Integrated MEG and fMRI Model

Abbas Babajani,[1] Mohammad-Hosein Nekooei,[1] Hamid Soltanian-Zadeh[1,2]

[1]Electrical and Computer Engineering Department, University of Tehran, Tehran 14399, Iran
[2]Image Analysis Lab., Radiology Department, Henry Ford Health System, Detroit, MI 48202, USA
E-mail: ababajani@yahoo.com

Abstract- For the first time, an integrated model for magnetoencephalography (MEG) and functional Magnetic Resonance Imaging (fMRI) is proposed. The MEG and fMRI outputs in the proposed model are related to the corresponding aspects of neural activities in a voxel. Post synaptic potentials (PSPs) and action potentials (APs) are two main signals generated by neural activities. In the model, both of MEG and fMRI are only correlated to PSPs and do not have correlation with APs. Each PSP is modeled by the direction and strength of its current flow which are treated as random variables. The overall neural activity in each voxel is used for equivalent current dipole (ECD) in MEG and as input of Balloon model for producing Blood Oxygen Level Dependent (BOLD) signal in fMRI. The proposed model shows the possibility of detecting activation by fMRI in a voxel while the voxel is silent for MEG and vice versa. The model also shows the possibility of different spatial responses in the two modalities. The proposed model is instrumental in evaluating and comparing different analysis methods of MEG and fMRI.

Keywords: Blood Oxygen Level Dependent (BOLD); Post Synaptic Potential (PSP); Action Potential (AP); Balloon model.

I. Introduction

Magnetoencephalography (MEG) detects weak magnetic fields generated by the flow of synchronized intracellular postsynaptic currents of pyramidal cells [1]. Functional Magnetic Resonance Imaging (fMRI) signal reflects oxygen level of the blood and thus is called blood oxygen level dependent (BOLD), which is a complex function of multiple physical parameters like blood flow, blood volume and blood oxygenation that changes by neural activities [2]. Neural activities are common source for both MEG and fMRI. Therefore, there should be a relationship between the responses of the two modalities, but this relation is not understood well heretofore.

It is known that if there are neural activities in a region and current sources from these activities are not synchronized and/or do not have the same direction, they may cancel each other and this region may be silent for MEG while having a detectable BOLD signal. Also, when there are synchronized and unidirectional current flows induced by a small quantity of active neurons, it is possible to detect MEG signal in a region that is silent in fMRI. To explain these facts and explore the relationship between the two modalities, we propose an integrated MEG and fMRI model (Fig. 1). In the proposed model, the external stimulus causes neural activities in a specific region of the brain (covering a few voxels). Based on the neural activities in the voxels, models of post synaptic potentials (PSPs) are used to generate MEG and fMRI signals. To this end, the activation of each neuron is modeled with several parameters. Since each voxel of the cortex contains a huge number of neurons whose activities are not deterministically known, we consider a stochastic model for each parameter.

The model is consistent with the fact that fMRI signal reflects the sum of PSPs' strengths (independent of their directions) but MEG signal reflects the vector sum of the PSPs (which depends on their directions). The model also shows that the crosstalk from neural activities of adjacent voxels in fMRI and properties of the inverse problem in MEG generate different spatial responses in the two modalities. The proposed model is instrumental in evaluating and comparing different analysis methods of MEG and fMRI. It is also useful in characterizing the upcoming integrated methods for simultaneous analysis of MEG and fMRI.

II. Proposed Model

Neuron is the principal building block of the brain. The overall activities of adjacent neurons in a region can be detected by MEG or fMRI. In the proposed model, the activities of neurons in a voxel are used for constructing MEG and fMRI signals. The voxel in the order of 1 mm^3 contains approximately 10^5 pyramidal cells and thousands of synapses per neuron [1]. Activity of each neuron starts with activities of its synapses that produce PSPs. The overall activities of synapses may produce action potentials (APs). PSPs and APs are two main indices for showing neural activities. MEG and fMRI are related to neural activities and so to PSPs and/or APs.

The proposed integrated model is constructed based on the fact that PSPs are the main link between the two modalities. We construct a stochastic model for PSPs so that each parameter (like direction and strength of each PSP) has a probability density function (pdf). The input of the model is the waveform of the external stimulation (Fig. 1). The number of PSPs at each time is constructed with a stochastic model according to the waveform of the input stimulus. The MEG signal is produced according to the pdfs of both direction and strength of the PSPs. The fMRI BOLD signal only depends on the overall strengths of PSPs, which is the input of the Balloon model for producing the BOLD signal. The overview of the relevant previous work and physiological facts that guide us for constructing the integrated model is presented in the following subsection before introducing the proposed model.

A. Neural Bases of MEG and fMRI

The intracellular potential of neurons increases by input through the excitatory synapses as excitatory post synaptic potential (EPSP), but decreases by inhibitory input as inhibitory post synaptic potential (IPSP). When the potential at the axon hillock reaches a certain threshold level, the neuron fires an action potential (AP) [1]. The relationship between PSPs (EPSPs or IPSPs) and APs with MEG and BOLD signals is inferred in this section. First, we deal with the MEG signal.

