NEURAL MASS INTEGRATED MODELING OF EEG/MEG AND FMRI

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ABSTRACT

In this paper, we introduce a model for integrating the EEG or MEG with the fMRI. The integrated model is based on the neural mass model. An extended neural mass model is proposed which is based on the physiological principles of cortical minicolumns and their connections. The fMRI signal is extracted from the proposed neural mass model by introducing a relationship between the stimulus and the neural activity and using the resultant neural activity as input of the extended Balloon model. The proposed model is instrumental in evaluating the upcoming combined methods for simultaneous analysis of MEG, EEG and fMRI.

1. INTRODUCTION

Although integrated MEG/EEG and fMRI model is an active area of research, there is limited work about it in the literature. The integrated model proposed by Riera *et al.* [1] is one of the most recent works in this field. They introduce a two-dimensional autoregressive model with exogenous variables (ARx) to describe the relationships between synaptic activity and hemodynamics. They use a static nonlinear function to describe the electro-vascular coupling through a flow-inducing signal. In this work, a linear filter for step from the stimulus to the synaptic activities is used, while experimental results report a nonlinear relationship between them [2]. Moreover, their assumption about linear relationship between cerebral blood flow (CBF) and BOLD is not generally valid, according to the nonlinearity of the Balloon model [3].

We propose an integrated model in this paper which is totally different from the integrated model in [1] and does not have the above limitations. The proposed integrated model is based on the neural mass model. We use the Jansen's model [4] as the base of the proposed model. However, the Jansen's model has few parameters and does not have the flexibility to generate various event related potentials (ERP). As the first contribution of this paper, we extend the Jansen's model and propose an extended neural mass model in a cortical area. The extended neural mass model is based on the physiological principles of cortical minicolumns and their connections.

We use the extended Balloon model (EBM) in the fMRI part of the proposed integrated model. In the EBM [3], the Balloon model is used for relating the CBF to the BOLD and a model of CBF autoregulation is added to the Balloon model which is linear and relates the synaptic activity to the CBF. The step from the stimulus to the synaptic activity is not proposed in the EBM which is reported nonlinear in experimental results [2]. We propose a nonlinear model for this step which is in agreement with the experimental results.

The second and main contribution of this paper is a new integrated M/EEG and fMRI model based on the neural mass model. Thanks to our extension of the neural mass model, the neural mass model that has so far been used for the M/EEG modeling only, has been used here for the first time for the fMRI modeling. The originality of our approach is to suggest a non-linear relationship between the stimuli and the neural activity using our extended neural mass model. With the combination of this new neural activity model and the EBM, we obtain an fMRI model that is naturally integrated with an M/EEG model. We justify our model of the neural activity by comparing the simulation results with experimental data.

2. PROPOSED INTEGRATED MODEL

2.1. Neural Mass Model

2.1.1. Jansen's Model

In the Jansen's model [4], a cortical column is modeled by a population of excitatory pyramidal cells, receiving inhibitory feedback from the local interneurons and excitatory input from the stellate cells. The solid box in Fig. 1 shows the Jansen's model. The impulse responses of the excitatory and the inhibitory synapses, shown by "h_e" and "h_i" in Fig. 1, are in the form of:

$$h(t) = H\frac{t}{\tau}\exp(-\frac{t}{\tau})\ ;\ t \geq 0 \qquad (1)$$

where H and τ are different for h_e and h_i. "S" operator in Fig. 1 transforms the average membrane potential of the population into an average rate of action potentials. For "S" operator, we use the following sigmoid function proposed by David *et al.* in [5]:

$$S(v) = \frac{2e_0}{1+\exp(-rv)} - e_0 \qquad (2)$$

where e_0 and r determine the shape of the sigmoid function. The four constants γ_i control the strength of the intrinsic connections and represent the total number of synapses in each subpopulation. The relative values of these constants are fixed: $\gamma_2=0.8\gamma_1$, $\gamma_3=\gamma_4=0.25\gamma_1$ ([4]). $x_i(t)$ in Fig. 1 show overall post synaptic potential (PSP) of different cells. The MEG/EEG signal is modeled by the PSP of the pyramidal cells as $y(t) = x_2(t) - x_3(t)$.

2.1.2. Proposed Extended Neural Mass Model

The minicolumn is the basic unit of the mature neocortex. Each minicolumn in primates contains roughly 80–100 neurons. The width of each minicolumn is 50 μm and the mean value for inter-columnar distance is 80 μm [6]. There are three basic cell types in minicolumns: the stellate cells, the local inhibitory interneurons and the pyramidal cells; the axon of the two former ones spread vertically in their minicolumn without any considerable outputs to the neighboring minicolumns. The output of a minicolumn is

mainly derived from its pyramidal cells and thus all cell types in a minicolumn receive input from pyramidal cells of the neighboring minicolumns. The stellate cells also receive afferent thalamic input [6]. We add the thalamo-cortical feed forward connection to the Jansen's model as shown in Fig.1.

