Qualitative Flux Control (QFC)

A Matlab package to calculate the driver reactions of metabolic networks

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qfc.zip (2.3 MB)
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Running the code

Requirements:
To run this code, you need Matlab (version 2014a or newer recommended) and Tomlab (http://tomopt.com/). A demo version of Tomlab is available here.

1. Extract the contents of the enclosed qfc.zip file to a local directory.
2. Start Matlab and include the directory containing the unzipped files, including its subdirectories, in the Matlab search path.
3. The input files of the metabolic networks analyzed in the paper are found in the exctracted subdirectory 'networks'. To run the analyes on a different network, the following files must be created and named accordingly:

- <name>.S
  Stoichiometric matrix as tab-separated table.
- <name>.rev
  List of reversible reactions, where each line in the file specifies either '0' for an irreversible reaction, or '1' for a reversible reaction.
- <name>.Reactions
  List of reaction names, where each line in the file contains the name of the correspnding reaction.
- <name>.Metabolites
  List of metabolite names, where each line in the file contains the name of the corresponding metabolite.

<name> is an arbitrary network name. See the 'networks' directory for examples of input files.

4. To run all analysis on a given network, execute 'runAll(<name>)', where <name> refers to the network name specifying the input files. This runs the following calculations:
   - calculation of blocked reactions, full, partial, and directional coupling using the F2C2 tool (Larhlimi et al. (2012). BMC Bioinformatics 13, 57)
   - calculation of anti-coupling and inhibitive coupling
   - creation of flux coupling profiles and flux coupling graph
   - sampling of 100 reaction activity patterns
   - calculation of driver reactions
5. The default Tomlab solver which will be used is cplex. If you want to use a different solver, specify the name as second string argument to runAll, e.g. runAll('Ecoli_Core', 'glpk') for using the glpk solver.

Example: The following command runs all analyses on the E. coli central metabolic network 'Ecoli_Core' contained in the extracted directory 'networks/Ecoli_Core':

- runAll('Ecoli_Core');

A description of the generated output files is given in the next section.

Output files

The following output files are generated by executing the 'runAll' command:

1. <name>.blocked
   Tab-separated list of blocked reactions, where the j-th entry indicates '1', if reaction j is blocked, and '0', if reaction j is non-blocked.
2. <name>.fctable
   Coupling table generated by the F2C2 tool, where an entry (i,j) specifies the following relation for the reactions i and j:
   - 0: the reactions are not fully, partially, nor directionally coupled
   - 1: the reactions are fully coupled
   - 2: the reactions are partially coupled
   - 3: reaction i is directionally coupled to reaction j
   - 4: reaction j is directionally coupled to reaction i

3. <name>.anticoupling
   Coupling table including full, partial, directional, and anti-coupling. This is a temporary table created before calculating inhibitive coupling. The final table including inhibitive coupling is described next.
4. <name>.coupling
   Coupling table including full, partial, directional, anti, and inhibitive coupling. An entry (i,j) specifies the following relation for the reactions i and j:
   - 0: the reactions are uncoupled
   - 1: the reactions are fully coupled
   - 2: the reactions are partially coupled
   - 3: reaction i is directionally coupled to reaction j
   - 4: reaction j is directionally coupled to reaction i
   - 5: the reactions i and j are anti-coupled
   - 8: the forward direction of i is inhibitively coupled to the forward direction of j
   - 16: the forward direction of i is inhibitively coupled to the reversed direction of j
   - 32: the reversed direction of i is inhibitively coupled to the forward direction of j
   - 64: the reversed direction of i is inhibitively coupled to the reversed direction of j

   For other values, the reactions are coupled by inhibitive coupling and another coupling type, which is specified by the sum of their values. For example, the value '12' indicates that the forward direction of i is inhibitively coupled to the forward direction of j (as with '8'), and reaction j is directionally coupled to reaction i (as with '4').
5. <name>.profile
   Absolute and relative frequencies of coupling types in the network, and the number of essential reactions. The flux coupling profile is obtained from the frequencies of coupling types divided by the total number of coupled reaction pairs.
6. <name>.profile.mat
   Same as <name>.profile, but in binary Matlab format.
7. <name>.fcgraph
   Flux coupling graph as adjacency list. Every line contains the tab-separated source reaction, target reaction, and coupling type. The coupling type is given by:
   - 1: the reactions are fully coupled
   - 2: the reactions are partially coupled
   - 3: reaction i is directionally coupled to reaction j
   - 5: the reactions i and j are anti-coupled
   - 6: reaction i is is inhibitively coupled to reaction j
8. <name>.split.fcgraph
   As <name>.fcgraph, but here reversible reactions are represented separately by their name, followed by [+] for the forward direction, or [-] for the reversed direction.
9. <name>.png
   Image of the plotted flux coupling profile.
10. <name>.samples
    Sampled reaction activity patterns, where each row corresponds to a sample, and each column corresponds to a reaction. '1' indicates that reaction j is active in sample i, and '0' indicates that reaction j is inactive in sample i.
11. <name>.drivers
    Driver reactions over sampled reaction activity patterns. An entry (i,j) of '1' indicates that reaction j is a driver for controlling the activity patterns given by sample i, while '0' indicates that reaction j is not a driver for the corresponding activity patterns.

Comments, suggestions

If you have comments on the tool, or if you receive an error message, please send us the error output and the file 'ErrorXYZ_<date,time>', which is created with the date and time the error occurred.