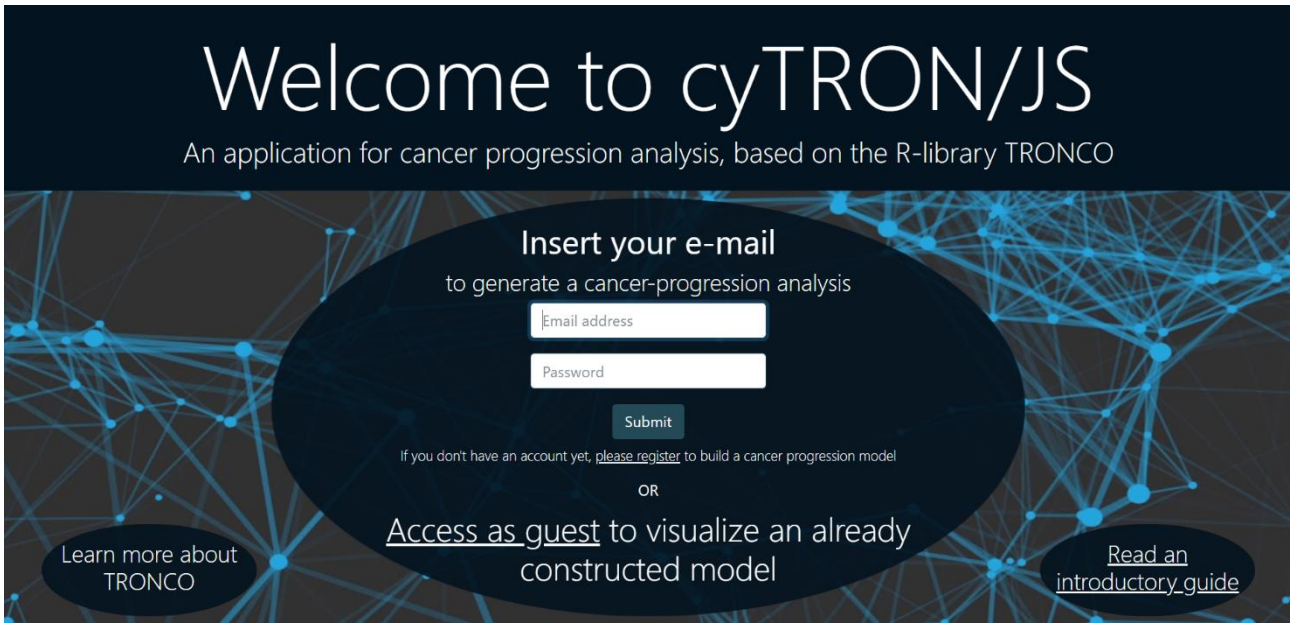
cyTRON/JS: Tutorial guide

Welcome to cyTRON/JS, a tool for the reconstruction of cancer progression models based on the R library TRONCO. This tutorial is a guide which shows examples about how to use this tool.



1) Exploring TRONCO graphs

By clicking on the *Access as guest* option in the home page displayed above, it is possible to start exploring some mutational graphs produced by TRONCO.

After selecting this option you will be redirected to this page:

Here, you have **two** options:

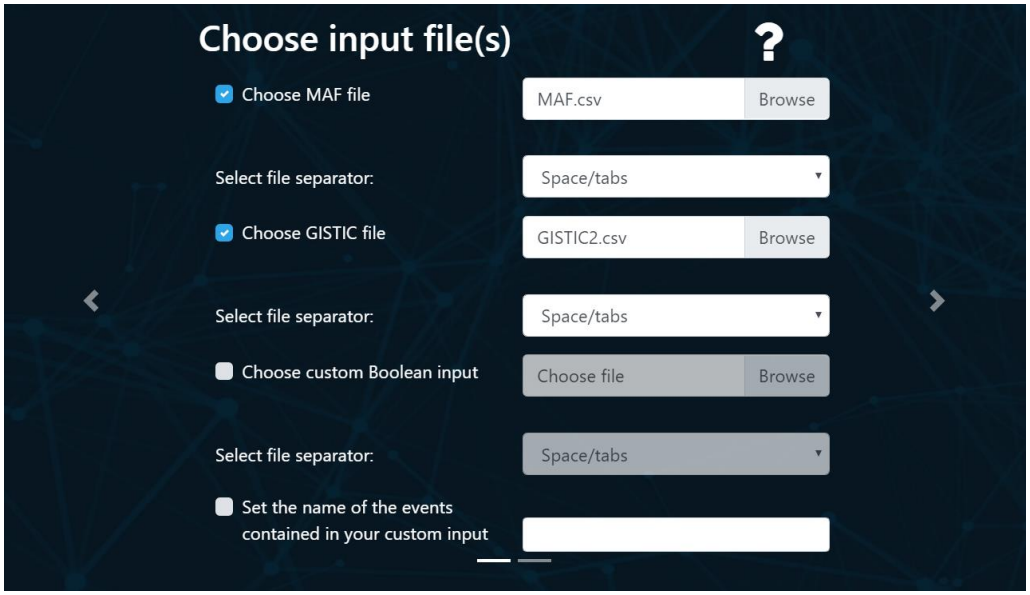
- On the **left** panel you can choose to visualize one of the publicly available results of a TRONCO analysis.
- On the **right** panel you can upload your local graphml file, which should contain the result of a TRONCO analysis.

