

## Accepted Manuscript

Variable neighborhood search for reverse engineering of gene regulatory networks

Charles Nicholson, Leslie Goodwin, Corey Clark

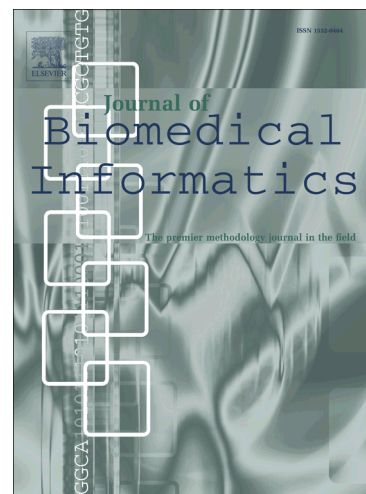
PII: S1532-0464(16)30173-3  
DOI: <http://dx.doi.org/10.1016/j.jbi.2016.11.010>  
Reference: YJBIN 2686

To appear in: *Journal of Biomedical Informatics*

Received Date: 4 December 2015  
Revised Date: 16 November 2016  
Accepted Date: 27 November 2016

Please cite this article as: Nicholson, C., Goodwin, L., Clark, C., Variable neighborhood search for reverse engineering of gene regulatory networks, *Journal of Biomedical Informatics* (2016), doi: <http://dx.doi.org/10.1016/j.jbi.2016.11.010>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



# Variable neighborhood search for reverse engineering of gene regulatory networks

Charles Nicholson<sup>a,\*</sup>, Leslie Goodwin<sup>a</sup>, Corey Clark<sup>b</sup>

<sup>a</sup>*School of Industrial and Systems Engineering, University of Oklahoma, Norman, OK*

<sup>b</sup>*Guidhall, Southern Methodist University, Dallas, TX*

---

## Abstract

A new search heuristic, Divided Neighborhood Exploration Search, designed to be used with inference algorithms such as Bayesian networks to improve on the reverse engineering of gene regulatory networks is presented. The approach systematically moves through the search space to find topologies representative of gene regulatory networks that are more likely to explain microarray data. In empirical testing it is demonstrated that the novel method is superior to the widely employed greedy search techniques in both the quality of the inferred networks and computational time.

*Keywords:* Gene regulatory networks, reverse engineering, variable neighborhood search

---

## 1. Background

A gene regulatory network (GRN) is a collection of genes, regulators, and regulatory connections that govern expression levels [1]. Analysis of GRNs has become essential for better understanding cellular systems because it provides insight into which genes control the activation of others [2, 3]. The network topology has various interpretations in literature: the nodes in the GRN may represent genes or their protein products, the undirected edges between nodes may indicate genes are co-regulated, share common functionality, location or process, or directly bind one another; and directed edges may imply a step in a metabolic pathway, signal transduction cascade, stage of development, or a causal relationship [4]. These networks create the blackprint of the cellular system structure and provide design details of the cell.

Research in computational systems biology revolves around inferring or reverse engineering GRNs based on gene expression levels [5]. A basic assumption within the field is that the observed data, which are the changes in mRNA expression profiles, can explain transcriptional regulation. By

---

\*Corresponding author

*Email addresses:* [cnicholson@ou.edu](mailto:cnicholson@ou.edu) (Charles Nicholson), [leslie.goodwin@ou.edu](mailto:leslie.goodwin@ou.edu) (Leslie Goodwin), [coreyc@smu.edu](mailto:coreyc@smu.edu) (Corey Clark)

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات