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Learning effective brain connectivity with dynamic Bayesian networks

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We propose to use dynamic Bayesian networks (DBN) to learn the structure of effective brain connectivity from functional MRI data in an exploratory manner. In our previous work, we used Bayesian networks (BN) to learn the functional structure of the brain (Zheng, X., Rajapakse, J.C., 2006. Learning functional structure from fMR images. NeuroImage 31 (4), 1601–1613). However, BN provides a single snapshot of effective connectivity of the entire experiment and therefore is unable to accurately capture the temporal characteristics of connectivity. Dynamic Bayesian networks (DBN) use a Markov chain to model fMRI time-series and thereby determine temporal relationships of interactions among brain regions. Experiments on synthetic fMRI data demonstrate that the performance of DBN is comparable to Granger causality mapping (GCM) in determining the structure of linearly connected networks. Dynamic Bayesian networks render more accurate and informative brain connectivity than earlier methods as connectivity is described in complete statistical sense and temporal characteristics of time-series are explicitly taken into account. The functional structures inferred on two real fMRI datasets are consistent with the previous literature and more accurate than those discovered by BN. Furthermore, we study the effects of hemodynamic noise, scanner noise, inter-scan interval, and the variability of hemodynamic parameters on the derived connectivity.

Keywords: Bayesian networks; Causal effects; Dynamic Bayesian networks; Effective connectivity; Functional MRI; Hemodynamic response function; Markov chains; Markov chain Monte Carlo methods

Introduction

The brain areas involved in various cognitive tasks can now be identified quite accurately and reliably through functional Magnetic Resonance Imaging (fMRI) experiments (Friston et al., 1995; Rajapakse and Piyaratna, 2001; Wang and Rajapakse, 2006). However, functional specialization of the brain does not provide a holistic view of brain function and does not describe how different brain regions communicate and interact with one another. Considering the multiple processes taking place at different brain regions and interacting with one another in executing a specific task, extracting brain connectivity from fMRI data facilitates our understanding of brain function (Buchel and Friston, 1997). Recently, there has been an increasing interest in functional integration studies to infer brain connectivity, especially for high-order brain functions. In fMRI, the activity of brain is measured by time-series of signals depending on blood-oxygenation-level-dependent (BOLD) contrast. Given multivariate voxel-based time-series, several techniques have been proposed to use fMRI to characterize effective connectivity of the brain (Friston, 2003; Goebel et al., 2003; McIntosh and Gonzalez-Lima, 1994; Rajapakse et al., 2006; Zheng and Rajapakse, 2006).

Structural equation modelling (SEM) decomposes interregional covariances of fMRI time-series to find functional interactions among brain regions (Bullmore et al., 2000; McIntosh and Gonzalez-Lima, 1994; Mechelli et al., 2002). The covariance structure models the interactions of underlying neural systems only in second-order statistical sense and therefore does not render effective connectivity or the "cause and effect" relationships among brain regions. Dynamic causal modelling (DCM) characterizes the dynamics of interactions among states (of brain regions) with bilinear approximations of intrinsic coupling (among neuronal states) and the influence of external inputs. An extended balloon model is used in DCM to model hemodynamic response, which enables inference of interactions at the neuronal level (Friston, 2003). Both SEM and DCM are confirmatory in the sense that the analysis of brain connectivity requires a priori model to begin with and is inapplicable for higher-order functions unique to human such as language or cognition (Bullmore et al., 2000).

Granger causality mapping (GCM) extends the vector auto-regressive (VAR) technique to capture interactions among brain regions, assuming a causal and dynamic system of linear interactions, driven by stochastic innovations (Goebel et al., 2003; Harrison et al., 2003). A graphical approach linking the notions

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of graphical models and Granger causality has been applied to describe dynamic dependencies in neural systems (Eichler, 2005). Nevertheless, a multi-step procedure fitting autoregressive models at each step is required to identify networks and therefore limits its applicability for large networks.

Recently, two techniques based on Bayesian networks (BN) (Zheng and Rajapakse, 2006) and independent component analysis (ICA) (Rajapakse et al., 2006) were proposed to derive effective connectivity of the brain from functional MRI data in an exploratory manner. Bayesian networks do not provide an explicit mechanism to represent temporal dependencies among multiple processes at brain regions and instead give one snapshot of brain connectivity, taking into consideration the whole experiment. Therefore, neural systems derived with BN do not fully describe causal relationships among brain regions. Moreover, because of equivalent properties of BN, directions of some edges are indeterminate and could be bi-directional (Chickering, 1995).

