Cyrface Manual

Cyrface is a bioinformatics Java library that provides a general interaction between Cytoscape and R. Cyrface offers a way to combine a friendly graphical interface within the Cytoscape environment with any R package. A GUI should benefit beginners and occasional users; as well as being useful for training and illustration purposes, it extends the accessibility of the tool to those not familiar with the R command line interface.

This tutorial is intended for Cyrface v2.0 that requires Cytoscape v3.1 and R 3.x. The following materials are all available online on Cyrface homepage: http://www.ebi.ac.uk/saezrodriguez/cyrface

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Software Requirements

Please unsure that you have the following software installed and working:

1. R framework (version 3.x) - http://www.r-project.org/
2. Cytoscape (version 3.1.x) - http://www.cytoscape.org/

It is very important that Cytoscape version is equal or greater than 3.1.0

Linux users must run the following commands before using Cytocopter

- sudo apt-get install libcairo2-dev
- sudo apt-get install libxt-dev

Introduction

http://www.ebi.ac.uk/saezrodriguez/cyrface

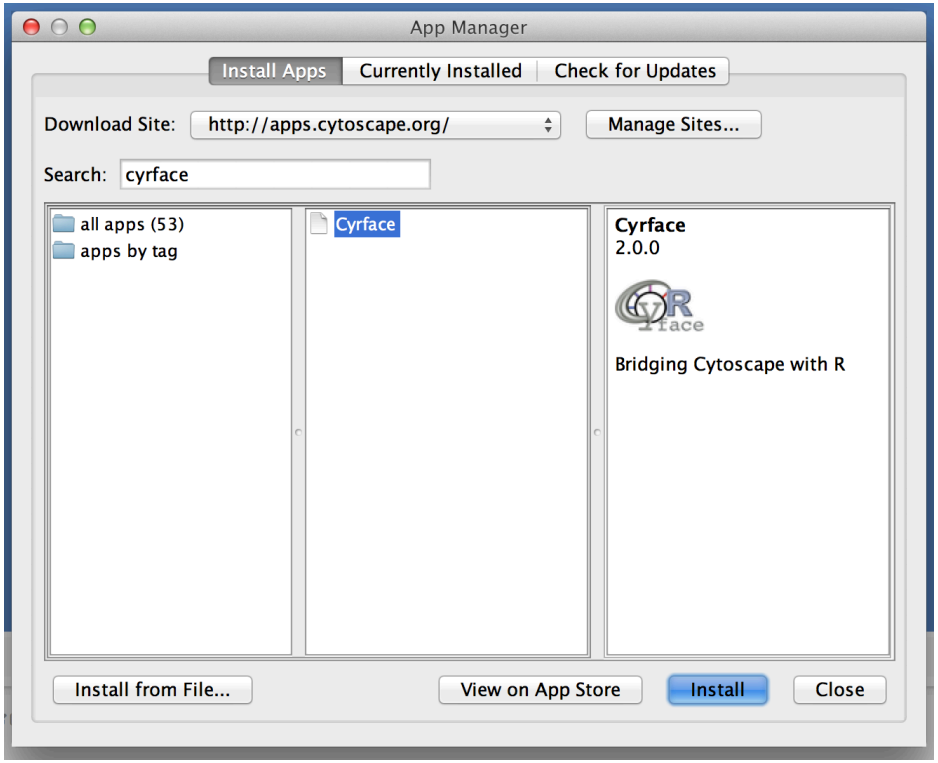
Cyrface[1] establishes an interface between R and Cytoscape[2,3] by using different Java-R libraries, e.g. Rserve, RCaller. Cyrface can be used as a Cytoscape plug-in, e.g. to run R commands within Cytoscape, or used as a library to allow your plug-in to connect to R.

This is developed under a GNU open-source license and the source code can be accessed from the respective GitHub project.

Installation

Install from Cytoscape

Click Apps on Cytoscape top bar followed by Apps Manager menu then search for Cyrface and click install. This may take a few minutes.



Install from file

Download the jar file of Cyrface from the following URL:

- www.ebi.ac.uk/saezrodriguez/cyrface

Click Apps on Cytoscape top bar followed by Apps Manager then click Install from file… button and search Cyrface jar file.

Install manually

Cyrface can also be installed manually by copying the jar file mentioned before to CytoscapeConfiguration folder. CytoscapeConfiguration folder is kept in the user home folder. Drag the App jar file into the following folder:

- ~/ CytoscapeConfiguration / 3 / apps / installed /

After moving the jar file start Cytoscape.

