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Current rates and reaction rates in the Stoichiometric Network Analysis (SNA)

Abstract: In stoichiometric network analysis (SNA) the instability condition is calculated by the current rates. Recently, we have shown that in the final result the current rates can be substituted by reaction rates, which is a more appropriate value for the examination of instability from experimental point of view. Here, we elaborate the problem of whether the current rates are necessary parameters in the calculation, with the aim of obtaining the region of instability. All calculations are performed on a model for Belousov-Zhabotinsky (BZ) reaction, which has not been examined by SNA.

Keywords: stoichiometric network analysis, current rates, reaction rates, instability condition, Belousov-Zhabotinsky reaction

1 Introduction

An examination of dynamic states of a complex nonlinear reaction system and the related stability of the corresponding model is a serious problem when the number of independent intermediate species, or, from a mathematical point of view, the number of variables in

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kinetic equations, is larger than three [1–11]. One method for solving this problem is to use the Stoichiometric Network Analysis (SNA) that was developed by Clarke [12]. In this method, instead of using reaction rates in the steady state, the current rates (see below) were introduced, to allow for stability conditions to be discussed for an *n*-dimensional system. The problem appeared when the relations expressed as a function of current rates had to be evaluated and compared with numerical simulations and experiments. The problem lies in the fact that the number of current rates is usually larger than the number of equations from which they can be determined. We have recently shown that evaluated instability condition in a function of current rates can always be expressed at the end as the function of reaction rates [13], thus contributing strongly to the application of the SNA. We shall discuss the common problem that appears: Is it possible to substitute the current rates with the reaction rates at some earlier phase in the SNA procedure, and, are the current rates necessary to analyze the stability of the dynamic states? In other words, why do we not work from the beginning with the reaction rates, *i.e.* the values close to almost all physical chemists?

All general equations necessary for consideration of the mentioned problem evaluated in Sect. 3 will be applied in the same section, to the model for Belousov-Zhabotinsky reaction [14] shown in Table 1 (Sect. 2), this model that has never been treated by SNA. The results of this assessment will be presented.

2 Theory and experiment

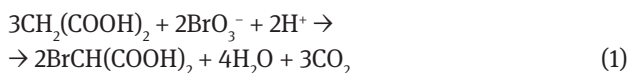### 2.1 Short overview of the Belousov – Zhabotinsky reaction

In this paper we focus our attention on the application of the SNA to the model describing a complex process under batch conditions. The selected complex process is the oscillatory catalytic oxidation of organic substrates

(malonic acid) in the presence of acid bromate and a metallic catalyst (cerium), known as the Belousov–Zhabotinsky oscillatory reaction (BZ) [15,16]. Although the malonic acid can be totally decomposed to water and carbon dioxide, the mentioned process is often presented in the literature by the following stoichiometric relation:

$$3CH_2(COOH)_2 + 2BrO_3^- + 2H^+ \rightarrow$$
$$\rightarrow 2BrCH(COOH)_2 + 4H_2O + 3CO_2 \quad (1)$$

The bromomalonic acid is the product of reaction [1,17].

The numerous dynamic states such as simple, mixed–mode and chaotic oscillations obtained in BZ reaction system under various experimental conditions [18–21], can be obtained by numerical simulations using different models. They all have an important role in the modeling of a BZ reaction [14,22–33].

With the aim of discussing the importance of current rates in examinations of dynamical states and their correlation with experimentally obtained results, we are going to apply the SNA to only one model which describes an oscillatory evolution of the BZ process under batch conditions; the model considered in our previous papers [14,34]. Table 1 contains the model of the BZ reaction consisting of twelve reactions (R1)–(R12) of which (R1), (R3), (R6) and (R7) are reversible.

The reaction (R12) was included in the model to regulate the evaporation of bromine from the solution [35–37].

