MEG/EEG source imaging using VBMEG

2019/11/27 Yusuke Takeda
ATR Neural Information Analysis Laboratories

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- Usage
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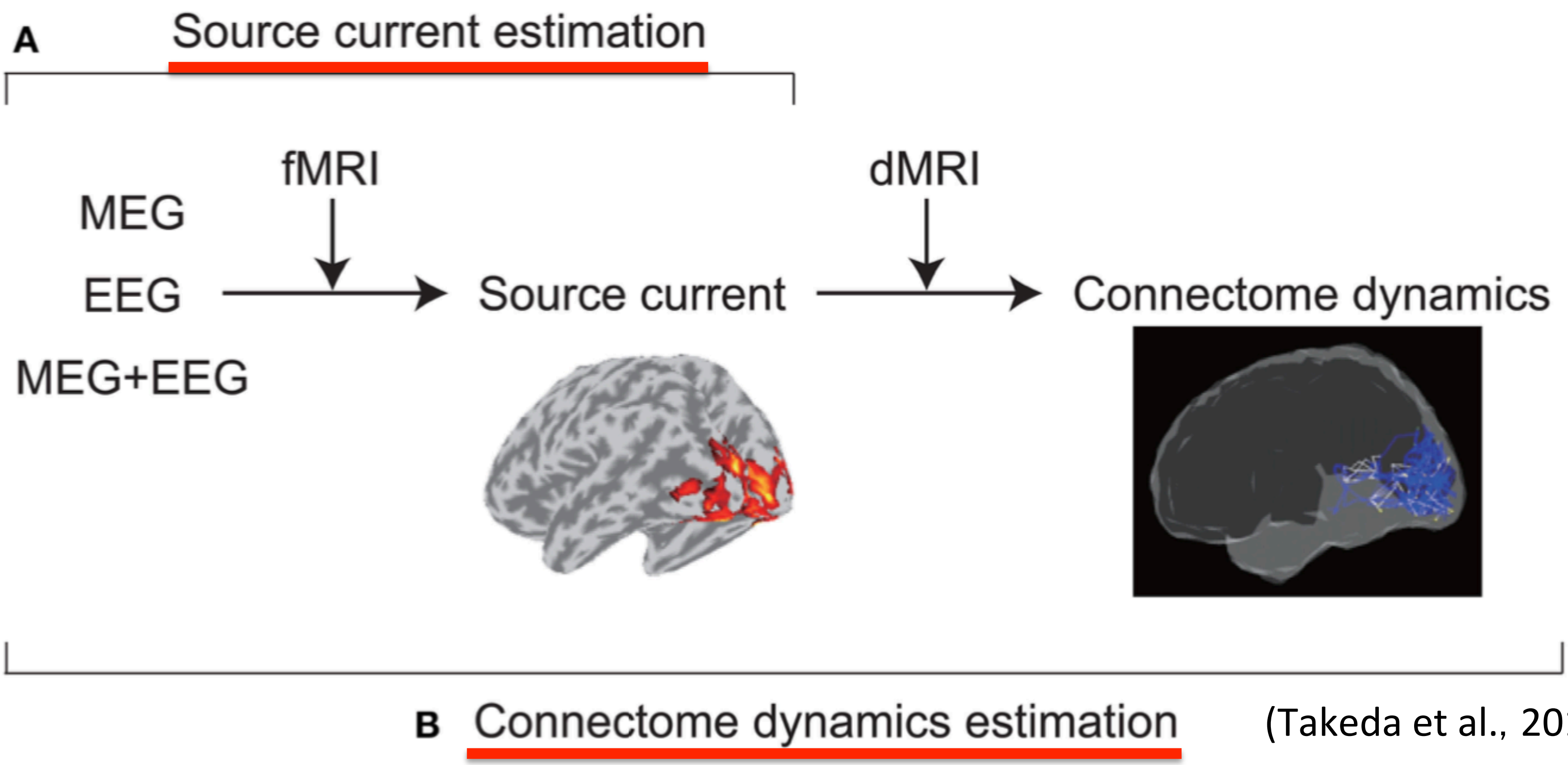
What is VBMEG?

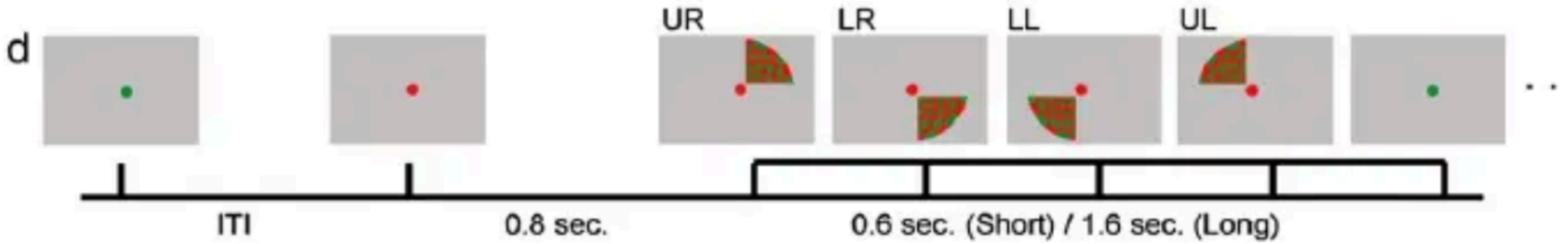
- VBMEG = Variational Bayesian Multimodal EncephaloGraphy
- A MATLAB toolbox for MEG/EEG source imaging

Main functions



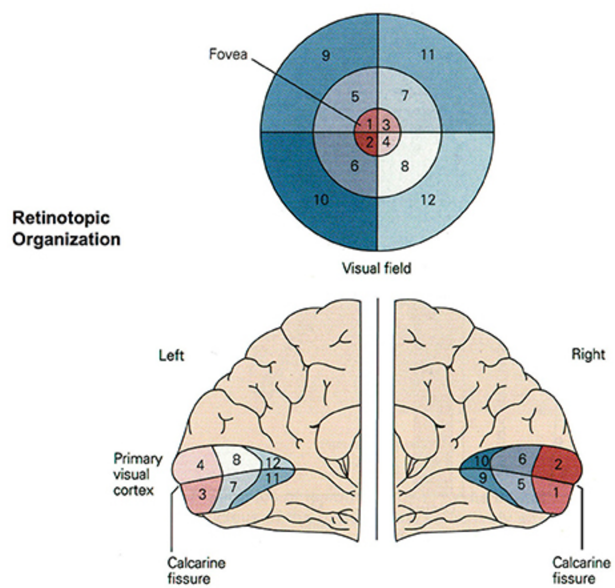
(Takeda et al., 2019)

Source current estimation



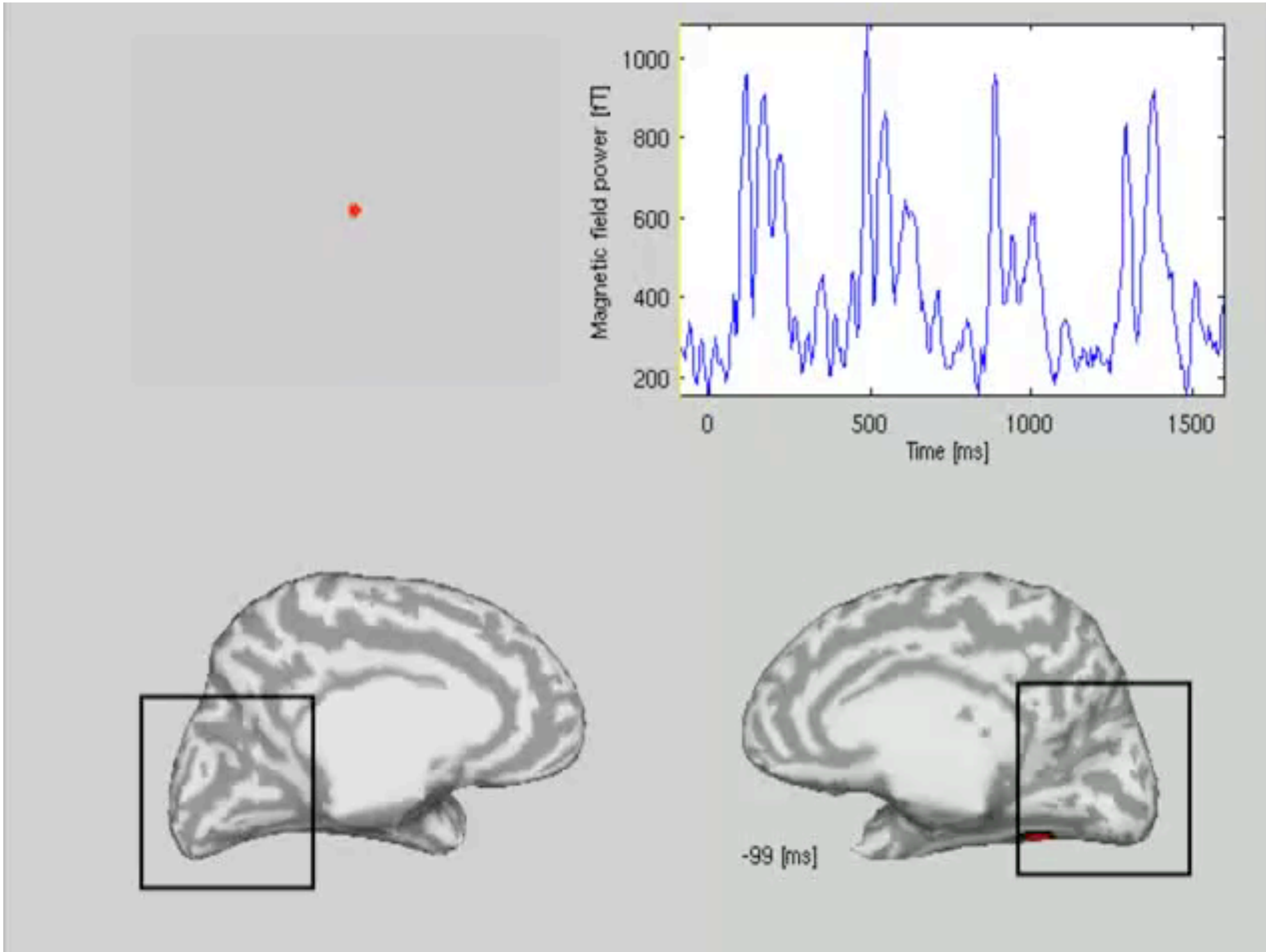
(Yoshioka et al., 2008)

Retinotopic map

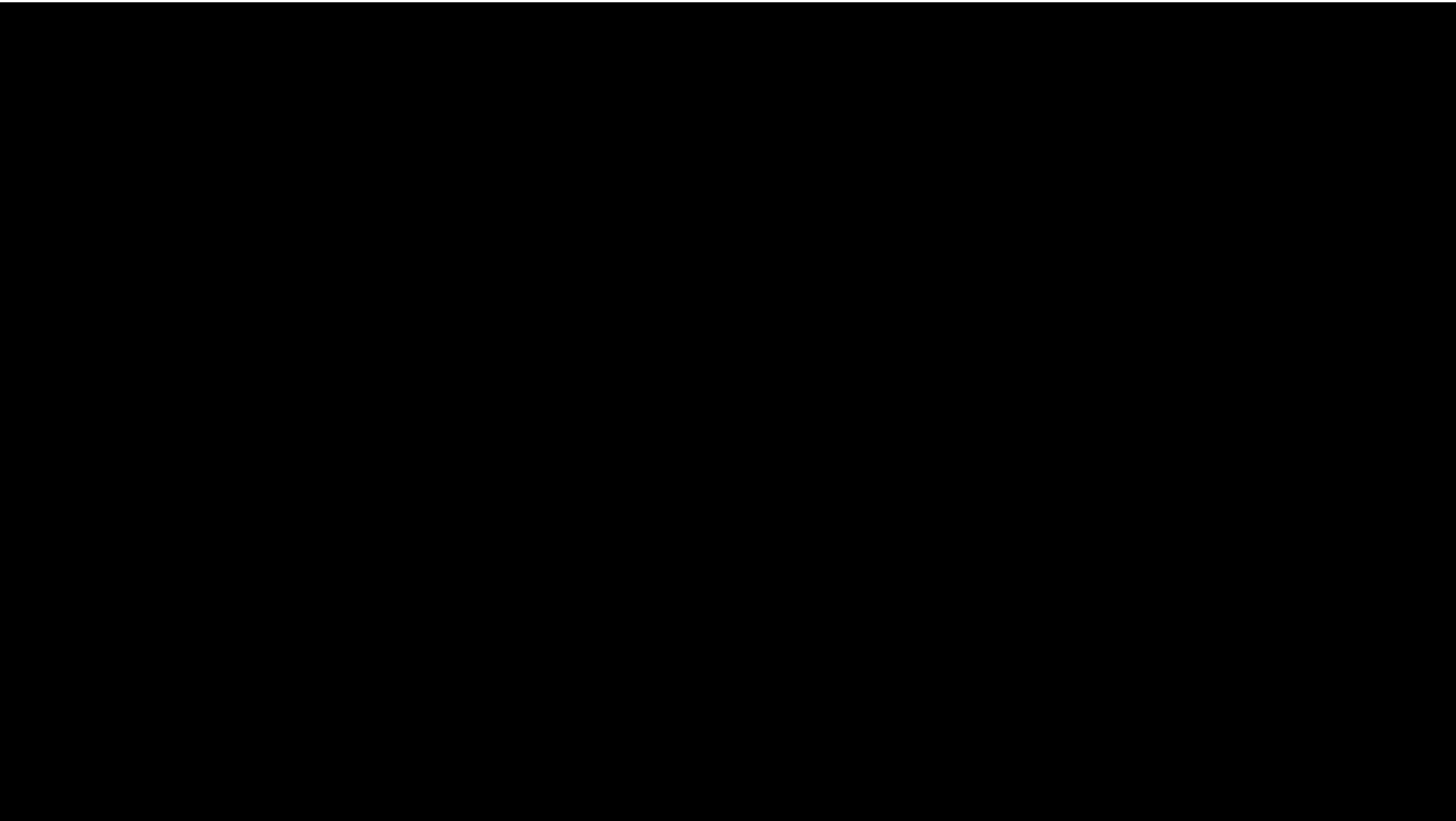


(Paulun et al., 2018)

Source current estimation

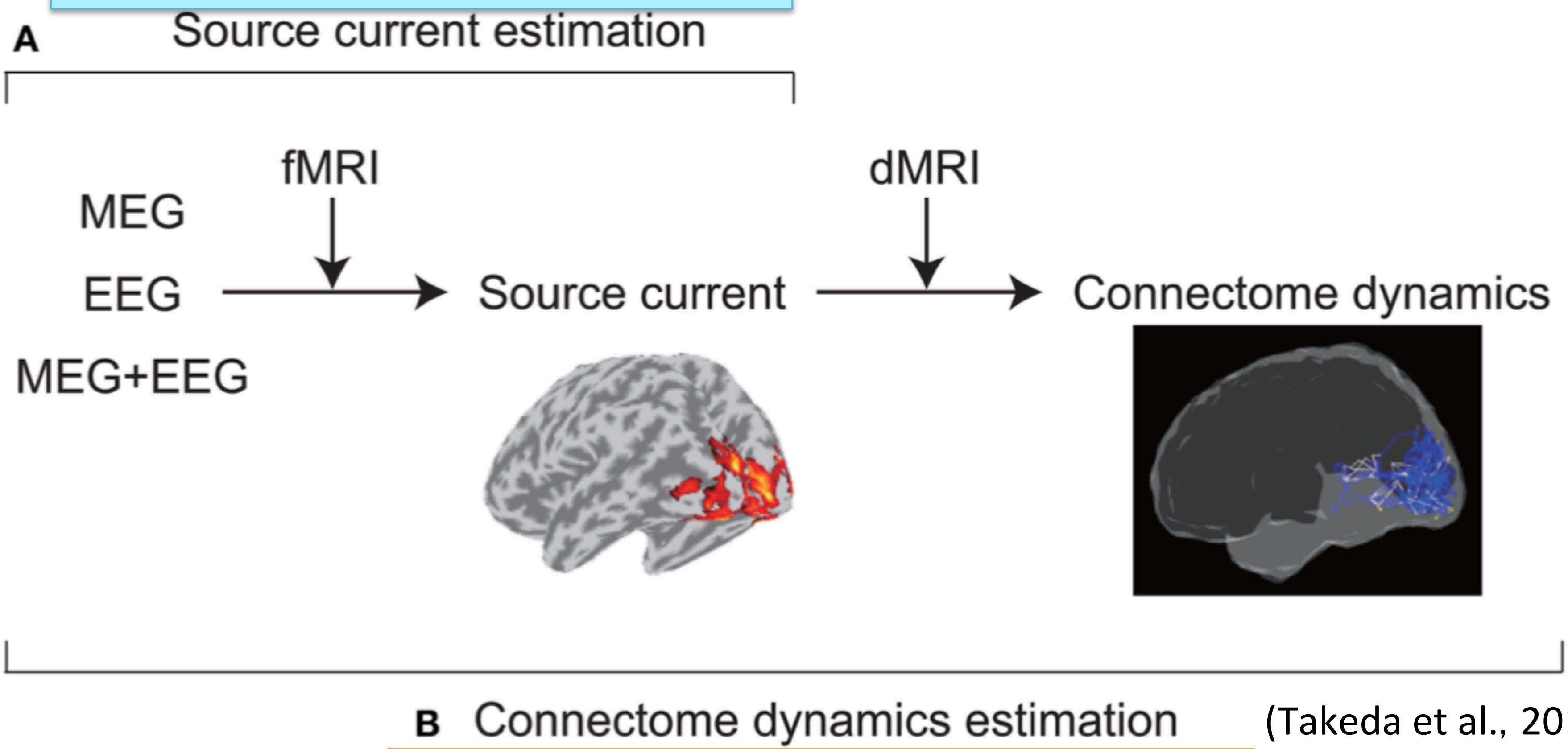


Connectome dynamics estimation



History

Sato et al., 2004 NeuroImage
VBMEG 1 (2011)

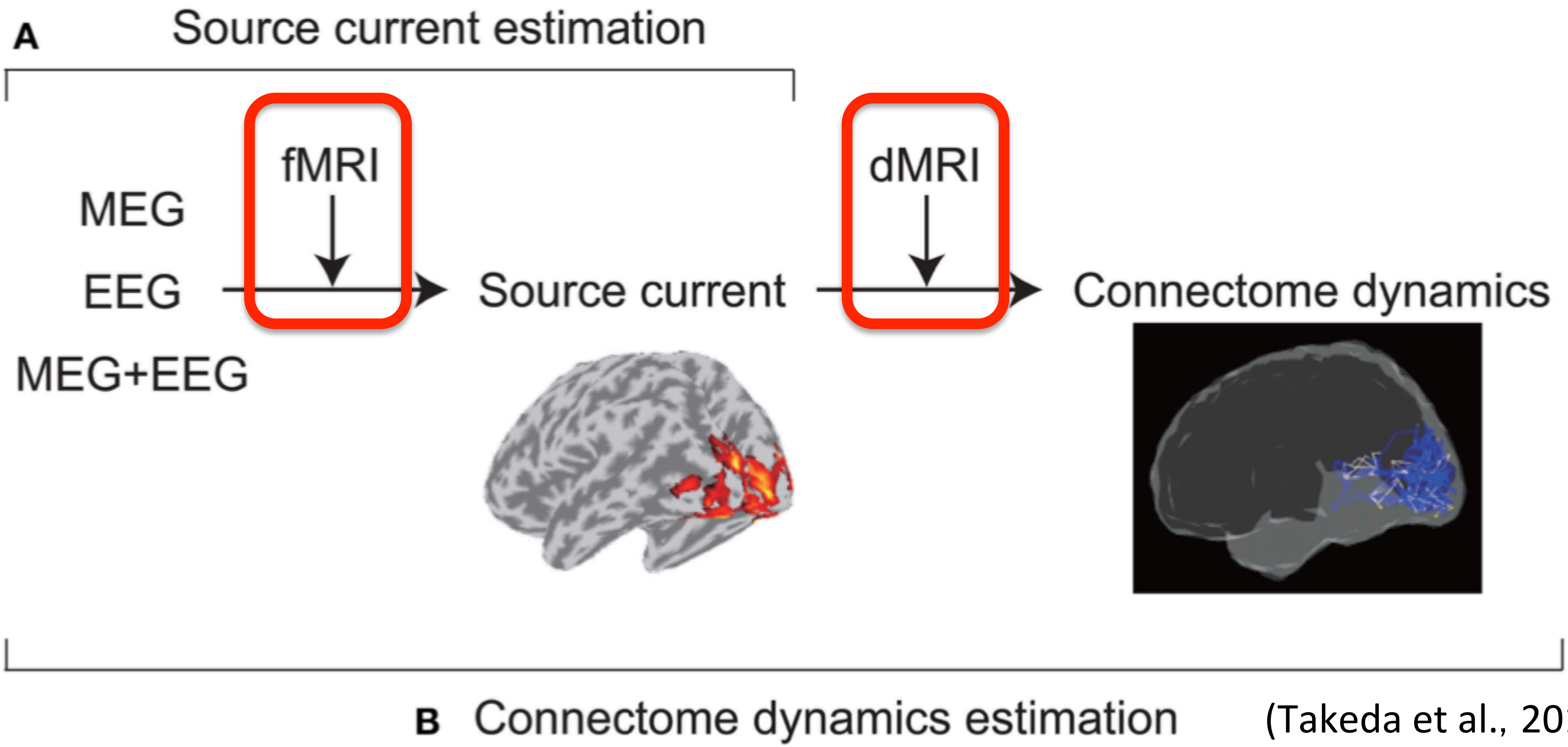


(Takeda et al., 2019)

