

Reviewer's report

Title: BiNoM, a Cytoscape plugin for accessing and analyzing pathways using standard systems biology formats

Version: 1 **Date:** 30 November 2012

Reviewer number: 3

Reviewer's report:

General

The authors present an overview of the functionality provided by BiNoM, a Cytoscape plugin for the conversion of standard systems biology file formats and the structural analysis and decomposition of large biological networks. A detailed view on the implemented BiNoM functions is given including a biological case study illustrating the principal functions of the software.

The presented software provides a valuable framework for the handling and analysis of large biological networks which should be of interest in its field of study. To justify publication, the manuscript in its present form requires major revisions.

Major Revisions

(1) As a variety of methods and tools for the conversion of standard systems biology file formats and the analysis and decomposition/reduction of large biological networks exist already, a more detailed consideration of related or previous work should be given and the benefit/novelty of the tool in comparison to already existing tools should be stated more clearly.

Some related work with respect to file conversion includes:

- Sybill: Rübenacker, O. et al. (2009) Integrating BioPAX pathway knowledge with SBML models. IET Syst. Biol., 3, 317–328.
- System Biology Format Converter (SBFC):
<http://www.ebi.ac.uk/compneur-srv/sbml/converters/SBMLtoBioPax.html>

Some related work with respect to network decomposition/clustering/modularization and structural analysis within Cytoscape include:

- ShortestPath Plugin
- GLay: Su, G. et al. (2010) GLay: community structure analysis of biological networks. Bioinformatics, 26, 3135–3137.
- MCode: Bader, G.D. and Hogue, C.W.V (2003) An automated method for finding molecular complexes in large protein interaction networks. BMC Bioinformatics, 4, 2

- ModuLand: Szalay-Beko M. et al. (2012) ModuLand plug-in for Cytoscape: determination of hierarchical layers of overlapping network modules and community centrality. *Bioinformatics* 28(16):2202-4
- ClusterMaker: <http://www.cgl.ucsf.edu/>
- NeMo: Rivera et al. (2010) NeMo: Network Module identification in Cytoscape. *BMC Bioinformatics* 18;11 Suppl 1:S61.

(2) Please state more clearly the novelty and progress of the current work with respect to the work published earlier (Zinovyev et al., 2008).

Minor Essential Revisions

(1) Tutorial:

There is no G1S.xml file provided on the website as mentioned in the tutorial. Instead a Cytoscape session file is provided, but the Material Component analysis of the given G1S network does not result into 36 subnetworks. Please correct and/or provide the xml-file mentioned.

(2) Figures/Tables:

- Figure 2: Due to its low informative value, it might be reasonable to change figure 2 and provide a smaller example providing node labels
- Table 1: As there is no difference between the listed path analysis algorithms with respect to the listed options, it is unclear why the table is provided instead of just mentioning the information in the text

(3) References in the text:

As already done for some algorithms implemented in BiNoM, in the text for each implemented method a respective literature reference should be given (if available). Implemented methods without a reference are for example:

- Material component decomposition (page 5)
- Path analysis algorithms: suboptimal shortest path, non self-intersecting paths (page 6)

(4) Network clustering, subsection Path analysis algorithms, 2nd paragraph:

Obviously, the result of some decomposition functions will result in subnetworks that share some components, as it is for example often the case with the decomposition in material components. Therefore, BiNoM also includes a function to cluster networks, based on common components such as protein or protein complexes. To determine the size of the clusters, the user can specify a percentage of intersection (ranging from 0 to 100%) that will be used as a threshold to create the clusters.

As the subject of network clustering rather belongs to network decomposition instead of path analysis, it might be useful to include this paragraph into the section of network decomposition.

(5) Recheck spelling and language, e.g.:

- Section Application of PIQuant on an influence network, 3rd paragraph:

The PIQuant score is then automatically calculated for each association between an annotated node and a target node.

- Section Results and Discussion, 4th paragraph:

This map contains a lot of valuable information but rather difficult to extract

(6) Recheck title of sections/subsection as they are sometimes written in capital letters and sometimes not

(7) Recheck formatting of the Reference section, e.g.:

- Ref. 24: journal name written in capital letters, instead of small ones as done by the others
- Ref. 30: journal name written in its abbreviated form, instead of its full name as done by the others

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.