Pathway Analyser

for FBA/MoMA analyses of metabolic pathways

11th SBML Forum

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October 12, 2006

Background

- Metabolic networks of several organisms have been reconstructed
- Constraint-based analyses are popular for genome-scale models
- FBA/MoMA have been used in various applications, from metabolic engineering to drug target identification

Implementation

- Written in C++
- Input:
  - Accepts (only) SBML input
    - Flux annotations?
  - Uses `modifiers` to keep track of gene–reaction associations for performing gene deletions
  - Lower and upper bounds specified in separate files
  - Objective function for FBA, specified in a sparse format
- Output:
  - Gene deletion report (essentiality)
  - Flux values — for deletions and wild-type

Implementation — Math

- The stoichiometric matrix is stored in sparse format (co-ordinate format $O(nz)$)
- FBA is a linear programming problem: solved using the interior point method from the GNU Linear Programming Toolkit (GLPK)
- MoMA is a quadratic programming problem: uses optimisation routines from Object Oriented Quadratic Programming (OOQP)

Mycolic Acid Pathway in *Mycobacterium tuberculosis*

- Model (Raman *et al*, 2005)
  - 197 metabolites
  - 219 reactions
  - 28 proteins
  - BIOMODELS.NET: MODEL8568434338 (Raman2006_MycolicAcid)
- Objective function: Maximise production of mycolates (α, methoxy and keto)
- Usage:
  `PA_FBA -f MAP` : Looks for `MAP.sbml`, `MAP.objfn`, `MAP.ub`, `MAP.lb` and solves the FBA. Similar for MoMA.
  Outputs `MAP.FBA.delReport`.

Essential genes in Mycolic Acid Pathway

```
Gene Deletion Report for MAP.sbml (MAP)

Mutant             Function Value   Essentiality

Wild                -0.012963
acpS                -0.012963       NON-ESSENTIAL
birA                -0.012963       NON-ESSENTIAL
accA3               -0.000000       ESSENTIAL
accD3               -0.000000       ESSENTIAL
fas                 -0.000000       ESSENTIAL
...
mmaA3               -0.012963       NON-ESSENTIAL
cmaA2               -0.012963       NON-ESSENTIAL
mmaA1               -0.012963       NON-ESSENTIAL
unk2                -0.012963       NON-ESSENTIAL
```

Availability and Requirements

- Project home page: *http://sourceforge.net/projects/pathwayanalyser*
- Operating system(s): Linux/UNIX
- Programming language: C++
- Other requirements: Libraries — GLPK, OOQP, SBML
- License: GNU GPL

References

- Karthik Raman, Preethi Rajagopalan and Nagasuma Chandra. Flux Balance Analysis of Mycolic Acid Pathway: Targets for Anti-Tubercular Drugs. *PLoS Comput Biol*, **1**:e46