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Stability of Stoichiometric Networks with Conservation Constraints: the case of catalytic carbonylation model

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Abstract

Stability analysis of stoichiometric networks with conservation constraint is described aiming to underlie specificities of this family of dynamic systems and to offer the procedure for their treatment. The main goal of this paper is to highlight complications and common mistakes, which may occur in stoichiometric network analysis of such systems. The model of catalytic carbonylation of alkyne-functionalized poly(ethylene glycol) is used as an example for the illustration of proper stability analysis. After several simplifications of the model, source of instability is determined.

Keywords: Stoichiometric network analysis, Conservation constraint, Catalytic carbonylation, Alkyne-functionalized poly(ethylene glycol)

1. Introduction

The stability of stoichiometric network is in general covered by the theory of Stoichiometric Network Analysis – SNA (Clarke 1980, Clarke 1988). However, systems with conservation constraints include one family of stoichiometric networks which is rather scarcely described within this theory. For example, it is discussed in only two pages within 216 pages long paper written by Clarke, (1980). Nevertheless, the analysis of stoichiometric networks with conservation constraints could lead to significant complications.

Subject of the present work is the stability of stoichiometric networks in the less explored case when some of essential intermediary species are linearly dependent on the others. Particularly, we will analyse the difference between the stability analysis (1) if linearly dependent species are simply removed from the equations and (2) if they are replaced with
corresponding conservation conditions. For this purpose we will use the model of the catalytic carbonylation of alkyne-functionalised poly(ethylene glycol) - PEGA (Donlon and Novaković 2014) for which we know that it can explain occurrence of experimentaly observed oscillations in turbidity, pH and in the flux of energy (Table 1). This oscillatory reaction is experimentally developed following extensive studies of palladium-catalysed oxidative carboylation of phenylacetylene (Novaković et al 2007, Parker and Novaković, 2016) and is of key interest for further transitioning of soluble chemical oscillators to insoluble oscillatory materials. Properties of constrained stoichiometric networks will be broadly discussed here, with application to the example of catalytic carbonylation model used as illustration. The model is given in Table 1:

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Stoichiometry</th>
<th>Rate Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEGA + PdI₂ + 2CH₃OH + 2CO → Prod + Pd + 2HI</td>
<td>$r_1 = k_1 \text{PEGA}[\text{PdI}_2][\text{HI}]^2$</td>
<td>R1</td>
</tr>
<tr>
<td>2HI + 0.5O₂ → I₂ + H₂O</td>
<td>$r_2 = k_2 [\text{HI}]^2$</td>
<td>R2</td>
</tr>
<tr>
<td>Pd + I₂ → PdI₂</td>
<td>$r_3 = k_3 [\text{Pd}][\text{I}_2]$</td>
<td>R3</td>
</tr>
<tr>
<td>Pd + 2I₂ → PdI₂</td>
<td>$r_4 = k_4 [\text{Pd}][\text{I}_2][\text{PdI}_2]$</td>
<td>R4</td>
</tr>
<tr>
<td>PdI₂ + CH₃OH + CO → IPdR + HI</td>
<td>$r_5 = k_5 [\text{PdI}_2]$</td>
<td>R5</td>
</tr>
<tr>
<td>IPdR + HI → PdI₂ + CH₃OH + CO</td>
<td>$r_6 = k_6 [\text{IPdR}][\text{HI}]$</td>
<td>R6</td>
</tr>
</tbody>
</table>

**Table 1.** Model of the catalytic carbonylation of PEGA. Sign R stands for the -COOCH₃ group.

Fundamental relations of SNA will be presented in Section 2. Application of the SNA to the catalytic carbonylation model will be given in Section 3. Essential conclusions are offered in Section 4.

**2. Fundamental relations of SNA**

The kinetic equations of any stoichiometric model presented by the set of differential equations such as equations (1) can be written in the form $d\{X\}/dt = S \cdot r$, where $d\{X\}/dt$ is the time derivative of the concentration vector $\{X\}$, $r$ the reaction rate vector and $S$ the matrix of the stoichiometric coefficients that can be read directly from the model (see Appendix). The rates at a steady state $r_{ss}$ are solutions of the relation $S \cdot r_{ss} = 0$. According to the SNA (Clarke 1980, Clarke 1988), reversible reactions are split into two forward irreversible reactions – one for each direction, and, therefore, whole process can be presented as linear combinations of several elementary reaction pathways with non-negative coefficients. These elementary reaction pathways are known as extreme currents $E_i$. The contributions of the extreme currents, named current rates $j_i$, are the components of the corresponding vector $j$, whereas the extreme currents $E_i$ are the components of the extreme current matrix $E$. The basic equation of the SNA is $r_{ss} = E \cdot j$.

