Bayesian Analysis of Single Trial Cortical Event-Related Components

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Abstract. A common technique in neurophysiology is the recording of electric potentials generated by cortical neuronal ensembles in relation to a specific event. The understanding of event-related potentials requires the identification of signals that are relatively phase-locked to a stimulus or event onset (event-related potentials) as well as non-phase locked activities. It is now widely accepted that the recorded phase-locked signal itself is not a homogeneous signal, but instead a combination of different components, which can vary in amplitude and latency from trial to trial. We approach the problem of identifying event-related component waveforms and their trial-to-trial variability from a Bayesian perspective. We employ a signal model consisting of a set of unknown source waveforms each with their own set of trial-to-trial amplitudes and latencies. Differential variability of the sources from trial to trial aids significantly in the identification of the component waveforms. The posterior probability density is derived for a specified number of event-related components using data from single or multiple sensors. The *Maximum A Posteriori* (MAP) solution is used to obtain the event-related component waveforms and their single trial parameters. The approach is demonstrated using a data set consisting of intracortically recorded local field potentials (LFP) in monkeys performing a visuomotor pattern discrimination task.

MODELING CORTICAL EVENT RELATED COMPONENTS

A common technique in neurophysiology is the recording of electric potentials generated by neuronal ensembles in relation to a specific event like the presentation of a sensory stimulus. The obtained recordings are commonly understood as the linear combination of event-related signals relatively phase-locked to the event onset, and ongoing activity. The ongoing activity includes event unrelated activity and possibly also event-induced components that are not phase-locked to the event onset. It is now widely accepted that the recorded event-related response itself is not a homogeneous signal, but instead a combination of different components, which can vary in amplitude and latency from trial to trial.

The separation between these components and the ongoing activity is fundamental for the interpretation of event-related modulation of statistical interdependence in multi-channel data [1]. Furthermore, the estimation of single trial amplitudes and

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latencies of event-related potentials provides essential information for the understanding of information processing stages in the cortex [2].

Several attempts to provide estimates of single trial event-related response following maximum likelihood approaches have been presented before, e.g.: single trial ICA [3], and latency and amplitude of single trial evoked responses [4,5,6,7]. In this work we present a more comprehensive formulation. We start from a multivariate generative linear model expressed as:

$$
\begin{pmatrix} x_{1r}(t) \\ \vdots \\ x_{Mr}(t) \end{pmatrix} = \begin{pmatrix} C_{11} & \cdots & C_{1N} \\ \vdots & \cdots & \vdots \\ C_{M1} & \cdots & C_{MN} \end{pmatrix} \begin{pmatrix} S_{1r}(t) \\ \vdots \\ S_{Nr}(t) \end{pmatrix} + \begin{pmatrix} \eta_{1r}(t) \\ \vdots \\ \eta_{Mr}(t) \end{pmatrix},
\tag{1}
$$

or in vector form:

$$
\mathbf{X}_r(t) = \mathbf{C}\mathbf{S}_r(t) + \mathbf{H}_r(t),
\tag{2}
$$

where $x_{mr}(t)$ is the mth channel recording at time t and at the rth realization or trial. $S_{nr}(t)$ represents a particular realization of the nth event or source activity at the trial r, C_{mn} are the entries of a mixing matrix representing instantaneous and stationary source-detector couplings, and $\eta_{mr}(t)$ refers to an unpredictable component. The source or components $S_{nr}(t)$ can be modeled in many diverse ways, as for example, ARMA processes, continuous or discrete time source waveforms, Taylor expansion of dynamical models, etc.

We approach the problem of solving for the components, noise and the matrix $\mathbf{C}$, from a Bayesian perspective. The posterior probability of the model parameters given the data and prior information I is:

$$
p(\mathbf{C}, \{\mathbf{S}(t)\}, \{\mathbf{H}(t)\} \mid \{\mathbf{X}(t)\}, I) =
$$
$$
\frac{p(\{\mathbf{X}(t)\} \mid \mathbf{C}, \{\mathbf{S}(t)\}, \{\mathbf{H}(t)\}, I) \ p(\mathbf{C}, \{\mathbf{S}(t)\}, \{\mathbf{H}(t)\}, I)}{p(\{\mathbf{X}(t)\})},
\tag{3}
$$

where $\{\cdot\}$ represents the set of a specific parameter or data for the whole ensemble of channels, trials, components and time points. A particular solution can be obtained by choosing the Maximum a Posteriori (MAP) solution, i.e., the set of parameters that maximize the posterior. It is known that the MAP solution of the above generative model gives origin to a set of very important techniques, depending on the choice of prior distributions for the model parameters. Examples constitute cluster analysis (K-means), PCA and Factor Analysis [8]. Also, with certain especial assumptions, as for example, noiseless recordings with invertible matrix $\mathbf{C}$ and spatially stationary and trial invariant sources, one can promptly derive the Bell and Sejnowski's ICA algorithm [9].