Fukushima et al., 2015 NeuroImage
VBMEG 2 (2017)

Advantage

Ability to integrate multimodal measurements



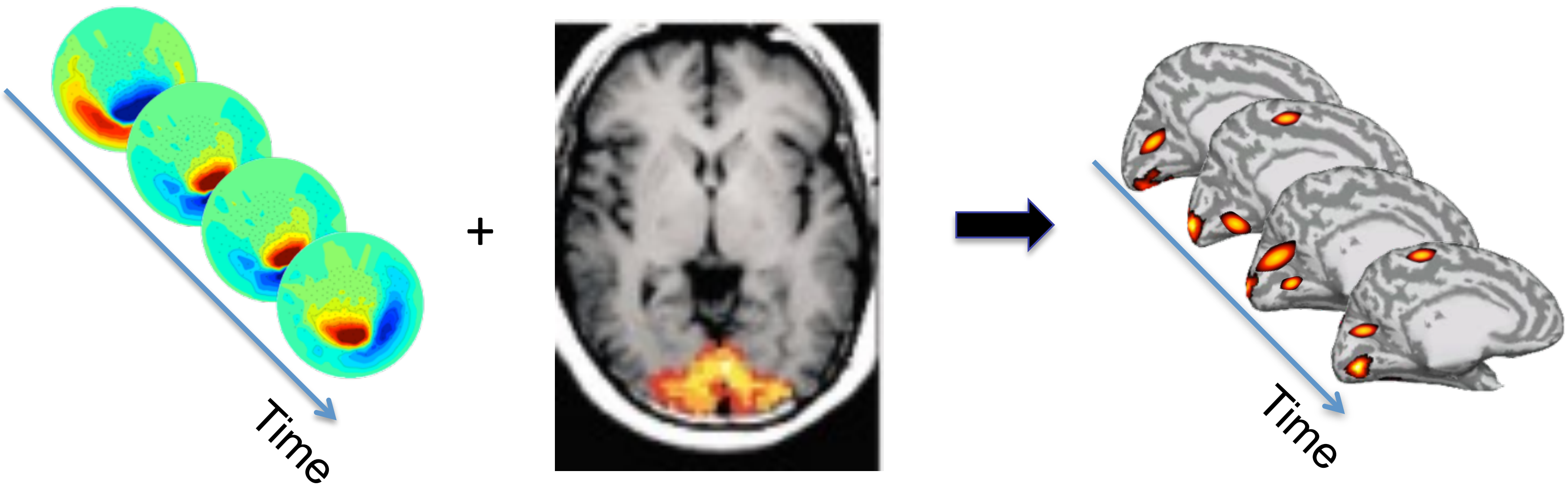
(Takeda et al., 2019)

Why is integrating multimodal measurements important?

MEG/EEG

fMRI

Current sources



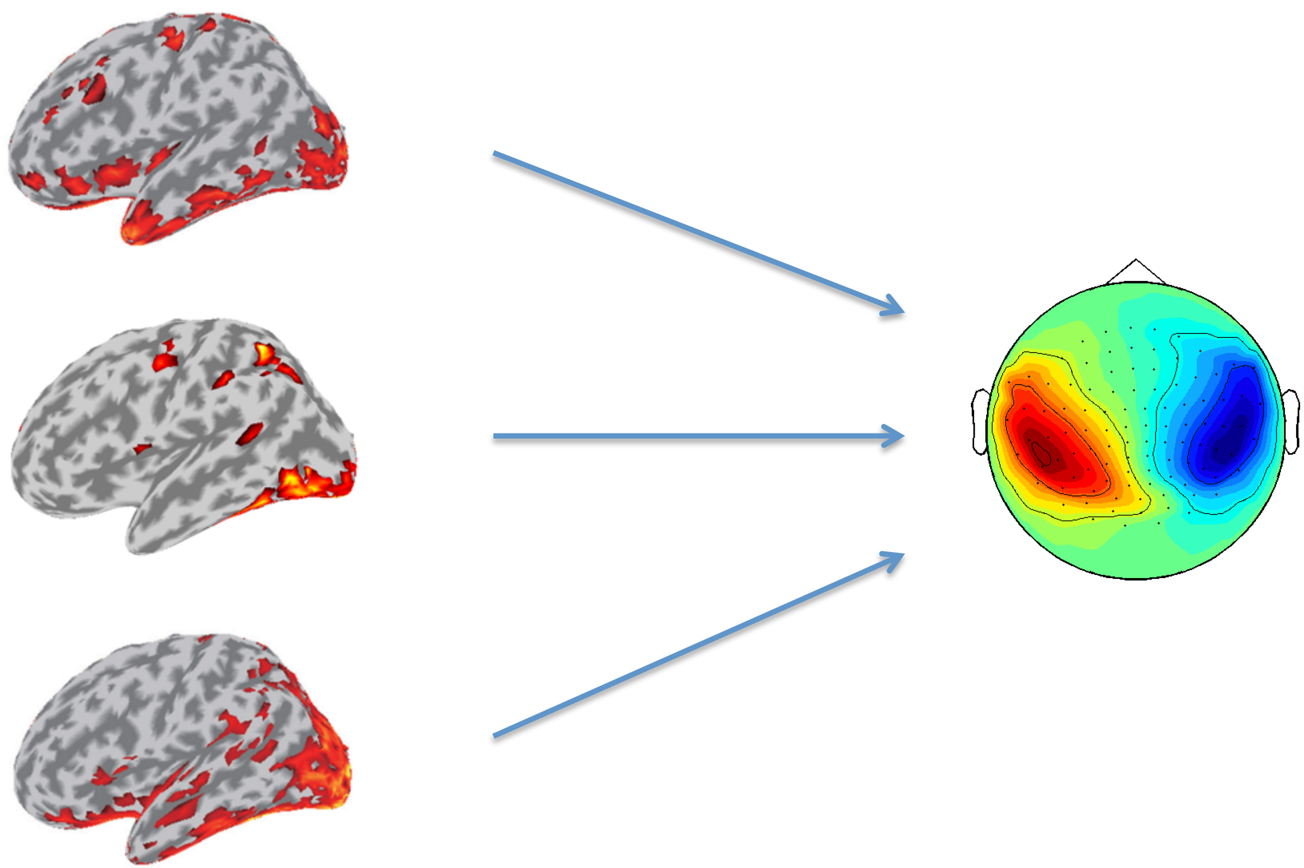
High temporal resolution

High spatial resolution

High spatiotemporal resolution

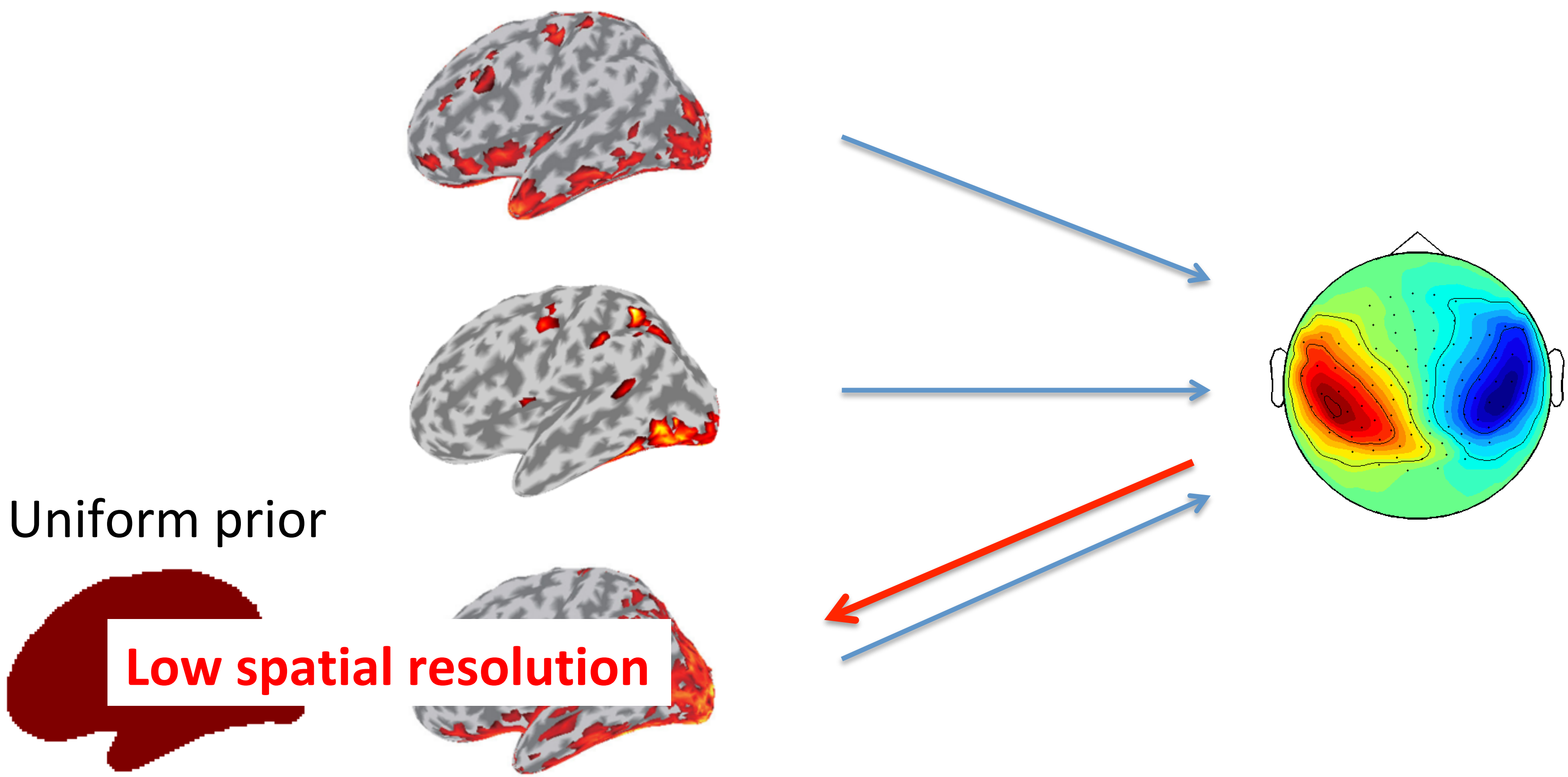
Why is integrating multimodal measurements important?

Estimating source current is ill-posed problem.



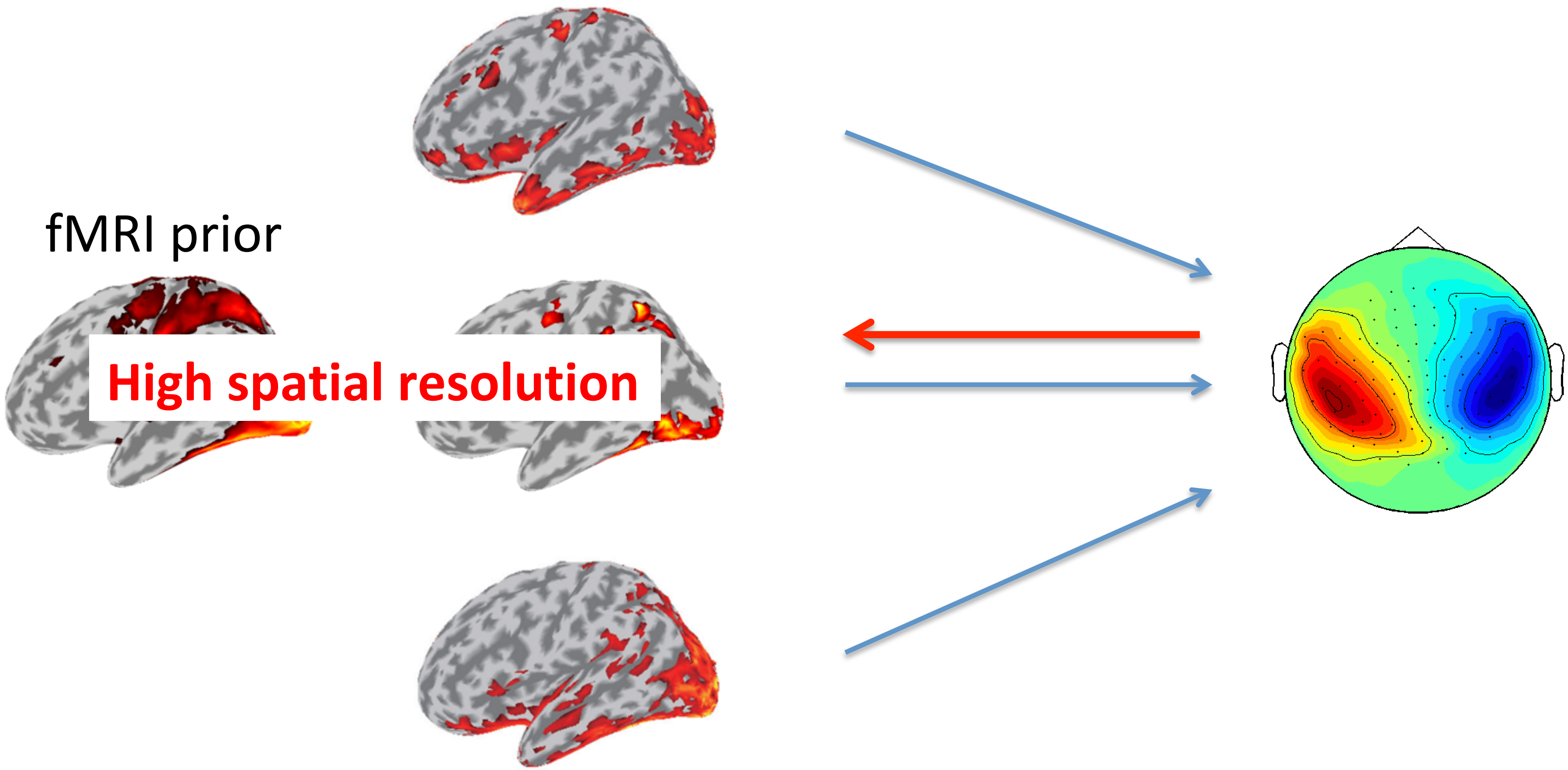
Why is integrating multimodal measurements important?

Prior information is necessary to reduce solution space.



Why is integrating multimodal measurements important?

By using fMRI as prior information, we can obtain source current with high spatial resolution.



Reliability of VBMEG

8 method studies on VBMEG

(Sato et al., NeuroImage 2004; Yoshioka et al., NeuroImage 2008; Fujiwara et al., NeuroImage 2009; Aihara et al., NeuroImage 2012; Morishige et al., NeuroImage 2014; Fukushima et al., NeuroImage 2015; Sato et al., PLoS One 2018; Takeda et al., Front Neurosci 2019)

14 neuroscience studies using VBMEG

(Shibata et al., Cereb Cortex 2008; Callan et al., NeuroImage 2010; Toda et al., NeuroImage 2011; Yoshimura et al., NeuroImage 2012; Yamagishi et al., PLoS One 2013; Morioka et al., NeuroImage 2014; Takeda et al., PLoS One 2014; Callan et al., Front Hum Neurosci 2016; Ohata et al., Sci Rep 2016; Yanagisawa et al., Nat Commun 2016; Yoshimura et al., Sci Rep 2017; Fukuma et al., Front Neurosci 2018; Mejia et al., Front Neurosci 2018; Filatova et al., Front Neural Circ 2018)

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References

- Source current estimation

Sato M, Yoshioka T, Kajihara S, Toyama K, Goda N, Doya K, Kawato M. Hierarchical Bayesian estimation for MEG inverse problem. Neuroimage. 2004 Nov;23(3):806-26.

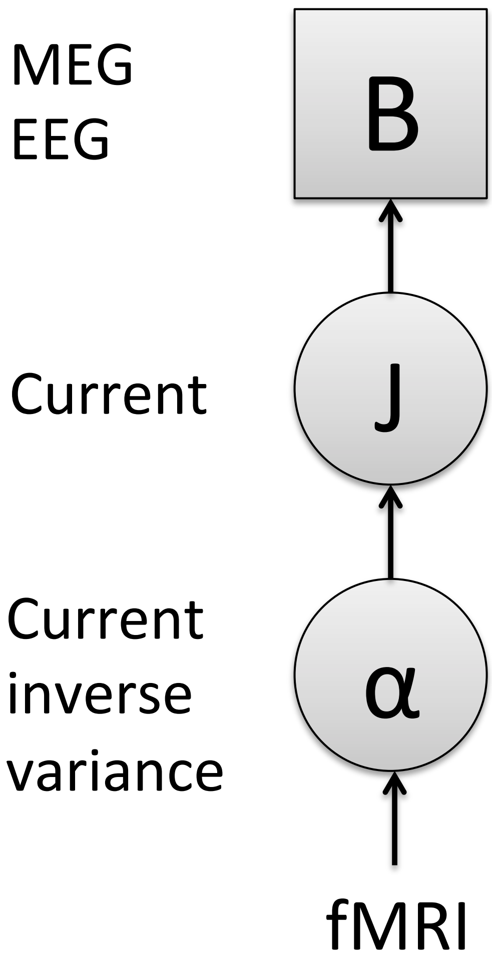
吉岡 琢、佐藤 雅昭. 階層変分ベイズ推定法（VBMEG）の原理と応用. 日本神経回路学会誌 2011 Vol. 18, No. 4:214-223.
https://www.jstage.jst.go.jp/article/jnns/18/4/18_4_214/_pdf

- Connectome dynamics estimation

Fukushima M, Yamashita O, Knösche TR, Sato M. MEG source reconstruction based on identification of directed source interactions on whole-brain anatomical networks. Neuroimage. 2015 Jan 15;105:408-27.
https://www.sciencedirect.com/science/article/pii/S1053811914008088?via%3Dihub

Source current estimation

Forward model of VBMEG



$$P(\boldsymbol{B}|\boldsymbol{J}) \propto \exp\left(-\frac{1}{2}\beta||\boldsymbol{B}-\boldsymbol{G}\cdot\boldsymbol{J}||^2\right)$$

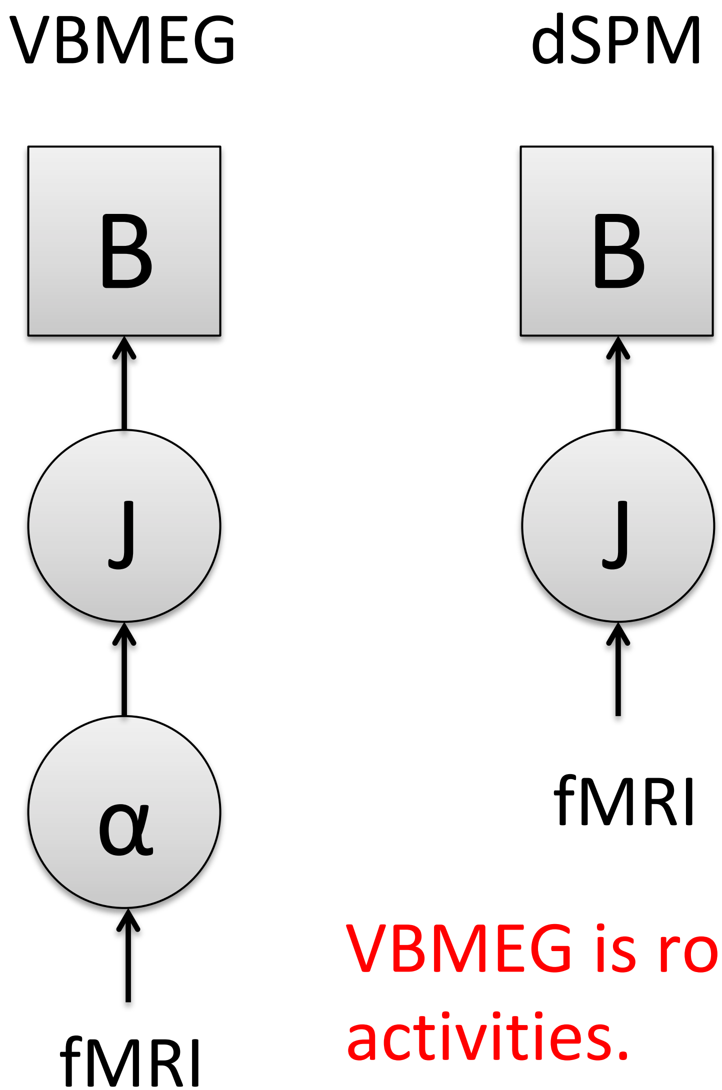
$$P_0(\boldsymbol{J}|\boldsymbol{\alpha}) \propto \exp\left(-\frac{1}{2}\boldsymbol{J}'\cdot\boldsymbol{A}\cdot\boldsymbol{J}\right)$$

$A = \mathrm{diag}(\alpha_1,\ldots,\alpha_I)$

$$P_0(\boldsymbol{\alpha}) = \prod_{i=1}^{I}\Gamma\left(\alpha_i|\bar{\alpha}_{0,i},\gamma_{0,i}\right)$$

fMRI

Difference from dSPM (Dale et al., 2000)



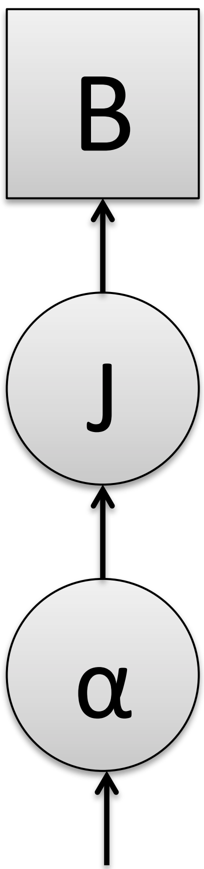
$$P_0(\boldsymbol{J}|\boldsymbol{\alpha}) \propto \exp\left(-\frac{1}{2}\boldsymbol{J}' \cdot \boldsymbol{A} \cdot \boldsymbol{J}\right)$$

VBMEG is robust to inaccurate fMRI activities.

