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Dynamic causal modelling of evoked responses in EEG/MEG with lead field parameterization

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Dynamical causal modeling (DCM) of evoked responses is a new approach to making inferences about connectivity changes in hierarchical networks measured with electro- and magnetoencephalography (EEG and MEG). In a previous paper, we illustrated this concept using a lead field that was specified with infinite prior precision. With this prior, the spatial expression of each source area, in the sensors, is fixed. In this paper, we show that using lead field parameters with finite precision enables the data to inform the network's spatial configuration and its expression at the sensors. This means that lead field and coupling parameters can be estimated simultaneously. Alternatively, one can also view DCM for evoked responses as a source reconstruction approach with temporal, physiologically informed constraints. We will illustrate this idea using, for each area, a 4-shell equivalent current dipole (ECD) model with three location and three orientation parameters. Using synthetic and real data, we show that this approach furnishes accurate and robust conditional estimates of coupling among sources and their orientations.

Keywords: Electroencephalography; Magnetoencephalography; Generative model; Hierarchical networks; Nonlinear dynamics

Introduction

In David et al. (2006), we described dynamic causal modeling (DCM) for event-related fields (ERFs) and potentials (ERPs). This new approach is grounded on a neuronally plausible, generative model that can be used to estimate and make inferences about category- or context-specific coupling among cortical regions. Context-specific coupling changes as a function of condition (i.e., experimental context such as “new” vs. “old” in memory paradigms) or stimulus-bound attributes (i.e., “house” vs. “face”). These changes can reconfigure neuronal interactions and produce different evoked responses for each category or context. The coupling parameters embody bottom-up, top-down, and lateral connections among remote cortical regions. Parameters are estimated with a Bayesian procedure using empirical data (ERPs/ERFs). With Bayesian model selection, one can use model evidences to compare competing models and identify the model that best explains the data.

In David et al. (2006), we constructed the spatial forward model using distributed dipole modeling on the grey matter surface. This procedure has the advantage of using the precise anatomical structure of the head. The subject's anatomy was derived from the high-resolution structural magnetic resonance imaging (sMRI). Critically, each area's lead field was predetermined so that each area had a fixed spatial expression in the sensors. Although this approach provides spatially precise expressions in the sensors, the true spatial configuration of an area may be different from our model and lead to biased conditional estimates of other [e.g., coupling] parameters. For example, the spatial model can be wrong because its parameters like location, orientation, or extent are specified inaccurately.

Alternatively, each lead field or its underlying spatial parameters can be regarded as a parameter of the model. In a Bayesian context, the above procedure is equivalent to using zero prior variance (i.e., infinite precision which expresses our belief that the specified lead field mediated the sensor data). If this belief is not supported by the data, the optimization algorithm will, at worst, fail to provide a good solution and compensate for the misspecified spatial model by biasing conditional estimates of other parameters like coupling. A way to avoid this is to decrease our strong belief in a specific lead field and use finite precision priors on the lead field parameters. There are several ways to parameterize the lead field. Although we could employ a surface-based forward model, we use equivalent current dipoles (ECDs). This has distinct advantages over other models. First, ECDs' spatial expression is analytic, i.e., the forward model computation is fast (Mosher et al., 1999). Secondly, the model is based on electrode positions only and does not need information from a structural MRI. Thirdly, many authors reported ECD location and orientation for specific ERP/ERF experiments in the peer-reviewed literature (e.g., Valeriani et al., 2001): Within our

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approach, these locations and orientations could be employed as prior expectations on ECD parameters. Finally, ECDs are a natural way to specify nodes in the probabilistic graphs that DCMs represent.

One can also view DCM for evoked responses as a source reconstruction approach with temporal, physiologically informed constraints imposed by our assumption that a hierarchical network of discrete areas generated the data. The reconstructed source activities over time fall out naturally as the system's states. Typically, most current source reconstruction approaches for EEG/MEG data are based exclusively on constraints given by the spatial forward model (Darvas et al., 2004). However, recently models have been proposed which use (spatio-) temporal constraints to invert the model (Darvas et al., 2001; Galka et al., 2004). These spatiotemporal approaches are closer to DCM but use generic constraints derived from temporal smoothness considerations and autoregressive modeling.