2.2 Experimental investigations

The isothermal BZ oscillatory reactions were performed at 30.0°C, in a thermostated batch reactor with a reaction volume of 51×10^{-3} dm^3 and equipped with a magnetic stirrer. The stirring rate was kept at 700 rpm. A bromide ion–sensitive electrode *versus* a double junction Ag/AgCl electrode as the reference one was used for the potentiometric monitoring of temporal evolution of the BZ reaction.The experiments were carried out with various initial malonic acid concentrations $8.00 \times 10^{-3} \leq$ $[CH_2(COOH)_2]_0 \leq 4.30 \times 10^{-2}$ mol dm^{-3}. In all experiments, the initial concentrations of potassium bromate, sulfuric acid, potassium bromide and cerium sulfate were kept constant: $[H_2SO_4]_0 = 1.00$ mol dm^{-3}, $[KBrO_3]_0 = 6.20 \times 10^{-2}$ mol dm^{-3}, $[KBr]_0 = 1.50 \times 10^{-5}$ mol dm^{-3}, $[Ce_2(SO_4)_3]_0 = 2.50 \times 10^{-3}$ mol dm^{-3}. The BZ reaction was started after an injection of 1×10^{-3} dm^3 of cerium sulfate solution into the 50×10^{-3} dm^3 mixture containing malonic acid, potassium bromate, sulfuric acid, and potassium

Table 1: A model of the Belousov–Zhabotinsky reaction [14].

Reactions	No.
$Br^- + HOBr + H^+ \rightarrow Br_2 + H_2O$	(R1)
$Br_2 + H_2O \rightarrow Br^- + HOBr + H^+$	(R–1)
$HBrO_2 + Br^- + H^+ \rightarrow Br_2O + H_2O$	(R2)
$Br_2O + H_2O \rightarrow 2HOBr$	(R3)
$2HOBr \rightarrow Br_2O + H_2O$	(R–3)
$Br^- + BrO_3^- + 2H^+ \rightarrow HOBr + HBrO_2$	(R4)
$2HBrO_2 \rightarrow BrO_3^- + HOBr + H^+$	(R5)
$BrO_3^- + HBrO_2 + H^+ \rightarrow 2BrO_2^{\bullet} + H_2O$	(R6)
$2BrO_2^{\bullet} + H_2O \rightarrow BrO_3^- + HBrO_2 + H^+$	(R–6)
$Ce^{3+} + BrO_2^{\bullet} + H^+ \rightarrow Ce^{4+} + HBrO_2$	(R7)
$Ce^{4+} + HBrO_2 \rightarrow Ce^{3+} + BrO_2^{\bullet} + H^+$	(R–7)
$CH_2(COOH)_2 + Br_2 \rightarrow CHBr(COOH)_2 + Br^- + H^+$	(R8)
$CH_2(COOH)_2 + Ce^{4+} \rightarrow Ce^{3+} + P_1 + H^+$	(R9)
$CHBr(COOH)_2 + Ce^{4+} \rightarrow Ce^{3+} + Br^- + P_2$	(R10)
$Br_2O + CH_2(COOH)_2 \rightarrow CHBr(COOH)_2 + HOBr$	(R11)
$Br_2 \rightarrow Br_2(g)$	(R12)*

*Note: Br_2 and $Br_2(g)$ denote bromine in aqueous solution and bromine in gas phase, respectively. P_1 and P_2 are products of the overall process

bromide solutions of the mentioned concentrations, at the moment when the potential of the bromide ion-sensitive electrode achieved the steady value of about 200 mV. A detailed description of the experiments is shown in a previous paper [14].

The typical potentiometric traces taken with the bromide ion–sensitive electrode of the investigated BZ systems at selected different initial concentrations of malonic acid are illustrated in Fig. 1a.

2.3 Numerical Simulations

The kinetic equations (2-12), based on the model given in Table 1 and law of mass action, which describe the time evolution of the concentrations of all species taking place in the model, are solved numerically using the rate constants presented in Table 2.

$$\frac{d[Br^-]}{dt} = -r_{+1} + r_{-1} - r_{+2} - r_{+4} + r_{+8} + r_{+10} \quad (2)$$

$$\frac{d[HOBr]}{dt} = -r_{+1} + r_{-1} + 2r_{+3} - 2r_{-3} + r_{+4} + r_{+5} + r_{+11} \quad (3)$$