Both action and synaptic currents generate magnetic fields. Approximately, the action potential can be considered as two opposite oriented current dipoles, which form a current quadrupole. The magnetic field produced by a quadrupole of AP decreases as $1/r^3$ where r is the distance between dipole and detection sensor. However, the magnetic field produced by a PSP is dipolar and decreases as $1/r^2$. Moreover, longer duration of a PSP (tens of ms) allows more effective temporal summation of neighboring currents than with the 1 ms lasting APs. Thus, the MEG signals are likely produced by the synaptic current flow [1]. Thus, we consider only the effect of PSP on the MEG signal and ignore the effect of AP.

Now, the relationship between the BOLD signal and the neural activities (PSPs and/or APs) is discussed. Logothetis, et al [3] have done many experimental studies for illustrating the relationship between BOLD signal and PSPs (synaptic activities) or APs (spike activities). The Multiple Unit spiking Activities (MUAs) are a weighted sum of the extracellular APs and the Local Field Potentials (LFPs) are the weighted average of synchronized dendro–somatic components of the synaptic signals. Thus, MUAs and LFPs are similar to the APs and PSPs, respectively. They simultaneously gather BOLD signal and also neural activities with microelectrode and then separate two types of neural signals (MUA and LFP) according to their different frequency property.

Logothetis, et al [4] saw that although MUA rises after activation, but it returns to baseline after 2-4 sec. Conversely, LFP was always elevated for the duration of the stimulus, similar to the BOLD signal. Both BOLD and LFP increased when the strength of stimuli increased, but the relation between BOLD and LFP is nonlinear. They concluded that the LFPs were the only neural signal to be associated with the BOLD response.

Lauritzen, et al [5] used the rat cerebellar cortex for detailed studies of the relationship among AP, synaptic activity, and changes in CBF. Their final result implies that it is impossible to conclude whether the spike activity (or APs) in a given brain region is increased or decreased on the basis of increases in CBF (and consequently the BOLD signal). They reported that the CBF or BOLD will be increased when the LFP is increased and the relation between LFP and CBF is an increasing function but may be nonlinear. This also indicates that PSPs affect the BOLD signal.

EPSP and IPSP have different polarizations and so they have canceling effect for MEG. Do they have same effect on the BOLD signal in fMRI? Experimental study of Caesar, et al [6] is one of the newest studies that answer this question. They stimulated the cerebellar climbing fibers (CF; excitatory) and parallel fibers (PF; inhibitory) alone and in combination and simultaneously recorded CBF with laser Doppler flowmetry (LDF). They reported that stimulation of the excitatory climbing fiber (EPSP) or inhibitory parallel fibers (IPSP) increases the CBF amplitude and there is no any difference between EPSP and IPSP in this regards. Thus, they

concluded that the EPSP and IPSP have similar effect on the BOLD signal.

In summary, considering the above facts and experimental studies, we conclude that both of equivalent current dipole (ECD) in MEG and BOLD signal in fMRI are mainly correlated to the PSPs and it is reasonable to ignore the effect of APs. The BOLD is an increasing but nonlinear function of PSPs. Although EPSP and IPSP have opposite effect in MEG, both of them have the same similar increasing effect on BOLD signal. We use these facts for constructing the proposed model.

B. Details of Proposed Model

The proposed model relates the MEG and fMRI signals in an active voxel of the brain. There are a huge number of neurons and synapses in a voxel. If during external stimulation a voxel belongs to the active region of the brain, there are many PSPs and APs in this voxel whose numbers and strengths show the rate of neural activities. According to our discussion in the previous section, we consider the PSPs as the single link between MEG and fMRI in the proposed model and ignore the effects of APs. The number and strengths of PSPs show the overall neural activities that produce MEG signal and change the blood flow for producing BOLD signal as shown in Fig. 1. The proposed model contains multiple blocks, which we will discuss in the following subsections.

B.1. PSP Production Mechanism

The first block of the proposed model is "PSP Production Mechanism" that shows at each time point during the external stimulation, how many PSPs are produced and what are their strengths and directions. After external stimulation, the activation in a voxel will start from activation of neurons that have peripheral nerve inputs or input connections with active neurons of another voxels. Gradually the number of active PSPs (also active neurons) in a voxel increases to its maximum number when most of the interconnection synapses are activated. After this time, it is logical to consider that the number of active PSPs does not almost change during the stimulation and this maximum number depends on the strength of the external stimulation.

After external stimulation, the background activity (no stimulation) reaches the maximum number of active PSPs in a duration of time which is proportional to the duration of a PSP (in the order of 10 ms). This delay for various stimuli is reported from 20 ms to 130 ms in [1]. For modeling this delay, we consider a first order system as the simplest model between external stimulation as input and the number of active PSPs as output as shown in Fig. 2. The relation between stimulation (*Stm*) and number of active PSPs (*N*) in this first order system is:

$$\tau_d \frac{dN(t)}{dt} + N(t) = N_{ss}\, Stm(t) \tag{1}$$

where N_{ss} is the steady state value of $N(t)$ which is proportional to strength of stimulation and τ_d models the delay time between stimulation and maximum neural activity.

