Stoichiometric Network Analysis and Associated Dimensionless Kinetic Equations. Application to a Model of the Bray−Liebhafsky Reaction

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The stoichiometric network analysis (SNA) introduced by B. L. Clarke is applied to a simplified model of the complex oscillating Bray−Liebhafsky reaction under batch conditions, which was not examined by this method earlier. This powerful method for the analysis of steady-states stability is also used to transform the classical differential equations into dimensionless equations. This transformation is easy and leads to a form of the equations combining the advantages of classical dimensionless equations with the advantages of the SNA. The used dimensionless parameters have orders of magnitude given by the experimental information about concentrations and currents. This simplifies greatly the study of the slow manifold and shows which parameters are essential for controlling its shape and consequently have an important influence on the trajectories. The effectiveness of these equations is illustrated on two examples: the study of the bifurcations points and a simple sensitivity analysis, different from the classical one, more based on the chemistry of the studied system.

Introduction

The stoichiometric network analysis (SNA) introduced by Clarke[1] is a powerful method for the examination of complex systems and for the stability analysis of steady-states. It is based on the definition of new variables and parameters leading to general equations of motion with several advantages over the classical ones. This paper discusses its application to complex reactions under batch conditions and show how important results can be easily obtained. Moreover, the SNA equations can be written in a dimensionless form that combines the advantages of this kind of equations with the advantages of the SNA. They simplify greatly not only the stability analysis but also the study of the state space properties. Our topic is illustrated using one variant of the model of the oscillating Bray−Liebhafsky reaction.[2,3] It was selected because it reproduces the main features of this reaction, allowing a connection between the theory and a real oscillating system, but avoids complications related with kinetics details clearly outside the scope of the present work. This paper shows how to apply the SNA and associated dimensionless equations in a batch reactor, referring the readers to the original papers for the underlying theory.[1]

The Bray−Liebhafsky reaction is the decomposition (D) of hydrogen peroxide in the presence of iodate and hydrogen ions.

$$2H_2O_2 \xrightarrow{IO_3^-,\ H^+} 2H_2O + O_2 \qquad (D)$$

This decomposition is the result of two complex reactions in which hydrogen peroxide acts as either a reducing (R) or an oxidizing (O) agent.

$$2IO_3^- + 2H^+ + 5H_2O_2 \rightarrow I_2 + 5O_2 + 6H_2O \qquad (R)$$

$$I_2 + 5H_2O_2 \rightarrow 2IO_3^- + 2H^+ + 4H_2O \qquad (O)$$

The sum of reactions R and O gives reaction D. When the rates of these two reactions are equal, the decomposition of hydrogen peroxide is monotonous. However, under some conditions discussed in this paper, the reactions R and O dominate alternately, resulting in a cascading consumption of hydrogen peroxide and an oscillatory evolution of the intermediates.[2−5] These reactions are themselves complex and numerous investigations of the role of possible intermediates appeared.[3−9] As our aim is to show the SNA usefulness when studying such systems, we will not discuss details requiring more complex models and will use the simple model presented in Table 1. The reactions numbers are taken from our earlier publications.[10−16]

The Extreme Currents

The fundamental idea of the SNA is to express the rates of reactions using new sets of variables and parameters.[1] The variables are the ratios between the actual concentrations and their values at a steady-state and the parameters are some rates at this steady-state. Thus we need to define the steady-state chosen as reference. Here it is the smooth decomposition of hydrogen peroxide (D) called “the disproportionation steady-state”. The decomposition of hydrogen peroxide under batch conditions is slow at the considered time scale, and therefore we can assume that the concentration of hydrogen peroxide, as well as iodate and acid concentrations, is constant during the time of interest. These compounds are called external. The evolutions of the concentrations of the other compounds appearing in Table 1 (I_2, I^-, IOH, IO_2H, and I_2O) occur on a faster time scale and these compounds are called internal.[1]

At the disproportionation steady state, we have specific relations between the rates of the steps of the model, where steps means complete stoichiometric form of reactions with

