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Nonoscillation in closed reversible chemical systems

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For a closed reversible chemical system obeying mass action kinetics, we prove that structurally stable closed orbits do not exist if there are no more reaction steps than reactants. We derive this using an appropriate Lyapunov function for a special case in which the number of reaction steps equals the number of reactants and a stationary point is shown to be unique and asymptotically stable.

KEY WORDS: closed chemical system, reversible, mass action kinetics, closed orbit, structurally stable, stationary point, Lyapunov function

1. Introduction

The dynamic behavior of chemical systems is generally governed by mass action kinetics. If the reaction steps are known, a corresponding system of ordinary differential equations for the concentrations of the reactants can be set up to describe the quantitative and qualitative properties of a given chemical system. To deal with a complicated model considerable simplifications may be necessary or advisable, e.g., by distinguishing fast and slow variables, applying the quasi-steady-state assumption and performing asymptotic analysis [1–4]. The most conspicuous qualitative feature then to detect is the type of attractor of a system. Here, stable equilibria and stable closed orbits are the simplest possibilities, the latter leading to the observation of oscillations. Many investigations have pursued the aim of finding or ruling out such oscillatory behavior, cf. [5–9] for a few existence and [10–12] for nonexistence results.

Not very much seems to be known in this respect about closed chemical systems modeled solely according to mass action kinetics, i.e., without any simplification as those mentioned above. Simon [13] proved that, in the case of two reactants with any finite number of reversible reactions, the concentrations of these are bounded, as well as bounded away from zero, in positive time direction. Tóth [12, theorem 3.2] showed nonexistence of periodic solutions in a very special case of nonreversible reactions.

In the present work, we propose to study closed reversible chemical systems in which the number of reaction steps does not exceed the number of reactants. In this situation, our principal result rules out the possibility of structurally stable closed orbits with positive concentrations (corollary 2.4). This is a consequence of other results making the assumption that the balance matrix, i.e., the matrix formed by the differences of the sto-

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ichiometric coefficients, is nonsingular. In that case, there is a unique equilibrium with positive coordinates, which is shown to be asymptotically stable and structurally stable. Every orbit is forward bounded and forward bounded away from the origin. There is no closed orbit that contains a point with all coordinates positive (theorem 2.2). Finally, if the chemical system has two reactants and reaction steps, then the equilibrium is globally asymptotically stable (corollary 2.3). All these results rely on a suitable Lyapunov function.

The terminology generally follows [14]. In particular, a *closed orbit* is one homeomorphic to a circle. We call it *structurally stable* if every eigenvalue of the linearization of a Poincaré map at the pertinent fixed point has absolute value different from 1. A stationary point is *structurally stable* if all the eigenvalues of the linearization of the vector field at that point have nonzero real parts.

2. Results

The general type of chemical system considered is a closed one, i.e., with $n \geqslant 2$ internal reactants $X_1, \ldots, X_n$, no external reactants, and $m \geqslant 1$ reaction steps with stoichiometric equations

$$m_{1j}X_1 + \cdots + m_{nj}X_n \underset{k'_j}{\overset{k_j}{\longleftrightarrow}} m'_{1j}X_1 + \cdots + m'_{nj}X_n, \quad j = 1, \ldots, m. \tag{1}$$

The stoichiometric coefficients m_{ij}, m'_{ij} $(i = 1, \ldots, n;\ j = 1, \ldots, m)$ are nonnegative integers. The system is assumed to be reversible, i.e., the forward and reverse rate constants, k_j and k'_j, respectively, in the jth reaction step are both positive $(j = 1, \ldots, m)$.

By the law of mass action in chemical kinetics, the concentrations x_i of the reactants X_i, for $i = 1, \ldots, n$, are described by the system of ordinary differential equations

$$\dot{x}_i = \sum_{j=1}^{m} k_j\big(m'_{ij} - m_{ij}\big)x_1^{m_{1j}} \cdots x_n^{m_{nj}} + \sum_{j=1}^{m} k'_j\big(m_{ij} - m'_{ij}\big)x_1^{m'_{1j}} \cdots x_n^{m'_{nj}}, \quad i = 1, \ldots, n, \tag{2}$$

where differentiation is with respect to time. The natural domain of definition of the differential system (2) is the *nonnegative orthant* in $\mathbb{R}^n$, i.e., $N := \{(x_1, \ldots, x_n) \in \mathbb{R}^n \mid x_1 \geqslant 0 \wedge \cdots \wedge x_n \geqslant 0\}$.

The following definition is convenient.

Definition 2.1. The *balance matrix* of system (2), or (1), is the matrix (a_{ij}) with

$$a_{ij} := m'_{ij} - m_{ij}, \quad i = 1, \ldots, n,\ j = 1, \ldots, m.$$

Theorem 2.2. In the chemical system (1) let the number of reactants coincide with the number of reaction steps, i.e., $n = m$. Assume that the balance matrix (a_{ij}) is nonsingular. Then the solution semiflow of system (2) has the following properties:

(i) The nonnegative orthant N is positively invariant.

(ii) There is a unique equilibrium point p in the (open) positive orthant $\mathrm{int}(N)$, the interior of N.

(iii) p is structurally stable and asymptotically stable.

(iv) A closed orbit does not contain a point of $\mathrm{int}(N)$. In particular, there is no closed orbit in the positive orthant $\mathrm{int}(N)$.

(v) Every orbit is forward bounded.

(vi) Every orbit different from $\{0\}$ is forward bounded away from the origin 0.

(vii) A compact set in a face $F_i := \{x \in N \mid x_i = 0 \wedge x_k > 0 \text{ for } k \neq i\}$ of N is not the ω-limit set of a point in $\mathrm{int}(N)$.

