Joint MEG/DOT brain functional imaging with state-space models

with Kalman filter and cortically constrained finite-element modelling

The Massachusetts
General Hospital
Martinos Center for
Biological Imaging

Qianqian Fang, Wanmei Ou, Theodore Huppert, Solomon Diamond,
Matti Hämäläinen, David Boas

Motivation: The neuronal evoke response measured from Magnetoencephalography (MEG) and the hemodynamic response captured by diffuse optical imaging (DOI) are both triggered by the same source, i.e. the electrophysiology (E-phys) of neuronal cells, and thus exhibit intrinsic correlations via a complex neural-vascular coupling process. Simultaneous MEG/DOI experiments enable use to explore this further and synegestically use both measurements to enhance estimation accuracy. In this study, we take advantage of this intrinsic correlation and develop a joint image reconstruction algorithm for MEG/DOI using a state-space model. A Kalman filter approach was used to estimate the non-stationary optical and MEG parameters. To reduce the computational burden, we constrain the MEG/DOI solutions to the cortex surface and developed a number of software tools to facilitate this analysis under a multimodality context.

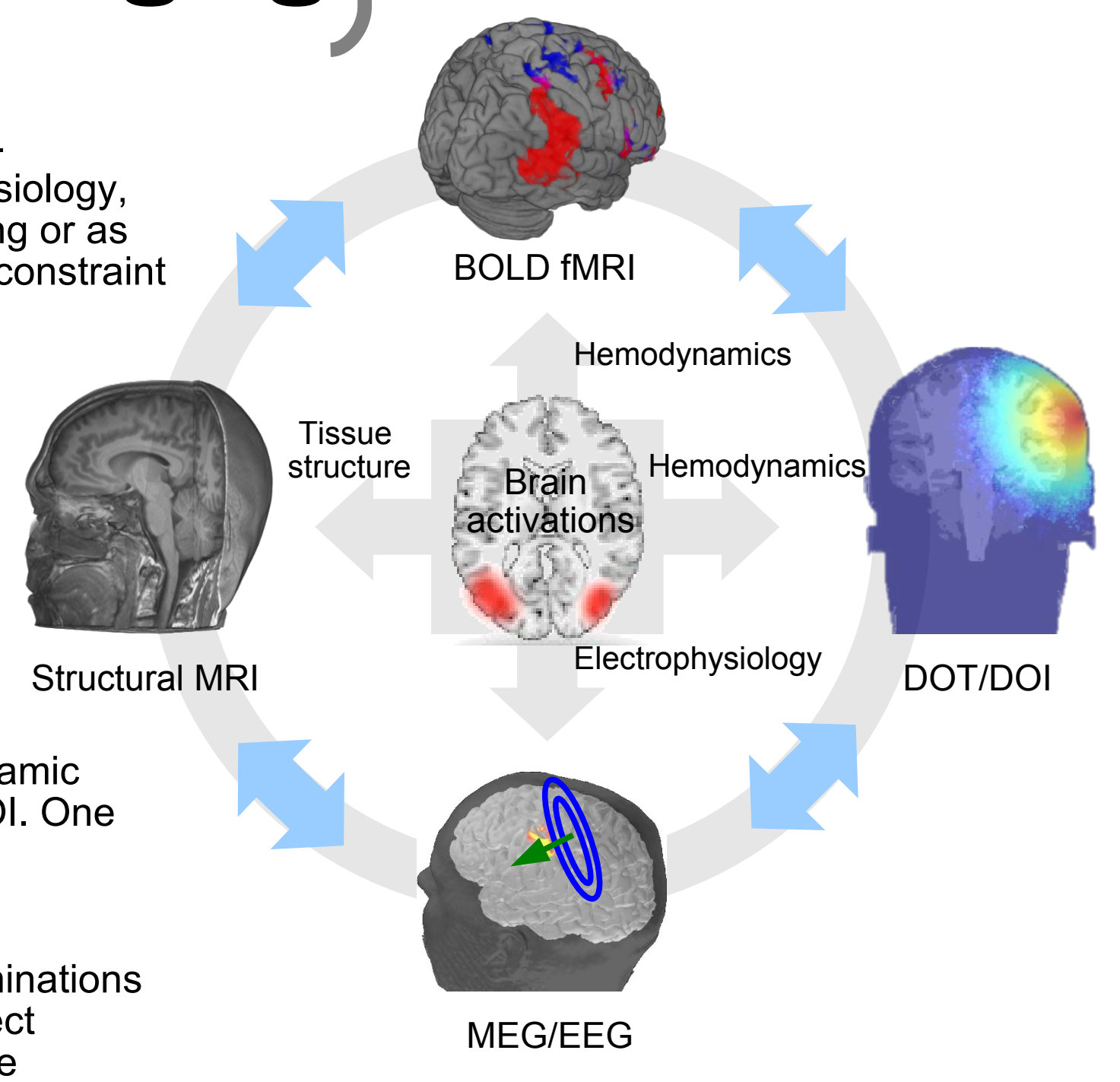
multi-modality brain functional imaging

Structural & functional image fusion (spatial)
For various reasons, the images produced from functional imaging modalities are typically low-resolution. To be able to accurately determine the physical origin and correlate with tissue physiology, one typically need to fuse the functional images with structural images, either in post-processing or as part of the image reconstructions. In the second case, the the structural images may sever as constraint for problem domain or spatial prior to influence the image reconstructions.

