Journal of Neuroscience Methods 285 (2017) 33–44

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

The dynamic programming high-order Dynamic Bayesian Networks learning for identifying effective connectivity in human brain from fMRI

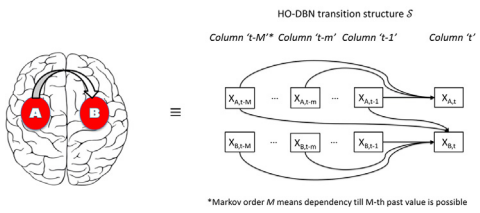
Shilpa Dang[a,*], Santanu Chaudhury[a,b], Brejesh Lall[a], Prasun Kumar Roy[c]

[a] Electrical Engineering Department, Indian Institute of Technology Delhi, New Delhi 110016, India
[b] Director, Central Electronics Engineering Research Institute, Pilani 333031, India
[c] National Brain Research Centre, Gurgaon, Haryana 122051 India

HIGHLIGHTS

- A novel approach proposing use of High-order Dynamic Bayesian Networks (HO-DBNs) for identifying Effective connectivity (EC) is presented.
- A fundamental problem faced in the structure learning of HO-DBN is low accuracy and high computational burden.
- The framework uses dynamic programming principle while exploiting properties of scoring function.
- This guarantees globally optimal solution for the structure learning problem.
- This overcomes the disadvantage of low accuracy and high computational burden of existing algorithms used for EC.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 23 January 2017
Received in revised form 5 May 2017
Accepted 5 May 2017
Available online 8 May 2017

Keywords:
Bayesian-Dirichlet score
High-order dynamic bayesian network
Dynamic programming
Effective connectivity
Functional magnetic resonance imaging
Structure learning

ABSTRACT

Background: Determination of effective connectivity (EC) among brain regions using fMRI is helpful in understanding the underlying neural mechanisms. Dynamic Bayesian Networks (DBNs) are an appropriate class of probabilistic graphical temporal-models that have been used in past to model EC from fMRI, specifically order-one.
New-method: High-order DBNs (HO-DBNs) have still not been explored for fMRI data. A fundamental problem faced in the structure-learning of HO-DBN is high computational-burden and low accuracy by the existing heuristic search techniques used for EC detection from fMRI. In this paper, we propose using dynamic programming (DP) principle along with integration of properties of scoring-function in a way to reduce search space for structure-learning of HO-DBNs and finally, for identifying EC from fMRI which has not been done yet to the best of our knowledge. The proposed exact search-&-score learning approach HO-DBN-DP is an extension of the technique which was originally devised for learning a BN's structure from static data (Singh and Moore, 2005).
Results: The effectiveness in structure-learning is shown on synthetic fMRI dataset. The algorithm reaches globally-optimal solution in appreciably reduced time-complexity than the static counterpart due to integration of properties. The proof of optimality is provided.

* Corresponding author at: Block–II, Room no. 405, Multimedia Lab, Electrical Engineering Department, Indian Institute of Technology Delhi, New Delhi, 110016, India.
E-mail address: shilpadrd@gmail.com (S. Dang).

http://dx.doi.org/10.1016/j.jneumeth.2017.05.009

Comparison: The results demonstrate that HO-DBN-DP is comparably more accurate and faster than currently used structure-learning algorithms used for identifying EC from fMRI. The real data EC from HO-DBN-DP shows consistency with previous literature than the classical Granger Causality method.
Conclusion: Hence, the DP algorithm can be employed for reliable EC estimates from experimental fMRI data.

1. Introduction

Functional brain imaging techniques have made substantial contributions towards improving our understanding of how and where our brain processes information, and how the regions interact (functional integration (Friston, 2002)) to support behaviour and cognition. Such interactions are directional in nature to have causal influences between neuronal activations, termed as *effective connectivity* (EC) (Friston, 1994). This could provide a basis for differentiating brain functioning under various conditions such as normal, diseased, and/or aging. Determination of effective connectivity has been a topic of persistent research in neuroscience community, both for task-based (Deshpande et al., 2009; Friston et al., 2003; McIntosh and Gozales-Lima, 1994; Roebroeck et al., 2005) and resting-state fMRI (Deshpande et al., 2011; Liao et al., 2010; Sridharan et al., 2008).

