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Single-Trial Extraction of Pure Somatosensory Evoked Potential Based on Expectation Maximization Approach

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Abstract—It is of great importance for intraoperative monitoring to accurately extract somatosensory evoked potentials (SEPs) and track its changes fast. Currently, multi-trial averaging is widely adopted for SEP signal extraction. However, because of the loss of variations related to SEP features across different trials, the estimated SEPs in such a way are not suitable for the purpose of real-time monitoring of every single trial of SEP. In order to handle this issue, a number of single-trial SEP extraction approaches have been developed in the literature, such as ARX and SOBI, but most of them have their performance limited due to not sufficient utilization of multi-trial and multi-condition structures of the signals. In this paper, a novel Bayesian model of SEP signals is proposed to make systemic use of multi-trial and multi-condition priors and other structural information in the signal by integrating both a cortical source propagation model and a SEP basis components model, and an Expectation Maximization (EM) algorithm is developed for single-trial SEP estimation under this model. Numerical simulations demonstrate that the developed method can provide reasonably good single-trial estimations of SEP as long as signal-to-noise ratio (SNR) of the measurements is no worse than ~26 dB. The effectiveness of the proposed method is further verified by its application to real SEP measurements of a number of different subjects during spinal surgeries. It is observed that using the proposed approach the main SEP features (i.e., latencies) can be reliably estimated at single-trial basis, and thus the variation of latencies in different trials can be traced, which provides a solid support for surgical intraoperative monitoring.

Index Terms—Bayesian model, cortical source, expectation Maximization (EM), log-likelihood, maximum likelihood (ML), regions of interest (ROI), somatosensory evoked potential (SEP) latency, single-trial, universal template.

I. INTRODUCTION

SOMATOSENSORY evoked potential (SEP) is a brain electrical response elicited by stimulation of the median nerve, common peroneal nerve and posterior tibial nerve [1]. SEP can be utilized to diagnose neurological disease which refers to the dysfunction of peripheral nerve, plexus, spinal root, spinal cord, brain stem and primary somatosensory cortex [2]. The acquisition of SEP depends on the signal collection during intra-operative SEP monitoring, which is noninvasive and applicable to any surgical level [3]. However, because of the large magnitude of background ongoing EEG, the SNR of directly obtained SEP signals is so low (~20 dB, even ~30 dB) that it is difficult to observe the features of SEP [4].

The across-trial averaging in the time domain is the most widely used extraction approach [5], [6]. The averaging procedure can recover the clean SEP, which describes the total effect of scalp potentials related to the onset of sensory event in a series of trials. But the prerequisite is that SEP must be stationary (e.g., The latency and morphology of SEPs are fixed generally in different trials) and unaffected by background EEG. While in some real cases of monitoring, SEP is not stable (e.g., Latencies are variable), then the averaging method is unable to generate reliable results reflecting real SEP features (e.g., latency and amplitude) in different trials. Thus, an approach that can extract accurately pure SEP in every single trial is needed.

In recent years, several approaches of single-trial detection of pure ERP (event-related potentials) signals including SEP have been developed. Rossi [7] applied Auto Regressive filter with eXogenous input (ARX) to track SEPs’ fast inter-trial changes emphasizing the relations between waveform variability and surgical maneuvers. Hu [8] proposed an approach based on wavelet filtering and multiple linear regression, which can promote the SNR of original single-trial ERP and detect the variability of the morphology, peak latencies and amplitudes corresponding to pure ERP signals. Hu [9] also explored a space-time-frequency filter combining probabilistic independent component analysis (ICA) with wavelet filtering in order to extract precisely the particular sensory modalities in different trials. Furthermore, since that the extraction of clean SEP can be regarded as an inverse recovery problem from collected SEP (observable signals), a series of blind source separation (BSS) methods may be adopted. Liu [10] has utilized several typical BSS approaches on SEP extraction tasks and compared the performances of these methods. In sum, second-order blind identification with six covariance matrix (SOBI6) is considered as an appropriate algorithm to handle SEP extraction from noise background.

All the above approaches belong to multi-linear algorithms, which can well exploit the spatial structure of multichannel ERP. However, such methods do not make use of the mul-
multiple-trial, multiple-condition structures or some standard features of ERP/EEG [11]. In addition, the prerequisite of executing these algorithms is that background EEG signals are uncorrelated and isotropic, which is often invalid in practice [12]. Besides, from the view of statistical inference, the modes corresponding to pure ERP may meet the risk of missing regions of significant probability mass [13]. Motivated by dealing with these disadvantages, Wu [11] constructed a hierarchical Bayesian model to utilize the inter-trial and inter-condition structure of EEG. In addition, Wu [12] proposed a specific Bayesian integrated statistical framework regarding some stereotyped ERP components on the scalp. The two approaches may provide comparatively reliable estimations of ERP features, but only statistical characteristic of original noisy ERPs is considered without combining the physiological generation mechanism of ERP. While in this paper, we integrate the cortical source potentials' effect and the basis waveforms of prior pure SEP features (extracted from a universal standard SEP template) into our methodology framework and propose a new Bayesian hierarchical model, in which SEP is denoted as the linear combination of cortical source signals. In addition, the source activities are regarded as an entire effect of several basis components of SEP features. So our model further simulates the physiological generation mechanism of SEP. Then based on the novel Bayesian framework, we deduce an innovative expectation maximization (EM) algorithm in order to give the estimation of pure SEP for every single trial. The new approach is applied to a series of synthetic and real SEP data. Finally, the results indicate that SEP latencies (an important index of SEP features) can be estimated well.