E-phys and hemodynamic fusion (temporal/spatial)
The neuronal electrical response triggers the arterial dilation which results in a cascade of dynamic processes in blood volume, blood flow and oxygenation in various vessel compartments. Using an appropriate transfer function, one can incorporate the E-phys into the estimation of hemodynamic parameters; additionally, this information fusion can be directed in the inverse direction: the hemodynamic measurement can also inform the estimation of E-phys parameters.

HbR and fMRI fusion
BOLD fMRI measures the intra-cellular and extra-cellular water signal variations in a hemodynamic process. These parameters exhibit correlations to HbR and oxygen saturation measured in DOI. One can use one measurement to inform the parameter estimations of the other modality.

Background physiology extraction and modelling
Background physiology, such as cardiac and respiration signals, is the major source of contaminations for DOI hemodynamic measurements. To be able to obtain more accurate DOI estimation, direct measurement and isolation of these components is very important. State-space models provide efficient tools for filtering these background signals.

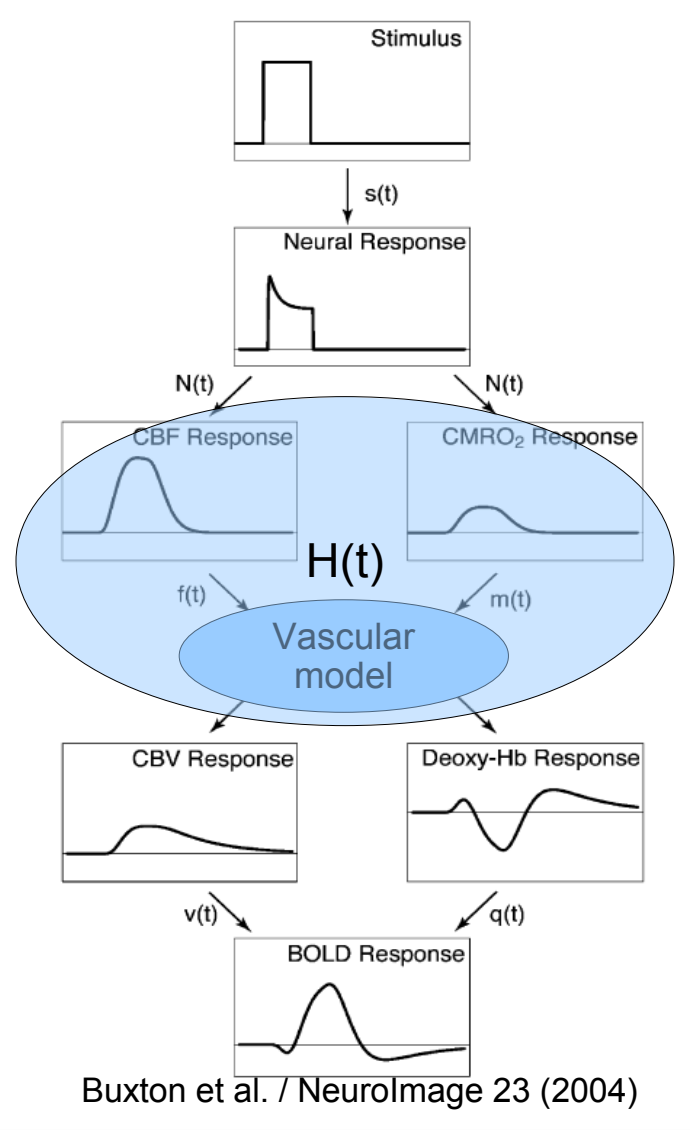


neural-vascular coupling

A accurate model of the neural-vascular coupling involves the modeling of arterial dilation and the subsequent changes in blood volume (CBV) and flow (CBF) with a vascular model, such as Windkessel, and oxygen transport and extraction in various compartments. As a result, this coupling relationship is non-linear. However, as the first step, we ignore the complex vascular model and approximate the neural-vascular coupling by a linear convolution model, i.e. the hemodynamics can be represented by