Source current estimation

Forward model of VBMEG

MEG
EEG



Localized currents tend to be estimated.

Current

$$P_0(\boldsymbol{J}|\boldsymbol{\alpha}) \propto \exp\left(-\frac{1}{2}\boldsymbol{J}' \cdot \boldsymbol{A} \cdot \boldsymbol{J}\right)$$

Current
inverse
variance

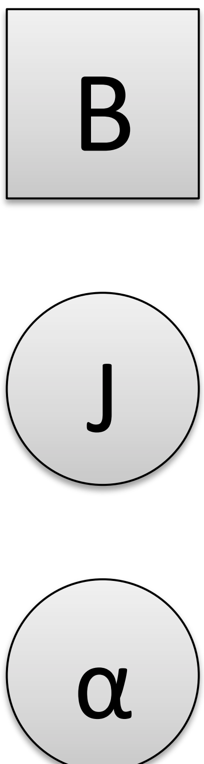
$$P_0(\boldsymbol{\alpha}) = \prod_{i=1}^{I} \Gamma\left(\alpha_i | \bar{\alpha}_{0,i}, \gamma_{0,i}\right)$$

fMRI

Automatic
Relevance
Determination
(ARD)

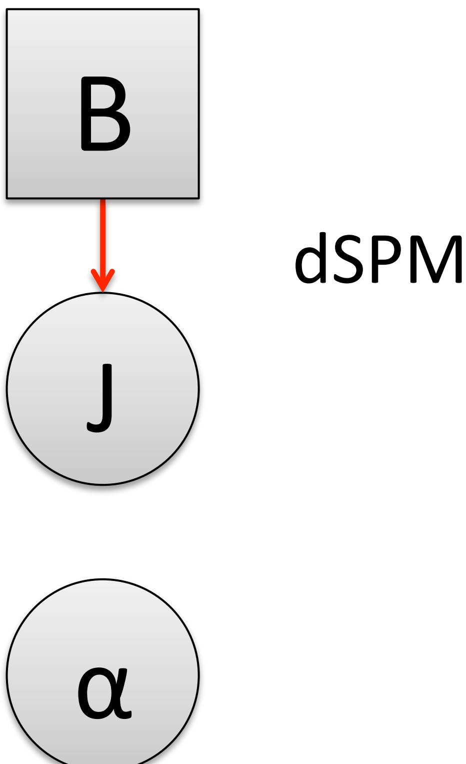
Source current estimation

Estimation algorithm



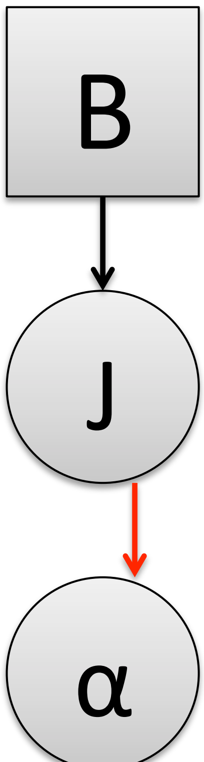
Source current estimation

Estimation algorithm



Source current estimation

Estimation algorithm



α-step

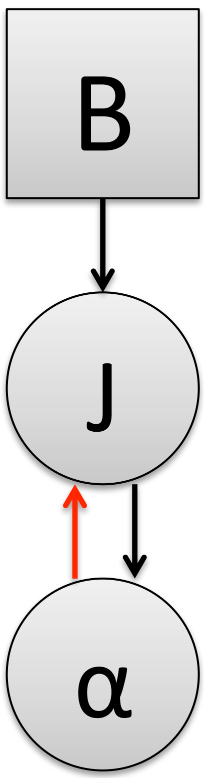
fMRI

$$\alpha_i^{-1} = w\bar{\alpha}_{0,i} + (1-w)\langle \frac{1}{T}\sigma \sum_{t=1}^{T} J_i^2(t) \rangle$$

$$w = \frac{\gamma_0}{\gamma_0 + \frac{T}{2}}$$

Source current estimation

Estimation algorithm



J-step

$$\boldsymbol{L}\left(\boldsymbol{\Sigma}_{\alpha}^{-1}\right) = \boldsymbol{\Sigma}_{\alpha}^{-1} \cdot \boldsymbol{G}' \cdot \left(\boldsymbol{G} \cdot \boldsymbol{\Sigma}_{\alpha}^{-1} \cdot \boldsymbol{G}' + \beta^{-1}\boldsymbol{I}_M\right)^{-1},$$

$$\boldsymbol{J}(t) = \boldsymbol{L}\left(\boldsymbol{\Sigma}_{\alpha}^{-1}\right) \cdot \boldsymbol{B}(t).$$

α-step

fMRI

Data

Current variance $$\alpha_i^{-1} = w\bar{\alpha}_{0,i} + (1-w)\langle \frac{1}{T}\sigma \sum_{t=1}^{T} J_i^2(t) \rangle$$

Prior weight $$w = \frac{\gamma_0}{\gamma_0 + \frac{T}{2}}$$ $(0 \le w \le 1)$

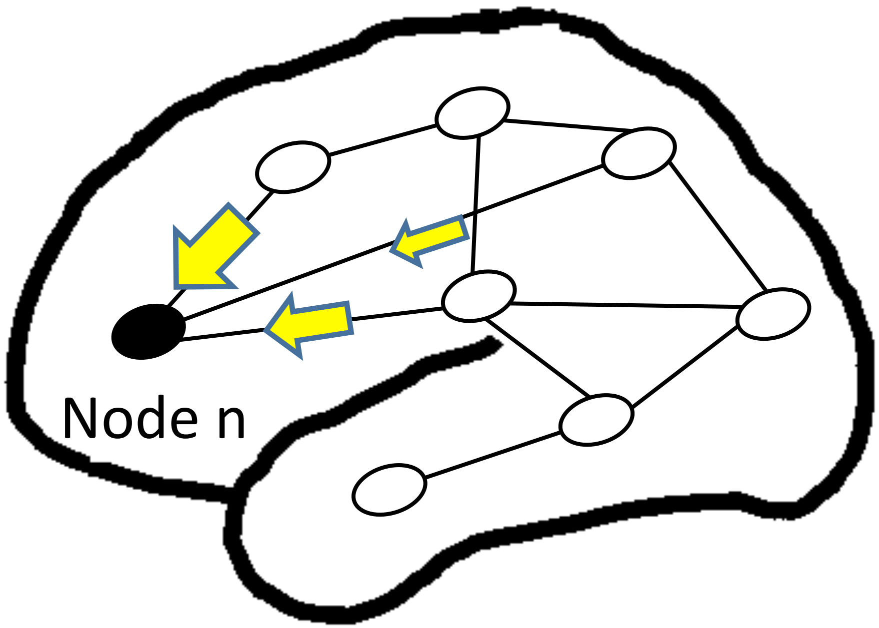
(Hyperparameter)

Prior weight	Current variance	
Small	Far from fMRI activity	Sparse
Large	Close to fMRI activity	Dense

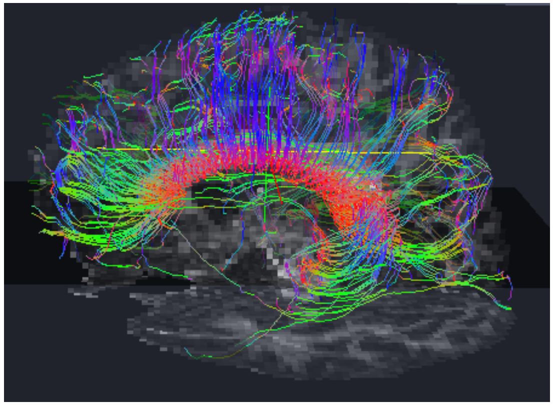
Connectome dynamics estimation

Generative model

$$z_{n,t} = \sum_{d=1}^{p} a_{nd} z_{n,t-d} + \sum_{v \in C_n} b_{nv} z_{v,t-\Delta_{v_n}} + \epsilon_n \qquad \Delta_{v_n} = \frac{L_{v,n}}{c} + D$$

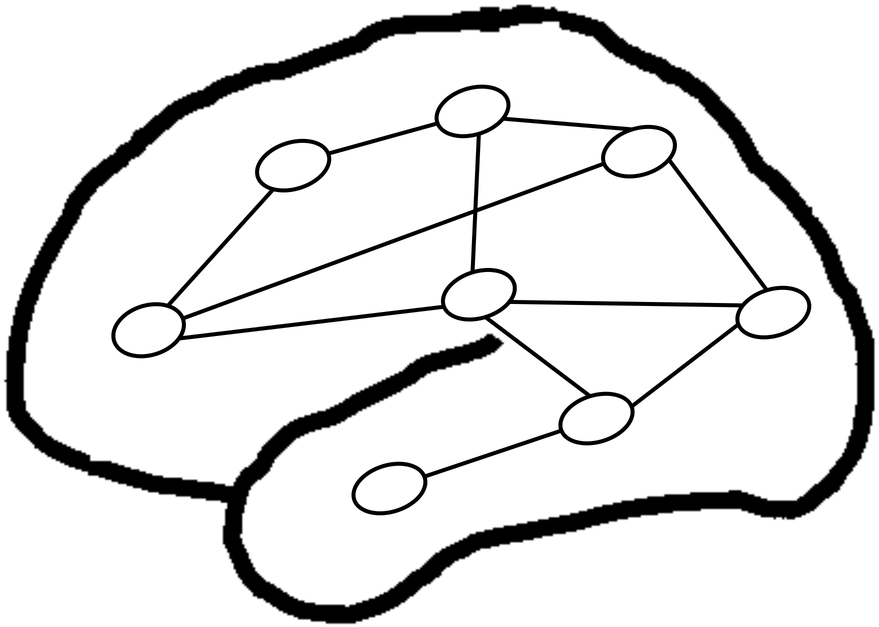


Anatomical connectivity derived from dMRI



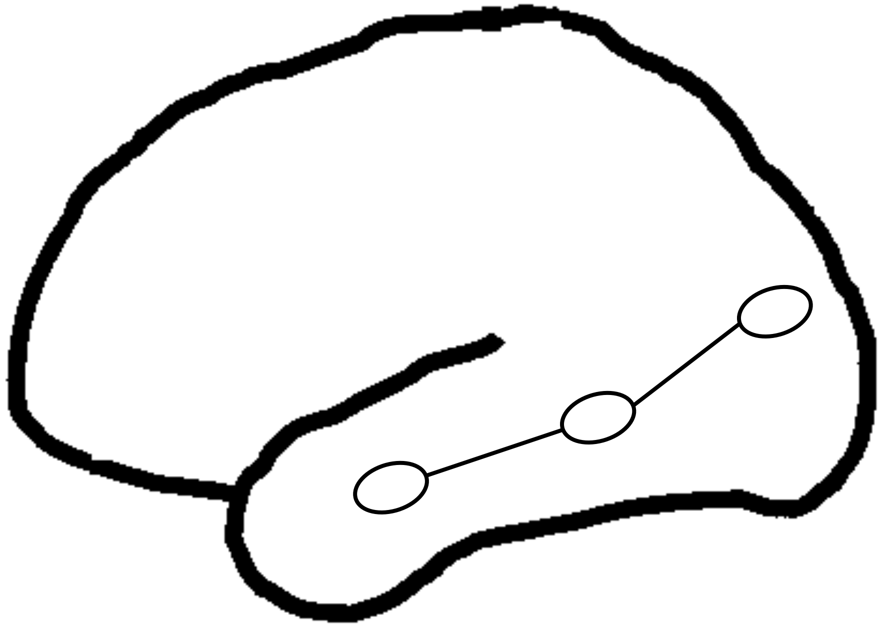
Relation with DCM

VBMEG



- Linear
- Whole-brain

Dynamic Causal Modeling
(DCM)



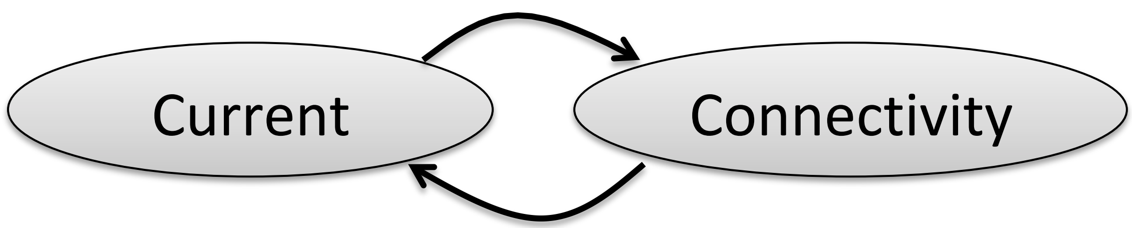
- Nonlinear
- Few ROIs

Connectome dynamics estimation

Estimation algorithm

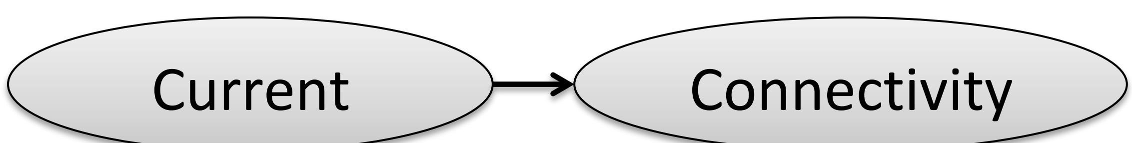
- Fukushima et al.'s method (2015)

  Current and connectivity are jointly estimated.



- Two-step method

  After estimating current, connectivity is estimated by the l2-regularized least squares method.



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How to learn VBMEG's usage

https://vbmeg.atr.jp/document/

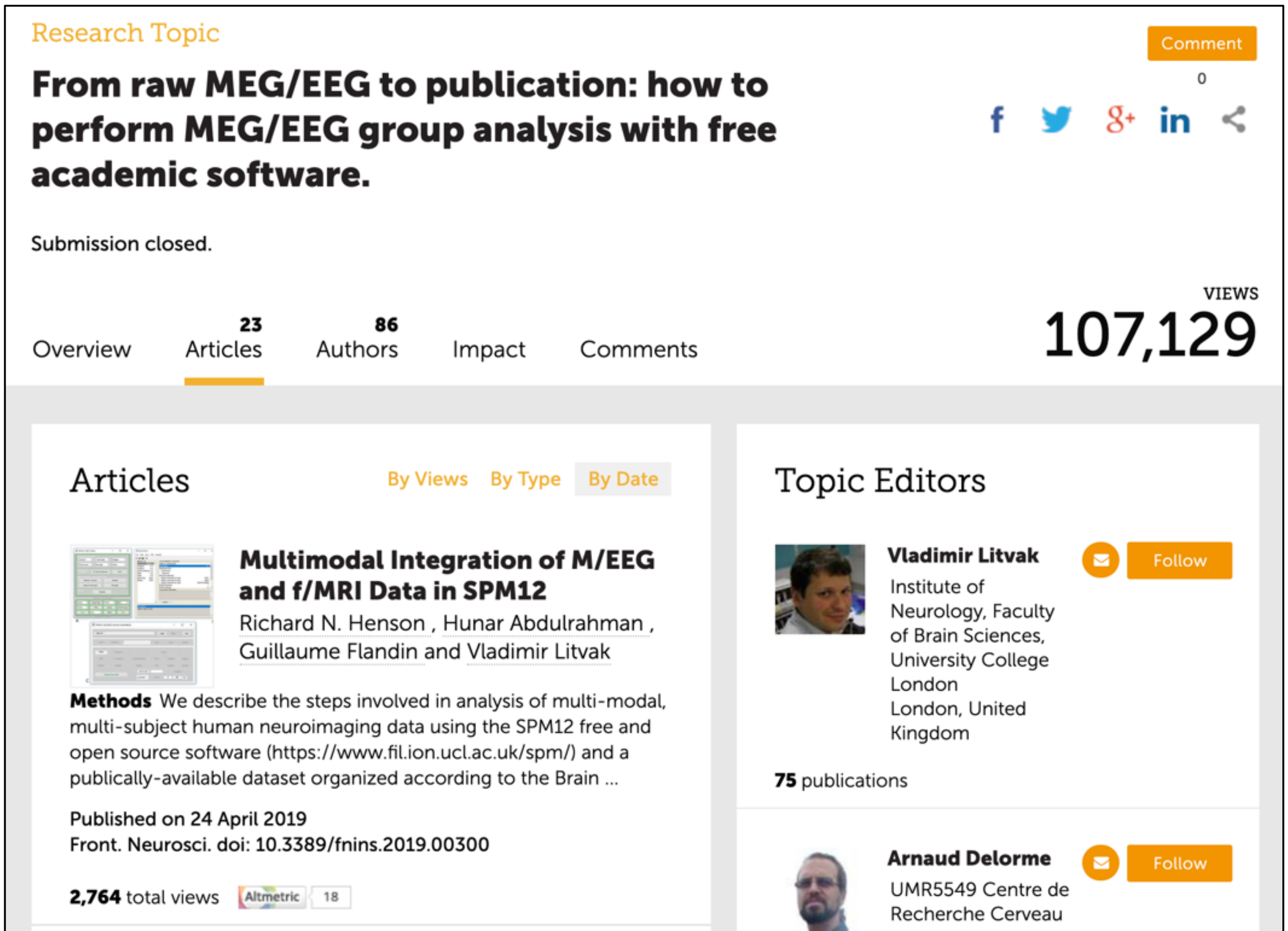
- Users manual — General manual of VBMEG (with function references and tips)

GUI
- Basic tutorial — MEG → Source current

Script
- Advanced tutorial — MEG/EEG → Source current → Connectome dynamics
- Easy VBMEG tutorial — EEG → Source current (without T1 image and sensor location)
- Neuromag tutorial — MEG/EEG → Source current → Group analysis → Connectome dynamics

Research topic in Front. Neurosci.

https://www.frontiersin.org/research-topics/5158/from-raw-megeeg-to-publication-how-to-perform-megeeg-group-analysis-with-free-academic-software#articles

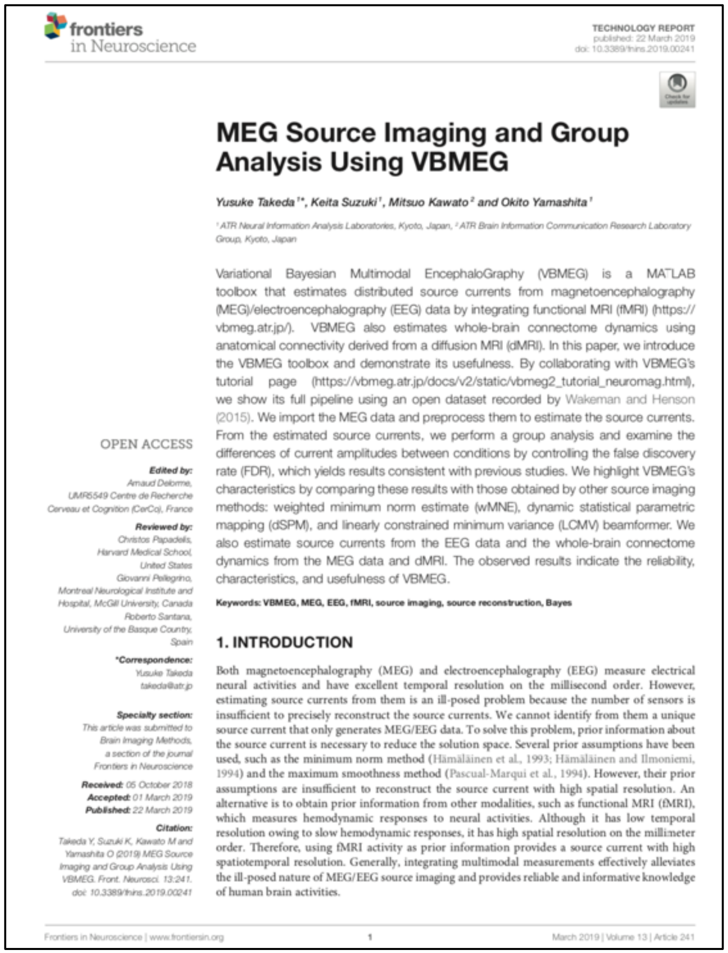


- VBMEG
- SPM12
- Brainstrom
- FieldTrip
- MNE
- etc.

