TrimGdel

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INTRODUCTION

TrimGdel determines a minimal gene deletion strategy to achieve growth-coupled production for a given target metabolite and a genome-scale model even in the worst-case analysis (ensures the weak-growth-coupled production). It should be noted that TrimGdel directly implements the Boolean functions of GPR rules, whereas gMCS-based methods convert GPR rules into a stoichiometric representation, which may introduce approximations in the Boolean functions. Consequently, the gene deletion strategies derived from TrimGdel often differ from those obtained using gMCS-based methods. On the other hand, the gMCS-based methods can ensure growth-coupled production even when the growth rate is not maximized. (ensures the strong-growth-coupled production)

MATERIALS - EQUIPMENT SETUP

MATLAB and Gurobi are required for this version.

PROCEDURE

1. Toy example (~5 sec)

In this tutorial, we apply TrimGdel to a toy example represented in Fig. 2 of [1].

First we load the small toy exapmle of Fig. 2 of [1]. The target metabolite is set as m6.

```
load('TrimGdelToyExample.mat');
targetMet = 'm6'
```

2. Step 1

As Step 1 of TrimGdel, gDel_minRN is applied. gDel_minRN identifies the gene deletion strategy that leads to growth-coupled production while maximizing the number of reppressed reactions.

gdel_minRN iteratively finds and verifies candidate solutions. If a candidate does not lead to growth-coupled production, it is added to the exclusion set, and the next candidate is explored. maxloop sets the upper limit on the number of iterations, which is set to 1 here.

When searching for candidate solutions, lower bounds are set for the growth rate and production rate, represented by GRLB and PRLB, respectively. Here, both are set to 1.

Step 1 (gDel_minRN) outputs gvalue, which represents the gene deletion strategy; gr, the maximum growth rate achieved; pr, the minimum production rate when the growth rate is maximized; it, the number of iterations required to find a solution; and success, indicating whether the process was successful or not.

The obtained strategy represented by gvalue deletes three genes, g1, g3, g4. gr = 5, pr = 5, it = 1, and success = 1 are obtained.

```
maxLoop = 1;
PRLB = 1;
GRLB = 1;

[gvalue gr pr it success] = gDel_minRN(model, targetMet, maxLoop, PRLB,
GRLB) % Step 1
```

3. Steps 2 and 3

Steps 2 and 3 reduces the size of gene deletions, starting with the gene deletion strategy obtained by Step 1. When Step 1 fails, Steps 2 and 3 are omitted and TrimGdel outputs failure.

The obtained strategy represented by gvalue deletes only one genes, g4. GR = 10, PR = 10, size1 = 3, size2 = 3, and size3 = 1 are obtained.

```
if success
     [gvalue, GR, PR, size1, size2, size3] = step2and3(model, targetMet,
gvalue) % Step 2 and 3


else
    gvalue = [];
    GR = 0;
    PR = 0;
    size1 = 0;
    size2 = 0;
    size3 = 0;
end
```

ANTICIPATED RESULTS

GR = 10, PR = 10, size1 = 3, size2 = 3, size3 = 1 gvalue indicates the deletion of only g4 (b0004).

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REFERENCES

1. Tamura, T. Trimming gene deletion strategies for growth-coupled production in constraint-based metabolic networks: TrimGdel. IEEE/ACM Transactions on Computational Biology and Bioinformatics. 20, 2, 1540-1549 (2023).