B.2. Constructing BOLD from PSPs

The second block in the model (Fig. 1) shows the relationship between different aspects of PSPs and MEG or fMRI. Each PSP is like a small current dipole that is a vector with direction and absolute value. Both direction and absolute value of this vector is important for MEG, but only the absolute value of this vector is important for fMRI. The kind of PSP (IPSP or EPSP) is important for MEG because of their opposite polarity, but not important for fMRI according to our previous discussions.

The absolute value or strength of each PSP depends on the kind of neuron, synapse and dendrite parameters. Also, the direction of current dipole for each PSP depends on the shape and structure of dendrite trees. Since it is not logical to introduce a deterministic model for these parameters, we consider each parameter as a random variable in the proposed model. The relationship between produced PSPs and MEG or fMRI signals is illustrated in block 3 of Fig. 1. We start discussing the fMRI part of the model and afterward deal with the MEG part of the model.

The "Balloon model" is used as the main mechanism for relating PSPs as the neural activity input and BOLD signal as output [7]-[8]. We use the extended Balloon model proposed by Friston and colleagues [8] in our proposed model.

In the Balloon model of Friston and colleagues, the neural activity ($u(t)$) is related to the BOLD signal ($y(t)$) by the following set of equations:

$$\dot{s} = \varepsilon u(t) - s/\tau_s - (f_{in} - 1)/\tau_f \tag{2}$$

$$\dot{f}_{in} = s \tag{3}$$

$$E(f_{in}, E_0) = 1 - (1 - E_0)^{1/f_{in}} \tag{4}$$

$$\tau_0 \dot{v} = f_{in} - f_{out}(v) \quad , \; f_{out} = v^{1/\alpha} \tag{5}$$

$$\tau_0 \dot{q} = f_{in} \frac{E(f_{in}, E_0)}{E_0} - f_{out}(v) q / v \tag{6}$$

$$\begin{cases} y(t) = V_0 \{k_1(1-q) + k_2(1-q/v) + k_3(1-v)\} \\ k_1 = 7E_0, k_2 = 2, k_3 = 2E_0 - 0.2 \end{cases} \tag{7}$$

where V_0 is resting blood volume fraction, E_0 is resting net oxygen extraction fraction by the capillary bed, v is normalized venous volume, q is

normalized total deoxyhemoglobin voxel content, f_{in} and f_{out} are inflow and outflow from the venous compartment, s is some flow inducing signal and another four fixed parameters must be estimated.

Friston, et al [8] accepted that, over normal ranges, blood flow and synaptic activity are linearly related and suggested that the nonlinearities between synaptic activity and BOLD is modeled by nonlinearity between blood flow and BOLD response. The $\varepsilon\, u(t)$ in (2) shows synaptic activities as the input of the Balloon model. We consider the overall synaptic activities as input of the Balloon model. Each PSP consumes a little energy and causes a small change in blood flow according to its peak potential value. We assume that the change in the blood flow is proportional to the PSP amplitude in our proposed model. For modeling various neurons and synapses, we consider a random variable for PSP amplitude and $u(t)$ is considered as:

$$u(t) = \frac{U(t)}{Max(U(t))}, U(t) = \sum_{k=1}^{N(t)} \Delta V_k \qquad (8)$$

where $N(t)$ is the number of active PSPs from (1), ΔV_k is the peak amplitude of the kth PSP and $u(t)$ is the input of the Balloon model with maximum value of 1. The variation in neural activity is modeled by ε as:

$$\varepsilon = \varepsilon_{\max} \frac{N_{ss}}{N_{\max}} \qquad (9)$$

where N_{ss} is defined in (1), $N_{\max}$ is maximum possible number of active synapse in a voxel with maximum external stimulation, and $\varepsilon_{\max}$ is maximum possible value of ε that produces maximum BOLD contrast in the output of the Balloon model.

The temporal resolution of MEG is in the order of ms and so we choose the sampling time of 1 ms for synaptic activities in our model. Thus, the sampling time of BOLD output in the Balloon model is 1 ms. With conventional imaging systems, the temporal resolution of the BOLD signal is in order of sec. Thus, we down sample the output of the Balloon model shown by "Down Sampling" box in Fig. 1. We choose the rate of 1ms /2s down sampling in the simulations.

Neural activities in a voxel change the blood flow of this voxel and also can affect the blood flow of the adjacent voxels. In an experimental study on rats, it is reported that the diameter of local arterioles (at the stimulation site) increases 26% and local blood flow increases 55% while in an up stream region with distance of about 2 mm from the stimulation site, the diameter of arterioles increases 8.7% and blood flow increases 15% [9]. In another experimental study on rats with electrical stimulation of the cerebellar parallel fiber, the local CBF at the stimulation site changes 55%. At sites with 4.5 mm horizontal and 1 mm vertical distance from the stimulation site, CBF changes 13% and 11%, respectively [10]. Thus, the synaptic activities in a voxel can affect the CBF and resultant BOLD signal in adjacent voxels. This is "Crosstalk from Neural Activities of Adjacent Voxels" in our model shown in Fig. 1.