The dynamics of small concentration perturbations $\Delta\{X\} = \{X\} - \{X\}_{ss}$ near a steady state $\{X\}_{ss}$ is given by the equation $d\Delta\{X\}/dt = M\Delta\{X\}$ obtained by linearization of the general equation of motion about this steady state. Its stability depends on the sign of the real part of the eigenvalues of the Jacobian matrix $M$ given in the form

$$M(r_{ss}) = S(\text{diag } r_{ss})K^T\left(\text{diag } [\{X\}]_{ss}^{-1}\right)$$

(1)

Here, $K$ is the matrix of the orders of reaction and $K^T$ is its transpose. In the SNA (Clarke 1980), the matrix $M$ is written as
\[ M(j,h) = S(\text{diag } E j)K^T(\text{diag } h) \]

where \( \text{diag } h \) is a diagonal matrix whose elements are the reciprocals of steady state concentrations and \( \text{diag } E j \) is a diagonal matrix whose elements are the reaction rates at the steady state.

The matrix \( M \) written as function of the SNA parameters has particular advantages for the stability analysis since the parameters \( j_i \) and \( h_i \) are non-negative, what is an essential feature of the SNA. The steady state stability is determined by the eigenvalues of \( M \), which are the roots \( \lambda \) of the characteristic polynomial

\[ |\lambda I - M| = \lambda^n + \alpha_1\lambda^{n-1} + \alpha_2\lambda^{n-2} + ... + \alpha_n = 0 \]

where \( n \) is the number of independent intermediate compounds and the \( \alpha_i \) the sums of all diagonal minors of dimensions \( i \) of matrix \( M \) multiplied by the product of the corresponding \( h_i \) values. Each diagonal minor of the matrix \( M \), as the determinant of square matrix having dimension \( i \), can be formed of any combinations of \( i \) independent intermediate species. In one \( \alpha_i \) the number of minors is equal to number of different combinations of \( i \) intermediates. It has been shown that the SNA allows to approximate the Routh-Hurwitz criteria with a much simpler condition: the steady state is unstable if any \( \alpha_i \) is negative (\( \alpha \) approximation) (Clarke 1980, Clarke 1992, Clarke and Jiang 1993). Besides, since \( \text{diag } h \) introduces only scaling factors, it is useful to define

\[ V(j) = -S(\text{diag } E j)K^T \]

giving \( M = -V(j) (\text{diag } h) \). As any \( \alpha_i \) is the sum of minors of \( V(j) \) with dimension \( i \) multiplied by the product of the corresponding \( h_i \) values, we look for a negative diagonal minors of \( V(j) \). If we find negative minors in one \( \alpha_i \) we ask if the sum of negative terms can be larger than the sum of positive terms in same \( \alpha_i \). Although it is an approximation, this criterion often gives very good results. (Schmitz et al. 2008, Jelić et al. 2009, Kolar-Anić et al. 2010, Maćešić et al. 2012, Maćešić et al. 2016, Maćešić et al. 2015, Marković et al. 2016; Čupić et al. 2016)

### 2.1 SNA equations of networks with conservation constraints

If concentrations of some intermediary species are linearly dependent on others due to some conservation constraint, their values are interconnected through the relation of the form \( \gamma X = C \), where \( \gamma \) is the conservation matrix, and \( C \) is the constant vector with total concentrations of conserved species. In this case, matrix \( M \) constructed from all species would be singular, leading to complications in evaluation of stability. The concentration of linearly dependent species could be separated from the independent ones. In such way their sum is formed by addition of these two terms:

\[ \gamma_1 X_1 + \gamma_D X_D = C \]

where subscripts \( D \) and \( I \) stands for dependent and independent species. Dependent variables are expressed as functions of independent ones:

\[ X_D = \gamma_D^{-1}C - \gamma_D^{-1}\gamma_1 X_1 \]
Jacobian matrix $M$ is then divided into four parts:

$$\frac{d}{dt} \begin{bmatrix} \Delta X_I \\ \Delta X_D \end{bmatrix} = \begin{bmatrix} M_{II} & M_{ID} \\ M_{DI} & M_{DD} \end{bmatrix} \begin{bmatrix} \Delta X_I \\ \Delta X_D \end{bmatrix}$$  \hspace{1cm} (7)

