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Multi-modal integration of MEG, EEG & fMRI

Rik Henson

MRC CBU, Cambridge

Multi-modal Integration

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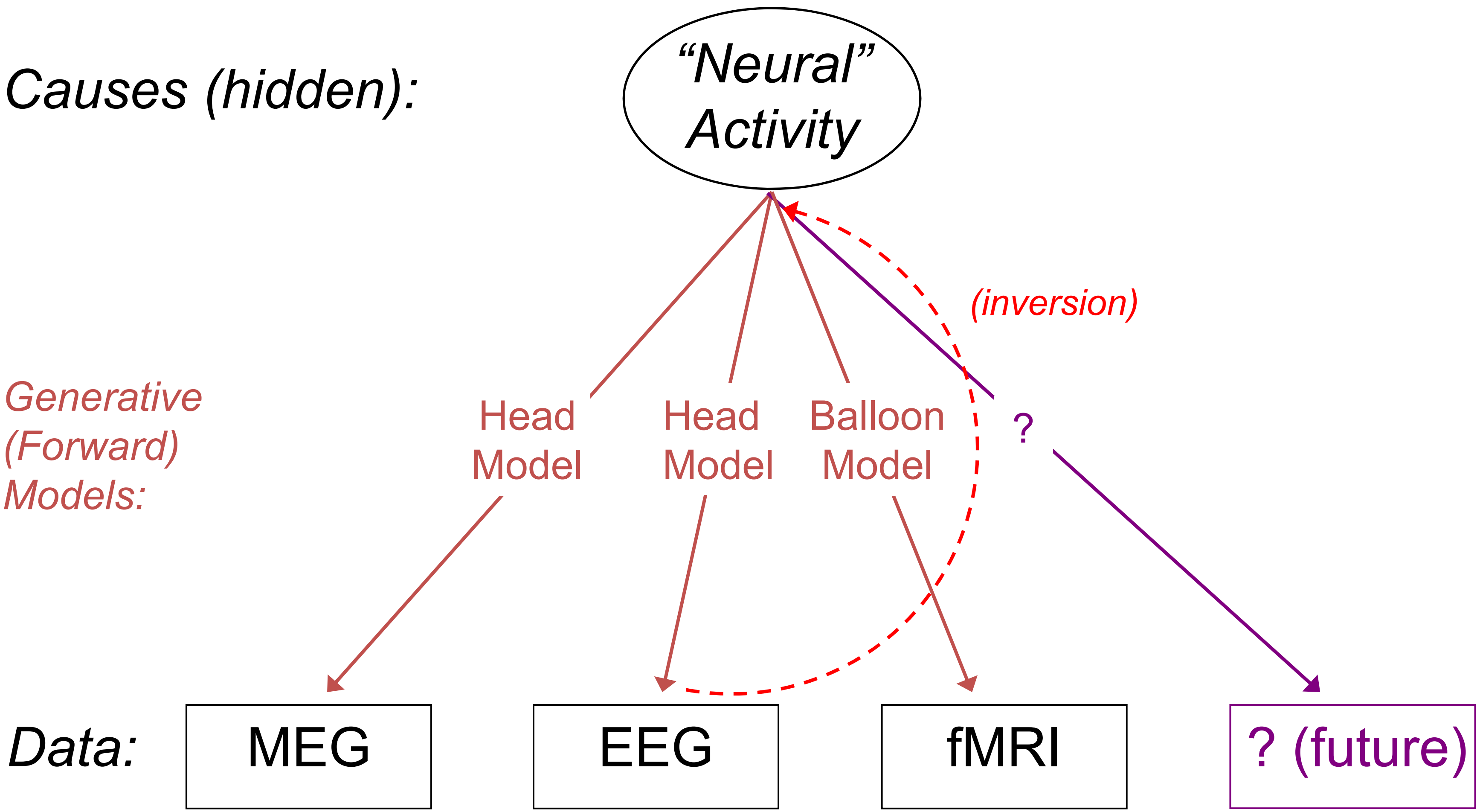
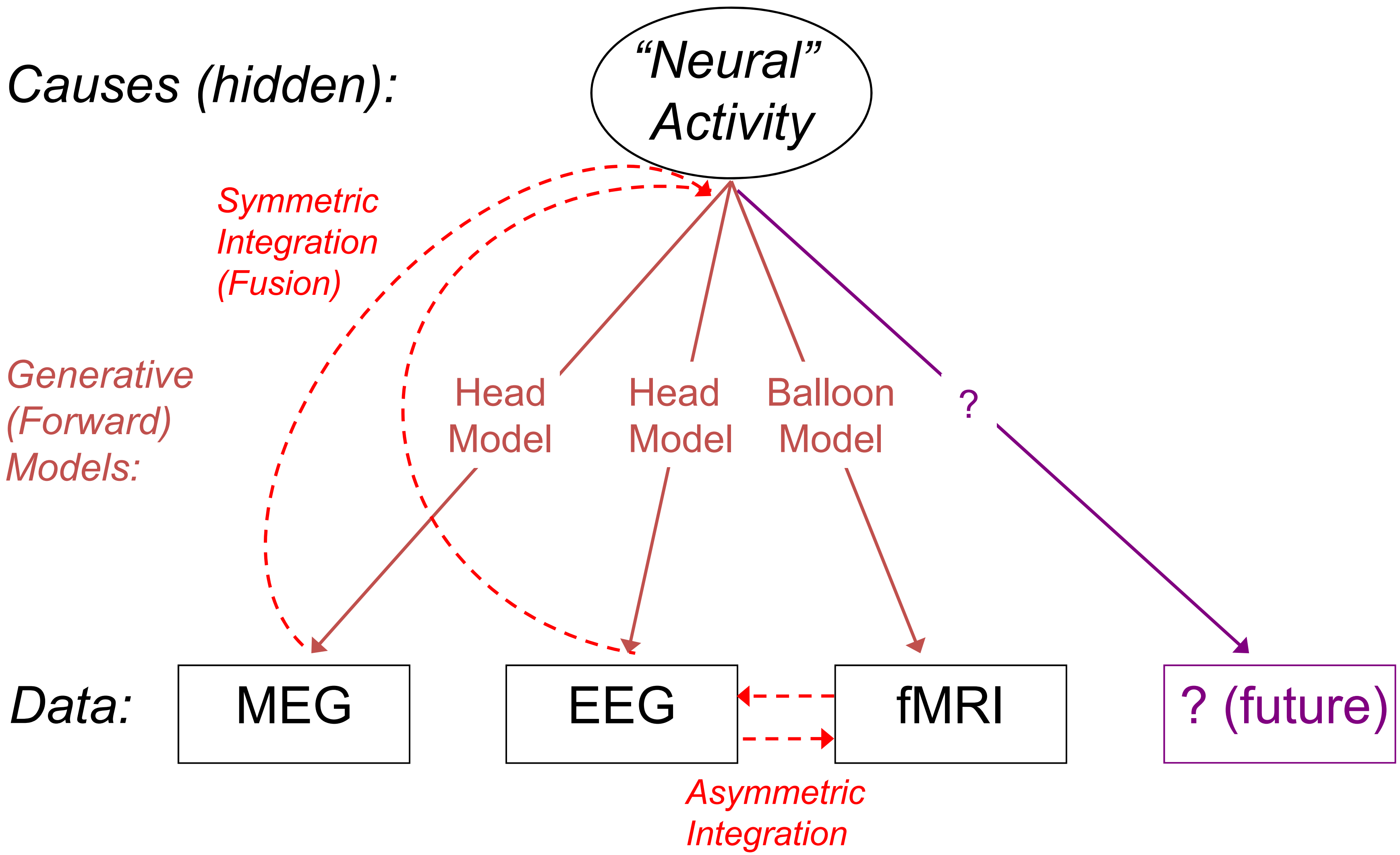


Multi-modal Integration



Daunizeau et al (2007), Neuroimage

Talk Overview

1. MEG + EEG symmetric integration (fusion)

2. M/EEG + fMRI asymmetric integration

Symmetric Integration of MEG+EEG Background

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- MEG generally has superior spatial resolution than EEG (less blurred by skull/scalp)

- MEG cannot detect radial component of current sources; EEG can!

Symmetric Integration of MEG+EEG Background

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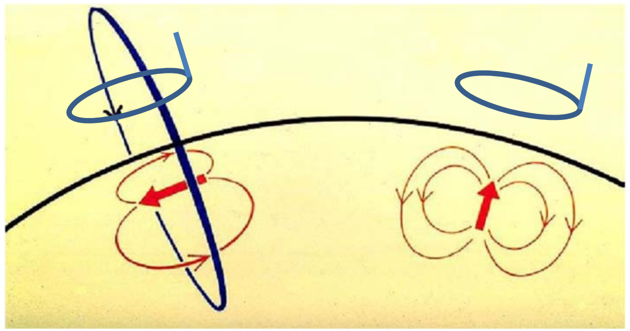
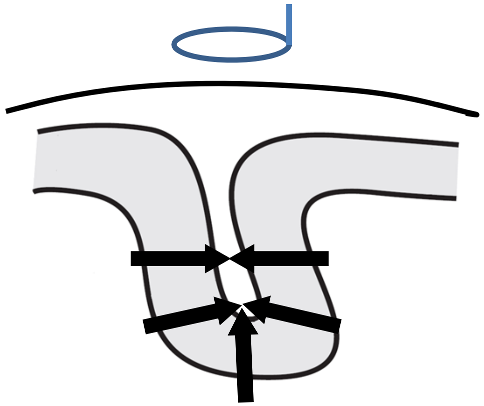
Dipolar Sources

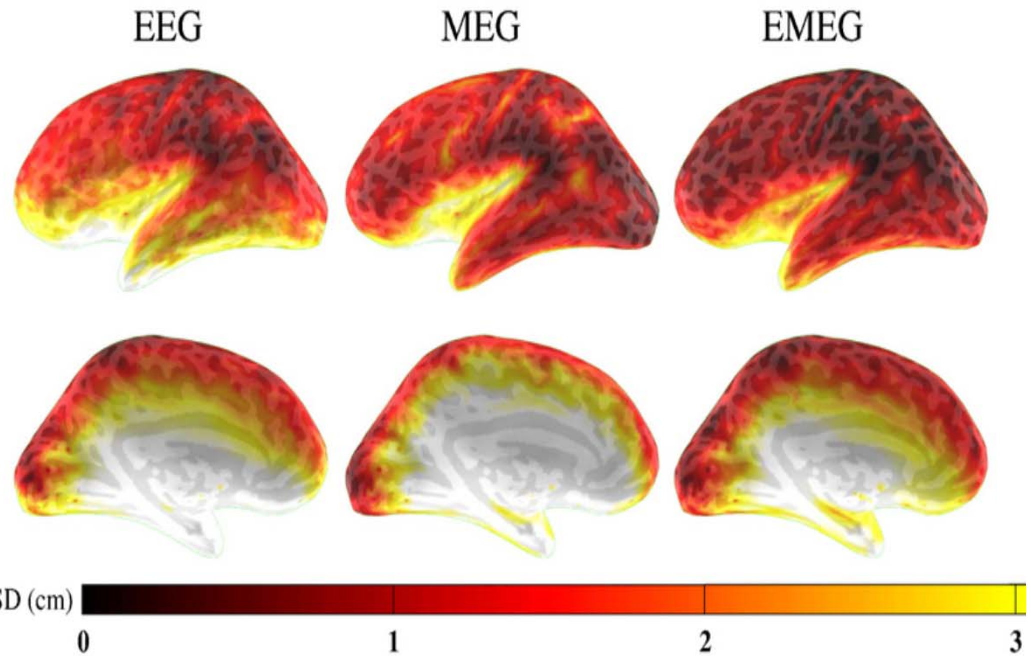


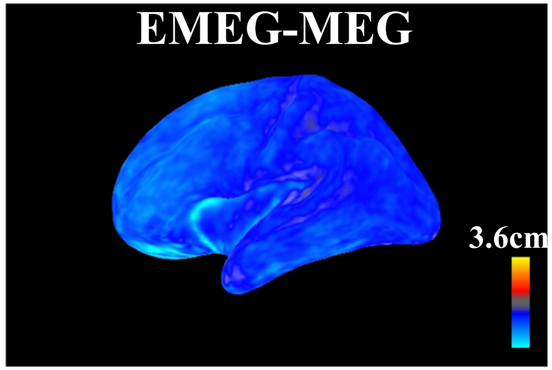
Extended Sources



Ahlfors et al., HBM 2010

Spatial Extent





Stenroos & Hauk, in prep

Molins et al., Neuroimage 2008

Symmetric Integration of MEG+EEG Background

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- MEG generally has superior spatial resolution than EEG (less blurred by skull/scalp)
- MEG cannot detect radial component of current sources; EEG can!
- And few practical problems acquiring concurrent EEG (apart from extra time attaching electrodes)
- …but EEG data is more sensitive to head geometry and conductivity (potentially biasing any joint-localisation)…
- …and has different noise characteristics…