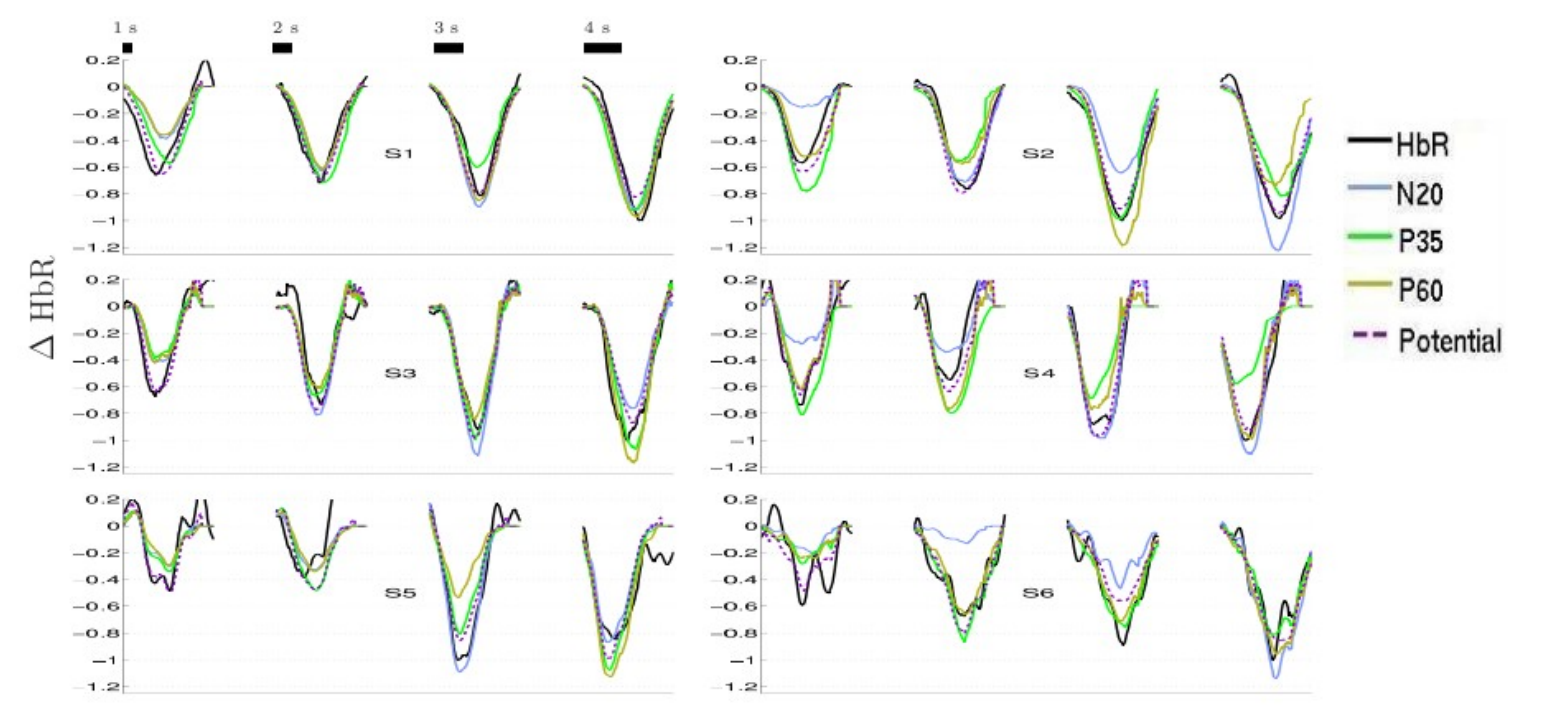
$$Hb(t)=H(t)*d(t)$$

where Hb(t) is the hemodynamic response (HbO or HbR), d(t) is the electrophysiology response, and H(t) is the impulse response function that connects the E-phys response to hemodynamic responses.

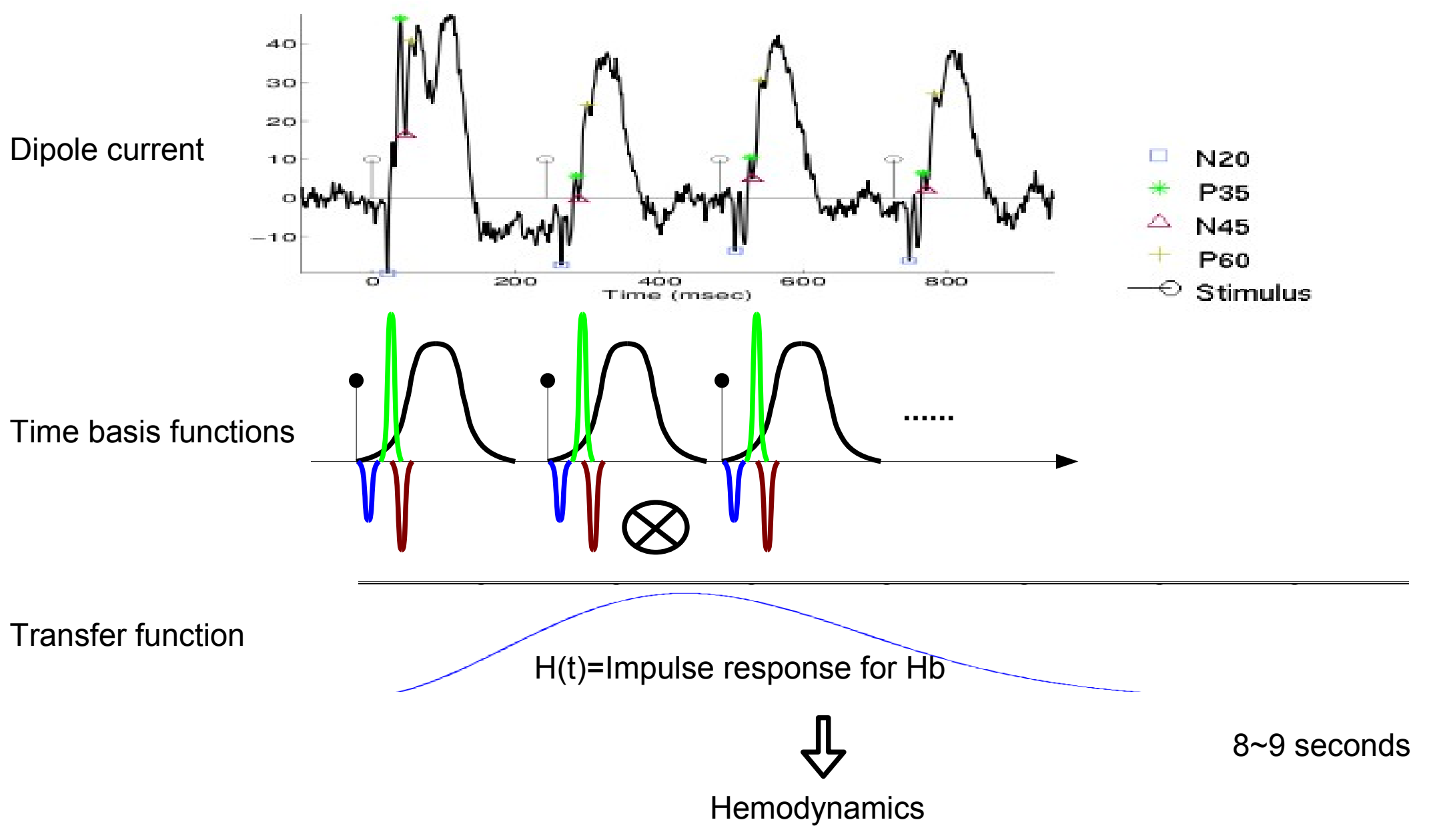


Buxton et al. / NeuroImage 23 (2004)

