Mathematica Notebook for Calculating Extreme Pathways

version 1.01 - April 4, 2006

Questions, Comments & Suggestions to myeung@be-research.ucsd.edu

1 Introduction

This documentation accompanies the Mathematica notebook created for the calculations of extreme pathways using the algorithm described in [2]. Two primary inputs are required from the users:

- The initial tableau $\mathbf{T}^0$, implemented as **InitialMtrx**; and
- the list of indices corresponding to the free metabolites, implemented as **FreeMet={}**.

Background of the theory of extreme pathways, as well as its use and the construction of the initial tableau $\mathbf{T}^0$ can be found in [2]. For a detailed explanation of the algorithm *and* the format of the tableau used in the notebook, please refer to [3].

2 Limitation

This Mathematica notebook is meant to be used on relatively small systems for either educational or demonstrative purposes only. Although it can handle larger systems (such as the *E.coli* core model provided), it is not recommended due to expensive computation time.

3 Procedure

The initial tableau, $\mathbf{T}^0$, and the list of free metabolites, **FreeMet**, were considered to be the minimal set of inputs required from the users. Given these two inputs, users must firstly evaluate the cell(s) containing these inputs. Once this is done, the user can then evaluate the cell that carries out preprocessing functions, such as calculating additional necessary parameters, as well as extreme pathways itself.

Once the calculation is completed, the users may choose to evaluate the additional cells for the removal of nullified part of the tableau and reveal the extreme pathway matrix $\mathbf{P}$, as well as exporting it as a text file for further analysis.

Three sample inputs are provided: the Red Blood Cell metabolic network, a small toy system, and the *E.coli* core metabolite network model. The *E.coli* model is located at the end of the notebook due to its size and calculation time required. Additional information about the layout of the notebook is given in the notebook itself.

For users using version 5+ of Mathematica, it is possible to store **InitialMtrx** as **SparseArray**[ ] by adjusting the inputs accordingly.

4 Technical Implementation

4.1 Ordering of Column of Iteration

The general extreme pathway algorithm presented in [2] was used. At each iteration, the column, not corresponding to a free metabolite, which produces the least number of rows in the subsequent tableau is chosen. Reason for this procedure is explained in [1].

4.2 Conical Independence Check

The first observation made was that at each iteration, rows with zero at the column of iteration (old rows) are automatically mutually independent. Hence it suffices to check for independence, firstly, amongst the newly formed rows and, secondly, amongst the independent new rows and the old rows. This method was found to be faster than checking all rows against all other rows or checking for independence of each newly formed row against existing one in the tableau before appending (a mathematical proof is available).

For the test itself, we firstly write $A_i = \left\{k : t_{i,k}^{(p)} = 0\right\}$ representing the set of indices of the zero element for row vector $\mathbf{t}_i$ at p-th iteration. For two given rows $\mathbf{t}_i$ and $\mathbf{t}_j$, let $\alpha = |A_i \cap A_j|$. If $\alpha = |A_i| \neq |A_j|$, then $A_i \subset A_j$ since $\alpha \leq \min\{|A_i|, |A_j|\}$, thus row i can be removed, and vice versa. Clearly if $\alpha = |A_i| = |A_j|$ then either one of the rows can be removed. For the actual test, whichever row that is appended in the tableau first takes presidence. Hence if $\alpha = |A_i| = |A_j|$, and assuming $\mathbf{t}_i$ is already in the tableau and the independence of $\mathbf{t}_j$ is the question, then $\mathbf{t}_j$ is simply not appended to the tableau. This implementation of conical independence test is possible in Mathematica by using built-in functions.

References

[1] Bell, S.L. and Palsson, B. (2004) **ExPA: A Program for Calculating Extreme Pathways in Biochemical Reaction Networks** *Journal of Bacteriology*, **187(16)**: 5818-5830.

[2] Schilling,C.H., Letscher, D.L., & Palsson, B.Ø. (2000) **Theory for the Systemic Definition of Metabolic Pathways and their use in Interpreting Metabolic Function from a Pathway-Oriented Perspective** *J. theor. Biol.,* **203**: 249-283.

[3] `http://binfo.ym.edu.tw/sb/pdf/BST_Section_9_1.pdf`