# **VBMEG** users manual

ATR Neural Information Analysis Laboratories (Aug 24, 2012)

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## **Revision History**

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## Overview

VBMEG is a free MATLAB toolbox that solves the M/EEG inverse problem using hierarchical Bayesian estimation (Sato et al., 2004). Using VBMEG one can:

- Import cortical surface model created by other software packages (i.e., FreeSurfer, BrainVoyager)
- Import M/EEG data (Yokogawa, Biosemi).
- Import fMRI activities (statistical parametric map) calculated with SPM2/5/8.
- Calculate M/EEG forward model (leadfield).
- Estimate M/EEG inverse filter.
- Estimate cortical current.

The following figure is a diagram of VBMEG processes for cortical current estimation.



To make SPM-voxel file ("fMRI (SPM)" in the diagram), you need to invoke a VBMEG function on a MATLAB console in which SPM is running. The preprocessing ("M/EEG", "Cortex", "Head", and "Activity/Area") and analysis ("Leadfield", "Current variance", and "Current timecourse") steps can be performed on GUI.

#### Hardware and software requirements

- VBMEG is running on MATLAB environment (version 7.0 or later). Since some MEX-files run only on Windows XP or Linux/x86, any other operating system is not supported.
- FreeSurfer (4.2 or later) or BrainVoyager (2000/QX) are needed to create cortical surface model (gray matter/white matter boundary).
- If you want to use fMRI data as prior information for cortical current estimation, a statistical parametric map of t-values obtained with SPM2/5/8 can be incorporated into VBMEG.
- If you use BEM (boundary element method) to calculate M/EEG forward model (leadfield), Curry or SPM8 software can be used to make skull and scalp surfaces. A simple sphere model can also be used for the forward model calculation.
- The following data are required for cortical current estimation by VBMEG:
  - Structural MRI data (ANALYZE/NIfTI).
  - o Cortical surface model (FreeSurfer/BrainVoyager).
  - M/EEG data (Yokogawa/Biosemi).
  - Positioning data (Fastscan).
  - fMRI data (SPM8; optional).
  - Head model (SPM8 and FreeSurfer/Curry; optional).

#### VBMEG file type

The following files are created by VBMEG:

- Cortical surface model file (.brain.mat) a polygon model of gray/white matter boundary, inflated model for displaying purposes, and information related to the model.
- **Cortical activity file (.act.mat)** consists of sets of some kind of activities (e.g., SPM t-value, cortical current at a time point) on the cortical surface model.
- **Cortical area file (.area.mat)** consists of sets of vertex indices representing a particular brain region (which can be the whole cortex) of the cortical surface model. For each vertex set, a string key is assigned, which is used to get the vertex set.
- M/EEG-MAT file (.meg.mat/.eeg.mat) has time-courses of M/EEG signals and extra channels.
- Head model file (.head.mat) has information about the structure of the subject's head. It is used to calculate the forward model by a numerical method (BEM).
- Leadfield file (.basis.mat) has leadfield matrix, which depends on the cortical surface model, head model, and M/EEG sensor position information included in the M/EEG-MAT file.

- **Current variance file (.bayes.mat)** has estimated current variance values and other model parameters of the hierarchical model of the M/EEG inverse problem.
- Cortical current file (.curr.mat) has estimated cortical currents.

#### Sample data

Sample data is available at <u>http://vbmeg.atr.jp/?lang=en#DOWNLOAD</u> Unzipping this file creates a directory which including "vbmeg1.0\_tutorial" directory. The data consist of

- MEG measurement (Yokogawa .ave file)
- fMRI analysis result (SPM voxel file)

of a passive viewing of a visual stimulus in the lower-right (LR) visual field (Yoshioka et al., 2008), and subject's

- MRI file ([.hdr/.img])
- cortical surface files (FreeSurfer)
- segmented gray matter file (SPM8)

The structure of the sample data is as follows:

- vbmeg1.0\_tutorial/
  - o subjects/
    - sbj\_test/
      - org/
        - sbj\_test.[hdr/img]
        - FS4.2/ % FreeSurfer data
        - SPM8/ % SPM8 data
        - Yokogawa % Yokogawa MEG data

"subjects" directory is defined as the project root directory (see below). "sbj\_test" directory includes all data for a subject.

### Preparation of files required for VBMEG

#### MR image preprocessing (DICOM to ANALYZE, bias correction)

MRI data are required to create subject's cortical surface model. MRI data is often provided with DICOM format. However, VBMEG supports ANALYZE format. DICOM files can be converted to ANALYZE files with VBMEG function *convert\_dicom\_nifti(dicom\_file, output\_dir)*. 'dicom\_file' is a filename of an arbitrary DICOM file consisting MRI. Running

this function, ANALYZE files (header and body of data) with prefix 'LAS\_' are created (NIfTI files are also created with prefix 'RAS\_').

Because of inhomogeneous magnetic field, MR images are sometimes contaminated by low frequency variation of signal values, which causes on extraction of cortical surface from the images. VBMEG function *vb\_bias\_correction\_by\_spm(analyze\_file)* can be used to correct signal values of MR images. Before executing this function, you need to set MATLAB path to SPM2/5/8 directory. After finished, bias corrected MRI files with prefix 'm' are created. The following figures are MR images before and after bias correction.



#### Cortical surface model

VBMEG can utilize cortex polygon models created with FreeSurfer or BrainVoyager. If you want to conduct inter-subject analysis, FreeSurfer is strongly recommended (see "Coregistration for inter-subject analysis"). BrainVoyager files can be used in VBMEG in their original format (.srf) while Freesurfer files have to be transformed within FreeSurfer. VBMEG assumes that the coordinate system of the poligon model coincides with the coordinate system of the MRI data. During preparation of the cortical surface model, the coordinate system is sometimes transformed into standard coordinates, so that structures other than the cerebral cortex (eg. cerebellum) can be discarded. In this case, the data has to be transformed back into their original coordinates before using them with VBMEG.

#### FreeSurfer

FreeSurfer automatically extracts the cortical surface model from the MRI data by the *recon-all* command. To use this command, an MRI file in MGZ format is required. ANALYZE format, which is widely used, can be converted to MGZ using the following FreeSurfer command: mri\_convert sbj\_test.img 001.mgz

'001' denotes that it is the 'first' MR image. FreeSurfer can construct the cortical surface model using two or more MR images (of the same subject) by averaging them to increase S/N ratio of the MR image from which the cortical surface model is extracted. In that case, subsequent MGZ filename should be '002', '003', etc.

To create the FreeSurfer's subject directory, you can use *mksubjdirs* command as follows:

mksubjdirs \$SUBJECTS\_DIR/sbj\_test

'sbj\_test' is ID of the subject. All MGZ files have to be put in the \$SUBJECTS\_DIR/[sbj\_id]/mri/orig/ directory as shown below:

cp 001.mgz (002.mgz 003.mgz ... if any) \$SUBJECTS\_DIR/sbj\_test/mri/orig

The *recon-all* command processes MR image(s): (GM/WM boundary extraction, coregistration to the template, etc.) as in the following example:

recon-all -all -subjid sbj\_test

It will take about 24 hours on a Linux PC with Xeon processor. After completion, surface files of the polygon model are saved in binary format. For VBMEG, the FreeSurfer data has to be saved in ASCII format. This can be done using the *mris\_convert* command included with FreeSurfer. Executing the following commands in a Unix shell generates the files necessary for import of the cortical surface model into VBMEG:

```
cd [freesurfer_sbjdir]/sbj_test/surf/
mris_convert [lh/rh]. smoothwm [lh/rh]. smoothwm. asc
mris_convert [lh/rh]. inflated [lh/rh]. inflated. asc
mris_convert -c curv [lh/rh]. smoothwm [lh/rh]. curv. asc
mris_convert [lh/rh]. sphere. reg [lh/rh]. sphere. reg. asc
```

#### BrainVoyager

VBMEG can directly read BrainVoyager .srf files. However, since the coordinate system of the cortical surface model is Talairach by default in BrainVoyager a backward transformation of the coordinate system to be the original one is required.