The organization of this paper is shown in the following. Section II describes our Bayesian model and the specific EM approach in detail. Section III shows the estimation results of some synthetic data with different SNRs. Section IV displays the estimation results of pure SEP signals originated from real spinal surgeries. Section V provides the discussion related to our novel approach and SEP estimation. In the end, Section VI gives the total conclusion.

II. Method

A. Problem Formulation

The physiological basis of ERP shows that scalp ERP signals come from composite effect of activation potentials related to some particular cortex regions under specific stimulations (e.g., pain stimulus in SEP). A simplified model of such mechanism is to consider EEG as linear combination of several cortical source potential signals corresponding to particular dipole sources or cortical source regions of interest (ROIs). Such model has been adopted widely in the literature [14]. For example, in [15] scalp potential signals are modeled as the multiplication between source-scalp forward fields and source activity potentials with a particular time dynamic relationship, and such model is adapted in this paper for the purpose of single-trial estimation. In order to represent single-trial variation about SEPs, we decompose the cortical source activities as a linear combination of the basis waveforms related to SEP features.

Denote the spatial distribution of cortical activities at time \( n \) as \( \alpha_n \). According to linear conductivity from the cortex to the scalp, the scalp EEG measurement \( y_n \) can be modeled as follows:

\[
y_n = H\alpha_n
\]  

(1)

where \( H \) is the leadfield matrix with each column representing the conductivity from a specified point on the cortex to the scalp. For ERP study such as SEP in this paper, we are interested in the cortical activities related to only the ERP under consideration, i.e., only a small number of ROIs on the cortex will be considered as the sources of SEP and all other regions on the cortex will be considered to contribute to background EEG in the context of SEP study. Denote part of \( H \) and \( \alpha_n \) corresponding to the \( m \)th ROI as \( H_m \) and \( \alpha^m_n \), respectively. In practice, \( H_m \) is often a low-rank matrix reflecting an ill-conditioning in the forward physics, so it is difficult to see all spatial degrees of freedom related to the measured SEP [16]. So, for the purpose of dimension reduction we make an approximation \( H_m \approx U_m^K \Sigma_m^K V_m^T \) using the leading \( K \) components of the singular value decomposition (SVD) of \( H_m \). Further simplifying \( \alpha^m_n \approx \alpha^m_x^m_n \), and denoting \( C_m = U_m^K \Sigma_m^K \) and \( \Lambda_m = V_m^T \alpha^m_n \), assuming we have a total of \( M \) ROIs, then according to (1) we have

\[
y_n = \sum_{m=1}^{M} C_m \Lambda_m \alpha^m_n + v_n \triangleq CAx_n + v_n
\]  

(2)

where \( v_n \sim N(0, R) \) is a vector of normal distribution with covariance matrix \( R \), representing a combination of model error and background EEG that have sources other than the ROIs, \( C = C_1 \cdots C_M \), \( \Lambda = \begin{pmatrix} \lambda_1 & 0 & \cdots & 0 \\ \vdots & \ddots & \vdots & \vdots \\ 0 & \cdots & \lambda_M \end{pmatrix} \), and \( x_n = [x^1_n \cdots x^M_n]^T \). In order to represent trial-to-trial variation of SEP, cortical SEP \( x_n \) is further decomposed by a set of basis components \( s_n \) as follows:

\[
x_n = As_n + w_n
\]  

(3)

where \( A \) represents the decomposition scores and \( w_n \sim N(0, Q) \) is a random vector of normal distribution with covariance matrix \( Q \), representing decomposition error.

Accordingly, the overall hierarchical Bayesian model of SEP measurements is described as follows:

\[
y_n = CAx_n + v_n
\]

\[
x_n = As_n + w_n
\]

\[
v_n \sim N(0, R)
\]

\[
w_n \sim N(0, Q)
\]  

(4)

In this model, \( \gamma_n \) is the known measured scalp EEG signal, \( s_n \) is the basis set that should be designed from SEP template, and \( C \) is the matrix which is calculated from the leadfield matrix \( H \). If needed to be determined from a head conduction model, while \( A, \Lambda, R \) and \( Q \) are model parameters that will be estimated using an EM algorithm developed later in this paper.