Cyrface DataRail Tutorial

Introduction

This tutorial assumes that Cytoscape as well as R is already installed. The necessary files for this tutorial is a network file in SBML-Qual format and the corresponding experimental data in MIDAS format.

Study case

To illustrate the usefulness of Cyrface we will use a simple implementation of the DataRail workflow[4].

The accompanying *in silico* data (MIDAS file format[4]) replicates biologically plausible behaviour that has been seen in intracellular signalling networks, such as the transient behaviour of ERK activation and the oscillatory dynamics of NFkB translocation from the cytoplasm to the nucleus.

MIDAS experimental data format

The MIDAS format (Minimum Information for Data Analysis in Systems Biology)[4] is a comma-separated file that specifies the layout of experimental data files.

Each row represents a single experimental sample; each column represents one sample attribute, such as treatment condition, or value obtained from an experimental assay.

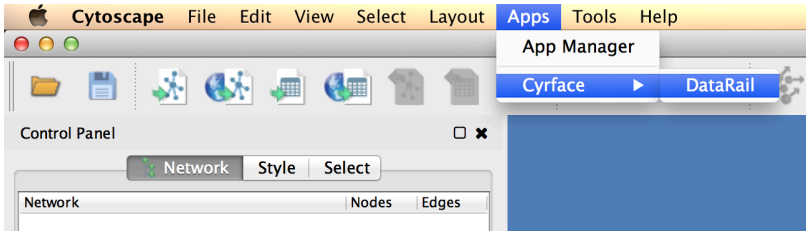
SBML-Qual network format

SBML-Qual format[5] is an extension to the System Biology Markup Language (SBML) for Qualitative Models (Qual). In one sentence, SBML-Qual is designed to provide a standard mean for the exchange of logical models or regulatory and signalling networks.

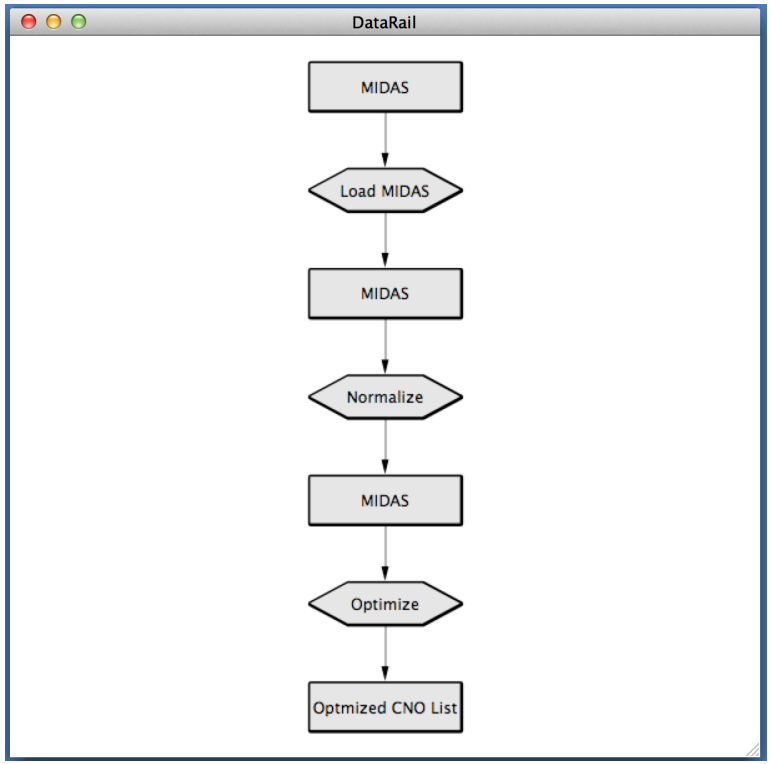
For more details regarding the specifications please see[5].