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TABLE 1: Model of the Bray−Liebhafsky Reaction

reactions	no.
$IO_3^- + I^- + 2\,H^+ \rightleftharpoons IOH + IO_2H$	(R1), (R-1)
$IO_2H + I^- + H^+ \rightarrow I_2O + H_2O$	(R2)
$I_2O + H_2O \rightleftharpoons 2\,IOH$	(R3), (R-3)
$IOH + I^- + H^+ \rightleftharpoons I_2 + H_2O$	(R4), (R-4)
$IOH + H_2O_2 \rightarrow I^- + H^+ + O_2 + H_2O$	(R5)
$I_2O + H_2O_2 \rightarrow IOH + IO_2H$	(R6)
$IO_3^- + H^+ + H_2O_2 \rightarrow IO_2H + O_2 + H_2O$	(R8)

power law kinetics, even if they are not elementary. The SNA express these relations in the rates space instead of the concentrations space. Clarke[1] has proved that any set of rates values satisfying the steady state equations can be represented in the rates space as a linear combination of vectors with non-negative coefficients, named the extreme currents $\boldsymbol{E}_i$.[17] The extreme currents can be interpreted geometrically as the edges of the corresponding cone in the reaction rates space.[1,18−20] Denoting by $\boldsymbol{S}$ the matrix of the stoichiometric coefficients in the model and by s its rank, all the extreme currents are obtained looking for all nontrivial solutions with no negative component of the s independent equations $\boldsymbol{S}\,\boldsymbol{E}_i = 0$. The $\boldsymbol{E}_i$ vectors are determined only up to a positive factor that is usually chosen to get round numbers. The set of extreme currents for a given factor is unique and is represented by the $\boldsymbol{E}$ matrix where each row comes from one step of the model. A MATLAB program Ematrix.m calculating this matrix is given in the Supporting Information. For the model in Table 1, we have the following matrices:

$$
\boldsymbol{S} =
\begin{array}{c}
\begin{array}{cccccccccc} (R1) & (R\text{-}1) & (R2) & (R3) & (R\text{-}3) & (R4) & (R\text{-}4) & (R5) & (R6) & (R8) \end{array} \\
\left|\begin{array}{cccccccccc}
0 & 0 & 0 & 0 & 0 & 1 & -1 & 0 & 0 & 0 \\
-1 & 1 & -1 & 0 & 0 & -1 & 1 & 1 & 0 & 0 \\
1 & -1 & 0 & 2 & -2 & -1 & 1 & -1 & 1 & 0 \\
1 & -1 & -1 & 0 & 0 & 0 & 0 & 0 & 1 & 1 \\
0 & 0 & 1 & -1 & 1 & 0 & 0 & 0 & -1 & 0
\end{array}\right|
\end{array}
\begin{array}{l} \\ I_2 \\ I^- \\ IOH \\ IO_2H \\ I_2O \end{array}
$$

$$
\boldsymbol{E} =
\begin{array}{c}
\begin{array}{ccccc} E_1 & E_2 & E_3 & E_4 & E_5 \end{array} \\
\left|\begin{array}{ccccc}
1 & 0 & 0 & 0 & 0 \\
1 & 0 & 0 & 0 & 1 \\
0 & 0 & 0 & 1 & 1 \\
0 & 1 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 1 & 1 \\
0 & 0 & 0 & 0 & 1
\end{array}\right|
\end{array}
\begin{array}{l} \\ (R1) \\ (R\text{-}1) \\ (R2) \\ (R3) \\ (R\text{-}3) \\ (R4) \\ (R\text{-}4) \\ (R5) \\ (R6) \\ (R8) \end{array}
$$

In the SNA, the rates at the steady state $\boldsymbol{r}_{ss}$ are expressed as linear combinations of the columns of $\boldsymbol{E}$, $\boldsymbol{r}_{ss} = \boldsymbol{E}\,\boldsymbol{j}$, giving in our example

$$
\begin{aligned}
&(r_{+1})_{ss} = k_{+1}[I^-]_{ss} = j_1 \\
&(r_{-1})_{ss} = k_{-1}[IOH]_{ss}[IO_2H]_{ss} = j_1 + j_5 \\
&(r_2)_{ss} = k_2[IO_2H]_{ss}[I^-]_{ss} = j_4 + j_5 \\
&(r_{+3})_{ss} = k_{+3}[I_2O]_{ss} = j_2 \\
&(r_{-3})_{ss} = k_{-3}[IOH]_{ss}^{\,2} = j_2 \\
&(r_{+4})_{ss} = k_{+4}[IOH]_{ss}[I^-]_{ss} = j_3 \\
&(r_{-4})_{ss} = k_{-4}[I_2]_{ss} = j_3 \\
&(r_5)_{ss} = k_5[IOH]_{ss} = j_4 \\
&(r_6)_{ss} = k_6[I_2O]_{ss} = j_4 + j_5 \\
&(r_8)_{ss} = k_8 = j_5
\end{aligned} \tag{1}
$$

where the subscripts ss denote the values of the concentrations and rates at the disproportionation steady state. The concentrations of the external compounds are included in the rate constants. An essential characteristic of the theory is that the components of $\boldsymbol{j}$, the current rates j_i,[21,22] are non-negative.

