Dynamic Causal Models for Human Electrophysiology: EEG, MEG, and Local Field Potentials

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Introduction

Dynamic causal models (DCMs) for EEG are a suite of neuroimaging analysis tools designed to provide estimates of the neurobiological mechanisms that generate electroencephalographic (EEG), magnetoencephalographic (MEG), and local field potential (LFP) recordings. The principal idea is that generative models of interconnected neural populations can be used as a substrate against which competing hypotheses about how empirical data are generated can be compared and investigated. Effective connectivity within and between brain regions, and their synaptic and cellular constituents, can be assessed using these DCMs.

Connectivity estimates using DCMs for EEG have been used to inform the mechanisms underlying a variety of neurological disorders: Parkinson's disease, epilepsy, the so-called vegetative state, and schizophrenia. Application of this methodology rests on a plausible generative model of neuronal dynamics from connected brain regions or "nodes" that can then be optimized, given empirical observations. These models describe, through sets of differential equations, mechanisms that are not directly observable, such as the strength of synaptic connections along extrinsic corticocortical pathways. Bayesian inference schemes are then used to map from recorded responses (in EEG/MEG/LFP data) back to the underlying cause. Hence, the estimates of intrinsic (within-region) and extrinsic (region-to-region) connections are deemed "effective" or model-based assessments.

This DCM procedure (Friston et al., 2003) of proposing a generative architecture and then fitting the model to data can be applied to a range of electrophysiological data features. These features include event-related potentials (ERPs), spectral densities, cross-spectral densities (CSDs), induced (time-frequency) responses (IRs), and phase coupling (PHA). DCMs for ERPs and DCMs for CSDs utilize an underlying neurobiological structure in the form of neural mass models to describe active brain regions. In contrast, DCMs for IR and DCMs for PHA use phenomenological models that recapitulate, with abstracted dynamic parameters, the interregional effects.

This chapter first outlines the types of neural mass models used in DCMs for ERP/CSDs. The second section outlines the forward-mapping that allows these models to generate scalp-level and sensor-level EEG and MEG data or invasive LFPs. It then describes how Bayesian inversion procedures are utilized to test competing hypotheses about the generative processes underlying empirical observations. The third section demonstrates how these models and procedures can be applied in the context of either ERP or CSD data. The fourth section outlines the phenomenological class of DCMs.

Neural Mass Models

Since Hodgkin and Huxley developed their biophysical model of ionic currents and action potential generation in the squid axon (Hodgkin and Huxley, 1952), scientists have considered how similar membrane potential mechanisms can be described at the level of neuronal populations. This pursuit of describing "neuronal activity in concert" has led to the development of neural mass models and their application in DCMs for EEG. Neural mass models use principles of statistical physics to mathematically describe how a population's dynamic characteristics emerge from single-cell dynamics. In particular, mean field reductions rely on the representation of probability densities to describe salient population features, such as the average current flow induced by particular ions. Neural mass models reduce the interaction of these types of neuronal states to interactions among the means, or modes, of their densities. This simplification reduces a potentially large parameter space (describing interactions among many orders of probability densities) to a simpler, one-dimensional characterization. DCMs for ERPs and CSDs use neural mass models that are assembled in this way (with options to include second-order interactions). From this dynamic and statistical starting point, the neural mass models that represent dynamics within a brain region are constructed based on known properties of neuroanatomy and neurophysiology.

Three important neurobiological properties are represented in DCMs' neural mass models: laminar-specific cellular subtypes within a region, laminar-specific extrinsic connections between regions, and glutamate and GABAergic receptor dynamics. Based on histological data, it is known that cortex has a layered structure (6-layered neocortex, and the less layered allocortex) and that different cell types populate these layers. The neural mass models used in DCMs capture this anatomical structure by specifying (currently 3 or 4) subpopulations of cell types, which represent occupancy in granular, supragranular, and infragranular layers. These are interconnected through plausible intrinsic connectivity structures and

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include representations of pyramidal cells, inhibitory interneurons, and spiny stellate cells. It is worth noting that these architectures are designed to be rearranged for particular investigations (e.g., in agranular primary motor cortex, by disconnecting certain layers/populations).

Whereas synapses formed by local gray matter axons are represented within a region, as "intrinsic connections," network-based brain dynamics (where multiple regions are coactivated) are generated through interregional (myelinated) connections. These extrinsic connections have the same mathematical form as intrinsic connections but are exclusively glutamatergic (excitatory) and impinge on cell populations in particular layers. For example, a thalamocortical or forward-corticocortical connection will excite granular layer IV stellate cells. In contrast, other backward, modulatory extrinsic connections will excite pyramidal cells and inhibitory interneurons outside of layer IV.