#### fMRI data

VBMEG function: vb\_job\_convert\_spm (MATLAB console)



SPM2/5/8 generated t-values can be used to determine the relative amplitude of the prior current variance in the hierarchical Bayesian estimation. When the statistical parametric map appears on the display (vis SPM), the VBMEG function *vb\_job\_convert\_spm* may be invoked to create a SPM-voxel file (.spm.mat), which can be imported into VBMEG. To do this, first add the VBMEG directory to MATLAB's path before running SPM. Next, run SPM to lunch its GUI, press "Result" button, choose the desired contrast and enter the appropriate parameters for determining probabilistic threshold. Then the following screen will appear:



(note that in this figure the bottom half of the SPM results window is missing) At this point, t-values and voxel coordinates are stored in the MATLAB workspace. Next, execute the VBMEG function *vb\_job\_convert\_spm* on the MATLAB console in which SPM is running. You may be asked:

Normalized functional data?

To which you can can respond "yes" or "no". If you analyze the data on a template model, the voxel coordinate values in the template space must be converted to the original subject's space. For the backward transformation, the "\_sn.mat" file is used. After that, enter the filename of the SPM-voxel file to which the SPM result is stored in a format readable by VBMEG.

#### Head model

You can use a spherical model to create the M/EEG forward model (leadfield). The spherical model is specified by the origin of the sphere and its radius. The MEG forward model with a spherical model is analytically calculated by the Sarvas equation which is not dependent on the radius of the sphere, while radii of spheres are also required for three-layers EEG forward model.

To obtain a more accurate forward model, VBMEG can create a cranial model from the subject's MRI. Required files for this calculation are:

 volumetric image of gray matter, created by using SPM8 "Segment" command (c1\*.[hdr/img]).

File       Edit       SPM       BasicIO         Module List       Current Module: Segment         Segment       Output Files      ial/subjects/sbj_test/org/sbj_test.img.1         Output Files      Grey Matter       Native Space        White Matter       Native Space        Cerebro-Spinal Fluid       None        Bias Corrected       Save Bias Corrected        Clean up any partitions       Dont do cleanup         Custom       Tissue probability maps       3 files        Gaussians per class       [2 2 2 4]        Migned Euglarisation      M space template - European brains        Warping Regularisation      M space template - European brains        Warping Regularisation       very light regularisation (0.0001)        Bias regularisation       very light regularisation (0.0001)        Bias FWHM       60mm cutoff         Current Item: Data       Nome/cbi-data5/taku-y/public/vbmeg1.0_tutorial/subjects/sbj_test/org/s         Select Files       Select Files	e O O 🔿 🛛 🕅 Batch Editor		
Module List       Current Module: Segment         Segment       Data      ial/subjects/sbj_test/org/sbj_test.ing,1         Output Files       Grey Matter       Native Space         White Matter       Native Space         White Matter       None         Bias Corrected       Save Bias Corrected         . Clean up any partitions       Dont do cleanup         Custom       Tissue probability maps       3 files         . Gaussians per class       [2 2 2 4]      M space template - European brains         . Warping Regularisation      M space template - European brains       1         . Warping Regularisation       very light regularisation (0.0001)       1         . Bias regularisation       very light regularisation (0.0001)       1         . Bias FeWHM       60mm cutoff       7         Current Item: Data       Inter/cbi-data5/taku-y/public/vbmeg1.0_tutorial/subjects/sbj_test/org/sig         . Select Files       Select Files	<u>File Edit SPM BasiclO</u>		
Module List       Current Module: Segment         Segment       Data      ial/subjects/sbj_test/org/sbj_test.img,1         Output Files      Grey Matter       Native Space        Grey Matter       Dont do cleanup         Custom       Dont do cleanup         Custom       Tissue probability maps       3 files        Gaussians per class       [2 2 2 4]        Mine Regularisation      M space template - European brains        Warp Frequency Cutoff       25        Bias FWHM       60mm cutoff	🗅 😅 🖬   🕨		
Segment       Data      ial/subjects/sbj_test/org/sbj_test/sbj_test/org/sbj_test/org/sbj_test/s	Module List	Current Module: Segment	
processing is not yet implemented for this method.	Segment Segment Data Select scans for processi multi-spectral (when ther processing is not yet impler	Data      ial/subjects/sbj_test/org/sbj_test.img, i         Output Files       Grey Matter         . Grey Matter       Native Space         . White Matter       Native Space         . Cerebro-Spinal Fluid       None         . Bias Corrected       Save Bias Corrected         . Clean up any partitions       Dont do cleanup         Custom       Tissue probability maps       3 files         . Gaussians per class       [2 2 2 4]         . Affine Regularisation      M space template - European brains         . Warping Regularisation       1         . Warp Frequency Cutoff       25         . Bias regularisation       very light regularisation (0.0001)         . Bias FWHM       60mm cutoff         Current Item: Data       forme/cbi-data5/taku-y/public/vbmeg1.0_tutorial/subjects/sbj_test/org/stime         Select Files       select Files         mg, This assumes that there is one scan for each subject. Note that e are two or more registered images of different contrasts) mented for this method.	

- 2. inner skull and outer skin surface files, created by FreeSurfer. To make these files, use *mri\_watershed* command:
- 3. cd \$SUBJECTS\_DIR/sbj\_test/mri
- 4. mri\_watershed -surf bem\_surf -useSRAS T1.mgz brain\_bem.mgz
- 5. mris\_convert lh.bem\_surf\_inner\_skull\_surface inner\_skull\_surface.asc
- 6. mris\_convert lh.bem\_surf\_outer\_skin\_surface outer\_skin\_surface.asc

These files are specified in the "Create head model" GUI.

## Setup and launch GUI

#### Installation

Execute the following commands in MATLAB in order to install the software:

> addpath(fullpath\_to\_vbmeg);

> vbmeg --- Find VBMEG program directory VBMEG program directory: /home/cbi/rhayashi/vbmeg --- Set program directories to MATLAB path --- Create global variable 'vbmeg\_inst'

Here, the variable fullpath\_to\_vbmeg indicates the path of the top directory of the VBMEG software ("vbmeg"). If only the relative path is given, part of the GUI might not work properly. While the path settings will be preserved until MATLAB is closed, the command *vbmeg* has to be executed every time the memory is cleared, since this command defines a global variable ("vbmeg\_inst").

#### Project manager startup

The **project manager** manages the execution of the various VBMEG GUIs and the parameters involved in each operation. It can be called after executing the *vbmeg* command by entering the following:

> project\_mgr

The project manager GUI is shown.

			projec	t_mgr	annen en
	Analysis I	ools			
Project nam	ne				
Root directo	bry				
Franklan a		(history)		- Chack model	
Function p	arameters	(history) —		Check model	
a rune nume		Spanniane		brain_parm	View cortical model
				1	view contrical model
				fmri parm	View inflated model
					View fmri activity
			-	meg parm(specify y	with
					View sensor position
A00 D0	терсемпрати	Interest of Decommun	r Dullasi		
Batch file t	builder —				
Builder			~		
Parameter					
					1
Comment					

The next step is to specify a **project file** (.prj.mat), which is saved in the **project root** directory. This file contains jobs that are called by the project manager as well as the parameters for each job. All of the filenames created by VBMEG are specified as relative path from the project root directory.

- Creating a new project file
  - 1. From the project manager menu select [File]->[New project], then "Create new project" GUI will pop up.

~	)	create new project	==×
		New project name and root directory	
	Project name	new_project	]
	Root directory		Select
		OK	CANCEL

## 2. Input "project\_name" and "project\_root", the directory in which the project should be saved. Press "OK" button.

•		create new project	= = ×
		New project name and root directory	
	Project name	new_project	
	Root directory	/home/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test	Select
	<b>-</b>	OK	CANCEL

- 3. Confirmation dialog will pop up. Press "OK" button.
- Specifying an existing project file
  - 1. From the project manager menu select [File]->[Load project], then the file select dialog will pop up.
  - 2. Specify the project file.
  - 3. "project\_name" and "project\_root" will be appeared in their respective line of the project manager dialog.

## Data import

This section gives how to import each of the files listed in the  $\rm ``VBMEG$  file format'' section.

#### Cortical surface model

• VBMEG function: vb\_job\_brain



From the project manager menu select [Data Import]->[Import cortical model].
 "Import cortical model" GUI will pop up. The default cortical model is FreeSurfer.
 You can also import cortical surface models of BrainVoyager.

