Variational Bayesian Framework for Estimating Parameters of Integrated E/MEG and fMRI Model

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Abstract: The integrated analysis of the Electroencephalography (EEG), Magnetoencephalography, and functional magnetic resonance imaging (fMRI) are instrumental for functional neuroimaging of the brain. A bottom-up integrated E/MEG and fMRI model based on physiology as well as a method for estimating its parameters are keys to the integrated analysis. We propose the variational Bayesian expectation maximization (VBEM) method to estimate parameters of our proposed integrated model. VBEM method iteratively optimizes a lower bound on the marginal likelihood. An iteration of the VBEM consists of two steps: a variational Bayesian expectation step implemented using the extended Kalman smoother (EKS) and the posterior probability of the parameters in the previous step, and a variational Bayesian maximization step to estimate the posterior distributions of the parameters. For a given external stimulus, a variety of multi-area models can be considered in which the number of areas and the configuration and strength of connections between the areas are different. The proposed VBEM method can be used to select an optimal model as well as estimate its parameters. The efficiency of the proposed VBEM method is illustrated using simulation results. The proposed VBEM method can be used to estimate parameters of other non-linear dynamical systems. This study proposes an effective method to integrate E/MEG and fMRI and plans to use these techniques in functional neuroimaging.

I. Description of Purpose (Introduction)

Variational Bayesian framework was used by Friston et al. [1,2] to estimate parameters of their proposed dynamic causal model (DCM). However, there are two limitations in DCM. First, its state equation is assumed to be noise-free; this is not a realistic assumption. Second, DCM is not an integrated E/MEG and fMRI model and models just one modality. To cover these limitations, we propose the variational Bayesian expectation maximization (VBEM) method to estimate parameters of our multi-area integrated E/MEG and fMRI model. The efficiency of the proposed VBEM method is illustrated using simulation results. In conclusion, this study proposes an effective method for estimating parameters of non-linear dynamical systems that can be particularly used for the integrated analysis of E/MEG and fMRI.

II. Method

Multi-Area integrated E/MEG and fMRI model: We propose a multi-area integrated E/MEG and fMRI model based on our previously developed integrated model [3]. The model is based on two connection types: Short-Range Connection (SRC) and Long-Range Connection (LRC). The SRCs are related to the connections between minicolumns within the areas. LRCs characterize configuration of the multi-area model and describe the connections among the cortical 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.

$$\begin{cases} \dot{X}_{8NL\times 1} = A_1 X + [A_2 + (G^s \otimes I_{8L\times 8L})A_3 + (G^l \otimes I_{8L\times 8L})A_4]S(X) + Bu + w \\ y_{ECDs} = CX \\ \kappa_n = \sum_{i=1}^{L} (|x_3^{(i)}| + |x_5^{(i)}| + |x_5^{(i)} - x_1^{(i)}| + |x_7^{(i)}|); n = 1,2,\ldots,N \end{cases} \quad (1)$$

where I is 8xL-by-8xL identity matrix, $\otimes$ is the *Kronecker product* operator, $A1$, $A2$, $A3$, $A4$, B, and C are fixed matrices which depend on some physiological parameters in the model, $S(.)$ is the 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 extended balloon model (EBM) [4] 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.

***Variational Bayesian Expectation Maximization Method*:** Consider a model (say model m) with hidden variable x and i.i.d. observed variable y where the unknown parameters θ describe stochastic dependencies between the variables. In the Bayesian learning, the following marginal likelihood of model m, $p(y|m)$, is maximized.

$$\ln p(y|m) = \ln \int d\theta \, dx \, p(x, y, \theta | m) \quad (2)$$

The marginal likelihood can be lower bounded by introducing free distributions over both hidden variables and parameters ($q_x(x)$ and $q_\theta(\theta)$).

$$\ln p(y|m) \geq \int d\theta \, q_\theta(\theta) \left[\int dx \, q_x(x) \ln \frac{p(x, y|\theta, m)}{q_x(x)} + \ln \frac{p(\theta|m)}{q_\theta(\theta)} \right] = F(q_x(x), q_\theta(\theta)) \quad (3)$$

By considering a particular class of graphical models, conjugate-exponential (CE) models, the VBEM algorithm will be more similar to the classical expectation maximization algorithm. The CE models satisfy the following conditions.