The interaction between different neurons in a minicolumn can be explained by the Jansen's model. According to the hierarchical structure of the cell assemblies, we extend the Jansen's model to a cortical area which contains several minicolumns. The proposed extended neural mass model is based on physiological principles explained in the previous paragraph and shown in Fig. 1. As proposed in [5], the model can be further extended by considering connections between multiple areas. For the sake of clarify, in the sequel we do not consider the inter-area connections and focus on a single area to present our extended model.

In our model, we consider a lattice form containing L minicolumns for the desired cortical area. The inter-columnar distance between minicolumns is D. The maximum permissible size of this lattice is limited by the available computational power only. Considering the first order kernel in Eq. (1) and Fig. 1, the activity of the ith minicolumn in our extended neural mass model is described by Eq. (3).

$$\ddot{x}_1^{(i)} = \frac{H_e}{\tau_e}\left(u^{(i)} + \gamma_1 S(y^{(i)}) + G_S \sum_{j=1, j\neq i}^{L} a_{ij} S\left(y^{(j)}(t-\delta_{ij})\right)\right) - \frac{2}{\tau_e}\dot{x}_1^{(i)} - \frac{1}{\tau_e^{\,2}} x_1^{(i)}$$

$$\ddot{x}_2^{(i)} = \frac{H_e}{\tau_e}\left(\gamma_2 S(x_1^{(i)}) + G_P \sum_{j=1, j\neq i}^{L} b_{ij} S\left(y^{(j)}(t-\delta_{ij})\right)\right) - \frac{2}{\tau_e}\dot{x}_2^{(i)} - \frac{1}{\tau_e^{\,2}} x_2^{(i)}$$

$$\ddot{x}_3^{(i)} = \frac{H_i}{\tau_i}\gamma_4 S(x_4^{(i)}) - \frac{2}{\tau_i}\dot{x}_3^{(i)} - \frac{1}{\tau_i^{\,2}} x_3^{(i)}$$

$$\ddot{x}_4^{(i)} = \frac{H_e}{\tau_e}\left(\gamma_3 S(y^{(i)}) + G_I \sum_{j=1, j\neq i}^{L} c_{ij} S\left(y^{(j)}(t-\delta_{ij})\right)\right) - \frac{2}{\tau_e}\dot{x}_4^{(i)} - \frac{1}{\tau_e^{\,2}} x_4^{(i)}$$

$$u^{(i)}(t) = e_i S\left(h_e(t) \otimes Stim(t-\Delta_i)\right) + \eta(t)$$

$$y^{(i)} = x_2^{(i)} - x_3^{(i)} \tag{3}$$

where $\otimes$ is convolution, H_e=3.25 mV, H_i=29.3 mV, τ_e=10 ms, τ_i=15 ms, γ_1=50, γ_2=40, γ_3=γ_4=12, e_0=2.5 and r=0.56e3 as given in [5]. The δ_{ij}=δ_c**dist*(*i*,*j*)/*D* is the propagation delay between minicolumn i and minicolumn j where δ_c is the unit delay between two adjacent minicolumns. It is selected as 0.1 ms in our simulations. The *dist*(*i*,*j*) is the Euclidean distance between the two minicolumns. The Δ_i≈40ms is the propagation delay between stimulus (*Stim*(.)) and the cortical columns. The physiological noise, represented by $\eta(t)$ as white Gaussian noise, models all inputs to the minicolumn that do not have correlation with the stimulus.

G_S, G_P and G_I represent the influence of the neighboring minicolumns on the stellate cells, pyramidal cells and interneurons in a minicolumn. Due to similar structure of the minicolumns in an area, we assume that these coefficients are fixed for all of the minicolumns in an area. The a_{ij}, b_{ij} and c_{ij} represent the strength of the connections of different cell populations between the ith and the jth minicolumns. We use a Gaussian kernel for modeling the connections between minicolumns based on the physiological principle that the greater the distance between the two minicolumns, the weaker their influence on each other:

$$a_{ij} = \exp\left(\frac{dist(i,j)^2}{-2\sigma_S^{\,2}}\right), b_{ij} = \exp\left(\frac{dist(i,j)^2}{-2\sigma_P^{\,2}}\right), c_{ij} = \exp\left(\frac{dist(i,j)^2}{-2\sigma_I^{\,2}}\right) \tag{4}$$

where σ_S=σ_P=σ_I=2**D*=160 μm as deduced from the data in [6]. The e_i in (3) represents the strength of the afferent input to the ith minicolumn:

$$e_i = \exp\left(-\frac{dist(i,m)^2}{2\sigma_E^{\,2}}\right) \tag{5}$$

where m is index of the minicolumn in the center of the area and σ_E=5**D*=400 μm as deduced from data in [6].