The Gaussian spatial smoothing function is used for modeling the spatial crosstalk of BOLD signal in our proposed model. We consider the effective synaptic activities as below:

$$\begin{cases} u_e(r;t) = G(r;0,\sigma) *** u(r;t) \\ r = (x,y,z), \sigma = (\sigma_x, \sigma_y, \sigma_z) \end{cases} \qquad (10)$$

where $u(r\ ;\ t)$ is synaptic activities at voxel in location (x,y,z), $G(r\ ;\ 0\ ,\ \sigma)$ is 3D Gaussian function with zero mean and standard deviation σ and "$***$" shows 3D convolution.

B.3. Constructing ECD from PSPs

The brain is a spherical structure and so the primary currents are the main sources of the magnetic field detected by MEG sensors and the volume currents are negligible [1]. Thus, we assume only the primary currents in the proposed model. With this assumption, the voxels of the brain will be independent and the detected signal in each MEG sensor will be the sum of the signals from all voxels.

From a distance, the PSP looks like a current dipole oriented along the dendrite. Approximately, the current dipole due to PSP is [1]:

$$\vec{q} = \frac{\pi}{4} d^2 \sigma_{in} \Delta V \cdot \vec{n} \qquad (11)$$

$$\vec{q} = \beta \Delta V \cdot \vec{n}\ ,\ \beta = \frac{\pi}{4} d^2 \sigma_{in} \qquad (12)$$

where d is the diameter of the dendrite, σ_{in} is the intracellular conductivity, ΔV is change of voltage during PSP and $\vec{n}$ is unit vector which shows current dipole orientation along the dendrite. Inserting typical values, d = 1 μm, $\sigma_{in} = 1\ \Omega^{-1}\mathrm{m}^{-1}$, ΔV = 25 mV, we find that q ≈ 20 f Am for a single PSP [1].

There are many types of neurons with different shapes and sizes of dendritic tree. We consider a random variable for the direction of current dipoles (of PSP) for modeling the different kinds of neurons and dendrite tree structures. We define "reference vector" as a vector that is perpendicular to the cortical surface in each voxel. The angle between the reference vector and each current dipole (θ) is considered as a truncated Gaussian random variable with the following pdf:

$$f_\Theta(\theta)=\frac{e^{\frac{-\theta^2}{2\sigma^2}}}{k};k=\sqrt{2\pi}\,\sigma\,erf(\frac{\pi}{\sqrt{2}\sigma}),-\pi<\theta\le\pi \quad (13)$$

where *erf*(.) is the error function. The pdf of θ is shown in Fig. 3 for some values of σ. The current dipole q in (12) is projected onto two vectors, first vector (q_p) is parallel to the reference vector with the value of $q\cos(\theta)$ and the second vector (q_n) is orthogonal to the reference vector with the value of $q\sin(\theta)$. The $E[q_n]$ is zero (due to odd property of sin(.) and even property of Gaussian function), thus, q_n acts as a noise for MEG sensors having no correlation with the stimulation. On the other hands, the $E[q_p]$ is nonzero and can be sensed by the MEG sensors as a signal.

If N active PSPs start to fire at time t, then the ECD from the sum of their activities at this time is:

$$\vec{q}(t)=\sum_{k=1}^{N} w_k\Delta V_k\beta_k\varphi_k(t)\cdot\vec{n}_k \quad (14)$$

where w_k is +1 for EPSP and -1 for IPSP, ΔV_k shows peak PSP value, β_k is a coefficient according to (12) that models parameters of the kth synapse and its neighboring dendrite and $\varphi_k(t)$ is a normalized (unitary peak) waveform for the kth PSP at time t. For modeling different kinds of neurons, we consider ΔV_k and β_k as random variables by using truncated Gaussian and uniform distributions. The truncated Gaussian variable denoted by $x \sim TN(\mu,\sigma;a,b)$ is a variable whose probability for $x<a$ or $x>b$ is zero and its pdf is like the Gaussian distribution (except a scalar normalization) with mean μ and standard deviation σ in the interval $x\in[a,b]$. The uniform distribution variable denoted by $x \sim uniform(a,b)$ is a random variable whose probability is constant in the interval of $[a,b]$ and zero outside this interval. We assume ΔV_k as a truncated Gaussian distribution ($\Delta V_k \sim TN(10,5;0,\infty)$ mV) [11] and β_k according to (12) as a function of two random variables ($d \sim uniform(0.1,2)$ μm and $\sigma_{in} \sim uniform(0.1,2)\ \Omega^{-1}\mathrm{m}^{-1}$).

Two functions are proposed for approximating the PSP waveform. First is the difference of two exponentials [12]:

$$\varphi(t)=\frac{e^{-t/\tau_d}-e^{-t/\tau_r}}{(c-1)c^{\frac{-c}{c-1}}},\ c=\frac{\tau_d}{\tau_r} \quad (15)$$

and second is the α-function [13]:

$$\varphi(t)=\frac{t\,e^{-\frac{(t-\tau_{PSP})}{\tau_{PSP}}}}{\tau_{PSP}} \quad (16)$$

Fig. 4 shows these two functions with typical values for EPSP and compares the resulting EPSP and IPSP. We choose α-function for PSP in the model. Since the waveform of PSP is different for different neurons and even it is different for synapses of the same neuron depending on their distance to the soma, we consider τ_{PSP} in (16) as a random variable with truncated Gaussian distribution $\tau_{PSP} \sim TN(2,1;0,\infty)$ ms according to the data reported in [11].