Clarke[23] has underlined that, since stoichiometry is the most essential element of a reaction network, and since the matrix $\boldsymbol{E}$ is determined solely by stoichiometry, $\boldsymbol{E}$ plays a fundamental role in the theory of reaction networks. In our example, the sum (R2) + (R5) + (R6) and the sum (R−1) + (R2) + (R6) + (R8) give the global reaction (D). Thus, the extreme currents $\boldsymbol{E}_4$ and $\boldsymbol{E}_5$ are two pathways leading to the observed stoichiometry. Therefore, we call them *stoichiometric currents*. On the other hand, reversible reactions are represented in the SNA by two reactions giving columns of $\boldsymbol{E}$ with no net contribution to the stoichiometry such as (R1) + (R−1), (R3) + (R−3) and (R4) + (R−4) giving $\boldsymbol{E}_1$, $\boldsymbol{E}_2$ and $\boldsymbol{E}_3$ in our example. These currents are characteristic of the reversibility of the corresponding reactions and we call them *exchange currents*. By analogy with a terminology used in electrochemistry, a high value of exchange current is characteristic of a highly reversible reaction. The name *equilibrium currents* used formerly[1] could be confusing because the corresponding reactions are not necessarily at equilibrium. For example, $(r_{+1})_{ss} = j_1$ is not equal to $(r_{-1})_{ss} = j_1 + j_5$. Our terminology underlines an important aspect of the SNA discussed hereafter, the relation between the currents and the experimental information.

Rate Equations and Stability Analysis

The stability of a steady state can be analyzed by linearization of the stoichiometric network general equation of motion about this steady state.[1,20,24−27] The SNA theory simplifies greatly this analysis using the j_i's as parameters and the ratios between the actual concentrations and their values at the steady-state as variables.[1] Thus, we define $x_1 = [I_2]/[I_2]_{ss}$, $x_2 = [I^-]/[I^-]_{ss}$, $x_3 = [IOH]/[IOH]_{ss}$, $x_4 = [IO_2H]/[IO_2H]_{ss}$, $x_5 = [I_2O]/[I_2O]_{ss}$, write the rate equations as functions of these variables, for example $r_{+1} = k_{+1}[I^-]_{ss}\,x_2 = j_1\,x_2$, and obtain the equations of motion in the following form.

$$
\begin{aligned}
&[I_2]_{ss} \quad dx_1/dt = j_3(x_2x_3 - x_1) \\
&[I^-]_{ss} \quad dx_2/dt = -j_1x_2 + (j_1 + j_5)x_3x_4 - (j_1 + j_5)x_2x_4 - j_3(x_2x_3 - x_1) + j_4x_3 \\
&[IOH]_{ss} \quad dx_3/dt = j_1x_2 - (j_1 + j_5)x_3x_4 + 2j_2(x_5 - x_3^{\,2}) - j_3(x_2x_3 - x_1) - j_4x_3 + (j_4 + j_5)x_5 \\
&[IO_2H]_{ss} \quad dx_3/dt = j_1x_2 - (j_1 + j_5)x_3x_4 - (j_4 + j_5)x_2x_4 + (j_4 + j_5)x_5 + j_5 \\
&[I_2O]_{ss} \quad dx_3/dt = (j_4 + j_5)x_2x_4 - j_2(x_5 - x_3^{\,2}) - (j_4 + j_5)x_5
\end{aligned} \tag{2}
$$

The matrix of currents $\boldsymbol{V}(\boldsymbol{j})$ is defined as

$$\boldsymbol{V}(\boldsymbol{j}) = -\boldsymbol{S}(\mathrm{diag}\,\boldsymbol{E}\,\boldsymbol{j})\boldsymbol{K}^{\mathrm{T}} \tag{3}$$

where $\boldsymbol{K}^{\mathrm{T}}$ is the transpose of the matrix of the order of reactions $\boldsymbol{K}$. Since $\boldsymbol{r}_{ss} = \boldsymbol{E}\,\boldsymbol{j}$, diag $\boldsymbol{E}\,\boldsymbol{j}$ is a diagonal matrix whose elements are the reaction rates at the steady states. The stability depends on the sign of the real part of the eigenvalues of the matrix $\boldsymbol{M} = -(\mathrm{diag}\ \boldsymbol{h})\ \boldsymbol{V}(\boldsymbol{j})$ where diag $\boldsymbol{h}$ is a diagonal matrix whose elements are the reciprocals steady state concentrations ($h_i = 1/[X_i]_{ss}$, $X_i = I_2$, I^-, HIO, HIO_2, I_2O). Although the stability analysis by this method is much simpler than by direct linearization of the kinetic equations, it becomes limited for real models by the number and size of the required polynomials and the following sufficient instability condition is used: If at least one negative term exists in a principal minor of $\boldsymbol{V(j)}$, the steady state is unstable for some values of the parameters. The MATLAB program Clarkestab.m given in the electronic supplement computes the coefficients of the $\boldsymbol{j}_i$ in $\boldsymbol{V(j)}$ and uses symbolic variables to locate all the destabilizing terms. For the model in Table 1, it reveals three negative terms proving that the steady state can be unstable.