Neuromag tutorial

https://www.frontiersin.org/articles/10.3389/fnins.2019.00241/full

https://vbmeg.atr.jp/docs/v2/static/vbmeg2_tutorial_neuromag.html


frontiers in Neuroscience

TECHNOLOGY REPORT
published: 22 March 2019
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MEG Source Imaging and Group Analysis Using VBMEG

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[1] ATR Neural Information Analysis Laboratories, Kyoto, Japan, [2] ATR Brain Information Communication Research Laboratory Group, Kyoto, Japan

Variational Bayesian Multimodal EncephaloGraphy (VBMEG) is a MATLAB toolbox that estimates distributed source currents from magnetoencephalography (MEG)/electroencephalography (EEG) data by integrating functional MRI (fMRI) (https://vbmeg.atr.jp/). VBMEG also estimates whole-brain connectome dynamics using anatomical connectivity derived from a diffusion MRI (dMRI). In this paper, we introduce the VBMEG toolbox and demonstrate its usefulness. By collaborating with VBMEG's tutorial page (https://vbmeg.atr.jp/docs/v2/static/vbmeg2_tutorial_neuromag.html), we show its full pipeline using an open dataset recorded by Wakeman and Henson (2015). We import the MEG data and preprocess them to estimate the source currents. From the estimated source currents, we perform a group analysis and examine the differences of current amplitudes between conditions by controlling the false discovery rate (FDR), which yields results consistent with previous studies. We highlight VBMEG's characteristics by comparing these results with those obtained by other source imaging methods: weighted minimum norm estimate (wMNE), dynamic statistical parametric mapping (dSPM), and linearly constrained minimum variance (LCMV) beamformer. We also estimate source currents from the EEG data and the whole-brain connectome dynamics from the MEG data and dMRI. The observed results indicate the reliability, characteristics, and usefulness of VBMEG.

Keywords: VBMEG, MEG, EEG, fMRI, source imaging, source reconstruction, Bayes

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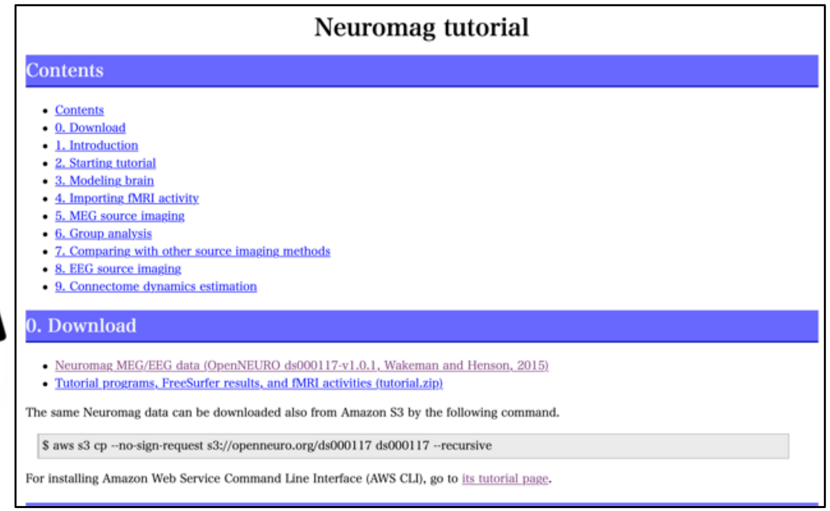
1. INTRODUCTION

Both magnetoencephalography (MEG) and electroencephalography (EEG) measure electrical neural activities and have excellent temporal resolution on the millisecond order. However, estimating source currents from them is an ill-posed problem because the number of sensors is insufficient to precisely reconstruct the source currents. We cannot identify from them a unique source current that only generates MEG/EEG data. To solve this problem, prior information about the source current is necessary to reduce the solution space. Several prior assumptions have been used, such as the minimum norm method (Hämäläinen et al., 1993; Hämäläinen and Ilmoniemi, 1994) and the maximum smoothness method (Pascual-Marqui et al., 1994). However, their prior assumptions are insufficient to reconstruct the source current with high spatial resolution. An alternative is to obtain prior information from other modalities, such as functional MRI (fMRI), which measures hemodynamic responses to neural activities. Although it has low temporal resolution owing to slow hemodynamic responses, it has high spatial resolution on the millimeter order. Therefore, using fMRI activity as prior information provides a source current with high spatiotemporal resolution. Generally, integrating multimodal measurements effectively alleviates the ill-posed nature of MEG/EEG source imaging and provides reliable and informative knowledge of human brain activities.

Frontiers in Neuroscience | www.frontiersin.org 1 March 2019 | Volume 13 | Article 241


Neuromag tutorial

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- 2. Starting tutorial
- 3. Modeling brain
- 4. Importing fMRI activity
- 5. MEG source imaging
- 6. Group analysis
- 7. Comparing with other source imaging methods
- 8. EEG source imaging
- 9. Connectome dynamics estimation

0. Download

- Neuromag MEG/EEG data (OpenNEURO ds000117-v1.0.1, Wakeman and Henson, 2015)
- Tutorial programs, FreeSurfer results, and fMRI activities (tutorial.zip)

The same Neuromag data can be downloaded also from Amazon S3 by the following command.

```
$ aws s3 cp --no-sign-request s3://openneuro.org/ds000117 ds000117 --recursive
```

For installing Amazon Web Service Command Line Interface (AWS CLI), go to its tutorial page.

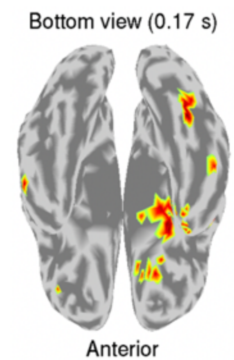
https://openneuro.org/datasets/ds000117/versions/1.0.1

Neuromag tutorial

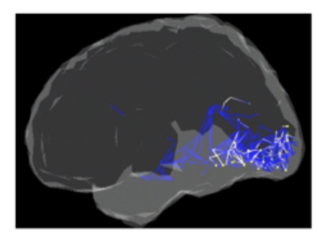
Neuromag MEG/EEG data

Source currents

Group analysis of source currents



Signal flow movie



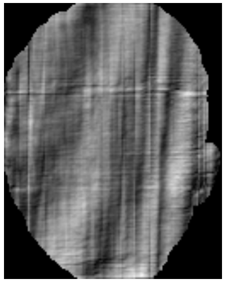
Neuromag MEG/EEG

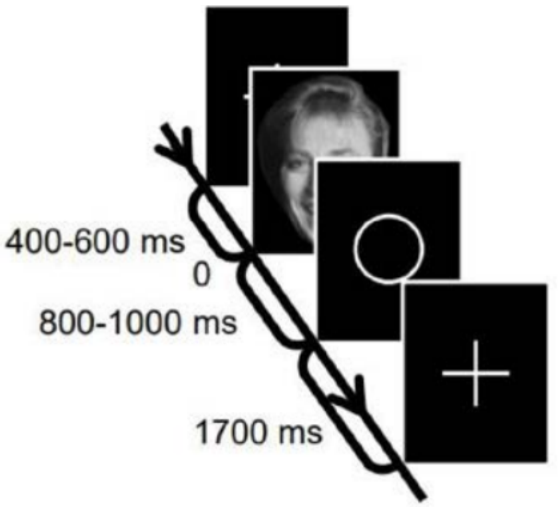
- Open dataset recorded by Wakeman and Henson (2015)
https://openneuro.org/datasets/ds000117/versions/1.0.1

- MEG and EEG were simultaneously recorded during a face recognition task by Neuromag system.

Face

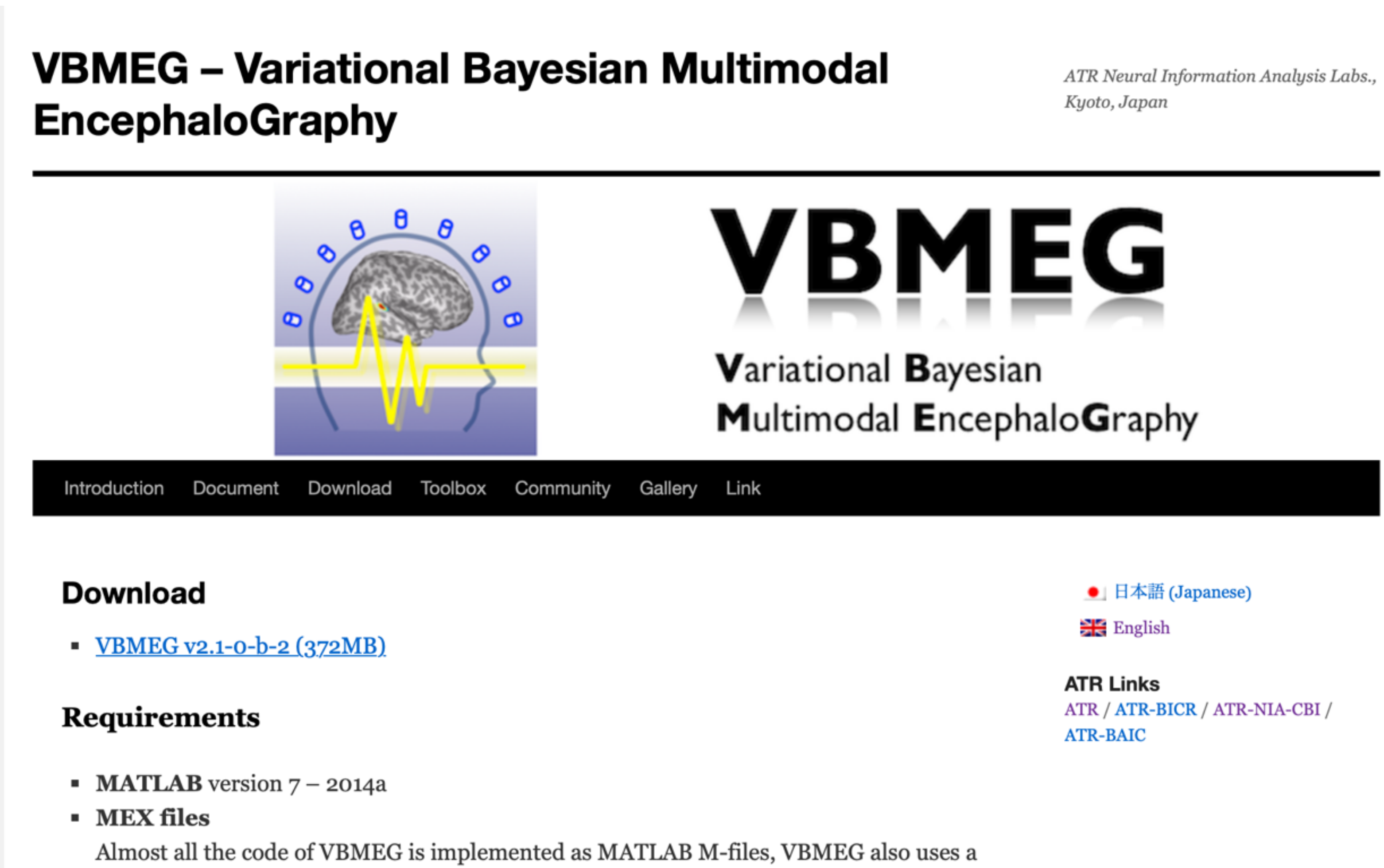
Scrambled





Starting VBMEG

https://vbmeg.atr.jp/download2/



VBMEG – Variational Bayesian Multimodal EncephaloGraphy

ATR Neural Information Analysis Labs., Kyoto, Japan

Introduction | Document | Download | Toolbox | Community | Gallery | Link

Download

- [VBMEG v2.1-0-b-2 (372MB)](https://vbmeg.atr.jp/download2/)

Requirements

- **MATLAB** version 7 – 2014a
- **MEX files**
  Almost all the code of VBMEG is implemented as MATLAB M-files, VBMEG also uses a

日本語 (Japanese)
English

ATR Links
ATR / ATR-BICR / ATR-NIA-CBI / ATR-BAIC

System requirements

OS : Linux

Software : MATLAB (R14–R2014a)

FreeSurfer4.2 or newer
SPM8
Modeling brain

Signal processing toolbox
M/EEG processing

MRtrix 0.2.1x
FSL 4.1 or newer
Connectome dynamics estimation

Procedure

- Brain modeling
- Import data
- Estimate source current from MEG
- Group analysis
- Estimate source current from EEG
- Estimate source current from MEG and EEG
- Estimate connectome dynamics

Procedure

- Brain modeling
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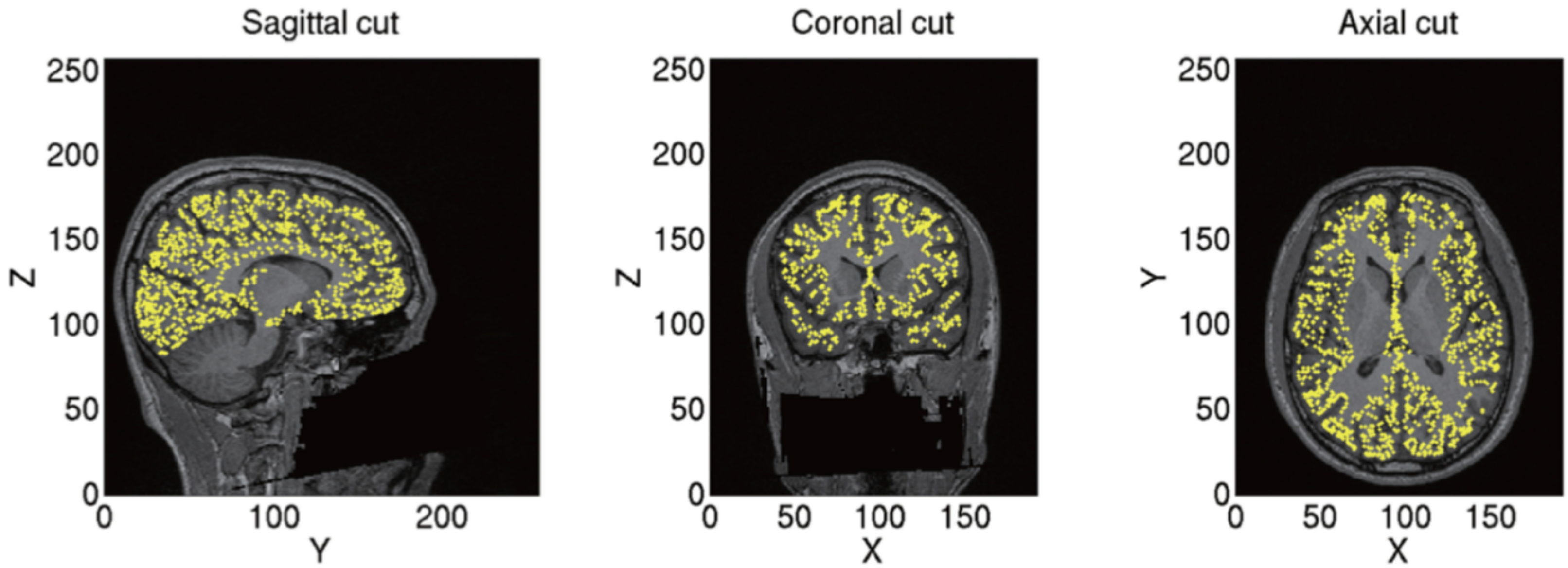
- Estimate connectome dynamics

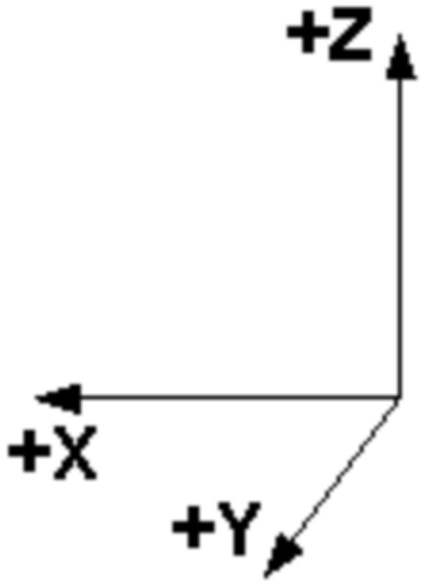
Brain modeling

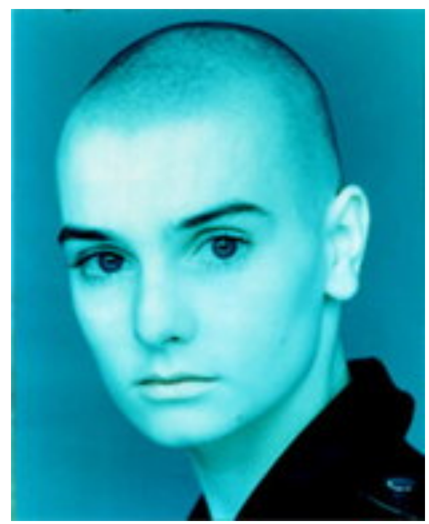
1. Import T1 image (convert coordinate system to that of VBMEG)
2. Extract cortical surface by FreeSurfer
3. Define sources on cortical surface



VBMEG's coordinate system

RAS, origin = center of T1



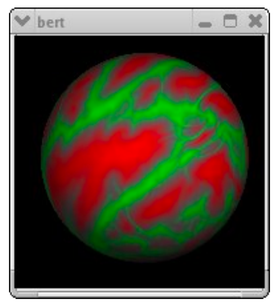


+X = Right
+Y = Anterior
+Z = Superior

How to define sources

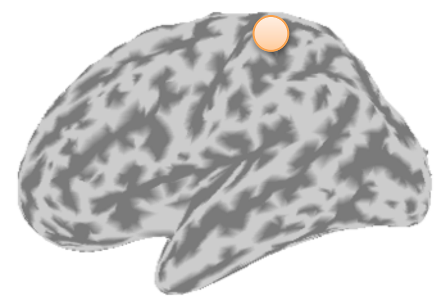
Standard brain
(MNI-ICBM152)

FreeSurfer's
sphere coordinate

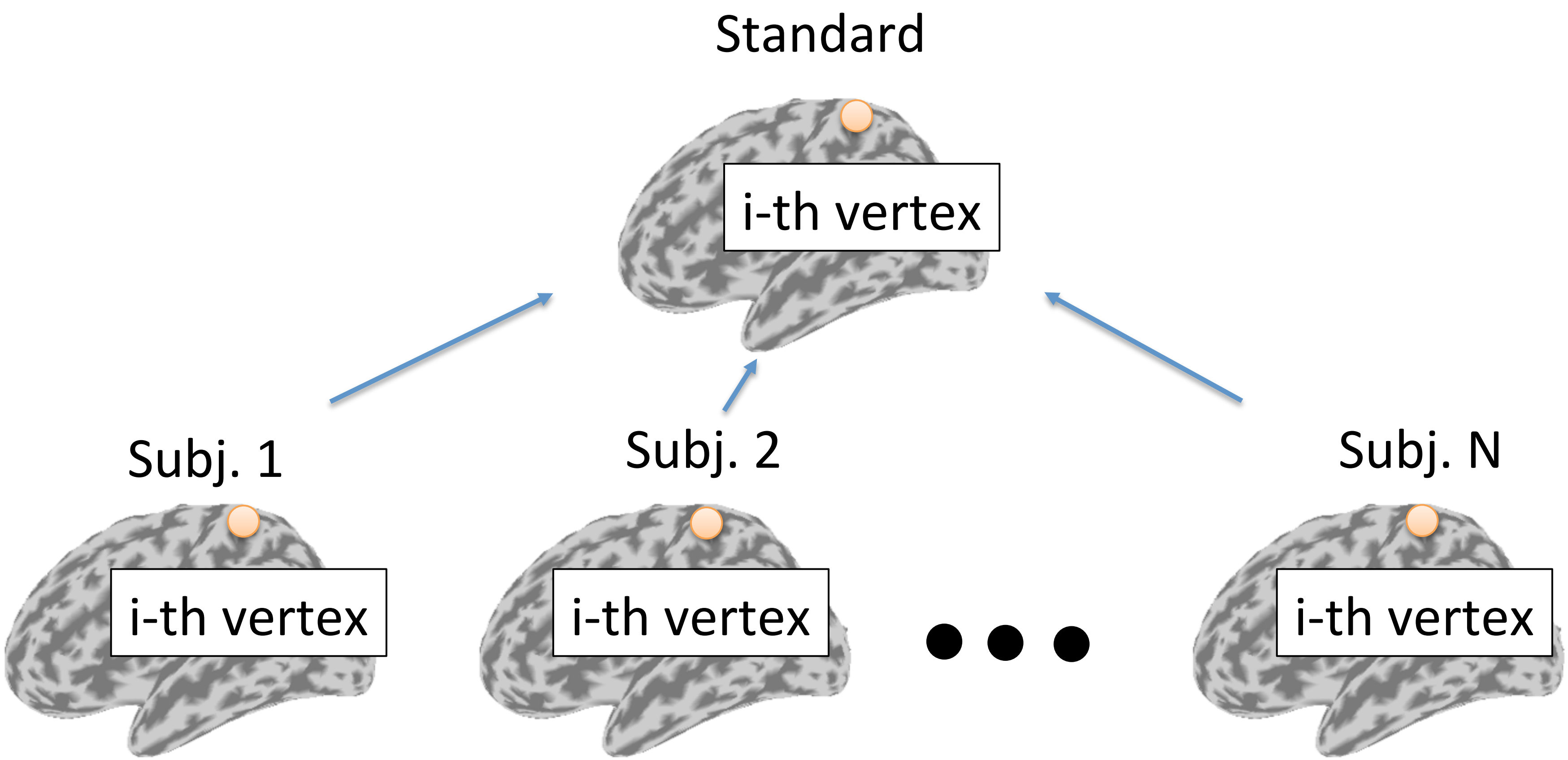


Mapping

Subject brain



Source locations are consistent across subjects



We can proceed to group analyses without any transformation.