The number of active PSPs at time t in a voxel is $N(t)$ from (1). The ECD in this voxel is derived from (14):

$$\vec{Q}(t)=\frac{1}{T}\int_{t_0=-T}^{0}\Big(\sum_{k=1}^{N(t)} w_k\Delta V_k\beta_k\varphi_k(t-t_0)\cdot\vec{n}_k\Big)dt_0 \quad (17)$$

$$\begin{cases}\vec{Q}(t)=\sum_{k=1}^{N(t)} w_k\Delta V_k\beta_k\widetilde{\varphi}_k(t)\cdot\vec{n}_k\\ \widetilde{\varphi}_k(t)=\frac{1}{T}\int_{t_0=-T}^{0}\varphi_k(t-t_0)dt_0\end{cases} \quad (18)$$

where $\varphi_k(t-t_0)$ is the waveform of the kth PSP whose activation started at time t_0, $\widetilde{\varphi}_k(t)$ is the average waveform of $\varphi_k(t-t_0)$ for possible range of t_0 and T is the maximum duration of PSP which we set as approximately T = 30 ms according to (16) and Fig. 4-b. The projections of $\vec{Q}(t)$ to two normal vectors can be found as:

$$\begin{cases}\vec{Q}(t)=\vec{Q}_p(t)\cdot\vec{n}_p+\vec{Q}_n(t)\cdot\vec{n}_n\\ \vec{Q}_p(t)=\sum_{k=1}^{N(t)} w_k\Delta V_k\beta_k\widetilde{\varphi}_k(t)\cos(\theta_k)\\ \vec{Q}_n(t)=\sum_{k=1}^{N(t)} w_k\Delta V_k\beta_k\widetilde{\varphi}_k(t)\sin(\theta_k)\end{cases} \quad (19)$$

where n_p is a unit vector parallel to the reference vector and n_n is the unit vector orthogonal to the reference vector.

The "Lead Field from Forward Problem" block is the final part of MEG modeling in block 3 of Fig. 1. As mentioned above, we consider only the primary current and ignore the volume current in our MEG model; therefore, the relationship between ECD in a voxel with the measured signal in a sensor is:

$$b_i(t)=\frac{\mu_0}{4\pi}\frac{\vec{Q}(t)\times(\vec{r}_i-\vec{r}_Q)\cdot\vec{e}_i}{\left|\vec{r}_i-\vec{r}_Q\right|^3}=\vec{l}\,(i)\cdot\vec{Q}(t) \quad (20)$$

where $\vec{r}_i$ is the location of the ith sensor, $\vec{r}_Q$ is the location of the dipole and $\vec{e}_i$ is the unit orientation of the ith sensor [14]. The measurement from m sensors in the matrix form is:

$$B(t)=\begin{bmatrix}\vec{l}(1)\\ \cdot\\ \cdot\\ \vec{l}(m)\end{bmatrix}[\vec{Q}(t)]=L(\vec{r}_Q)\,\vec{Q}(t) \qquad (21)$$

where L is called as lead field matrix.

The final block in our integrated model is related to the noise. Some sources of noise in MEG are electrical activity of the heart, environment electromagnetic parasites, and the APs of neurons ignored in the proposed model. To cover these, white Gaussian noise is usually considered in MEG. On the other hands, there are many more physiological and instrumental sources of noise in the BOLD signal. We consider white Gaussian noise for fMRI simulations.

III. Relation between MEG and fMRI

Now, we intend to quantitatively survey the effects of pdf of θ and ratio of IPSP number to number of EPSP (IPSP ratio) on MEG and fMRI signals. After the number of active synapses reaches its final steady state value according to (1), the number of active synapses becomes almost fixed. Referring to (19), we have:

$$\vec{Q}=\sum_{k=1}^{N} w_k \Delta V_k \beta_k \tilde{\varphi}_k \cos(\theta_k)\cdot\vec{n}_p+\sum_{k=1}^{N} w_k \Delta V_k \beta_k \tilde{\varphi}_k \sin(\theta_k)\cdot\vec{n}_n \qquad (22)$$

where N is the average number of active synapses after steady state. If the random variables in (22) are considered independent, the mean value of ECD is:

$$\overline{\vec{Q}}=\{\sum_{k=1}^{N} E[w_k]E[\Delta V_k]E[\beta_k]E[\tilde{\varphi}_k]E[\cos(\theta_k)]\}\cdot\vec{n}_p=\overline{Q}.\vec{n}_p \qquad (23)$$

$$\overline{Q}=N(1-2r)\;\overline{V}\;\overline{\beta}\;g(\sigma_\theta) \qquad (24)$$

where $E[.]$ is "expected value", r is the mean value of IPSP ratio, $\overline{V}$ is mean amplitude of PSP, $\overline{\beta}$ is mean of β according to (12), $\overline{\tilde{\varphi}}=1$ because of unity peak value of $\varphi(t)$ according to (16) and (18) and $g(\sigma_\theta)$ shows average effects of projected ECD onto the reference vector. The second term of (22) vanishes in averaging because of odd property of "sin" function.

