IWBBIO 2016

INTERNATIONAL WORK-CONFERENCE ON BIOINFORMATICS AND BIOMEDICAL ENGINEERING

PROCEEDINGS EXTENDED ABSTRACTS

Godel Editorial

20-22 April, 2016
Granada (SPAIN)

IWBBIO 2016
International work-conference on Bioinformatics and biomedical engineering

Proceedings Extended abstracts
20-22 April,2016
Granada (SPAIN)

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I.S.B.N: 978-84-16478-75-0
Legal Deposit: Gr- 500-2016
Edit and print : Editorial Godel S.L.

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Network-inspired approaches for transcriptomic analyses

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Keywords. Network analysis, gene co-expression network, transcriptomics

1 Biological network analysis

Network models have long been used in biological contexts to model interactions between biological entities, with applications to gene regulation, metabolic and signaling pathways, and protein-protein networks, among others [1-4]. Analyzing these network models allows exploring both local and global properties of the networks, which may provide insights that other methods cannot readily offer. Quantifiable network properties include connectivity, average degree, density, distance distribution, scale-freeness, critical nodes and edges, partitionability into clusters, and much more; thus providing a valuable approach to study biological systems.

In the field of transcriptomics, network analysis is carried out by constructing gene co-expression networks. A *gene co-expression network* (GCN) is an undirected graph, where each node corresponds to a gene, and a pair of nodes is connected by an edge if there is a significant co-expression relationship between them [5]. Co-expression relationships between genes can be quantified as a function of their gene expression profiles (e.g., Pearson correlation coefficient). Therefore, with this approach, we can identify pairs of genes with strongly correlated behavior (both positive and negative). GCNs allow generating hypotheses involving genes that may be controlled by the same regulatory element, genes that may be functionally related, or genes that may play a coordinated role in one or more biological processes [6-11].

Transcriptomic data in the form of gene expression profiles may be obtained using technologies such as microarray and, more recently, using the next generation sequencing (NGS) technology named RNA-Seq. While the former focuses on targeted genes, the latter provides an unbiased profile of the organism being studied. Transcriptomic data can be studied from a systems biology perspective in order to unravel potential relationships between expressed genes, and this is the main goal of the present work.

[*] The first two authors contributed equally to this paper.

2 Application to transcriptomic data analysis

In marine environments, abiotic factors, such as temperature and salinity, have an impact on living organisms as well as entire ecosystems. Furthermore, mankind has altered natural balances leading to additional changes in the environment. As a consequence, marine organisms must adapt to environmental variations in order to survive. Transcriptomic analysis helps us to elicit how such adaptations are achieved.

In this work, a network-based analysis approach was applied to transcriptomic data from the Pacific oyster, *Crassostrea gigas*, challenged with different temperature and salinity conditions [12]. Raw RNA-Seq data was first processed using standard pipelines [13, 14]. Next, co-expression networks were built as described in prior work [15, 16]. Figures 1 (a) and (b) show the GCNs for *C. gigas* under two different environmental stressors. In these figures, edges between nodes (genes) indicate the strength and nature (positive or negative) of their relationship. Also, connected components with the same color correspond to co-expressed clusters of genes.

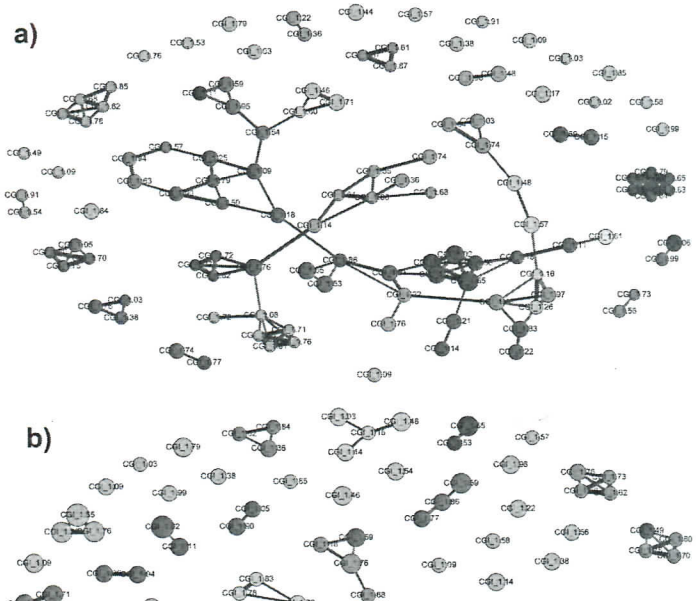

Fig 1. Co-expression networks of *Crassostrea gigas* genes challenged with (a) temperature and (b) salinity

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Many useful conclusions can be drawn from these networks. First, we can identify pairs of genes that show strongly correlated expression profiles across a set of conditions. This can be generalized to identify clusters of genes with correlated expression profiles. In this specific application, some clusters represent the same gene (from different loci on the genome), showing strong co-expression. Other clusters may indicate direct or indirect relationships between genes involved in the same biological process or metabolic pathway. Within each cluster, positive correlations (green edges) could indicate cooperative roles, while negative correlations (red edges) could indicate incompatible roles or opposite effects.

If multiple networks are compared, common responses and differences between expression patterns can be pinpointed. Clusters that are conserved across networks can be attributed to processes that are independent of the specific environmental stressor (i.e., temperature and salinity), whereas clusters that show changes may highlight specific effects that are characteristic of a stressor, and may lead to the identification of biomarkers.

Understanding the changes that result from variations in the environment is crucial to shed light on the adaptive mechanisms of marine organisms. Such information could be of great value in order to monitor specific environments and has the potential for the development of multi-gene biomarkers. Hence, network-based approaches represent a valuable tool to study changes in gene expression, enabling the further generation of targeted hypotheses for wet-lab validation.

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Genetic Algo

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1 Introduction

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