Procedure

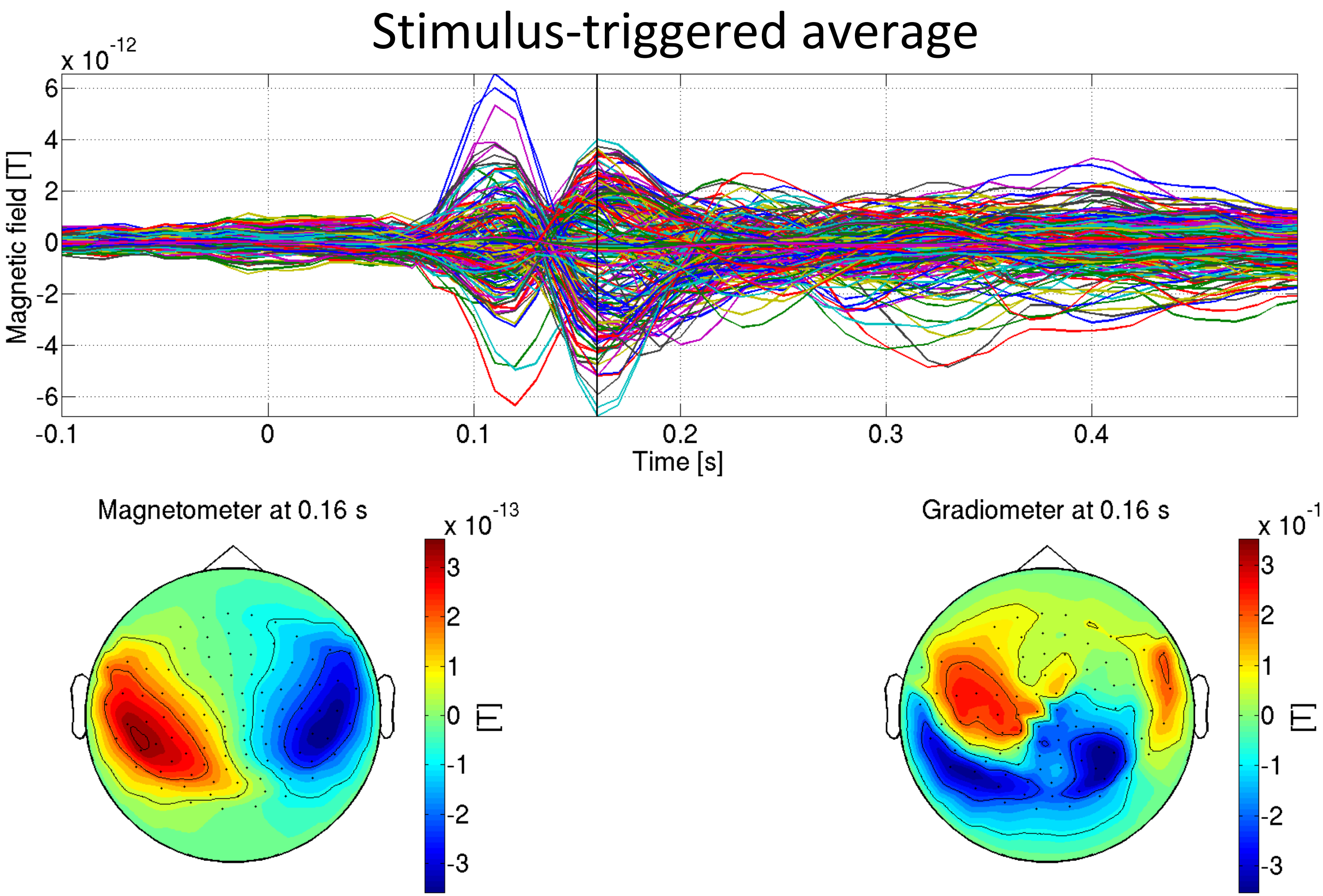
- Brain modeling
- Import data
- Estimate source current from MEG
- Group analysis
- Estimate source current from EEG
- Estimate source current from MEG and EEG
- Estimate connectome dynamics

Importing data

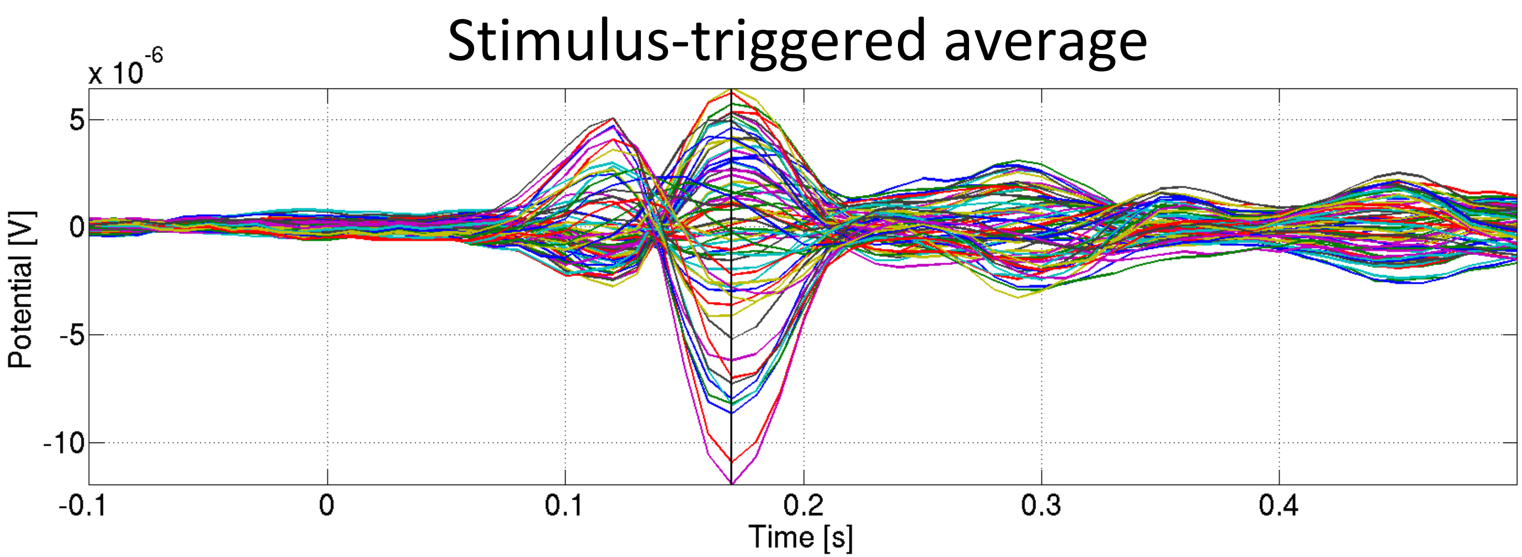
Supported format: Yokogawa and Neuromag MEG
Biosemi and Brainamp EEG

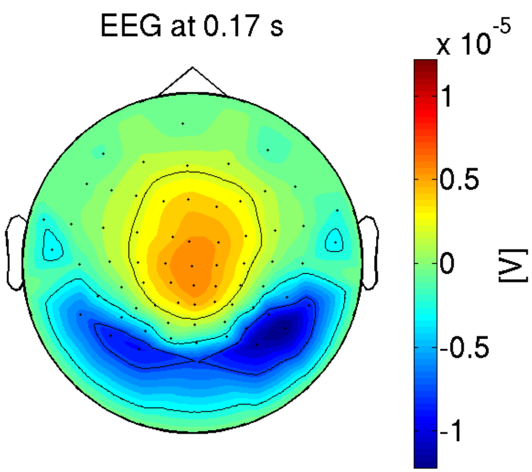
If you have any requests for the supported format, please inform us.

Preprocessed MEG



Preprocessed EEG





Procedure

- Brain modeling
- Import data
- Estimate source current from MEG
- Group analysis
- Estimate source current from EEG
- Estimate source current from MEG and EEG
- Estimate connectome dynamics

Estimate source current from MEG

Important parameters

- bayes_parm.prior_weight
- bayes_parm.twin_meg
- bayes_parm.twin_noise
- bayes_parm.trial_average

bayes_parm.prior_weight

α-step

fMRI

Data

$$\alpha_i^{-1} = w\bar{\alpha}_{0,i} + (1 - w)\langle \frac{1}{T}\sigma \sum_{t=1}^{T} J_i^2(t) \rangle$$

Prior weight $w = \frac{\gamma_0}{\gamma_0 + \frac{T}{2}}$ $(0 \leq w \leq 1)$

(Hyperparameter)

In Neuromag tutorial, bayes_parm.prior_weight = 0.3

bayes_parm.twin_meg

α-step

fMRI

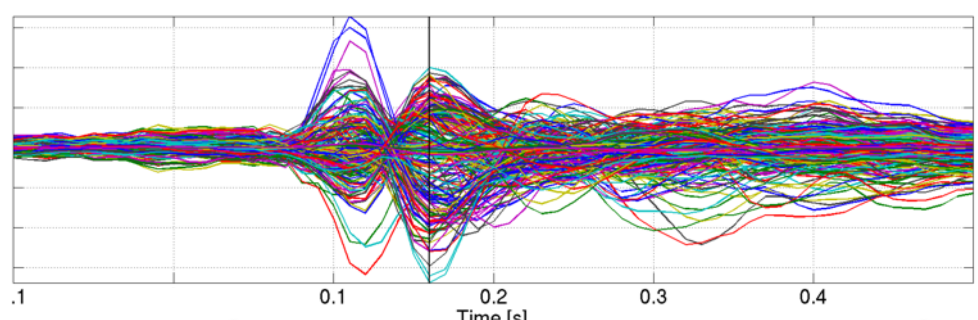
Data

$$\alpha_i^{-1} = w\bar{\alpha}_{0,i} + (1-w)\langle \frac{1}{T}\sigma \sum_{t=1}^{T} J_i^2(t) \rangle$$

Prior weight
(Hyperparameter)

$$w = \frac{\gamma_0}{\gamma_0 + \frac{T}{2}} \qquad (0 \le w \le 1)$$

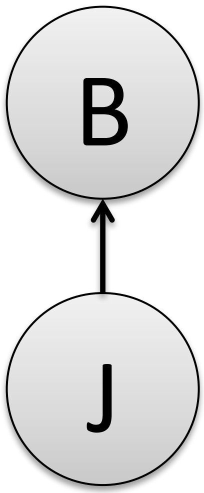
In Neuromag tutorial



0 ⟷ 0.5 s

bayes_parm.twin_noise

MEG
EEG

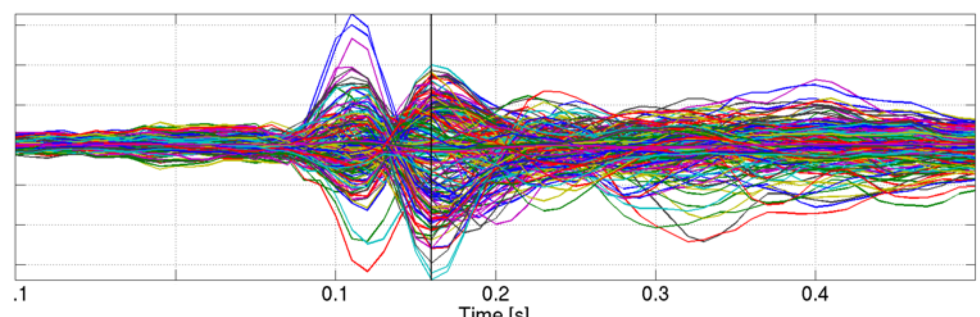


Current

$$P(\boldsymbol{B}|\boldsymbol{J}) \propto \exp\left(-\frac{1}{2}\beta||\boldsymbol{B}-\boldsymbol{G}\cdot\boldsymbol{J}||^2\right)$$

Observation noise covariance

In Neuromag tutorial



-0.3 s ⟷ 0

bayes_parm.trial_average

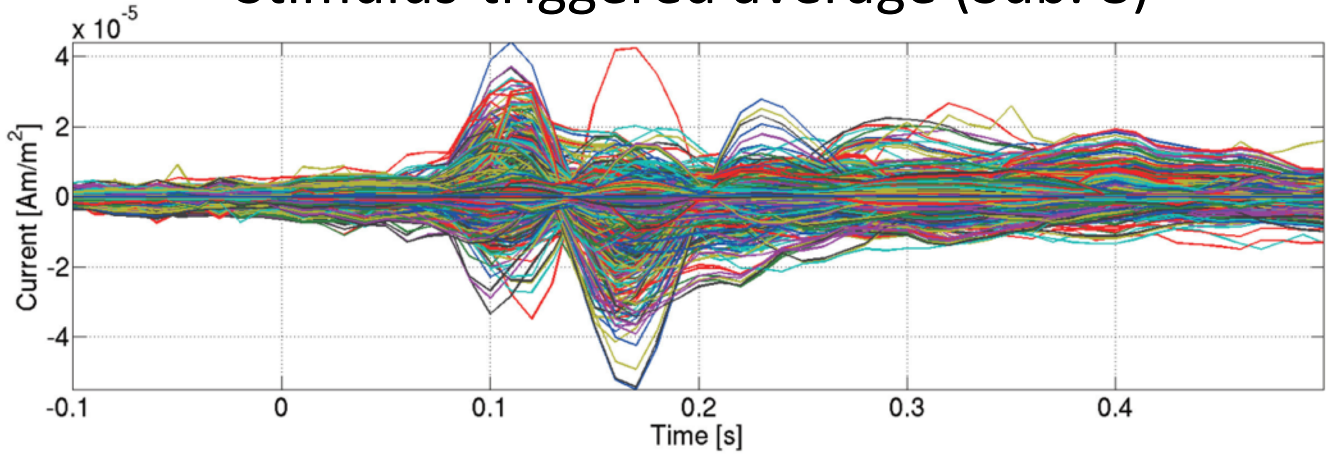
This parameter determines whether noise covariance and current variances are calculated from trial-averaged data.

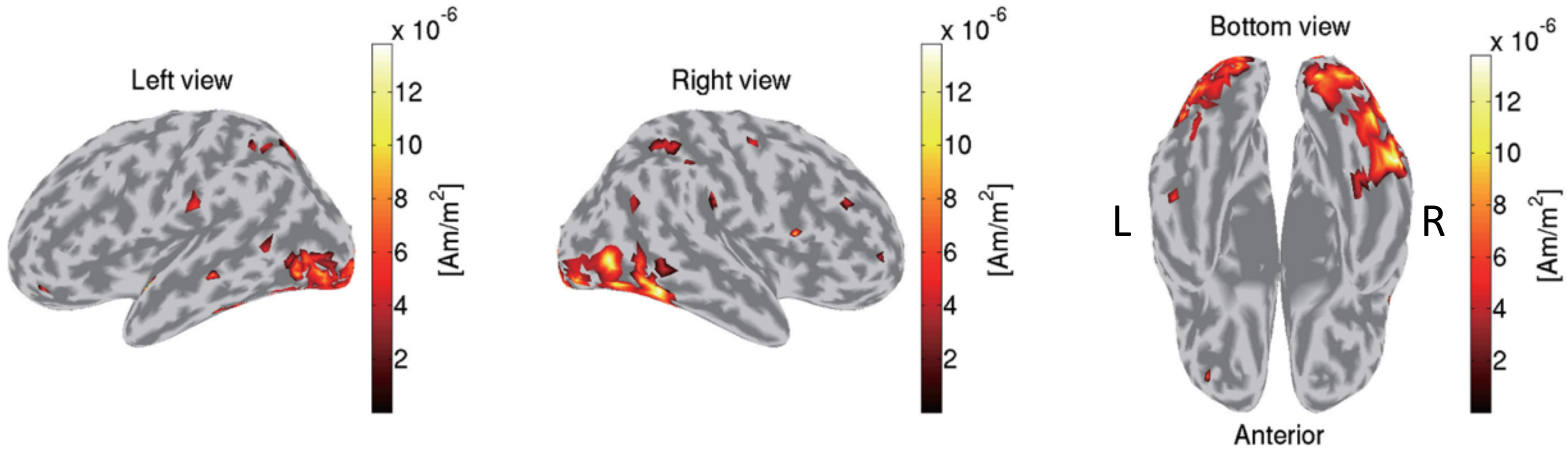
We highly recommend

bayes_parm.trial_average = OFF (default)

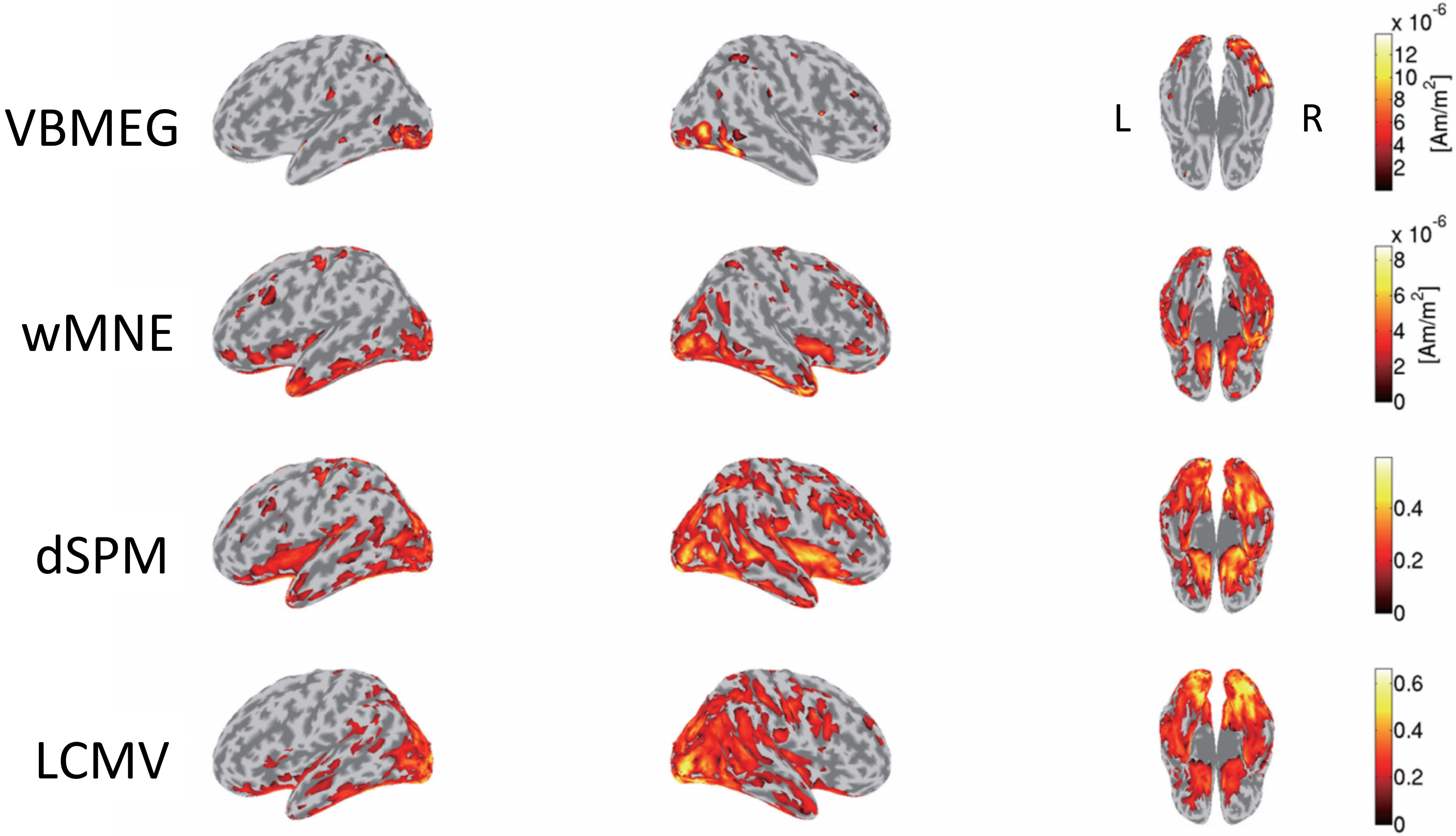
Estimated source current from MEG

Stimulus-triggered average (Sub. 8)





Comparison with other methods



Thanks to fMRI and ARD priors, VBMEG's source current is localized around visual processing areas.