The $g(\sigma_\theta)$ is defined by:

$$\begin{cases} g(\sigma_\theta)=\int_{-\pi}^{\pi}\cos(\theta)f_\theta(\theta;\sigma)d\theta=\int_{-\pi}^{\pi}\cos(\theta)\dfrac{e^{\frac{-\theta^2}{2\sigma^2}}}{k}d\theta \;\;;\;\; k=\sqrt{2\pi}\,\sigma\,erf(\dfrac{\pi}{\sqrt{2}\sigma}) \\ \sigma_\theta^2=\sigma^2(1-\dfrac{2\pi\sigma^2}{k}e^{\frac{-\pi^2}{2\sigma^2}}) \end{cases} \qquad (25)$$

where σ_θ is the standard deviation of θ. When $\sigma\to 0$, then $\sigma_\theta\to 0$ and the pdf of θ is like the Dirac delta function and $g(\sigma_\theta)\to 1$. When $\sigma\to\infty$, then $\sigma_\theta\to\pi^2/3$ and the pdf of θ is uniform and $g(\sigma_\theta)\to 0$.

The relation between synaptic activities and the index of ε for fMRI is derived from (8)-(9):

$$\begin{cases} \varepsilon\propto\sum_{k=1}^{N}\Delta V_k \\ \bar{\varepsilon}\propto N\overline{V} \;\Rightarrow\; \bar{\varepsilon}=\bar{\varepsilon}_m\dfrac{N\overline{V}}{\max(N\overline{V})} \end{cases} \qquad (26)$$

where $\bar{\varepsilon}_m$ and $\max(N\overline{V})$ are maximum values of $\bar{\varepsilon}$ and $N\overline{V}$ in a voxel for maximum external stimulus. Inserting (26) in (24), we have:

$$\overline{Q}=\max(N\;\overline{V})\,\overline{\beta}\,(1-2r)g(\sigma_\theta)\frac{\bar{\varepsilon}}{\bar{\varepsilon}_m}=\overline{Q}_m(1-2r)g(\sigma_\theta)\frac{\bar{\varepsilon}}{\bar{\varepsilon}_m}$$

(27) Considering (2)-(7) in the Balloon model and (27), the relation between BOLD signal and ECD is:

$$\begin{cases} \overline{Q}=\overline{Q}_m(1-2r)g(\sigma_\theta)\dfrac{\bar{\varepsilon}}{\bar{\varepsilon}_m} \\ BOLD\ Output=Balloon\ Model\ (\bar{\varepsilon}) \end{cases} \qquad (28)$$

Relation between ECD ($\overline{Q}$) in MEG, average synaptic activities ($\bar{\varepsilon}$) and BOLD output in fMRI are summarized in (28). If r tends to 50% or $g(\sigma_\theta)\to 0$, there is a detectable BOLD signal and the MEG signal is very weak. On the other hands, If r and $\bar{\varepsilon}$ tend to zero and $g(\sigma_\theta)\to 1$, there is a detectable MEG signal and BOLD signal cannot be detected.

IV. Simulation

Fig. 5 shows simulation results in a voxel of $1\,mm^3$ with $N_{ss}=10^6$ active PSPs (according to (1)) and IPSP ratio of 10%. The stimulus duration is 1 second. The number of active PSPs (sum of EPSPs and IPSPs) during stimulation is depicted in Fig. 5-a. The current dipole produced by each PSP has an angle (θ) with the reference vector, in the [-π , π] range. Fig 5-b illustrates its pdf which is close to a uniform pdf.

The projected ECD to the reference vector ($Q_p(t)$) and normal to this vector ($Q_n(t)$) are depicted in Figs. 5-c and 8-d, respectively. According to (19) and the odd property of the "sin" function, the average value of ECD will be zero as shown in Fig. 5-d. Assuming the ECD peak value in the order of 10 nAm can be detected by the MEG sensors [1], the $Q_p(t)$ in Fig. 5-c can be detected, although the pdf of θ tends to a uniform pdf and it is expected that PSPs cancel each other. This is because the small difference between the pdf of θ and uniform pdf is amplified by the huge number of active PSPs and thus detectable MEG signal is produced. The normalized synaptic activities according to (8) is shown in Fig. 5-e and used as input to the Balloon

model. For this stimulation, the value of $\varepsilon / \varepsilon_{\max}$ is considered 7.2% according to (9). Finally, Fig. 5-f shows the BOLD signal output of the model without considering additive noise. The maximum contrast of the BOLD signal is 1.58%.

V. Conclusion

The purpose of this paper is to present an integrated MEG and fMRI model (Fig. 1). The MEG and fMRI BOLD signals are related to neural activities. The number of PSPs and APs show the overall neural activities. Based on the existing experimental studies and physiological facts, both MEG and fMRI signals are mainly related to PSPs and have almost no correlation with APs. The proposed stochastic model is based on the parameters of PSPs that are considered as random variables. In our model, the overall effect of PSPs is related to ECD in MEG and average neural activities as the input of the Balloon model in fMRI. Neural activities in a voxel can change CBF and produce BOLD signal in the neighboring voxels. We model this spatial blurring property of BOLD signal as "Crosstalk from Neural Activities of Adjacent Voxels". The parameters of the model can explain conditions for which there is a detectable fMRI signal in a voxel but this voxel is silent for MEG and vice versa. The proposed model is instrumental in evaluating and comparing different analysis methods of MEG and fMRI. It is also useful in characterizing the upcoming combined methods for simultaneous analysis of MEG and fMRI.