~		Import cortical model	_ = ×
	Project root directory	/home/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test	Select
ſ		Import cortical model	
	Analyze file (.hdr)		Select
	Model type	© FreeSurfer OBrainVoyager	
	Left-brain file (.smoothwm.asc)		Select
	Right-brain file (.smoothwm.asc)		Select
	Left-inflate file (.inflated.asc)		Select
	Right-inflate file (.inflated.asc)		Select
	Left-curvature file (.curv.asc)		Select
	Right-curvature file (.curv.asc)		Select
	SPM normalization file (_sn.mat)		Select
	Keyword		
	Comment		A 
I	Save directory		Select
	Cortical model file (.brain.mat)		
1	Cortical area file (.area.mat)		
	Cortical activity file (.act.mat)		
	Reset	Exec	Advanced parameter

#### 2. Specify the files required.

• Specify ANALYZE (or NIFTI) header file of subject's MRI from which the cortical surface model was extracted (BrainVoyager or FreeSurfer).

Analyze file ( hdr)	vralski dotoQ/toku u/vkrag1. O tutoriol/cubicate/chi tast/org/chi tast.hdv
Analyze me (analy	ome/cbi=data9/taku=y/vbmeg1.0_tutonai/subjects/sbj_test/org/sbj_test.ndr

 $_{\odot}$  Specify FreeSurfer files. Required files are smoothwm, inflated, curv for lh/rh.

Left-brain file (.smoothwm.asc)	a9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/lh.smoothwm.asc
Right-brain file (.smoothwm.asc)	a9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/rh.smoothwm.asc
Left-inflate file (.inflated.asc)	-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/lh.inflated.asc
Right-inflate file (.inflated.asc)	-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/rh.inflated.asc
Left-curvature file (.curv.asc)	cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/lh.curv.asc
Right-curvature file (.curv.asc)	bi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/FS4.2/rh.curv.asc

 Specify SPM normalization file \_sn.mat (optional). It is used to calculate the standard (template) brain coordinate values for vertices of the (individual) subject's cortical surface model.

SPM normalization file (_sn.mat)	ata9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/org/SPM8/sbj_test_sn.mat

 $_{\odot}$   $\,$  Specify the directory to which created files are saved.

Save directory

• Filenames are automatically set using MRI filename.

Cortical model file (.brain.mat)	./sbj_test.brain.mat
Cortical area file (.area.mat)	./sbj_test.area.mat
Cortical activity file (.act.mat)	./sbj_test.act.mat

3. Press "Exec" button to start import of the cortical model.

After processing three files will be created: the cortical surface model file (.brain.mat), cortical activity file (.act.mat) and cortical area file (.area.mat). The following figures will be shown. Check if the cortical surface model (yellow line) is aligned with the gray/white matter boundary in MR image.



If you specified the SPM normalization file (\_sn.mat) in the GUI, the standard brain coordinate values of the Talairach and MNI305 templates are appended to the cortical surface model file. In addition, VBMEG creates 3 files: \_brodmann.area.mat, \_aal.area.mat, and \_atlas.act.mat, which include anatomical label data on the cortical surface model.

#### MEG data

• VBMEG function: vb\_job\_meg



VBMEG can import MEG data measured by a Yokogawa system (MegLaboratory; .raw, .ave, .con). The MEG sensor position should be transformed into SPM-Analyze (RAS, origin at the center of MRI volume) coordinate system. The coregistration methods supported by VBMEG are the standard method offered by MegLabotory (determination of the marker location by means of MRI) and the method developed by Shimadzu and ATR (three dimensional matching of the face; Kajihara et al., 2004). To import MEG data, follow the below steps:

1. Select [Data Import]->[Import MEG data]->[Yokogawa] from the project manager menu. "Import YOKOGAWA MEG data" GUI will pop up.

	Import YOKOGAWA MEG data		
Project root directory	taku-y/vbmeg1.0_tutorial/subjects/sbj_test	Select	
	Import YOKOGAWA MEG data		
Yokogawa MEG file(.raw .ave		Select	
Channel pos file (.pos.mat)		Select	
EXT channel gain	Setting None		
Keyword			
Comment			
Save directory		Select	
MEG file (.meg.mat)			
Binary data directory (relative path from MEG file)			
Reset	Exec		

- 2. Specify the required MEG data files.
  - Specify Yokogawa MEG file (.raw, .ave, .con).

Yokogawa MEG file(.raw .ave average/sbj\_test\_HPF\_LPF\_BC-TriggerLR.ave

• Specify positioning file (.pos.mat). This is used to transform sensor coordinate values.

Channel pos file (.pos.mat)	s/sbj_test/org/Yokogawa/marker1.pos.mat
• • • •	

• Specify the directory to which created file will be saved.

- · · ·	
Save directory	
-	

• The MEG-MAT file name is automatically set. In addition, the directory, in which the MEG time course is saved, is also created.

MEG file (.meg.mat)	./sbj_test_HPF_LPF_BC-TriggerLR.meg.mat
Binary data directory (relative path from MEG file)	./sbj_test_HPF_LPF_BC-TriggerLR_bin

3. Press "Exec" button to start import.

The data, now formatted for VBMEG, are saved in a MEG-MAT file.

To check signals of MEG data, you can M/EEG viewer. Select [Tools]->[View MEG/EEG data] from the project manager menu. Then "View MEG/EEG data" dialog will pop up.

	View MEG/EEG data	
*MEG/EEG file([.meg./.eeg].mat)	al/subjects/sbj_test/sbj_test_HPF_LPF_BC-TriggerLR.meg.mat	select
	OK	CANCEL

Select MEG-MAT file and press "OK" button. MEG/EEG viewer GUI will pop up.



Spatial map and time course of MEG signals are shown in the left and right panel. You can select arbitrary time window, from which the spatial map is obtained, by dragging the cursor on the right panel.



Then, the spatial map will be updated.



The spatial map may be discontinuous because of the configuration of the direction of sensors of some MEG systems is arbitrary (as of MEG system in ATR). You can select axial sensors to be plotted from the menu of GUI.



If the direction of axial sensors is continuous spatially, the spatial map of MEG signals is smooth as in the figure.



#### EEG data

• VBMEG function: vb\_job\_meg

Data obtained by a Biosemi EEG system (.bdf) can also be imported. Screening of the individual session and trial data for artifacts is recommended before import, but can also be conducted after import into VBMEG. The EEG sensor position has to be transformed into SPM-Analyze (RAS, origin at the center of MRI volume) coordinate system before import. The coregistration method supported by VBMEG is the one developed by Shimadzu and ATR (three dimensional matching of the face; Kazihara et al., 2004). EEG data can be imported by following the steps below:

 Select [Data Import]->[Import EEG data]->[Biosemi] from the project manager menu. "Import Biosemi EEG data" GUI will pop up.

00	X Import BIO	SEMI EEG data	
Project root directory	/home/cbi-data5/	taku-y/public/vbmeg1.0_tutorial/subjects	Select
	Import BIOSEMI	EEG data	
Biosemi EEG file ( .bdf )			Select
Channel pos file ( .pos.mat )			Select
Keyword			
Comment			
Save directory			Select
EEG file ( .eeg.mat )			
Binary data directory (relative path from EEG file)			
Res	set	Elec	

- 2. Specify the required EEG data files.
- 3. Press "Exec" button to start the import, then the channel lists, included in the BDF file and the POS-MAT file, are shown. The order of channels does not matter, but you should check if all the EEG channels (on the scalp) in the BDF file are included in the POS-MAT file. Some extra channel (EOG, EMG, trigger recording) can be included in the BDF file, so the lengths of the lists can also be different. Pressing "Sort" button sorts the order of display and does not affect to import process.

BDF-file Channel list = 73         POS-fil           AF7         AF7           AF7         AF7           F1         Fp2           F3         AF7           F5         AF2           F7         AF8           FC5         F7           FC3         F5           FC1         F3           C1         C3           C5         F2           T7         F4	
Fp1         A         Fp1           AF7         Fp2         Fp2           AF3         Fp4         Fp2           F1         AF3         AF7           F3         F5         F7           F7         AF4         F7           FC5         F7         FC3           FC1         F3         C1           C3         C5         F2           T7         F4	e Channel list = 64
TP7 CP5 CP3	
Sort Sort	DK Cancel

4. The data, now formatted for VBMEG, are save in an EEG file (.eeg.mat).

#### fMRI data

• VBMEG function: vb\_job\_fmri



SPM-Voxel file (.spm.mat) can be imported by following the steps below:

1. Select [Data Import]->[Import SPM data] from the project manager menu. "Import SPM voxel data" GUI will pop up.

	Import SPM voxel data	×
Project root	bmeg1.0_tutorial/subjects/sbj_test	Select
	Import SPM voxel data	
Cortical model file		Select
SPM voxel file		Select
Activity II	Area ID	
Commen		
Cantinal area file		
		Select
Cortical activity file		Select
Reset	Exec	dvanced parameter

- 2. Specify the required files.
  - Specify the cortical surface model file (.brain.mat), onto which voxels are projected.