$$\begin{cases} p(x_i, y_i | \theta) = g(\theta) f(x_i, y_i) \exp[\Phi(\theta)^T . z(x_i, y_i)] \\ \\ p(\theta | \eta, \nu) = h(\eta, \nu) g(\theta)^\eta \exp[\Phi(\theta)^T \nu] \end{cases} \quad (4)$$

where the sufficient statistics $z(.,.)$ and function $f(.,.)$ define the exponential family functions, $\Phi(\theta)$ is the vector of natural parameters, η and ν are hyperparameters of the prior, and g and h are the normalization constants. Two steps of the VBEM algorithm for CE models are as follows.

$$\text{VB E Step}: \begin{cases} q_{x_i}^{(k+1)}(x_i) \propto f(x_i, y_i) e^{\overline{\Phi}^T . z(x_i, y_i)} = p(x_i | y_i, \overline{\Phi}^{(k)}) \quad \forall i = 1,\ldots,n \\ \\ \overline{\Phi}^{(k)} = \int d\theta \, q_\theta^{(k)}(\theta) \Phi(\theta) \end{cases} \quad (5)$$

$$\text{VB M Step}: \begin{cases} q_\theta^{(k+1)}(\theta) \propto h(\tilde{\eta}, \tilde{\nu}) g(\theta)^{\tilde{\eta}} e^{\Phi(\theta)^T . \tilde{\nu}}; \tilde{\eta} = \eta + n \\ \tilde{\nu} = \nu + \sum_{i=1}^{n} \bar{z}(y_i); \bar{z}(y_i) = \langle u(x_i, y_i) \rangle_{q_{x_i}^{(k+1)}(x_i)} \end{cases} \quad (6)$$

where super-script k represents the iteration number. In the linear dynamical model, the solution of the Kalman smoother is equivalent to the VB E-step in Eq. (5) [5]. For the nonlinear model according to Eq. (1), the solution of the extended Kalman smoother (EKS) is equivalent to the VB E-step in Eq. (5). We derived the formulation of the variational EKS for the time-variant dynamical system in Eq. (1).

Estimation of the Model Parameters**:** For a specific model, the locations and configuration of connections among its areas are given. Then, the Bayesian framework along with the MEG/fMRI data can be used to estimate unknown parameters of the model. Here, G^s and G^l in Eq. (1) which are parameters of the SRCs and LRCs as well as hemodynamic parameters are the unknown parameters that can be estimated using the proposed VBEM method and the MEG/fMRI data. For an N-area model, G^s and G^l contain 3xN and 3xNx(N-1) unknown parameters, respectively. Considering five hemodynamic parameters in each area, the N-area model has 5xN unknown hemodynamic parameters. After preprocessing and assigning a prior distribution to the parameters, the proposed VBEM method can be used to estimate the parameters as well as the activation in the multi-area model. Following pseudocode shows algorithm of the VBEM method.

1. Initialization
    - Initialize precision hyperparameters (η and ν in Eq. (4)) where unknown parameters of the model are: $\theta \equiv \{G^s, G^l\}$
    - Initialize hidden state priors (mean and variance of the state initial value in Eq. (1))
    - Initialize hidden state sufficient statistics (z(.,.) in Eq. (4))
    - Initialize noise hyperparameters
2. Variational Bayesian M step (VBM)
    - Infer parameter posteriors $q_\theta(\theta)$
    - Calculate expected natural parameters ($\Phi(\theta)$ in Eq. (4))
3. Variational Bayesian E step (VBE)
    - Infer distribution over hidden state $q_x(x)$
        - ⇨ extended Kalman smoother (EKS)
    - Calculate hidden state sufficient statistics
4. Compute the lower bound of the Log-likelihood (F(.,.) in Eq. (3))
5. Update hyperparameters
    - Update precision hyperparameters (η and ν in Eq. (4))
    - Update hidden state priors
    - Update noise hyperparameters
6. Go to step 2 if F(.,.) is increasing

