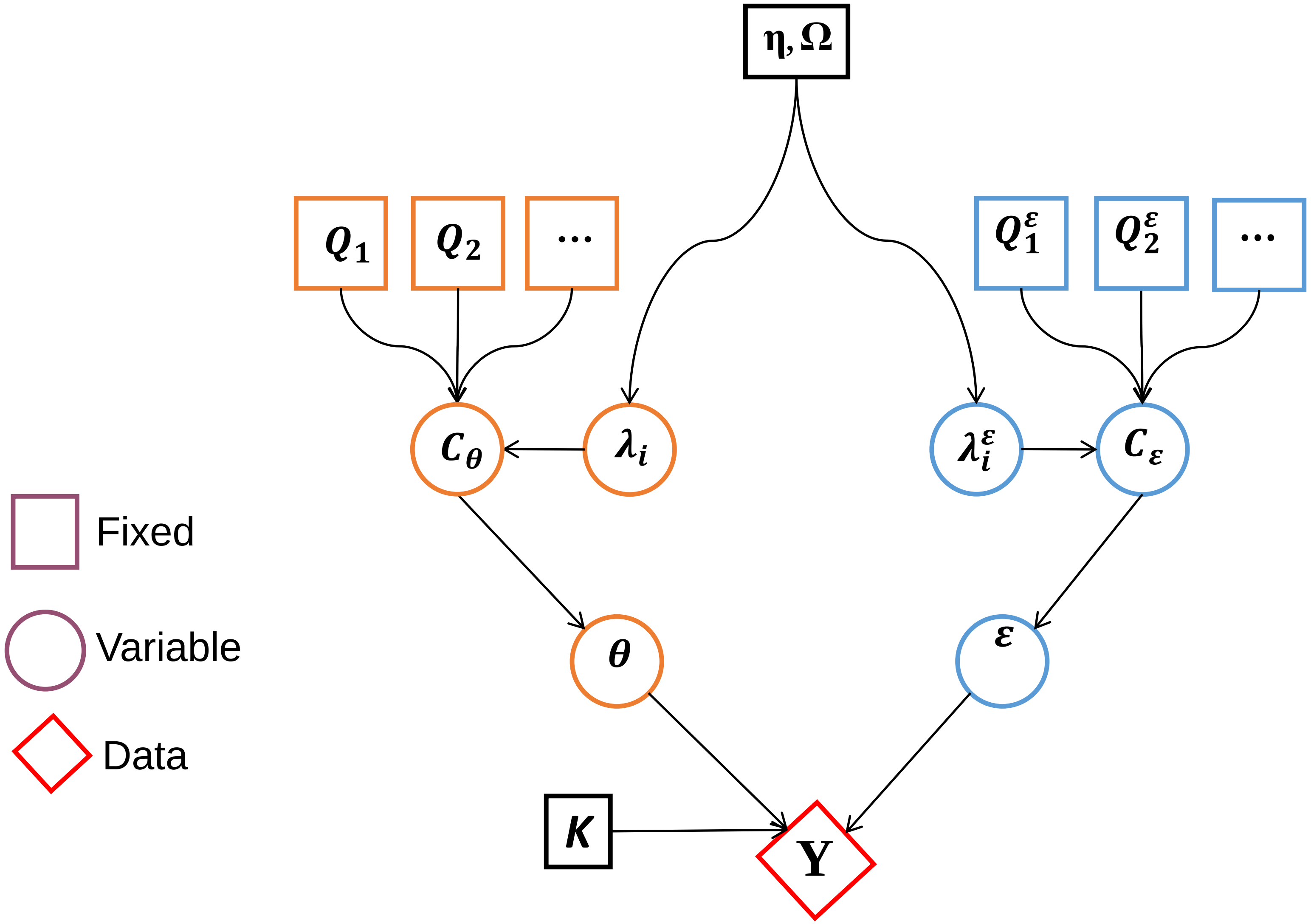
Group inference

- <u>MSP based source reconstruction for **a single subject**</u>

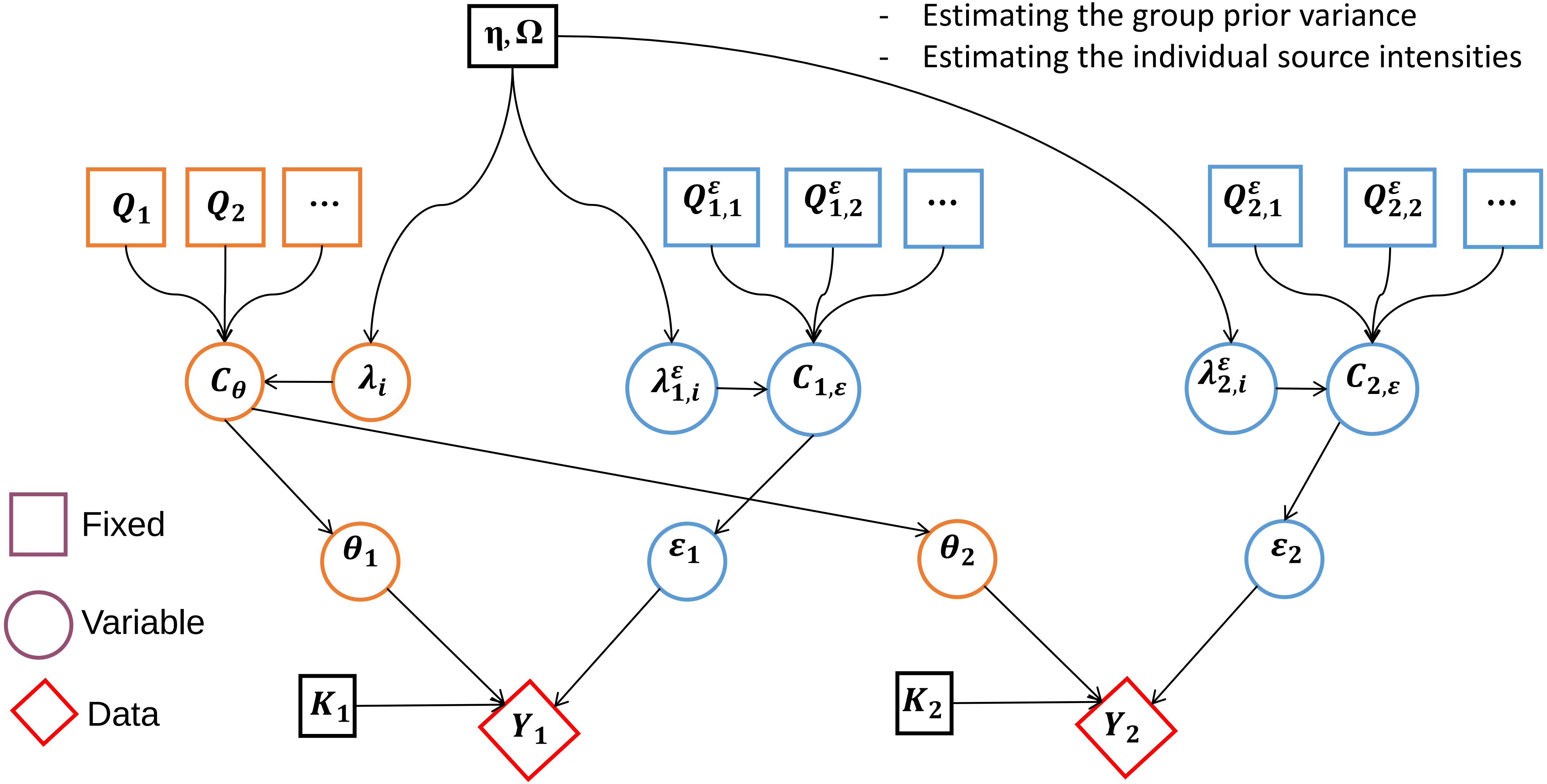


Friston et al., NeuroImage, 2008

Group inference

- MSP based source reconstruction for **multiple subjects**

A two-step procedure:
- Estimating the group prior variance
- Estimating the individual source intensities