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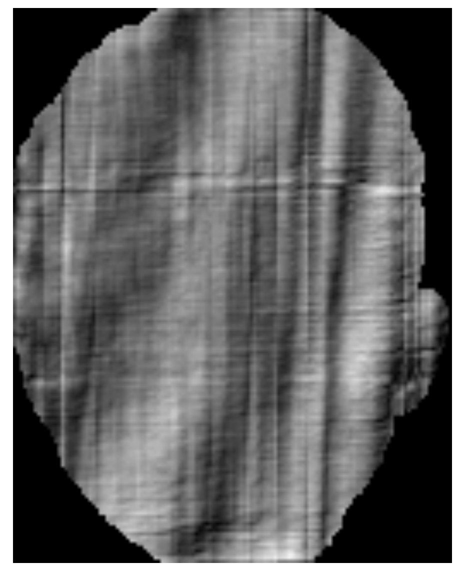
Group analysis

Detect face-selective activity

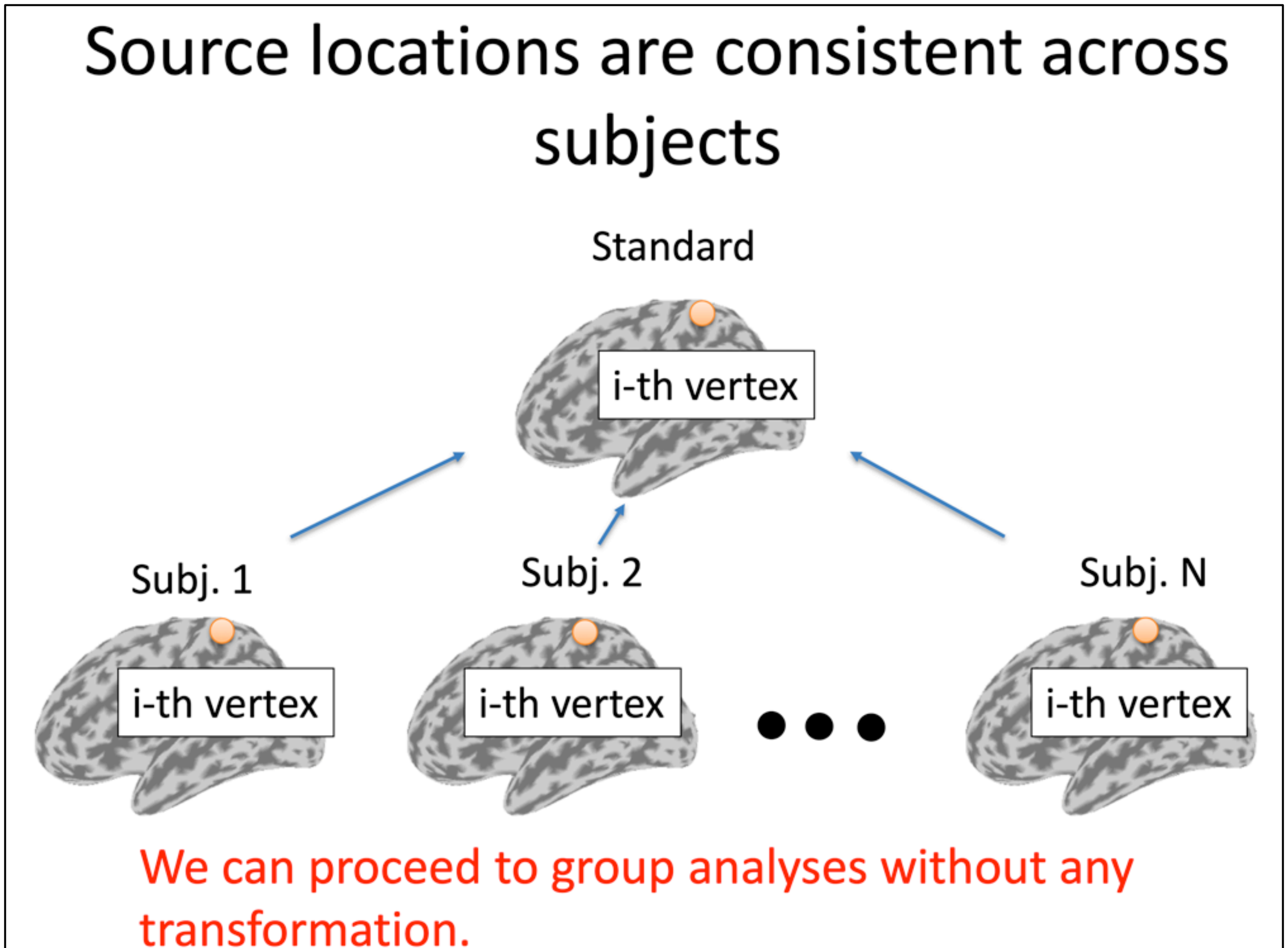
Face

–

Scrambled



No transformation is necessary



Caution

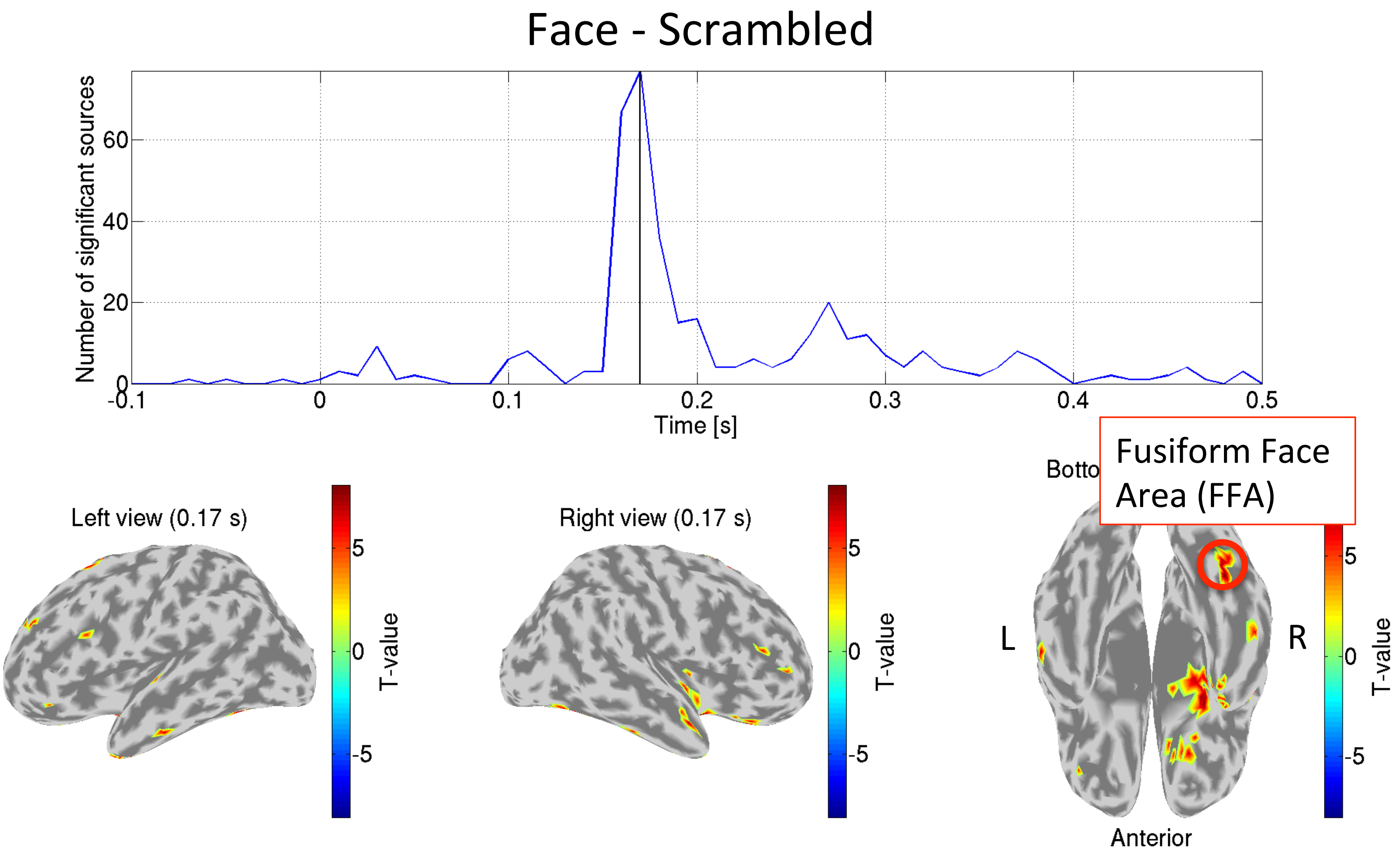
Absolute values (or powers) of currents should be used.

In Neuromag tutorial

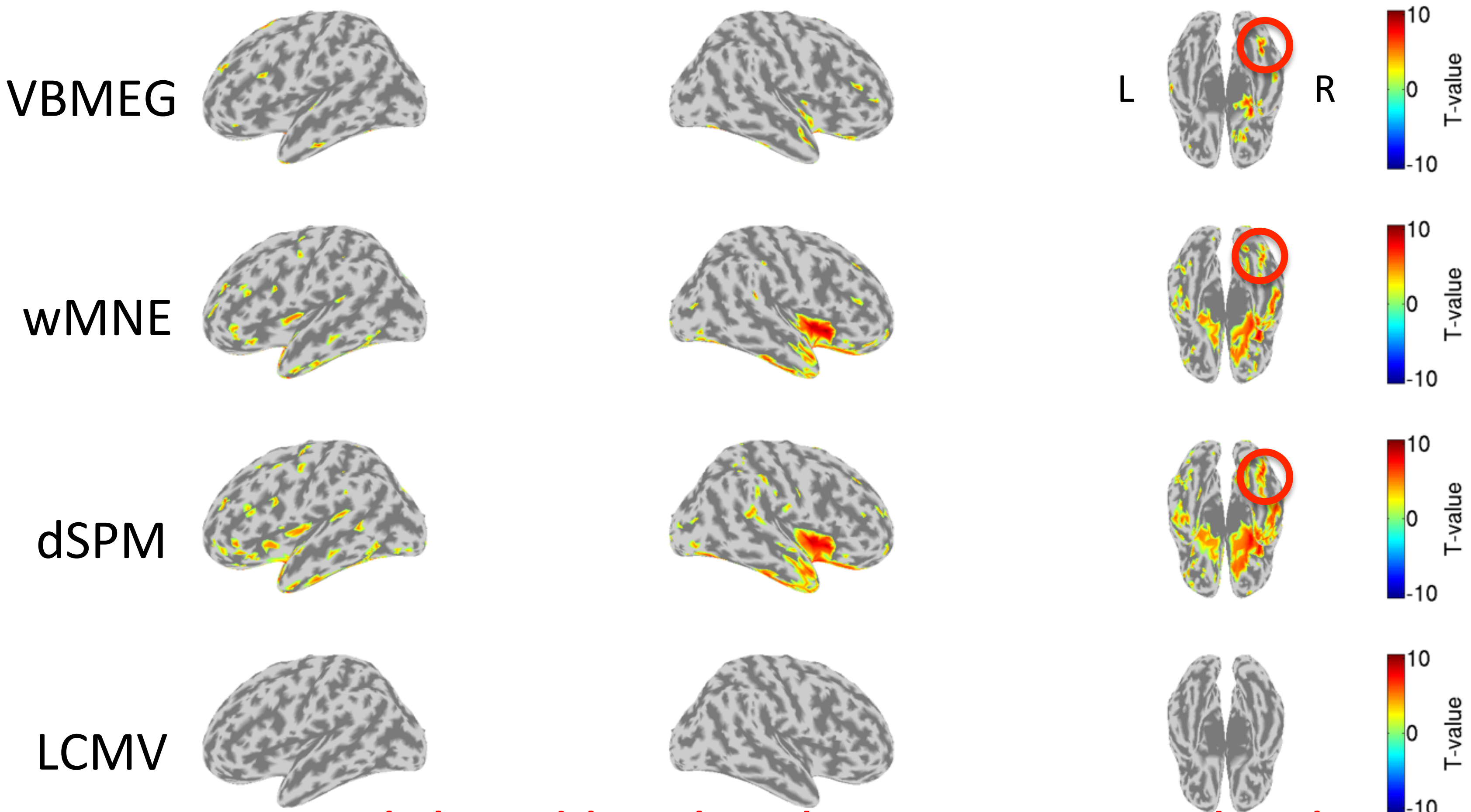
- Calculate stimulus-triggered average of currents
- Normalize it so that baseline period (-0.3–0 s) has mean 0 and SD 1
- Calculate amplitude

- For each source and time, compared 16 subjects' amplitudes between face and scrambled conditions
- Multiple comparison problem is controlled by False Discovery Rate (FDR)

Group analysis result



Comparison with other methods



VBMEG exhibited localized activity around right FFA. This might be because integrating fMRI suppressed signal leakage.

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Estimating source current from EEG

Caution

We need to take a reference from EEG and its leadfield.

In Neuromag tutorial

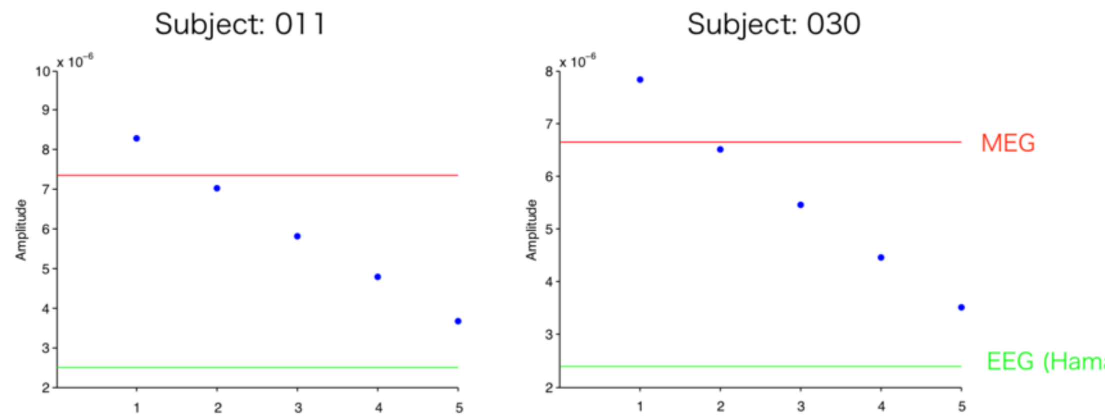
```
% Take common average
> basis_file = fullfile(p.proj_root, basis_parm.basis_file);
> load(basis_file, 'basis’)
> for v = 1:size(basis, 1);
    basis(v, :) = basis(v, :)-mean(basis(v, :), 2);
> end
> vb_save(basis_file, 'basis');
```

Estimating source current from EEG

Default conductivities are set to

Brain, Skull, Scalp
0.62, 0.03, 0.62 S/m

Estimated current sources day1 (14 deg/s)

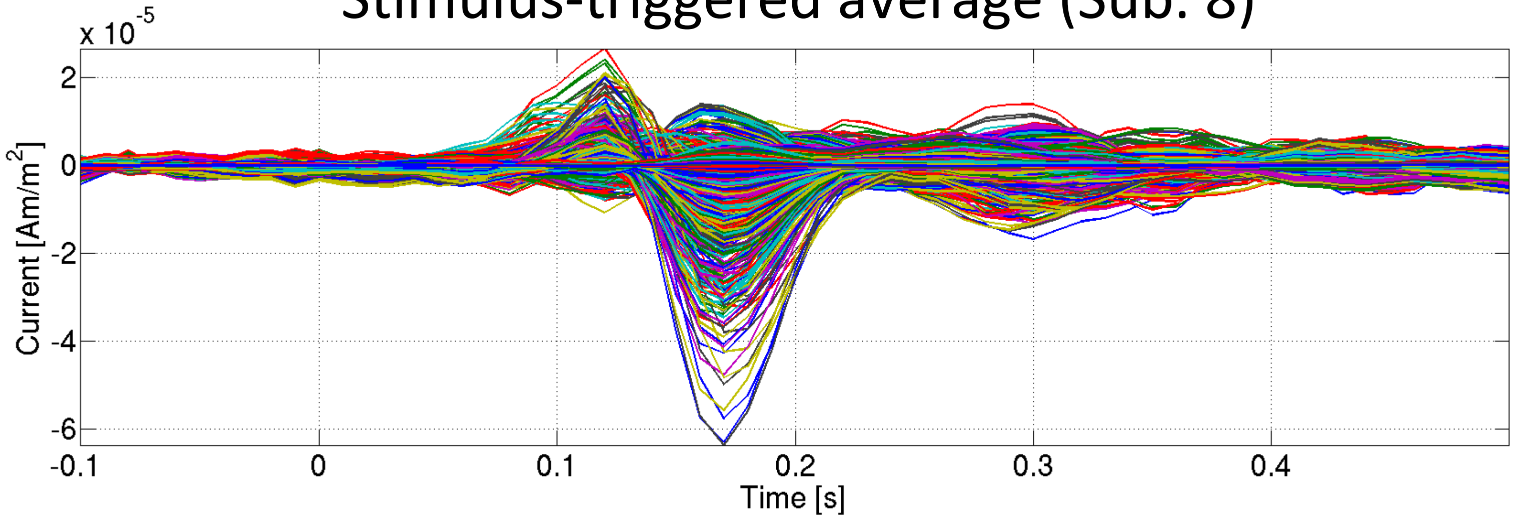


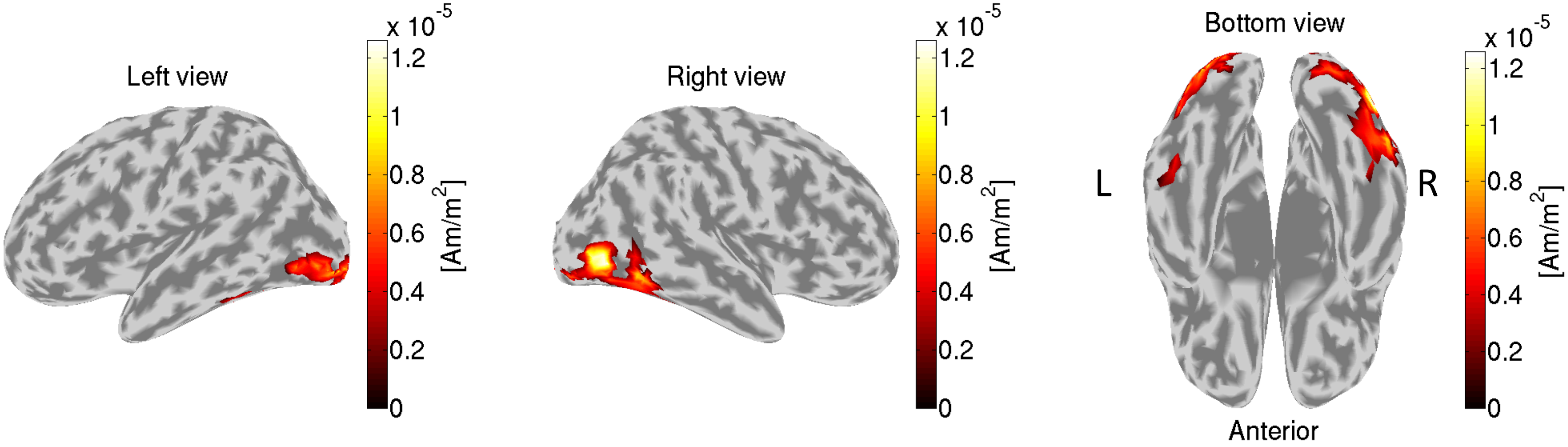
	brain	skull	skin
VBMEG default (brainstorm)	1.0	0.0125	1.0
1	0.67	0.026	0.67
2	0.62	0.030	0.62
3	0.55	0.034	0.55
4	0.48	0.038	0.48
5	0.40	0.042	0.40
Hamalainen	0.3	0.06	0.3

From Fujiwara-san’s slide

Estimated source current from EEG

Stimulus-triggered average (Sub. 8)