Here we consider a particular formulation of the above generative model applied to the problem of signal separation in cortical event-related local field potential (LFP) recordings. Consider the specific type of source activity representation:

$$\mathbf{S}_r(t) = \begin{pmatrix} a_{1r}s_1(t - \tau_{1r}) \\ \vdots \\ a_{Nr}s_N(t - \tau_{Nr}) \end{pmatrix}, \tag{4}$$

and re-express model Eq. (1) in component form:

$$x_{mr}(t) = \sum_{n=1}^{N} C_{mn} a_{nr} s_n(t - \tau_{nr}) + \eta_{mr}(t), \tag{5}$$

where $s_n(t)$ is the nth event-related response component with a trial-to-trial variable amplitude and latency given, respectively, by $a_{nr}(t)$ and $\tau_{nr}(t)$. The unpredictable component $\eta_{mr}(t)$, henceforth simply referred as ongoing activity, refers now to a zero mean activity including both the true ongoing activity and other uncertainties originating from measurement noise.

In the absence of any knowledge about the temporal correlations in the ongoing activity, we take $\mathbf{H}(t)$ to be independent identically distributed with a (unknown) time independent diagonal covariance matrix with diagonal entries given by σ_η^2. The principle of maximum entropy then requires that we assign a Gaussian density to the likelihood function. The posterior can thus be rewritten as

$$p(\mathbf{C}, \{a_{nr}\}, \{s_n(t)\}, \{\tau_{nr}\}, \sigma_\eta \mid \{\mathbf{X}(t)\}, I) \propto p(\mathbf{C}, \{a_{nr}\}, \{s_n(t)\}, \{\tau_{nr}\}, \sigma_\eta \mid \{\mathbf{X}(t)\}, I)$$

$$(2\pi\sigma_\eta^2)^{\frac{-MRT}{2}} \exp\left(-\frac{1}{2\sigma_\eta^2} \sum_{m=1}^{M} \sum_{r=1}^{R} \sum_{t=1}^{T} [x_{mr}(t) - \sum_{n=1}^{N} C_{mn} a_{nr} s_n(t - \tau_{nr})]^2\right) \tag{6}$$

For simplicity we assume that the matrix $\mathbf{C}$ and the source parameters a_{nr}, τ_{nr} and $s_n(t)$ are independent and uniformly distributed, with appropriate cutoffs denoting a range of physiologically reasonable values. Treating the ongoing noise variance as a nuisance parameter and assigning the Jeffreys prior $p(\sigma) = \sigma^{-1}$, we marginalize the posterior over σ_η, obtaining:

$$p(\mathbf{C}, \{a_{nr}\}, \{s_n(t)\}, \{\tau_{nr}\} \mid \{\mathbf{X}(t)\}, I) \propto \left(\sum_{m=1}^{M} \sum_{r=1}^{R} \sum_{t=1}^{T} [x_{mr}(t) - \sum_{n=1}^{N} C_{mn} a_{nr} s_n(t - \tau_{nr})]^2\right)^{\frac{-MRT}{2}} \tag{7}$$

The partial derivatives and the Hessian matrix of the posterior are easily derived, and the MAP solution can be obtained by numerical methods (e.g. conjugate gradients

or quasi-Newton trust region methods). As we are estimating simultaneously the waveforms, amplitudes and latencies, there is degeneracy in the model, which is eliminated by constraining the ensemble average of the amplitudes across trials to be unity and the ensemble mean of the latency components to be zero. Intuition about the solutions for the optimal parameters can be gained by examining the partial derivatives.

