LARGE-SCALE KERNELIZED GRANGER CAUSALITY TO INFERENCE TOPOLOGY OF DIRECTED GRAPHS WITH APPLICATIONS TO BRAIN NETWORKS

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ABSTRACT

Graph topology inference of network processes with co-evolving and interacting time-series is crucial for network studies. Vector autoregressive models (VAR) are popular approaches for topology inference of directed graphs; however, in large networks with short time-series, topology estimation becomes ill-posed. The present paper proposes a novel nonlinearity-preserving topology inference method for directed networks with co-evolving nodal processes that solves the ill-posedness problem. The proposed method, large-scale kernelized Granger causality (lsKGC), uses kernel functions to transform data into a low-dimensional feature space and solves the autoregressive problem in the feature space, then finds the pre-images in the input space to infer the topology. Extensive simulations on synthetic datasets with nonlinear and linear dependencies and known ground-truth demonstrate significant improvement in the Area Under the receiver operating characteristic Curve (AUC) of the receiver operating characteristic for network recovery compared to existing methods. Furthermore, tests on real datasets from a functional magnetic resonance imaging (fMRI) study demonstrate 96.3 percent accuracy in diagnosis tasks of schizophrenia patients, which is the highest in the literature with only brain time-series information.

Index Terms— topology inference, causal inference, vector autoregressive models, nonlinear interactions, graphical models

1. INTRODUCTION

Graph topology inference is crucial in network studies, especially emphasized by recent surges in graph signal processing. Understanding the underlying interactions of network processes shed light on knowledge discovery in multiple domains, e.g., chemistry and medicine, genealogy, climatology, and neuroscience, to name a few. Representing the influences beneath a complex network has diverse applications. Nevertheless, to infer the graph topology, the edges are not directly observable, restricting the nodal observations to the sole source of data acquisition. For instance, in the human brain, time-series data may be recorded from distinct regions of interest (ROI) using resting-state functional magnetic resonance imaging (rs-fMRI); however, the interactions among the recorded time-series are not measurable.

Vector autoregressive models (VAR) or Granger causality [1] are widely adopted to infer directional dependencies among the nodal processes. Various methods are proposed to infer the directional topology of graphs; see [2, 3]. Lasso-Granger learns the causal dependencies based on the variable selection using the Lasso algorithm [4]. Authors in [5] propose a linear VAR to infer the topology in the original space by translating the VAR model in the linear principal space [5]. Authors in [6] estimate a nonlinear function to assess the latent interactions of the time-series, to unravel the nonlinear dependencies, and in [7], the authors propose a conditional nonlinear independence hypothesis test in the Granger causality framework using Peter and Clark momentary conditional independence hypothesis tests (PCMCI) [7]. Contemporary methods investigate linear time-lagged dependencies between the time-series vulnerable to confounding connections, see e.g. [3, 2]; however, various methods have been proposed to infer the topology of networks with nonlinear interactions, see e.g. [6, 7, 2, 3, 8, 9, 10].

The present paper extends the merits of the prior works, large-scale Granger causality [5], and puts forth a more general, nonlinear method, the lsKGC, for topology inference of directional time-series graphs. Unlike previous nonlinear efforts [6, 9, 8], the present paper leverages the kernel principal component analysis as an encompassing framework to preserve the nonlinearity in low-dimensional space by projecting data into their principal components and utilizes pre-images of the feature space representations to infer the topology in the

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input space. The present work estimates the model parameters in the low-dimensional feature space while estimates the topology of the graph in the linear framework of the input space.

2. PRELIMINARIES

Consider an $N$-node directed graph, whose topology is unknown, but time-series $\{y_{it}\}_{i=1}^T$ are observed per node $i$, over $T$ time intervals. Linear VAR model states that each $y_{jt}$ is a linear combination of the time-lagged versions of the measurements $\{y_{i(t-\ell)}\}_{\ell=1}^N$; see e.g., [11, 12, 14].