In [Wanmei2009], this linear model was tested and used to predict the HbR changes from various deflections in the neural responses. An empirical impulse response were fitted from 5 concurrent MEG/DOT measurements. From the following plot,the changes predicted from the evoke responses roughly match the shape of HbR changes estimated from DOI measurement; the potential appears to give the best match.



state-space model



State-space model for filtering after independent MEG/DOI estimations

Measurement

$$\mathbf{y}=\begin{pmatrix}HbO(t)\\HbR(t)\\D(t)\end{pmatrix}$$

Dipoles response

$$D(t)=\sum_{s=1}^{M}\left(\sum_{k=1}^{4}d_k G(t-t_s,\tau_k,\sigma_k)\right)$$

HbO and HbR

$$Hb(t)=a_{Hb}\times H_{Hb}(t)\otimes D(t)+\sum_i a_{fi}\sin(\omega_i t)+b_{fi}\cos(\omega_i t)$$

$$=a_{Hb}\times H_{Hb}(t)\otimes\left(\sum_{s=1}^{M}\left(\sum_{k=1}^{4}d_k G(t-t_s,\tau_k,\sigma_k)\right)\right)+\sum_i a_{fi}\sin(\omega_i t)+b_{fi}\cos(\omega_i t)$$

States

$$\mathbf{x}=[a_{HbO}\quad a_{HbR}\quad d_1\quad d_2\quad d_3\quad d_4\quad a_{f1}\quad b_{f1}\quad c]^T$$

Jacobian

$$J=\frac{d\mathbf{y}}{d\mathbf{x}}=\begin{pmatrix}H_{HbO}(t)\otimes D(t) & 0 & 0 & 0\ \ 0 & 0 & \sin(2\pi f_1 t) & \cos(2\pi f_1 t) & \dots\\ 0 & H_{HbR}(t)\otimes D(t) & 0 & 0\ \ 0 & 0 & \sin(2\pi f_1 t) & \cos(2\pi f_1 t) & \dots\\ 0 & 0 & \sum_s G(t-t_s,\tau_1,\sigma_1) & \dots\ \ \dots & \sum_s G(t-t_s,\tau_4,\sigma_4) & 0 & 0 & \dots\end{pmatrix}$$

```
Loop over time step k {
    State prediction (transition)
        $\bar{x}_k = K x_{k-1}$
    State covariance prediction
        $\bar{C}_k = K C_{k-1} K^T + Q_k$
    Kalman Gain
        $G_k = \bar{C}_k J_k^T (J_k \bar{C}_k J_k^T + R_k)^{-1}$
    State update
        $x_k = \bar{x}_k + G_k (y_k^M - y_k(\bar{x}_k))$
    State covariance update
        $C_k = (I - G_k J_k) \bar{C}_k$
}
```

State-space model for joint MEG/DOI estimation

Observations

$$y(t)=\begin{pmatrix}\Phi(t)\\M(t)\end{pmatrix}$$

states:

$$x=[a_{HbO},a_{HbR},d_1,d_2,d_3,d_4,a_{f1},p_{f1},a_{f2},p_{f2},c]^T$$

sensitivity matrix:

$$J=\frac{dy}{dx}=\begin{pmatrix}\dfrac{d\Phi}{dx}\\[2mm]\dfrac{dM}{dx}\end{pmatrix}$$

where

$$\frac{d\Phi}{dx}=\left(J_{HbO}(H_{HbO}(t)*d(t))\quad J_{HbR}(H_{HbR}(t)*d(t))\quad 0\quad 0\quad 0\quad 0\quad (J_{HbO}+J_{HbR})\sin(2\pi f_1 t)\quad (J_{HbO}+J_{HbR})\cos(2\pi f_1 t)\right)$$