Let $Q = \sum_{m=1}^{M} \sum_{r=1}^{R} \sum_{t=1}^{T} [x_{mr}(t) - \sum_{n=1}^{N} C_{mn} a_{nr} s_n(t - \tau_{nr})]^2$. Then the logarithm of the posterior can be written as:

$$\ln P = -\frac{MRT}{2} \ln Q + const.$$ (8)

The first partial derivative with respect to $s_j(q)$ is:

$$\frac{\partial \ln P}{\partial s_j(q)} = -\frac{MRT}{2} Q^{-1} \frac{\partial Q}{\partial s_j(q)},$$ (9)

where

$$\frac{\partial \ln Q}{\partial s_j(q)} = -2 \sum_{m=1}^{M} \sum_{r=1}^{R} [WC_{mj} a_{jr} - (C_{mj} a_{jr})^2 s_j(q)],$$ (10)

and

$$W = x_{mr}(q + \tau_{jr}) - \sum_{\substack{n=1 \\ n \neq j}}^{N} C_{mn} a_{nr} s_n(q - \tau_{nr} + \tau_{jr}).$$ (11)

Solving $\frac{\partial Q}{\partial s_j(q)} = 0$ for the optimal parameters $\hat{s}_j(q)$ results in:

$$\hat{s}_j(q) = \frac{\sum_{m=1}^{M} \sum_{r=1}^{R} WC_{mj} a_{jr}}{\sum_{m=1}^{M} \sum_{r=1}^{R} (C_{mj} a_{jr})^2}.$$ (12)

The above equation does not have a closed form solution since the right hand side depends on the other estimated parameters. Some intuition about the solution can be obtained by examining the term W. Basically, it involves: the time shifting of the data according to the latencies of the estimated component, i.e. $x_{mr}(q + \tau_{jr})$; the subtraction from the data of the other scaled and time shifted components, i.e. $C_{mn} a_{nr} s_n(t - \tau_{nr} + \tau_{jr})$, $n \neq j$; and the average of the scaled residuals, where the

scaling is given by the terms $C_{mj}a_{jr}$. Similarly, for the parameters a_{jp} and C_{ij} we obtain:

$$\hat{a}_{jp} = \frac{\sum_{m=1}^{M}\sum_{t=1}^{T}UV}{\sum_{m=1}^{M}\sum_{t=1}^{T}V^2}, \tag{13}$$

where $U = x_{mp}(t) - \sum_{\substack{n=1 \\ n\neq j}}^{N}C_{mn}a_{nr}s_n(t-\tau_{np})$ and $V = C_{mj}s_j(t-\tau_{jp})$; and

$$\hat{C}_{ij} = \frac{\sum_{r=1}^{R}\sum_{t=1}^{T}ZY}{\sum_{r=1}^{R}\sum_{t=1}^{T}Y^2}, \tag{14}$$

where $Z = x_{ir}(t) - \sum_{\substack{n=1 \\ n\neq j}}^{N}C_{in}a_{nr}s_n(t-\tau_{nr})$ and $Y = a_{jr}s_j(t-\tau_{jr})$.

Notice that the formulas derived for $\hat{a}_{jp}$ and $\hat{C}_{ij}$ are related to matching filter solutions. For example, $\hat{a}_{jp}$ is given by the projection of the detector-scaled component, i.e. V, and the data after subtraction of the other scaled and time shifted components, i.e. U.

For the latency parameter, setting $\dfrac{\partial Q}{\partial \tau_{jp}} = 0$ leads to the following equation[1]:

$$\tag{15}$$

$$2\sum_{m=1}^{M}\sum_{t=1}^{T}\left([x_{mp}(t) - \sum_{\substack{n=1 \\ n\neq j}}^{N}C_{mn}a_{np}s_n(t-\tau_{np})]C_{mj}a_{jp}s'_j(t-\tau_{jp}) - a_{jp}^2 s'_j(t-\tau_{jp})s_j(t-\tau_{jp})\right)=0$$

where $s'_j(t-\tau_{jp})$ is the time derivative of $s'_j(t)$ evaluated at $(t-\tau_{jp})$. The solution for τ'_{jp} seems more difficult since τ_{jp} appears as an implicit parameter in the waveform function. An alternative and more intuitive solution can be obtained by directly examining the condition for maximization of the logarithm of the posterior, which is equivalent to minimization of the quadratic term Q. Expansion of this term results in:

$$\sum_{n=1}^{M}\sum_{r=1}^{R}\sum_{t=1}^{T}\left(x_{mr}^2(t) + [\sum_{n=1}^{N}C_{mn}a_{nr}s_n(t-\tau_{nr})]^2 - 2x_{mr}(t)\sum_{n=1}^{N}C_{mn}a_{nr}s_n(t-\tau_{nr})\right). \tag{16}$$

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[1] To deal with continuous latency values, we need a continuous time model of the component waveform, which can be implemented using a spline model, for example.