$$y_{jt} = \sum_{\ell=1}^N \sum_{i=1}^N a^\ell_{ij} y_{j(t-\ell)} + e_{jt}, \quad (1)$$

with $a^\ell_{ij}$ as model coefficients encoding the causal structure of the network over a $\ell$ time points. Based on the error covariance matrix $\Sigma$ of the full model and the error covariance matrix $\Sigma_{ij}^\ell$ of the model without $\{y_{it}\}_{i=1}^T$, the degree of information flow from node $i$ to node $j$ can be quantified by $\delta_{ij} = \ln(\Sigma_{ij}^\ell / \Sigma_{jj})$, where $\Sigma_{ij}^\ell$ and $\Sigma_{jj}$ denote the diagonal entries of $\Sigma_{ij}^\ell$ and $\Sigma$ associated to $\{y_{jt}\}_{t=1}^T$, respectively. Within this framework, a Granger Causality Index (GCI) [5] can be defined in terms of linear predictability [1], that is, a causal link exists between nodes $i$ and $j$ only if there exist $\delta_{ij} \neq 0$. Consequently, the topology of the graph directly will be obtained by adjacency matrix $[\Delta]_{ij} = \delta_{ij}$.

Let $A^\ell \in \mathbb{R}^{N \times N}$ denote the “time-lagged” VAR model parameters matrix, with $[A^\ell]_{ij} = a^\ell_{ij}$. Given the multivariate time-series $\{y_t\}_{t=1}^T$, where $y_t := [y_{1t}, \ldots, y_{Nt}]^\top$, the goal is to estimate the model parameter matrices $\{A^\ell\}_{\ell=1}^L$, and consequently unveil the hidden network topology. Although generally known, one can readily deduce $L$ via standard model order selection tools, e.g., the Bayesian information criterion (BIC) [12], or Akaike’s Information Criterion (AIC) [13].

In a well-defined system with known topology, several approaches have been proposed to learn the model parameters; see e.g., [11, 12, 14]. However, the model’s complexity increases by increasing $N$ for the same $T$ in the system since redundant variables can lead to ill-posed problems [15, 5].

Accordingly, a method that estimates multivariable interactions while reducing redundancy would be desired. In [5], a VAR model is proposed to learn linear causal influences for large-scale systems by reducing redundancy through projecting data to principal space. Albeit conceptually simple and computationally tractable, the linear VAR of [5] is incapable of capturing nonlinear dependencies inherent to complex networks, e.g., the human brain. The present paper proposes a nonlinear VAR model by reducing the redundancies in [1] using a nonlinear transformation of data to the feature space.

**Problem Statement.** Given nodal measurements $\{y_{it}\}_{i=1}^T$ in [1], the goal is to estimate $\{\hat{y}_{jt}\}_{j=1}^T$ in a low-dimensional feature space, encompassing nonlinear dependencies between time-series, to bypass estimation of parameter matrix $\{A^\ell\}_{\ell=1}^L$ in the input space, subsequently transform the predicted $\{\hat{y}_{jt}\}_{j=1}^T$ to the input space to obtain the unknown adjacency matrix $\Delta$ of causal relationships.

3. LARGE-SCALE KERNELIZED GRANGER CAUSALITY

Time-series $\{y_{jt}\}_{j=1}^T$ for $j = 1, \ldots, N$ are series with linear or nonlinear causal dependencies between $N$ nodes. The aim is to transfer the equation (1) to the space of the principal components with lower dimensions, encompassing nonlinear dependencies. Defining $P < \infty$ as the dimensions of the feature space, $\{\phi_p(.)\}_{p=1}^P$ as the basis of feature space with (possibly) known kernel function, where $\{\phi_p(.)\}_{p=1}^P$ spans a finite subspace of the Hilbert space related to finite input space, and $\phi(y_{jt}) := [\phi_1(y_{1t}), \ldots, \phi_P(y_{jT})]^\top$. A projection of input data $y_{jt}$ onto the $p$-th principal component would be desired, such that the major proportion of data variation is explained by a few principal components; see [16].