When we have found that a steady state can be unstable, we would like to know when it is actually unstable. This remains a difficult task unless we use an *a priori* knowledge of the orders of magnitude of the parameters to locate the dominating negative terms. For the BL reaction, we know that the iodine concentration is much larger than the concentration of the other internal compounds. This means that $h_1 = 1/[I_2]_{ss}$ is much smaller than the other h_i and that we can discard all the terms multiplied by h_1 in the development of the characteristic equation. We also know that reaction (R4) remains nearly at equilibrium, meaning that its exchange current rate j_3 is much larger than the values of stoichiometric current rates. This reduces drastically the number of terms in the instability condition given by the program Clarkestab.m, leaving

$$23j_1j_2j_4 + 21j_1j_2j_5 + 14j_1j_4j_5 + 8j_1j_4^2 + 6j_1j_5^2 + 12j_2j_4j_5 + 12j_2j_5^2 + 10j_4j_5^2 + 6j_4^2j_5 + 4j_5^3 - 2j_2j_4^2 < 0 \quad (4)$$

The identification of the dominating negative terms based on experimentally known orders of magnitude is a striking advantage of the SNA.

Dimensionless Equations

The expressions (2) of the kinetic equations throw some light on classical concepts in chemical kinetics, quasi-steady state approximation, nullclines and slow manifold. They are closely related and their use rests on the relative magnitude of some concentrations. We illustrate this after a transformation of eqs 2. The variables are already dimensionless and, since the number of dimensionless parameters is always less than classical ones,[28] it is useful to define dimensionless parameters and dimensionless time based on a proper choice of the reference values:

$$c_2 = [I^-]_{ss}/[I_2]_{ss}, \quad c_3 = [IOH]_{ss}/[I_2]_{ss},$$
$$c_4 = [IO_2H]_{ss}/[I_2]_{ss}, \quad c_5 = [I_2O]_{ss}/[I]_{ss}, \quad \alpha = j_2/(j_4 + j_5),$$
$$\beta = j_1/(j_4 + j_5), \quad \gamma = j_3/(j_4 + j_5), \quad \delta = j_5/(j_4 + j_5)$$

We take $[I_2]_{ss}$ as the reference concentration because it is larger than the concentrations of the other internal compounds $[I^-]_{ss}$, $[IOH]_{ss}$, $[IO_2H]_{ss}$, and $[I_2O]_{ss}$, such that c_2, c_3, c_4, and c_5 are small parameters. We take $(j_4 + j_5)$ as reference current rate because it is the rate of reaction (D) at the catalytic disproportionation steady state. We will see that this choice simplifies the relations between the dimensionless parameters and the properties of the chemical system. The corresponding dimensionless time is $\tau = t \times (j_4 + j_5)/[I_2]_{ss}$. Introducing these parameters, the equations of motion (2) take the dimensionless form (5).

$$\begin{aligned}
&dx_1/d\tau = \gamma(x_2x_3 - x_1)\\
&c_2dx_2/d\tau = -\beta(x_2x_3 - x_4) - \gamma(x_2x_3 - x_1) + \\
&\qquad \delta x_3(x_4 - 1) - x_2x_4 + x_3\\
&c_3dx_3/d\tau = \beta(x_2x_3 - x_4) - \gamma(x_2x_3 - x_1) + \\
&\qquad 2\alpha(x_5 - x_3^2) - \delta x_3(x_4 - 1) - x_3 + x_5\\
&c_4dx_4/d\tau = \beta(x_2 - x_3x_4) + \delta(1 - x_3x_4) - x_2x_4 + x_5\\
&c_5dx_5/d\tau = -\alpha(x_5 - x_3^2) + x_2x_4 - x_5
\end{aligned} \quad (5)$$

These equations are similar to the classical SNA equations (eqs 2) and have all their advantages together with the ones coming from their dimensionless form resulting from Pi theorem.[28] Relations between the dimensionless parameters and the kinetic constants are easily derived from eqs 1. The following study of the slow manifold and the sensitivity analysis show the advantages of these equations over the classical ones.