Cortical model file	./sbj_test.brain.mat
$_{\odot}$ Specify the SPM-Voxel fil	e, which includes voxels of SPM t-values.
SPM voxel file (.spm.mat)	st/org/SPM8/sbj_test_LR_SPM8.spm.mat
$_{\circ}$ Specify IDs of activity ma	p and cortical area.
Activity ID LR	Area ID LR
<ul> <li>Specify the cortical activition cortical area are stored in</li> </ul>	ty file and cortical area file. The activity map and these files with specified IDs.

Cortical area file (.area.mat	./sbj_test.area.mat
Cortical activity file (.act.mat)	./sbj_test.act.mat

3. Press "Exec" button to start the data import.

The t-values provided by the SPM-Voxel file are mapped onto the cortex vertices and regirstered in the cortical activity file with the identifier you specified. Additionally, voxles with a t-value exceeding the threshold will be registered an individual area of the cortex and as such saved in the cortical area file. The following figure shows the result of the import of the "LR" result of SPM8.



#### Head model

• VBMEG function: vb\_job\_head\_3shell



You can make a realistic head model to improve accuracy of the leadfield calculation by following the steps below:

1. Select [Data Import]->[Import head model]->[SPM/FreeSurfer/Curry v4.5] from the project manager menu. "Create head model" GUI will pop up.

	Create head model
Project root directory	/home/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test Select
	Create head model
Model	◯CSF
The number of Vertices in each sur	face 2000 Voxel size 1 [mm]
Analyze file (.hdr)	Select
Source type	SPM segmentation file + Cortical model file [+ FreeSurfer file(inner skull)]
SPM gray matter file(.hdr)	Select
Cortical model file (.brain.mat)	Select
FreeSurfer surface file(.asc)	Select
Source type	use Scalp thickness
Scalp thickness	4 [mm] Minimum skull thickness 2 [mm]
Scalp source	
Source type	FreeSurfer surface file(outer skin)
FreeSurfer surface file(.asc)	Select
Comment	-
Save directory	Select
Head file (.head.mat)	_3shell_6000.head.mat
	Exec 2D view 3D view

- 2. Specify files and parameters.
  - Specify head model type. For MEG check "CSF", making a head model consisting of single layer (celebro-spinal fluid; CSF). Then the number of vertices of the CSF layer are automatically set (6,000 by default). The Analyze/NIfTI image is also required.

Model	CSF	⊖CSF, Skull, Scalp		
The number of Vertices in each surface	6000	Voxel size 1	[mm]	
Analyze file (.hdr) 9/	taku-y/vbmeg1.0_	.tutorial/subjects/sbj_test/org/sbj_test.h	dr	Select

 For EEG, check "CSF, Skull, Skalp", which will make a head model consisting of three layers (CSF, Skull, Scalp). The number of vertices for each of the three layers is 2,000.

Model	CSF	◆ CSF, Skull, Sc		
The number of Vertices in	eact 2000	Voxel si:1	[mm	
Analyze file (.hdr)	orial/subjects/sbj_	test/org/sbj_test.hdr		Select

 Specify files and parameters for creating the CSF surface. Required files are the SPM8 gray matter file (c1\*.hdr), VBMEG cortical surface model file, and FreeSurfer inner skull surface file (see section "Head model" of "Preparation of files required for VBMEG").

CSF source	SPM segmentation fi	ile + Cortical model file	[+ FreeSurfer file(inner skull	)]	•
SPM gray matter file(.hdr)	//vbmeg1.0_tutorial,	/subjects/sbj_test/org,	/SPM8/c1sbj_test.hdr	Select	
Cortical model file (.brain.mat)			./sbj_test.brain.mat	Select	
FreeSurfer surface file(.asc)	.0_tutorial/subjects	;/sbj_test/org/FS4.2/in	ner_skull_surface.asc	Select	
Morphological operation[mm]	for Gray matter	[6 6 -7]	for FreeSurfer surface	[4 -4]	

 Specify parameters for creating the skull surface. You can use the default parameters.

<ul> <li>Skull source</li> <li>Source type</li> </ul>	use Scalp thickness	•
Scalp thickness	4 [mm] Minimum sku	II thickness 2 [mm]

 Specify files and parameters for creating the scalp surface. The required files is FreeSurfer outer skin surface file (see section "Head model" of "Preparation of files required for VBMEG").



• Specify the directory to which the head model file is saved.

Save directory		Select
Head file (.head.mat)	./c1sbj_test	_CSF_6000.head.mat

3. Press "Exec" button to start making the head model.

A head model file will be created and figures as below will be appeared. In this example there is a CSF single layer (yellow line) model for MEG. Check if the CSF surface correctly aligned with the MR image.



Specifying a three layer model for EEG gives the following figures, consisting of CSF (yellow), skull (red), and scalp (light blue) surfaces. In the last figure, the scalp surface is superimposed on the face model.





## Cortical current estimation

The estimation of the electric current source with VBMEG is done in three steps: Leadfield calculation, current variance estimation and finally, current timecourse estimation.

#### Leadfield calculation

• VBMEG function: vb\_job\_leadfield



Leadfield can be calculated by following the steps below:

1. Select [Analysis]->[Calculate leadfield] from the project manager menu. The "Leadfield calculation" GUI will pop up.

	Leadfield calculation	
Project root directory	ta9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test	Select
	Leadfield parameters	
MEG/EEG file ([.meg/.eeg].mat)		Select
Cortical model file ( .brain.mat )		Select
Cortical area file ( .area.mat )		Select
Calculation method	BASIS_MEG_SPHERE •	
Head model file ( .head.mat )		Select
Center of the head		View / Edit
Conductivity( inner to outer )	1, 0.0125, 1	
Radius( inner to outer )	0.87, 0.92, 1	
Basis mode	CURRENT_NORMAL -	
Normal mode	NORMAL_ADJACENT_MEAN 🗸	
ArealD		
Keyword		
Comment		
Save directory		Select
Leadfield file ( .basis.mat )		
Reset	Exec	Check

- 2. Specify the required files and parameters.
  - Specify the M/EEG-MAT file and cortical model file. You do not need to specify the cortical area file (the field is not necessary and will be removed in a future version).

MEG/EEG file ([.meg/.eeg].mat)	./sbj_test_HPF_LPF_BC-TriggerLR.meg.mat
Cortical model file ( .brain.mat )	./sbj_test.brain.mat
Cortical area file ( .area.mat )	

• Specify the method for leadfield calculation. "BASIS\_MEG\_BEM" is the option to use BEM for calculation of the leadfield.

Calculation method BASIS_MEG_BEM
----------------------------------

• The head model file must be specified for BEM.

Head model file ( .head.mat )	./c1sbj_test_CSF_6000.head.mat
	· · · ·

 Do not modify parameters here. These parameters are used for advanced users.

Basis mode	CURRENT_NORMAL -
Normal mode	NORMAL_ADJACENT_MEAN

• Specify the directory to which the leadfield file is saved. The filename is automatically set using the MEG-MAT filename.

Save directory	
Leadfield file ( .basis.mat )	./sbj_test_HPF_LPF_BC-TriggerLR.basis.mat

- 3. Press "Exec" button to start the leadfield calculation.
- 4. The result is saved in the leadfield file (.basis.mat).

The leadfield at M/EEG sensors are calculated for every vertex of the cortical surface model.

#### Current variance estimation

• VBMEG function: vb\_job\_vb



The hierarchical Bayesian method for estimation of brain activity estimates variance of the electric current from the MEG data. Once the current variance is obtained, we can calculate the linear inverse filter, which will yield the electric current estimation when multiplied with the MEG data matrix. Here, we explain how to arrive at the electric current variance using VBMEG. From the project manager menu, choose [Analysis]->[Estimate current variance] to open the "Current variance estimation" GUI. This GUI displays a variety of parameters, which have to be chosen carefully. The following provides information on how to choose the parameters and gives examples.