MEG Linear Forward Model

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Given *n* sensors and *p* sources fixed in location and orientation (e.g, on a cortical mesh), then linear Forward Model (for single timepoint):

$$\begin{bmatrix} d_1 \\ \vdots \\ d_n \end{bmatrix} = \begin{bmatrix} L_{11} & L_{12} & \cdots L_{1p} \\ \vdots & \ddots & \vdots \\ L_{n1} & \cdots & \cdots L_{np} \end{bmatrix} \begin{bmatrix} s_1 \\ s_2 \\ \vdots \\ s_p \end{bmatrix} + \begin{bmatrix} e_1 \\ \vdots \\ e_n \end{bmatrix}$$

d = Data	*n* sensors
s = Sources	*p*>>*n* sources
L = Leadfields	*n* sensors *x p* sources
e = Error (noise)	*n* sensors…

Equivalent matrix format:

$$\mathbf{d} = \mathbf{L}\mathbf{s} + \mathbf{e}$$

Assume sensor noise is zero-mean Gaussian with error covariance $\mathbf{C}^{(e)}$:

$$e \sim N(0, \mathbf{C}^{(e)})$$

Assume sources similarly Gaussian with source covariance $\mathbf{C}^{(s)}$:

$$s \sim N(0, \mathbf{C}^{(s)})$$

MEG Linear Forward Model Assumptions to Solve

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$$\mathbf{d} = \mathbf{L}\mathbf{s} + \mathbf{e}$$

$$\mathbf{e} \sim N(0, \mathbf{C}^{(e)})$$

$$\mathbf{s} \sim N(0, \mathbf{C}^{(s)})$$

d = Data — *n* sensors
s = Sources — *p*>>*n* sources
L = Leadfields — *n* sensors *x* *p* sources
e = Error (noise) — *n* sensors…

General solution is:

Hauk (2004), Neuroimage

$$\hat{\mathbf{s}} = \mathbf{C}^{(s)}\mathbf{L}^T(\mathbf{L}\mathbf{C}^{(s)}\mathbf{L}^T + \lambda\mathbf{C}^{(e)})^{-1}\mathbf{d}$$

λ = Regularisation (hyperparameter)

But how calculate $\mathbf{C}^{(e)}$ and $\mathbf{C}^{(s)}$?

MEG Linear Forward Model
Assumptions to Solve

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One approach is to model sources and noise by variance components:

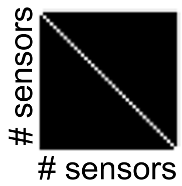
$$\mathbf{C} = \sum_i \lambda_i \mathbf{Q}_i$$

C = Sensor/Source covariance
Q = Covariance components
λ = Hyper-parameters

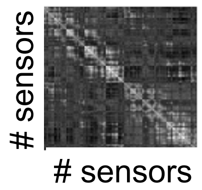
Friston et al (2008) Neuroimage

1. Sensor components, $\mathbf{Q}_i^{(e)}$ (error):

"IID" (white noise):

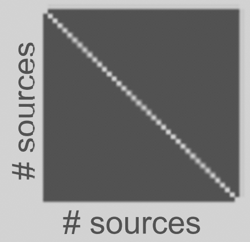


Empty-room:

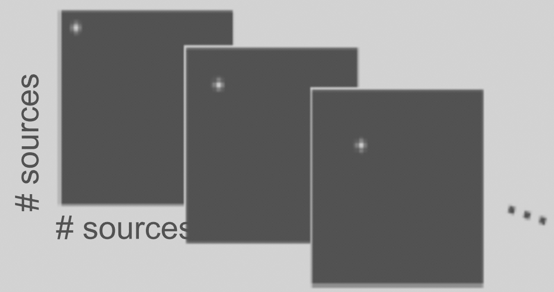


2. Source components, $\mathbf{Q}_i^{(s)}$ (priors/regularisation):

"IID" (min norm):



Multiple Sparse Priors (MSP):



MEG Generative Model

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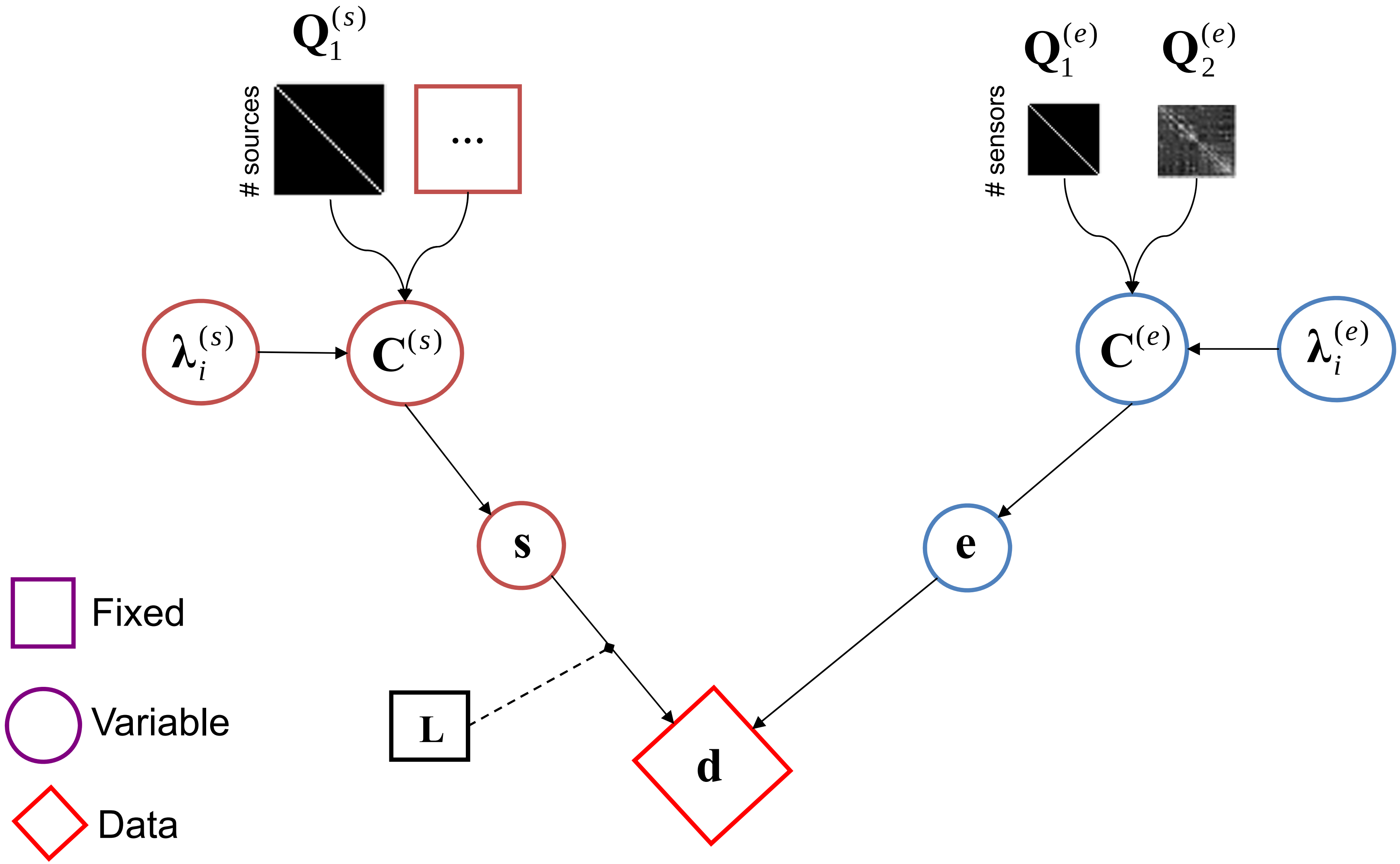

Henson et al (2009) Neuroimage

Symmetric Integration of MEG+EEG Generative Model

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For fusing MEG and EEG, we can simply concatenate the MEG+EEG data:

$$\begin{bmatrix} \mathbf{d}_{(MEG)} \\ \mathbf{d}_{(EEG)} \end{bmatrix} = \begin{bmatrix} \mathbf{L}_{(MEG)} \\ \mathbf{L}_{(EEG)} \end{bmatrix} \mathbf{s} + \begin{bmatrix} \mathbf{e}_{(MEG)} \\ \mathbf{e}_{(EEG)} \end{bmatrix}$$

$$\mathbf{e} \sim N(0, \mathbf{C}^{(e)})$$

$$\mathbf{s} \sim N(0, \mathbf{C}^{(s)})$$

Note same sources, eg, for Minimum (L2) Norm solution:

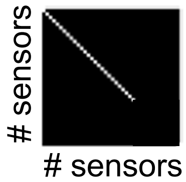
$$\mathbf{C}^{(s)} = \mathbf{I}$$

$$\hat{\mathbf{s}} = \mathbf{L}^T (\mathbf{L}\mathbf{L}^T + \hat{\mathbf{C}}^{(e)})^{-1} \mathbf{d}$$

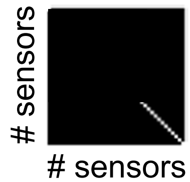
Noise expressed by MEG and EEG terms (e.g, white noise):

$$\hat{\mathbf{C}}^{(e)} = \lambda_1^{(e)} \mathbf{Q}_{(MEG)}^{(e)} + \lambda_2^{(e)} \mathbf{Q}_{(EEG)}^{(e)}$$

$$\mathbf{Q}_{(MEG)}^{(e)} =$$



$$\mathbf{Q}_{(EEG)}^{(e)} =$$



The separate hyperparameters allow for different noise levels (SNR)

The multiple hyperparameters are estimated by maximising **model evidence** (using a variational Bayesian approach, eg EM algorithm)

Symmetric Integration of MEG+EEG Generative Model

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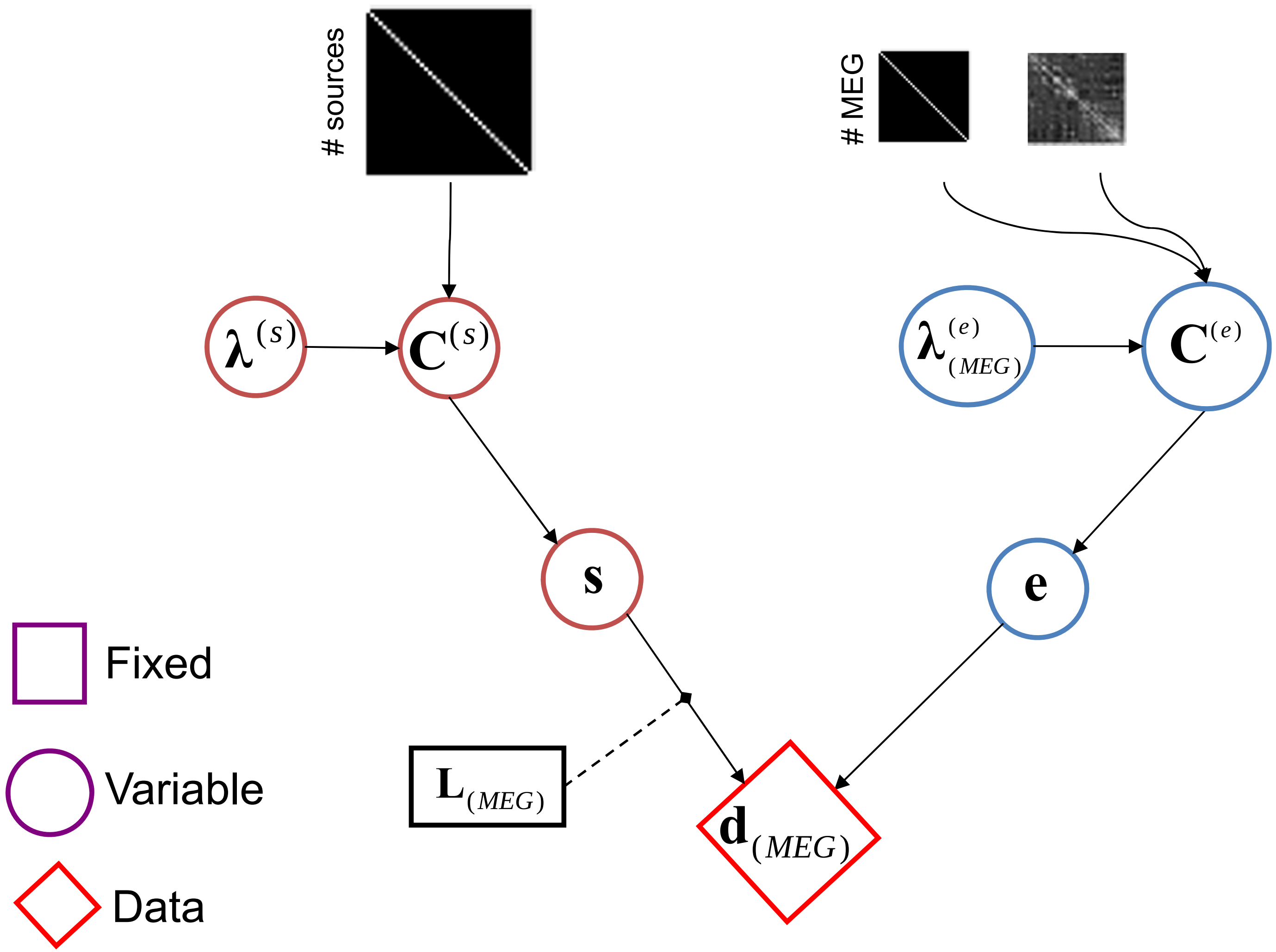