Slow Manifold and Time Evolutions

The iodine concentration is much larger than the concentrations of the other internal compounds and taking $[I_2]_{ss}$ as reference concentration in eqs 5 simplifies greatly the study of the motion. The last four equations have the form $\epsilon\ dx_i/dt = f_i(x, c)$ where ϵ is small, so that the trajectories in the state space are strongly attracted by the nullclines $f_i(x, c) = 0$. The equations of the four nullclines define the slow manifold. It is one-dimensional in the five-dimensional state space. This is a first advantage of eqs 5 over the classical ones: they give directly simple equations of the slow manifold and show that the main effect of the parameters c_2, c_3, c_4, and c_5 is to determine its attracting power. The equations (eqs 5) simplify also greatly the study of the shape of the slow manifold. They reveal that this shape depends only on the four parameters α, β, γ, and δ and not on the individual values of the ten rate constants.

At this point, we would like to underline the relation between the concepts of nullclines or slow manifold and the classical quasi-steady state approximation. The equations of the nullclines are identical to the equations we would write using the quasi-steady state approximation but their meaning is clearer and this approach reveal a frequent misunderstanding in chemical kinetics. Taking for example the concentration $[I^-]$, the steady-state approximation does not mean that $d[I^-]/dt$ is equal to zero, what is clearly untrue. The slow manifold approach gives the exact condition: c_2 is small.

Figure 1 shows examples of time evolutions calculated by numerical integration of eqs 5 and of slow manifolds calculated analytically when the disproportionation steady state is stable or unstable. The instability condition (eq 6) is obtained replacing the j_i in eq 4 with the dimensionless parameters. The simplification is striking.

$$(4\beta - \beta\delta + 3\delta - \delta^2)/\alpha + (11.5 - \delta)\beta < \delta^2 - 8\delta + 1 \quad (6)$$

The parameter α, equal to k_{+3}/k_6, is the main parameter controlling the stability. The orders of magnitude of the other parameters are dictated by experimentally known orders of magnitude. The equilibrium of reaction (R4) being only weakly disturbed during the Bray–Liebhafsky reaction, its exchange current rate j_3 is much larger than the sum of current rates $j_4 + j_5$. The value of $\gamma = j_3/(j_4 + j_5)$ must be much larger than one and has a minor influence on the shape of the calculated curves. The current rate j_3 does not appear in eq 4 and the parameter γ does not appear in eq 6 for the same reason. On the contrary, the equilibrium of reaction (R1) is strongly disturbed, its exchange current rate j_1 must be relatively small and $\beta = j_1/(j_4$

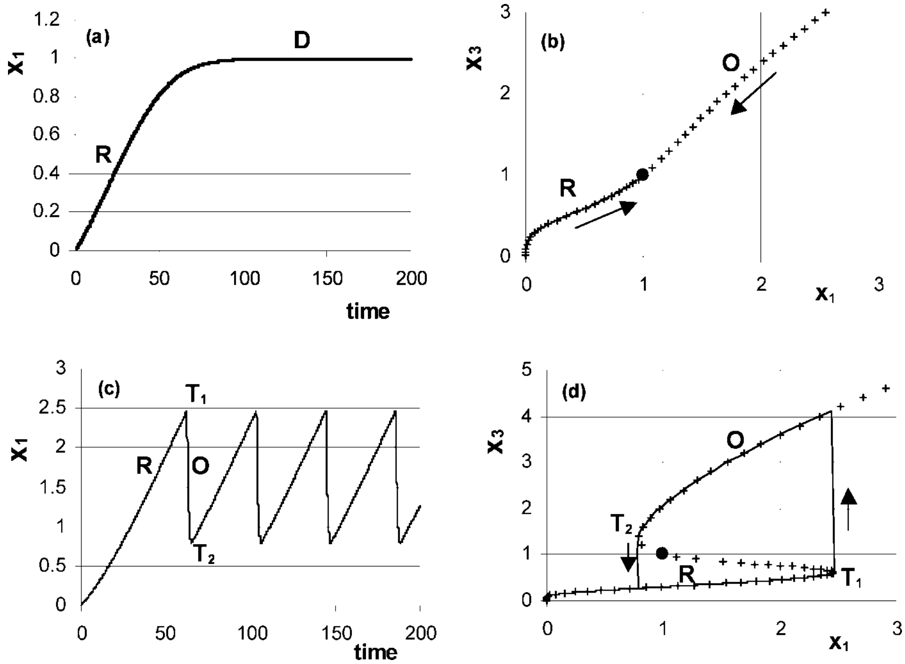

Figure 1. (a, b) Time evolution for α = 0.2, $\beta = 0.01$, $\gamma = 100$, $\delta = 0.05$, $c_2 = 2 \times 10^{-4}$, $c_3 = 5 \times 10^{-4}$, $c_4 = 2 \times 10^{-4}$, and $c_5 = 2 \times 10^{-6}$ and projections of the trajectory (—) and the slow manifold (+ + +) onto the x_3-x_1 plane. The disproportionation steady state (●) is stable. (c, d) Same as parts a and b, except α = 2. The disproportionation steady state (●) is unstable.