B. Calculation of Leadfield Matrix \( C \)

Based on a standard three-sphere head model, the forward field from each cortical mesh point to the scalp EEG electrode
positions can be calculated by surface integral [17], resulting as a column of the leadfield matrix $\mathbf{H}$, and in this paper such calculation is performed by Fieldtrip toolbox [18] embedded in the SPM software [19]. To determine the ROIs related to SEP, we use an empirical Bayesian method included in SPM to generate cortical source imaging based on scalp SEP signals that are estimated from the standard multi-trial averaging of the measured scalp EEG signals under the SEP experiments. Fig. 1 displays possible cortical SEP sources estimated by SPM from a subject's scalp SEP. According to the particular SEP experiment (stimulating electrodes were placed over the posterior tibial nerve at ankle), we have the prior knowledge of possible cortical source positions (postcentral gyrus and cingulate sulcus [32]). In addition, the number of cortical source regions should be smaller than EEG channel number because of the matrix singularity of $(\mathbf{C}^T \mathbf{R}_{yy}^{-1} \mathbf{C})^{-1}$ in $\mathbf{W} = \mathbf{R}_{yy}^{-1} \mathbf{C} (\mathbf{C}^T \mathbf{R}_{yy}^{-1} \mathbf{C})^{-1}$ of (14). Then we choose 2 main cortical regions, referring to postcentral gyrus and cingulate sulcus, which are also the two most activated regions at 40 ms (time of the P37-N45 complex of the SEP). The two areas, marked with red rectangles in Fig. 1, are chosen as the two ROIs in this paper. Accordingly, $\mathbf{H}_1$ and $\mathbf{H}_2$, corresponding to the two ROIs, respectively, are extracted from $\mathbf{H}$, and then $\mathbf{C}_1$ and $\mathbf{C}_2$ are obtained from SVD approximation described previously, and finally we get $\mathbf{C} = \mathbf{C}_1 \mathbf{C}_2$. In the SVD of $\mathbf{H}_1$ and $\mathbf{H}_2$, a good approximation can be obtained using at most 4 leading components, $(K \leq 4)$ when the area of ROI is 590 mm² or less as in our situation [20]. In this study, $\mathbf{C}_1$ occupies 85.65% of total variance of $\mathbf{H}_1$, while $\mathbf{C}_2$ holds 72.62% related to $\mathbf{H}_2$. 

C. Design of SEP Basis set $\mathbf{s}_n$

The basis set $\mathbf{s}_n$ is designed as to be able to represent the basic waveform of SEP, especially the P37 and N45 components of traditional SEP [30], and trial-to-trial variations of the latencies of the two components. We design such a basis set from a SEP template, which can be either a multi-trial averaged SEP waveform from the subject’s own scalp EEG, or a universal one that is common for all subjects. For the ease of application, a universal SEP template is adopted in this paper, as shown in Fig. 2.

With the given SEP template, the whole process of building up the basis set is described as follows. At first, two segments of the SEP template are extracted, with Segment I covering the period 30–50 ms and Segment II covering 50–70 ms. Then a series of time-delayed version of each segment are obtained, where time delay is $0.4k$ ms with $k = -15, -14, \ldots, -2, -1, 0, 1, 2, \ldots, 14, 15$, as shown in Fig. 3(a) and (b). These set of signals will be able to cover a latency variation ranging from $-6$ ms to 6 ms. Since these total

![Fig. 1. 2 selected cortical source regions generating SEP signals.](image1)

![Fig. 2. Universal SEP template.](image2)

![Fig. 3. (a) Delayed version of Segment I of the SEP template. (b) Delayed version of Segment II of the SEP template.](image3)
of 62 signals shown in Fig. 3(a) and (b) are highly correlated, we use their leading 3 principal components (2 for Segment I and 1 for Segment II), which cover more than 70% of the total variation of 2 signal sets, as the final basis set $s_n$ for the purpose of model simplification, as shown in Fig. 4.

D. EM Algorithm for Model Parameter Estimation

With scalp EEG signals $y_n$ measured, SEP basis set $s_n$ designed, and leadfield matrix $C$ determined, our final step is to estimate the set of unknown model parameters in (4), $\mathbf{A}, \lambda_1, \lambda_2, \ldots, \lambda_M$, $\mathbf{Q}$, and $\mathbf{R}$, denoted as variable set $\theta$. In the following we develop an expectation maximization (EM) algorithm [21] for a maximum likelihood (ML) estimation of $\theta$. The development of our EM algorithm for our SEP model is in some sense similar to that for the state-space model (SSM) described in [22].

To develop the EM algorithm, we first get the likelihood and log-likelihood of our model as follows.