2) TCGA-prostate example

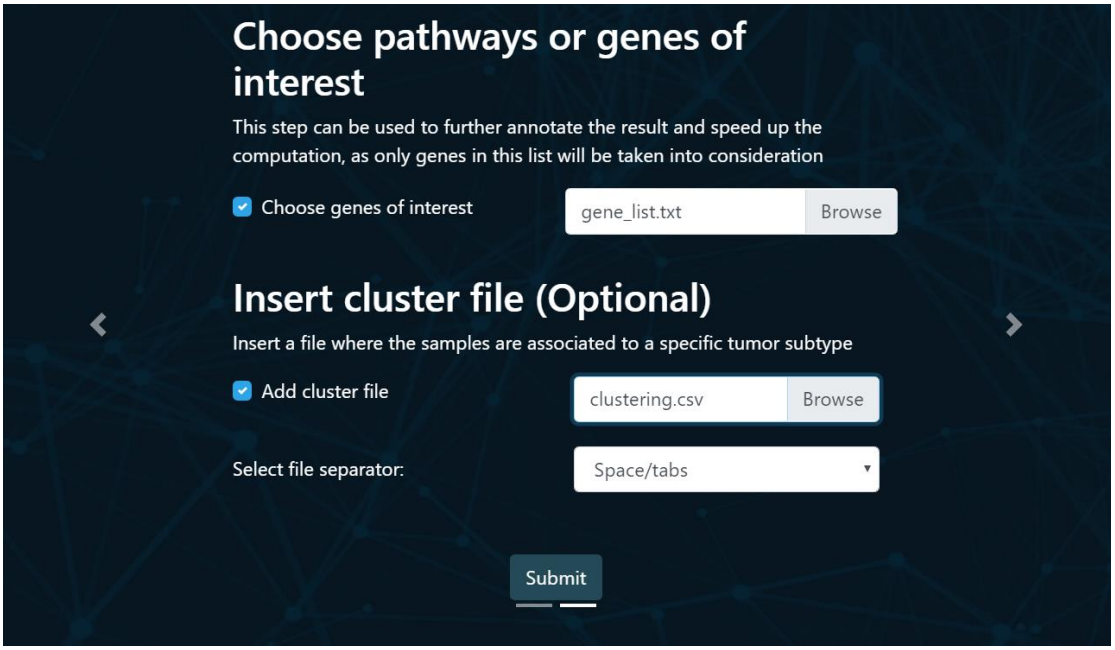
The files needed for every step can be found here: https://github.com/BIMIB-DISCo/cyTRON-js/tree/master/examples/TCGA-prostate

First, in order to proceed further you need to create an account or to sign-in from he home page. After this step is complete, you will be redirected to a page where you need to insert a name for the analysis you are about to run.

1: Selecting input



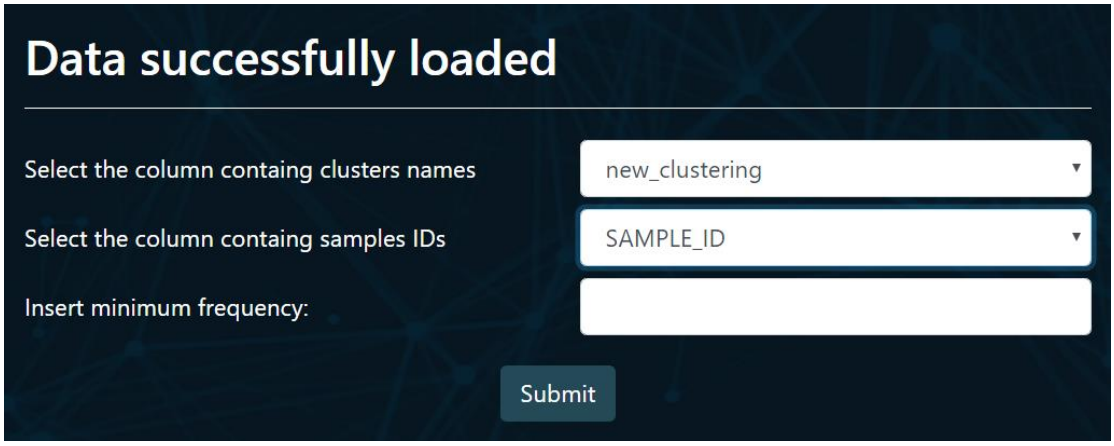
The image above shows the page which is displayed after inserting the study name. There are three different possible input files: MAF, GISTIC and a custom Boolean file, which contains a matrix indicating which mutation is present in each sample. For this example we are going to use the first two types of input.