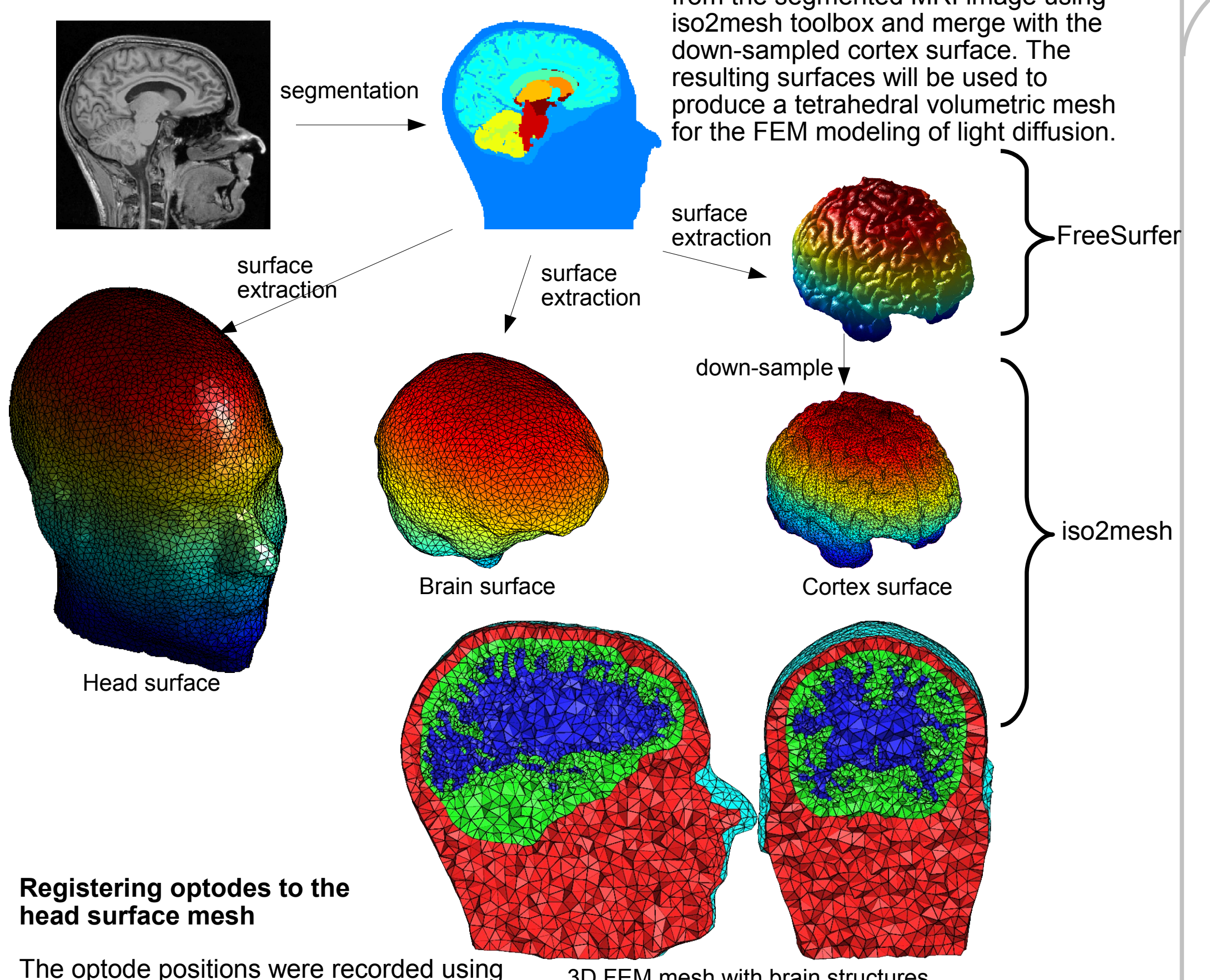
$$\frac{dM}{dx}=\left(0\quad 0\quad J_{MEG}\sum_s G(t-t_s,\tau,\sigma_1)\quad J_{MEG}\sum_s G(t-t_s,\tau,\sigma_2)\quad J_{MEG}\sum_s G(t-t_s,\tau,\sigma_3)\quad J_{MEG}\sum_s G(t-t_s,\tau,\sigma_4)\quad 0\quad 0\quad \dots\right)$$

The above equation will be solved for each node within the region-of-interest at every time point. The full history of d(t) will be stored and used to compute d*M*/d*x*. This formula informs DOI parameter estimations using the dipole response from MEG.

cortically constrained reconstruction

Using structural information in the image reconstruction

First, the structural MRI images will be segmented into different tissue types using FreeSurfer; the high resolution cortex surface is then downsampled to limit the unknown space. The surface of the head and brain will be extracted from the segmented MRI image using iso2mesh toolbox and merge with the down-sampled cortex surface. The resulting surfaces will be used to produce a tetrahedral volumetric mesh for the FEM modeling of light diffusion.