Neural mass models also allow one to infer the synaptic connections that are mediated by different neurotransmitters and receptor types. We explicitly model GABAergic and glutamatergic processes. This third component of biophysical plausibility is provided by describing the dynamic mathematical effects (and differences) of, for example, glutamate arriving at an AMPA receptor (fast excitatory) versus an NMDA receptor (slow, excitatory, and gated). Describing these different channel-membrane responses generates more realistic brain dynamics and provides for fine-grained inference on neurophysiological contributions to EEG recordings. From this perspective, DCM represents a "mathematical microscope" and can assess local synaptic physiology.

Together, these dynamic descriptions, comprising coupled nonlinear differential equations, form a mathematical state space. These states describe the dynamic elements of a neural mass, such as fluctuations in membrane depolarization. Thus, the states of the neuronal model evolve over time according to the value of a set of neuronal parameters. These parameters include the strength of intrinsic connections within each region, the strength of extrinsic connections, and parameters controlling synaptic adaptation (namely, synaptic time constants) (Fig. 1). A forward-observation model is then required to transform these depolarizations into the observed EEG or MEG output.

Forward Models, Model Comparison, and Hypothesis Testing

Forward models in these DCMs comprise a linear mixture of depolarizations, which are then transformed via a parameterized lead field into scalp-level or sensor-level data (Fig. 2). This mapping can accommodate different lead fields that depend on the imaging modality (e.g., invasive LFPs or noninvasive EEG and MEG). Since dendrites of interneurons are roughly symmetrically positioned around the cell body, whereas dendrites of pyramidal cells align tangentially to the cortical surface, the net dipolar output is modeled primarily as the output of these pyramidal subpopulations.This fully parameterized generative model can then recapitulate electrophysiological data.

An inversion routine can then be applied to a particular model given empirical EEG/MEG or LFP recordings. The inversion routine is central to the utility of these neural masses and is a fundament of DCM methodology. So far, we have outlined a generative model of electrophysiological data. DCM is designed to map backward from real measured responses to the underlying neuronal generators (Fig. 2). This inverse mapping or model inversion provides an estimation of the model parameters that are conditional on a given set of data. In DCM, this procedure is prescribed by a variational scheme, which optimizes the conditional density of parameters under a fixed-form (Laplace) assumption. This optimization entails using the expectation maximization method to maximize a free-energy bound on the log evidence. The inversion scheme requires both a form for the observation noise (to produce a likelihood function of the modeled parameters) and prior probabilities based on model parameters. These priors are specified in terms of a prior mean and variance (the prior variance determines how far the parameter can move from its prior mean during inversion). Parameters that have been investigated empirically, such as the time constants of different receptors, are ascribed relatively small prior variance. In contrast, flat (higher variance) priors are used for effective connectivity measures to ensure that their posterior estimates are determined primarily by the data.

Once optimized, the inversion routine returns both an approximation to the log-model evidence, known as the "free energy," and a set of posterior or conditional model parameters. The first of these is used to assess competing hypotheses about the structure of a model, independent of their parameters.

