Multi-Area Integrated E/MEG and fMRI Modeling

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Abstract: Functional MRI (fMRI) has complementary spatiotemporal resolution compared to Electroencephalography (EEG) as well as Magnetoencephalography (MEG). Thus, their integrated analysis should improve the overall resolution. To integrate analysis of E/MEG and fMRI, we extend our previously proposed integrated E/MEG and fMRI neural mass model to a multi-area model by defining two types of connections: the Short-Range Connections (SRCs) between minicolumns within the areas and Long-Range Connections (LRCs) between inter-areas minicolumns. The nonlinear input/output relationship in the proposed model is derived from the state space representation of the multi-area model. The E/MEG signals are originated from the overall synaptic activities of the pyramidal cells of all minicolumns and can be calculated using the lead field matrix (i.e., forward electromagnetic model). The fMRI signal is extracted from the proposed integrated model by calculating the overall neural activities in the areas and using it as the input of the extended balloon model (EBM). Using the simulation results, the capabilities of the proposed model to generate E/MEG and fMRI signals is shown. In addition, change of the dynamics of the model to variations of its parameters is evaluated that lead us to find the appropriate ranges for the parameters. Overlay, this work proposes an effective method to integrate E/MEG and fMRI and hopes to more effectively use these techniques in functional neuroimaging.

1. Description of Purpose (Introduction)

Although integrated E/MEG and fMRI model (bottom-up modeling) is an active area of research, there is limited work on it in the literature [1-6]. To introduce an integrated multi-area model, we extend our previously proposed integrated model in [2] from one cortical area to a multi-area model. In addition, the appropriate ranges for the parameters of the proposed model are extracted.

2. Method

Our proposed integrated E/MEG and fMRI model in [1] was based on the physiological principles of the cortical minicolumns and their connections in one cortical area. The interaction among different cell populations (i.e., the stellate cells, the pyramidal cells, and the inhibitory interneurons) within a minicolumn was modeled by the Jansen's neural mass model [7]. We extended the Jansen model to a cortical area which contains several minicolumns. The proposed extended neural mass model (ENMM) is shown in Fig. 1. Based on the connection in Fig. 1, we extracted the state space representation of the dynamics within the single cortical area that models the interactions among different cell populations within the minicolumns as well as the interactions with other minicolumns within the area. The EEG and MEG signals originate from the overall synaptic activities of the pyramidal cells ($y^{(i)}$ in Fig. 1) of all minicolumns and can be calculated using the lead field matrix. We extracted the fMRI signal from the proposed ENMM by calculating the overall neural activities in the area and using it as input of the extended balloon model (EBM) [8].

To extend the proposed model in [2] to a multi-area model, we define two connection types: Short-Range Connection (SRC) and Long-Range Connection (LRC). SRC is made by cortical neurons whose local branches can reach a maximum of about 10 mm. The SRCs between minicolumns within an area is exactly same as what we proposed in [2]. LRCs characterize configuration of the multi-area model with describing the connections among the cortical areas. LRCs are mainly created by axons of pyramidal cells that pass through the white matter to connect the cortical areas and its length may be more than 100 mm. While the effective strength of SRCs between two minicolumns within an area diminishes exponentially with their distance, LRCs do not show such a regular and smooth pattern [6].

To define LRC between two areas, we consider that the three cell populations of all minicolumns in the destination area are affected by the excitatory efferent of the pyramidal cells of all minicolumns in the source area as illustrated in Fig. 2. Based on the uniform structure of the minicolumns within the cortical area in the proposed model, strengths of the LRCs between all pairs of the minicolumns in the source and the destination areas are assumed to be equal. Unknown parameters of the multi-area model are three SRCs parameters within each area and three LRCs parameters among the areas.

Consider a multi-area model which contains N cortical areas where connections among minicolumns within and between the areas are specified by the SRCs and LRCs, respectively. Each area contains L uniform minicolumns which are perpendicular to the cortical surface. The following equations show dynamics of the multi-area model.