Likelihood

$$P(Y, X; \theta) = \prod_{n=1}^{N} P(y_n|x_n) P(x_n)$$

Log-likelihood

$$\log P(Y, X; \theta) = \sum_{n=1}^{N} -\frac{1}{2} \log |\mathbf{R}| - \frac{1}{2} \log |\mathbf{Q}| - \frac{N}{2} \text{tr}(\mathbf{R}^{-1}(y_n - \mathbf{C}a(x_n))(y_n - \mathbf{C}a(x_n))^T) - \frac{N}{2} \text{tr}(\mathbf{Q}^{-1}(x_n - \mathbf{A}s_n)(x_n - \mathbf{A}s_n)^T).$$

1) E-Step: In the E-step of our EM algorithm, the conditional expectation of log-likelihood, given an estimate of the model parameter in the previous ($r$th) iteration denoted as $\theta^r$, is shown as follows:

$$q(\theta | \theta^r) = E_{X|Y, \theta^r} \{ \log P(Y, X; \theta) \} = -\frac{N}{2} \log |\mathbf{R}| - \frac{N}{2} \log |\mathbf{Q}| - \frac{N}{2} \text{tr}(\mathbf{R}^{-1}(y_n - \mathbf{C}a(x_n))(y_n - \mathbf{C}a(x_n))^T) - \frac{N}{2} \text{tr}(\mathbf{Q}^{-1}(x_n - \mathbf{A}s_n)(x_n - \mathbf{A}s_n)^T).$$

2) M-Step: In the M-step of our EM algorithm, the partial derivatives of each variable $\theta$ with respect to $q$ are derived and set as 0, resulting in the following:

$$\frac{\partial q}{\partial \mathbf{Q}} = 0 \Rightarrow \mathbf{Q} = \mathbf{\Sigma} + \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T + \mathbf{A} \left( \frac{1}{N} \sum_{n=1}^{N} s_n s_n^T \right) \mathbf{A}^T - \mathbf{A} \left( \frac{1}{N} \sum_{n=1}^{N} s_n \mu_n^T \right) - \left( \frac{1}{N} \sum_{n=1}^{N} \mu_n s_n^T \right) \mathbf{A}^T$$

$$\frac{\partial q}{\partial \mathbf{A}} = 0 \Rightarrow \mathbf{A} = \left( \frac{1}{N} \sum_{n=1}^{N} s_n \mu_n^T \right) - \left( \frac{1}{N} \sum_{n=1}^{N} \mu_n s_n^T \right)^{-1}$$

$$\frac{\partial q}{\partial \mathbf{R}} = 0 \Rightarrow \mathbf{R} = \frac{1}{N} \sum_{n=1}^{N} y_n y_n^T - \mathbf{C} \left( \frac{1}{N} \sum_{n=1}^{N} \mu_n y_n^T \right) - \mathbf{C} \left( \frac{1}{N} \sum_{n=1}^{N} y_n \mu_n^T \right) \mathbf{A}^T \mathbf{C}^T + \mathbf{C} \left( \mathbf{\Sigma} + \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T \right) \mathbf{A}^T \mathbf{C}^T$$

$$- \mathbf{C} \left( \mathbf{\Sigma} + \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T \right) \mathbf{A}^T \mathbf{C}^T - \mathbf{C} \left( \mathbf{\Sigma} + \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T \right) \mathbf{A}^T \mathbf{C}^T - \mathbf{C} \left( \mathbf{\Sigma} + \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T \right) \mathbf{A}^T \mathbf{C}^T$$

$$\frac{\partial q}{\partial \mathbf{\mu}} = 0 \Rightarrow \lambda = \mathbf{C}^T \mathbf{\Sigma}^{-1} \mathbf{C}^T \mathbf{\lambda}$$

$$\mathbf{C}^T \mathbf{\Sigma}^{-1} \mathbf{C}^T \mathbf{\lambda} = \begin{pmatrix} \mathbf{C}^T \mathbf{R}^{-1} \mathbf{C} \mathbf{r}_{1,1} \mathbf{M} & \cdots & \mathbf{C}^T \mathbf{R}^{-1} \mathbf{C} \mathbf{r}_{1,M} \mathbf{M} \\ \vdots & \ddots & \vdots \\ \mathbf{C}^T \mathbf{R}^{-1} \mathbf{C} \mathbf{r}_{M,1} \mathbf{M} & \cdots & \mathbf{C}^T \mathbf{R}^{-1} \mathbf{C} \mathbf{r}_{M,M} \mathbf{M} \end{pmatrix} \begin{pmatrix} \lambda_1 \\ \vdots \\ \lambda_M \end{pmatrix}$$