The image above displays the second slide of the input selection. Here a user can decide to upload a **list of genes** to take into consideration during the analysis. This step can speed up the computation, as only genes contained in this list will be taken into consideration.

The cancer type involved in the study might also be divided into different subtypes: to achieve this goal, a user can upload a **cluster file,** which should contain a list of samples with an associated subtype.

2: Cluster selection

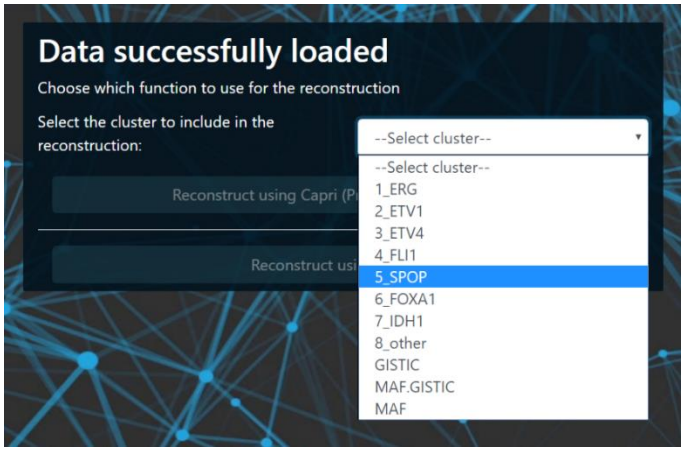


This is the page displayed after the input selection. Here the user can access the names of the columns contained in the cluster file, and can indicate which columns contain the samples IDs and the subtype names related to each sample.

3: Model reconstruction

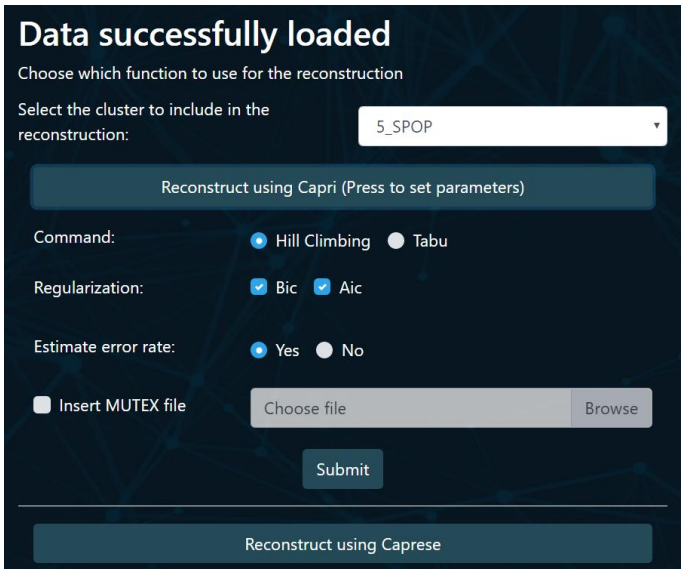
After the clustering step, the user will be redirected to a page for the model reconstruction.

These images on the left show the interface for the reconstruction:



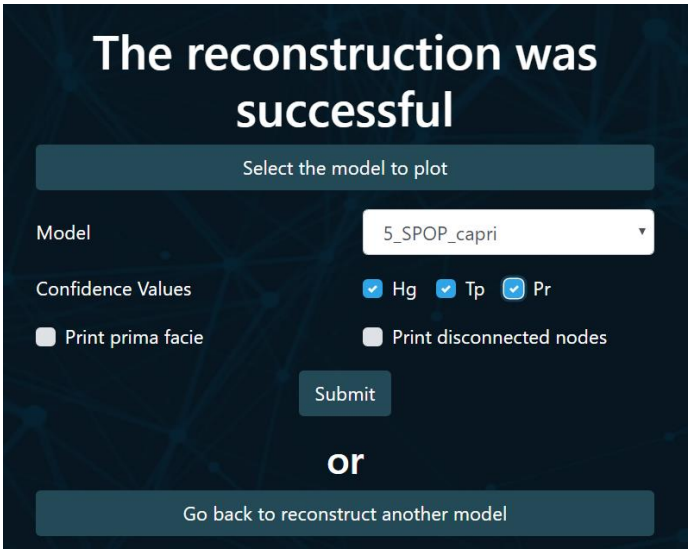
First, the user needs to select which one among the clusters will be used.

