

Chemical Reaction Networks Formalism

(notes for Rutgers 640:336, E.D. Sontag, Sep 2006)

1 Chemical Networks

We next discuss a formalism that allows one to easily write up differential equations associated with chemical reactions given by diagrams like



In generally, we consider a collection of chemical reactions that involves a set of n_s “species”:

$$S_j, \quad j \in \{1, 2, \dots, n_s\}.$$

These “species” may be ions, atoms, or molecules (even large molecules, such as proteins). We’ll just say “molecules”, for simplicity. For example, (1) represents a set of two reactions that involve the following $n_s = 3$ species (hydrogen, oxygen, water):

$$S_1 = H, \quad S_2 = O, \quad S_3 = H_2O,$$

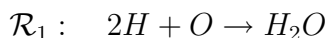
one going forward and one going backward. In general, a *chemical reaction network* (“CRN”, for short) is a set of chemical reactions $\mathcal{R}_i, i \in \{1, 2, \dots, n_r\}$:

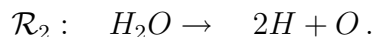
$$\mathcal{R}_i: \quad \sum_{j=1}^{n_s} \alpha_{ij} S_j \rightarrow \sum_{j=1}^{n_s} \beta_{ij} S_j \quad (2)$$

where the α_{ij} and β_{ij} are some nonnegative integers, called the *stoichiometry coefficients*.

The species with nonzero coefficients on the left-hand side are usually referred to as the *reactants*, and the ones on the right-hand side are called the *products*, of the respective reaction. (Zero coefficients are not shown in diagrams.) The interpretation is that, in reaction 1, α_{11} molecules of species S_1 combine with α_{12} molecules of species S_2 , etc., to produce β_{11} molecules of species S_1 , β_{12} molecules of species S_2 , etc., and similarly for each of the other $n_r - 1$ reactions.

The forward arrow means that the transformation of reactants into products only happens in the direction of the arrow. For example, the reversible reaction (1) is represented by the following CRN, with $n_r = 2$ reactions:





So, in this example,

$$\alpha_{11} = 2, \quad \alpha_{12} = 1, \quad \alpha_{13} = 0, \quad \beta_{11} = 0, \quad \beta_{12} = 0, \quad \beta_{13} = 1,$$

and

$$\alpha_{21} = 0, \quad \alpha_{22} = 0, \quad \alpha_{23} = 1, \quad \beta_{21} = 2, \quad \beta_{22} = 1, \quad \beta_{23} = 0.$$

It is convenient to arrange the stoichiometry coefficients into an $n_s \times n_r$ matrix, called the *stoichiometry matrix* $\Gamma = \Gamma_{ij}$, defined as follows:

$$\Gamma_{ji} = \beta_{ij} - \alpha_{ij}, \quad i = 1, \dots, n_r, \quad j = 1, \dots, n_s \quad (3)$$

(notice the reversal of indices).

The matrix Γ has as many columns as there are reactions. Each column shows, for all species (ordered according to their index i), the net “produced–consumed”. For example, for the reaction (1), Γ is the following matrix:

$$\begin{pmatrix} -2 & 2 \\ -1 & 1 \\ 1 & -1 \end{pmatrix}.$$

Notice that we allow degradation reactions like $A \rightarrow 0$ (all β 's are zero for this reaction).

Homework: Find the matrix Γ for each of the reactions shown in Section 6.1 of the notes as well as in the homework problems in the course website.

We now describe how the state of the network evolves over time, for a given CRN. We need to find a rule for the evolution of the vector:

$$\begin{pmatrix} [S_1(t)] \\ [S_2(t)] \\ \vdots \\ [S_{n_s}(t)] \end{pmatrix}$$

where the notation $[S_i(t)]$ means the concentration of the species S_i at time t . For simplicity, we drop the brackets and write S_i also for the concentration of S_i (sometimes, to avoid confusion, we use instead lower-case letters like s_i to denote concentrations). As usual with differential equations, we also drop the argument “ t ” if it is clear from the context. Observe that only nonnegative concentrations make physical sense (a zero concentration means that a species is not present at all).

The graphical information given by reaction diagrams is summarized by the matrix Γ . Another ingredient that we require is a formula for the actual rate at which the individual reactions take place.