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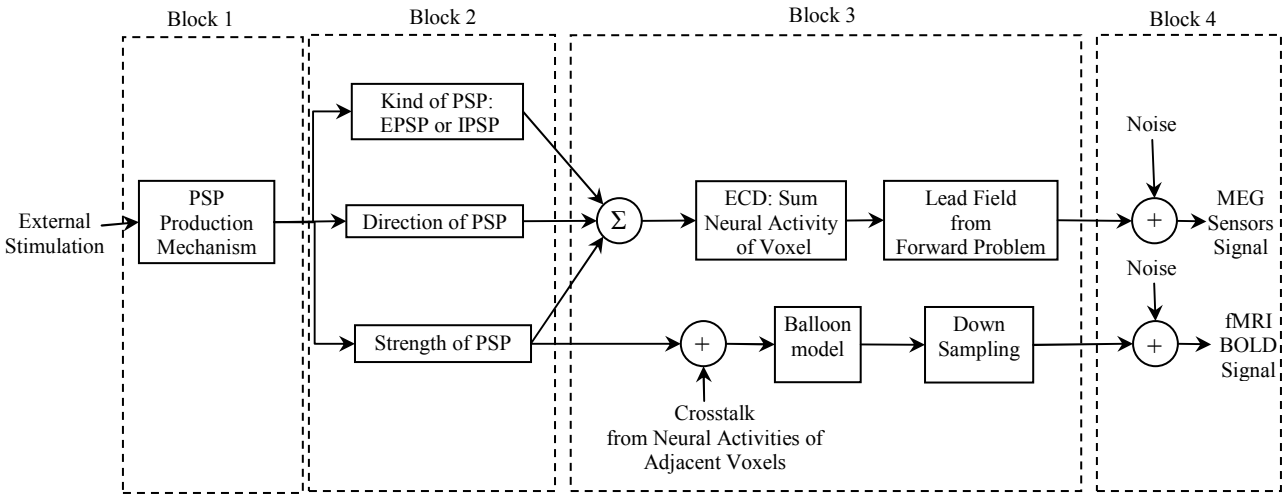

Fig. 1. Schematic Diagram for the proposed integrated MEG and fMRI model.

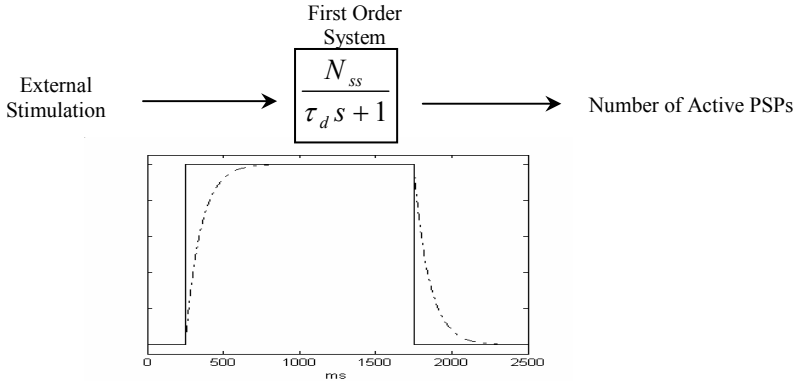

Fig. 2. Illustration of PSP production mechanism. Top: first order system for modeling the delay between external stimulation and number of active PSPs in an active voxel of the brain; Bottom: external stimulation (solid line) and number of active PSPs (dashed line) with $\tau_d = 100$ ms.

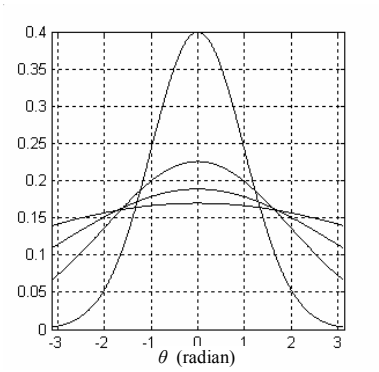

Fig. 3. pdf of θ (angle between current dipole and reference vector) according to (13). The values of σ are 1, 2, 3 and 5 from maximum to minimum peak value of the 4 plotted functions.