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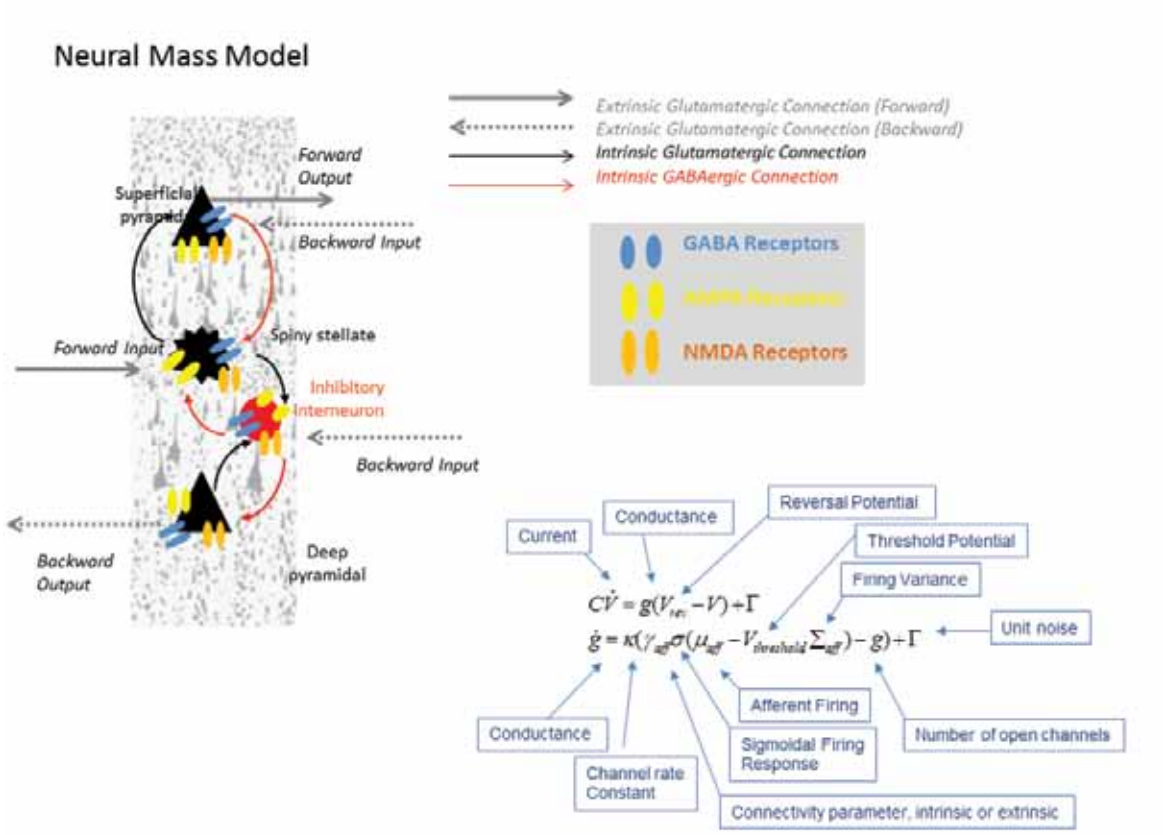


Figure 1. A neural mass model used in DCM for EEG to represent an active brain region. This 4-subpopulation model uses Morris Lecar–type differential equations to describe the time evolution of current and conductance states at different cell types. Cells can possess AMPA, $GABA_A$, and NMDA receptors with ion-channel time constants ($1/\kappa$). Layers and regions are connected with strengths parameterized by γ. V_{rev} are reversal potentials for ions through these channels, and $V_{threshold}$ is the threshold potential. The neuronal architecture comprises interconnected neuronal subpopulations, including inhibitory interneurons and pyramidal cells (supragranular and infragranular layers) and spiny stellate cells (granular layer IV). Pyramidal cells send signals to regions outside of the neural mass. These deliver forward signals (from superficial layer) and backward signals (from deep layers). The spiny stellates, in turn, receive extrinsic forward connections, while the inhibitory cells and superficial pyramidal cells receive extrinsic backward connections.

This is used to identify the most plausible architecture subtending observed responses. Individual parameter posteriors can then be investigated to assess relative contributions to network dynamics or to compare across populations (e.g., using an identical model but fitted to data from healthy controls and a pathological cohort).

DCM for ERP and DCM for Cross-spectral Densities

Both DCM for ERPs (Kiebelet al., 2006) and DCM for cross-spectral densities (Moran et al., 2009) utilize the neural mass models outlined above to describe activity within a region in a cortical network. For ERPs, exogenous inputs, timed according to experimental stimuli, serve as the input to the deterministic state equations of the neural masses.This input is represented as a thalamic input volley, with the form of a delayed (by a few tens of milliseconds) narrow Gaussian impulse function. This can be entered into plausible cortical nodes from whose extrinsic efferent dynamics will propagate throughout connected nodes in the modeled network. The inversion procedure will then determine how parameters are weighted (including biophysical and forward parameters) to best fit the empirical scalp, sensor, or electrode ERPs.

Cross-spectral densities are modeled in the same way, with the exception of specific exogenous inputs. Instead, a mixture of parameterized white and pink noise components provides the input to the neural mass equations. This system of differential equations is linearized around a fixed point, to

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describe the response of a node in the frequency domain. This linearization allows one to compute the transfer function mapping from the endogenous (neuronal) fluctuations to the scalp, sensor, or electrode data. This transformation assumes that the system operates in a stationary regime, with fluctuations around a stable fixed point. The DCM for CSDs also returns coherence, covariance, and phase lags at the level of neuronal sources and the scalp or sensor level.

DCM for Induced Responses and DCM for Phase Coupling

DCM for IRs (Chen et al., 2008) and DCM for PHA (Penny et al., 2009) are based on identical principles to those outlined above. These comprise the description of a generative model and the description of priors on model parameters, and Bayesian model inversion. These DCMs are distinct from DCM for ERPs and DCM for CSDs in two ways. The first difference is that they do not explicitly describe a neurobiological architecture in the generative model; instead, they prescribe an abstracted mathematical form that is flexible enough to accommodate highly nonlinear generative mechanisms. The second difference is that data are modeled directly in source space, so they require preliminary source localization and time-series extraction.

