Dynamic causal modelling for functional near-infrared spectroscopy

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ABSTRACT

Functional near-infrared spectroscopy (fNIRS) is an emerging technique for measuring changes in cerebral hemoglobin concentration via optical absorption changes. Although there is great interest in using fNIRS to study brain connectivity, current methods are unable to infer the directionality of neuronal connections. In this paper, we apply Dynamic Causal Modelling (DCM) to fNIRS data. Specifically, we present a generative model of how observed fNIRS data are caused by interactions among hidden neuronal states. Inversion of this generative model, using an established Bayesian framework (variational Laplace), then enables inference about changes in directed connectivity at the neuronal level. Using experimental data acquired during motor imagery and motor execution tasks, we show that directed (i.e., effective) connectivity from the supplementary motor area to the primary motor cortex is negatively modulated by motor imagery, and this suppressive influence causes reduced activity in the primary motor cortex during motor imagery. These results are consistent with findings of previous functional magnetic resonance imaging (fMRI) studies, suggesting that the proposed method enables one to infer directed interactions in the brain mediated by neuronal dynamics from measurements of optical density changes.

Introduction

Functional near-infrared spectroscopy (fNIRS) is a noninvasive method for monitoring hemodynamic changes in the brain (Jobsis, 1977; Villringer et al., 1993; Hoshi, 2007; Ferrari and Quaresima, 2012; Scholkmann et al., 2014). fNIRS works by shining near-infrared light in the spectral range between 650 and 950 nm from fiber-optic emitters placed on the scalp. Because the absorption of chromophores in tissue is relatively low within this spectral range, near-infrared light can propagate several centimeters through tissue. Changes in light photon density reaching the detectors correspond to changes in the optical properties of the tissue, reflecting changes in oxygenated and deoxygenated hemoglobin (HbO and HbR). The loss of light levels can then be used to calculate the changes in hemoglobin concentrations in underlying brain regions (Delpy et al., 1988). As neuronal processes require extra delivery of oxygen, this provides a marker of underlying neuronal activity.

fNIRS has many advantages that make it highly useful in cognitive and clinical neuroscience studies. Compared to other imaging modalities, such as functional magnetic resonance imaging (fMRI), fNIRS is mobile and compact, and the data acquisition is quiet. Furthermore, as compared to fMRI, fNIRS provides a more direct measure of changes in HbO, HbR, and total hemoglobin (HbT), and the time series

are sampled at high temporal resolution. It has therefore proved to be an effective tool for studying physiological mechanisms in the healthy brain and in cerebrovascular disease (Highton et al., 2010; Wolf et al., 2012; Obrig, 2014). It is also finding unique applications in clinical areas, including bedside monitoring of infants, and studies of auditory and language systems (Lloyd-Fox et al., 2010; Eggebrecht et al., 2014).

There is currently a surge of interest in characterizing brain connectivity using fNIRS. Recent fNIRS studies have assessed the coupling between brain regions in terms of a measure of functional connectivity (Homae et al., 2010; Sasai et al., 2011) and effective connectivity (Im et al., 2010; Yuan, 2013). Specifically, Homae et al. (2010) explored developmental changes of brain networks in early infancy, using functional connectivity defined as temporal correlation between pairs of fNIRS measurements. Sasai et al. (2011) investigated the frequency-specific characteristics of functional connectivity based on spontaneous oscillation in the low-frequency range in HbO and HbR signals. However, functional connectivity does not provide any insight into the directed causal interactions among brain regions underlying cognitive processing. To address this shortcoming, Im et al. (2010) and Yuan (2013) applied Granger causality analysis to fNIRS data, which provides estimation of the directed functional connectivity between brain regions. The analyses of both functional connectivity and effective (via Granger causality) connectivity are usually performed at the level of measured hemodynamic signals, such as HbO, HbR, and HbT responses (White et al., 2009; Im et al., 2010; Homae et al., 2010; Sasai et al., 2011; Yuan, 2013). However, connectivity estimates at the level of

hemodynamic measurements are not direct measures of connectivity changes at the neuronal level, because the hemodynamic response to neuronal activation depends on the balance of the changes in cerebral blood flow and oxidative metabolism, and also on the changes in cerebral blood volume (Fox and Raichle, 1986; Buxton, 2012). This complex interplay between processes can cause functional connectivity to differ with the type of hemoglobin changes (e.g., HbO and HbR), while underlying interactions between neuronal populations do not vary (Lu et al., 2010). This highlights the importance of estimating causal influences among neuronal populations, referring to a biophysical model of how neuronal activity is transformed into fNIRS measurements.

Several fNIRS studies have used biophysical models relating blood inflow to HbO and HbR changes, or neuronal activity to HbO and HbR changes during brain activation. Specifically, Cui et al. (2010) generated synthetic HbO and HbR responses induced by blood inflow using the Balloon model in a study that investigated the effect of head motion on the fNIRS signal. Dubeau et al. (2012) recovered neuronal inputs from hemodynamic measurements by deconvolving the extended Balloon model (Friston et al., 2000), and showed significant correlation between estimated neural inputs and measurements of local field potentials and multiunit activity. However, to our knowledge, there have been no studies focusing on model-based estimation of neuronal interaction among multiple regions from the optical density changes using fNIRS.