Different from (8) and (9) that provide an estimate for $\mathbf{C}$ and $\mathbf{A}$, respectively, (10) and (11) cannot provide explicit expression for $\mathbf{C}$ and $\mathbf{A}$ since they are coupled in these two equations.
A way of decoupling is to give an approximation of $R$ as following as in [15]

$$R = \frac{1}{N} \sum_{n=1}^{N} y_n y_n^T - \frac{1}{N} \sum_{n=1}^{N} y_n \mu_n (\Sigma + \mu_n \mu_n^T)^{-1} \mu_n y_n^T$$  \hspace{1cm} (12)$$

and then calculate $A$ according to (11). While (12) can be further simplified into (13) based on Woodbury matrix identity—$(\Sigma + \mu_n \mu_n^T)^{-1} = \Sigma^{-1} - \Sigma^{-1} \mu_n \mu_n^T \Sigma^{-1} / 1 + \mu_n \Sigma^{-1} \mu_n$ [24]

$$R = \frac{1}{N} \sum_{n=1}^{N} y_n y_n^T / 1 + \mu_n \Sigma^{-1} \mu_n.$$  \hspace{1cm} (13)$$

3) Initialization: To complete our EM algorithm, we need to set initial values for the model parameters. While $A$ and $Q$ can be given randomly, $R$ and $\Lambda$ can be better initialized through solving a linearly constrained minimum variance (LCMV) problem.

If we have a matrix $W$ with $W^T C = I$, from (2) we have a rough estimate of $x_n$ as $W^T y_n = Ax_n + w^T v_n$, and we want to minimize the error $\sum_{n=1}^{N} \text{tr}(W^T y_n y_n^T W)$ by choosing $W$ properly according to the following optimization:

$$\min_{W} \text{tr}\left\{ W \left( \sum_{n=1}^{N} y_n y_n^T \right) W^T \right\}$$  \hspace{1cm} s.t. $C^T W = I$$

which can be solved through the LCMV beamformer [25] as $W = R_{yy}^{-1} C (C^T R_{yy}^{-1} C)^{-1}$, where $R_{yy} = 1/N \sum_{n=1}^{N} y_n y_n^T$ and $W^T R_{yy} W = \Lambda x_n A^T$.

Then we set the initial value of $R$ and $\Lambda$ as follows:

$$R = \text{diag}\{ R_{yy} \} - C (C^T R_{yy}^{-1} C)^{-1} C^T,$$  \hspace{1cm} (14)$$

$\lambda_i$ is the first eigenvector of $(W^T R_{yy} W)^T$.

4) Convergence Criterion: Convergence of the EM algorithm can be considered as achieved if the relative change of log-likelihood drops below a small threshold, for example $10^{-5}$. The log-likelihood in our model can be determined as

$$\log P(Y; \theta) = \sum_{n=1}^{N} \log P(y_n; \theta) = -\frac{N}{2} \log \text{CA\Lambda}^T C^T + R - \frac{1}{2} \sum_{n=1}^{N} [(y_n - \text{CA\Lambda s_n})^T (\text{CA\Lambda}^T C^T + R)^{-1} (y_n - \text{CA\Lambda s_n})] + \text{constant}.$$  \hspace{1cm} (15)$$

5) Complete EM Algorithm: In summary, our EM algorithm for model parameter estimation can be described as below.

1) Initialization

Let $R_{yy} = 1/N \sum_{n=1}^{N} y_n y_n^T$, $R_{ss} = 1/N \sum_{n=1}^{N} s_n s_n^T$, $D = (C^T R_{yy}^{-1} C)^{-1}$, $D_i$ is the $i$th $K \times K$ diagonal block of $D$. Make:

$$\lambda_i^0 = \text{largest eigenvector of } D_i^0,$$  \hspace{1cm} (16)$$

$$R^0 = \text{diag}\{ R_{yy} - \text{CDCT} \},$$  \hspace{1cm} (17)$$

$$A^0 = \alpha \cdot \text{rand}(M, L), \ M \text{ sources, } L \text{ bases}.$$  \hspace{1cm} (18)$$

2) EM iteration (r: the iteration number).

E-step:

$$B = \text{CA}^T, \ \mu_s = \text{A}^T s_n, \ \mu_y = B \mu_s, \sum_{21} = B Q;$$  \hspace{1cm} (19)$$

$$\sum_{22} = \sum_{21} B^T + R; \ \sum_{11} = Q$$  \hspace{1cm} (20)$$

$$\sum_{21} = Q' - \sum_{22}^{11} \sum_{21} + \mu_n \Sigma^{-1} \mu_n.$$  \hspace{1cm} (21)$$

$$\mu_n - \mu_y + \sum_{21}^{11} \sum_{22} (y_n - \mu_y)$$  \hspace{1cm} (22)$$

Define : $R_{\mu\mu} = \frac{1}{N} \sum_{n=1}^{N} \mu_n \mu_n^T, \ R_{\mu\mu} = \sum_{21} + R_{\mu\mu},$  \hspace{1cm} (23)$$

$$R_{\mu\mu} = \frac{1}{N} \sum_{n=1}^{N} \sum_{22}^{11} \sum_{21} (y_n - \mu_y^T) \mu_n.$$  \hspace{1cm} (24)$$

