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GALANT: a Cytoscape plugin for visualizing data as functional landscapes projected onto biological networks

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ABSTRACT

Summary: Network-level visualization of functional data is a key aspect of both analysis and understanding of biological systems. In a continuing effort to create clear and integrated visualizations that facilitate the gathering of novel biological insights despite the overwhelming complexity of data, we present here the GrAph LANdscape VisualizaTion (GALANT), a Cytoscape plugin that builds functional landscapes onto biological networks. By using GALANT, it is possible to project any type of numerical data onto a network to create a smoothed data map resembling the network layout. As a Cytoscape plugin, GALANT is further improved by the functionalities of Cytoscape, the popular bioinformatics package for biological network visualization and data integration.

Availability: http://www.lbbc.ibb.unesp.br/galant.

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Supplementary Information: Supplementary data are available at *Bioinformatics* online.

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1 INTRODUCTION

The network modeling of biological systems has been demonstrated to be a formidable tool to decipher the collective behavior of various biological processes. However, the construction of a biological network per se is not sufficient to accomplish this task. To better understand the biological systems and their responses, it is necessary to extend and complement these networks with data collected from different sources, such as gene or protein expression profiles (Bebek *et al.*, 2012). Moreover, owing to the human natural strengths in rapid visual pattern recognition, the visualization of these data through maps overlaid on interaction networks would be an efficient way to extract information that could be missed by a purely statistical or numerical approach.

Virtually, all existing tools capable to map data to biological networks perform this task by coloring the nodes according to data values (for a review, see Gehlenborg *et al.*, 2010). Although these tools have proven to be useful, these 'colored networks'–specially the large and dense networks–are often noisy, and, therefore, the visual identification of patterns in the data mapped to these networks are difficult. To facilitate this task, these large colored networks could be transformed in smoothed data maps. To the best of our knowledge, only the ViaComplex (Castro *et al.*, 2009), an open source software implemented in Fortran, is currently able to generate smoothed data maps by projecting data as functional landscapes onto biological networks. To expand the collection of tools providing this functionality, we developed in this work a Cytoscape plugin version of ViaComplex: the GrAph LANdscape VisualizaTion (GALANT). Although GALANT provides the same essential functionality found in the original ViaComplex, its main advantage over ViaComplex is the well-known versatile network visualization and data integration environment provided by Cytoscape (Shannon *et al.*, 2003).

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2 DESCRIPTION

GALANT projects any type of numerical data onto a network to create landscapes resembling the network layout. For this purpose, GALANT uses the java class 'HeatMap' created by Matthew Beckler (http://www.mbeckler.org/heatMap/). 'HeatMap' defines the color gradient by finding the minimum and maximum values in a matrix superposed to the network. The values of this matrix are calculated from the data mapped to nodes in the network through three different functions: Gaussian, Moving Average or Power Law (see 'Supplementary Data' for details on these functions).

GALANT offers a friendly interface fully integrated with Cytoscape where users can easily build their landscapes of interest by using one of the previously mentioned functions. Users can project their functional data either as raw values by selecting the 'Attribute' option or as normalized ratios between raw values from two different conditions by selecting the 'Exp X Control' option (see details at http://www.lbbc.ibb.unesp.br/galant). Moreover, in both options, users can set parameters to control smoothness ('sigma' in Gaussian mode, 'smoothness' in Moving Average mode and 'exponent' in Power Law mode) and resolution to get the desired landscape more appropriate for their analyses (see details at http://www.lbbc.ibb.unesp.br/galant).