As τ_{jp} is varied only the cross-terms in $x_{mp}(t)\sum_{n=1}^{N}C_{mn}a_{np}s_n(t-\tau_{np})$ corresponding to j^{th} component change (as long as the evoked components $s_n(t)$ are zero outside a closed time interval $[t_0,t_f]$). Thus the optimal parameter $\hat{\tau}_{jp}$ is found by maximizing

$$\sum_{m=1}^{M}\sum_{t=1}^{T}\left(C_{mj}a_{jp}s_j(t-\tau_{jp})[x_{mp}(t)-\sum_{\substack{n=1\\n\neq j}}^{N}C_{mn}a_{np}s_n(t-\tau_{np})]\right), \qquad (17)$$

which is the cross-correlation between the estimated component and the data after the contributions from the other components has been subtracted off. This is then averaged over all the detectors.

APPLICATIONS

We apply the derived approach to intra-cortically recorded LFP from a monkey performing a GO-NOGO visuomotor pattern recognition task (Bressler, Coppola, & Nakamura, 1993). Because the channel recordings are very localized we believe that the mixing of distant sources is very unlikely. In this case, we reduce the problem to the estimation of event related components recorded from a single channel, i.e., $M = 1$ and $C_{mn} = 1$. Also, we employ a discrete time model for the sources waveforms, such that the time resolution of latencies is equal to the sampling interval. The striate channel was selected for the example to be presented here. The ensemble was constituted of the GO response trials for one of the visual patterns, totaling 222 trials. An example of a single trial recording is given in Figure 1.

In this data set, some simplifications were tried for the MAP solution. The choice of the number of components was based on the inspection of the Average Event-Related Potential (AERP), computed as $\text{AERP}(t) = <x_r(t)>_r$. Extrema of the AERP provided information for the choice of the number of components to be estimated, as well as information about their localization in time. For instance, the three main extrema of the AERP (Figure 2) happening around 110, 170 and 230 msec, respectively, suggest the activation of three main source signals. The local shapes of the AERP around the extrema were taken as initial guesses for the component waveforms. These simplifications proved to give good results. Evidence for the efficacy of the estimation is obtained by considering the following situation. Previous work [1] has demonstrated that the trial-to-trial variability of the amplitude and latency of the event-related responses was the main source of observed event-related increases in ensemble variance, $\sigma^2(t) = <[x_r(t)-<x_r(t)>]^2>_r$, of the channel recordings. Thus, if one is able to correctly estimate the waveforms of the event-related responses together with their corresponding single trial amplitudes and latencies, one should be able to remove the transient increase in variance by subtracting the estimated single trial event-related responses from the data. Indeed this

is verified to be the case by computing the new ensemble variance
$\sigma^2(t) =< [x_r(t) - \sum_{n=1}^{N} a_{nr} s_n(t - \tau_{nr})]^2 >_r$, as shown in Figure 2.
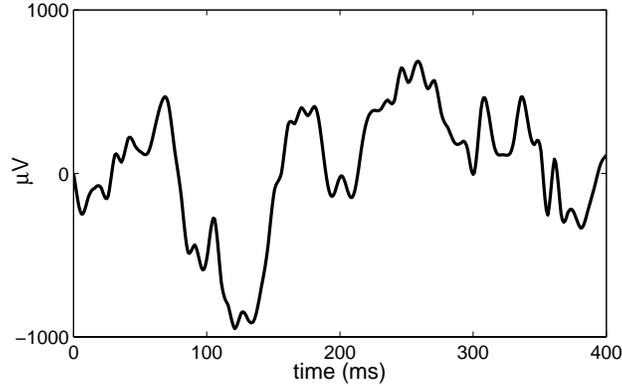