In this paper, we apply Dynamic Causal Modelling (DCM) to fNIRS data, to estimate effective connectivity at the neuronal level from the measurement of optical density changes. Effective connectivity is defined as the (model-based) influence of one (neuronal) system on another. DCM is a framework for fitting differential equation or state space models of neuronal activity to brain imaging data using Bayesian inference (Friston et al., 2003). There is now a library of DCMs and variants differ according to their level of biological realism and the data features which they explain. The DCM approach can be applied to fMRI (Friston et al., 2003, 2014), electroencephalographic (EEG), and Magnetoencephalographic (MEG) data (Moran et al., 2007; Penny et al., 2009; Daunizeau et al., 2009b).

This paper extends the DCM approach to fNIRS. Because the variational Bayesian estimation algorithm is the same as that used for DCMs for other imaging modalities, this paper focuses on development of a generative model of how observed fNIRS data are caused by the interactions among hidden neuronal states. In particular, we extend the neurodynamic and hemodynamic models used for DCM-fMRI analysis (Friston et al., 2003) to additionally include the total hemoglobin state (Cui et al., 2010), and optics model that describes the detected optical density changes as a linear combination of light absorption changes due to HbO and HbR (Delpy et al., 1988; Arridge, 1999). The model is further augmented by including spatially extended hemodynamic sources (Shmuel et al., 2007) and pial vein contamination effects (Gagnon et al., 2012). In short, the proposed method allows fNIRS to be used for making inference about changes in directed connectivity at the neuronal level.

This paper is structured as follows: In the Methods section we first describe a generative model of fNIRS data, and then describe the model optimization procedure for estimating the connectivity parameters from this data. In the Results section we provide an illustrative analysis using fNIRS data acquired during the motor imagery and motor execution tasks. In the Discussion section we discuss future extensions of the proposed method.

Methods

The generative model for fNIRS data comprises three components: (i) neurodynamics describing neural activity in terms of inter-regional interactions and its experimentally induced modulation (Friston et al., 2003), (ii) hemodynamics linking neural activity with the changes in total hemoglobin, and deoxy-hemoglobin based on the Balloon model

(Friston et al., 2000; Buxton et al., 2004; Cui et al., 2010), and (iii) optics relating the hemodynamic sources to optical density changes (Delpy et al., 1988; Arridge, 1999). A schematic of the generative model is summarized in Fig. 1. The following subsections describe each of these components. These are followed by sections on computing the optical sensitivity matrix and confounding effects that underlie the optical model, and a section on model estimation.
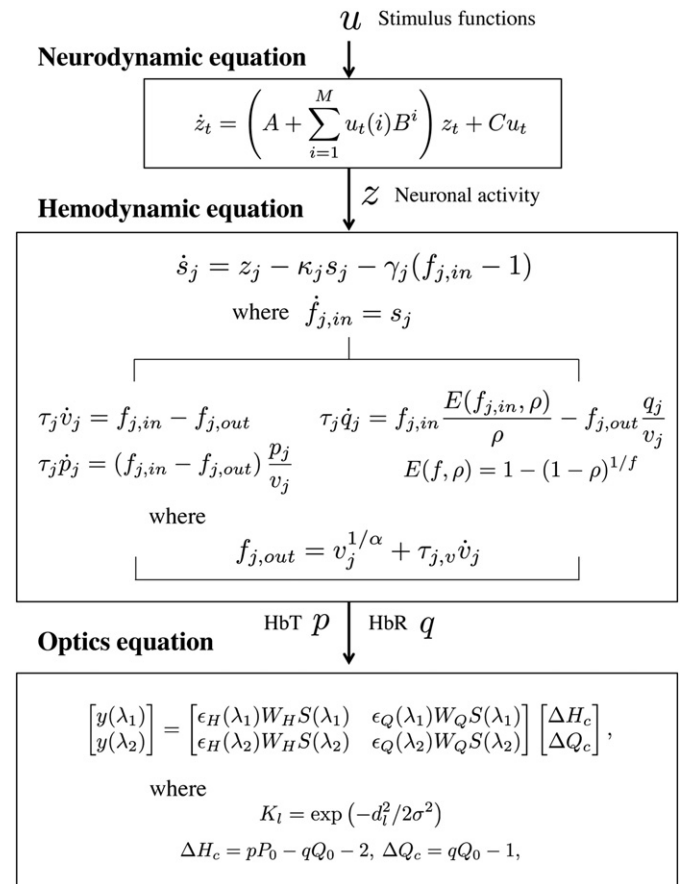
Neurodynamics

The neurodynamics are described by the following multivariate differential equation

$$
\begin{aligned}
\dot{z}_t &= \Im_t z_t + C u_t \\
\Im_t &= A + \sum_{i=1}^{M} u_t(i) B^i,
\end{aligned}
\tag{1}
$$

where t indexes continuous time and the dot notation denotes a time derivative. The entries in z correspond to neuronal activity in $j = 1,\ldots,L$ cortical source regions, and $u(i)$ is the ith of M experimental inputs. An $[L \times L]$ matrix, $\Im$, denotes the effective connectivity between

Fig. 1. Schematic of the generative model of fNIRS data. The neurodynamic equation uses linear differential equations and a single state variable per region describing neural activity. Coupling parameter matrices A, B^i, and C represent the average connectivity among regions, the modulation of effective connectivity by experimental manipulation, and the influence of inputs on regions, respectively. The hemodynamic equation uses the Balloon model and its extensions to describe how neural activity causes a change in a flow inducing signal which in turn causes an increase in blood flow with concomitant changes in relative blood volume and deoxy-hemoglobin. The optics equation uses a sensitivity matrix, S, describing how changes in hemodynamic sources cause changes in optical measurements. Potential pial vein contamination of the fNIRS measurements is corrected using matrices W_H and W_Q. Spatially distributed hemodynamic source is generated using Gaussian spatial smoothing kernel K.