Sparse Network Inference using the k-Support Norm

Position Paper

Aman Gupta*
Language Technologies Institute
School of Computer Science
Carnegie Mellon University
Pittsburgh
amang@cs.cmu.edu

Haohan Wang*
Language Technologies Institute
School of Computer Science
Carnegie Mellon University
Pittsburgh
haohanw@cs.cmu.edu

Rama Kumar Pasumarthi*
Language Technologies Institute
School of Computer Science
Carnegie Mellon University
Pittsburgh
rpasumar@cs.cmu.edu

ABSTRACT

Network inference is an important problem in a variety of domains. Understanding gene interaction networks is an important problem in Biology. DNA microarrays provide a cheap and efficient mechanism of measuring mRNA expression levels of thousands of genes in one go. The computational problem then reduces to taking gene mRNA expression time series data and using inference/reverse-engineering techniques to learn a gene interaction network. In the context of social network analysis, network inference refers to the problem of inferring underlying network of influence, given time series data of when users performed certain actions (e.g., post, retweet, share). These networks capture the dynamics of influence and information diffusion.

In this position paper, we discuss various strategies to learn sparse networks with the help of the k-support norm, which corresponds to the tightest convex relaxation of sparsity combined with an l2 penalty. This norm encourages sparsity and also controls the influence of individual parameters. We also discuss strategies to incorporate various constraints on learned networks.

Keywords

network inference, sparsity, K-support norm

1. INTRODUCTION

Inference of complex networks from data is a vital problem in a variety of domains like computational biology, social network analysis, operations research etc. With an explosion in the availability of data, the need of the hour is algorithms adept at modeling complex networks.

In the domain of biology, an important goal is understanding the regulation of various cellular processes and their responses to stimuli. Genes and proteins are at the core of all cellular processes. Genes produce messenger RNA during a process known as transcription, and mRNA in turn is processed into proteins. Proteins synthesized by genes may act as transcription factors for the synthesis of mRNA from other genes, or may be used in other important cellular activities. A set of genes can either promote or suppress the production of mRNA from a target gene. These interactions can be visualized as complex gene regulatory networks (GRNs). Inference of these networks then becomes crucial to understanding the underpinnings of cellular processes. This insight can be used to analyze altered gene expression, a result of conditions like cancer, for potential drug targets.

In social networks, information diffusion is often modelled as a stochastic process that occurs over an underlying network of influence. The diffusion of a single piece of *contagion* (a news snippet/meme/hashtag) occurs in a cascade like fashion. What is usually observed is the time series data of when users performed certain actions (also referred to as when a user is *infected*), for each contagion, but the underlying network is unobserved, or partially observed, where we have information such as who follows whom. Inferring this underlying network of influence, a directed graph where the pairwise edges indicate strength of influence, is essential to understand the dynamics of information diffusion, and to solve problems such as influence maximization, design of viral marketing campaigns, or to stem the flow of malicious information.

Networks in both of the domains described above, although complex, involve a small number of interacting entities and can be represented using sparse models [5]. The lasso [12] technique has proved very popular in learning parsimonious models. However, the lasso, despite acting as a good surrogate for cardinality, is not very good at controlling the magnitude of parameters. This can be especially problematic in cases where the magnitude of parameters is of importance. In this position paper, we discuss approaches to learn sparse networks with the help of the k-support norm. The k-support norm is the tightest convex relaxation of sparsity combined with l2-regularization. Thus, k-support ensures that . Since the k-support norm is not differentiable, we discuss fast proximal gradient descent algorithms for optimization. We also discuss various approaches for incorporating constraints on network learning during optimization.

2. BACKGROUND AND RELATED WORK

In computational biology, the low connectivity property [11] of biological networks and sparsity of gene regulatory networks have

*these authors contribute equally

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introduced challenges in employing sparsity prior knowledge. This sparsity prior knowledge has been used as explicit constraints on the connectivity of network components [4]. Other works adopt L1-norm [12] regularization to build sparse networks. For example, [9] uses sparse regression with an L1-penalty induced for selecting the non-zero partial correlations and discover an undirected network encoding direct relations between genes. [3] infers gene regulatory network with the L1 norm method based on the autoregressive model. [14, 13] propose a linear program that fits the data and satisfies the sparse structure with weighted L1 relaxation as the cost function, with additional linear constraints. Recently, Zavlanos et al. [14, 13] have shown that the inference performance is significantly improved by explicitly imposing the stability condition on the network.