3D FEM mesh with brain structures

Registering optodes to the head surface mesh

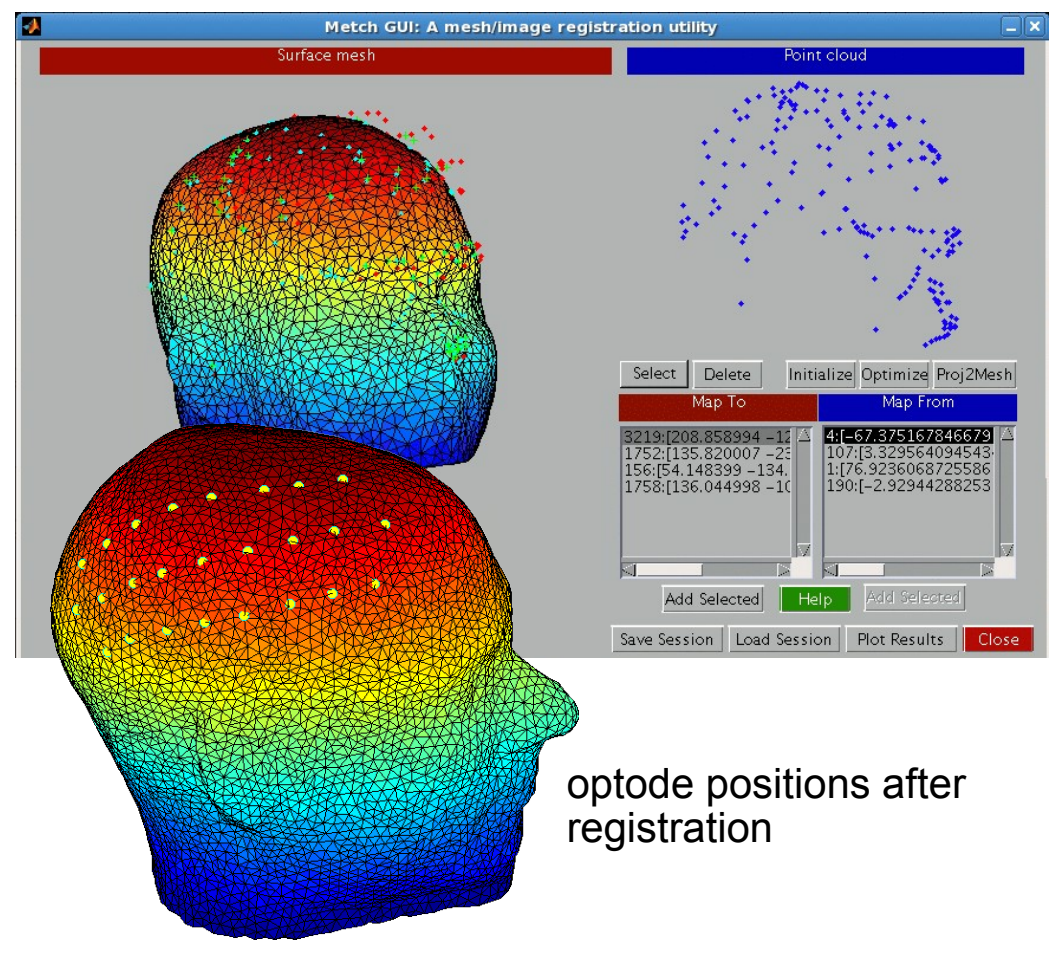
The optode positions were recorded using a EM position tracker (Polhemus), as well as the contour of the head surface.

We register the optode positions to the head surface mesh using the following procedures:

1. select a number of landmarks based on the 10-20 systems (inion, nasion, Cz etc) on both surface mesh and the tracker recording, compute a initial rigid-body transformation matrix using least-squares;

2. use the above matrix, iteratively minimize the distances of the entire point cloud to the surface mesh and produce an optimized transformation.

3. project the transformed optodes onto the surface (make sure they locate on the surface).

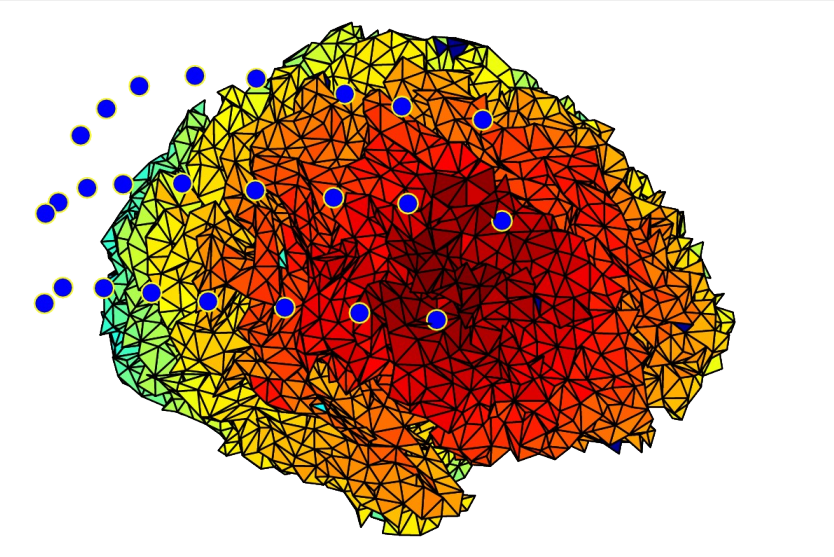


optode positions after registration

Computing Jacobian for DOT and obtaining cortical mapping

Using the FEM mesh and tissue segmentation generated previously, we compute the forward solutions for each optode by solving the diffusion equation with the FE method.

From these forward solutions, we compute the Jacobian matrix distributed through the entire mesh using the adjoint method.