Tutorial

1. To start Cyrface's DataRail workflow go to *Apps -> Cyrface -> DataRail*

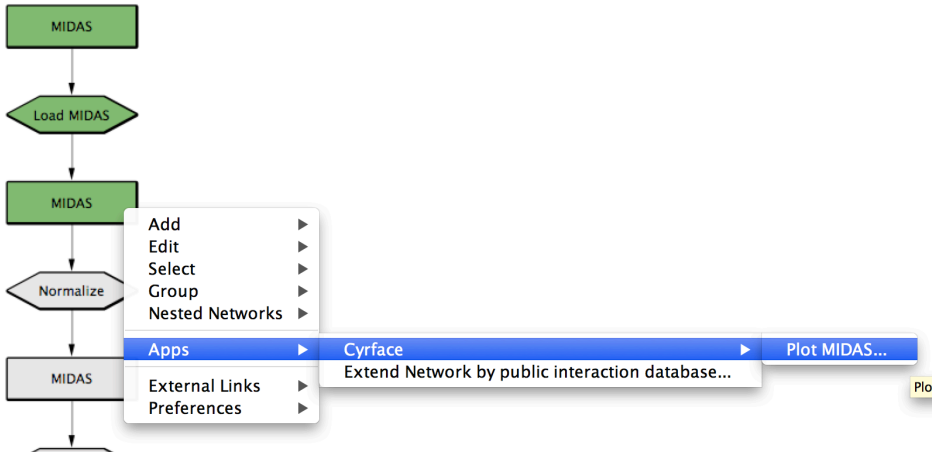


2. The full workflow should now be visible



3. Right-click on the top MIDAS node and then select *Cyrface -> Set MIDAS file*... to select the desired MIDAS file. After the MIDAS file is selected the node should turn green.

   Raw data MIDAS file:
   www.ebi.ac.uk/saezrodriguez/cyrface/resources/ToyDataPB10raw.csv



4. Right-click on *Load MIDAS* node and then select *Cyrface -> Load MIDAS...* option to load the previously selected MIDAS file. After the file is loaded the node should turn green.

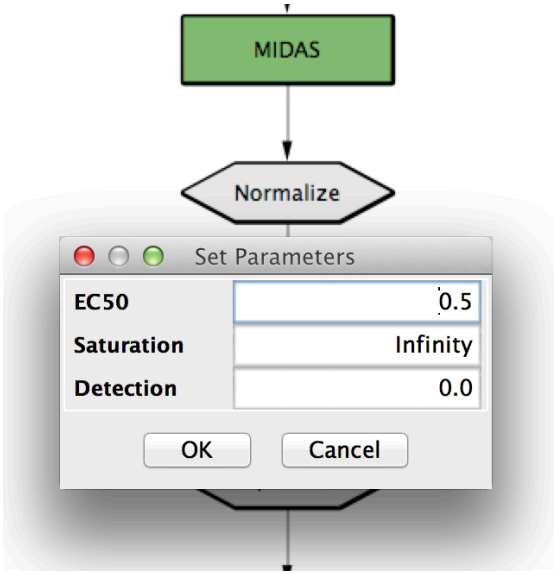
5. After the MIDAS file is successfully loaded the second MIDAS node is now green showing that it's ready to be normalized or visualized.

6. Right-click on the respective MIDAS node and the selecting the *Cyrface -> Plot MIDAS...* option will pop-up a plot of the data
   a. The plot SVG file can be exported click *File -> Save R plot...*

7. Right-click on the *Normalize* node to run the normalization function. A pop-up window will show up to allow the user to define the Normalization function arguments:

   a. **EC50Data:** parameter for the scaling of the data between 0 and 1, default=0.5
   b. **Detection:** minimum detection level of the instrument, everything smaller will be treated as noise (NA), default to 0
   c. **Saturation:** saturation level of the instrument, everything over this will be treated as NA, default to Inf