$+ j_5$) must be small. The parameter δ, equal to $j_5/(j_4 + j_5)$, is the relative contribution of reaction (R8) to reaction D. The values of c_2 and c_3 used in Figure 1 are based on experimentally known orders of magnitude of the concentrations while the values of c_4 and c_5 are unknown. However, as explained before, their values have nearly no influence on the calculated curves as long as they remain small.

Parts a and b of Figure 1 illustrate the motion when the disproportionation steady state is stable. As expected, the trajectories calculated numerically are close to the slow manifold calculated analytically. The evolution begins with reaction R because the initial value of x_1 (iodine) is zero. When the initial value of x_1 is larger than one, the evolution begins with reaction O. Parts c and d of Figure 1 illustrate the motion when the disproportionation steady state is unstable. The x_1 oscillations obtained by numerical integration of the eqs 5 are very similar to the experimental ones.[4,5,29] The oscillations can be divided into two periods separated by transition points. During the period R the rate of reaction R is larger than the rate of reaction O and x_1 increases; during the period O, it is the opposite and x_1 decreases. Figure 1d shows the projections of the slow manifold and of the trajectory from the five dimensional state space onto the $x_3 - x_1$ plane explaining the transition points T_1 and T_2. The slow manifold has an S shape with upper and lower stable branches and an intermediate unstable branch between points T_1 and T_2. The calculated trajectory follows the lower branch until it reaches point T_1. At this point, dx_1/dt is still positive and the trajectory must leave the slow manifold. It jumps quickly (more or less quickly depending on the smallness of the c_i) to the stable upper branch where dx_1/dt is negative and follows this branch to point T_2. Then it must again leave the slow manifold, jumps to its lower branch and closes the limit cycle.

The Bifurcation Points

We have studied the transitions between stability and instability using $\alpha = j_2/(j_4 + j_5) = k_{+3}/k_6$ as bifurcation parameter. When the steady state is stable and is far from a bifurcation, the slow manifold has a shape like in Figure 1b leading to the smooth disproportionation. When the disproportionation steady state is unstable, the slow manifold has an S shape as in Figure 1d leading to oscillations. Between these two situations surprising behaviours are observed. At the transitions between stability and instability, the slow manifold has still an S shape and the steady state is close to one of the points T_1 or T_2. The first case is favored by low δ values and will be illustrated by the example in Figure 2. The second case is favored by high δ values and will be illustrated by the example in Figure 3. The parameter δ has always a stabilizing effect and the meaning of “high δ values” is defined by the instability condition 6. As $\delta = j_5/(j_4 + j_5) < 1$, its left-hand side is positive and the instability condition 6 cannot be satisfied if its right-hand side is negative, that is, if $\delta^2 - 8\delta + 1 < 0$ or $\delta > 0.127$. The parameter β has also a stabilizing effect and the amplitude of the studied phenomena increases when β decreases because the left-hand side term decreases. The other parameters were chosen as explained before.

Figure 2 gives an example of bifurcation when the steady state is close to T_1. A supercritical Hopf bifurcation is found by numerical simulations for $\alpha = 4.0473 \times 10^{-3}$, very close to $\alpha = 4.0465 \times 10^{-3}$ given by condition 6. The small difference comes from the numerous small terms neglected in the characteristic equation. When α increases over $\alpha = 4.0473 \times 10^{-3}$ the limit cycle born at the Hopf bifurcation grows and a situation similar to that in Figure 1d is finally obtained. However, this growth can be more or less fast depending on the values of the other parameters. Figure 2a gives an example of abrupt increase of the oscillations amplitude near $\alpha_C = 4.04897475 \times 10^{-3}$, known as a canard explosion.[30−33] This phenomenon is characteristic of systems with very different time scales, which is our case, and can be continuous or not.[30] The insert in Figure 2a suggests that it is discontinuous for the used values of the parameters. Such canard explosions are often associated with excitability,[31] and Figure 2b shows the behavior for $\alpha = 4.0489 \times 10^{-3}$, just before the explosion. The unstable