M-step:

$$\text{update}\ A^{r+1} = R_{\mu\mu}^{-1} R_{\mu\mu}^{-1},$$  \hspace{1cm} (25)$$

$$Q^{r+1} = R_{\mu\mu} + A^{r+1} R_{\mu\mu} A^{r+1} - A^{r+1} R_{\mu\mu} A^{r+1} + R_{\mu\mu}$$  \hspace{1cm} (26)$$

$$R^{r+1} = \frac{1}{N} \sum_{n=1}^{N} y_n y_n^T / 1 + \mu_n^T \sum_{n=1}^{N} \mu_n y_n^T.$$  \hspace{1cm} (27)$$

3) Check convergence and output

If $(\log P(Y; \theta))^{r+1} - (\log P(Y; \theta))^r / (\log P(Y; \theta))^r < 10^{-5}$, $(\log P(Y; \theta))$ given in (15), output:

$$\lambda_1^{r+1}, \lambda_2^{r+1}, \ldots, \lambda_M^{r+1}, A^{r+1}, \ R^{r+1}, Q^{r+1}; \text{ else, return step (2) and continue the EM iteration.}$$  \hspace{1cm} (28)$$

III. SYNTHETIC SEP DATA EXPERIMENT

The synthetic SEP data is generated based on the EEG generation model through the effect of cortical leadfield potentials ([15], (10) and (11)). The acquisition of EEG conforms to a distributed source model [26]. SNR is defined in (16)

$$\text{SNR} = 10 \log_{10} \frac{\text{tr} \{ \sum_{j=1}^{J} \sum_{n=1}^{N} \text{tr}(H_i^j \alpha_{n,j}^i) (H_i^j \alpha_{n,j}^i)^T \}}{\text{tr} \{ \sum_{j=1}^{J} \sum_{n=1}^{N} (v_n, i) (v_n, i)^T \}}.$$  \hspace{1cm} (29)$$

We provide six cases of synthetic data, which are respectively related to the SNR of observed data (synthetic SEP data) as $-30 \text{ dB}, -25 \text{ dB}, -20 \text{ dB}, -10 \text{ dB}, -5 \text{ dB}, 0 \text{ dB}$. The SNRs fit different cases of real collected SEP signals [27]. Referring to each SNR case, 100 teams of data are generated.

We adopt our Bayesian model and the novel EM algorithm to estimate pure synthetic SEP signals from the generated data.
synthetic SEP data corresponding to various noise levels. The evaluation of estimation effects depends on calculating the Pearson correlation coefficient between the presumed pure synthetic SEP data and the estimated clean synthetic SEP signal \([CAx_0\text{ in (1)}]\). Fig. 5 shows the total estimation situations of all synthetic SEP data corresponding to different SNR cases. From the figure, we know that the extracted synthetic SEPs are reasonable when SNR is larger than \(-20\) dB, because the mean Pearson correlation coefficient values are greater than 0.8 related to these cases. In contrast, the cases of SNRs as \(-30\) dB and \(-25\) dB can only respectively give the mean correlation values as 0.4 and 0.5, which indicates a terrible estimation effect. In addition, the standard deviations corresponding to SNRs as \(-30\) dB and \(-25\) dB are smaller than those for SNRs as \(-20\) dB and \(-10\) dB. Thus, our EM approach can give more stable estimations referring to the cases of SNRs larger than \(-25\) dB. Based on Fig. 5, we observe that the SNR as \(-20\) dB can be regarded as the threshold of the feasible SEP noisy data adaptive to our Bayesian model and EM algorithm. When noises follow Gaussian distribution with \(\frac{1}{\sqrt{2\pi}}\), our approach has the capability of generating the feasible estimation of pure SEP signals.

IV. REAL SEP DATA EXPERIMENT

In our task, the clinical SEP data is originated from the spinal surgery. Referring to elicit SEP signals, a pair of stimulating electrodes was placed over both sides of subjects’ posterior tibial nerve at ankle [28]. The time period of collecting SEP is 100 ms with the sampling rate as 5000 Hz. There exist six subjects. Corresponding to each subject, the measurement of more than 100 trials is executed. We give the average of SEPs related to all trials and consider it as the reference of pure SEP signals for the purpose of verification. Then our model and EM approach are applied to all single-trial cases. Referring to the feedback of activating crura, SEP is more evident in Channel Cz than that in other channels. So we intend to care the estimated signals of Channel Cz. The SEP latency we concern is the time period from the starting point (0 ms) to the minimum wave trough (P-peak) point. Based on clinical guideline for short-latency SEP [31], average SEP from 300 trials was used as the standard SEP for evaluation of single trial SEP extraction. Notch filter is applied to the EEG signals to reduce power line noise of 50 Hz in frequency, and an additional low-pass filter is used to reduce the harmonics (mainly 100 Hz) to better fit the Gaussian noise assumption in our model. However, results show that such a low-pass filter has very little effect on the estimation of our proposed EM algorithm.