In this paper, we propose dynamic Bayesian networks (DBN) to derive the effective connectivity of the brain by modelling fMRI time-series in a Markov chain. DBN, an extension of BN, admits a class of nonlinear continuous time interactions and provides a direct mechanism to model temporal relationships among brain regions. Functional MRI time-series of activated voxels are modelled with first-order stationary Markov chains. The inter-scan interval (ISI) of fMRI is used as the interval between two consecutive instances of the Markov chain. The connectivity between two time instances (or scans) is modelled in a transition network of two layers of brain regions (or nodes). In a stationarity setting, the connectivity of the transition network renders the effective connectivity of the brain.

Dynamic Bayesian networks may assume a known or unknown structure, and full or partial observability of states at the nodes. The states of activated brain regions are fully observed as intensity variations of fMRI time-series. Beginning with an unknown connectivity structure, we find the best structure fitting fMRI data in an exploratory manner. A greedy search or an expectation maximization (EM) provide only a local search of the structure of DBN. Starting with a partly connected structure, we use a Markov chain Monte Carlo (MCMC) method to derive the structure of the connectivity among brain regions from fMRI data. The MCMC method attempts to find a globally optimal solution by sampling a collection of highly probable structures from the equilibrium distribution of the Markov chain (Husmeier, 2003b).

We describe DBN and structure learning algorithm in the Method section. In experiments, synthetic fMRI data is used to illustrate the robustness of our approach and compare with GCM. The method is further demonstrated by exploring functional structures from real fMRI data obtained in two experiments: a silent word reading task and a counting Stroop task. A comparison between structures derived from BN and DBN is also provided.

Method

This section introduces DBN for modelling effective brain connectivity from functional MRI data. Then, a MCMC algorithm for structure learning is described.

Neural system modelling with DBN

When modelling the brain connectivity, the nodes in the Bayesian network are associated with activated brain regions while the edges characterize the interactions among regions. Consider a neural system of n brain regions activated by a sensory or cognitive task and let the regions be indexed in a set $I=\{i : i=1, 2, \ldots n\}$. The activation of a brain region is measured by the average fMRI time-series over the region. Let x_i be the activation measuring the hemodynamic response of region i.

Bayesian networks (BN) describe the probability distribution over the activation of brain regions, where the graphical structure provides an easy way to specify conditional interdependencies for a compact parameterization of the distribution. The BN is defined by a structure s and a joint distribution over the set of time-series $x=\{x_i : i\in I\}$. The BN structure is a directed acyclic graph (DAG) characterized by the absence of directed cycles. If a_i denote the set of activations of the parents of the region i, a DAG offers a simple and unique way to decompose the likelihood of activation in terms of conditional probabilities:

$$P(x|\theta) = \prod_{i\in I} P(x_i|a_i, \theta_i) \tag{1}$$

where $\theta=\{\theta_i : i\in I\}$ represents the parameters of the conditional probabilities.

Dynamic Bayesian network extends BN model to incorporate temporal characteristics of the time-series x. Let us explicitly represent temporal processes of brain regions and $x(t)=\{x_i(t): i\in I\}$ representing the activations of n brain regions at time t. The instances $t=1, 2, \ldots T$ correspond to the times when brain scans are taken and T denotes the total number of scans. In order to model the temporal dynamics of brain processes, we need to model a probability distribution over the set of random variables $\bigcup_{t=1}^{T} x(t)$ which is rather complex and practically prohibitive.

To avoid an explosion of the model complexity, we assume the temporal changes of activations of brain regions are stationary and first-order Markovian:

$$P(x(t+1)|x(t), \ldots x(1)) = P(x(t+1)|x(t)) \tag{2}$$

where the transition probabilities $P(x(t+1)|x(t))$ are independent of t. The transition network represents the connectivity structure between two consecutive brain scans, which renders the joint distribution of all possible trajectories of temporal processes. The structure of the DBN is obtained by unrolling the transition network over consecutive scans for all $t=1, 2, \ldots T$. The first-order stationary assumption provides a tractable causal model that explicitly takes into account the temporal dependencies of brain processes. Higher-order and non-stationary Markov models allow more complex temporal processes and connectivity patterns. However, such complex models pose obvious challenges in estimating structures and parameters.

Unlike BN, DBN is capable of modelling recurrent networks while still satisfying the acyclic constraint of the transition network. This is an important advantage of modelling neural system with DBN as there exist cyclic functional networks in the brain, such as cortico-subcortical loops. Inter-scan connections to same brain region itself are considered as default prior connections and their parameters are allowed to adapt. We do not allow intra-scan connections because the effect on a brain region takes place with a time delay after its cause. Although instantaneous interactions may exist due to low temporal sampling and hemodynamic modulation of fMRI, the determination of such interactions remains as a limitation of neural systems modelling with functional MRI.