In social network inference, survival theory has been used to model information propagation, where the instantaneous rate of infection of a user (*hazard rate*) depends on the infection times of previously infected users, as explanatory variables or covariates. The hazard rate has been modeled using parametric distributions such as Weibull and power law, or using non-parametric methods. The objective function for network inference has been shown to be convex in the space of pairwise influence parameters. Since these networks are in general sparse, Daneshmand *et al* [2] have used an L1 norm penalty to promote sparsity in the solution.

There is ample evidence for the importance of learning parsimonious models for both gene and social networks. In the following subsections, we discuss two popular models for inferring sparse gene and social networks.

2.1 Modeling gene networks as Linear Dynamical Systems

Gene regulatory networks of a set of p genes can be modeled as $p-$dimensional non-linear dynamical systems:

$$\frac{d\mathbf{x}}{dt} = f(\mathbf{x}, u) \tag{1}$$

Where **x** represents gene expression concentrations for genes and **u** represents perturbations applied to each gene. Both **x** and **u** are p-dimensional vectors. This is an effective model because the expression of a gene depends on the current gene expression of itself and its neighbours. **u** represents a systematic perturbation applied to a gene expression system at equilibrium.

Non-linear dynamical systems reach equilibrium when the rate of change of gene expression for all genes becomes zero, i.e. all genes attain steady-state values of mRNA concentrations.

Under small-perturbations on a steady-state system, these non-linear systems can be approximated to a first-order model [4]. The change in concentrations can be approximated using the following linear model:

$$\frac{d\mathbf{x'}}{dt} = \mathbf{Ax + u} \tag{2}$$

x' is the change in concentration of mRNA for all genes from previous equilibrium. The matrix **A** is $n \times n$ dimensional and encodes pairwise relationships between genes. Specifically, $\mathbf{A}_{ji}$ represents the influence of gene j on gene i. The vector **u** represents perturbations applied to all genes. The problem is then reduced to learning a sparse and consistent matrix A.

At steady-state, the system reaches equilibrium and the rate of change of gene expression is almost zero. Moreover, multiple perturbation experiments can be carried out to help make better inference. If there are m such experiments, then the steady-state matrix form of equation 2 is:

$$0 \approx \mathbf{AX + U} \tag{3}$$

X and **U** are $p \times m$ matrices. This model was introduced by [4]. They used the assumption that $m < n$, and imposed restrictions on the number of connections each gene can have to solve for an under-determined system by using multiple linear regressions.

A simple objective function for learning sparse **A** is:

$$\begin{aligned} \min t||\mathbf{A}||_1 + (1-t)\epsilon \\ \text{subject to} \\ ||\mathbf{AX} + \mathbf{U}||_1 <= \epsilon, \epsilon > 0 \end{aligned} \tag{4}$$

where t is a factor that controls the relative importance of sparsity and ϵ is the desired error threshold. This objective can be minimized using interior point methods.

2.2 Objective Formulation for Social Network Inference

We shall use the objective formulation in [2] for network inference. Let there be N nodes in the network. Let **A** be the matrix of influence parameters for each pair of nodes. Let $\mathbf{A_i} = \{\mathbf{A_{ji}}, 1 \leq j \leq N, j \neq i\}$.

In [2], it is shown that the objective function decomposes into a convex formulation per node, in the following form:

$$\begin{aligned} \min l_i(\mathbf{A_i}) + \lambda||\mathbf{A_i}||_1, \\ s.t. \\ \mathbf{A_{ji}} \geq 0, 1 \leq j \leq N, j \neq i \end{aligned}$$

where $l_i(\mathbf{A_i})$ corresponds to the negative log-likelihood of observing the infection times corresponding to node i.

3. METHODS

3.1 K - support norm

Networks in biology - gene, protein or of other kinds - are generally sparse in nature [5]. It is well-understood that only a handful of genes affect the expression of a particular gene. So is the case for social networks, where one person can affect only a handful of people directly. Learning parsimonious models thus becomes a necessity. A strategy to learn these networks is to use a sparsity regularizer such as the lasso [12]. In this work, we propose the use of the k-support norm[1] to ensure sparsity of the learned network.

The k-support norm has been previously used for classification [1]. Its superiority to Lasso has been shown in different settings [10],[7]. To the best of our knowledge, this is the first time it is being used for gene regulatory network inference.