$$\dot{X}_{8NL\times 1} = A_1 X + [A_2 + (G^s \otimes I_{8L\times 8L})A_3 + (G^l \otimes I_{8L\times 8L})A_4]S(X) + Bu + w \tag{1}$$

$$\begin{cases} y_{ECDs} = CX \\ \kappa_n = \sum_{i=1}^{L} (|x_3^{(i)}| + |x_5^{(i)}| + |x_5^{(i)} - x_1^{(i)}| + |x_7^{(i)}|); n = 1,2,...,N \end{cases} \tag{2}$$

where I is 8xL-by-8xL identity matrix, $\otimes$ is the *Kronecker product* operator, $A1$, $A2$, $A3$, $A4$, B, and C are fixed matrixes which depend on some physiological parameters in the model, $S(.)$ is non-linear sigmoid function, u is the external stimulus, X is the state vector, w is the Gaussian state noise, κ_n represents the overall neural activities as input of the EBM in the nth area that generates the fMRI signals in the area, and y_{ECDs} contains all equivalent current dipoles (ECDs) in the areas that generate E/MEG signal. G^s and G^l in Eq. (1) contain unknown SRCs and LRCs parameters of the model. In addition, hemodynamic parameters of the EBM in each area are unknown parameters of the model that can be estimated from the fMRI data.

3. Results

Fig. 3 illustrates simulation results of a three area model where each area contains four minicolumns. Configuration of the LRCs among the areas is shown in Fig. 3-a. It should be noted that the SRCs between minicolumns within the areas are not shown in Fig. 3-a. The generated E/MEG and fMRI signals are illustrated in Figs. 3-b and 3-c, respectively. The strength of the generated E/MEG and fMRI signals in Area 1 are more than the generated signals in other areas that is in agreement with this fact that the Area 1 receives direct afferent input. Although Area 2 and Area 3 generate different E/MEG signals, the generated fMRI signals from these areas are similar due to this fact that the generated neural activities of these areas are in the same order.

To verify the effects as well as the valid ranges of parameters of the proposed model, behavior of the dynamical state space model in Eq. (1) are investigated. If the dynamic range of the strength of the input is considered to be small, the nonlinear sigmoid function in Eq. (1) can be linearly approximated. Thus, the state space equation will be linear and its dynamics can be represented by locations of its poles. Considering linear approximation of Eq. (1), locations of poles of a model which contains one cortical area is illustrated in Fig. 4. As shown in this figure, the model tends to become unstable as the parameters of the model (i.e. G^S, G^P, and G^I) increase. Parameter values less than the thresholds shown inside parenthesis should be chosen to generate stable output.

4. Conclusion

In this study, we extend our previously proposed integrated MEG and fMRI neural mass model to a multi-area model by defining two types of connections: Short-Range Connections (SRCs) between minicolumns within an area and Long-Range Connections (LRCs) betweens minicolumns of two areas. The nonlinear input/output relationship in the proposed model is derived from the state space representation of the multi-area model. Using simulation studies, capabilities of the proposed model to generate E/MEG and fMRI signals are shown. In addition, changes of the dynamics of the model to variations of its parameters are evaluated for the purpose of finding appropriate ranges for the parameters. This study proposes an effective method to integrate MEG and fMRI and hopes to more effectively use these techniques in functional neuroimaging.

5. References

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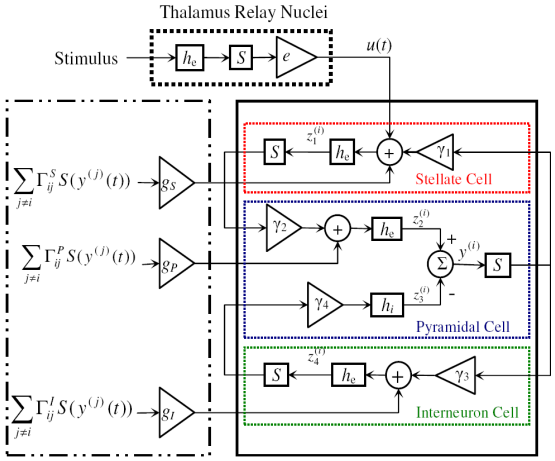

Fig 1. Illustration of the connections related to the *i*th minicolumn in the single area integrated model proposed in [2]. The left dash-dot box illustrates contributions of the neighboring minicolumns to the *i*th minicolumn.