Henson et al (2009) Neuroimage

Symmetric Integration of MEG+EEG Generative Model

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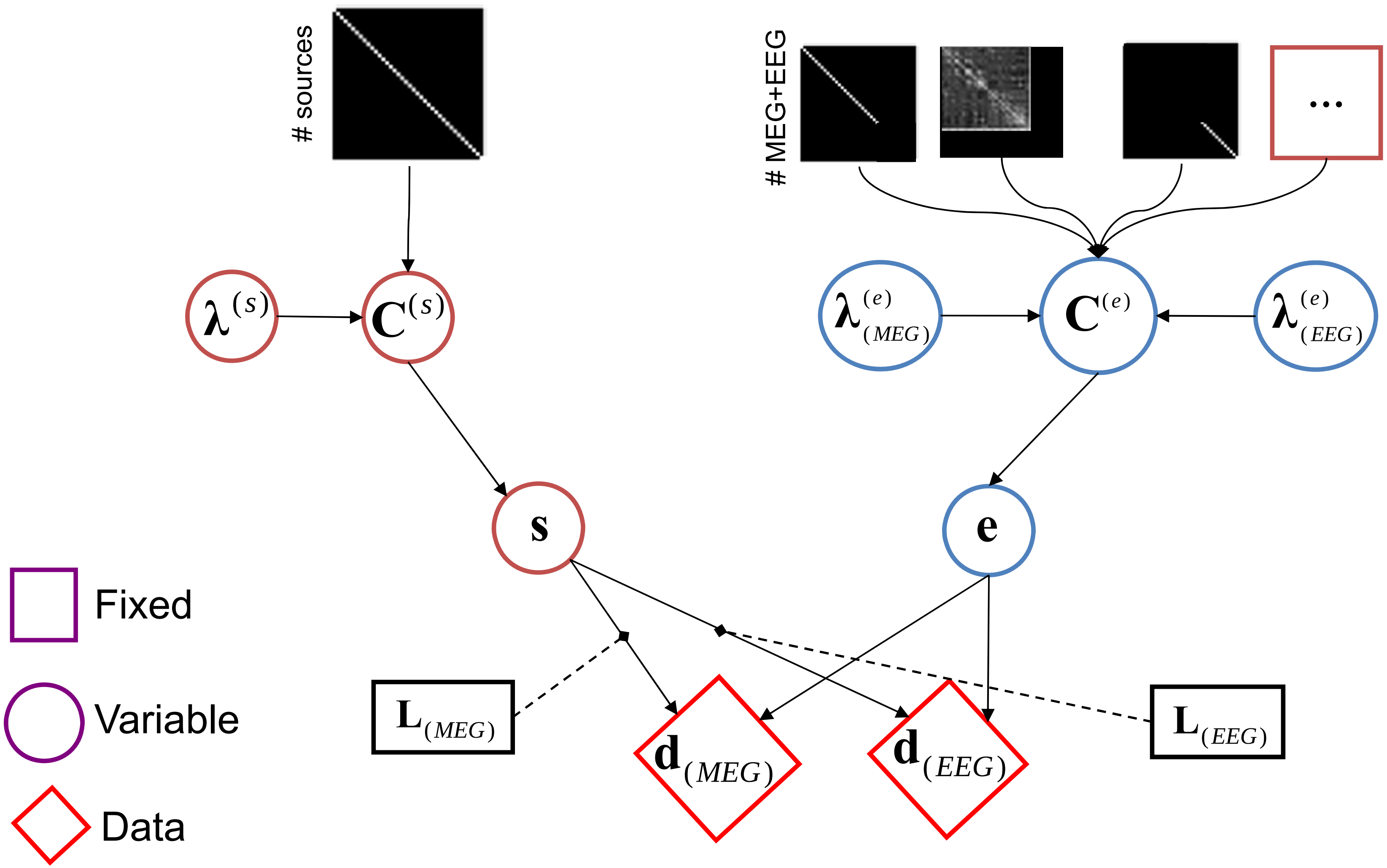

Henson et al (2009) Neuroimage

One final problem…

- Though this allows for different additive noise levels in MEG and EEG…
- …we are assuming mapping from common electrical sources to sensor values (in terms of Telsa and Volts) is known precisely…
- …whereas in reality, this depends on several unknowns (e.g, precise conductivity of skull/scalp)

- One solution is to scale data/leadfields to have same variance:

$$\tilde{Y}_i = \frac{Y_i}{\sqrt{\frac{1}{n_i} tr(Y_i Y_i^T)}} \qquad \tilde{L}_i = \frac{L_i}{\sqrt{\frac{1}{n_i} tr(L_i L_i^T)}}$$

i = ith modality, ie MEG or EEG
n_i = Number of sensors for modality *i*

Henson et al (2009) Neuroimage

Symmetric Integration of MEG+EEG Example

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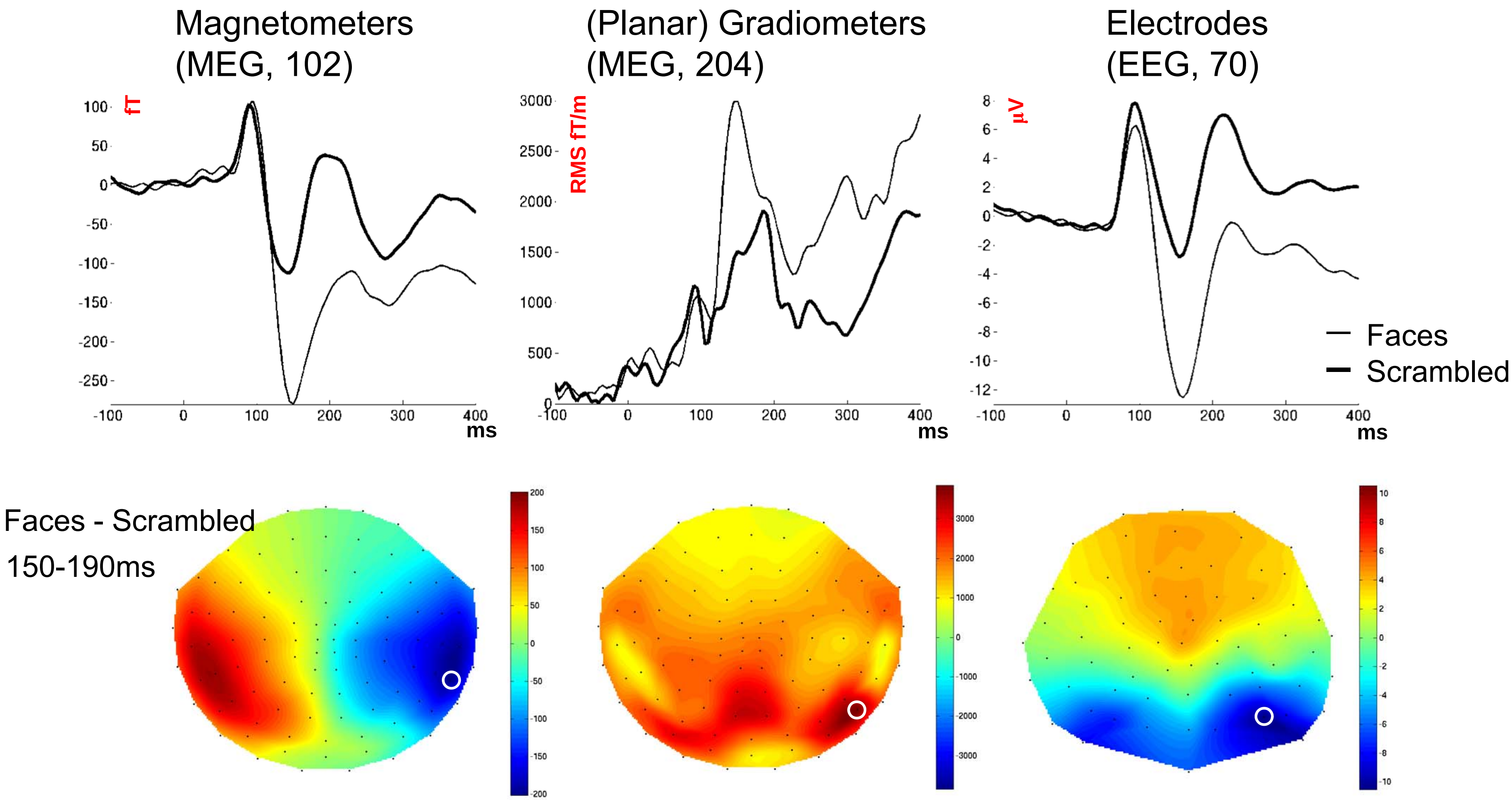
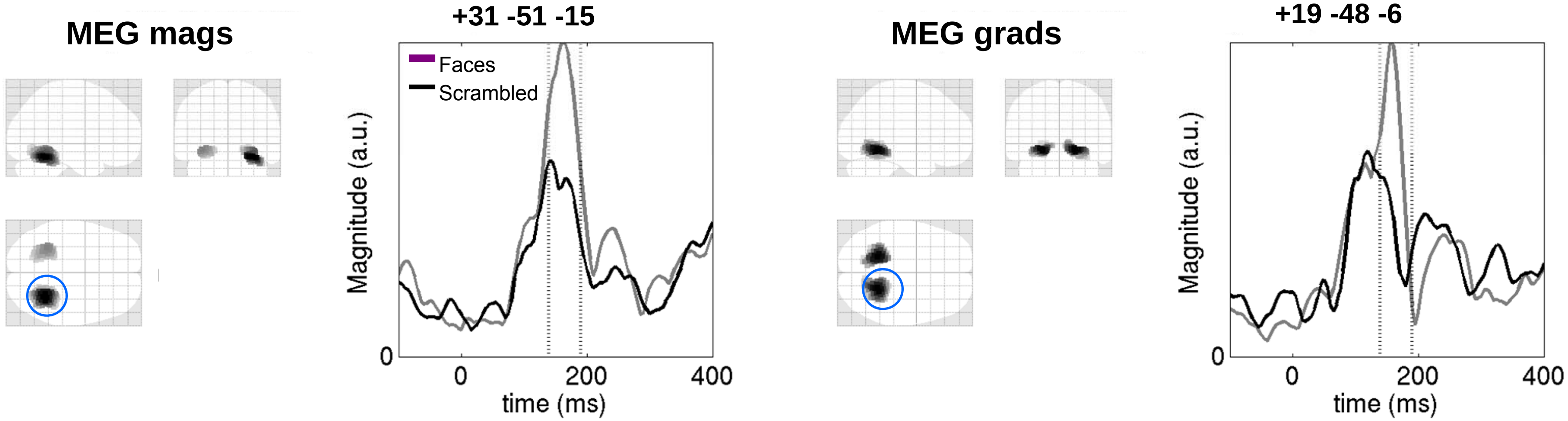
ERs from 12 subjects for 3 simultaneously-acquired Neuromag sensor-types:

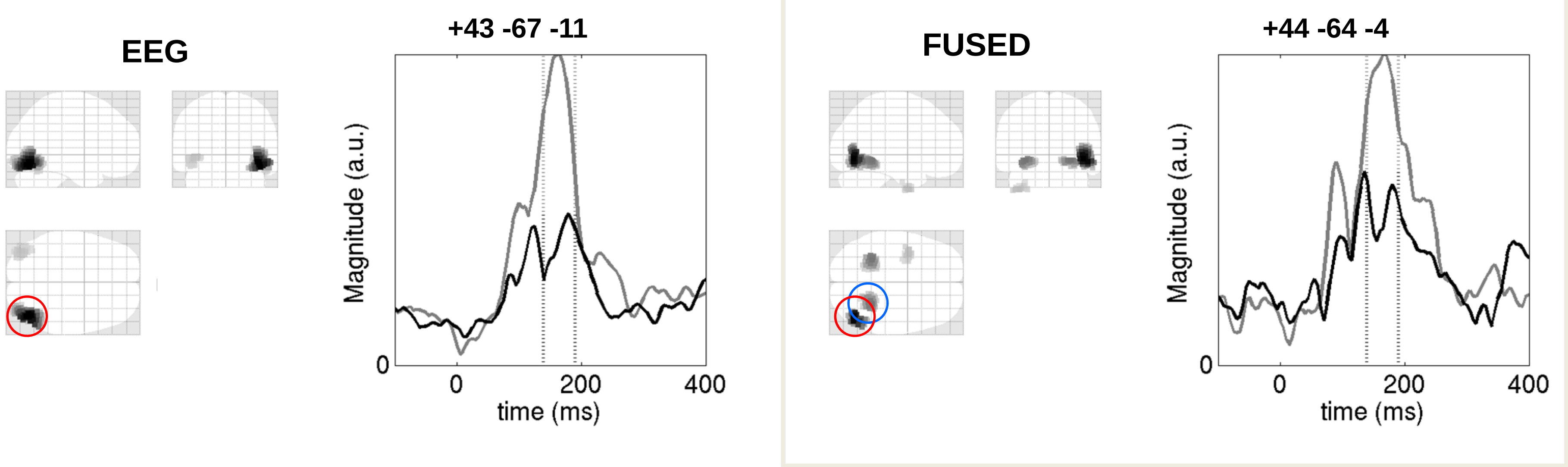


Henson et al (2009) Neuroimage

Symmetric Integration of MEG+EEG



Faces – Scrambled, 150-190ms



IID noise for each modality; common MSP for sources

Henson et al (2009) Neuroimage

Other Approaches to M/EEG fusion

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- Estimate noise covariance from pre-stimulus baseline (**b**):

$$\mathbf{C}^{(e)} = \begin{bmatrix} cov(\mathbf{b}_{(MEG)}) & \mathbf{0} \\ \mathbf{0} & cov(\mathbf{b}_{(EEG)}) \end{bmatrix}$$

Molins et al (2008), Neuroimage

(which can also be used to pre-whiten data and leadfields, scaling to noise units)…
…but downside is that **baseline contains source activity**, so not estimate of true sensor noise

- Maximise mutual information between MEG and EEG

Baillet et al (1999), IEEE

- Re-parameterise leadfields in terms of radial/tangential components

Huang et al (2007), Neuroimage

Talk Overview

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1. MEG + EEG symmetric integration (fusion)

2. M/EEG + fMRI asymmetric integration

Asymmetric Integration of MEG+fMRI Background

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- fMRI has superior spatial resolution (~mm) than M/EEG, but inferior temporal resolution (integrating over seconds)
- fMRI and M/EEG measure similar, but not identical, neural activity
- Eg, some source configurations give detectable fMRI signal, but no detectable M/EEG signal…
- …and vice versa

Asymmetric Integration of MEG+fMRI
Background

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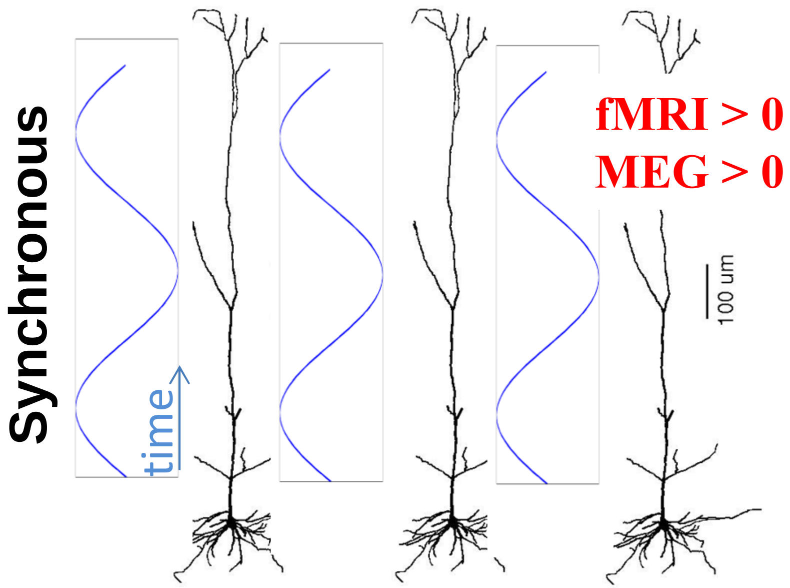

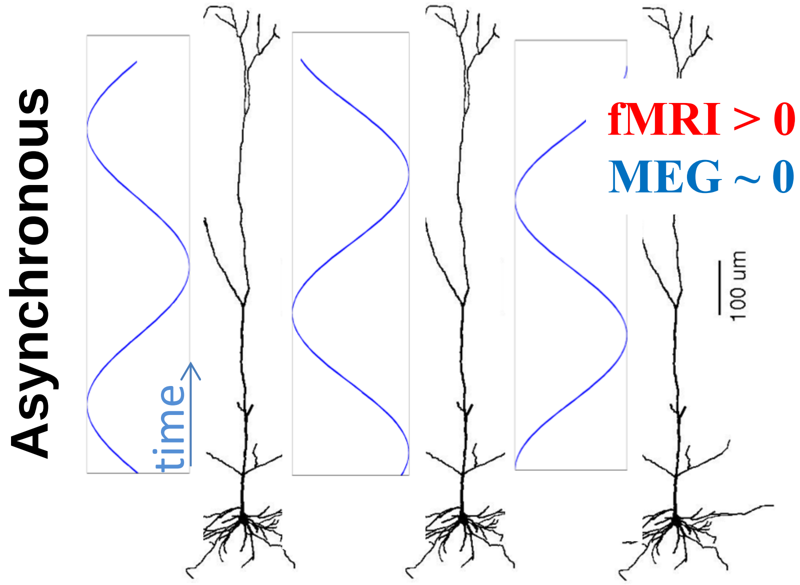

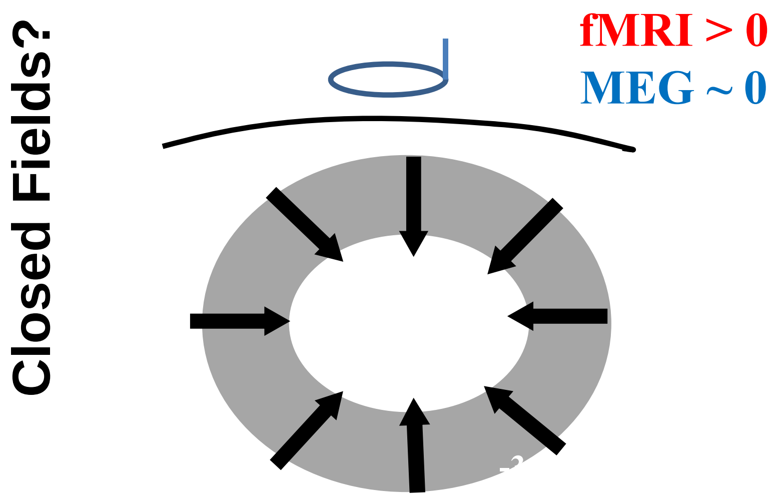

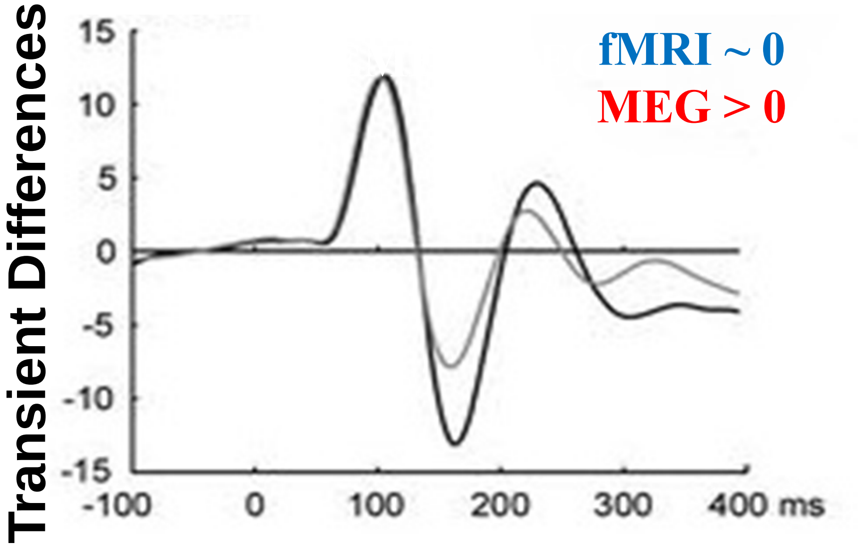

Asymmetric Integration of MEG+fMRI Background

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- fMRI has superior spatial resolution (~mm) than M/EEG, but inferior temporal resolution (integrating over seconds)
- fMRI and M/EEG measure similar, but not identical, neural activity
- Eg, some source configurations give detectable fMRI signal, but no detectable M/EEG signal…
- …and vice versa
- Use fMRI as a soft, rather than hard, constraint on localisation of sources of M/EEG data…

Asymmetric Integration of MEG+fMRI

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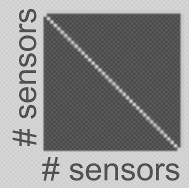
Specifying (co)variance components (priors/regularisation):

$$\mathbf{C} = \sum_i \lambda_i \mathbf{Q}_i$$

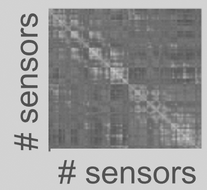
C = Sensor/Source covariance
Q = Covariance components
λ = Hyper-parameters

1. Sensor components, $Q_i^{(e)}$ (error):

"IID" (white noise):

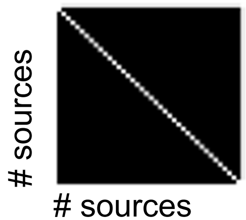


Empty-room:

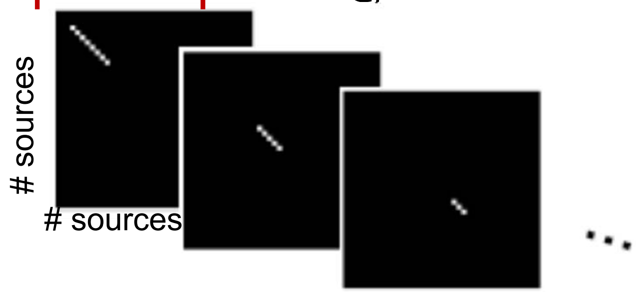


2. Each suprathreshold fMRI cluster becomes a separate prior $\mathbf{Q}_i^{(s)}$

"IID" (min norm):



fMRI Priors:



Henson et al (2010) Hum. Brain Map.

Asymmetric Integration of MEG+fMRI

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General solution again:

$$\hat{\mathbf{s}} = \mathbf{C}^{(s)}\mathbf{L}^T(\mathbf{L}\mathbf{C}^{(s)}\mathbf{L}^T + \lambda\mathbf{C}^{(e)})^{-1}\mathbf{d}$$

$$\mathbf{e} \sim N(0, \mathbf{C}^{(e)})$$
$$\mathbf{s} \sim N(0, \mathbf{C}^{(s)})$$

Now source covariance expressed as number of fMRI clusters:

$$\mathbf{C}^{(s)} = \lambda_1^{(s)}\mathbf{Q}^{(s)}_{(fMRI\,1)} + \lambda_2^{(s)}\mathbf{Q}^{(s)}_{(fMRI\,2)} + \ldots$$

When $\mathbf{Q}_i^{(s)}$ does not help maximise model evidence, $\lambda_i^{(s)} \rightarrow 0$, i.e, constraints ignored…

…catering for situations where fMRI signal does not reflect same activity as in M/EEG signal (e.g, occurring later than time-window than M/EEG data)

Symmetric Integration of MEG+EEG Generative Model

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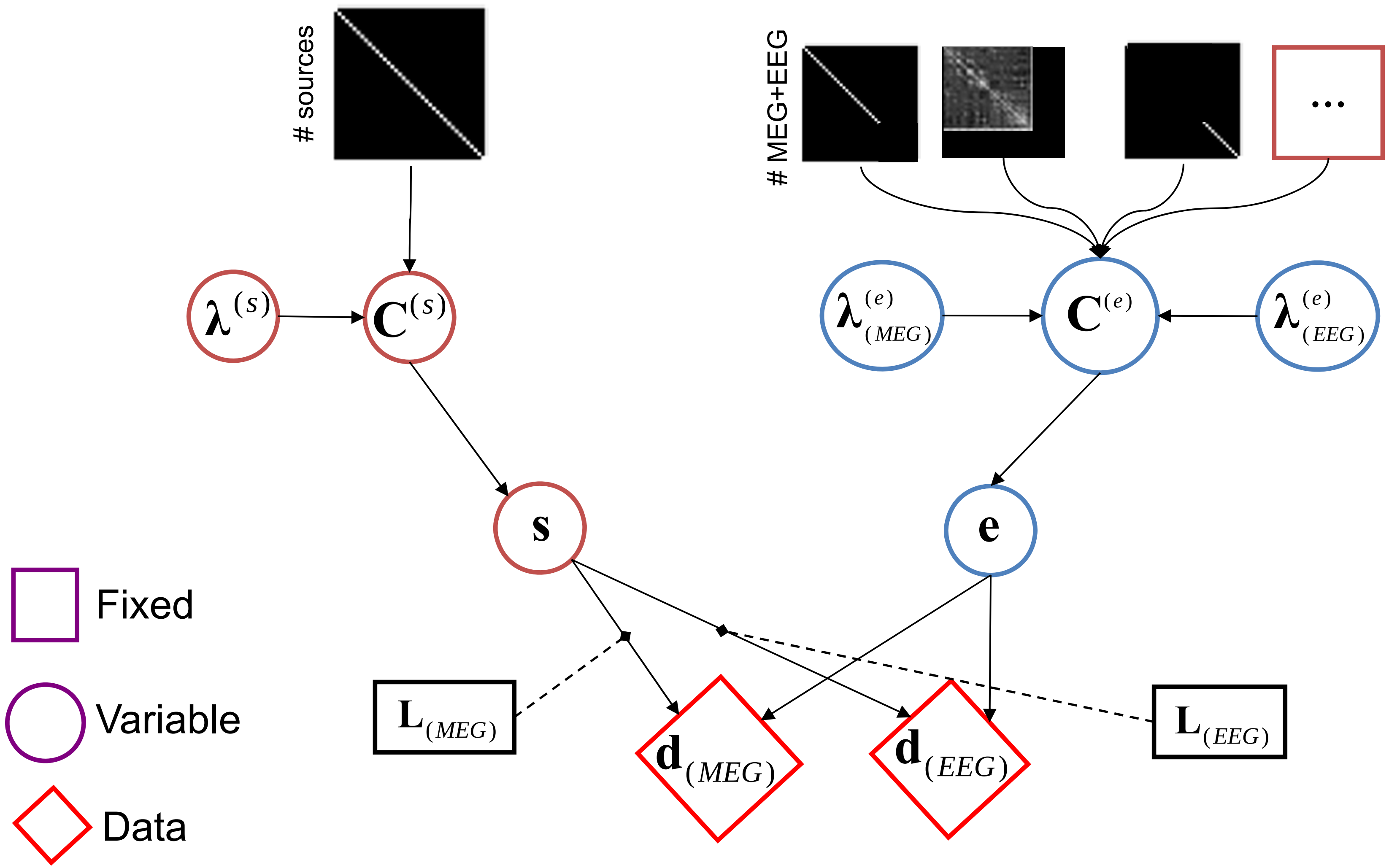
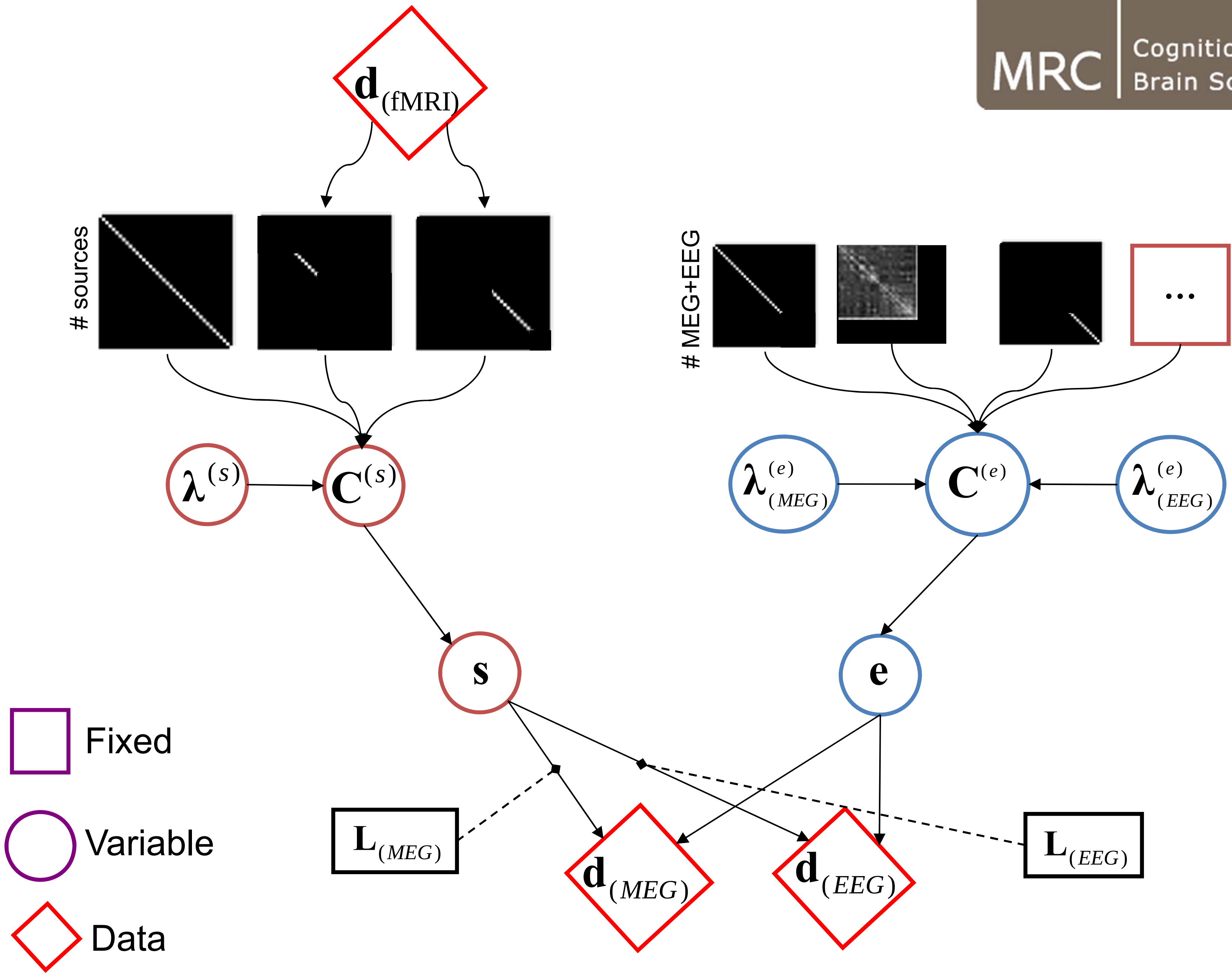


Henson et al (2009) Neuroimage



Henson et al (2010) Hum. Brain Map.

Asymmetric Integration of M/EEG+fMRI

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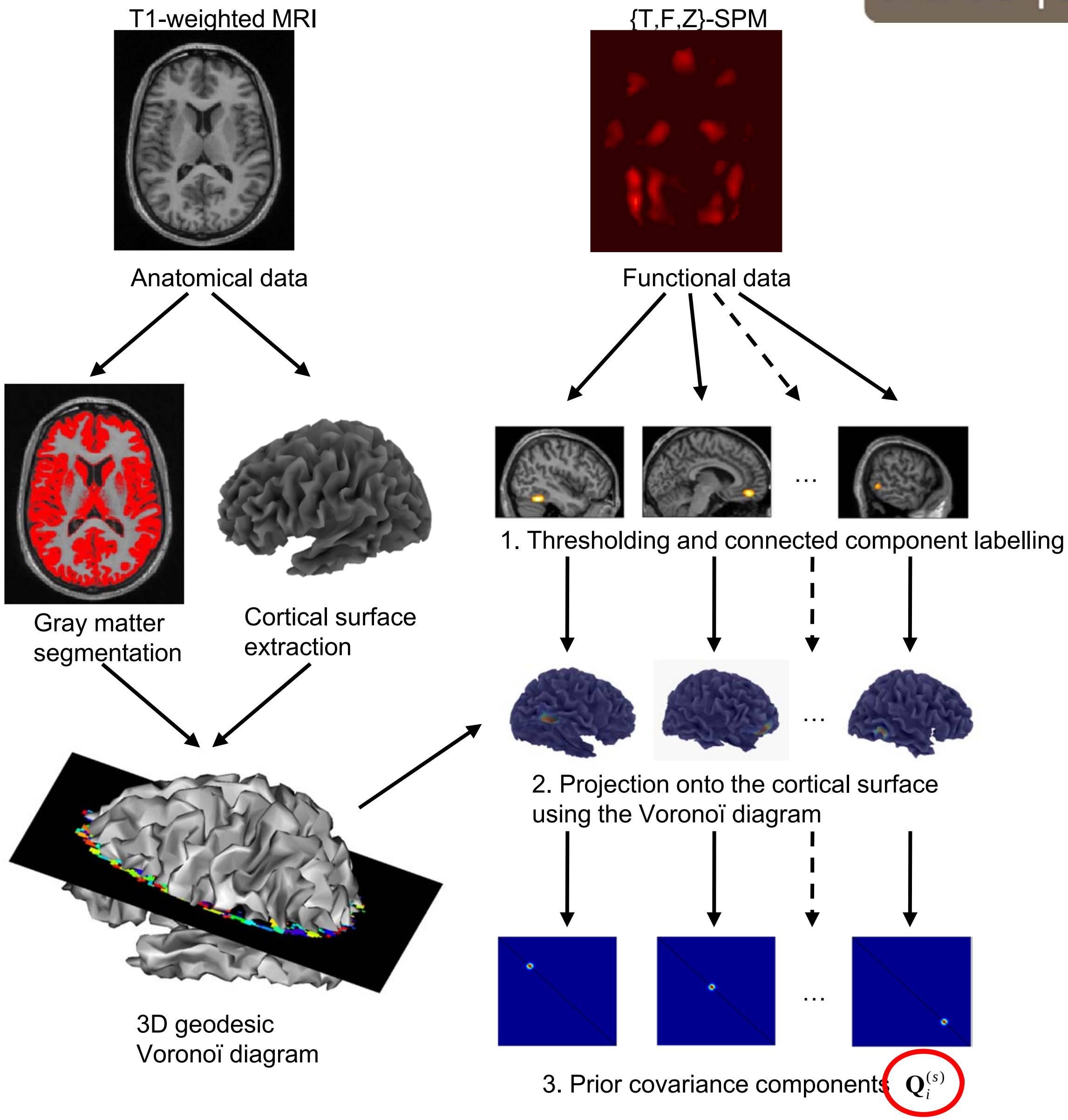

Henson et al (2010) Hum. Brain Map.

Asymmetric Integration of M/EEG+fMRI

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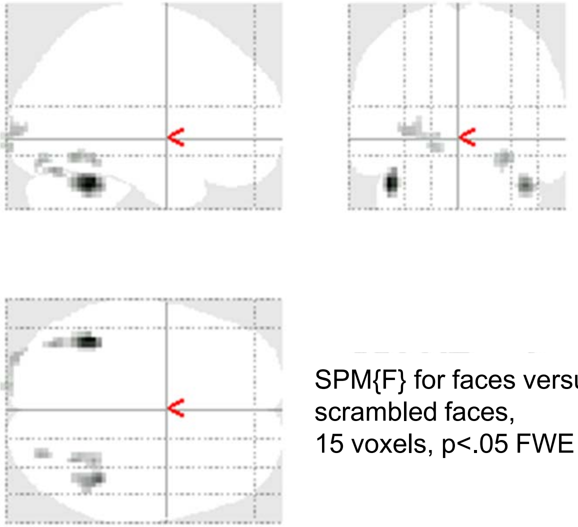
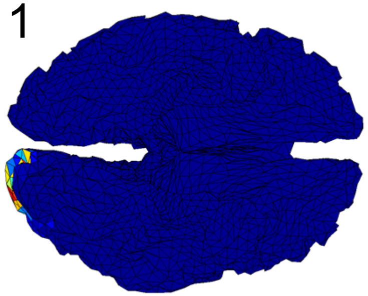


SPM{F} for faces versus
scrambled faces,
15 voxels, p<.05 FWE

1



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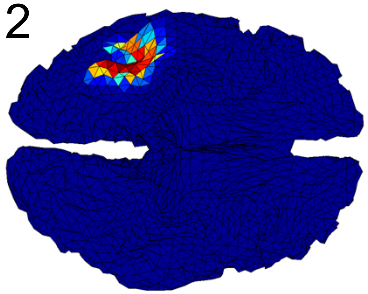

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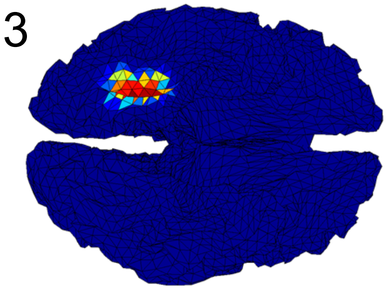
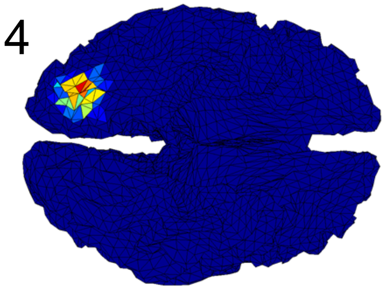
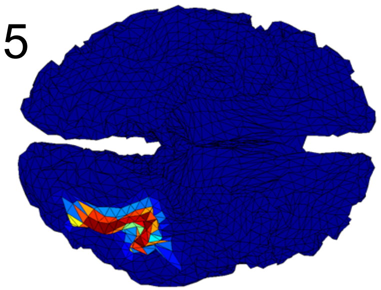


4



5



5 clusters from SPM of fMRI data from separate group of (18) subjects in MNI space

Henson et al (2010) Hum. Brain Map.