(The elements of four parts $M_{II}$, $M_{ID}$, $M_{DI}$ and $M_{DD}$ of the Jacobian matrix are $\partial \Delta \dot{X}_I / \partial \Delta X_I$, $\partial \Delta \dot{X}_I / \partial X_D$, $\partial \Delta \dot{X}_D / \partial \Delta X_I$ and $\partial \Delta \dot{X}_D / \partial X_D$, respectively.) Hence, the dynamics of the independent species can be expressed as:

$$d\Delta X_I/dt = M_{II}\Delta X_I + M_{ID}\Delta X_D$$  \hspace{1cm} (8)

Since $\Delta[X] = [X] - [X]_{ss}$ and using Eq. (6) we can find that $d\Delta[X]/dt = M^*\Delta[X]$, where

$$M^* = M_{II} - M_{ID} \gamma_D^{-1} \gamma_I.$$  \hspace{1cm} (9)

In terms of SNA parameters new linearized operator finally has a form (Clarke 1980):

$$M^*(j,h) = S_I (\text{diag } E_j) \begin{bmatrix} K_I^T (\text{diag } h_I) - K_D^T (\text{diag } h_D) \gamma_D^{-1} \gamma_I \end{bmatrix}.$$  \hspace{1cm} (10)

This is the form which should be analysed in case when some intermediary species are dependent on the others, instead of Eq. (2). The procedure will be clarified in an example of the catalytic carbonylation reaction.

### 3. Example

Due to some peculiarities we will slightly adapt the model from Table 1 to be self consistent but keep the kinetic properties of the original one. Namely, stoichiometry of reactions R1 and R4 does not correspond to the rate laws of the same reaction, given in the same Table. If we use rate laws from the Table 1, numerical simulation indeed leads to oscillations (Fig. 1). However, if we use the mass action rate law there are no oscillations in simulation (Fig. 2). Hence, the model is first modified by addition of two molecules of HI on both sides of R1, and one molecule of PdI$_2$ on both sides of reaction R4. This is how we achieved that rate laws given in Table 1 are consistent with reaction stoichiometry given in the same Table. Furthermore, in the original paper (Donlon and Novaković 2014) assumption was adapted that concentrations of CH$_3$OH, O$_2$ and CO are much higher than others and do not change significantly. Therefore we can include these species concentrations in the rate constants, and remove them from the formal model. Finaly, we can note that species PEGA, Prod and H$_2$O are not intermediary species but either reactants or products of the proces. In this case, reaction rates either does not depend on their concentrations, or they depend only at the parametrical level. Such species are not essential for the occurance of the instability. Therefore, for the present purpose, we can eliminate these species from the model. As a result of all these changes, we obtained Model given in Table 2. This is the Model we will analyse, actually.
Fig. 1. Oscillatory evolution of HI concentration in the simulation based on Model given in Table 1, with given rate expressions.

Fig. 2. Monotonous evolution of HI concentration in the simulation based on Model given in Table 1, with rate expressions corresponding to the mass action kinetics consistent with stoichiometry of the model.

\[
PdI_2 + 2HI \xrightarrow{k_1} Pd + 4HI \\
2HI \xrightarrow{k_2} I_2 \\
Pd + I_2 \xrightarrow{k_3} PdI_2 \\
Pd + I_2 + PdI_2 \xrightarrow{k_4} 2PdI_2 \\
PdI_2 \xrightarrow{k_5} IPdR + HI \\
IPdR + HI \xrightarrow{k_6} PdI_2
\]

\[\begin{align*}
    r_1 &= k_1 [PdI_2][HI]^2 & \text{R1} \\
    r_2 &= k_2 [HI]^2 & \text{R2} \\
    r_3 &= k_3 [Pd][I_2] & \text{R3} \\
    r_4 &= k_4 [Pd][I_2][PdI_2] & \text{R4} \\
    r_5 &= k_5 [PdI_2] & \text{R5} \\
    r_6 &= k_6 [IPdR][HI] & \text{R6}
\end{align*}\]

Table 2. Modified Model of the catalytic carbylation.

