

## Introduction

**Gene4x** is a pipeline for the identification of communities on a gene multiplex composed of four layers: co-expression network, transcriptional and post-transcriptional co-targeting network and protein-protein interaction network.

The pipeline performs the following operations:

1. Multiplex reconstruction
2. Layers filtering
3. Community detection on the multiplex

**ATTENTION! The alpha thresholds for step 2. has to be chosen from the user.**

**We suggest to follow the three criteria proposed in the paper.**

**ATTENTION! The community detection algorithm for step 3. has to be chosen from the user, the suggested one is OSLOM.**

## Installation

The following software components are required to run **Gene4x**:

- **Gene4x**
- R (<http://www.r-project.org/>)
- R packages: igraph and BioPhysConnectoR
- package Ganet [REF] (<https://sites.google.com/site/gokmenaltay/ganet>). To install the package download the file Ganet\_1.0.tar.gz at the above link. Set the working directory in the same folder that ganet is placed. Then, in the R console, write the following: `install.packages("GAnet_1.0.tar.gz", type="source")`.
- Python

- Python modules: networkx and scipy

In principle, **Gene4x** should run under Linux and Mac.

## Usage

To run **Gene4x**:

- download the net\_mirna\_and\_tf.zip file at the link <http://personalpages.to.infn.it/~caselle/BioPhys/Gene4x/>
- unzip net\_mirna\_and\_tf.zip -d /path\_to\_Gene4x/data/
- Set the working directory in Gene4x (cd path\_to\_Gene4x/)
- ./ Gene4x\_run.sh

## Inputs

While running, the program requires the following inputs:

- The path to the file containing the mRNA expression matrix in log2 with the first column containing genes names, the second column containing gene annotations (or gene names) and the first row containing sample names.
- Integer corresponding to the optimal alpha value, choosing among (0=0.005,1=0.01,2=0.02,3=0.03,4=0.05,5=0.1,6=0.2,7=0.3,8=0.4,9=0.5) for the expression network, transcription factor co-targeting network and microRNA co-targeting network. To choose the optimal alpha value you can use the three criteria suggested in the paper taking advantage of the files:
  - Gene4x/temp/selection\_links\_EXP.txt for the co-expression layer.

- Gene4x/temp/selection\_links\_TF.txt for the transcription factor co-targeting layer.
  - Gene4x/temp/selection\_links\_MIRNA.txt for the microRNA co-targeting layer.
- The integer corresponding to the algorithm you want to use for network clustering, choosing among:
    - 0: oslom undirected,
    - 2: infomap undirected
    - 4: louvain
    - 5: label propagation method,
    - 8: modularity optimization

## Outputs

During **Gene4x** running some intermediate outputs are created in Gene4x/temp/ the folder will be deleted when the execution is completed.

The final output comm\_final\_genesymbol.txt is in the folder Gene4x. The file reports in the first column an integer used as identifier for the communities. Then in each row the list of genes belonging to that community is reported. Communities are ordered in respect to their dimension.

## Data

The datasets to reproduce the results of our paper are available at:

- gastric GSE13911

- lung GSE10072,
- pancreas GSE15471
- colon GSE44076

## Contact

Please feel free to contact us at

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Moreover, feel free to change the code according to your needs.

**For every use of the original or modified pipeline cite us:**

Cantini et al., Community detection on genomic multiplex networks reveals cancer drivers