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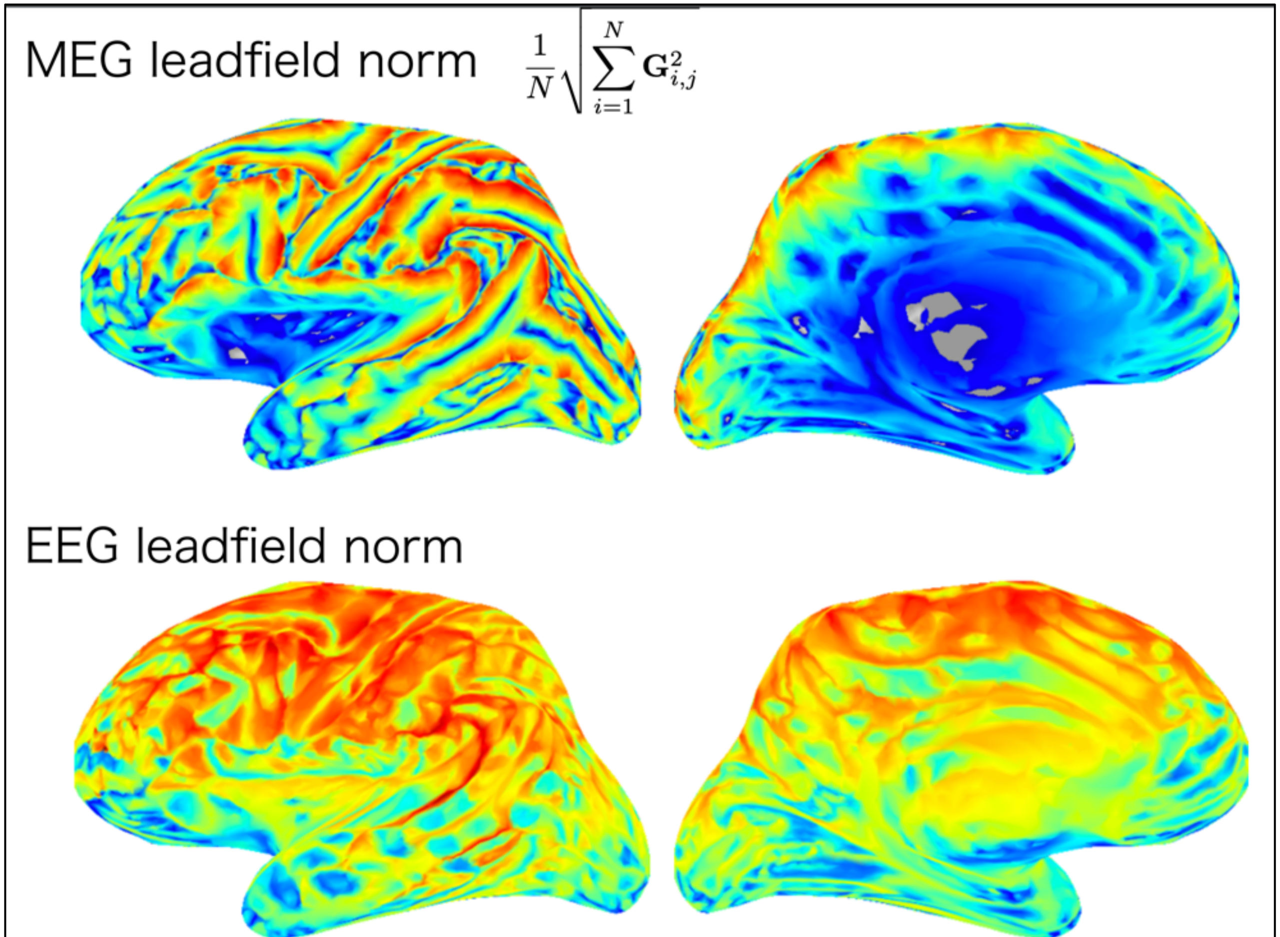
Estimating source current from MEG and EEG

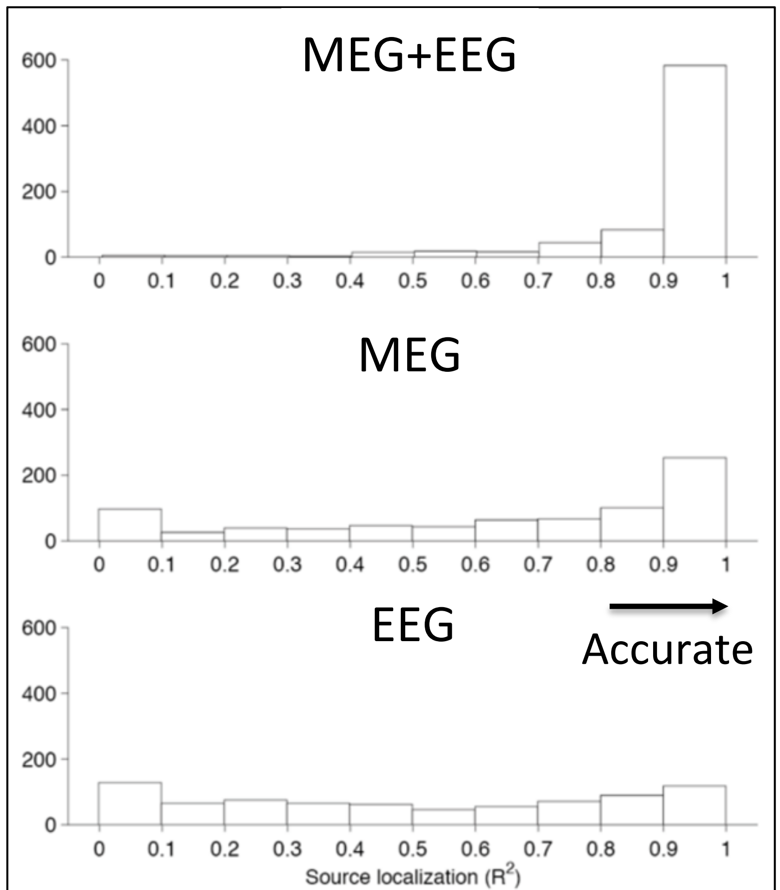
MEG and EEG have different sensitivities.



From Fujiwara-san's slide

Estimating source current from MEG and EEG

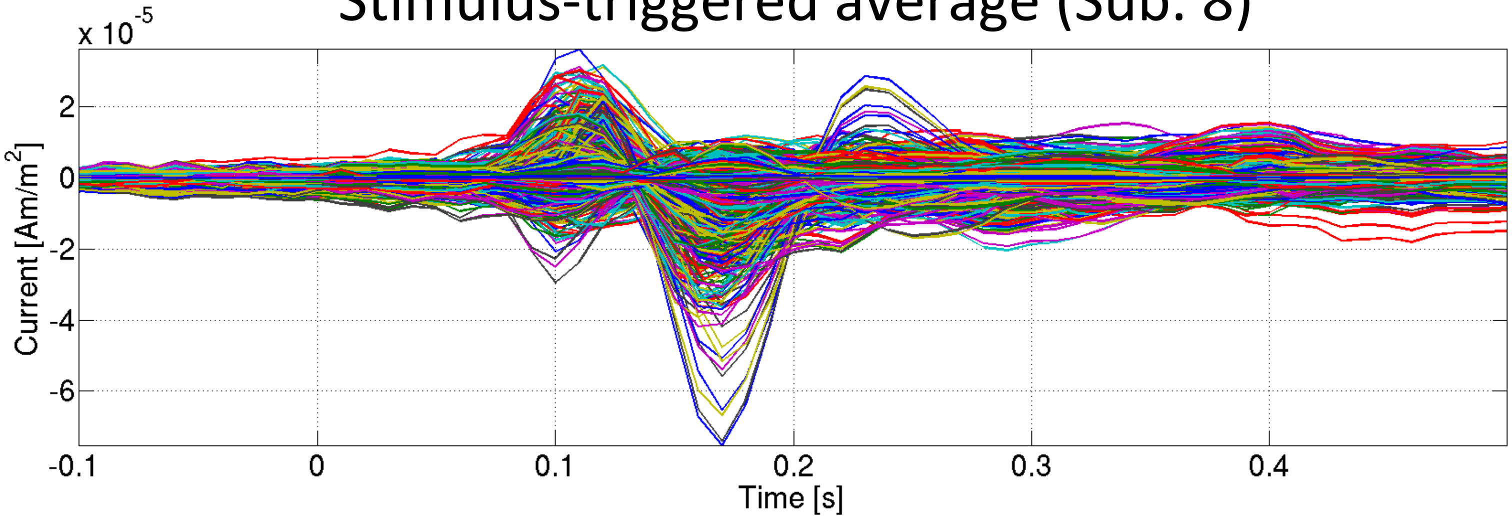
Combining MEG and EEG improves the estimation accuracy of source current.

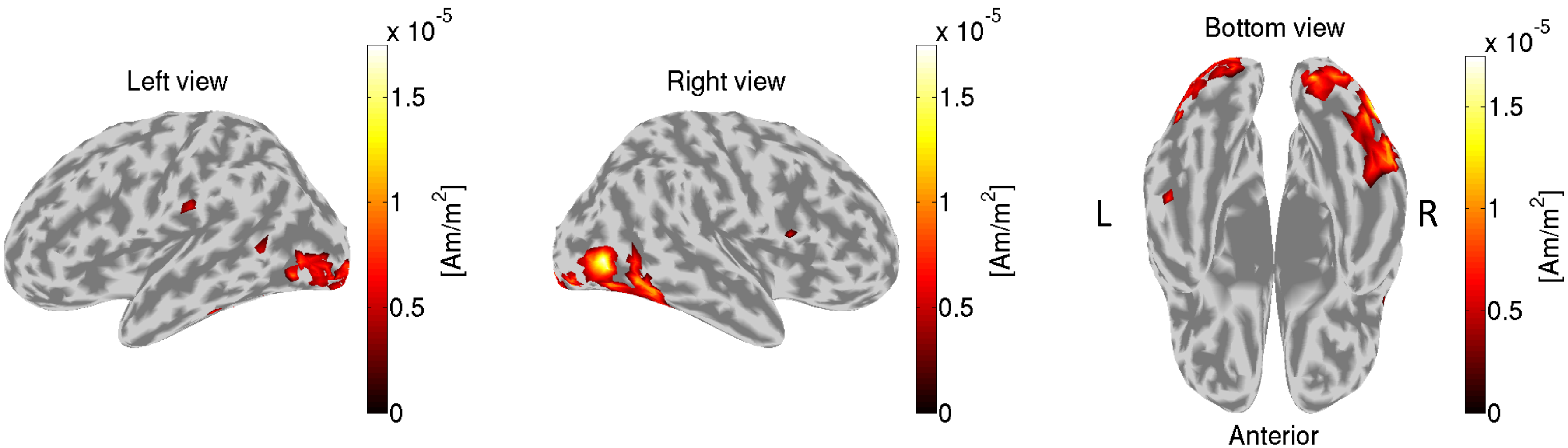


From Fujiwara-san's slide

Estimated source current from MEG and EEG

Stimulus-triggered average (Sub. 8)





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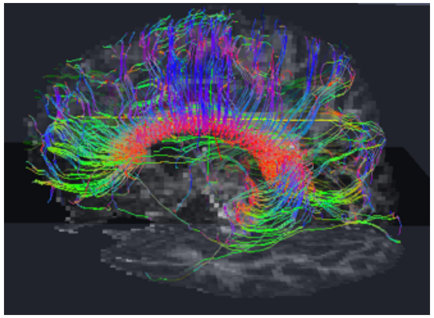
Estimate connectome dynamics

1. Estimate anatomical connectivity



2. Estimate connectome dynamics

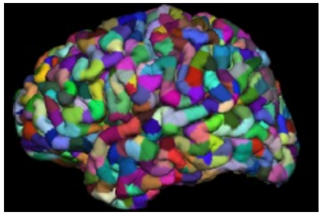
$$z_{n,t} = \sum_{d=1}^{p} a_{nd} z_{n,t-d} + \sum_{v \in C_n} b_{nv} z_{v,t-\Delta_{v_n}} + \epsilon_n \qquad \Delta_{v_n} = \frac{L_{v,n}}{c} + D$$

Estimate anatomical connectivity

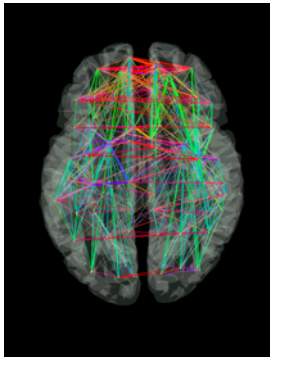
Necessary software: MRtrix 0.2.1x
FSL 4.1 or newer

Procedure

1. Parcellation



2. Fiber tracking



3. Thresholding

Estimate connectome dynamics

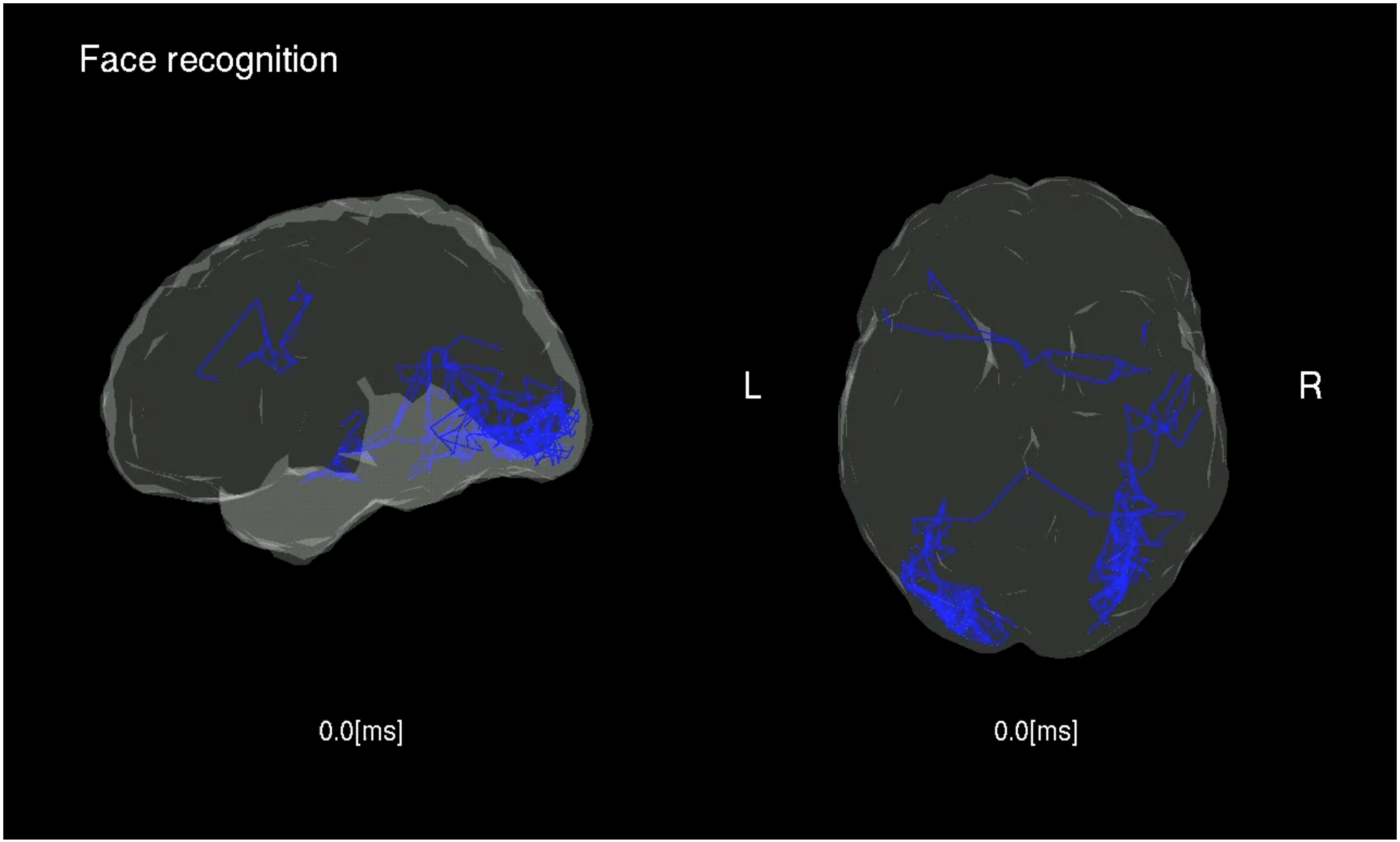
1. Estimate connectome dynamics
   by l2-regularized least squares method

$$z_{n,t} = \sum_{d=1}^{p} a_{nd} z_{n,t-d} + \underline{\sum_{v \in C_n} b_{nv} z_{v,t-\Delta_{v_n}}} + \epsilon_n \qquad \Delta_{v_n} = \frac{L_{v,n}}{c} + D$$

(default) p = 2, c = 6 m/s, D = 27 ms

2. Generate a movie displaying signal flows

Generated movie



Contents

- Overview
- Theory
- Usage
- FAQ and News

FAQ and News

- I don’t have fMRI
- How to determine prior weight
- Brodmann area labels are strange
- Optically-pumped magnetometer

FAQ and News

- I don’t have fMRI
- How to determine prior weight
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I don't have fMRI

- Use uniform prior by setting

  bayes_parm.act_key = 'Uniform'

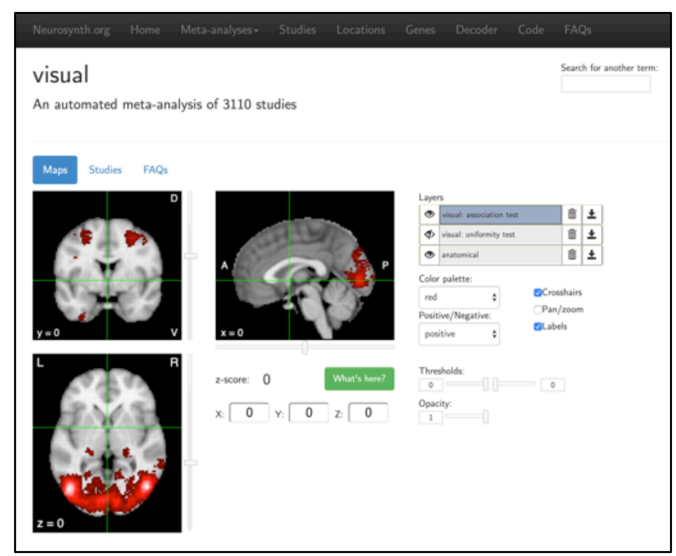
  bayes_parm.prior_weight = very small value

  (e.g. 0.0001)

Or

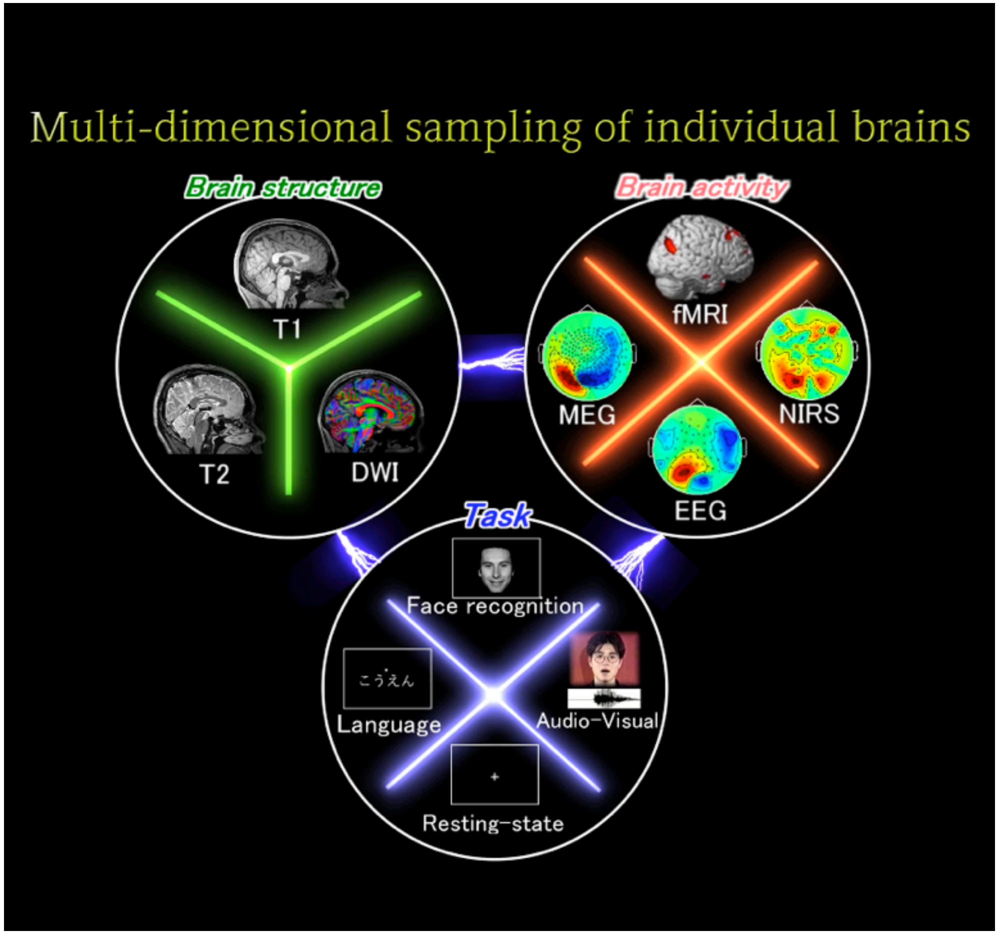
- Use meta-analysis results of fMRI studies

  Suzuki-kun's talk



I don't have any data～

Please use our dataset (n=5)!