Second, the user can decide which algorithm to use. In case ‘Capri’ is chosen, some parameters need to be set:



- **Command**: it defines the heuristic search to be performed.
- **Regularization**: it selects the regularization for the likelihood estimation.
- **Error rate**: it enables or disables the estimation of the error rates give the reconstructed model.
- **Mutex**: this can be used to insert a file containing a list of mutually exclusive mutations, created through the MUTEX tool.
For more information visit https://github.com/PathwayAndDataAnalysis/mutex.

4: Plot

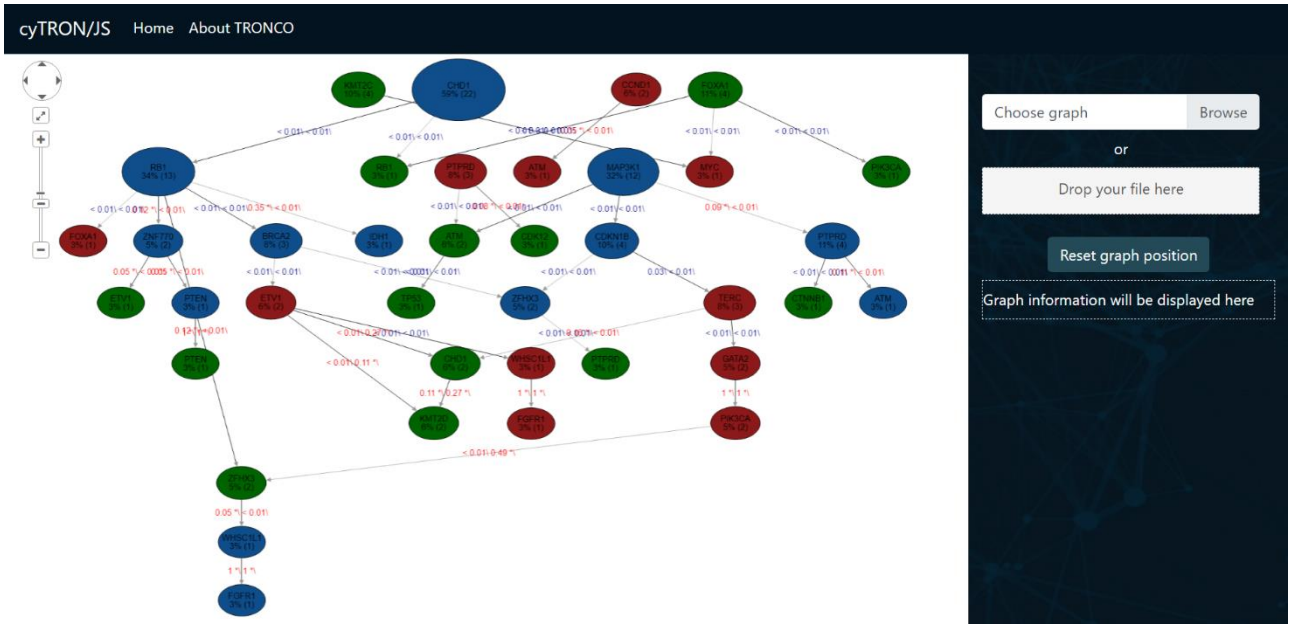


This is the page displayed after the reconstruction has finished. Here the user can decide to either reconstruct another model or plot one which has already been constructed.

To plot a model, the user needs to indicate which confidence values have to be displayed for every edge in the model, if *prima facies* needs to be displayed, and if disconnected nodes should be included in the visualization.

4: Visualization

After the previous step, a .graphml file containing the progression model is created, and it is displayed in the following page:



Here a user can click on the model's nodes to get more information about a gene and can read confidence information for each edge by clicking on them.

3) COADREAD example

Pre-requisites:

The input data for this example can be found here: https://github.com/BIMIB-DISCo/cyTRON-js/tree/master/examples/COADREAD

Before starting this example you should follow the link and download the data.

In order to complete the coadread analysis, you should also authenticate and select a new name for this study.