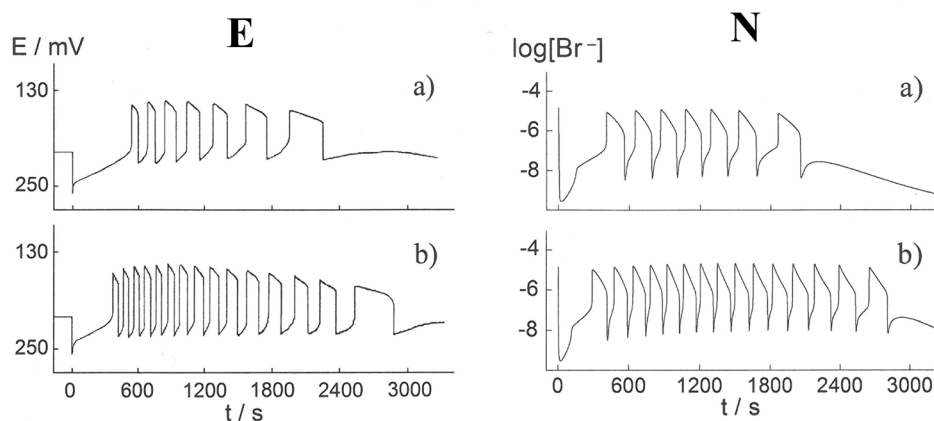$$\frac{d[Br_2]}{dt} = r_{+1} - r_{-1} - r_{+8} - r_{+12} \quad (4)$$

Figure 1: The oscillograms obtained experimentally E, and by the numerical simulation N, at T = 30°C, for $[CH_2(COOH)_2]_0$ values (in mol dm^{-3}): a) 1.60×10^{-2} and b) 2.20×10^{-2}. Experimental results E, present the potentiometric traces of the bromide ion-sensitive electrode. Calculated results N, present the time dependence of log[Br$^-$] obtained by the numerical simulation according the kinetic scheme given in Table 1 [14].

$$\frac{d[HBrO_2]}{dt} = -r_{+2} + r_{+4} - 2r_{+5} - r_{+6} + r_{-6} + r_{+7} - r_{-7} \quad (5)$$

$$\frac{d[Br_2O]}{dt} = r_{+2} - r_{+3} + r_{-3} - r_{+11} \quad (6)$$

$$\frac{d[BrO_2^\bullet]}{dt} = 2r_{+6} - 2r_{-6} - r_{+7} + r_{-7} \quad (7)$$

$$\frac{d[Ce^{3+}]}{dt} = -r_{+7} + r_{-7} + r_{+9} + r_{+10} \quad (8)$$

$$\frac{d[Ce^{4+}]}{dt} = r_{+7} - r_{-7} - r+_9 - r_{+10} \quad (9)$$

$$\frac{d[BrO_3^-]}{dt} = -r_{+4} + r_{+5} - r_{+6} + r_{-6} \quad (10)$$

$$\frac{d[BrMA]}{dt} = r_{+8} - r_{+10} + r_{+11} \quad (11)$$

$$\frac{d[MA]}{dt} = -r_{+8} - r_{+9} - r_{+11} \quad (12)$$

Table 2: Rates and rate constants of the Model (Table 1) used in the numerical simulations of the Belousov–Zhabotinsky reaction.