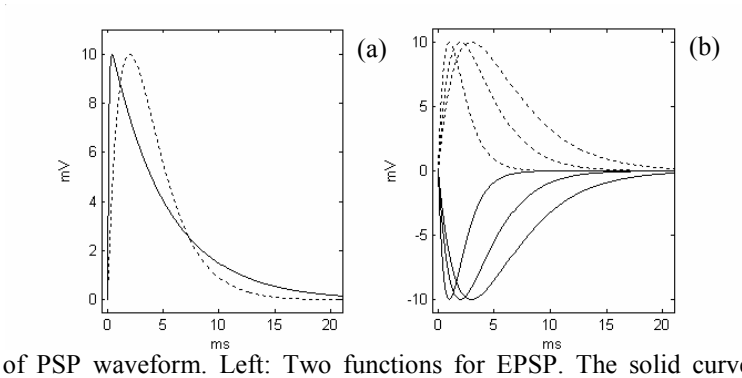

Fig. 4. Illustration of PSP waveform. Left: Two functions for EPSP. The solid curve shows EPSP with function of $\varphi(t) = k(e^{-t/\tau_d} - e^{-t/\tau_r})$ with τ_d = 5 ms, τ_r = 0.1 ms and k = 11 mV. The dashed curve is α-function ($\varphi(t) = \frac{kt\, e^{-t/\tau_{PSP}}}{\tau_{PSP}}$) for EPSP with τ = 2 ms and k = 27.18 mV. Right: EPSP (dashed) and IPSP (solid) of α-function with τ = 1, 2 and 3 ms, k = 27.18 mV for EPSP and k = -27.18 mV for IPSP.

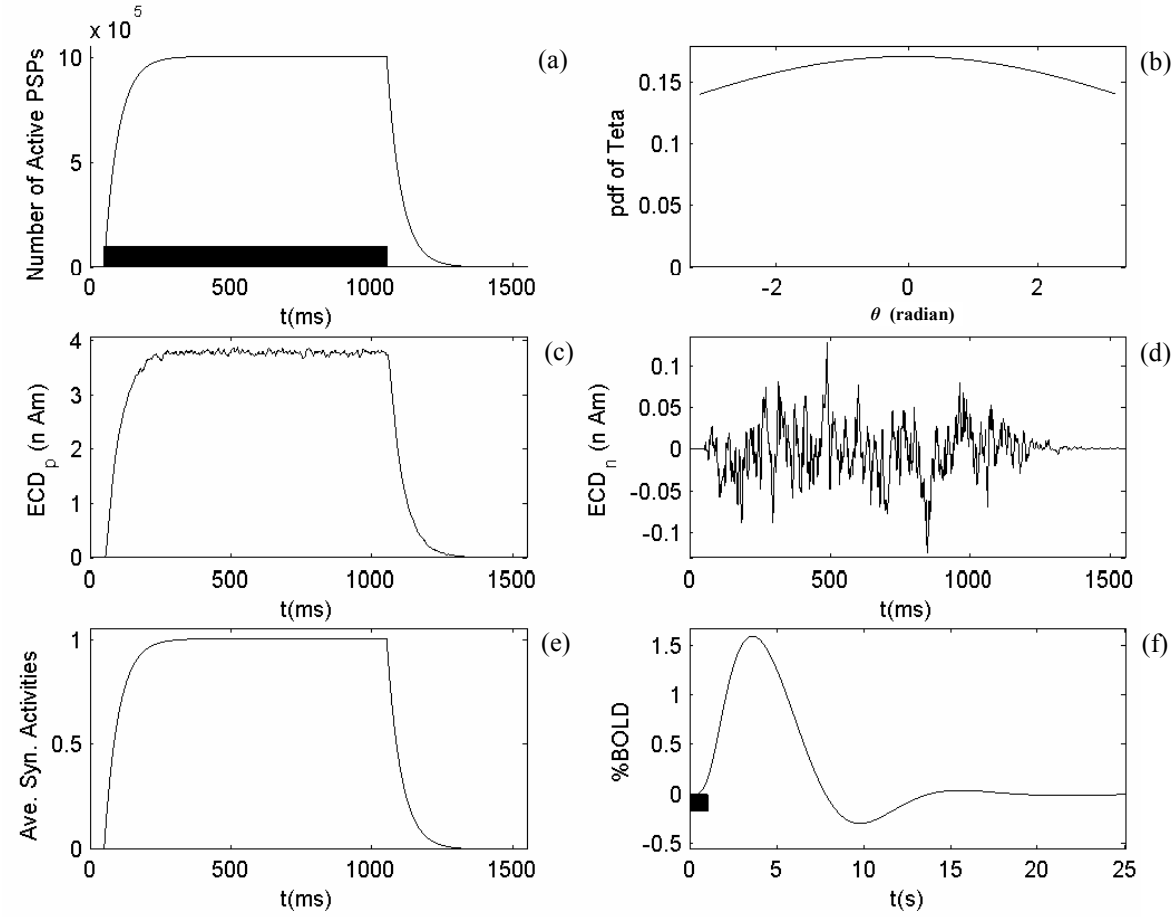

Fig. 5. Illustration of the capability of the proposed model to generate both MEG and fMRI signals. The small black rectangle shows the duration of stimulation. (a) Number of active synapses according to (1) with τ_d = 50 ms. (b) pdf of θ where θ is the angle between PSP dipole and direction perpendicular to the cortical surface. (c) Projected ECD in the direction perpendicular to the cortical surface, $Q_p(t)$ in (19). (d) Projected ECD in the direction tangent to the cortical surface, $Q_n(t)$ in (19). (e) Average synaptic activity according to (8). (f) BOLD output according to (2)-(7) with $\varepsilon / \varepsilon_{\max}$ = 0.2 and $u(t)$ from (e).