Enumerate reaction networks composed with elementary reactions
November 2014

This particular code is to enumerate all possible reaction networks (with certain dimensions, $n \times m$ where n is speciese number m is reaction number) composed of three types of interactions:

$$A + B \rightarrow C$$
$$\mathrm{D} \rightarrow E + F$$
$$G \rightarrow H$$

Those are heterodimerization, disassociation and single transformation. However, we did not include $I \rightarrow 2J$ and $2K \rightarrow L$ those two type of elementary reaction here, we should implement those in near future.

With three types of elementary reactions above, we could construct a set of reaction networks, then we could use DSR graphs and/or bipartie graph to characteristic those networks whether they are multistationary and has closed competition loop (as well as interchangeable competitors).

The main purpose of this document is to explain the procedures that how to construct and enumerate all possible reaction networks when given fixed reaction number and species number.

If a chemical reaction network has m reactions driven by n chemical species, we could have a stoichiometric matrix $N_{m \times n}$ with dimension

But before to go through such checking, we need to preclude situations that clearly not a complex balanced reaction network, by which mean it obeys the following three constraints:

0. Only allow elementary reactions described above, which is the starting point to construct the matrix; (NB: we don't consider birth-death process like $\varnothing \rightarrow X$ and $Y \rightarrow \varnothing$)

a). list all possibly reaction vectors N_i $(i = 1 \,..n)$ and select m of those into matrix (sequence does not matter)

The total number of reaction vectors for $G \rightarrow H$ is $\binom{n}{2} \cdot 2$ (since we need to consider the sides of two species in a reaction);

The total number of reaction vectors for $A + B \rightarrow C$ and $\mathrm{D} \rightarrow E + F$ are both $\binom{n}{3} \cdot 3$ (same here);

We get $r = \binom{n}{2} \cdot 2 + \binom{n}{3} \cdot 3$ number of reaction vectors, we store it in matrix $R_{r \times n}$, then we construct all the stoichiometric matrix by choosing m reaction vectors from $R_{r \times n}$ into $N_{m \times n}$, therefore we have total number of $\binom{r}{m}$ matrices to construct. Each constructed matrix $N_{m \times n}$ will go through balanced checking, mass conservation checking to become a valid stoichiometric matrix to go through further bistability check and competition check.

b). (Optional) We could further reduce the number of matrices when constructing them, in the set of constructed matrices there are huge number of matrices are isomorphic, which means any matrix in the set

with column permutation is another matrix in the set. (I did not prove this, I am thinking because I enumberated all possibility in each reaction vector which means no matter how to permutate the columns in a matrix, after permutation the matrix always falls in the same set). Now the set is closure for column permutation, so does the set of $N_{(m-1)\times n}$, then if we construct the set of $N_{m\times n}$ from $N_{(m-1)\times n}$, we just need to add one in three reaction vectors (because with any column permutation we always get an isomorphic graph, the number of nth reaction vector is 3:
[1, −1, 0, 0, ... , 0], [1, 1, −1, 0, ... , 0], [1, −1, −1, 0, ... , 0], because the position of 1 and −1 are not important), in this treatment, we can reduce the number of matrices from $\binom{r}{m}$ to $\binom{r}{m-1}\cdot 3$.

c). Further, we could reduce the number to $\binom{r}{m-2}\cdot 43$ for $n = 5$, or $\binom{r}{m-2}\cdot 46$ for $n \geq 6$. 43 and 46 are the unique reaction patterns for two reactions between n species. I listed these reaction vectors manually, and implemented it in the code.

1. Mass conservation;

Based on the stoichiometric matrix $N_{m\times n}$, we can construct a vector of mass values $\boldsymbol{m}$, m_i is the mass value of species S_i. Then we have the equation $N\boldsymbol{m} = \mathbf{0}$, because in each reaction the mass of left (reactants) is equal to mass of right (products). We need to make sure $\boldsymbol{m}$ is strictly positive.

a). firstly we check the rank of N (or linearly dependent), if $Rank(N) < m$, then it is linearly dependent, otherwise reject the matrix.

b). then caculate the nullspace basis of N. Then if the ith element in all basis is 0 or negative then m_i is 0 or negative. (This is not clear, may need some prove. When Maple compute the nullspace basis, it always return basis with 1s in $\boldsymbol{e}_j$ which means in the solution space $\sum x_j\boldsymbol{e}_j$, x_j must be strictly positive.)

2. Complex banlanced: each species has at least one in flow and one out flow (this is very easy to check);

Then we need to:

4. check competition: there are at least one species has two −1 and there is another −1 in each of the according reactions;

a). Get the N_- which only have the negative elements in N. In negative matrix, check the RowSum get indices I of −2 and check the ColumnSum get indices J of $Cs_i \leq -2$, if there are two indices $i, h \in I$ and one index $j \in J$ with which $N_{hj} = N_{ij} = -1$, $i = 1..m$, then there is competition.

5. check loop: take indices of competitors, do the network searching, find the loop from one to another and then from the other to this one.

this is fairly easy to understand, I use breadth-first search. For now, there are some small problem with competition loop checking.

Cluster matrix into four categories: bistable with closed competition loop, bistable without closed competition loop, monostable with closed competition loop, monostable without closed competition loop.

All the procedure are implemented in the code. Any suggestions and corrections are more than welcome.

- **Initializations**

- **Functions for constructing stoichiomatric matrix and examine the existence of competition and closed loop.**
  - **1. To enumerate stoichiomatric vectors (reaction patterns)**
  - **2. Now we can construct stoichiomatric matrix based on the reaction patterns, and examine their properties.**

- **Testing**