Fig. 6 shows the estimation of pure SEP signal in a single-trial test (Trial 216) corresponding to Subject 1. The first sub-figure gives the original SEP signal of Channel Cz in Trial 216. The second shows the estimated pure SEP signal in this trial. The third one is the average of original SEP signals related to all trials (300 trials). The mean values of multiple-trial SEPs can be regarded as the reference and the upper bound of estimated SEP. In the first sub-figure, we see nothing about SEP features. Regarding the second sub-figure, we observe that the latency of estimated SEP signal is around 33 ms, which is nearby that of average SEP signal (34 ms) shown in the third sub-figure. Thus, referring to this trial, our approach gives a reasonable estimation of the SEP latency. In addition, our method gives the same waveform estimation as that of average-trial SEP signals during the SEP feature period, which is the interval from 30 ms to 60 ms. So in this trial, the SEP features are extracted accurately.

In order to check the total estimation effect of latencies related to the extracted pure SEPs, we display the potential amplitudes of estimated and original SEPs of all trials in one figure. The function of ERP image in EEGLAB [29] is adopted to plot 2-D images of amplitudes of SEP potentials, which can show the SEP latencies in all trials accurately and smoothly. Fig. 7 is such a smoothed 2-D colormap of potential amplitudes of Subject 1’s SEPs in 522 trials. Dark blue points represent the minimum wave troughs, while bright red parts indicate the maximum wave peaks. Referring to calculate troughs and peaks, we set a range between 30 ms and 50 ms, which belongs to the area of obligated SEP waveform. Then in this region, find out the minimum time point as a trough and the maximum time
point as a peak. Based on Fig. 7, we notice that it is not evident that there exist particular regions of wave troughs in the left sub-figure (original SEP), while the right sub-figure (estimated SEP) clearly displays an area of wave troughs appearing in the interval from 30 ms to 40 ms. The entire effect of amplitudes is summarized by the waveform under the colormap. We see that the integrated waveform in the right sub-figure displays the main SEP features. The average estimated SEP latency is located nearby 34 ms, which is marked by a vertical line. The composite estimation result is approximate to the average-trial SEP shown in the third sub-figure of Fig. 6. In addition, the results lie in the latency range of identifiable P37–N45 wave, which is one of features of traditional SEP wave [30]. Therefore, our approach can give a totally feasible and stable estimation of SEPs in all trials.

With respect to find out the change tendency of latencies in all trials, we draw a colormap showing the specific wave troughs and peaks of potential amplitudes, which are displayed in Fig. 8. Based on this figure, we observe that the left panel (original SEPs) almost provides no information about the latencies, while the right panel clearly reflects the time points of wave troughs (latencies) of estimated SEPs in different trials. It is evident that there exist some variations corresponding to latencies in various trials. Thus, the diversification of latencies related to the whole trials is displayed evidently. Furthermore, Fig. 8 demonstrates that our approach can trace the change of SEP latencies among multiple trials. With respect to the scale difference between Figs. 7 and 8, it is caused by smoothness. Fig. 8 is our original result. Fig. 7 is a smoothed result processed by a smooth function in EEGLAB software. Smoothness is realized through moving-average of potentials across several trials. The major procedures refer to split total trials into several partitions and each partition's potential averaging within the regions of moving non-rectangular windows. The purpose of smoothness is to emphasize trough and peak regions from the view of total trials. Through averaging operations, the values of previous peaks and troughs are replaced by means across the selected trials. So the scale of smoothed estimated SEPs (Fig. 7) is lower than those without smooth operations (Fig. 8).

Referring to the verification of total effects of extracted pure SEPs in multiple trials, we calculate the relative error $|\varepsilon|$, defined in (17) between the latency of average-trial original SEP and that of single-trial estimated SEP

$$
|\varepsilon| = \frac{L_{a} - L_{u}}{L_{a}} .
$$

In (17), $L_{u}$ is the latency of average-trial estimated SEP based on the universal template of SEP feature signal, while $L_{a}$ is the latency of average-trial original SEP signal. Corresponding to every subject, we extract the results in different trials of data and calculate their relative errors $|\varepsilon|$ of average-trial estimated SEP. The results are shown in 3rd column of Table I. We know that the relative errors of six subjects are lower than 0.025. Specifically, Subject 6 gives the zero-error. So the latency of entire extracted SEPs based on a universal SEP template is almost the same as that of average-trial original SEP. In addition, if $L_{u}$ is the latency of single-trial estimated SEP signal, (17) defines single-trial relative error. Then we calculate six subjects’ single-trial relative errors and gives the statistic of mean and standard deviation related to each subject. The results are provided in fourth and fifth columns of Table I. We observe that the means of single-trial relative errors for six subjects are lower than 0.055. The standard deviations are around 0.02. Therefore, our approach can provide a reasonable estimation of pure single-trial SEP from the view of total trials.