3.1.1 Definition

Consider a general vector w, which could be a regression vector. The k-support norm is the gauge function associated to the set $conv\{w | \|w\|_0 \leq k, \|w\|_2 \leq 1\}$. It can be computed as

$$\|w\|_k^{sp} = \left(\sum_{i=1}^{k-r-1} (|w|_i^{\downarrow})^2 + \frac{1}{r+1} \Big(\sum_{i=k-r}^{d} |w|_i^{\downarrow} \Big)^2 \right)^{\frac{1}{2}}$$

with $|w|_i^{\downarrow}$ the i^{th} largest element of vector w and r is the unique

integer in the set {1,...,k-1} such that

$$|w|^{\downarrow}_{k-r-1} > \frac{1}{r+1}\sum_{i=k-r}^{d}|w|^{\downarrow}_i \geq |w|^{\downarrow}_{k-r}$$

3.1.2 Relationship to lasso and ridge penalty

We observe that in the $k = 1$ case, the k-support norm is actually the same as the l_1 norm. When $k = d$ and $w \in R^d$, the k-support norm is equivalent to the l_2 norm. While the Lasso leads to sparse solutions, it doesn't capture group structure and randomly selects one variable among a group correlated variables. By tuning the parameter k, we can choose the cardinality of the solution and therefore choose to keep groups of correlated variables. Hence, less sparse, but with more predictive power solutions can be chosen.

As observed by the authors of [10], for an objective $\min_w \lambda\|w\|^{sp}_k + f(w, X, y)$, when $k = d$, this minimization problem is equivalent to $\min_w \lambda\|w\|_2 + f(w, X, y)$. This problem differs from the traditional l_2 regularized one. However, by noting that this objective is the Lagrangian of the constrained minimization problem that minimizes f subject to $\|w\|_2 \leq B$ and that this constraint is equivalent to $\|w\|_2 \leq B^2$, we have, for any constant λ the existence of a constant $\tilde{\lambda}$ such that:

$argmin_w \lambda\|w\|_2 + f(w, X, y) = argmin_w \tilde{\lambda}\|w\|^2_2 + f(w, X, y)$

which is the usual l_2 regularizer.

3.1.3 Relationship to the elastic net

One common setting in microarray studies is to have high dimensional data with few examples. In this situation, the Lasso saturates as it can select a number of variables at most equal to the number of features. To address this limitation, [15] introduced the elastic net, which linearly combines the l_1 and the l_2 regularizations:

$$argmin_w \frac{1}{2}\|Xw - y\|_2 + \lambda_1\|w\|_1 + \lambda_2\|w\|^2_2 \quad (5)$$

Like k-support, the elastic net interpolates between the l_1 and the l_2 norms. [1] show that the k-support norm is tighter than the elastic net by a factor of$\sqrt{2}$

3.2 Optimization

A general cost function for network inference involves an error term and a regularization term. Since the l1-norm is not differentiable, we resort to proximal algorithms. The cost function can be split into two terms, the first term aims to learn the gene regulatory network, which is convex and differentiable and the second term is inducing sparsity control with K-support norm, which is convex, but not differentiable. Therefore, the cost function is convex. The formulation of these two terms naturally suits proximal gradient descent, which we use to solve the problem [8].

The proximal computation can be done within $O(d(k + \log k))$ steps which is given in the algorithm 1 of [1], indicated in Algorithm 1 This proximal operator offers us the freedom to treat the cost function as a differentiable one and we can use standard algorithms to solve it. Here we considered interior point method [6].

Algorithm 1 Computation of the proximal operator

Input: $v \in R^d$

Output: $q = prox_{\frac{1}{2\beta}(\|\cdot\|^{sp}_k)^2}(v)$

Find $r \in \{0, ..., k-1\}$, $l \in \{k, ..., d\}$ such that

$$\frac{1}{\beta+1}z_{k-r-1} > \frac{T_{r,l}}{l-k+(\beta+1)r+\beta+1} \geq \frac{1}{\beta+1}z_{k-r} \quad (6)$$

$$z_l > \frac{T_{r,l}}{l-k+(\beta+1)r+\beta+1)} \geq z_{l+1} \quad (7)$$

where $z := |v|^{\downarrow}$, $z_0 := +\infty$, $z_{d+1} := -\infty$, $T_{r,l} := \sum_{i=k-r}^{l} z_i$

$$q_i \leftarrow \begin{cases} \frac{\beta}{\beta+1} & \text{if } i = 1, ..., k-r-1 \\ z_i - \frac{T_{r,l}}{l-k+(\beta+1)r+\beta+1} & \text{if } i = k-r, ..., l \\ 0 & \text{if } i = l+1, ..., d \end{cases}$$

reorder and change signs of q to conform with v

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5. APPENDIX

5.1 Proximal Gradient Descent

Consider an objective function $g(x)$ of the following form:

$$f(x) = g(x) + h(x)$$

where $g(x)$ is a smooth function (and represents the negative log-likelihood or a similar quantity) and $h(x)$ is a convex but non-smooth function like the k-support