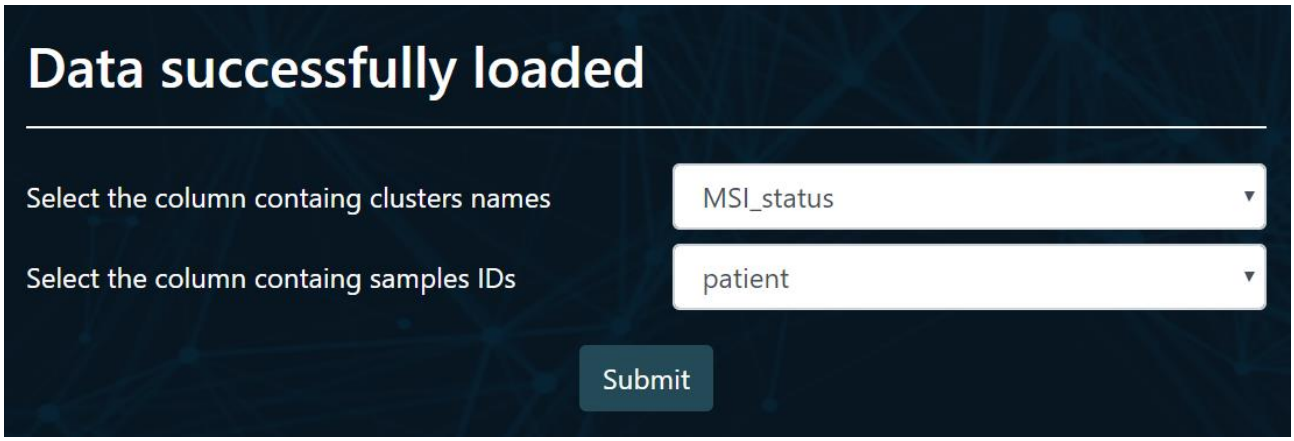
Input selection:

In the input page, you need to select the following files from the data folder you downloaded:

- MAF: for this file you need to select the ";" separator.
- GISTIC
- Genes_list: this is the file that needs to be selected in the *genes of interest* section.
- TCGA-clusters: select the ";" separator for this file

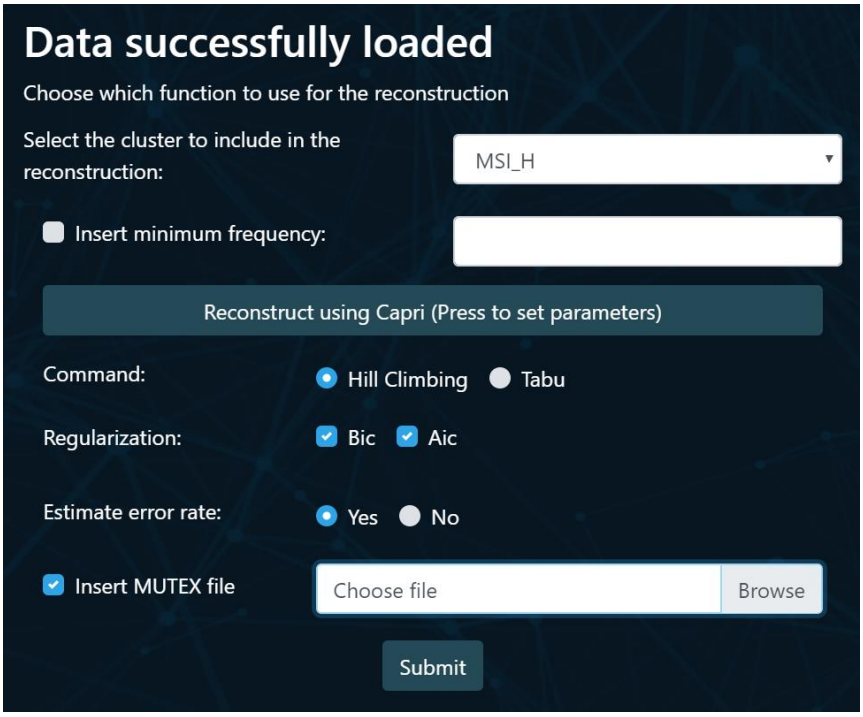
Cluster selection

After the previous step is complete, you will be redirected to a page where you need to select which columns of the clusters file contain the cluster names and the samples ID. Here you need to select the options as it is shown in the next figure:



Model reconstruction

The next step is the reconstruction of the cancer progression model. Select the parameters as it is shown below:



For this example we also consider the MUTEX file. For this reason you need to open the data folder you previously downloaded, open the *mutex* folder, and select the *msi_results* file.

Finally, click on the *submit* button, and then visualize the model.