Defining $\Phi_j := [\phi(y_{jt}), \ldots, \phi(y_{jT})]^\top$, the covariance matrix of the data in $\mathcal{H}$ will be $C = \frac{1}{N} \sum_{j=1}^N \Phi_j \Phi_j^\top$. To find $\{\phi_p(.)\}_{p=1}^P$ as the basis of feature space, eigenvalues $\lambda_p \geq 0 : \{\lambda_1 \geq \ldots \geq \lambda_P\}$ would be desired. Consequently, in the feature space $\exists v_p \in \mathcal{H} \setminus \{0\}$ such that $\lambda_p v_p = C v_p$, and $< v_p, v_{p'} >= 1$ to ensure orthonormality of eigenvectors $\{v_p\}_{p=1}^P$ in the feature space. Consequently, exists $\exists \{\beta_j\}_{j=1}^N : \beta_j \in \mathbb{R}^P$, that eigenvectors can be written as a linear combination for features $v_p = \sum_{j=1}^N \beta_j \Phi_j$. Acknowledging that $\phi(.)$ is probably a known function, e.g. radial basis function (RBF), obtaining the eigenvectors is equivalent to estimating the coefficients $\beta_j$. Thus, any function $\phi(.)$ (equivalently $\{\phi_p(.)\}_{p=1}^P$) can be written as a linear combination of $\{v_p\}_{p=1}^P$ to project data onto eigenvectors with the highest explained variance in the feature space. Using the transformation of $\{\phi_p(.)\}_{p=1}^P$, the feature space representation of the autoregressive equation (1) can be written as [17]

$$\eta_{pt} = \sum_{\ell=1}^L \sum_{j=1}^N a^\ell_{jp} \phi_p(y_{j(t-\ell)}) + \varepsilon_{pt}, \quad (3)$$

where $\{\eta_{pt}\}_{t=1}^T$ for $p = 1, \ldots, P$ is the transformed time-series into the feature space, and $\varepsilon_{pt}$ is the error at time slot $t$ in the feature space. One can use models such as linear regression, LS with $l_1$-regularization (the lasso), $l_2$-regularization (ridge regression), or elastic-net regression to minimize error $\{\eta_{pt}\}_{p=1}^P$ and obtain the unknown coefficients
\{\alpha_{jp}\}; \text{ see } [18]. \text{ Once the } \{\eta_{pt}\}_{p=1}^{P} \text{ in (3) are obtained, the predictions } \{\hat{\eta}_{pt}\}_{p=1}^{P} \text{ will be transformed into the input space to infer the graph topology. To transform } \{\hat{\eta}_{pt}\}_{p=1}^{P} \text{ into the input space, the pre-image } \gamma(\hat{\eta}_{pt}) : \mathcal{H} \to \mathcal{Y}; \quad \hat{\eta}_{pt} \mapsto \gamma(\hat{\eta}_{pt}), \text{ would require the estimation } [16]

\[
\hat{y}_{jt} = \arg \min_{y_{jt} \in \mathcal{Y}} \| y_{jt} - \gamma(\phi(\hat{y}_{jt})) \|^2,
\]

which is a nonlinear optimization, lacking the computational efficiency, applicability to pre-images with discrete variables, and a guaranteed optimum solution in general; \text{ see } [16] [19]. Interestingly, both the inputs \(y_{jt}\) and \(\eta_{pt}\) will be inferred in the input space by the corresponding mappings are present for \(\phi(y_{jt}) : \mathcal{Y} \to \mathcal{H}\). Defining \(\hat{\gamma} := [\hat{\gamma}_1, \ldots, \hat{\gamma}_N]\), \(\gamma := [\gamma_1, \ldots, \gamma_N]\), \(\gamma(\hat{\eta}_{pt}) := [\gamma_1(\hat{\eta}_{pt}), \ldots, \gamma_N(\hat{\eta}_{pt})]\), \(\Gamma := [\Gamma_1, \ldots, \Gamma_p]\), and \(\Phi := [\Phi_1, \ldots, \Phi_N]\), and using the learning problem \(\text{ [19] [20]}\)

\[
\mathcal{L} = \min_{\Gamma, \Phi} \| \mathcal{Y} - \Gamma \Phi \|^2,
\]

one can obtain the coefficients \(\gamma_{jp} := [\Gamma]_{jp}\), and consequently the predictions \(\hat{y}_{jt} = \sum_{p=1}^{P} \gamma_{jp} \eta_{pt}\) will be obtained; \text{ see } [19] [20]. Simultaneously, the adjacency matrix \(\Delta\) will be inferred in the input space by the corresponding MSE of the error covariance. The complete algorithm is shown in Algorithm. 1 and the notations \(Y^- := [y_1, \ldots, y_{j-1}, y_{j+1}, \ldots, y_N]\), \(\hat{\eta}_p := [\eta_{pt}, \ldots, \eta_{pt}]\), \(H := [\eta_1, \ldots, \eta_P]\) are defined for the sake of simplicity.