A traditional and most-widely employed measure of effective connectivity is Granger Causality (Granger, 1969). It is based on the idea of "temporal precedence" of one time series over another. Traditional GC analysis is a model-based approach where model assumptions make GC vulnerable to violations for fMRI data, as shown in our previous work (Dang et al., 2015). Confirmatory model-driven approaches, such as structural equation modelling (SEM) (McIntosh and Gozales-Lima, 1994) and classical dynamic causal modelling (DCM) (Friston et al., 2003), require prior candidate structures with assumptions about existence and direction of influence between any two regions and identifying the most likely candidate. However, advances in more efficient ways of searching for larger search spaces (Friston et al., 2011) have made DCM more exploratory as compared to the classical one proposed initially, while it still being deterministic in nature. In contrast, probabilistic graphical techniques such as Bayesian Networks (BNs) for fMRI EC (Ramsey et al., 2010) are exploratory in nature. However, BNs have their own limitations. They do not consider the delayed or time-lagged interactions between time-series and assume acyclicity over graphs and thus, cannot model cyclic interactions such as self-regulations and feedbacks present in a system as complex as the brain. Unlike BNs, Dynamic Bayesian Networks (DBNs) can model delayed and cyclic interactions by unrolling a BN over time (Friedman et al., 1998), and order-one DBNs have been proposed (Rajapakse and Zhou, 2007) and used (Burge et al., 2009; Wu et al., 2014a) for causal modelling of fMRI time series. In DBNs, a transition network S between any two consecutive time-points characterizes the EC. This is first-order assumption allowing to model causal dependencies among brain regions. With the advent of fast sampling rates such as multiband EPI (Feinberg et al., 2010), *first-order* DBNs (FO-DBNs), however, cannot model interactions which are longer than one time step. Thus, posing a necessity for using *high-order* DBNs (HO-DBNs) (Xing and Wu, 2006) for EC detection from fMRI, which has not been done yet. Moreover, Gaussian FO-DBN (Wu et al., 2014a) and discrete FO-DBN (Rajapakse and Zhou, 2007) have been used in past for EC detection from fMRI. Gaussian DBNs model EC with continuous data but are limited to linear relationships by considering DBN as a group of linear regression equations assuming Gaussian hypothesis; which risks missing non-linear relationships present between fMRI signals (Lahaye et al., 2003). In contrast, discrete DBNs require discretization of data and can detect non-linear relationships as well by assuming multinomial distribution over network parameters. Thus, we propose employing discrete HO-DBNs for identifying EC from fMRI.

The problem of identification of connectivity between the brain regions using fMRI time series is structure learning of a network from data where brain regions are denoted by nodes of the network, and connectivity between them is denoted by the directed edges between nodes of the network. Friedman et al. (1998) were the first to look at structure learning of DBNs. Thereafter, the literature for DBN has been developed widely and finds many interesting applications such as for causal modelling of temporal processes from biomedical to economics (Husmeier, 2003; Rajapakse and Zhou, 2007; Sandoval and Hernandez, 2014). A complete state-of-the-art of Bayesian learning approaches can be found in (Daly et al., 2011).

Most of the structure learning algorithms proposed for BN can be adapted for the "dynamic" counterpart. A fundamental problem faced in the structure learning of DBN is high computational burden by the existing search techniques. The algorithm REVEAL for Dynamic Bayesian Networks (Murphy and Mian, 1999) for inference of gene regulatory pathways is an exhaustive search strategy. Various algorithms for structure learning of DBN have been proposed, majorly in the field of genetics using sampling based and hybrid approaches, (Husmeier, 2003; Li and Ngom, 2013; Rajapakse and Chaturvedi, 2010). Applications in the domain of fMRI connectivity have been limited though. Heuristic local learning approaches, such as greedy search (Burge et al., 2009), simulated annealing (Eldawlatly et al., 2010) have been applied to reduce the time complexity of the search but they only provide locally optimum solutions (low accuracy).

Sampling based strategy such as Markov Chain Monte Carlo (MCMC) methods (Gibbs Sampling, Metropolis-Hastings (MH) algorithm) have been extensively used for EC detection from fMRI using complete data frameworks (Friedman et al., 1998), discrete FO-DBN (Rajapakse and Zhou, 2007) and Gaussian FO-DBN (Wu et al., 2014a); and our recent incomplete or missing data framework for fMRI (Dang et al., 2017, 2016). MCMC methods deliver good accuracy in structure learning, however, at the cost of high computational burden by sampling a collection of highly probable structures from the Markov chain which has converged to a stationary distribution.

In this paper, we propose search-and-score based exact learning using Dynamic Programming (DP) principle for searching over the parent trees of the nodes of the DBN while evaluating a possible candidate parent set using a score function. DP is a step-wise search method for optimization problems where solutions can be considered as an outcome of sequential decisions. The most attractive property of this approach is that during the search for a solution it avoids full enumeration by pruning early partial solutions that cannot possibly lead to optimal solution. The optimal solution can be reached in polynomial number of steps by exploring only the optimal solutions at each step. A full enumeration will be done only in the worst case. DP delivers global optimal solution in comparably much less computational burden. Because of its power there are algorithms developed on this principle for structure learning of different types of networks, training and inference (El-Sebakhy et al.,