Rates	Rate constants		Reactions
$r_{+1} = k_1 [Br^-][HOBr][H^+]$	$k_1 = 2.55 \times 10^9$	M^{-2} s^{-1}	(R1)
$r_{-1} = k_{-1} [Br_2]$	$k_{-1} = 3.18$	s^{-1}	(R−1)
$r_2 = k_2 [HBrO_2][Br^-][H^+]$	$k_2 = 5.93 \times 10^6$	M^{-2} s^{-1}	(R2)
$r_3 = k_3 [Br_2O]$	$k_3 = 3.21 \times 10^3$	s^{-1}	(R3)
$r_{-3} = k_{-3} [HOBr]^2$	$k_{-3} = 3.22 \times 10^8$	M^{-1} s^{-1}	(R−3)
$r_4 = k_4 [Br^-][BrO_3^-][H^+]^2$	$k_4 = 2.86$	M^{-3} s^{-1}	(R4)
$r_5 = k_5 [HBrO_2]^2$	$k_5 = 3.49 \times 10^3$	M^{-1} s^{-1}	(R5)
$r_6 = k_6 [BrO_3^-][HBrO_2][H^+]$	$k_6 = 44.70$	M^{-2} s^{-1}	(R6)
$r_{-6} = k_{-6} [BrO_2^\bullet]^2$	$k_{-6} = 6.70 \times 10^7$	M^{-1} s^{-1}	(R−6)
$r_7 = k_7 [Ce^{3+}][BrO_2^\bullet][H^+]$	$k_7 = 3.20 \times 10^4$	M^{-2} s^{-1}	(R7)
$r_{-7} = k_{-7} [Ce^{4+}][HBrO_2]$	$k_{-7} = 1.12 \times 10^4$	M^{-1} s^{-1}	(R−7)
$r_8 = k_8 [CH_2(COOH)_2][Br_2]$	$k_8 = 4.24$	M^{-1} s^{-1}	(R8)
$r_9 = k_9 [CH_2(COOH)_2][Ce^{4+}]$	$k_9 = 0.36$	M^{-1} s^{-1}	(R9)
$r_{10} = k_{10} [CHBr(COOH)_2][Ce^{4+}]$	$k_{10} = 47.17$	M^{-1} s^{-1}	(R10)
$r_{11} = k_{11} [Br_2O][CH_2(COOH)_2]$	$k_{11} = 4.23 \times 10^{-2}$	M^{-1} s^{-1}	(R11)
$r_{12} = k_{12} [Br_2]$	$k_{12} = 1.10 \times 10^{-2}$	s^{-1}	(R12)

Remark: M ≡ mol dm^{-3}

Where r_i, r_{+i} and r_{-i} denotes the rates of the irreversible reaction i, forward and reverse parts of the reversible ones, respectively. The concentration of X_i is denoted as $[X_i]$.

The numerical simulations were carried out under the same conditions as the ones used in the experiments. One of the numerically obtained results, the time evolution of the log[Br$^-$], is presented in Fig. 1N. All experiments were performed in 1.00 mol dm^{-3} H$_2$SO$_4$ and in all

the simulations we use $[H^+]_0 = 1.29$ mol dm^{-3} according to Robertson and Dunford [38]. In the simulations, the initial concentration of intermediate species HOBr was $[HOBr]_0 = 1.50 \times 10^{-8}$ mol dm^{-3}, whereas the initial concentrations of other intermediates were zero. Under the batch conditions, the concentrations of reactants decrease with time, for chosen model and numerical simulation to accurately describe the evolution of BZ reaction in closed

reactor, it is necessary to integrate the concentrations of the reactants. Therefore, only the concentration of water $[H_2O] = 55$ mol dm^{-3} is included in the rate constants of corresponding reactions [27].

The simulations were performed using the MATLAB program package. The differential equations derived from the model (2-12) were integrated using the ode15s solver. All numerical simulations were performed with a numerical precision of 10^{-20}.

3 Results

3.1 Stability analysis

In general, as well as in SNA, the stability analysis is based on examination of the stability of the non-equilibrium stationary states or steady states. Steady states are defined as time independent states that are observed when a reaction system is driven and maintained out of equilibrium by external forces, such as the temperature or the concentration of external species as control parameters. When a system is found in a nonequilibrium stationary state, its properties are defined by the independent intermediate species. For this reason, if we want to analyze the stability of nonequilibrium stationary states, we need to consider the kinetic equations of independent intermediate species only. However, for an analysis of the time evolution of the overall process, we need to examine the complete set of kinetic equations including reactants and products. Numerical simulation using a complete set of kinetic equations provides insight into the properties of the sequence of steady states, that system pass through, forced by slowly changing concentrations of reactants.