Asymmetric Integration of M/EEG+fMRI

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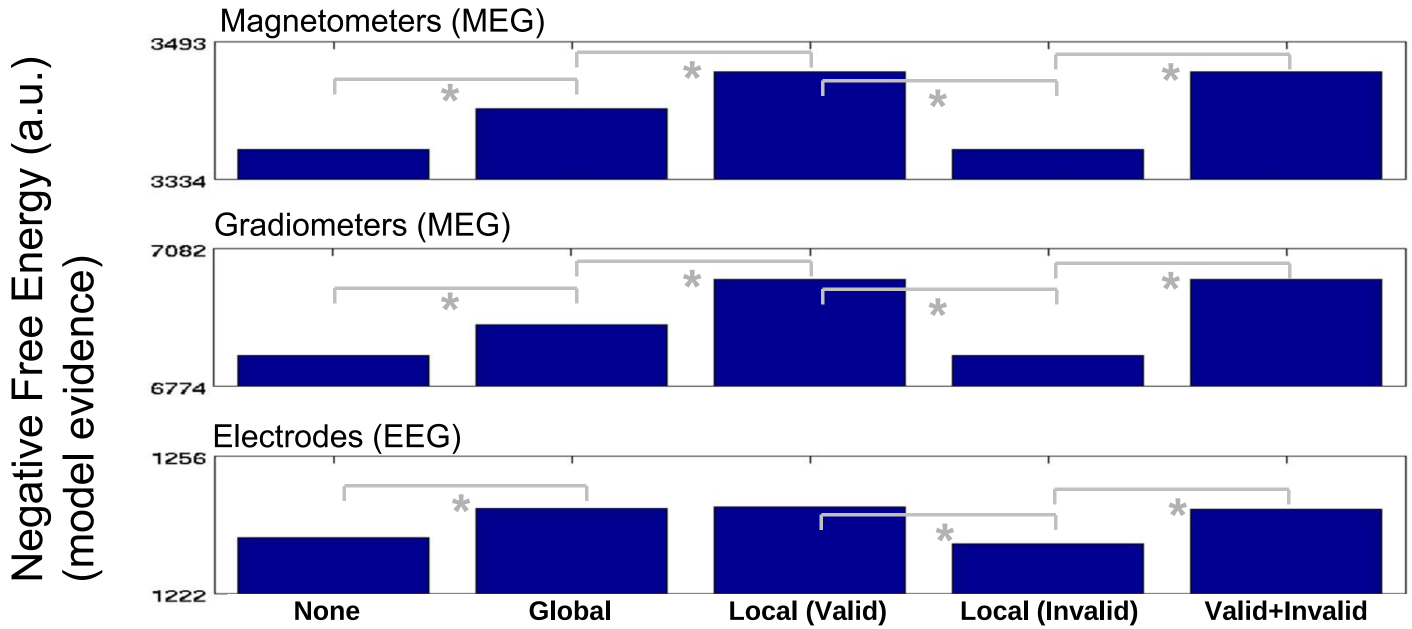

Henson et al (2010) Hum. Brain Map.

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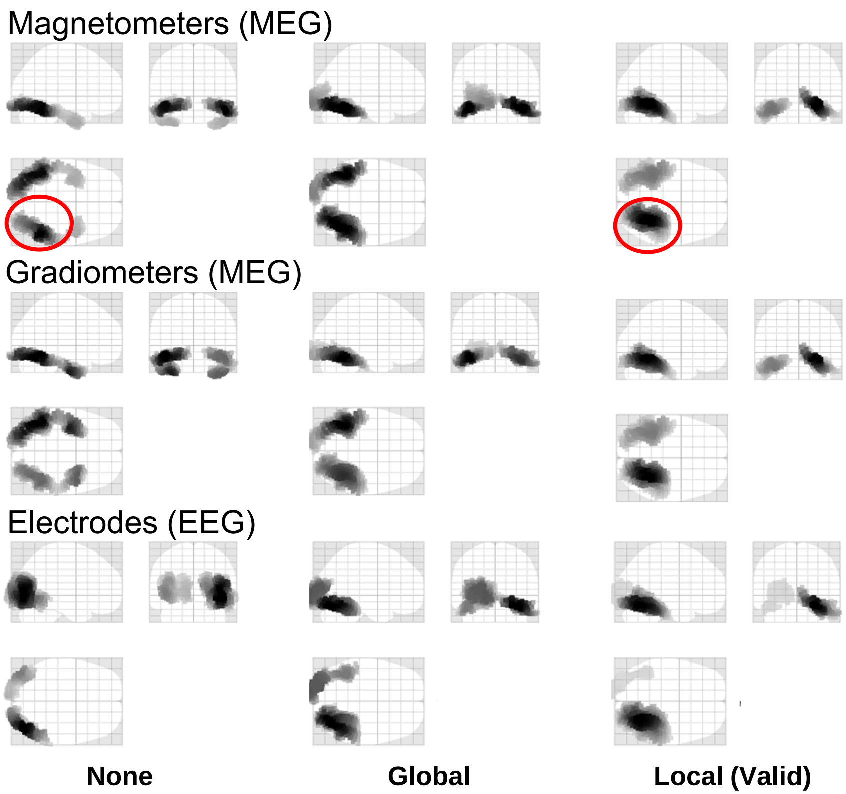
IID sources and IID noise (L2 MNM)



fMRI priors counteract superficial bias of Min Norm

Henson et al (2010) Hum. Brain Map.

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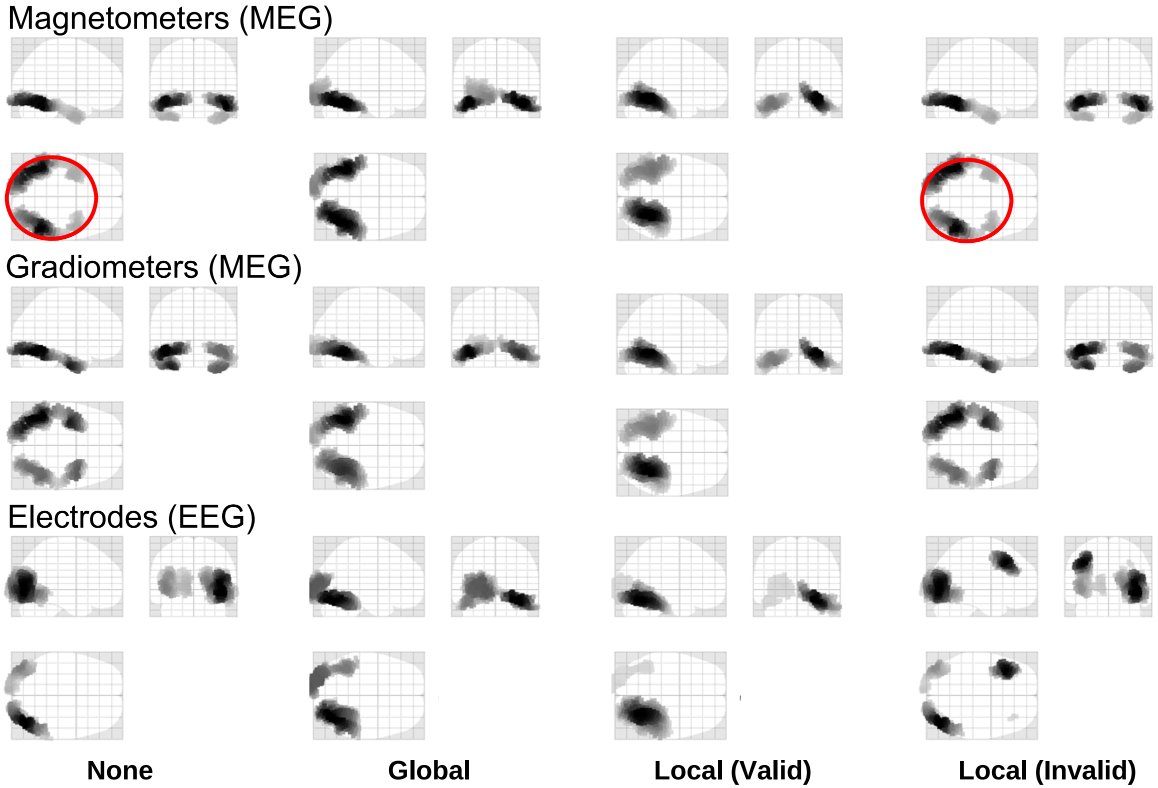
IID sources and IID noise (L2 MNM)



Invalid priors generally discounted (at least for MEG)

Henson et al (2010) Hum. Brain Map.

Asymmetric Integration of M/EEG+fMRI

- Adding a single, global fMRI prior increases model evidence
- Adding multiple valid priors increases model evidence further
- Adding invalid priors does not necessarily increase model evidence, particularly in conjunction with valid priors
  Helpful if some fMRI regions produce no MEG/EEG signal (or arise from neural activity at different times)
- Can counteract superficial bias of, e.g, minimum-norm
- Makes some allowance for different sensitivities of fMRI and M/EEG to certain types of neural activity

Henson et al (2010) Hum. Brain Map.

Other Approaches to fMRI/MEG/EEG

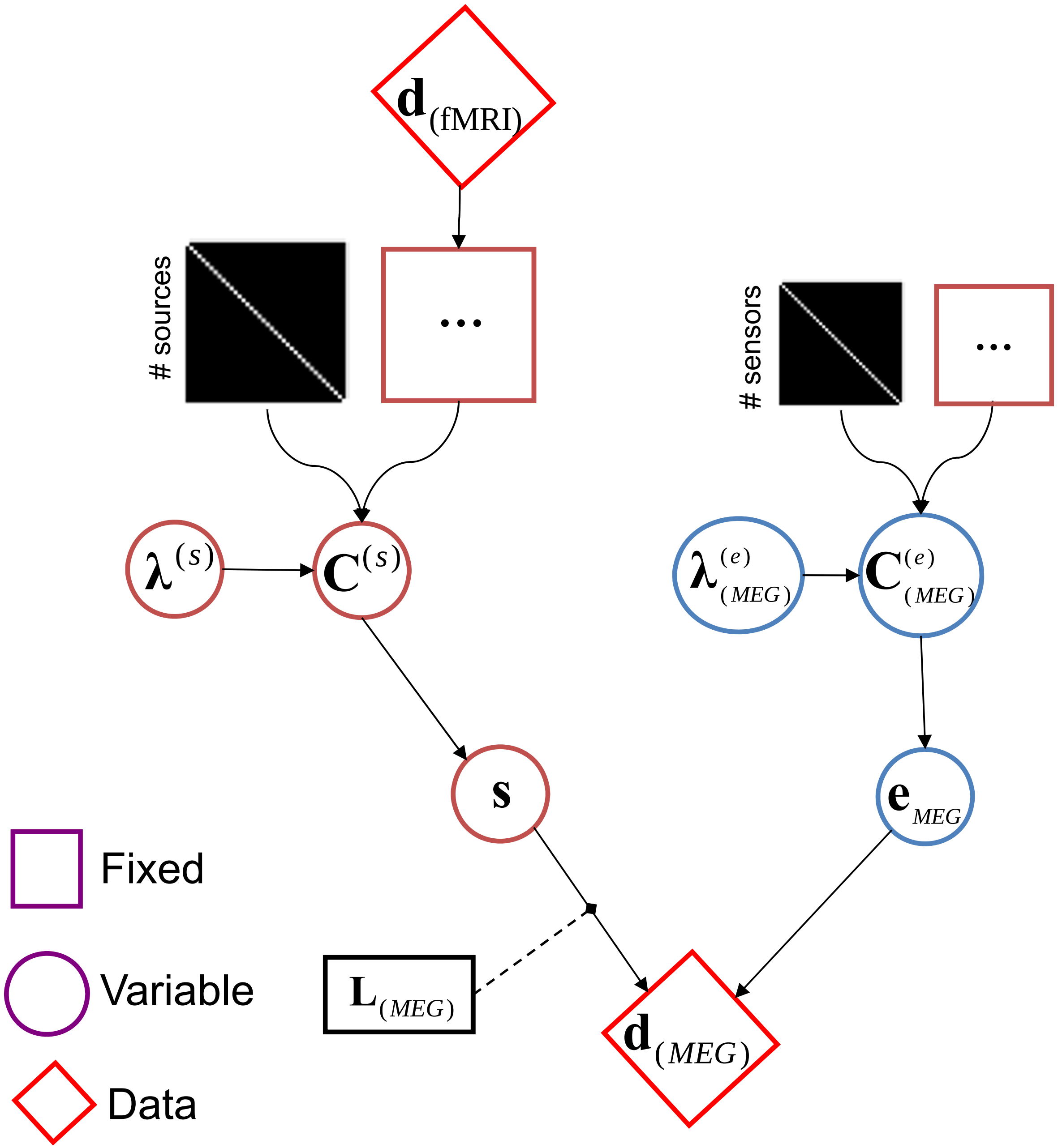
Symmetric Integration (fusion) of fMRI and M/EEG

- e.g based on ROIs:

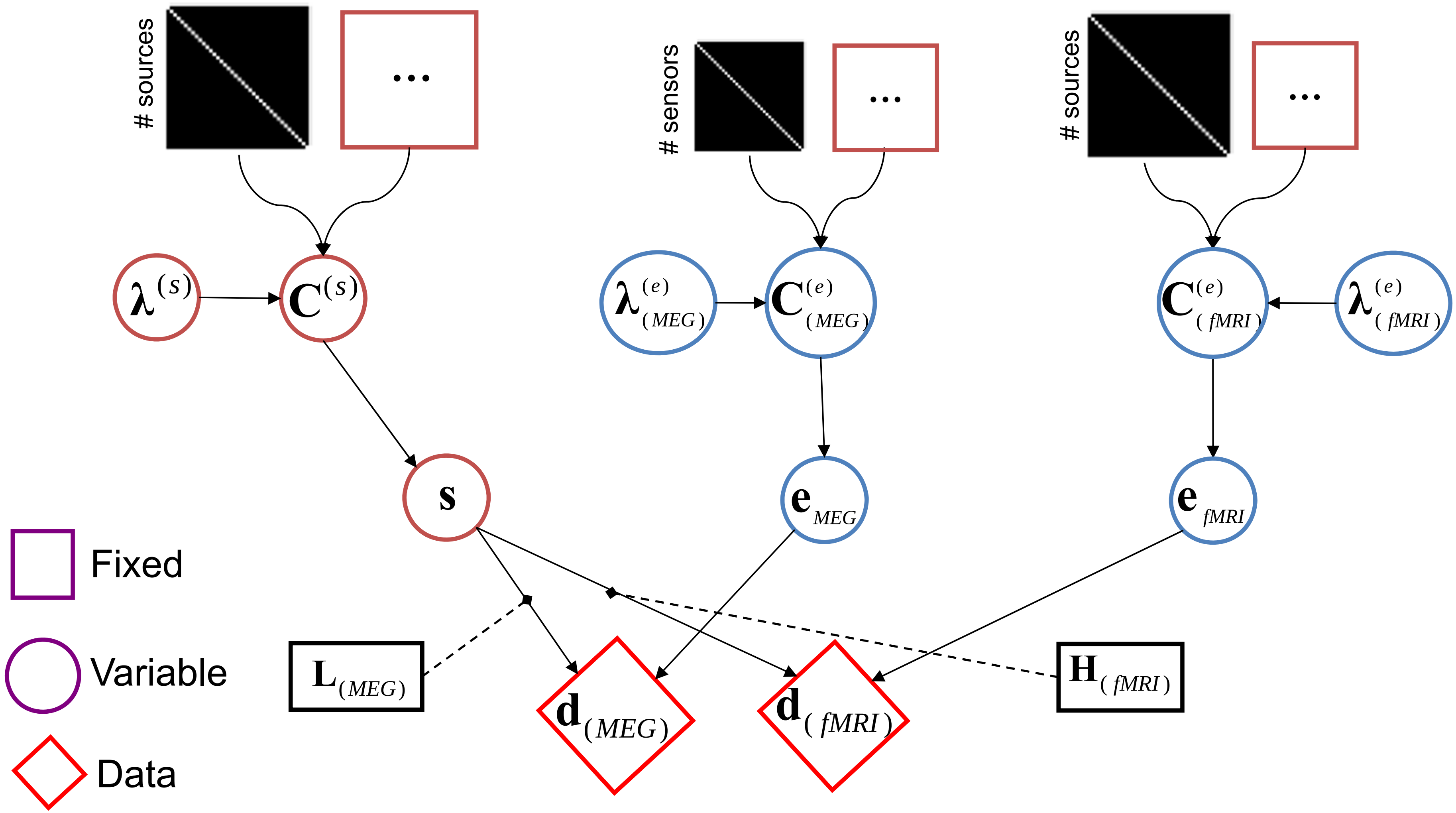
Ou et al (2010), Neuroimage

- e.g, full biophysical model

Sotero & Trujillo-Barreto (2008), Neuroimage



Henson et al (2011) Frontiers

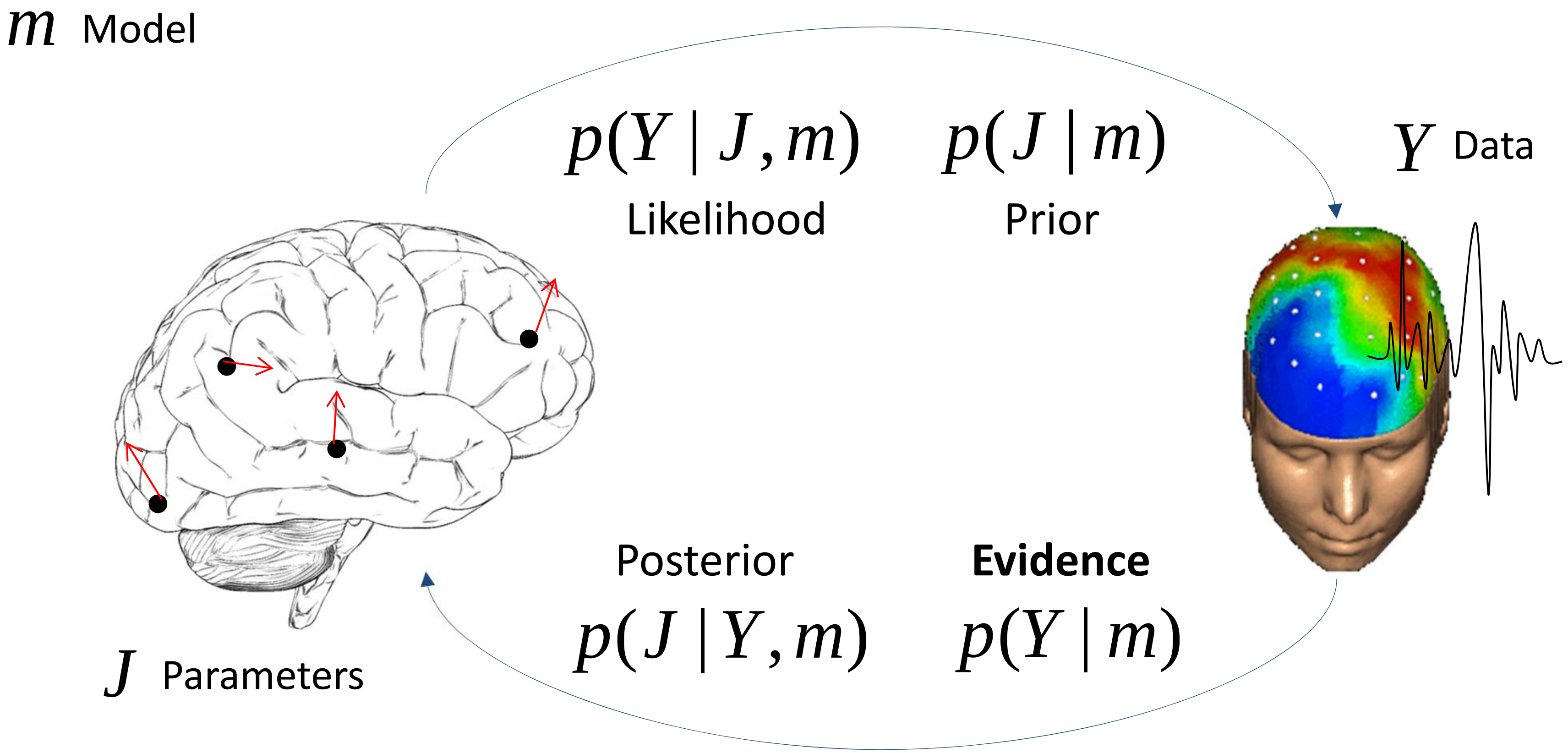


Henson et al (2011) Frontiers

The End

Bayesian Perspective

Forward Problem



Inverse Problem

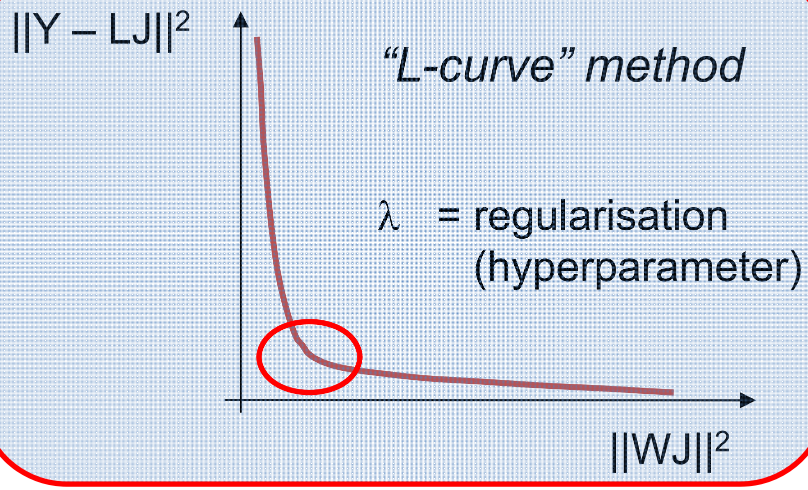
Inverse Problem: Standard L2-norm

$$\mathbf{Y} = \mathbf{LJ} + \mathbf{E} \qquad \mathbf{E} \sim N(\mathbf{0}, \mathbf{C}^{(e)})$$

$$\mathbf{J} = \arg\min\{\left\| \mathbf{C}^{(e)^{-1/2}} (\mathbf{Y} - \mathbf{LJ}) \right\|^2 + \lambda \left\| \mathbf{WJ} \right\|^2\}$$

$$= (\mathbf{W}^T\mathbf{W})^{-1}\mathbf{L}^T[\mathbf{L}(\mathbf{W}^T\mathbf{W})^{-1}\mathbf{L}^T + \lambda\mathbf{C}^{(e)}]^{-1}\mathbf{Y}$$

"Tikhonov Solution"



$\mathbf{W} = \mathbf{I}$	"Minimum Norm"
$\mathbf{W} = \mathbf{DD}^T$	"Loreta" (**D**=Laplacian)
$\mathbf{W} = diag(\mathbf{L}^T\mathbf{L})^{-1}$	"Depth-Weighted"
$\mathbf{W}_p = diag(\mathbf{L}_p^T C_y^{-1} \mathbf{L}_p)^{-1}$	"Beamformer"
$\mathbf{W} = \ldots$	

Phillips et al (2002), Neuroimage

Inverse Problem: Equivalent PEB

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Parametric Empirical Bayesian (PEB) 2-level hierarchical form:

$$\mathbf{Y} = \mathbf{LJ} + \mathbf{E}^{(e)} \qquad \mathbf{E}^{(e)} \sim N(0, \mathbf{C}^{(e)})$$

$$\mathbf{J} = 0 + \mathbf{E}^{(j)} \qquad \mathbf{E}^{(j)} \sim N(0, \mathbf{C}^{(j)})$$

$C^{(e)}$ = n x n Sensor (error) covariance

$C^{(j)}$ = p x p Source (prior) covariance

Likelihood:

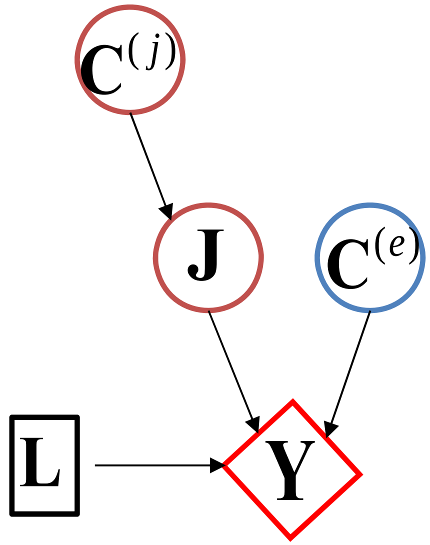
$$p(\mathbf{Y} \mid \mathbf{J}) = N(\mathbf{LJ}, \mathbf{C}^{(e)})$$

Prior:

$$p(\mathbf{J}) = N(0, \mathbf{C}^{(j)})$$

Posterior:

$$p(\mathbf{J} \mid \mathbf{Y}) \propto p(\mathbf{Y} \mid \mathbf{J})\, p(\mathbf{J})$$



Maximum A Posteriori (MAP) estimate:

$$\hat{\mathbf{J}} = \mathbf{C}^{(j)}\mathbf{L}^T[\mathbf{L}\mathbf{C}^{(j)}\mathbf{L}^T + \mathbf{C}^{(e)}]^{-1}\mathbf{Y}$$

cf Classical Tikhonov:

$$(\mathbf{W}^T\mathbf{W})^{-1}\mathbf{L}^T[\mathbf{L}(\mathbf{W}^T\mathbf{W})^{-1}\mathbf{L}^T + \lambda\mathbf{C}^{(e)}]^{-1}\mathbf{Y} \qquad \Rightarrow \mathbf{C}^{(j)} = (\mathbf{W}^T\mathbf{W})^{-1}$$

Phillips et al (2005), Neuroimage

PEB: Estimation

1. Obtain Restricted Maximum Likelihood (ReML) estimates of the hyperparameters (λ) by maximising the variational "free energy" (F):

$$\hat{\boldsymbol{\lambda}} = \max_{\lambda} p(\mathbf{Y} \mid \boldsymbol{\lambda}) = \max_{\lambda} F$$

2. Obtain Maximum A Posteriori (MAP) estimates of parameters (sources, J):

$$\hat{\mathbf{J}} = \max_{j} p(\mathbf{J} \mid \mathbf{Y}, \hat{\boldsymbol{\lambda}}) = \max_{j} F$$