2.2. BOLD Signal in Proposed Model

EEG is related to $y^{(i)}(t)$ in (3) that shows the synaptic activations of the pyramidal cells. The sum of $y^{(i)}(t)$ in all minicolumns is assumed to represent the ERP or the EEG signal. In the following, we introduce a relationship between the external stimulus and the BOLD signal in a single minicolumn. Then, using our extended neural mass model, we extend the idea to an area containing several minicolumns. The relationship between the stimulus and BOLD can be segregated into two separate steps: a step from the stimulus to the neural activity, another step from the neural activity to the BOLD. We use the EBM for relating the neural activity to the BOLD and introduce a new relationship between the stimulus and the neural activity.

In the neural mass model, ERP is only related to the synaptic activity of the pyramidal cells, but the neural activity as an index for increasing the CBF could be related to the activity of all cell types. The PSPs and action potentials (APs) are two main indices for showing the activity in a neuron. It is assumed that increasing the CBF is only related to the PSPs and there is no significant correlation between CBF and APs [7]. Thus, neural activity should be related to the $x_1(t)$, $x_2(t)$, $x_3(t)$ and $x_4(t)$ in Fig. 1 which illustrate the overall synaptic activities of different neurons.

Considering the neural mass model for a single minicolumn, each $x_i(t)$ represents the activation of several synapses fired with different time lag δ_j:

$$x_k(t) = \sum_j h_k(t-\delta_j)\ ; k = 1,2,3,4 \tag{6}$$

where $h_k(.)$ is the same as that in (1). Based on the physiological principle that the neural activity and CBF are proportional to the consumed energy by the PSPs [7], we propose the following representation for the neural activity $N(t)$ in a minicolumn:

$$N_k(t) \propto \sum_j I\left(h_k(t-\delta_j)\right) h_k(t-\delta_j)\ ; k = 1,2,3,4 \tag{7}$$

where $I(h(t))$ is the current due to voltage $h(t)$ and the product of $I(h(t))$ by $h(t)$ shows the instantaneous power of the corresponding PSP. For simplicity, we consider a constant value for the synaptic current:

$$N_k(t) \propto \sum_j h_k(t-\delta_j)\ ; k = 1,2,3,4 \tag{8}$$

The total neural activity of the neurons considering (6) and (8) is therefore:

$$N(t) = \sum_{k=1}^{4} N_k(t) \propto \sum_{k=1}^{4} x_k(t) \tag{9}$$

Since $N(t)$ is some representation of the power consumed in an area, it is expected to have a positive value, as it is the case in [1]. In ERP regime of the Jansen's model, all $x_i(t)$ are positive when the sigmoid function is positive. Since the sigmoid function in (2) is designed to produce a zero resting state for all variables, its value

may become negative. Thus, we consider the absolute value of $x_i(t)$ in our model to comply with the positivity of $N(t)$:

$$N(t) \propto \sum_{k=1}^{4} \left| x_k(t) \right| \tag{10}$$

We believe that both of the excitatory and inhibitory postsynaptic activities induce comparable increases in the neural activity and CBF. Hence, there are no differences between the inhibitory and excitatory PSPs in our model as illustrate in (10).

The neural activity in an area with L minicolumns is the sum of all neural activities in each minicolumn:

$$N(t) \propto \sum_{i=1}^{L} \sum_{k=1}^{4} \left| x_k^{(i)}(t) \right| \tag{11}$$

where $x_k^{(i)}(t)$ for k=1,…,4 are the overall synaptic activities of the ith minicolumn in the proposed extended neural mass model and can be calculated from (3). The relationship between $x_k^{(i)}(t)$ and the stimulus in our model is nonlinear due to the nonlinearity of the sigmoid function, thus the relation between the stimulus and the neural activity is nonlinear. The neural activity computed in (11) is used as the input of the EBM from which the output BOLD signal is obtained. Instead of the proportionality (11), we consider its equality form, considering the proportional gain in the "neuronal efficacy ε" in the EBM.