We denote by $R_i(S)$ be algebraic form of the j th reaction. The most common assumption is that of *mass-action kinetics*, where:

$$R_i(S) = k_i \prod_{j=1}^{n_s} S_j^{\alpha_{ij}} \text{ for all } i = 1, \dots, n_r.$$

This says simply that the reaction rate is proportional to the products of concentrations of the reactants, with higher exponents when more than one molecule is needed. The coefficients k_i are “reaction constants” which usually label the arrows in diagrams. Let us write the vector of reactions as $R(S)$:

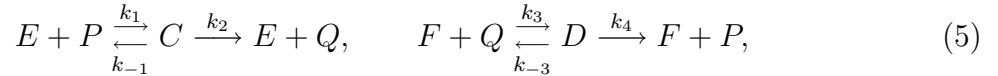
$$R(S) := \begin{pmatrix} R_1(S) \\ R_2(S) \\ \vdots \\ R_{n_r}(S) \end{pmatrix}.$$

With these conventions, the system of differential equations associated to the CRN is given as follows:

$$\frac{dS}{dt} = \Gamma R(S). \quad (4)$$

Example

As an illustrative example, let us consider the following set of chemical reactions:



which may be thought of as a model of the activation of a protein substrate P by an enzyme E ; C is an intermediate complex, which dissociates either back into the original components or into a product (activated protein) Q and the enzyme. The second reaction transforms Q back into P , and is catalyzed by another enzyme (a phosphatase denoted by F). A system of reactions of this type is sometimes called a “futile cycle”, and reactions of this type are ubiquitous in cell biology. The mass-action kinetics model is then obtained as follows. Denoting concentrations with the same letters (P , etc) as the species themselves, we have the following vector of species, stoichiometry matrix Γ and vector of reaction rates $R(S)$:

$$S = \begin{pmatrix} P \\ Q \\ E \\ F \\ C \\ D \end{pmatrix}, \quad \Gamma = \begin{pmatrix} -1 & 1 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & -1 & 1 & 0 \\ -1 & 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & -1 & -1 \end{pmatrix} \quad R(S) = \begin{pmatrix} k_1 EP \\ k_{-1} C \\ k_2 C \\ k_3 FQ \\ k_{-3} D \\ k_4 D \end{pmatrix}.$$

From here, we can write the equations (4). For example,

$$\frac{dP}{dt} = (-1)(k_1 EP) + (1)(k_{-1} C) + (1)(k_4 D) = k_4 D - k_1 EP + k_{-1} C.$$

Conservation Laws

Let us consider the set of row vectors c such that $c\Gamma = 0$. Any such vector is a *conservation law*, because

$$\frac{d(cS)}{dt} = c \frac{dS}{dt} = c\Gamma R(S) = 0$$

for all t , in other words,

$$cS(t) = \text{constant}$$

along all solutions (a “first integral” of the motion). The set of such vectors forms a linear subspace (of the vector space consisting of all row vectors of size n_s).

For instance, in the previous example, we have that, along all solutions, one has that

$$P(t) + Q(t) + C(t) + D(t) \equiv \text{constant}$$

because $(1, 1, 0, 0, 1, 1)\Gamma = 0$. Similarly, we have two more linearly independent conservation laws, namely $(0, 0, 1, 0, 1, 0)$ and $(0, 0, 0, 1, 0, 1)$, so also

$$E(t) + C(t) \quad \text{and} \quad F(t) + D(t)$$

are constant along trajectories. Since Γ has rank 3 (easy to check) and has 6 rows, its left-nullspace has dimension three. Thus, a basis of the set of conservation laws is given by the three that we have found.

Homework. Find, for each of the problems in the notes and web-posted homework assignment, a basis of conservation laws.

Optional homework. This one is a bit more complicated, but also very interesting. The example covered before can be summarized as in Figure 1(a). Many cell signaling processes involve double instead of single transformations such as addition of phosphate groups. A model for a double double-phosphorylation as in Figure 1(b) corresponds to

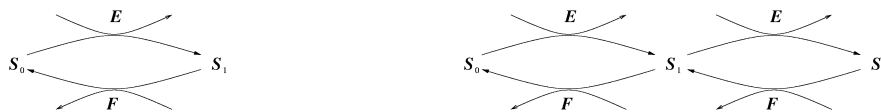
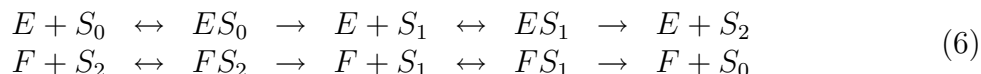


Figure 1: (a) *One-step* and (b) *two-step transformations*

reactions as follows (we use double arrows for simplicity, to indicate reversible reactions):



where “ ES_0 ” represents the complex consisting of E bound to S_0 and so forth. You should attach constants to all arrows and write up the system of ODE’s. Show also that there is a basis of conservation laws consisting of three vectors.