3. Maximal F approximates Bayesian (log) "model evidence" for a model, *m*:

$$\ln p(\mathbf{Y} \mid m) = \ln \int\int p(\mathbf{Y}, \mathbf{J}, \boldsymbol{\lambda} \mid m) d\mathbf{J} d\boldsymbol{\lambda} \approx F(\mathbf{Y}, \hat{\boldsymbol{\alpha}}, \hat{\boldsymbol{\Sigma}}) \qquad m = \{\mathbf{L}, \mathbf{Q}, \boldsymbol{\eta}, \boldsymbol{\Omega}\}$$

$$F(\mathbf{Y}, \hat{\boldsymbol{\alpha}}, \hat{\boldsymbol{\Sigma}}) \propto -tr(\mathbf{C}^{-1}\mathbf{Y}\mathbf{Y}^{T}) - \ln|\mathbf{C}| - (\hat{\boldsymbol{\alpha}} - \boldsymbol{\eta})^{T} \boldsymbol{\Omega}^{-1} (\hat{\boldsymbol{\alpha}} - \boldsymbol{\eta}) + \ln|\hat{\boldsymbol{\Sigma}}\boldsymbol{\Omega}^{-1}|$$

Accuracy   Complexity

(…where $\hat{\boldsymbol{\alpha}}$ and $\hat{\boldsymbol{\Sigma}}$ are the posterior mean and covariance of hyperparameters)

Friston et al (2002) Neuroimage

PEB: Multiple Sparse Priors

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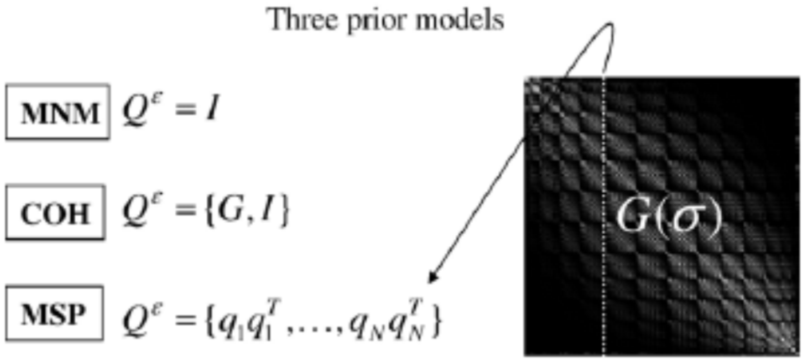
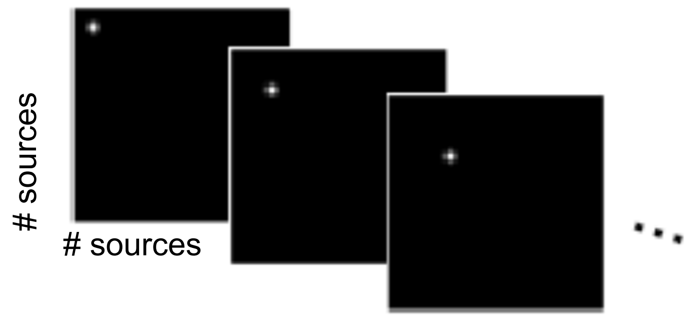
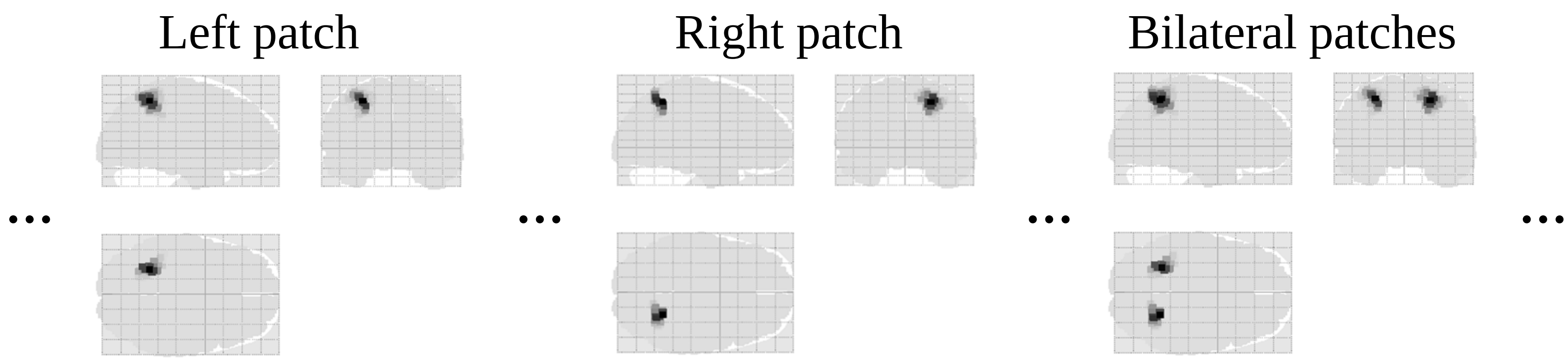
Hyperpriors allow the extreme of 100's source priors, or MSP





$$G(\sigma) = [q_1, \ldots, q_N] = \sum_{i=0}^{8} \frac{\sigma^i}{i!} A^i \approx \exp(\sigma A)$$



Friston et al (2008) Neuroimage

PEB: Multiple Sparse Priors

Hyperpriors allow the extreme of 100's source priors, or MSP

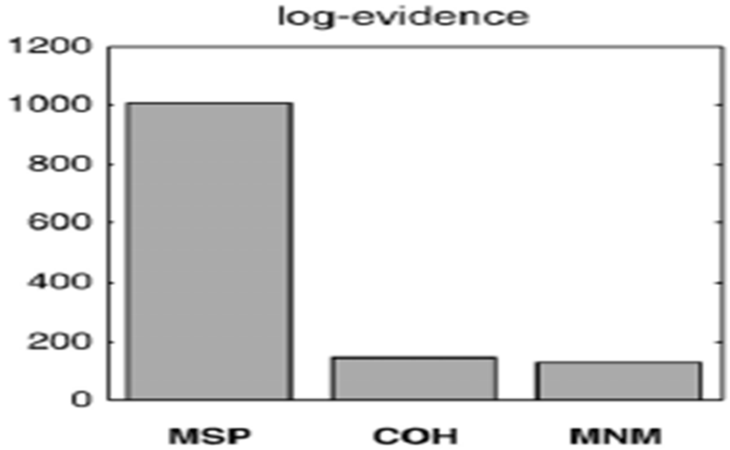
Three prior models

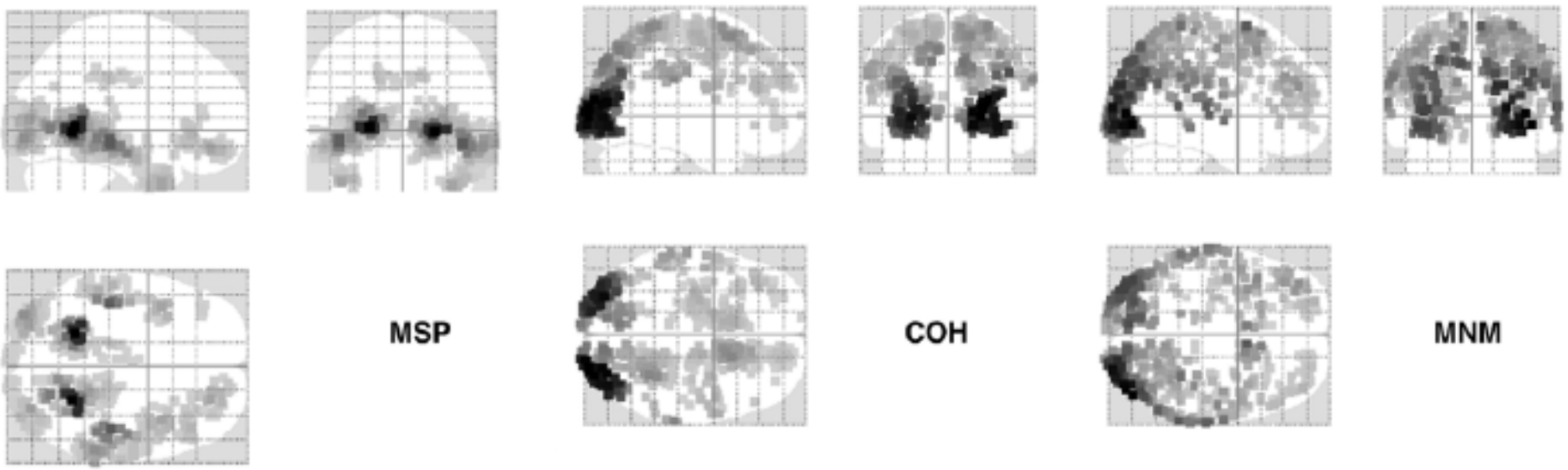
MNM $Q^{\varepsilon} = I$

COH $Q^{\varepsilon} = \{G, I\}$

MSP $Q^{\varepsilon} = \{q_1 q_1^T, \ldots, q_N q_N^T\}$

$$G(\sigma) = [q_1, \ldots, q_N] = \sum_{i=0}^{8} \frac{\sigma^i}{i!} A^i \approx \exp(\sigma A)$$





Friston et al (2008) Neuroimage

Asymmetric Integration of M/EEG+fMRI

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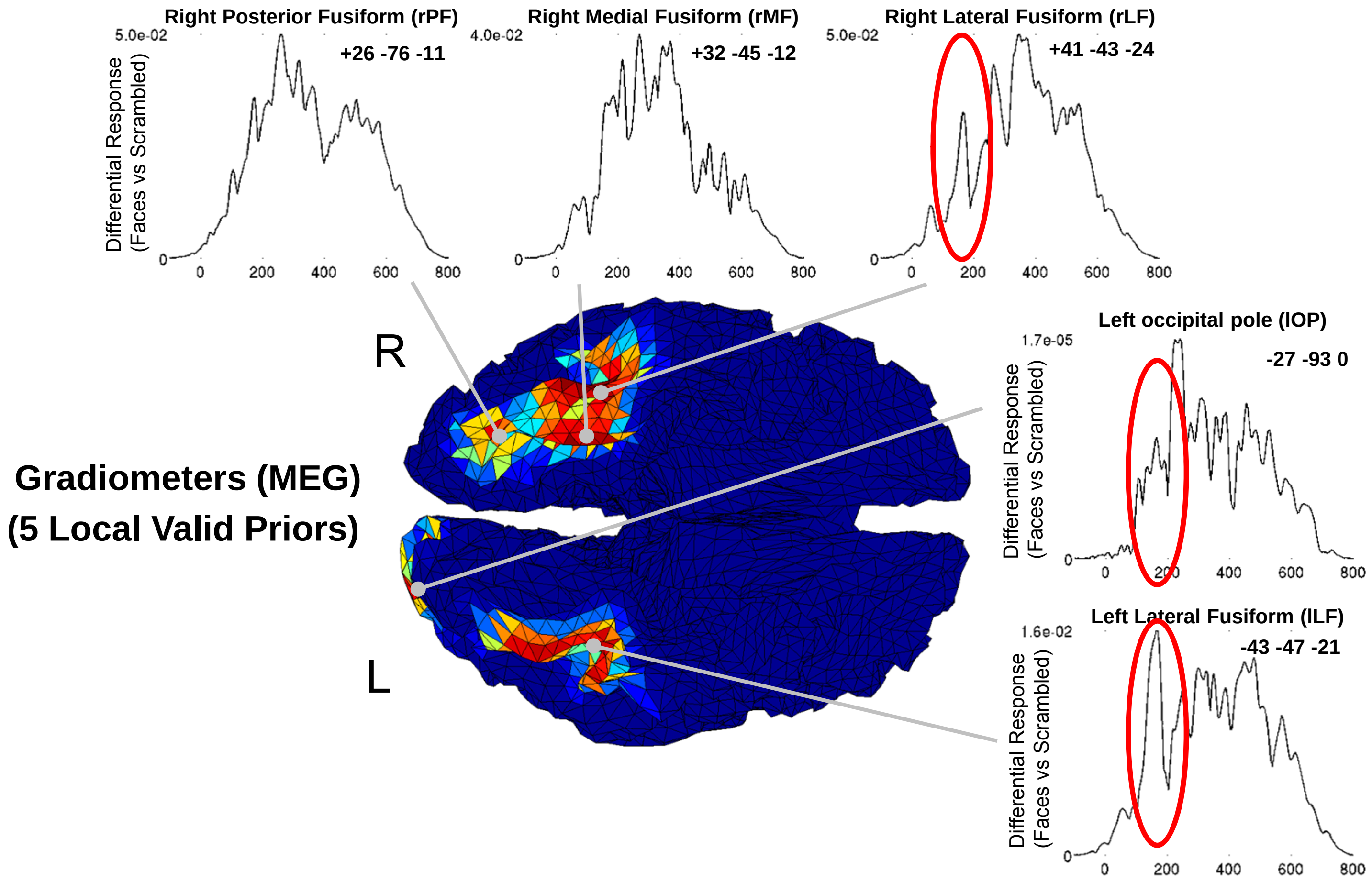

NB: Priors affect variance, not precise timecourse…

Henson et al (2010) Hum. Brain Map.

PEB Summary

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Summary:

- Automatically "regularises" in principled fashion…
- …allows for multiple constraints (priors)…
- …to the extent that multiple (100's) of sparse priors possible (MSP)…
- …(or multiple error components or multiple fMRI priors)…
- …furnishes estimates of model evidence, so can compare constraints