	Current variance estimation	//////////////////////////////////////
Project root directory	me/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test	Select
Cortical model file (.brain.mat)		Select
Leadfield file (.basis.mat)		Add
	-	Remove
MEG/EEG file (.meg.mat, .eeg.mat)		Add
		Remove
Cortical area file (area mat)	Cortical activity file ( act mat)	
Contical area me (larealmat)	Control activity file (.act.mat)	Select
Area ID	Activity ID	
Cortex	- Uniform	<b></b>
lime window parameters	Time window list	
MEG time range [ms] -		
Time window format  Equally shift	OManual Check	
Analysis time range [ms]	-	
Time window size [ms]		
Shift size [ms]		<b></b>
Estimation model parameters		
Variance magnification parameter	100 Smoothness filter radius [mm]	6.00
Confidence parameter	10 Dipole reduction ratio	1.00
Time range for baseline signal [ms]	-	
Noise model COVARIANCE N	ioise 👻	
Current variance file output directory		Salact
Current variance filename (.baves.mat)		Jeleot
Comment		
Save	Exec Advance	ed Parameters

#### Input files

First, the cortical model file, leadfield file and MEG-MAT file have to be specified. To select leadfield file and MEG file, press the "Add" button. VBMEG can estimate the current distribution for multiple sessions at the same time. The below figure displays an example with a single session.

Cortical model file (.brain.mat)	./sbj_test.brain.mat
Leadfield file (.basis.mat)	./sbj_test_HPF_LPF_BC-TriggerLR.basis.mat
MEG/EEG file (.meg.mat, .eeg.mat)	./sbj_test_HPF_LPF_BC-TriggerLR.meg.mat

You can specify multiple leadfield/MEG-MAT files across sessions. The leadfield file and MEG-MAT file must correspond with each other: the first leadfield file is calculated from the first MEG-MAT file. The same holds for the second, third ones.

#### Cortical area and activity

In the next step, cortical area and cortical activity is selected. The cortical area information is used to specify the areas in which dipoles are assumed. The cortical activity information is used to determine the hyper parameters. In case you are importing fMRI data with VBMEG, it is recommended to label the cortical areas and the related activity according the conducted MEG study. The standard cortical area ("Cortex") and cortical activity ("Uniform") are registered without fMRI data.

The cortical area ID "Cortex" includes all vertices of the cortical model; when "Cortex" is selected dipoles are assumed at all vertices of the cortex. The cortical activity ID "Uniform" assumes that the whole cortex activation follows a uniform pattern. If no fMRI data is given, the cortical area ID "Cortex" will be used for the estimation with the cortical activity ID "Uniform". Here we have imported fMRI data, so cortical activity ("LR") is used to determine hyper parameters.

Cortical area file (.ar	ea.mat)	
	./sbj_test.area.mat	Select
Area ID		
Cortex		<b>▲</b>
LR		-
Cortical activity file (	.act.mat)	
Cortical activity file (	.act.mat) ./sbj_test.act.mat	Select
Cortical activity file ( Activity ID	.act.mat) ./sbj_test.act.mat	Select
Cortical activity file ( Activity ID Uniform	.act.mat) ./sbj_test.act.mat	Select

#### Time window parameters

VBMEG divides the MEG data into time windows of suitable length and estimates the current distribution separately for each of these windows. Based on the MEG-MAT file specified, the dafault parameters in the "Time window parameters" sections will automatically be set to the default values. In the default setting, a single time window covers the whole time series. That is to say, the prior distribution of the electric current is assumed to be the same at each time point.

Time window parameters			
MEG time range [ms]	-500.00 -	499.00	Time
Time window format	● Equally shift	⊖Manual	Check
Analysis time range [ms]	-500.00	- 499.00	
Time window size [ms]	1000.00		
Shift size [ms]	1000.00		

Time windows separation is favorable in case the cortical activity changes in location with time (Shibata et al., 2008, Callan et al., 2010). To divide the time window, two options are available: you can either set time window width and window shift (equally shift) or manually set every time window (manual). The two options can be selected with the "Time window format" check box. In case of multiple time windows, window width and time shift have to be set accordingly. In our example, the MEG data was divided into 100 ms time windows. The "Shift size" is set to 50 ms, i.e. the windows overlap 50 ms. In the overlapping regions, the electric current distribution is estimated independently. However, the electric current itself will be estimated as the average over the estimations for each window.

Time window parameters	
MEG time range [ms]	-500.00 - 499.00
Time window format	●Equally shift ○Manual
Analysis time range [ms]	-500.00 - 499.00
Time window size [ms]	100.00
Shift size [ms]	50.00

Pressing the "Check" button returns a list of the individual time windows.

	Time window list	
	-500.00401.00	<b></b>
Check	-450.00351.00	**
	-400.00301.00	335
	-350.00251.00	
	-300.00201.00	
	-250.00151.00	
	-200.00101.00	
	150.00 51.00	

#### Estimation parameters

The figure below shows how the estimation parameters in the GUI should be set.

1	<ul> <li>Estimation model parameters</li> </ul>		
	Variance magnification parameter	500 Smoothness filter radius [mm]	6.00
	Confidence parameter	500 Dipole reduction ratio	0.2
	Time range for baseline signal [ms]	-500.001.00	
	Noise model	COVARIANCE NOISE	

VBMEG has the following estimation parameters:

- Smoothness filter radius: VBMEG makes use of a smoothing filter that can be described by exp(-(d/R)<sup>2</sup>), where d is the distance between two vertices measured along the cortical surface and R is the "Smoothness filter radius". The standard value for R is 6mm.
- Dipole reduction ratio: In case the number of vertices in the cortical model should be too high, it can be reduced by setting the value for "Dipole reduction ratio", e.g.

for a cortical model with 20,000 vertices, setting the Area ID to "Cortex" and " Dipole reduction ratio" to 0.2, will reduce the number of dipoles left over to 4,000.

- Noise model parameters: The standard for the "Noise estimation model" is "
   COVARIANCE NOISE". The time interval set in "Time range for baseline signal"
   determines which part of the MEG data. VBMEG uses to estimate 1) the
   covariance matrix of the observation noise and 2) the baseline current variance.
   Usually, this time interval is set as the baseline interval (time before trigger onset).
- Hyper parameters: In the hierarchical Bayesian estimation, two hyper parameters control the electric current estimation, the "Variance magnification parameter" (in the following refered to as m0) which controls the current strength and the "Confidence parameter" (in the following gamma0), a coefficient of confidence in the fMRI data. The higher the value of m0, the higher the power of the electric current is estimated. In standard cases a value of m0 = 100 is recommended. If extremely high electric currents are expected, such as in visual color grading experiments, m0 can be set as high as 500. If fMRI data is available, the standard value for the confidence parameter gamma0=100. If no fMRI data is available or the conditions for fMRI and MEG experiment differ significantly set gamma0=10. Conversly, if the experiments for fMRI and MEG are equal, the value can be set as high as gamma0=500. A high value of gamma0 (e.g., 100000) results in the Wiener filter estimation (Kajihara et al., 2004).

#### Output file

Finally, select the "Current variance file directory" and the "Current variance filename", where the results will be stored. Note that "Current variance file" does not include current time course, but consists of current variances and other model parameters, from which the inverse filters are calculated.

Current variance file output directory	
Current variance filename (.bayes.mat)	LR.bayes.mat

After having set the parameters, press the "Exec" button to start the estimation.

#### Current timecourse estimation

• VBMEG function: vb\_job\_current



Cortical current time course can be calculated by multiplying the inverse filters, obtained using the estimated current variance and other model parameters. This calculation can be performed by following the steps below:

1. From the project manager menu, select [Analysis]->[Estimate current]. The "Current estimation" GUI will pop up.

	Current estimation
Project root directory /ho	ome/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test Select
	Current estimation parameters
Current variance file (.bayes.mat)	Select
MEG/EEG file (.meg.mat, .eeg.mat)	Select
Trial average	● OnOff
Time Window [ms]	- Select time window
Cortical area file (.area.mat)	Select Reset
Area ID	
Comment	
Current file format	Single file     OMultiple files
Current file directory	Select
Current file name (.curr.mat)	current.curr.mat
Ехес	Advanced parameters

- 2. Specify the files and parameters required.
  - Specify current variance file (.bayes.mat). GUI will automatically put M/EEG-MAT file (.meg.mat/.eeg.mat) from which current variance was estimated. You can overwrite this parameter.

Current variance file (.bayes.mat)	./LR.bayes.mat
MEG/EEG file (.meg.mat, .eeg.mat)	./sbj_test_HPF_LPF_BC-TriggerLR.meg.mat

 Specify estimation parameters. If "Trial average" is "On", current timecourses are calculated for MEG data averaged across trials. You also can set a time window sorter than one used in the "Current variance estimation". By default, the time window covering whole data is used.