III. Results

Fig. 2-a illustrates the configuration of the LRCs in a three-area model which is used in the simulation. Each area contains four minicolumns. Note that the SRCs between minicolumns within the areas are not shown. Two SRCs parameters in each area and two LRCs parameters between each pairs of the areas are given non-zero values and other six parameters are given zero. 12 unknown SRCs and LRCs parameters are estimated using the VBEM method. Using Eq. (1) and given values

of the parameters, y_{ECDs} as the E/MEG signal in the areas are generated which is shown with the red plot in Fig. 3-b. Using the VBEM method, the unknown parameters are estimated. Fig. 3-c shows the Log-likelihood of the iterations of the VBEM method. Convergence of the estimated parameters to their final values is illustrated in Fig. 3-d. As shown in Fig. 3-e, the estimated values of the parameters is in good agreement with the real values of the parameters. In addition, the small difference between the estimated and real MEG signals in Fig. 3-b illustrates the performance of the VBEM method in estimating the model parameters and the activation map.

IV. Conclusion

To estimate parameters of our multi-area integrated E/MEG and fMRI model and detect activations in the areas of the model, we proposed the VBEM method. This method iteratively optimizes a lower bound on the marginal likelihood. The solution of the extended Kalman smoother (EKS) is equivalent to the VB E-step in Eq. (5). Using properties of the conjugate-exponential models, we derived the formulation of the variational EKS as the solution of the VB E-step. The efficiency of the proposed VBEM method is illustrated using simulation results where the real and estimated parameters were in good agreement. In conclusion, we propose an effective method for estimating parameters of non-linear dynamical systems and used it for integrated analysis of the E/MEG and fMRI.

5. References

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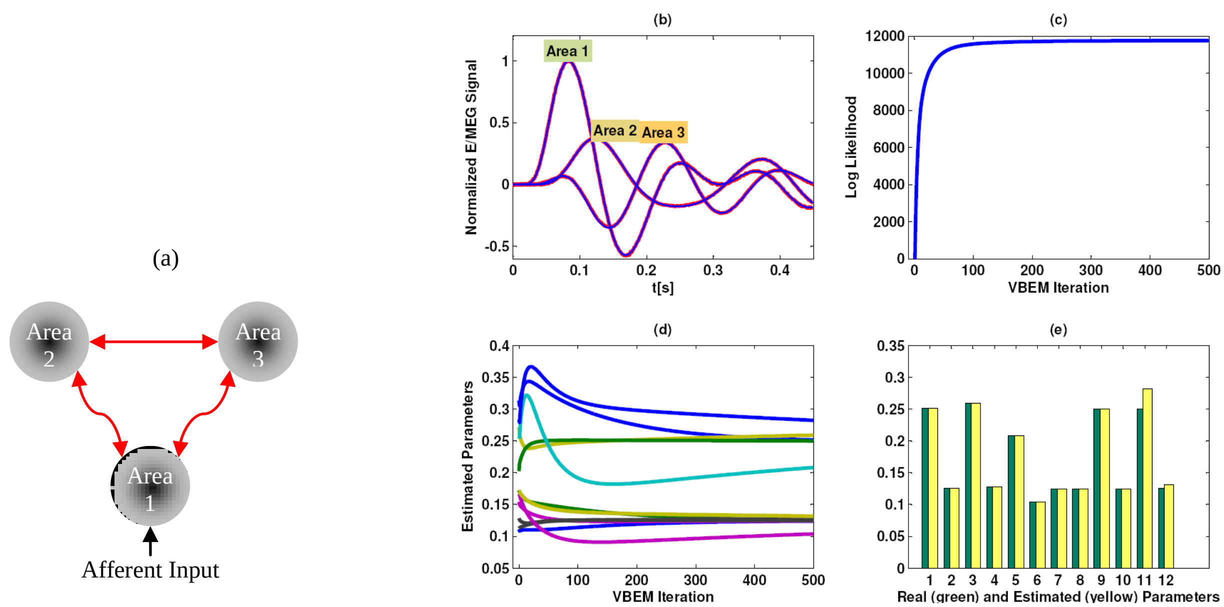

Fig 2. Simulation results of the three-area model. (a) Illustration of the LRCs in the three-area model. (b) Normalized real (red) and Estimated (blue) E/MEG Signals. (c) Log-likelihood of the estimation. (d) Convergence of the estimated parameters to their final values. (e) Real (green) and estimated (yellow) values of the parameters.