Litvak and Friston, NeuroImage, 2008

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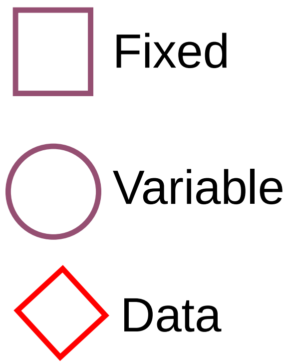
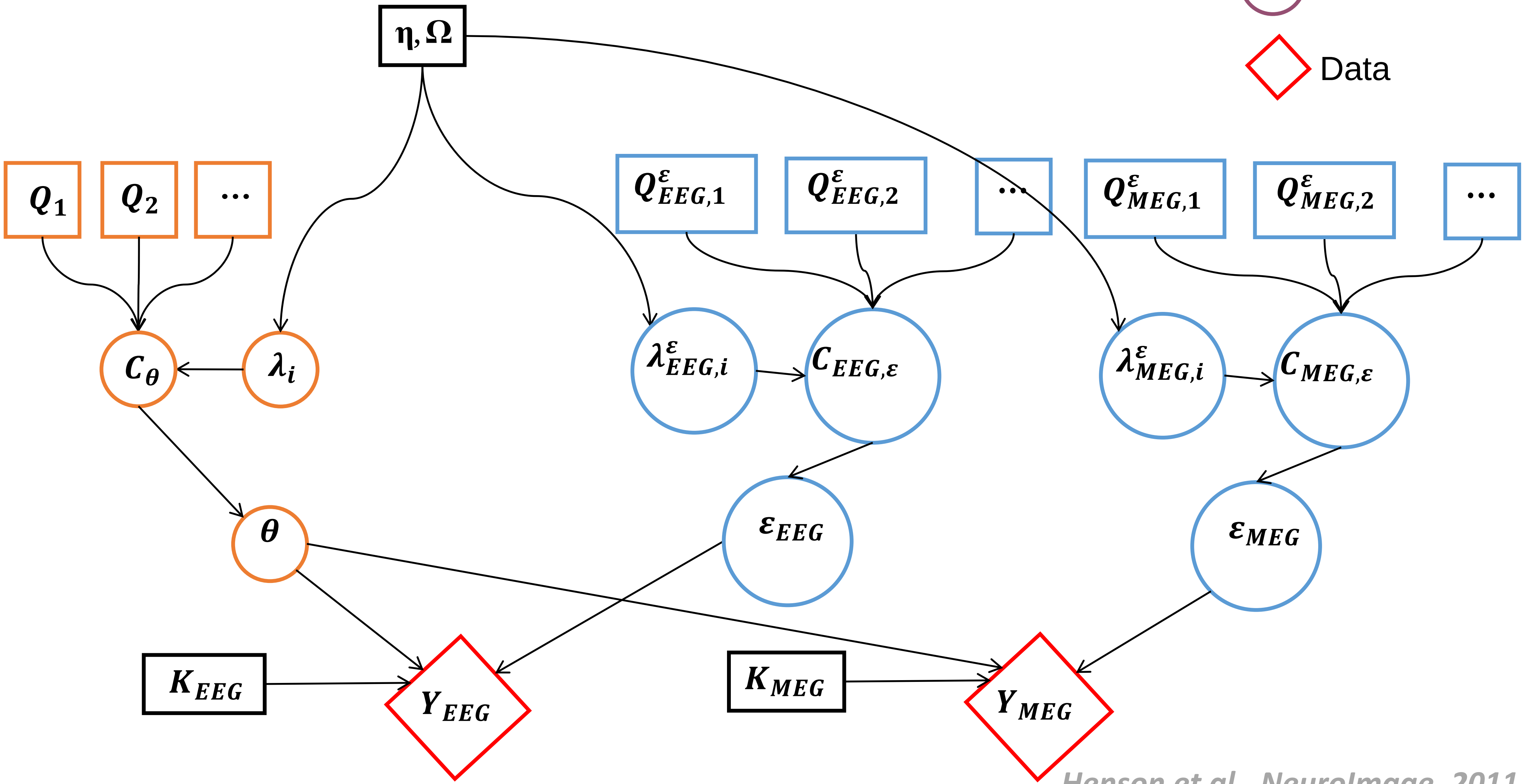
EEG/MEG fusion

- <u>MSP based source reconstruction for **multimodal data**</u>





Henson et al., NeuroImage, 2011

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