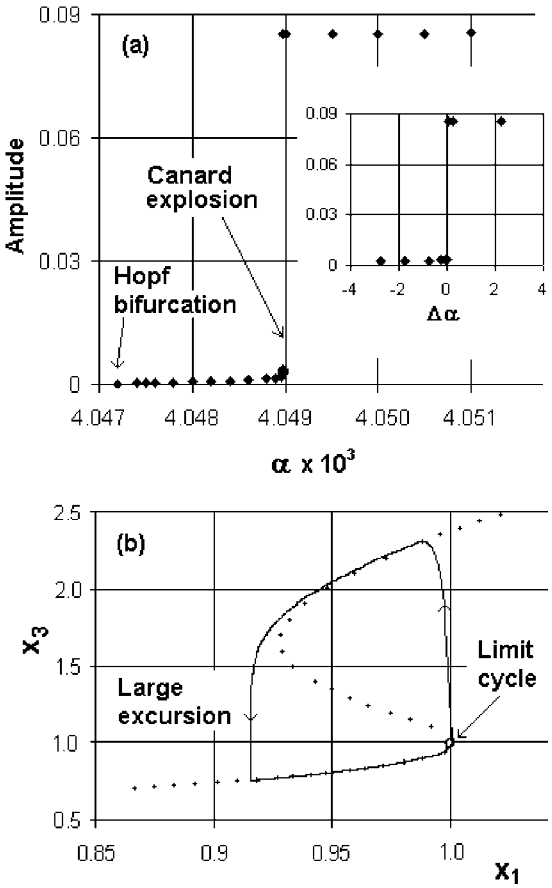

Figure 2. Bifurcations for $\beta = 0.001$, $\gamma = 100$, $\delta = 0$, $c_2 = 2 \times 10^{-4}$, $c_3 = 5 \times 10^{-4}$, $c_4 = 2 \times 10^{-4}$, $c_5 = 2 \times 10^{-6}$. (a) Amplitudes of the x_1 oscillations vs α. The insert, where $\Delta\alpha = (\alpha - \alpha_C) \times 10^9$, shows the discontinuity. (b) Projections of the trajectory (—) and the slow manifold (+ + +) on the $x_1 - x_3$ plane for $\alpha = 4.0489 \times 10^{-3}$ and initial values vector $x_i = [1.001\ 1\ 1\ 1\ 1]$.

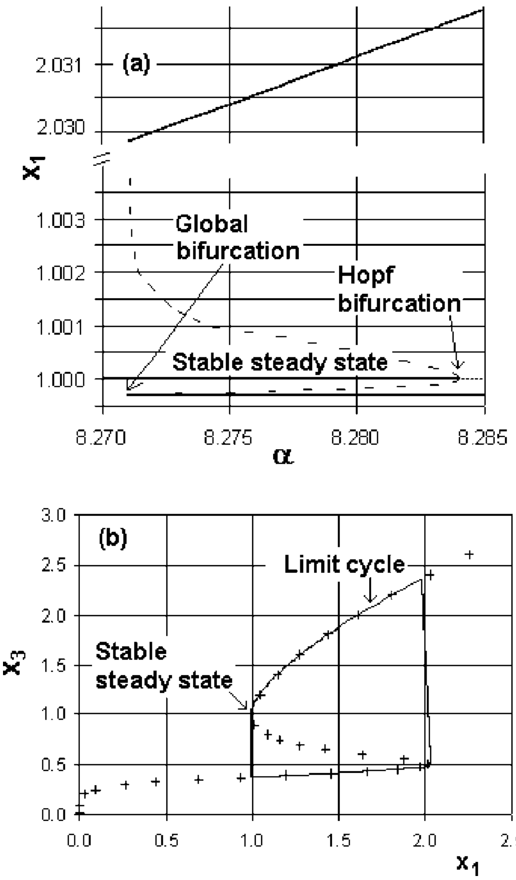

Figure 3. Bifurcations for $\beta = 0.001$, $\delta = 0.120$ and other parameters as in Figure 2. (a) Maximum (upper part) and minimum values of x_1 during the oscillations (—) and section in the separatrix (- - -). (b) Projections of the trajectory (—) and the slow manifold (+ + +) showing the bistability for α = 8.272.

steady state is surrounded by a very small limit cycle and the system is highly excitable because the trajectory is strongly attracted by the slow manifold. For the chosen initial values, the system makes a large excursion near the slow manifold before cycling toward the small limit cycle. This excursion announces the large limit cycle that will appear at the canard point.