Frequency-to-frequency interactions are a popular topic in human electrophysiological research. For example, it arises when assessing whether alpha spectra suppress other spectral features locally or at different regions of the brain. This type of hypothesis can be addressed formally using a DCM for IR, in which a full time-frequency interaction can be deconstructed using a model of connected brain nodes. DCMs for IR show spectral dynamics in terms of a mixture of frequency modes obtained from source space with singular value decomposition. The differential equations employed in this routine represent the time evolution of energy interactions across all frequencies, where linear or nonlinear source interactions can prescribe within- and between-frequency empirical effects.

To understand how regions of the brain may become phase-locked or drift out of phase, DCM for phase coupling optimizes a generative model comprising weakly coupled oscillators. These sets of differential equations describe how the phase of one region (modeled as an oscillator) influences the change of phase of another. These time-evolving phase couplings are described in terms of a Fourier series to any order. Given empirical data series from EEG/MEG or LFP, a Hilbert transform of source-space time-series data (band-passed to a frequency of interest) reveals how networks interact in that spectral domain. This is an increasingly studied principle of cortical organization, one prominent example being the investigation of hippocampal-based network interactions in theta and gamma bands.

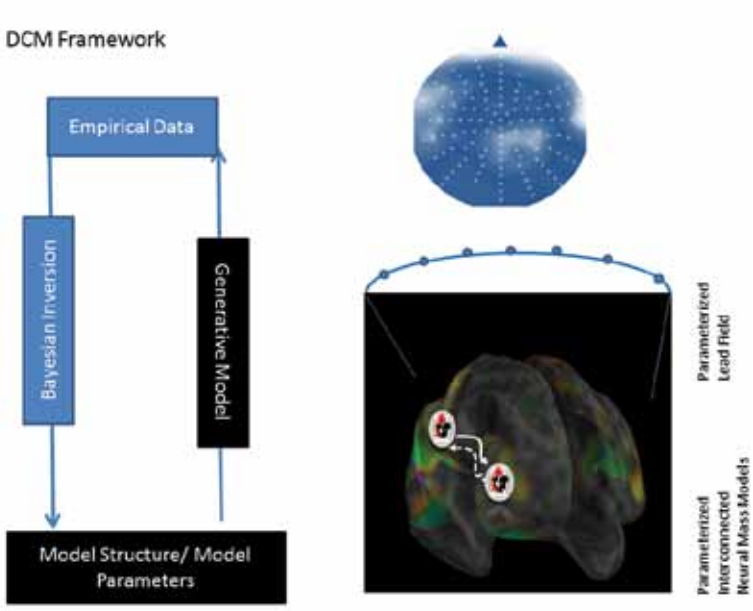


Figure 2. Elements of the DCM framework. Generative models (physiological for DCM for ERP/CSD and phenomenological for DCM for IR/PHA) produce a repertoire of empirical recordings. A particular data set acquired in humans (or animals) can then be fitted to these models using a variational Bayesian inversion, to reveal the density of model parameters conditional on those particular data.

Conclusion

The DCM approach to analyzing electrophysiological data takes advantage of the large and rich body of literature surrounding neural physiology and neuronal codes. It is an informed analysis method that allows us to formally address how our EEG/MEG/LFP data could have been generated by the brain.

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Acknowledgments

All the DCM components described in this chapter can be implemented using MATLAB routines available as part of the academic freeware package SPM (Statistical Parametric Mapping) from http://www.fil.ion.ucl.ac.uk/spm/software/spm12/. This software was written by members and honorary members of the FIL Methods Group at University College London.

References

Chen C, Kiebel S, Friston K (2008) Dynamic causal modelling of induced responses. Neuroimage 41:1293–1312.

Friston K, Harrison L, Penny W (2003) Dynamic causal modelling. Neuroimage 19:1273–1302.

Hodgkin AL, Huxley AF (1952) Propagation of electrical signals along giant nerve fibres. Proc Roy Soc London B Biol Sci 140:177–183.

Kiebel S, David O, Friston K (2006) Dynamic causal modelling of evoked responses in EEG/MEG with lead field parameterization. Neuroimage 30:1273–1284.

Moran RJ, Stephan KE, Seidenbecher T, Pape HC, Dolan RJ, Friston KJ (2009) Dynamic causal models of steady-state responses. Neuroimage 44:796–811.

Penny W, Litvak V, Fuentemilla L, Duzel E, Friston K (2009) Dynamic causal models for phase coupling. J Neurosci Methods 183:19–30.

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