Trial average	€On	⊖Off	
Time Window [ms]	-500.00	- 499.00	Select time wi

 Specify cortical area on which current time courses are calculated. If the size of the MEG data is too large (many trials, long time window), this option is preferable to reduce the size of current timecourses.

Cortical area file (.area.mat)	./sbj_test.area.mat Select Reset
Area ID	Cortex A

 Specify how to store the body of current timecourse data. If the "Single file" option is selected, estimated current time courses for all trials are saved into a single file, while if the "Multiple files" option is selected, current time courses are saved into different files for each trial.

Current file format	●Single file	OMultiple files

• Specify the directory to which the cortical current file is saved. The filename is automatically set using current variance filename.

Current file directory	. Select
Current file name (.curr.mat)	./LR.curr.mat

3. Press "Exec" button to start estimation of cortical current time course.

The estimated current timecourse is then saved into a cortical current file (.curr.mat).

View cortical current

• VBMEG function: job\_plot\_currentmap

To look at the estimated cortical current, select [Tools]->[View estimated current] from the project manager menu. Then file select dialog will pop up. You need to specify the cortical current file and the cortical model file. The cortical currents will be mapped on the cortical surface model. You can also specify cortical area and activity map files.

		Input files		- • ×
apply		······		
V	Cortical model file	i-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/sbj_test.brain.mat	select	
$\checkmark$	*Current file	me/cbi-data9/taku-y/vbmeg1.0_tutorial/subjects/sbj_test/LR.curr.mat	select	
		load mode 💿 average 📿 raw : Trial 🔢 /1		
	Cortical area file		select	
	Cortical act file		select	
	Description	Information		
	*: required paramet	er(s).		•
		ОК	CANCEL	

GUI of the cortical current viewer will pop up. In the left, the selected cortical surface model is plotted. The time course on the bottom is the estimated current of the selected vertex. Just after launch the GUI, the 1st vertex is selected ("Vertex index" edit box). The selected vertex is marked by a green cross (left hemisphere in the figure).



Push "Right" button to change the viewpoint to look at the cortical surface model from right.





You can choose which hemisphere is shown. To suppress the right hemisphere plot, uncheck the "Right" check box.

Hemisph	⊾Left	Right
Model	⊖Fold	●Infla

The the right hemisphere will disappear and the left hemisphere is shown in the medial view.



In the time course plot, you can specify an arbitrary time window. Here the latency of visual evoked field (around 100ms) is chosen.



Accordingly, the spatial pattern of the cortical current is shown with averaging across the time window.



To choose a vertex (current dipole), push "Select vertex" button and click a point of the cortical surface model.



Then the green cross moves to the point specified,



and the time course plot is changed to the one on the selected vertex.



By pressing "Temporal peak" button, you can find the peak of the timecourse within the time window.



The width of the time window after the temporal peak search is in the "TOI" editbox.



The spatial pattern of the cortical current is also updated reflecting the update of the time window.



## Advanced topics

#### Coregistration for inter-subject analysis

• VBMEG function: vb\_job\_add\_sphcoord, vb\_job\_coreg\_brain

To conduct inter-subject analysis, a **coregistration matrix** to a template cortical surface model is required for each subject's cortical surface model. A template cortical surface model "fsaverage" from FreeSurfer (see FreeSurfer's web site for more detail about this data) is attached with VBMEG software. An activity map (e.g., cortical current at a timepoint) of the cortical surface model of an individual subject (referred to as "source"), J\_s, is transferred to the one on another cortical surface model (referred to as "target", usually a template brain), J\_t, by multiplying the coregistration matrix C: J\_t=C\*J\_s.. Each component of the projection matrix, C\_{ij}, is proportional to  $exp(-(d_{ij}/R)^2)$ , where R is a tunable coefficient and d\_{ij} is the distance between the i-th vertex of the template model and the j-th vertex of the source model, on a common coordinate system (3D volume coordinate and 2D cortical surface coordinate supported by VBMEG). Intuitively, the coregistration matrix represents closeness of the vertices of the template and source models.

The calculation of the coregistration matrix for each subject's model consists of 2 steps:

- 1. (optional, but strongly recommended) import coordinate values commonly used in the template model (*vb\_job\_add\_sph\_coord*).
- 2. calculate the coregistration matrix using the coordinate values (vb\_job\_coreg\_brain).

If you used FreeSurfer, spherical coordinate values are assigned to each vertex. These are calculated such that sulci and gyri of the subject's cortex align to the ones of "fsaverage" model and saved to "[lh/rh].sphere.reg(.asc)". To import them into the cortical surface model file, *vb\_job\_add\_sphcoord* is used. The following is an example:

```
>> proj_root = './subjects/';
>> brain_parm.brain_file = 'sbj_test/sbj_test.brain.mat';
>> brain_parm.brain_sphL = 'subjects/sbj_test/org/FS4.2/lh.sphere.reg.asc';
>> brain_parm.brain_sphR = 'subjects/sbj_test/org/FS4.2/rh.sphere.reg.asc';
>> brain_parm.key = 'sphere.reg'; % arbitrary string available
>> vb_job_brain_add_sphcoord(proj_root, brain_parm);
```

The spherical coordinate values are then added to the cortical surface model file. Note that "brain\_file" specifies a relative path from the project root directory ("proj\_root"), while "brain\_sph[L/R]" specifies the source file directly. "demo/vb\_test\_gave2.m" in "demo" directory is a sample script.

A coregistration matrix is calculated by using *vb\_job\_coreg\_brain*. Before running this function, you should copy the "fsaverage" model to subject's directory:

```
mkdir your_work_dir/vbmeg1.0_tutorial/subjects/fsaverage
cp your_vbmeg_dir/functions/tool_box/freesurfer4.5/*
your_work_dir/vbmeg1.0_tutorial/subjects/fsaverage
```

Then run *vb\_job\_coreg\_brain* as below:

>> coreg\_parm.source\_file = './subjects/sbj\_test/sbj\_test.brain.mat';

```
>> coreg_parm. source_key = 'sphere. reg';
>> coreg_parm. target_file = './subjects/fsaverage/fsaverage. brain. mat';
>> coreg_parm. target_key = 'sphere. reg'; % prospectively registered to
fsaverage. brain. mat
>> coreg_parm. key = 'fsaverage. sphere. reg';
>> vb_job_coreg_brain(coreg_parm);
```

The coregistration matrix is added to "sbj\_test.brain.mat".

#### Grandaverage

• VBMEG function: vb\_job\_grandaverage

The grand average of cortical current across trials and subjects is calculated by *vb\_job\_grandaverage*. In the above example we only have the cortical current timecourse of a single subject. An example of the calculation of cortical current timecourse on the template brain (fsaverage.brain.mat) is shown below:

>> avr\_parm.curr\_file = {'./subjects/sbj\_test/LR.curr.mat'};

```
>> avr_parm.brain_file = {'./subjects/sbj_test/sbj_test.brain.mat'};
```

```
>> avr_parm.key = {'fsaverage.sphere.reg'};
```

```
>> avr_parm.tbrain_file = './subjects/fsaverage/fsaverage.brain.mat';
```

- >> avr\_parm.curr\_file\_out = './subjects/fsaverage/LR.curr.mat';
- >> vb\_job\_grandaverage(avr\_parm);

#### Artifact rejection with extra-dipole

M/EEG signals are sensitive to eye movement artifacts. VBMEG support the **extra-dipole** method, which models eyeball artifact sources by current dipoles and estimates their current simultaneously the cortical current (Fujiwara et al., 2009; Morishige et al., 2009). It has been shown that eye movement artifacts are successfully removed while not affecting the estimation of the cortical current correlated with the eye movements (Fujiwara et al., 2009). In addition, cardiac artifacts are also removed (Morishige et al., 2009). To use the extra-dipole method, follow the steps below:

- 1. Create **extra-dipole position file (.mps.mat)** using the GUI to place the extradipoles on the eyes.
- 2. Calculate the leadfield for the extra-dipoles.
- 3. Estimate current variance on the MATLAB console (the extra-dipole method not supported on "Current variance estimation" GUI).

#### Create extra-dipole position file (.mps.mat)

 Run the VBMEG command vb\_mri\_point\_select on the MATLAB console and choose the subject's MR image. Then "MRI point select" GUI will pop up.



2. Choose the left eyeball position on the MR image.



 Press the "get point" button then the "Enter the point name" dialog will pop up. Choose "Left eye".



4. "Left eye" is added to "Save points" list.