3. SIMULATION RESULTS

In this section, we illustrate simulation results of the extended neural mass model in a cortical area. The area contains 31*31=961 minicolumns where inter-columnar distance is D=80 μm. Minicolumns uniformly spread in a square area of 2.5*2.5 mm^2. The Simulink toolbox of the MATLAB is used for solving Eq. (3) after converting it to a matrix state space form with 961*8 =7688 state variables.

3.1. ERP in Extended Neural Mass Model

The effects of the parameters of the extended neural mass model on ERP are illustrated in Fig. 2. The top row illustrates the saturations in thalamus and stellate cells to strong input stimuli. With weak input, the response is linear, leading to a linear relationship between the stimulus and peak ERP responses. However, with strong input, the neuronal activity leaves the linear domain of the sigmoid function in Eq. (2) and the shape of ERP changes due to the spiking saturation. The second row illustrates the effect of stellate cell's gain (G_S) to inputs from neighboring pyramidal cells. There is a shift on the positive and negative peaks of ERP when G_S increases. The peak times are N70/P200, N100/P330 and N180/P600 when G_S is 1, 2 and 2.5, respectively. The ERP will be unstable for large values of G_S. The third row illustrates the effect of G_P. The ERP tends to oscillate when G_P increases. Larger values of G_P make ERP unstable. Very large values of G_P saturate the sigmoid functions of all pyramidal cells and produce saturated ERP. The effect of the inhibitory interneuron's gain (G_I) is illustrated in the bottom row of Fig. 2. Increasing G_I causes more oscillation in the ERP. This is not surprising because the inhibitory interneurons with negative feedbacks are the main sources of the oscillation in the Jansen's model.

3.2. Nonlinearity in Proposed Integrated Model

Before dealing with the nonlinearities in the proposed integrated model, the sample waveform of the ERP, the neural activity and the BOLD responses to the impulse stimulus are illustrated in Fig. 3. The conditions generating the left column in Fig. 2 leads to the neural activities illustrated in the middle column of Fig. 3. The normalized BOLD responses for four different conditions are shown in the right side of Fig. 3.

The relationships between the neural activity, BOLD and EEG signals for different strengths of the external stimulus are illustrated in Fig. 4. The input stimulus is the unit step function and the steady state values of all variables are plotted in this figure. Figs. 4.a and 4.b summarize one contribution of this paper. The relationship between the stimulus' strength and the neural activity or the EEG signal is nonlinear. When there is a strong stimulus, the sigmoid function of the output pulse rate of the thalamus relay nuclei and also the stellate cells saturate, thus the EEG and the neural activity saturate. With a weak input, the sigmoid function behaves linearly, thus the relationship is linear. There are several experimental results in the literature reporting a nonlinear relationship between the neural activity and the stimulus. For example, Jones and colleagues report that the relationship between the stimulus and the neural activity is like a sigmoid function [2]. Surprisingly, their reported curve is quite similar to Fig 4.a.

Fig. 4.c shows the saturated curve of the BOLD signal as a function of the neural activity, a direct consequence of the nonlinearity in the EBM. Both curves in Figs. 4.a and 4.c have saturation characteristics, thus the saturating relationship between the stimulus and the BOLD signal intensifies in Figs. 4.e. Fig. 4.d illustrates that although both of the EEG and the neural activity saturate with strong stimulus, their relationship remains linear. It should be noted that the proportionality between the EEG steady state values and the neural activity in Fig. 4.d cannot be extended to their time series as shown in Fig. 3. The relationship between the EEG and fMRI signals is illustrated in Fig. 4.f.

4. CONCLUSION

For the first time, the neural mass model is used to propose a new integrated M/EEG and fMRI model in this paper. The external stimulus is the input of the model and simultaneous EEG and BOLD signals are the outputs of the model. In our method, we extend the classical neural mass model according to the physiological principles of the cortical minicolumns and their connections. The populations of different cells interact with themselves in a minicolumn and also receive inputs from the axons of the pyramidal cells in the neighboring minicolumns. Our simulations illustrate that the proposed extended neural mass model is capable of generating various types of ERP. Moreover, the extended neural mass model is the base of a new fMRI model. Indeed, it allows introducing a new nonlinear model of the neural activity. The resulting neural activity is used as the input of the extended Balloon model in order to generate the BOLD signal. Different applications could be foreseen for this new integrated model. It is possible that certain neurological diseases change the behavior of some minicolumns in a brain region. These behaviors are characterized in our model by the values of some parameters, which can be estimated using M/EEG and fMRI data. Thus, our model and its parameterization can help to diagnose or characterize the related neurological diseases.

5. REFERENCES

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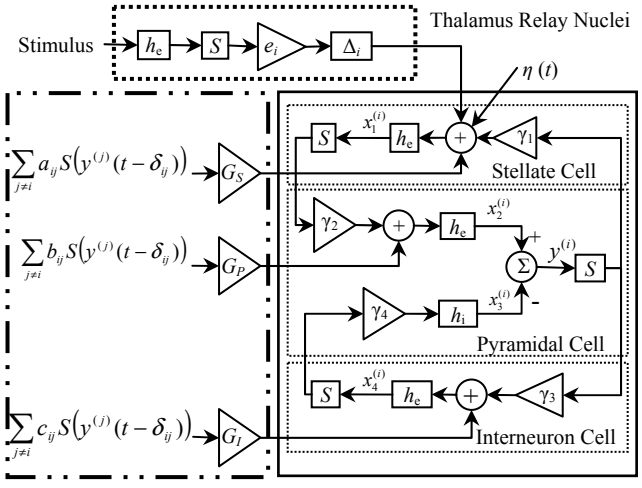

Fig. 1. An illustration of the proposed extended neural mass model for the *i*th minicolumn. The solid box shows the classical Jansen's model. The upper dotted box ("Thalamic Relay Nuclei") shows the feed forward model of the thalamus. The left dash-dot box illustrates contributions of the neighboring minicolumns to the *i*th minicolumn. The physiological noise is represented by $\eta(t)$.

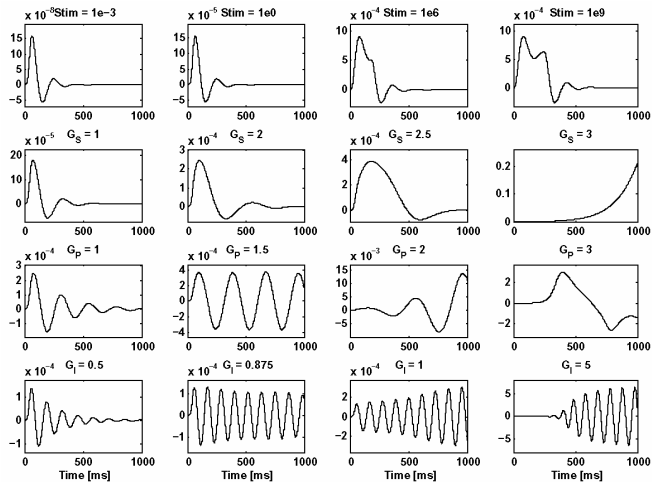

Fig. 2. Illustration of the capability of the proposed extended neural mass model for producing the ERPs. *Top row*: effect of the stimulus strength on ERP. *Second row*: effect of the stellate cells gain (G_S) on ERP. *Third row*: effect of the pyramidal cells gain (G_P) on ERP. *Bottom row*: effect of the inhibitory interneurons gain (G_I) on ERP.

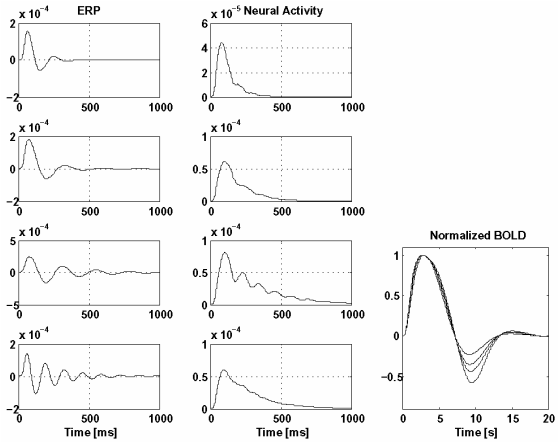

Fig. 3. Illustrations of the effects of the proposed integrated model's parameters on the ERP, the neural activity and the BOLD signals. All conditions are similar to the left column in Fig. 2.

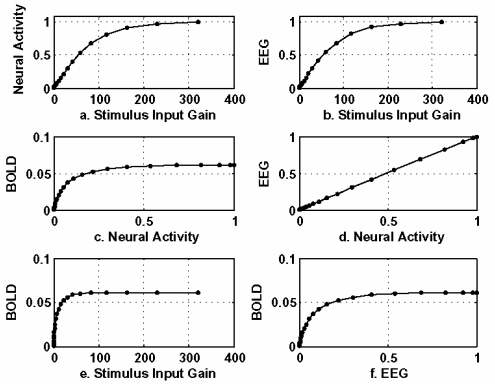

Fig. 4. Illustrations of the relationship between the stimulus, the neural activity, the ERP and the BOLD in the proposed integrated model.