8. After normalizing the MIDAS file it can be plotted as previously and/or exported.



Optional steps

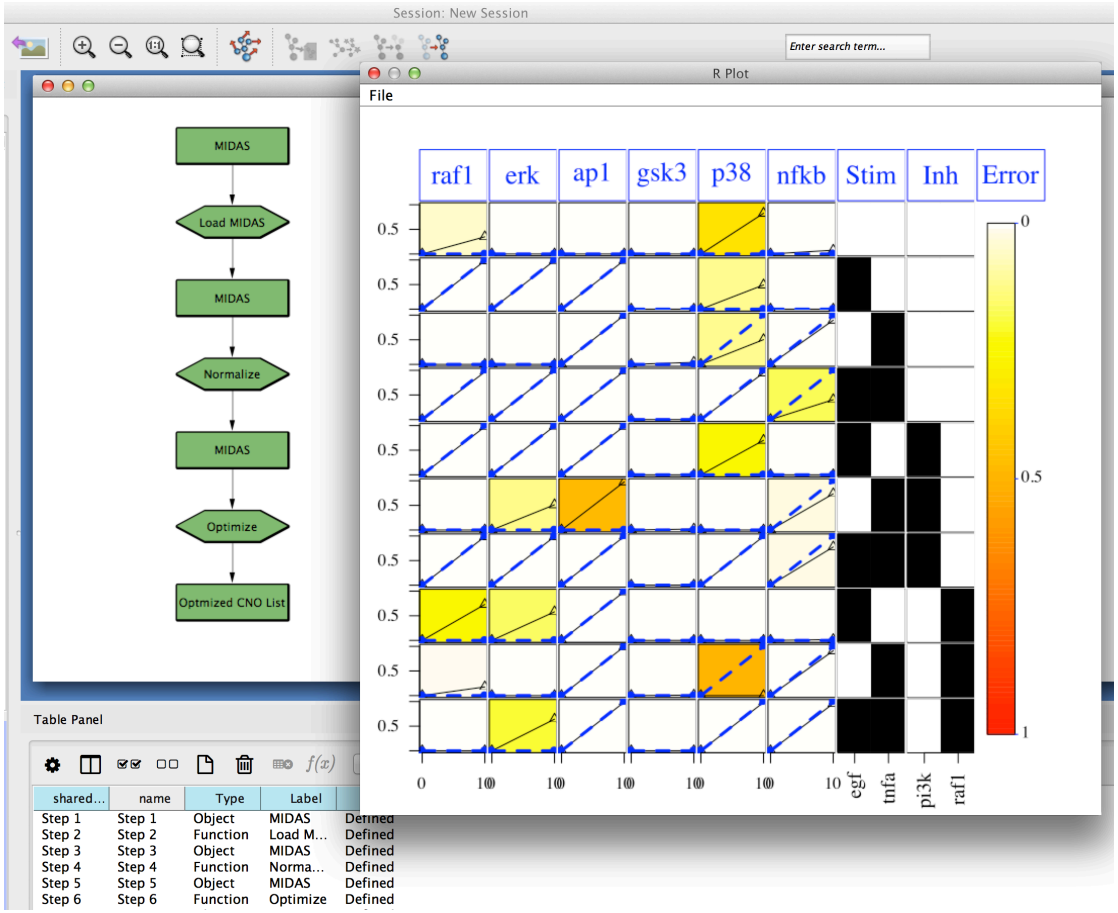
Cyrface's DataRail[4] Workflow is also linked to the CellNOptR[6] R package allowing the users to optimize a selected prior knowledge network against the just normalized MIDAS file.

9. Right-click on the *Optimize* node and select *Cyrface -> Optimize...* function will pop-up a file browser to select the model file. Both SIF and SBML-Qual[5] formats are supported.

10. The optimization may take awhile and it's executed using the defaults values defined in CellNOptR

11. Right-click on the *Optimized CNO List* will show how well the optimized model fit the data.

12. For more details about the normalization function and the optimization method please visit CellNOptR package in Bioconductor or CellNOpt homepage



a. www.bioconductor.org/packages/2.12/bioc/html/CellNOptR.html
b. www.cellnopt.org

Links

- ***Cyrface*** - http://www.ebi.ac.uk/saezrodriguez/cyrface
- ***Cyrface (Github)*** - https://github.com/EmanuelGoncalves/cyrface
- ***Cytoscape*** - http://www.cytoscape.org/
- ***R*** - http://www.r-project.org/
- ***Rserve*** - http://www.rforge.net/Rserve/
- ***Rcaller*** - http://www.mhsatman.com/rcaller.php

References

1. Gonçalves, E. & Saez-Rodriguez, J. Cyrface: An interface from Cytoscape to R that provides a user interface to R packages. *F1000Res* **2,** 192 (2013).

2. Shannon, P. *et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome Research* **13,** 2498–2504 (2003).

3. Smoot, M. E., Ono, K., Ruscheinski, J., Wang, P. L. & Ideker, T. Cytoscape 2.8: new features for data integration and network visualization. *Bioinformatics* **27,** 431–432 (2011).

4. Saez-Rodriguez, J. *et al.* Flexible informatics for linking experimental data to mathematical models via DataRail. *Bioinformatics* **24,** 840–847 (2008).

5. Chaouiya, C. *et al.* SBML qualitative models: a model representation format and infrastructure to foster interactions between qualitative modelling formalisms and tools. *BMC Syst Biol* **7,** 135 (2013).

6. Terfve, C. *et al.* CellNOptR: a flexible toolkit to train protein signaling networks to data using multiple logic formalisms. *BMC Syst Biol* **6,** 133 (2012).