Left eye :	62	193	135	get point
				emove poir
				check point

- 5. Choose the right eyeball the same way.
- 6. Press "Save" button to save the coordinate values of the selected points.

#### Manually create .mps.mat file

If you want to place extra-dipoles at places other than eye balls, you should use the following MATLAB code.

```
% directories and files
work_dir = '/home/cbi-data9/taku-y/public/extdip/';
         = [work_dir 'subjects/sbj_test/'];
sbj_dir
proj_root = sbj_dir;
% put extra-dipoles
Pointlist = cell(3, 1);
% ---- left eye
Pointlist{1}.coord_type = 'SPM_Right_m';
Pointlist{1}.name
                        = 'Left eye';
Pointlist {1}.point
                        = 1e-3*[-33.5 64 0];
% ---- right eye
Pointlist{2}.coord_type = 'SPM_Right_m';
Pointlist{2}.name
                        = 'Right eye';
Pointlist{2}.point
                        = 1e-3*[28.5 65 0];
% ---- heart
Pointlist{3}.coord_type = 'SPM_Right_m';
Pointlist {3}. name
                        = 'Heart';
Pointlist {3}. point
                        = 1e-3*[0 \ 0 \ -300];
% make .mps.mat file
save([sbj_dir 'brain/sbj_test.mps.mat'],'Pointlist');
```

Here 30cm below  $(1e-3*[0\ 0\ -300])$ the center of MR image, which is the origin of the coordinate system used in VBMEG ('SPM\_Right\_m'), is tentatively defined as a place from which cardiac artifacts come. In this code, extra-dipoles are assumed at three places and nine dipoles for x, y, z directions at each place. You can add four or more extra-dipoles by modifying the code.

#### Calculate leadfield for extra-dipoles

To calculate the leadfield for the extra-dipoles, you need to run *vb\_job\_leadfield\_extra* from the MATLAB console. The following is an example (note that "meg\_file", "mps\_file" and "basis\_file" are relative path from proj\_root):

>> proj\_root = './subjects/';

>> extra\_basis\_parm.meg\_file = 'sbj\_test/sbj\_test\_HPF\_LPF\_BC-TriggerLR.meg.mat'; % MEG file including sensor position of the session to be analyzed >> extra\_basis\_parm.mps\_file = 'sbj\_test/sbj\_test.mps.mat'; % Extra-dipole position file you created >> extra\_basis\_parm.basis\_file = 'sbj\_test/sbj\_test\_HPF\_LPF\_BC-TriggerLR\_eyes.basis.mat'; % arbitrary filename to which the leadfield matrix of the extra-dipoles will be stored. >> vb\_job\_leadfield\_extra(proj\_root, extra\_basis\_parm);

After finished, the leadfield file for the extra-dipoles are created.

#### Check leadfield of extra-dipole

Before conducting estimation, you should make sure that the spatial pattern of the extradipole matches with the spatial pattern of the artifact you want to remove. The following code plot the leadfield of the 7-th component of the extra-dipole created with the MATLAB code in "Manually create .mps.mat file", corresponding to x-direction placed at the heart:

```
% directories and files
work_dir = '/home/cbi-data9/taku-y/public/extdip/';
           = [work_dir 'subjects/sbj_test/'];
sbi dir
meg_file = [sbj_dir 'meg/sbj_test_UR.meg.mat'];
basis_file = [sbj_dir 'basis/sbj_test_extdip.basis.mat'];
% get MEGinfo (sensor type depends on the system you use)
MEGinfo = vb load meg info(meg file, 5);
        = find (MEGinfo. ChannelInfo. Type==2); % axial sensor
ix1
ix2
        = find (MEGinfo. ChannelInfo. Type==3); % planar sensor
% get sensor position
pick = vb_load_sensor(meg_file);
pick = pick (1: (size(pick, 1)/2), 1:3);
% load leadfield
load(basis_file, 'basis');
% plot leadfield
pick1 = pick(ix1, :); % axial sensor
pick2 = pick(ix2, :); % planar sensor
```

```
% --- heart (x)
clim_val = 1e-6*[-0.1 0.1];
figure('Name', 'Heart (x)');
subplot(2, 1, 1);
vb_plot_sensor_2d(pick1, basis(7, ix1), clim_val);
axis equal off;
colorbar;
subplot(2, 1, 2);
vb_plot_sensor_2d(pick2, basis(7, ix2), clim_val);
axis equal off;
colorbar;
```

The following figure will appear:



The above and below show spatial patterns of the leadfield at axial and planar sensors, respectively, of Yokogawa 400ch system in ATR. The actual figure you will see depends on the sensor configuration of your system.

#### Estimate current variance on MATLAB console

To estimate current variance, you need to manually set the parameters for extra-dipoles in **bayes\_parm.extra**:

```
>> proj_root = './subjects/';
>> ...
>> bayes_parm.extra.basisfile = 'sbj_test/sbj_test_HPF_LPF_BC-
TriggerLR_eyes.basis.mat'; % Multiple sessions not supported yet
>> bayes_parm.extra.extra.a0 = (5e-9)^2*ones(6,1);
>> bayes_parm.extra.Ta0 = 100*ones(6,1);
>> bayes_parm.extra.a0_physical = true;
>> ...
>> vb_job_vb(proj_root, bayes_parm);
```

The following two issues should be noted:

- 1. Number of extra-dipoles: we have specified 2 position (left and right eyes) when creating .mps.mat. At each position, 3 current dipoles are assumed in the x, y, and z axis, leading to each hyperparameter having 6 components. This allows for estimation of current direction.
- The magnitude of the prior current variances are specified as having a physical unit (Am, current dipole moment), specified by parameter "a0\_physical". (5e-9)<sup>2</sup> (5[nAm] is squared to produce the variance) is a tentative value of current dipole moment induced by tremor when fixating the eyes (Morishige et al., 2009).

#### **VBMEG** functions

#### **Plotting function**

- vb\_plot\_cortex: Plot cortical surface.
- vb\_plot\_sensor\_2d: Plot spatial pattern of M/EEG signal.

#### File access function

- vb\_add\_act: Add activity map (vector whose dimension is the number of vertices of cortical surface model) to cortical activity file.
- vb\_add\_area: Add area (index set of cortical surface model) to cortical area file.
- vb\_get\_act: Get activity map (vector whose dimension is the number of vertices of cortical surface model) from cortical activity file.
- vb\_get\_area: Get area (index set of cortical surface model) from cortical area file.
- vb\_load\_basis: Load leadfield matrix.
- vb\_load\_channel\_info: Load information of M/EEG channel.
- vb\_load\_cortex: Load cortical surface model.
- vb\_load\_meg\_data: Load M/EEG signal timecourses.
- vb\_load\_meg\_info: Load information of M/EEG data.
- vb\_load\_sensor: Load information of M/EEG sensor position.

## FAQ

#### What is the unit of cortical current estimated with VBMEG?

 By default, the unit of cortical current is Ampere meter (Am). If patch normalization is applied during estimation, the unit is Am/m<sup>2</sup>. As a supplement, all physical variables of VBMEG have standard SI units (e.g., MEG signals have "Tesla" as its unit as opposed to pico/femto Tesla). The same holds for the cortical current.

#### Which direction does estimated cortical current at each vertex flow?

• In cortical current files (.curr.mat), a positive current is defined as one directed toward the outside of the cortex. However, the direction is automatically flipped when plotting cortical currents by *job\_plot\_currentmap*; current directed toward the inside of the cortex is shown as positive.

#### Which kind of information does positioning files (.pos.mat) include?

• Positioning files include a 4-by-4 affine transformation matrix (trans\_info, obtained by vb\_posfile\_get\_transinfo.m). The affine matrix transforms the sensor coordinate system (position and direction) in the hardware space (measurement system dependent) to the 'SPM\_Right\_m' space (MRI dependent).