Figure 3 shows an example of bifurcation when the steady state is close to T_2. When α increases from 8.2710 to 8.2711, a large limit cycle seems to appear from nowhere and to understand what happens it is easier to consider decreasing α values. For high α values the disproportionation steady state is unstable and surrounded by a limit cycle. Near α = 8.284 a subcritical Hopf bifurcation is observed. The steady state becomes stable but is still surrounded by a limit cycle. For α < 8.284 bistability is observed as in Figure 3b. They are two basins of attraction, one for the steady state, the other for the limit cycle. They are separated in the five-dimensional state space by a four-dimensional manifold called the separatrix. Figure 3a shows a section in it. When α continue to decrease a new bifurcation is encountered: the separatrix collides with the limit cycle near α = 8.2711 and breaks it. The large limit cycle disappears suddenly. For lower α values the only attractor is the stable steady state but the system can perform large excursions near the former limit cycle before reaching it. Let us note that the difference between the α values at the two bifurcations is so small that they could probably not be resolved experimentally. Only a sudden transition between a stable steady state and a limit cycle with a finite size would be observed. Our example shows that this sudden transition would be an illusion and that normal transitions lay under it.

Sensitivity Analysis

The dimensionless equations derived from the SNA offer a simple approach to the sensitivity analysis different from the classical one and more based on the chemistry of the studied system. Instead of ten rate constants and three external concentrations (iodate, acidity and hydrogen peroxide), we have two scaling factors, $[I_2]_{ss}$ and the reference current rate ($j_4 + j_5$), four main parameters, α, β, γ and δ, and four c_i. The reference concentration $[I_2]_{ss}$ and the reference current rate ($j_4 + j_5$) have no effect on the structure of the state space or on the shape of the trajectories. The four main parameters determine the stability of the steady state and the properties of the slow manifold. The four c_i determine the attracting power of the slow manifold. Their values affect weakly the trajectories, as long as they remain small. Thus, the sensitivity analysis reduces to the study of the effect of the four main dimensionless parameters. Moreover, if reaction (R4) is at quasi-equilibrium, the value of γ is large, the trajectories are rather insensitive to it, and we have only three important parameters. The SNA parameters are related by the instability condition 4 and the introduction of the dimensionless parameters simplifies it further to condition 6. This offers some qualitative sensitivity analysis: the oscillations are highly sensitive to only three parameters, α, β and δ, and exist only when they satisfy condition 6. Some direct conclusions about the rate constants can also be obtained. For example, the ratio $\alpha = k_{+3}/k_6$ is important, not the individual values of these two rate constants. A direct conclusion is also obtained about reaction (R8). If k_8 is such that δ is very small, this reaction has no effect and can be neglected. If k_8 is such that δ is larger than 0.127, it suppress any possibility of oscillations. After the analysis of the sensitivity to the dimensionless parameters it is easy to go back to the kinetic constants solving the eqs 1. Hence, if we want to adjust rate constants it is easier to begin with the dimensionless parameters, to adjust independently the shape and the scales of the calculated curves and calculate afterward the rate constants using the eqs 1.

Conclusions

Since it was proposed by Clarke,[1] the SNA appears occasionally in the literature[34−40] but the importance of the concept of currents in chemical kinetics remains underestimated. We have illustrated the main features of the method taking as an example a simplified model of the BL reaction and proposed MATLAB programs in the electronic supplement computing the extreme currents $\boldsymbol{E}$ matrix and locating the destabilizing terms in matrix of currents $\boldsymbol{V}(\boldsymbol{j})$. Then, we have shown that the usefulness of the SNA is not limited to the stability analysis of steady states. This powerful method for the examination of complex systems gives equations of motion that can be written easily in a dimensionless form simplifying greatly the study of the slow manifold, revealing the parameters controlling its shape and showing which parameters have or have not a noticeable influence on the trajectories. Moreover, the orders of magnitude of most SNA parameters, and consequently of the derived dimensionless parameters, are related to experimental information. This relation is important for locating the dominating terms in the instability condition and selecting the parameters values used in the numerical simulations.

We have given two examples of the effectiveness of these equations, the study of the bifurcations points and the sensitivity analysis. The observed bifurcations are well-known theoretically but we are not aware of another example of such a complex behavior in a realistic chemical reaction mechanism consisting of stoichiometric steps with integer coefficients and mass action kinetics. It occurs in a small range of parameters values and would have probably not been discovered by integration of the usual differential equations using the rate constants as parameters. We also establish here that the dimensionless parameters derived from the SNA offer a nonclassical sensitivity analysis showing directly which functions of the rate constants have an important influence on the dynamics of the studied model.

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Supporting Information Available: Matlab file Ematrix.m used for determination of the extreme currents in the SNA theory and files SNAStab.m and OutSNAStab.m used for the search of the destabilizing terms. This material is available free of charge via the Internet at http://pubs.acs.org.

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