If the reversible reactions are decomposed into two forward irreversible reactions – one for each direction, the kinetic equations of any stoichiometric model presented by a set of differential equations of the independent intermediate species only, can be written in the form:

$$\frac{d[X]}{dt} = \mathbf{S} \cdot \boldsymbol{r} \tag{13}$$

where $d[X]/dt$ is the time derivative of the concentration vector $[X]$, $\boldsymbol{r}$ is the reaction rate vector and $\mathbf{S}$ is the matrix of the stoichiometric coefficients that can be assigned directly from the model (Sect. A in Supplementary material). According to SNA [12,39], reversible reactions are decomposed into two forward irreversible reactions – one for each direction.

The rates at a steady state (r_{ss}) are solutions of the relation:

$$\mathbf{S} \cdot \boldsymbol{r}_{ss} = 0 \tag{14}$$

and the overall process can be presented as a linear combination of several elementary reaction pathways from the proposed model, with non-negative coefficients (Sect. A in supplementary material). These elementary reaction pathways are known as extreme currents (E_i) and they all contribute to the steady state values of reaction rates. The contributions of the extreme currents (E_i) denoted as the current rates (j_i) are the components of the corresponding current rate vector ($\boldsymbol{j}$), whereas the extreme currents (E_i), are the columns of the extreme current matrix ($\mathbf{E}$). The basic equation of the SNA is:

$$\boldsymbol{r}_{ss} = \mathbf{E} \cdot \boldsymbol{j} \tag{15}$$

Eq. 15 simply describes the decomposition of the steady-state reaction rates into the current rates which are by definition non-negative numbers.

The stability analysis of a particular steady state is usually performed on a linearized form of the general equation of motion of the system around it. When we consider the system in a steady state, a small perturbation of the concentrations of intermediate species can be described as a linear deviation from the steady-state concentrations [1,3,4,6,40−44]:

$$[X] = [X]_{ss} + [\Delta X] \tag{16}$$

We can then expand time derivative of concentration vector $[X]$ in Taylor series near the steady state $[X]_{ss}$ and retaining the leading terms only.

$$\frac{d[X]}{dt} = \frac{d([X]_{ss} + [\Delta X])}{dt} = \frac{d[\Delta X]}{dt} = \mathbf{M} \cdot [\Delta X] \tag{17}$$

The leading term $\mathbf{M}$ is a Jacobian matrix which in SNA has the form [12,45]:

$$\mathbf{M}(\boldsymbol{h}, \boldsymbol{r}_{ss}) = \mathbf{S} \cdot \mathrm{diag}(\boldsymbol{r}_{ss}) \cdot \mathbf{K}^T \cdot \mathrm{diag}(\boldsymbol{h}) \tag{18}$$

or by using the relation (15):

$$\mathbf{M}(\boldsymbol{h}, \boldsymbol{j}) = \mathbf{S} \cdot \mathrm{diag}(\mathbf{E} \cdot \boldsymbol{j}) \cdot \mathbf{K}^T \cdot \mathrm{diag}(\boldsymbol{h}) \tag{19}$$

where $\mathrm{diag}(\boldsymbol{h})$ is a diagonal matrix whose elements (h_i) are the reciprocal of the steady state concentrations of the species i, $(i = 1,...,n)$ where n is the number of independent

intermediate species, and $\mathbf{K}$ is the matrix of the order of reactions with its transpose $\mathbf{K}^T$. For the model under consideration, matrix $\mathbf{K}$ is given in Appendix B.

The steady-state stability is determined by the sign of the eigenvalues of $\mathbf{M}$, which are the roots (λ) of the characteristic polynomial: [46]

$$\left| \lambda \mathbf{I} - \mathbf{M} \right| = \sum_{i=0}^{n} \alpha_i \lambda^{n-i} \tag{20}$$

If the real compoments of all of the eigenvalues are negative, a steady state is stable. If one or more eigenvalues have positive real parts the steady state is unstable.