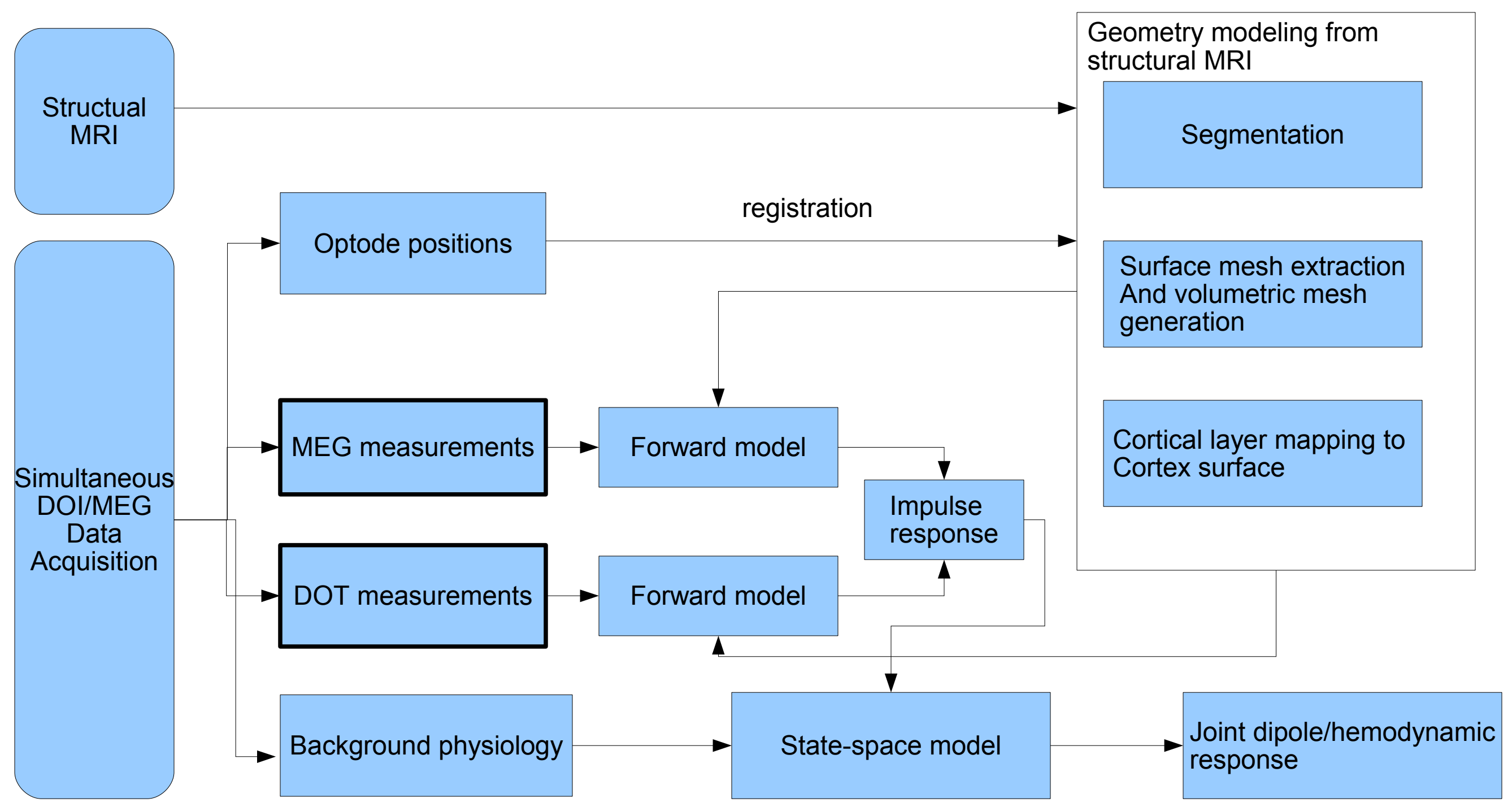


Sensitivity map computed on the cortex surface (for a specified source/detector pair)

Because in brain functional studies, the activations are mostly located within the gray-matter layer, therefore, we zerorize all the non-gray-matter entries in the Jacobian. To further reduce problem space, we collapse all gray-matter nodes and merge their sensitivities to their nearest cortex surface mesh nodes. This reduce the unknown space dramatically and greatly facilitate the analysis. One can further reduce the unknown space by thresholding the sensitivity values on the cortex surface and only include those nodes within the coverage of the optodes.

algorithm workflow

In this analysis, we jointly use the structural information from MRI, E-phys from MEG and hemodynamics information from DOI to estimate the hemodynamic and dipole current response. The overall estimation workflow is shown below.