The matrices of stoichiometric coefficients \( S \) and orders of reactions \( K \) for the model in Table 2, are:
Here we come to the main problem. The matrix \( S \) has a rank equal to 3. It means that two rate equations are linearly dependent on the others, due to some conservation constraints. Hence, we can use two algebraic equations, representing two conservation constraints, to simply calculate concentrations of two dependent species from the remaining independent ones. These two constraints represent the conservation of the Pd and I atoms in the system:

\[
\begin{align*}
\text{PdI}_2 & + 0\text{Pd} + 1\text{IPdR} = \text{Pd}_\text{tot} \\
2\text{PdI}_2 & + 2\text{HI} + 2\text{I}_2 + 1\text{IPdR} = \text{I}_\text{tot}
\end{align*}
\]

We can choose without losing generality that two dependent species are Pd and I₂. Then, according to Eq (5) conservation laws (15) and (16) may be expressed in matrix form:

\[
\begin{align*}
&\begin{bmatrix}
1 & 1 & 0 \\
2 & 1 & 1
\end{bmatrix}
\begin{bmatrix}
PdI_2 \\
\text{IPdR}
\end{bmatrix}
+ 
\begin{bmatrix}
1 & 0 \\
0 & 2
\end{bmatrix}
\begin{bmatrix}
Pd \\
\text{I}_2
\end{bmatrix}
= 
\begin{bmatrix}
Pd_{\text{tot}} \\
\text{I}_{\text{tot}}
\end{bmatrix}
\end{align*}
\]

For solving the stability problem we would need to use Eq. (10), but since it is much more complicated than Eq. (2) it is common practice to eliminate dependent species as if they would have a constant concentrations. In this case only part of the Jacobian matrix is used

\[
M_\Pi = S_1 (\text{diag}\ E_j) K_1^T (\text{diag}\ h_I)
\]

for the stability evaluation.

In this case we use matrix of the stoichiometric coefficients in the form:

\[
S_1 = \begin{bmatrix}
-1 & 0 & 1 & 1 & -1 & 1 \\
2 & -2 & 0 & 0 & 1 & -1 \\
0 & 0 & 0 & 1 & -1 & 1
\end{bmatrix}
\]

and

\[
K = \begin{bmatrix}
1 & 0 & 1 & 1 & 0 \\
2 & 2 & 0 & 0 & 0 & 1 \\
0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 1 & 1 & 0 & 0 \\
0 & 0 & 1 & 1 & 0 & 0
\end{bmatrix}
\]
and matrix of the reaction orders:

\[
R = \begin{bmatrix}
R_1 & R_2 & R_3 & R_4 & R_5 & R_6 \\
1 & 0 & 0 & 1 & 1 & 0 \\
2 & 2 & 0 & 0 & 0 & 1 \\
0 & 0 & 0 & 0 & 0 & 1 \\
\end{bmatrix}
\]

\[K_1 = \begin{bmatrix}
PdI_2 \\
HI \\
IPdR \\
\end{bmatrix}
\]

From these matrices we easily obtain extreme current matrix:

\[
E = \begin{bmatrix}
1 & 1 & 0 \\
1 & 1 & 0 \\
1 & 0 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1 \\
0 & 0 & 1 \\
\end{bmatrix}
\]

Furthermore, the corresponding current matrix is:

\[
V(j) = \begin{bmatrix}
-j_1 + j_3 & 2j_1 + 2j_2 - j_3 \\
-2j_1 - 2j_2 - j_3 & j_3 & j_3 \\
-j_3 & j_3 & j_3 \\
\end{bmatrix}
\]

And finally, Jacobian matrix is:

\[
M_{H}(j, h) = \begin{bmatrix}
(j_1 + j_3)h_1 & (2j_1 + 2j_2 - j_3)h_2 & -j_3h_3 \\
(-2j_1 - 2j_2 - j_3)h_1 & j_3h_2 & j_3h_3 \\
-j_3h_1 & j_3h_2 & j_3h_3 \\
\end{bmatrix}
\]

where \(h_1\)–\(h_3\) stands for reciprocal steady state concentrations of species PdI_2, HI and IPdR, and later on \(h_4\) and \(h_5\) will be used for Pd and I_2.