Figure 1. Example of single trial recording from the striate cortical site. Stimulus onset is at 0 msec.
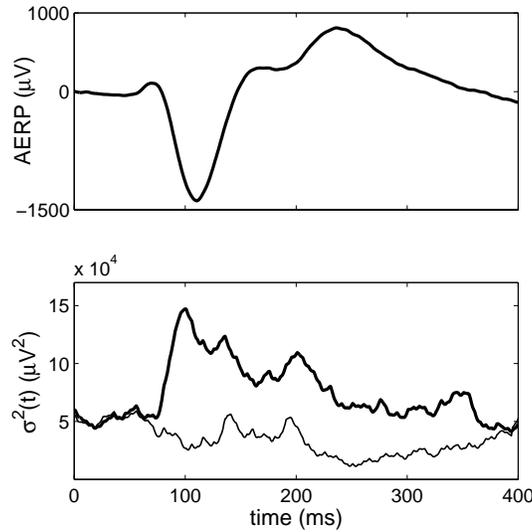
Figure 2. Separation of the single trial evoked components from the recorded time series. Top: ensemble mean (AERP) from a striate channel. Bottom: ensemble variance as a function of time derived from the original time series by subtracting the AERP (thick curve) and of the same time series ensemble but after the subtraction of the estimated single trial event-related components (see text). The onset of the event-related response happens around 70 msec (top plot) and, simultaneously, the onset of a transient increase in the ensemble variance is observed. Previous work has shown that this transient increase originates mainly from the trial-to-trial variability of the amplitude and latency of the event-related response components. Indirect evidence of the efficacy of the estimation procedure is provided by the fact that the removal of this transient increase is obtained by subtracting the estimated single trial event-related components from the time series. We also conjecture that the dips in the variance time function of the subtracted time series, around ~ 100 msec and ~ 250 msec, are related to true decreases in the ongoing activity variability.

The estimated component waveforms are shown in Figure 3. The estimated components have different variances for their single trial amplitudes and latencies. Across trial variances for the amplitudes are $\sigma_a^2 = \{0.05, 1.0, 0.14\}$ for the first, second and third components respectively (top to bottom panels in Figure 3), with latency variances $\sigma_\tau^2 = \{24.0, 123.0, 132.6 \text{ ms}^2\}$.
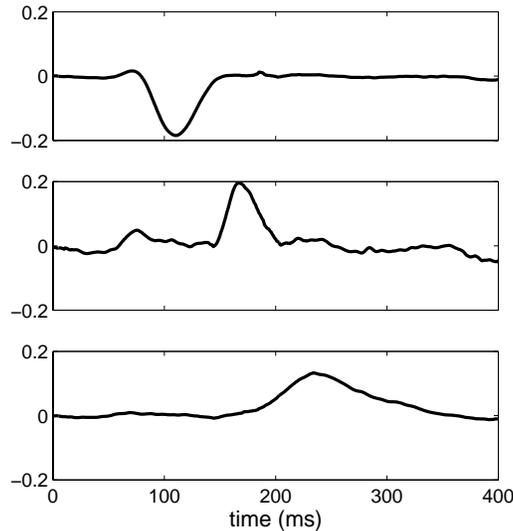
Figure 3. Estimated event-related component waveforms. Waveforms are normalized such that the integral of the square amplitude equals unity.

DISCUSSION

A principled way of estimating single trial multi-component event-related responses was presented. The approach is very promising especially from a methodological point of view. The Bayesian formulation offers a modeling based strategy in the sense that short-comings of the solutions can promptly point to the necessary reformulation of the model and prior probabilities.

From our experience, there is ample evidence in the present LFP data that the ongoing activity can be highly non-stationary during the transition from the pre- to the post-event period [10]. As a consequence, it is difficult to introduce any knowledge about the power spectrum of the ongoing activity based on power spectrum estimates of the pre-event period recordings. Careful consideration of the dependence of the derived algorithm on the signal-to-noise ratio is necessary to avoid spurious results originated from "locking" of the estimated waveforms onto the ongoing activity. The current approach seems to be especially well suited for the estimation of relatively slow and large amplitude event-related components. Fast components (e.g. evoked gamma bursts) represent a very difficult task to the current available methodologies because of the low signal-to-noise ratio and of the larger impact of trial-to-trial latency variability. Another important issue is the choice of the number of event-related components, especially in the case of single channel recordings. Although differential

variability in latency and amplitude of different components can add significantly to the separation of the components [11,12], we believe that the knowledge about the underlying physiology still is a strong requirement for the choice of the number of event-related components, and for the initial guesses of their relative position in time and ranges for their trial-to-trial variability in latencies and amplitudes. A detailed discussion of all these issues is to appear in Truccolo et al. (*in preparation*).

Initial analysis of the relationships between this algorithm and popular blind source separation algorithms is given in [11]. In addition, the utility of including information about the propagation of the signals to the detectors (forward problem), in similar Bayesian derivations, can be found in previous works [13,14,15].

ACKNOWLEDGMENTS

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