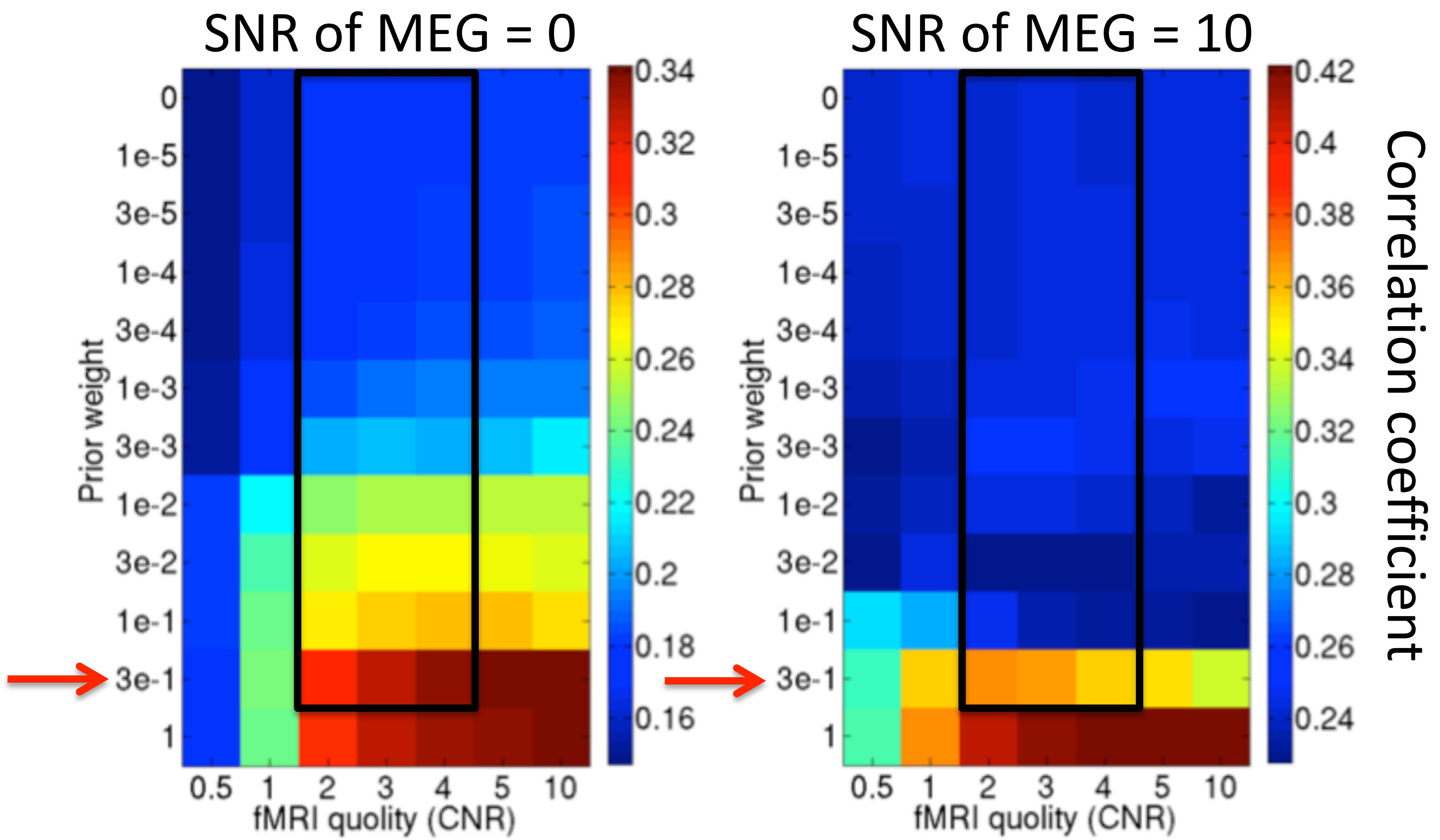
https://bicr-resource.atr.jp/mulds/

FAQ and News

- I don’t have fMRI
- How to determine prior weight
- Brodmann area labels are strange
- Optically-pumped magnetometer

How to determine prior weight

Simulation test conducted by Suzuki-kun



prior weight = 0.3 is good

How to determine prior weight

Practically, try prior weights from 0.01 to 0.3 by few subjects' data and determine the prior weight which provide reasonable result.

FAQ and News

- I don’t have fMRI
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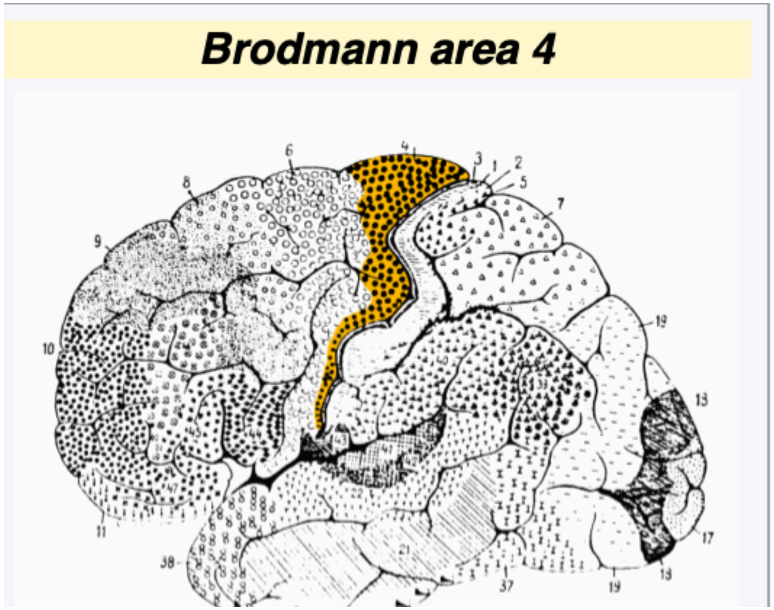
- Optically-pumped magnetometer

Brodmann area labels are strange

BA4 in
*_brodmann.area.mat

BA4

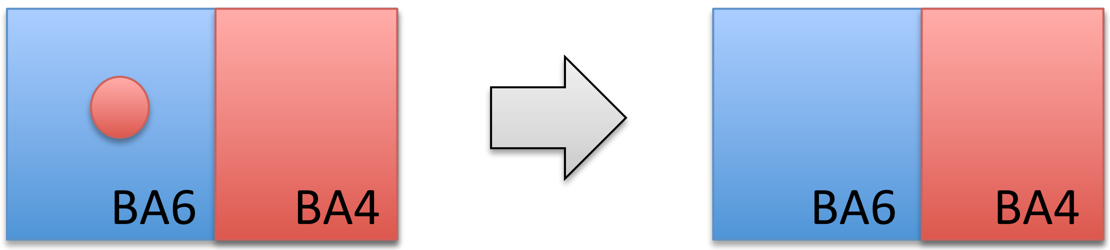


(https://en.wikipedia.org/wiki/Brodmann_area_4)

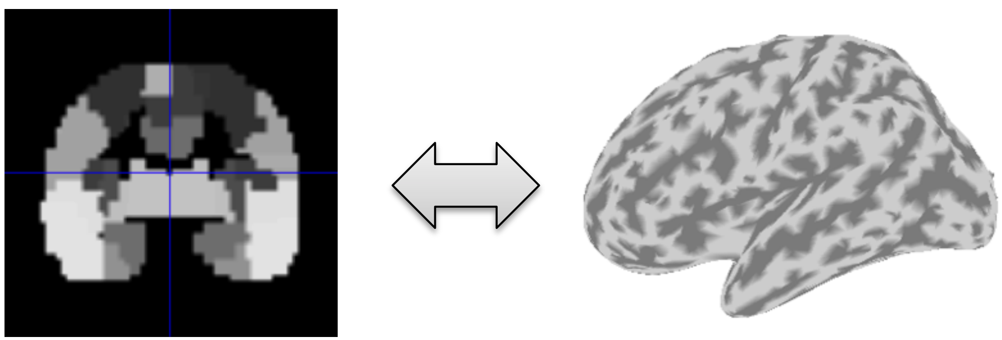
- Left-right asymmetry
- Bad location

Causes

- Removing island made scattered area small



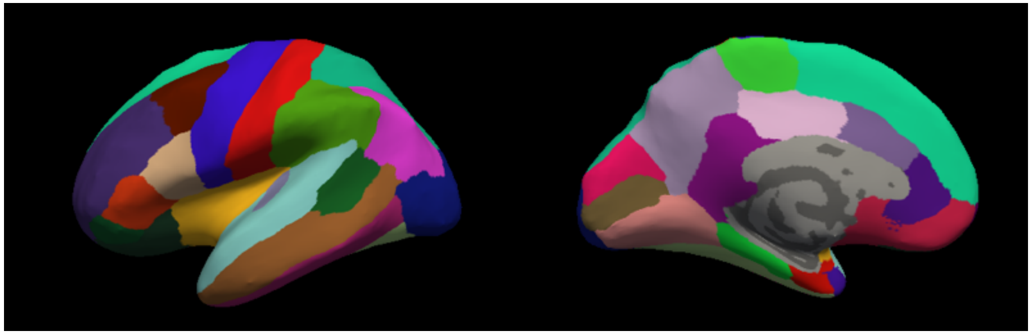
- Bad matching between voxel and surface



Solution

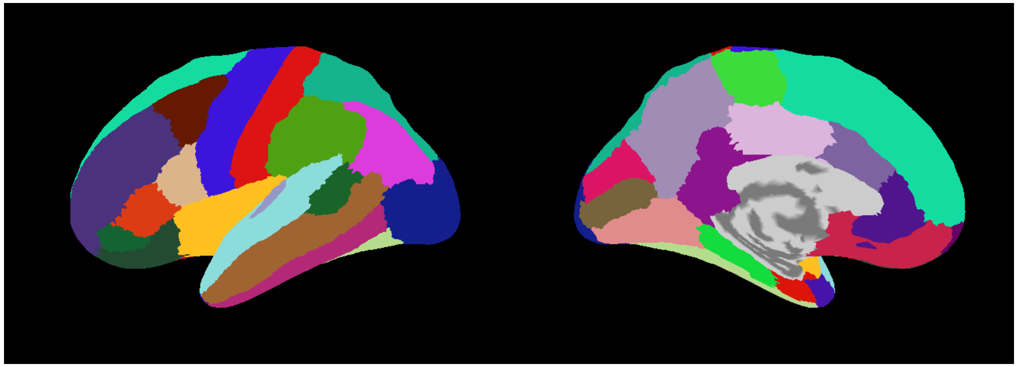
Import FreeSurfer's label file

FreeSurfer's label file
(aparc.annot)



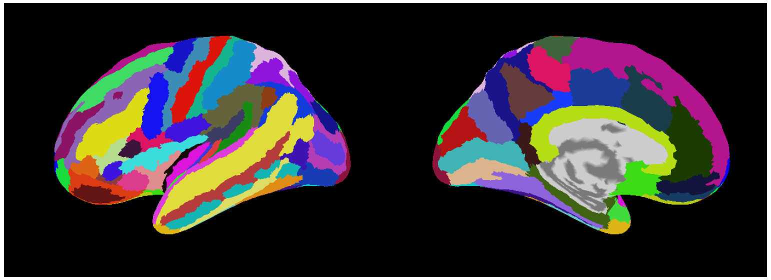
Import

VBMEG brain model
(80000 vertices)

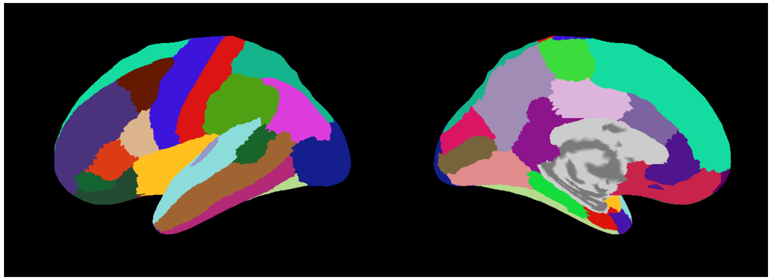


New area files in new VBMEG

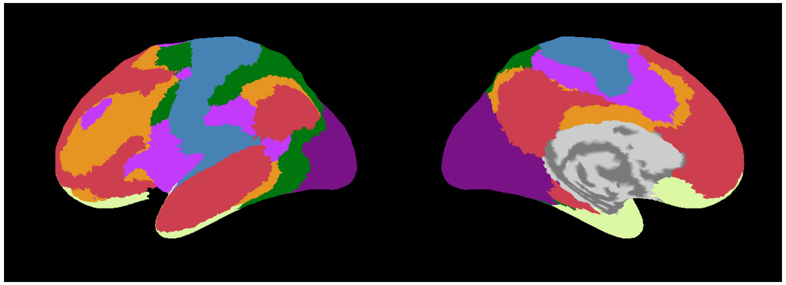
*_Destrieux.area.mat



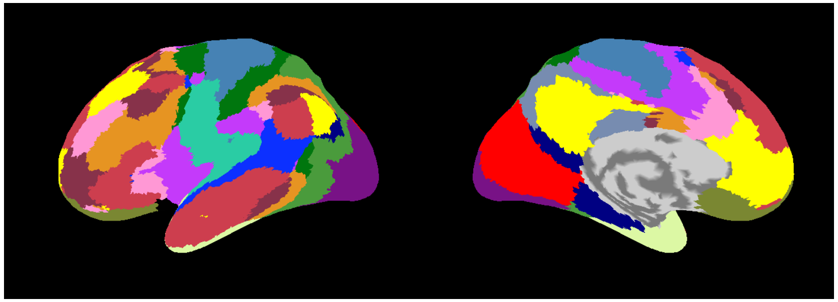
*_Desikan-Killany.area.mat



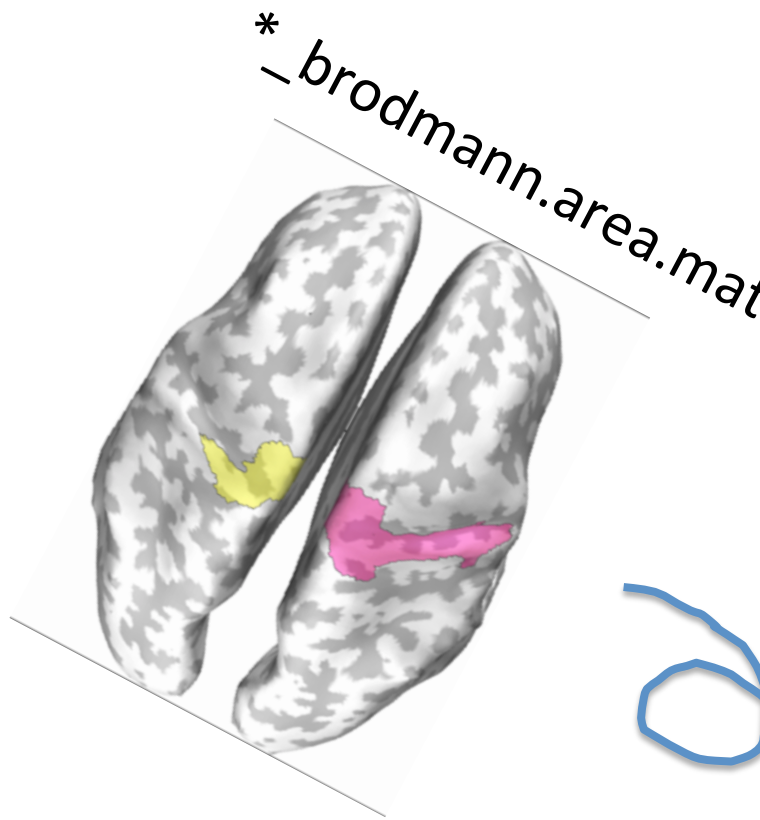
*_Yeo2011_7Networks_N1000
.area.mat



*_Yeo2011_17Networks_N100
0.area.mat



To be removed area file



FAQ and News

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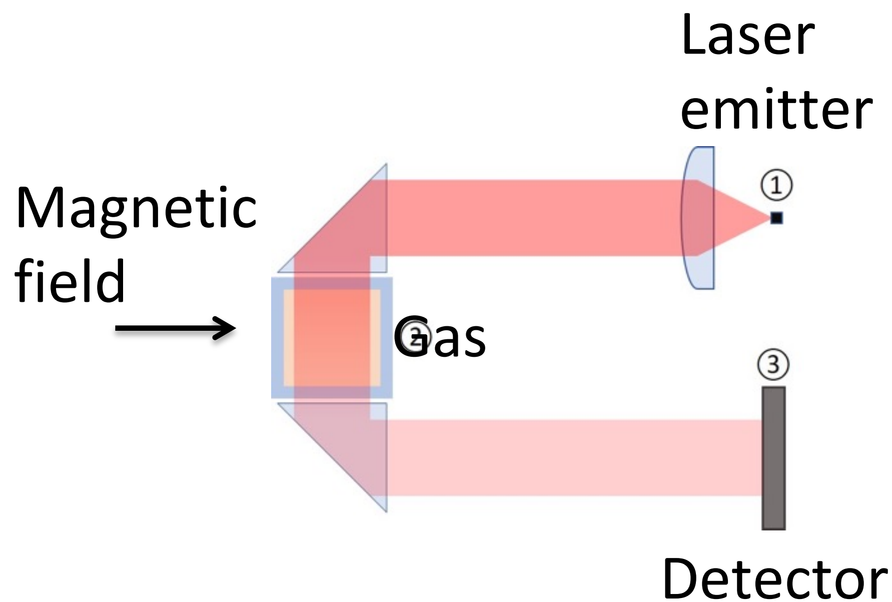
Optically-Pumped Magnetometer

Sensor



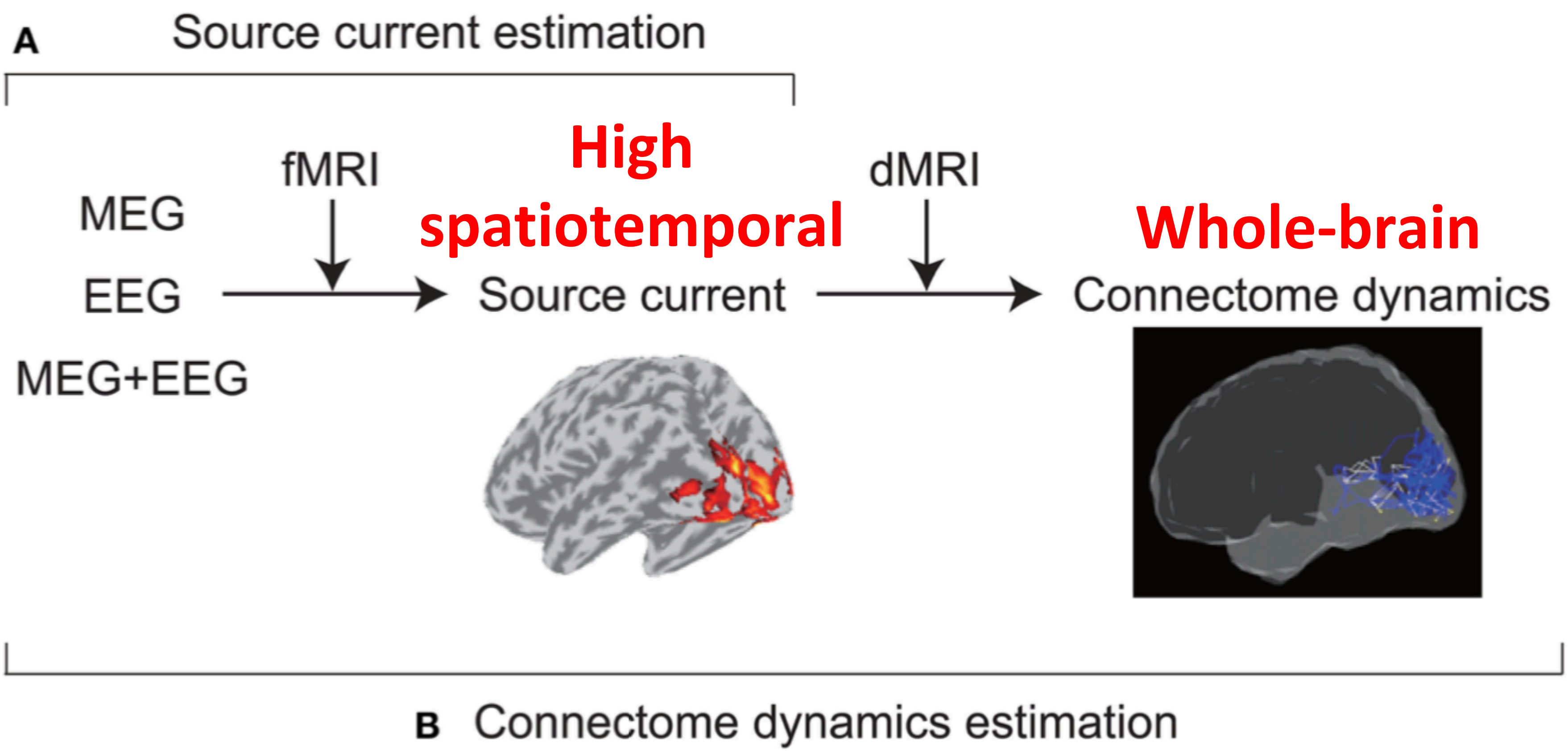
- Closer to the brain
- No maintenance cost
- Subject can move

Future plan

Estimate source current from simultaneous recordings of OPM and EEG

Cap image

Summary of VBMEG' advantages



Limitation

VBMEG does not support source imaging from resting-state MEG/EEG.

→ Ito-kun's talk

Thank you for your attention!