The sign of the real part of the eigenvalues of the Jacobian matrix can be evaluated by using several criteria such as the Hurwitz determinants [46,47] or an α approximation (a system is unstable if at least one coefficient of the characteristic polynomial α is negative). Since our main goal is to derive an equation which yields an (in)stability condition, two of the mentioned criteria are impractical to use, because the equations derived for large models consist of hundreds or even thousands of terms. Moreover, a direct calculation of the roots of a characteristic Eq. 20 of the order n, where n is the number of independent intermediate species is often impossible to calculate. A much simpler method to examine the steady-state stability is to use a matrix of current rates [$\mathbf{V}(j)$], where:

$$\mathbf{V}(j) = -\mathbf{S} \cdot \mathrm{diag}(\mathbf{E} \cdot j) \cdot \mathbf{K}^T \tag{21}$$

or by using relation (15):

$$\mathbf{V}(r_{ss}) = -\mathbf{S} \cdot \mathrm{diag}(r_{ss}) \cdot \mathbf{K}^T \tag{22}$$

A steady state is considered unstable if there is at least one negative diagonal minor of $\mathbf{V}(j)$ [12] and it is possible only if the polynomials from corresponding determinants contain, at least, one negative term. Namely, a negative minor actually represents a destabilizing term since it can make a coefficient of the characteristic polynomial, α_i, become negative. This occurs as a consequence of the fact that α_i represents the sum of the diagonal minors of dimension $i \times i$. Although it is an approximation, this criterion often gives a very good result [48–50].

The instability criterion calculated by the above mentioned procedure when the system is in a steady state is a function of the reaction rates, and consequently, the related rate constants and steady state concentrations. Steady state concentrations, obtained by solving a steady-state equation (14) are functions of the reactant

concentrations in a selected steady state. Consequently, the instability criterion, as well as the dynamic state of the considered reaction system in a closed reactor, changes in time as the concentration of reactants varies during the course of a reaction. In other words, under batch conditions the reaction system passes through an infinite number of pseudo-steady states.

3.2 Implementation of SNA

With an aim to discuss the role of current rates under stability condition, we need to apply the SNA to a system of differential equations which describe the time evolution of the concentrations of independent intermediate species from a selected model, *i.e.* the model of BZ reaction. Therefore, the selection of the independent intermediate species is the first and necessary step in the stability analysis and are (Br^-, $HOBr$, Br_2, $HBrO_2$, Br_2O, BrO_3^-, $BrO_2^{\bullet}$, Ce^{3+} and $CHBr(COOH)_2$). Malonic acid is a simple reactant that decomposes, whereas $Br_2(g)$, P_1 and P_2 are products of the overall process. (Note, the final products of malonic acid decomposition are CO_2 and H_2O, but our aim is to apply SNA to the previously published model where further decomposition of P_1 and P_2 is not taken into account.) As we have already mentioned in Sect. 2.3, the concentration of water was included in the rate constants of corresponding reactions. Moreover, only one of the two cerium species are considered independent intermediate since the sum of their concentrations are constant. We accept the approximation that $[H^+]$ is constant since its concentration is much higher than those of the intermediate. Thus, we have nine independent intermediate species for the SNA. The oscillating dynamics is typically evolved during the initial phase of the reaction, when bromomalonic acid is the main product, and final oxidation products are formed only in small amounts. Hence, we want to analyze the malonic acid decomposition by the overall stoichiometric reaction (1) and therefore we have to recognize that bromate is the reactant while bromomalonic acid is a product. In that case, we shall consider to have seven independent intermediate species (Br^-, $HOBr$, Br_2, $HBrO_2$, Br_2O, $BrO_2^{\bullet}$, Ce^{3+}), which turns out to be a very serious problem from a mathematical point of view. However, the SNA gives us the possibility of finding instability conditions in such a reaction system which enables us to avoid the direct calculations of the roots of a characteristic Eq. 20 of the seventh order that appears in the model with seven variables [12,13,51].

In this already known procedure, where the instability condition is calculated by means of the negative minors

Table 3: Diagonal minor M_{146} in points where inequality (23) change sign and where bifurcation occurs in Fig. 1N, given as a function of malonic acid concentration.