Algorithm 1 Large-scale kernelized Granger causality

Require: \(L, P, Y, \phi(.)\)

Ensure: \(\Delta = [\Delta_i]_{i=1}^{N}\)

\[
\Gamma = \text{ arg } \min_{\Gamma} \| \mathcal{Y} - \Gamma \Phi \|^2
\]

for \(i = 1\) to \(N\) do

\[
H \leftarrow \mathcal{Y}
\]

for \(\ell = 1\) to \(L\) do \(\hat{Y} \leftarrow H\)

end for

end for

for \(j = 1\) to \(N\) do

\[
H_j \leftarrow \mathcal{Y}
\]

for \(\ell = 1\) to \(L\) do \(\hat{Y}_j \leftarrow H_j\)

end for

end for

\[
[\Delta_i] := \left\{ \left[ \frac{\text{cov}(Y_j, \hat{Y}_j)}{\text{diag}(\text{cov}(Y_j, Y_j))} \right] \right\}_{j=1}^{N}
\]

4. NUMERICAL TESTS

Simulations to evaluate and compare the proposed technique’s performance include synthetic network datasets with known ground-truth and real fMRI datasets. The ensuing explains the description and results of tests on the datasets.

\footnote{The codes are available at https://github.com/ali-vosoughi/lsKGC}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig1.png}
\caption{An instant graph of the underlying ground-truth network for the synthesized model with nonlinearities for \(N = 6\). The color-bar represents the coupling’s strength for the edges, and the number on the edges represents the lag.}
\end{figure}
This paper put forth a novel method for the topology inference in large-scale networks and uncovers nonlinear interactions between the nodal processes. By leveraging the feature space, the proposed method preserves the nonlinearities inherent to complex networks by transforming data into their principal components in the feature space. Further, the pre-images were used to infer the directional network topology in the original space by adopting the learning from mappings between the input and feature spaces. Tests on the synthetic datasets with nonlinear and linear processes and known underlying relationships demonstrate significant improvement in the topology inference of networks. Moreover, tests on the real data from an fMRI study demonstrated 96.3 percent accuracy in the diagnosis of patients with schizophrenia (COBRE), while the same classification procedure using cross-correlation for the same dataset is 72.8%. The literature of classification accuracies on the COBRE dataset is listed in Table 1.

**5. CONCLUSIONS**

### Table 1: COBRE and ACPI datasets accuracies

| Dataset          | Paper Accuracy (%) | Table 1: COBRE and ACPI datasets accuracies |
|------------------|--------------------|--------------------------------------------|
| COBRE dataset, Schizophrenia |                   |                                            |
| Paper Accuracy (%) |                   |                                            |
| [28]             | 86.2               |                                            |
| [29]             | 61-72              |                                            |
| [30]             | 82.42              |                                            |
| [31]             | 69                 |                                            |
| [32]             | 93.1               |                                            |
| [33]             | 70.5               |                                            |
| [34]             | 71.8               | This paper **96.28 ± 1.41**               |

33 healthy and 29 diseased subjects, totaling 62 individuals. Functional connectivity measurements were generated from the COBRE dataset [22], a publicly available sample which we accessed through the Nilearn Python library [23]. The images were already preprocessed using the NIAK resting-state pipeline [24][22]. The number of regions of interest has been selected to be 122 with functional brain parcellations [25].

**Real dataset results.** In the present study, brain connections served as features for classification and are estimated by the proposed large-scale kernelized method. Feature selection is performed on each training data set with k-fold cross-validation using Kendall’s Tau rank correlation coefficient [26] and 10% – 90% of test-to-train split ratio. For the 100 iteration cross-validation scheme for classification, the data set is divided into two groups: a training data set (90%) and a test data set (10%) in a way that the percentage of samples for each class was preserved. A Support Vector Machine (SVM) [27] is used for classification between healthy subjects and schizophrenia patients. All procedures are implemented in Python 3.8. We show 96.3% (P=17, L=4) accuracy in the diagnosis of patients with schizophrenia (COBRE), while the same classification procedure using cross-correlation for the same dataset is 72.8%. The literature of classification accuracies on the COBRE dataset is listed in Table 1.
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