After generating the landscape according to the selected parameters, users can also select the type of color gradient that is more appropriate to represent their mapped data. GALANT

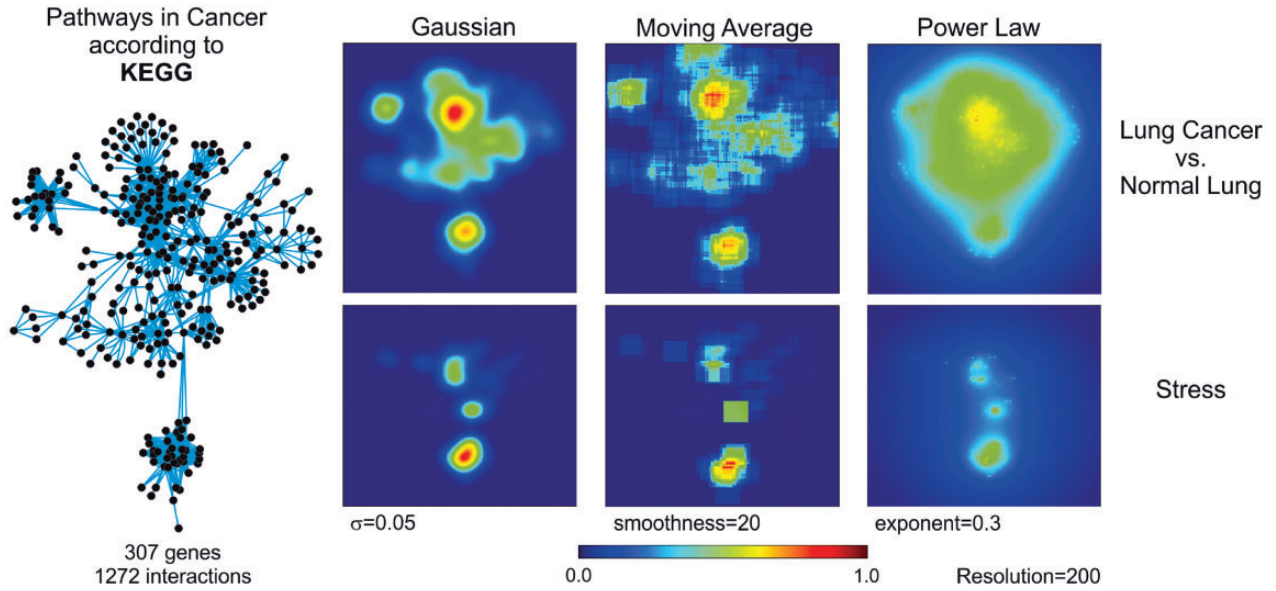

Fig. 1. Case study showing how GALANT can be used to integrate functional data into a biological network. These are projections of ratios between gene expression values from lung cancer versus normal lung (upper panel) and values of stress centrality (lower panel) onto a signaling cancer network by using the three methods for generating landscapes

provides 10 different types of color gradient through the Matthew Beckler's 'HeatMap' class (http://www.mbeckler.org/heatMap/). In addition, users can export the landscapes as images in PNG format.

Detailed instructions on how to construct a landscape can be found in a tutorial page at http://www.lbbc.ibb.unesp.br/galant.

3 CASE STUDY

As a simple example of GALANT application (additional examples can be found in the 'Supplementary Data'), we sought to verify the projection of two different types of data onto a cancer signaling network constructed by merging cancer pathways provided by the KEGG PATHWAY database (Kotera *et al*., 2012): stress centrality and the differential gene expression in lung cancer in comparison with normal lung (Fig. 1). First, we imported to Cytoscape the cancer signaling network. We then calculated the stress centrality for each node by using NetworkAnalyzer (Assenov *et al*., 2008) and imported the gene expression values (dataset GSE19804) from the Gene Expression Omnibus database (Barrett *et al*., 2011). By using GALANT, we generated the functional landscape maps shown in Figure 1. The lower and upper panels of Figure 1 show, respectively, the projection of stress values and the ratio between gene expression values of cancer and normal tissues onto the cancer signaling network by using the available methods for image smoothing. As an example of analysis, it is possible to observe that the subnetworks showing the highest stress centrality values match those containing genes highly expressed in lung cancer.

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Conflict of Interest: none declared.

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