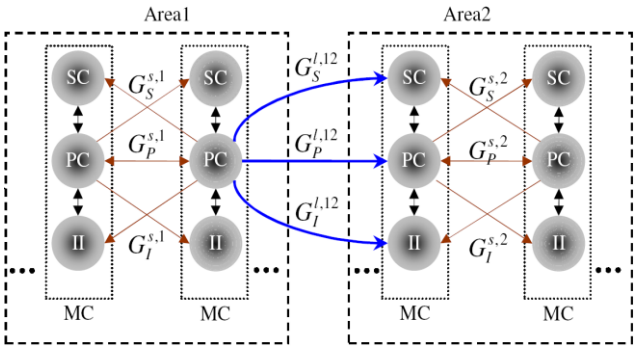

Fig 2. Illustration of the SRCs and LRCs in a two-area model. Within each area, pyramidal cells (PC) of all minicolumns affect the three cell populations (SC, PC, and II) of other minicolumns as SRC (brown arrows). Pyramidal cells of minicolumns of Area1 affect the three cell populations of all minicolumns in area2 as LRC (blue arrows). SC: Stellate Cells; PC: Pyramidal Cells; II: Inhibitory Interneurons; MC: Minicolumn.

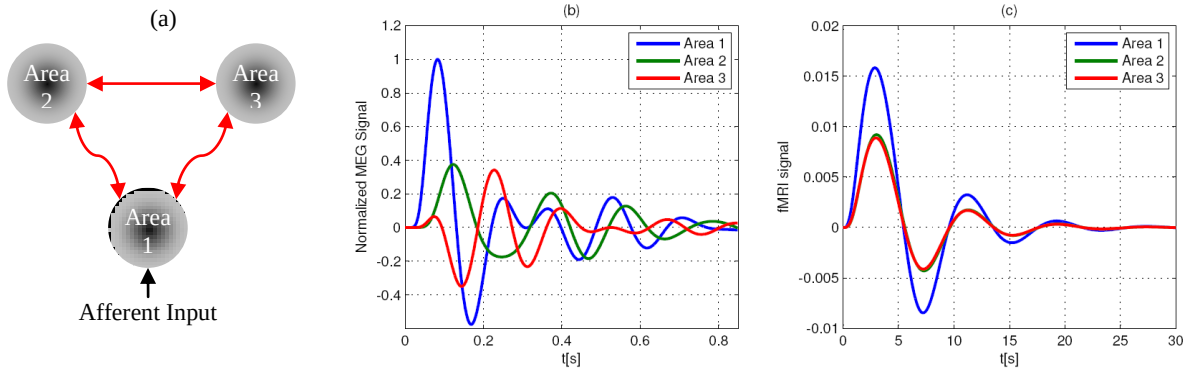

Fig 3. Simulation results of a three area integrated model. (a) Illustration of the LRCs in the three area model used in the simulation. The SRCs between minicolumns within the areas are not shown. (b) Normalized generated E/MEG signals. (c) Generated fMRI signals

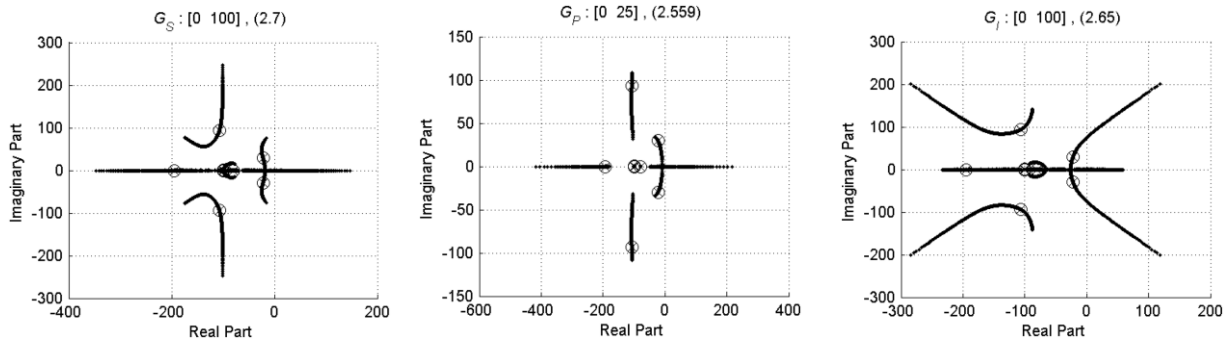

Fig. 4. Illustration of the locations of poles of Eq. (1) for a model contains one cortical area. Eq. (1) is linearized in this analysis. Model becomes unstable as the values of parameters of the model (i.e. G^S, G^P, and G^I) increase. Values of the parameters inside the square brackets represent minimum and maximum values of the parameter that generate the shown pole locations (root locus). Values of the parameters inside the parentheses represent the maximum value of the parameters that generate stable output.