This paper is structured as follows. In the Theory section, we will describe briefly the temporal generative model for ERP/ERFs (for a detailed description, see David et al., 2005). This is followed by a description of the spatial forward model, its parameterization and typical prior distributions we adopt for ERP data. In the Results section, we illustrate the operational details of the procedures on two ERP datasets. In the first ERP experiment, we repeat the analysis of an auditory oddball dataset (David et al., 2006) to show that the mismatch negativity can be explained by changes in connectivity to and from the primary auditory cortex. This analysis shows that biologically meaningful results can be obtained in terms of the parameters governing the neuronal architectures generating ERPs. In the second experiment, we establish face validity in terms of the spatial parameters; we analyze sensory-evoked potentials (SEPs) elicited by unilateral median nerve stimulation and measured with EEG. With this model, we can explain the observed SEP to 200 ms. We find strong connectivity among areas during the course of the SEP. The estimated orientations of these sources conform almost exactly to classical estimates in the literature. Furthermore, we observe short transmission delays among sources within the contralateral hemisphere (~6 ms) but long delays (~50 ms) between homologous sources in both hemispheres. Finally, using synthetic data, we show that finite precision priors on lead field parameters result in models with greater evidence and more accurate and robust conditional estimates, in relation to models with infinitely precise priors.

Theory

Intuitively, the DCM scheme regards an experiment as a designed perturbation of neuronal dynamics that are promulgated and distributed throughout a system of coupled anatomical sources to produce region-specific responses. This system is modeled using a dynamic input–state–output system with multiple inputs and outputs. Responses are evoked by deterministic inputs that correspond to experimental manipulations (i.e., presentation of stimuli). Experimental factors (i.e., stimulus attributes or context) can also change the parameters or causal architecture of the system producing these responses. The state variables cover both the neuronal activities and other neurophysiological or biophysical variables needed to form the outputs. Outputs are those components of neuronal responses that can be detected by MEG/EEG sensors. In our model, these components are depolarizations of a 'neural mass' of pyramidal cells.

DCM starts with a reasonably realistic neuronal model of interacting cortical regions. This model is then supplemented with a spatial forward model of how neuronal activity is transformed into measured responses, here, MEG/EEG scalp-averaged responses. This enables the parameters of the neuronal model (i.e., effective connectivity) to be estimated from observed data. For MEG/EEG data, this spatial model is a forward model of electromagnetic measurements that accounts for volume conduction effects (Mosher et al., 1999).

Hierarchical MEG/EEG neural mass model

We have developed a hierarchical cortical model to study the influence of forward, backward, and lateral connections on ERFs/ERPs (David et al., 2004). This model is used here as a DCM and embodies directed extrinsic connections among a number of sources, each based on the Jansen and Rit (1995) model, using the connectivity rules described in Felleman and Van Essen (1991). These rules, which rest on a tri-partitioning of the cortical sheet into supra-, infra-granular layers and granular layer 4, have been derived from experimental studies of monkey visual cortex. Under these simplifying assumptions, directed connections can be classified as (i) bottom-up or forward connections that originate in agranular layers and terminate in layer 4; (ii) top-down or backward connections that connect agranular layers; (iii) lateral connections that originate in agranular layers and target all layers. These long-range or extrinsic cortico-cortical connections are excitatory and comprise the axonal processes of pyramidal cells. For simplicity, we do not consider thalamic connections but model thalamic output as a function operating on the input (see below).

The Jansen and Rit (1995) model emulates the MEG/EEG activity of a cortical source using three neuronal subpopulations. A population of excitatory pyramidal (output) cells receives inputs from inhibitory and excitatory populations of interneurons, via intrinsic connections (intrinsic connections are confined to the cortical sheet). Within this model, excitatory interneurons can be regarded as spiny stellate cells found predominantly in layer 4 and in receipt of forward connections. Excitatory pyramidal cells and inhibitory interneurons occupy agranular layers and receive backward and lateral inputs. Using these connection rules, it is straightforward to construct any hierarchical cortico-cortical network model of cortical sources.

The ensuing DCM is specified in terms of its state equations and an observer or output equation

$$\dot{x} = f(x, u, \theta)$$

$$h = g(x, \theta) \tag{1}$$

where x are the neuronal states of cortical areas, u are exogenous inputs, and h is the output of the system. θ are quantities that parameterize the state and observer equations (see also below under 'Prior assumptions'). The state equations are ordinary second-order differential equations and are derived from the behavior of the three neuronal subpopulations which operate as linear damped oscillators. The integration of the differential equations pertaining to each subpopulation can be expressed as a convolution (David and Friston, 2003). This convolution trans-