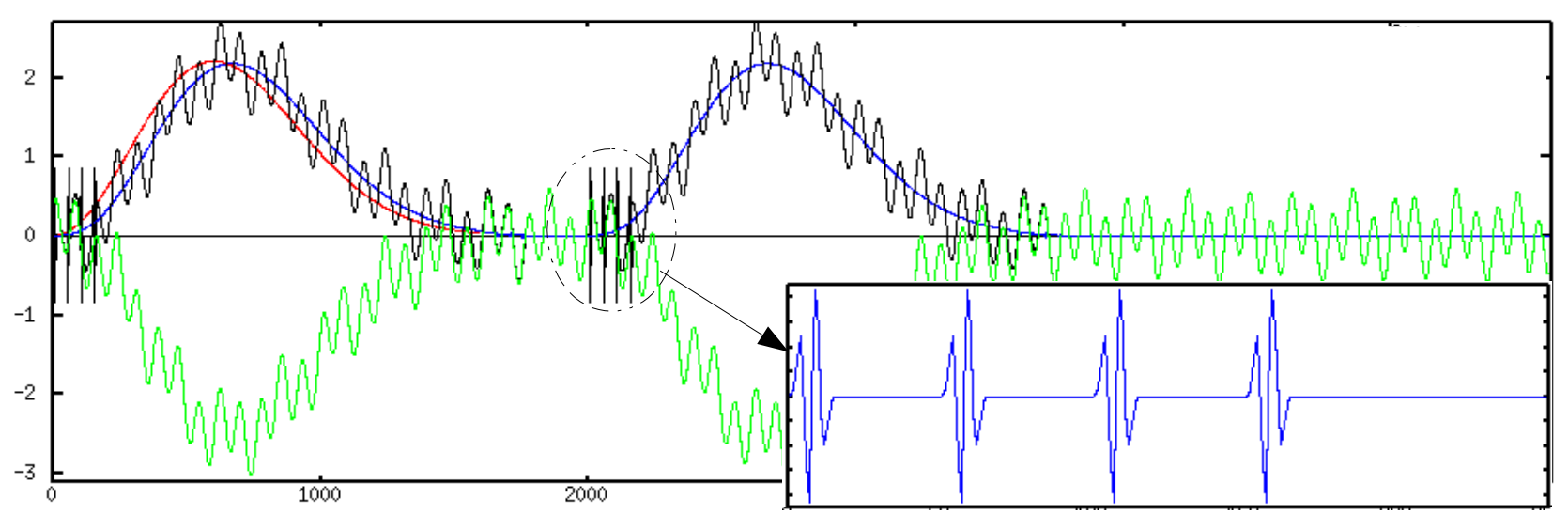


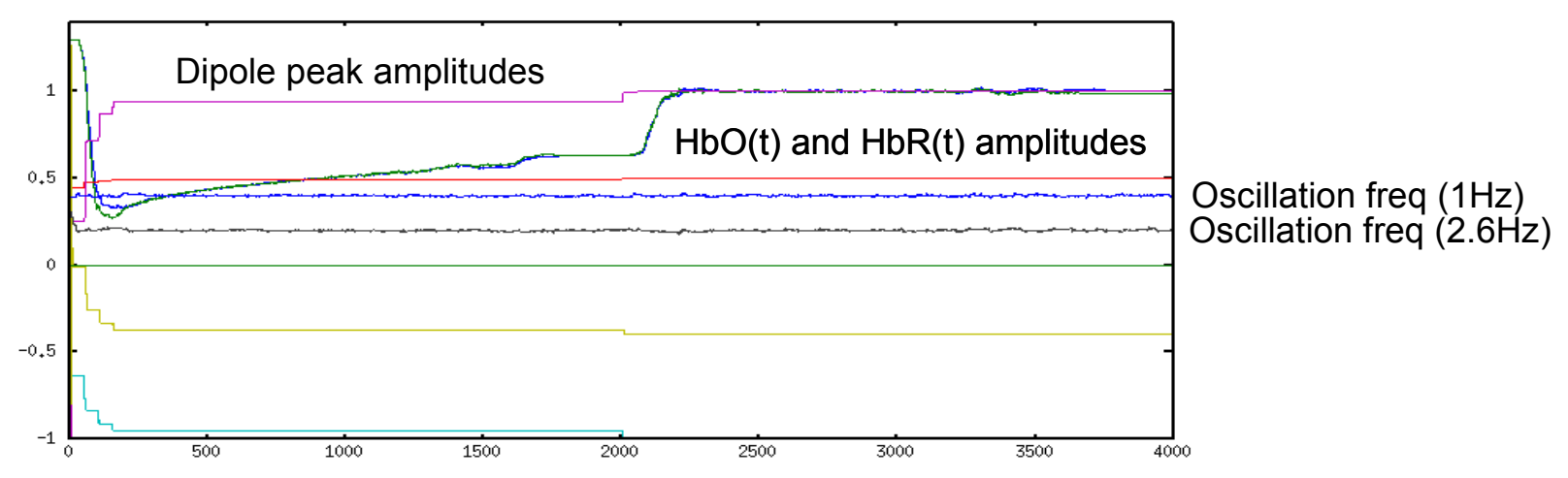
simulations

We simulated a concurrent MEG/DOT measurement using an assumed impulse response function. The stimulus consists of 4 consecutive pulses with ¼ second spacing, followed by 9 seconds baseline. This stimulus is repeated with the same or different amplitudes.

The dipole response was decomposed into 4 basis functions corresponding to the deflections at 20ms, 35ms, 45ms and 60ms from the on-set of the stimulus. Two background oscillation signals were added to simulate cardiac and respiration.

Using the Kalman filter, we estimated the amplitudes of HbO, HbR, the amplitudes for each deflection peaks in the dipole response and the amplitudes of the background signals. These parameters were estimated correctly shortly after the full length of the impulse response function.





in vivo human experiments

A total of 5 human subjects were measured with a concurrently MEG/DOT experiment protocol. Head probes made of fiber optics were used to acquire RF and CW optical measurements. The stimulus trains are medium nerve stimulation pulses repeated at 4 Hz. The duration of the stimulus varies from 1 second to 4 seconds.

The DOI instrument is a multi-channel continuous wave (CW) system with 9 source fibers, 16 detector fibers, and a total of 32 active source/detector pairs. The separation of the shortest source/detector separation is 3cm. We acquired optical measurements at 40k sample/second and filtered to 10Hz.

The MEG data were acquired simultaneously with the optical data using a 306-channel Neuromag VectorView MEG device (Elekta-Neuromag Oy, Helsinki, Finland), in a magnetically shielded room (Imedco AG, Switzerland). The MEG measurement data was sampled at 1kHz [Wanmei2009].

what's next

We will apply the developed state-space model and the cortically constrained FEM modeling to the analysis of the concurrent DOI/MEG human experiments. This will require to perform a spatial-temporal reconstruction simultaneously using MEG/DOI measurements and recover the dipole and hemodynamic response on the cortex surface. The improvement using the joint model will be assessed by comparing with the single modality estimation.

As we incorporate more measurements into the estimation, the computational efficiency becomes the bottleneck. We will use the sensitivity map to further constrain the optical unknown space.

The utilities for the cortically constrained mesh processing will be released as open-source software. This will be listed at our development website at

`http://orbit.nmr.mgh.harvard.edu/`

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THE pmi lab OF MARTINOS CENTER FOR BIOMEDICAL IMAGING
MASSACHUSETTS GENERAL HOSPITAL, 13th street, building 149, CHARLESTOWN, MA 02129
`http://nmr.mgh.harvard.edu/PMI/`

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