$[MA]_0 / 10^{-2}$ M	1.60		2.20	
	$[MA] / 10^{-2}$ M	$M_{146} / 10^{-14}$	$[MA] / 10^{-2}$ M	$M_{146} / 10^{-12}$
Last positive value	1.55209	0.04371	2.11650	1.08600
First negative value	1.55183	-0.73271	2.11611	-0.01154
1st oscillations	1.36560	-1.37174	1.99310	-0.00884
Last oscillation	0.41080	-4.23458	0.25918	-0.08000
Last negative value	0.27398	-1.59243	0.25007	-0.02130
First positive value	0.27395	1.47311	0.24995	0.11609

of the order less than seven, current rates will have an important role. To demonstrate this, we have to start with a corresponding set of differential equations (2-8) that describe the time evolution of the concentrations of the seven selected independent internal species. By equating (2-8) with zero we obtain steady state equation (14), that upon solving yields matrix **E** (Sect. A in supplementary material) which is required to perform the stability analysis.

For the considered model, $\mathbf{V}(j)$ is given in Appendix C. Stability analysis is performed by calculating the determinants of the corresponding diagonal minors, and by detecting ones that can be negative (the others are always positive). The first step is to calculate the matrix $\mathbf{V}(j)$ by Eq. 21, and then to calculate the determinants of the diagonal minors that are functions of the current rates. By analyzing polynomials from the related determinants of all diagonal minors having dimension 1 to 7, only 8 were identified with negative terms. The lowest dimension of a negative minor is 3, and this a diagonal minor which is a part of all other negative diagonal minors; therefore we can conclude that the core of instability was located within it. This minor (M_{146}) consists of the elements of the first, fourth and sixth rows, and the columns of matrix $\mathbf{V}(j)$ corresponding to intermediate species Br^-, $HBrO_2$, $BrO_2^\bullet$. (given in Appendix E). The common characteristics for all of the negative minors are that they all contain combinations of rows and columns corresponding to intermediate species Br^-, $HBrO_2$, $BrO_2^\bullet$ and this means that the feedback among those species could be responsible for the instability which causes oscillations.

Since the relations between reaction rates and currents rates in a steady state are known (15), the instability condition expressed in the function of current rates can be rewritten as a function of reaction rates, by using MATLAB symbolic toolbox. Thus:

$$r_{+6,ss} r_{+7,ss} (r_{+1,ss} + r_{+2,ss} + r_{+4,ss}) >$$
$$> 2r_{-6,ss} r_{-7,ss} (r_{+1,ss} + r_{+2,ss} + r_{+4,ss}) + (4r_{-6,ss} + r_{+7,ss})$$
$$(r_{+1,ss} + r_{+2,ss} + 4r_{+1,ss} r_{+5,ss} + 2r_{+2,ss} r_{+4,ss} + \qquad (23)$$
$$+ 4r_{+2,ss} r_{+5,ss} + 4r_{+4,ss} r_{+5,ss})$$

The inequality obtained from the selected negative minor, as well as the one expressed in the function of current rates (Eq. E1 in supplementary material) describes the instability condition which most probably must be fulfilled so that the system can become unstable. Validity of the inequality (23) was verified by comparing it with numerical simulations carried out for different initial concentrations of malonic acid given in Fig. 1. Since the malonic acid concentration is decreasing during reaction, it behaves as a control parameter of the system and steady state concentrations of other species are calculated as functions of its instantaneous value. The reaction rates and all minors depend on it as well. From the results given in Table 3, a good agreement between malonic acid concentrations for which diagonal minor M_{146} shifts from a positive to a negative value, and the malonic acid concentrations where oscillations start and terminate can be established.

Once an instability condition in a function of reaction rates is in a steady state, it can be expressed in different combinations by means of their steady-state relations such as the ones given in Eq. 14. Namely, the number of reaction rates in a steady state is equal to the number of reactions in the model, because in the SNA all reversible reactions are separated in two forward reactions. In the case considered here, there are 16 reactions. Since we have selected 7 independent intermediary species (independent internal variables) with aim of describing a time-evolution of the system and define the steady state, the number of equations in (14) is equal to this number,

and the values for the reaction rates in the steady state can neither be uniquely determined, nor chosen arbitrarily. The instability condition can be expressed as a function of the different linear combinations of the reaction rates in the steady state, where all of them satisfy the relation (14).