Coefficients of the corresponding characteristic polinomial are always positive:

\[
\alpha_1(j, h) = j_1h_1 + j_3h_1 + j_3h_2 + j_3h_3
\]

\[
\alpha_2(j, h) = 4j_1^2h_1h_2 + 8j_1j_2h_1h_2 + j_1j_3h_1h_2 + 4j_2^2h_2h_2h_3 + j_1j_3h_1h_3
\]

\[
\alpha_3(j, h) = 4j_1^2j_3h_1h_3h_3 + 8j_1j_2j_3h_1h_2h_3 + 4j_2^2j_3h_2h_2h_3
\]

According to \(\alpha\) approximation this model would not have a chance to give instability.

We will now show that this is a consequence of the fact that influence of dependent species concentrations on rates of independent ones is neglected.

One can express dependent variables according to Eq. (6) using conservation matrices given in eq. (17):
The matrix of reaction orders for dependent species is:

$$\begin{bmatrix} Pd_l \\ I_2 \end{bmatrix} = \begin{bmatrix} 1 & 0 \\ 0 & \frac{1}{2} \end{bmatrix} \begin{bmatrix} Pd_{tot} \\ I_{tot} \end{bmatrix} = \begin{bmatrix} 1 & 1 \\ 0 & \frac{1}{2} \end{bmatrix} \begin{bmatrix} Pd_{tot} \\ I_{tot} \end{bmatrix} = \begin{bmatrix} 1 & 1 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} \end{bmatrix} \begin{bmatrix} Pd_{tot} \\ I_{tot} \\ HI \end{bmatrix} = \begin{bmatrix} 1 & 1 & 0 \\ 0 & \frac{1}{2} & \frac{1}{2} \end{bmatrix} \begin{bmatrix} Pd_{tot} \\ I_{tot} \\ HI \end{bmatrix}$$ (26)

The matrix of reaction orders for dependent species is:

$$R_1 ~ R_2 ~ R_3 ~ R_4 ~ R_5 ~ R_6$$

$$K_D = \begin{bmatrix} 0 & 0 & 1 & 1 & 0 & 0 & Pd \\ 0 & 0 & 1 & 1 & 0 & 0 & I_2 \end{bmatrix}$$ (27)

Then we can use complete Eq. (10) to finally obtain Jacobian matrix, which is here given in its transposed form just from the convenience:

$$M^T(j, h) = \begin{bmatrix} j_1 h_1 + j_2 h_1 + j_3 h_4 + j_2 h_4 + j_3 h_5 + j_2 h_5 \\ 2j_1 h_1 + 2j_2 h_1 + j_3 h_4 + j_3 h_5 \end{bmatrix} - \begin{bmatrix} 2j_2 h_2 + j_1 h_4 + j_2 h_4 + j_3 h_3 + \frac{j_1 h_8}{2} + \frac{j_3 h_5}{2} - j_3 h_4 \\ j_3 h_2 + j_3 h_2 \end{bmatrix}$$ (28)

In this case, linearized operator poses additional terms indicating possibilities to generate instability. We found negative terms in:

$$\alpha_3(j, h) = 4 h_1 h_2 h_3 j_1^2 j_3 + 4 h_1 h_2 h_3 j_2^2 j_3 - h_1 h_2 h_5 j_1^2 j_3 + 2 h_1 h_3 h_4 j_1^2 j_3$$

$$- h_1 h_2 h_5 j_2^2 j_3 + 2 h_1 h_3 h_4 j_2^2 j_3 + h_1 h_3 h_5 j_1^2 j_3 + h_1 h_3 h_5 j_2^2 j_3$$

$$+ 8 h_1 h_2 h_3 j_1 j_2 j_3 - 2 h_1 h_2 h_5 j_1 j_2 j_3 + 4 h_1 h_3 h_4 j_1 j_2 j_3 + 2 h_1 h_3 h_5 j_1 j_2 j_3$$ (29)

and this is sufficient to explain instability in the system.

It can be concluded that elimination of linearly dependent species from the equations of linearized problem may lead to wrong conclusion about the stability of the system.

4. Conclusions

Stability analysis of stoichiometric networks with conservation constraint is described aiming to underlain specificities of this family of systems. Complications are highlighted, which may occur in stoichiometric network analysis of such systems. Elimination of linearly dependent species from the Jacobian matrix was identified as critical step which may lead to inaccurate stability evaluation. The simplified model of catalytic carbonylation of alkyne-functionalized poly(ethylene glycol) is used as an example to illustrate application of stability analysis.

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