**V. DISCUSSION**

The model of generating SEP is originated from the generation model of VEP in [15]. We modify the state equation (2nd equation in our model) through utilizing the basis components
and regulatory weight matrix to fit the source activities. It is a rough approximation of the physiological generation of SEP.

The polarity of traditional P37-N45 waveform related to SEP is opposite to that of ERP. P37 of the traditional SEP refers to a negative peak, while N45 marks a positive peak [30]. All of figures corresponding to the estimated SEP waveforms are consistent with the marks on P37 and N45 of the traditional SEP.

The basic components \([s_\alpha]\) in (1) may generate some impacts to the estimated pure SEP signals. In Section IV, corresponding to each subject, our approach utilizes a standard SEP feature signal (wave trough point is located at 37 ms) as the universal template to calculate the values of \(s_\alpha\) (details shown in Section II-B). Here we make use of each subject's average-trial SEP as the basis component template of their own. Then EM is applied to six subjects' data in Section IV.

Through comparing latencies, we find that there exist only small discrepancies. So the individual SEP template can provide the similar estimation solution as that upon the universal SEP template. Therefore, the variation of the basis component template gives a small influence to the estimation of SEP latencies.

The leadfield matrix \([L]\) also gives a large influence related to the estimated SEP. Based on our model (1), the pure SEP should be the multiplication of \([C, A, x]\). Thus, a precise \(C\) will be a strong prior and constraint guaranteeing the accurate estimation of other variables.

Referring to Gaussian noises and the influence of SNRs, we concern the range of suitable SNRs for our approach as SNRs larger than –20 dB. A large numbers of synthetic data experiments have given the verification in Section III. In real cases, if main noises follow Gaussian distribution with originally collected SEP signals conforming to the feasible SNR range, our approach can be effective to extract real SEP signals.

In order to check the estimation effect of our approach (EM) compared to other single-trial SEP detection methods, we make the comparison of estimated latencies among EM (our approach), CSOBI, PICA and WFMLR (referred in Section I). We adopt the software of STEP1 [32], which integrates these algorithms. Fig. 9 shows the single-trial estimation results among four approaches. We observe that SEP latency point (red framework) in Subfigure EM is nearest to that of average SEP (upper bound) in Fig. 6. In addition, the feature waveforms of estimated SEP related to three other approaches are far from the average SEP. Referring to the total estimation effect, Figs. 10 and 11 gives the smoothed colormap of estimated SEPs corresponding to all trials of Subject 1 and Subject 3. We know that EM can provide the most stable estimation of SEP latencies. Referring to other subjects, we provide the statistic of single-trial relative estimation errors of SEP latencies in Table II. Compared with Table I, it is evident that EM can gain smaller relative errors than three other approaches involving all subjects.
As a matter of fact, our proposed EM method has the same clear superiority for all six subjects under study, but due to space limitation, results for subjects 4–6 are not shown in the manuscript, and instead we compared the relative errors of extracted SEP signals for all six subjects in Table I of Section IV for our proposed method and Table II of Section V for the other three methods under comparison.

Considering our algorithm’s stability across different subjects, we shows the subject 2 (Fig. 11 first sub-graph) and 3’s estimation effect figures of SEP latencies (Fig. 12). From the two figures we know that the latencies of estimated SEPs locate in the range between 35 ms and 45 ms. Altogether with Figs. 7 and 8, it shows that our algorithm can give a stable estimation of pure SEP across multiple subjects.

Finally, considering the algorithm strategy of EM, EM approach owns the limitation of local convergence. In addition, as described in Section II-D, three approximations are adopted to decouple $\mathbf{A}$ and $\mathbf{R}$ in (10) and (11) and set the initial value of $\mathbf{A}$ and $\mathbf{x}_n$, respectively. While a good initialization can help an iterative algorithm converge close to global optimum, when latencies vary in different trials, our approach can trace the changing tendency precisely and fast, which is quite important in SEP intraoperative monitoring.

VI. CONCLUSION

Referring to the SEP feature extraction, we propose a particular Bayesian model of SEP signal generation considering the effects of cortical source potentials. In addition, a specific Expectation Maximization (EM) approach is proposed. Through utilizing a universal feature SEP signal template, our approach can fast acquire the accurate pure SEP estimation similar to that adopting the across-trial averaging (a conventional approach) in a single-trial level. Specially, in original collected SEP signals with a low SNR ($-20 \text{ dB} \sim -10 \text{ dB}$), when latencies vary in different trials, our approach can trace the changing tendency precisely and fast, which is quite important in SEP intraoperative monitoring.


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