4 Discussion

As we mentioned earlier, the main goal of this paper is to answer the question as to whether the stability analysis can be performed using only reaction rates in a steady state as those parameters that can be more or less satisfactorily evaluated from experimentally determined rate constants and steady-state concentrations of reactants. We have calculated instability condition as a function of reaction rates in a steady state by using the procedure of selecting the negative minor by means of current rates and then the current rates have been transformed to reaction rates. What will happen if we calculate the negative minors directly from $\mathbf{V}(r_{ss})$, that is, from Eq. 22 using steady-state relations (14)? In that case, the number of negative minors is larger than it should be. Why? Although all the coefficients of the current rates in the $\mathbf{V}(j)$ matrix are positive numbers, it is not the case with the $\mathbf{V}(r_{ss})$ matrix. In the case considered, instead of 8 there are 16 of negative minors (Sect. D in supplementary material). Therefore we obtain incorrect solution. If we want to know which minor are negative, we need to calculate the negative ones as a function of the current rates.

On the other hand, the matrix $\mathbf{V}(j)$ given as a function of the current rates offers the exact set of negative minors. In order to illustrate the problem that can arise from the stability analysis based only on the reaction rates, an analysis of the diagonal minor of dimension 2, which consists of the first two elements of the first and second rows and columns of the matrices $\mathbf{V}(j)$ and $\mathbf{V}(r_{ss})$ is required. (As we have shown earlier in Eq. 23, the source of instability is located within diagonal minor of dimension 3, and no minor of the dimension 2 contains negative Terms). When expressed using reaction rates (Eq. 22), a polynomial of the determinant of the considered diagonal minor of dimension 2 has the form:

$$M_{12}(r_{ss}) = r_{+7,ss}\left(r_{+2,ss} + 4r_{+5,ss} - r_{+6,ss}\right) + \\ + 2r_{-6,ss}\left(2r_{+2,ss} + 8r_{+5,ss} + r_{-7,ss}\right) \tag{24}$$

There is one negative term given in the form of $r_{+6,ss}$ and therefore, one can consider this diagonal minor as the

source of instability. However, this polynomial cannot become negative since there are no negative terms when it is expressed via current rates using Eq. 21 (see Eq. F1 in supplementary material).

The existence of diagonal minors is a significant problem in stability analysis based solely on the reaction rates, but since the number of current rates is usually larger than the number of equations from which they can be determined and numerical values of current rates most often cannot be calculated, the main problem of using current rates as parameters in stability analysis is the inability to compare the derived equations with experimental results.

5 Conclusion

Based on the presented discussion we can see that the SNA is a very powerful method for stability analysis of very complex chemical models such as the one investigated in this paper. This paper provides support for an efficient stability analysis where both parameters (current and reaction rates) are equally important. Since each parameter has unique features which introduce significant improvements in both detecting instabilities in the model and fitting numerical simulations with experimental results. Current rates provide an accurate method for detecting instabilities in the investigated system, but the inability to calculate their numerical values prevents comparing them with experimental results and makes them impractical to use for a system optimization. On the other hand, reaction rates can be easily calculated and compared with experimental results, which allows for system optimization, but they do not provide an accurate method for detecting instabilities. Therefore, for efficient stability analysis we suggest the next scheme:

1. Calculate matrix E, and then calculate matrices $\mathbf{V}(j)$ and $\mathbf{V}(r_{ss})$.
2. Analyze diagonal minors of matrix $\mathbf{V}(j)$ and detect those with negative terms.
3. By analyzing the core of instability, select the smallest, yet most important negative minor.
4. Extract negative minor selected in the previous step, but this time directly from the matrix $\mathbf{V}(r_{ss})$ and calculate the instability condition as a function of r_{ss}.

The previously presented model for the Belousov-Zhabotinsky reaction [14] shown in Table 1 (Sect. 2), is analyzed here by SNA. We found that the core of instability in the considered model is a result of the interplay between the intermediate species Br^-, $HBrO_2$, and $BrO_2^{\bullet}$. We also

obtained the necessary conditions for the appearance and disappearance of oscillations (Eq. 23).

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