#### How do I get axial sensors of Yokogawa MEG system?

• You can use VBMEG function vb\_load\_channel\_info:

>> ch\_info = vb\_load\_channel\_info('your\_meg\_file.meg.mat');

'ch\_info' is a struct including information of sensors.

```
>> ch_info
```

```
ch_info =
```

```
Active: [400x1 double]
Name: {400x1 cell}
Type: [400x1 double]
ID: [400x1 double]
```

'ch\_info.Type' includes sensor type. In Yokogawa MEG system at ATR with 400 channels, 2 and 3 indicates axial and planar sensors, respectively. Indices of axial sensors can be obtained with the following code:

ix\_axial = find(ch\_info.Type==2);

## How do I get the original vertex indices for estimation results with reduce parameter less than 1?

If you performed current estimation with a vertex reduction parameter <1, you may
want to get vertex indices for the reduced vertices. Specifically, cortical current
estimation with the reduced vertices use the equation J=WZ, where J is the
cortical current, W is the smoothing matrix, and Z is the auxiliary variable. You can
transform Z to J using the following MATLB code:</li>

```
۷
        = vb_load_cortex('your_brain_file.brain.mat');
Jinfo = vb load current info('your current file.curr.mat');
W
       = Jinfo.Wact;
       = 100; % number of time points
Т
I
        = size(V,1);
I ext = size(W, 1); % note: it can be different with I=size(V, 1) because the
maximum radius of the smoothing filter can not be large enough to cover the
cortical region
I act = size(W, 2);
Z = rand(I_act, T); % pseudo data on the reduced model
J = zeros(I, T);
ix trans = (I ext, 1);
ix_trans(1:I_ext, :) = Jinfo.ix_act_ex;
J(ix_trans,:) = W*Z; % transformation from reduced model to the original
```

model

Note that size(W,2) can be less than size(J,1) (==I). It means that W can include only a subset of the whole cortical model. To compensate this inconsistency, here, indices are transformed via variable ix\_trans.

#### How do I get the nearest neighbors to a vertex?

The cortical model file includes distances from each vertex to neighbors. The following code is an example to get neighbors to a vertex within 10mm radius.

```
[nextDD, nextIX] = vb_load_cortex_neighbor('your_brain_file.brain.mat');
ix_center = 100; % center of ROI
ixx = find(nextDD{ix_center}<=10e-3);
ix_roi = nextIX{ix_center}(ixx); % ix_roi is the set of
vertices within 10mm from ix center
```

#### How do I make my own fMRI prior?

You may want to combine two or more fMRI prior to estimate cortical current during multiple conditions but with the single prior. The following code is an example to calculate average of cortical activity data already stored and store the averaged activity data to a cortical activity file.

```
act_file1 = 'your_act_file1.act.mat';
act_file2 = 'your_act_file2.act.mat'; % this can be the same with act_file1.
act1 = vb_get_act(act_file1, 'act_key_cond1');
act2 = vb_get_act(act_file2, 'act_key_cond2');
act_new.xxP = (act1.xxP+act2.xxP)./2;
act_new.key = 'act_key_new'; % ID of new activity map
```

vb\_add\_act(act\_file2,act\_new); % store new activity map

The average activity map will be stored in act\_file2 with ID 'act\_key\_new'.

#### Troubleshooting

How to resolve the error 'Output argument "z" (and maybe others) not assigned during call to "\$VBMEG¥vb\_repmultiply...>vb\_repmultiply".'?

- You need to recompile MEX-files for your system. It can be done just by running following functions.
  - vb\_mex\_compile.m
  - vb\_mex\_compile\_utilities.m

How to resolve the error 'Invalid MEX-file <mexfilename> The specified module could not be found.' on Windows?

- You need to install Microsoft Visual C++ 2010 Redestributable Package (x86/x64) on your system. see the following URLs.
  - for x86: vcredist\_x86.exe: <u>http://www.microsoft.com/en-us/download/details.aspx?id=5555</u>
  - for x64: vcredist\_x64.exe: <u>http://www.microsoft.com/en-us/download/details.aspx?id=14632</u>

#### The result of fMRI import looks strange. How do I fix it?

- It is possible that the coordinate system of the voxel data (in .spm.mat) does not match with that of the cortical surface model on which the voxel data are projected.
  - You can check this by using the following MATLAB commands:
  - >> V1 = vb\_load\_cortex('your\_brain\_file.brain.mat');
  - o >> load('my\_voxel\_data.spm.mat','SPM');
  - >> V2 = (SPM. XYZmm. /1000)';
  - $\circ$  >> figure;
  - >> plot3(V1(:, 1), V1(:, 2), V1(:, 3), 'b.');
  - $_{\circ}$   $\longrightarrow$  hold on;
  - >> plot3(V2(:,1), V2(:,2), V2(:,3), 'r.');
  - $\circ$  >> view([0 90])
  - If coordinate systems matches, cortical vertices (blue) and voxel positions (red) are overlapped as shown in the figure:



- If you use the normalization file (\_sn.mat) for another subject, these positions will not match. In addition, you need to use the same T1 image for SPM analysis and FreeSurfer cortical surface extraction. Check that your \_sn.mat file are created from the MR image of the subject you deal with.
- Otherwise, the problem may stem from the origin of the T1 image on which EPI images are registered. Load the T1 image on SPM.



• Check the origin of the T1 image. If the origin does not the center of the image, the voxel positions in the .spm.mat file can be shifted, leading to a

misalignment of the cortical surface model and voxel positions on VBMEG. The following figure shows a valid T1 image. The size of this image is 191x256x256.



• If the origin is not the center of the image, you may need to modify the header file. On SPM8 GUI, you can use "Reset" button.

right {mm} forward {mm} up {mm} pitch {rad} roll {rad} yaw {rad} resize {x}	0 0 0 0 0 0 1	Vox size:-1 x 1 x 1 Origin:96 105 113 Dir Cos: 1.000 0.000 0.000 0.000 1.000 0.000 0.000 0.000 1.000
resize {y} resize {z}	1	Full VolumeHide CrosshairsWorld Spacebilin interp
Reorient images	Reset	Auto Window 👻 🛛 Add Blobs

• Select the T1 image file in the file dialog. Then the origin will be set to the center of the T1 image.

Vox size: <b>-1 x 1 x 1</b>					
Origin:96.5 128 128					
Dir Cos: 1.000 0.000 0.000					
0.00	0 1.000 0.000				
0.00	0 0.000 1.000				
Full Volume 👻	Hide Crosshairs				
World Space 👻	bilin interp 👻				
Auto Window 🛛 👻	Add Blobs				

 After reset the origin, you need to perform SPM precessing and make .spm.mat file again.

## MATLAB Scripts

Add new area information into cortical area file (.area.mat)

```
Extract area on which some activity (e.g., t-value) is larger than a threshold
% files and ids
area_file = 'sbj.area.mat';
act_file = 'sbj.act.mat';
% thresholding
act = vb_get_act(act_file,'t_value'); % get activity map 't_value' stored
in act_file
ix = find(a, xxP \ge threshold);
% make and add new area
area_new.Iextract = ix; % thresholded area
area_new.key = 'area_new_id'; % any identifier
vb_add_area(area_file, area_new); % area_new is added to area_file
Concatenate two areas (union)
% files
area_file = 'sbj.area.mat';
% get areas
area1 = vb_get_area(area_file, 'area1');
area2 = vb_get_area(area_file, 'area2');
```

```
% concatenation
ix = union(area1.lextract, area2.lextract);
```

```
% make and add new area
area_new.Iextract = ix;
area_new.key = 'area_new_id'; % any identifier
vb_add_area(area_file, area_new); % area_new is added to area_file
```

#### Plot cortical surface model

```
Plot vertices of cortical surface model superimposed on the inflated model
% files
brain_file = 'sbj.brain.mat';
```

```
% plot cortical surface model
[V,F,tmp,inf_C] = vb_load_cortex(brain_file,'Inflate');
plot_parm = vb_set_plot_parm;
vb_plot_cortex(plot_parm, V, F, inf_C, J);
hold on;
```

```
% vertex indices
ix = [1; 10; 100; 1000];
```

```
% plot vertices
plot3(V(ix, 1), V(ix, 2), V(ix, 3), 'r.');
```

```
Plot vertices of cortical surface model superimposed on the inflated model (left
hemisphere only)
% files
brain_file = 'sbj.brain.mat';
```

```
% plot cortical surface model (left hemisphere only)
[V,F,tmp,inf_C] = vb_load_cortex(brain_file, 'Inflate');
plot_parm = vb_set_plot_parm;
plot_parm.LRflag = 'L'; % 'L' for LH, 'R' for RH, 'LR' for both hemispheres
vb_plot_cortex(plot_parm, V, F, inf_C, J);
hold on;
```

```
% vertex indices
ix = [1; 10; 100; 1000];
```

```
% choose vertices of LH
ix_lh = F.F3L(:); % F.F3L(:) including vertex indices of LH
ix = intersect(ix,ix_lh);
```

```
% plot vertices
plot3(V(ix, 1), V(ix, 2), V(ix, 3), 'r.');
```

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