# Metabolic Modelling, Spring 2009, Exercises
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# Solutions

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1. Building the stoichiometric matrix.

   Nothing produces A, B and D; and nothing consumes J and H. Thus the system as such is a closed one, where likely no meaningful steady state exists. To make the system an open one, we add exchange reactions:

$$
\begin{aligned}
r_8 : &\quad \rightarrow A \\
r_9 : &\quad \rightarrow B \\
r_{10} : &\quad \rightarrow D \\
r_{11} : &\quad H \rightarrow \\
r_{12} : &\quad J \rightarrow
\end{aligned}
$$

   The stoichiometric matrix is:

```
-1     0     0     0     0     0     0     1     0     0     0     0
 0    -1     0     0     0    -1     0     0     1     0     0     0
 1    -1     0     0     0     0     0     0     0     0     0     0
 0     0    -1     0     0     0     0     0     0     1     0     0
 0     1    -1    -1     0     0     0     0     0     0     0     0
 0     0     1     0    -2     0     0     0     0     0     0     0
 0     0     0     1     0    -1     0     0     0     0     0     0
 0     0     0     0     1     0     0     0     0     0    -1     0
 0     0     0     0     0     1    -1     0     0     0     0     0
 0     0     0     0     1     0     1     0     0     0     0    -1
```

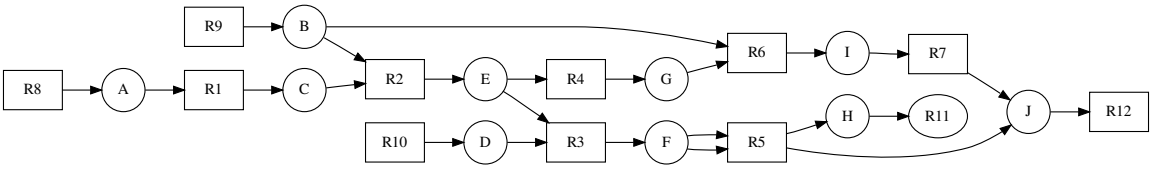


Figure 1: Metabolic network.

2. The kernel matrix found by solving the null space of stoichiometric matrix:

```
 0.0270    0.3907
 0.0270    0.3907
 0.4060    0.2918
-0.3790    0.0989
 0.2030    0.1459
-0.3790    0.0989
-0.3790    0.0989
 0.0270    0.3907
-0.3519    0.4897
 0.4060    0.2918
 0.2030    0.1459
-0.1760    0.2448
```

The dead ends can be found by checking whether any zero rows exist in the kernel matrix. There are no dead ends.

An enzyme subset consists of reactions which must operate in fixed ratio in any steady state. This is computed from kernel matrix: enzyme subset rows are scalar multiples of each other. Here the subsets are $\{1, 2, 8\}$, $\{3, 5, 10, 11\}$, $\{4, 6, 7\}$ and $\{9, 12\}$.

Conserved pools of metabolites are seen from the left null space. It's empty and no conserved pools of metabolites exist.

Elementary flux modes can be found by visual inspection. There are no cycles in the model, which makes our job easier. There are two EFM's, the first one producing both H and J, and the other one producing only J.

```
2     1
2     1
2     0
0     1
1     0
0     1
0     1
2     1
2     1
2     0
1     0
1     1
```

In the first EFM metabolites A,C,B,E,D,F,H,J are active. In the second one A,C,B,E,J,G,I,J are active.

3. Let's formulate the problem:

$$\max \sum_{i=1}^{12} c_i v_i = \max 1 \cdot v_{12}$$
$$\mathbf{Sv} = \mathbf{0}$$
$$v_9 \leq 1$$
$$v_i \geq 0$$

To solve this in matlab, we need optimization function (zero vector except for 12'th position 1), stoichiometric matrix, zero vector for stoichiometric matrix, upperbound vector (infinities except for 9th entry 1) and lowerbound vector (zeros). Also, because matlab's linprog minimizes, we negate the optimization vector to get a maximum.

```
f =

     0
     0
     0
     0
     0
     0
     0
     0
     0
     0
     0
     1

b =

     0
     0
     0
     0
     0
     0
     0
     0
     0
     0
     0

b_lb =

     0
     0
     0
     0
     0
```

```
     0
     0
     0
     0
     0
     0
     0

b_ub =

   Inf
   Inf
   Inf
   Inf
   Inf
   Inf
   Inf
   Inf
     1
   Inf
   Inf
   Inf

>> [flux, yield] = linprog(-f, [], [], S, b, b_lb, b_ub)
Optimization terminated.

flux =

    0.8121
    0.8121
    0.6242
    0.1879
    0.3121
    0.1879
    0.1879
    0.8121
    1.0000
    0.6242
    0.3121
    0.5000


yield =

   -0.5000
```

The maximum production of J is 0,5. This solution most likely is unique.

4. With input set $\{r_8, r_9\}$ the reachable nodes are A, B, C, D, E, G, I, J. F and H are not reachable. Reachable reactions are 8,9,1,2,4,6,7,12. Reactions

3,5,10 and 11 are not reachable.

In the procedure, one first adds the products of reactions 8 and 9: A and B. Reaction 1 is now reachable, and it produces C. This makes reaction 2 available, and E with it. Now reaction 4 is available, which produces G. Next reaction 6 can be produced with B and G, and then I, R7, J and R12. Reaction 3 remains unreachable because D is not reachable.

With also $r_{10}$ in the input set, all the reactions and metabolites are reachable.

J is possible to produce without uptake of D, which was seen in the reachable sets. This could also be computed using linear programming and FBA, where one would set the reaction $v_{10} = 0$ and try to produce J.