Statement (vii) in particular implies that no attracting stationary point or closed orbit can exist in a face F_i of N. Moreover, by proposition 3.6 below, if a face of N contains a stationary point or a closed orbit, then the closure of that face is invariant.

For a two-dimensional system, we have:

Corollary 2.3. If $n = m = 2$ in theorem 2.2, then p is globally asymptotically stable in $\mathrm{int}(N)$.

We cannot prove global asymptotic stability of p for $n \geqslant 3$ in theorem 2.2, nor do we have a counterexample at this stage. Dropping the hypothesis of $n = m$ makes the situation much more complicated. We have an example of a two-dimensional system (i.e., two reactants) with three reaction steps and at least three stationary points (cf. example 3.7).

For $n \geqslant m$ we can at least deduce the following from theorem 2.2, by a perturbation argument.

Corollary 2.4. For $n \geqslant m$, system (2) has no structurally stable closed orbit in $\mathrm{int}(N)$.

3. Proofs

First we do not restrict n or m. Using the balance matrix, system (2) reads

$$\dot{x}_i = \sum_{j=1}^{m} a_{ij}\left(k_j x_1^{m_{1j}} \cdots x_n^{m_{nj}} - k'_j x_1^{m'_{1j}} \cdots x_n^{m'_{nj}}\right), \quad i = 1, \ldots, n. \tag{3}$$

Remark 3.1. We have to allow for real $m_{ij}, m'_{ij} \geqslant 0$. We understand $x^a = \mathrm{e}^{a \ln x}$, so $0^a = 0$ for any $a > 0$ and $0^a = 1$ for $a = 0$, in order to have a continuous vector field on N. For $m_{ij}, m'_{ij} \in \{0\} \cup [1, \infty[$, the vector field satisfies a local Lipschitz condition.

Proposition 3.2. Consider a system (3) with $m_{ij}, m'_{ij} \in \{0\} \cup [1, \infty[$, $a_{ij} = m'_{ij} - m_{ij}$, any n and m. For $x \in N$, $x_i = 0$ implies $\dot{x}_i \geqslant 0$. The nonnegative orthant N is positively invariant, and (3) has a solution semiflow with nonextendible solutions defined on intervals which are open on the right-hand side.

Proof. Let $x \in N$ such that $x_i = 0$ for some i. If $a_{ij} = 0$ then s_j, the jth summand in the expression for $\dot{x}_i$, is zero. Let $a_{ij} < 0$, i.e., $m'_{ij} < m_{ij}$. Then $m_{ij} > 0$, hence, $x_i^{m_{ij}} = 0$ for $x_i = 0$, and thus, $s_j \geqslant 0$. If $a_{ij} > 0$ then $m'_{ij} > 0$, $x_i^{m'_{ij}} = 0$ for $x_i = 0$ and $s_j \geqslant 0$. Therefore, $\dot{x}_i \geqslant 0$ at x. By remark 3.1 the vector field satisfies a local Lipschitz condition. Now the statements in the last sentence of proposition 3.2 follow from [6, appendix, lemma A.1]. □

As a special case of proposition 3.2 we have part (i) of theorem 2.2 which is thereby proved.

To continue the proof of theorem 2.2 we first detect a unique stationary point, then transform it to the point $(1, \ldots, 1)$ and finally apply a particular Lyapunov function.

Proof of 2.2(ii). We now assume $n = m$.

As $\det(a_{ij}) \neq 0$, a point $x \in \operatorname{int}(N)$ is stationary if and only if

$$k_j x_1^{m_{1j}} \cdots x_n^{m_{nj}} - k'_j x_1^{m'_{1j}} \cdots x_n^{m'_{nj}} = 0, \quad j = 1, \ldots, n, \tag{4}$$

or

$$x_1^{a_{1j}} \cdots x_n^{a_{nj}} = \frac{k_j}{k'_j}, \quad j = 1, \ldots, n.$$

Putting $\kappa_j := \ln(k_j/k'_j)$, $j = 1, \ldots, n$, this is equivalent to

$$\sum_{i=1}^{n} a_{ij} \ln x_i = \kappa_j, \quad j = 1, \ldots, n.$$

Again, as $\det(a_{ij}) \neq 0$, this system of linear equations for the $\ln x_i$ has a unique solution. Therefore, (3) has a unique stationary point p with positive coordinates, the solution of

$$\sum_{i=1}^{n} a_{ij} \ln p_i = \kappa_j, \quad j = 1, \ldots, n. \tag{5}$$

This proves part (ii) of theorem 2.2. □

Proof of 2.2(iii). Let

$$\mu_j := k_j p_1^{m_{1j}} \cdots p_n^{m_{nj}} = k'_j p^{m'_{1j}} \cdots p_n^{m'_{nj}}, \quad j = 1, \ldots, n. \tag{6}$$

(The latter equation holds by (4).)

Transform system (3), by $y_i := x_i/p_i$, $i = 1, \dots, n$, to the form

$$\dot{y}_i = \frac{1}{p_i} \sum_{j=1}^{n} a_{ij}\mu_j \left(y_1^{m_{1j}} \cdots y_n^{m_{nj}} - y_1^{m'_{1j}} \cdots y_n^{m'_{nj}} \right), \quad i = 1, \dots, n. \tag{7}$$

The domain of this system is still N, the stationary point in $\operatorname{int}(N)$ is $(1, \dots, 1)$.

A second coordinate change, $z_i := \ln y_i$, $i = 1, \dots, n$, transforms $\operatorname{int}(N)$ to $\mathbb{R}^n$, the stationary point $(1, \dots, 1)$ to the origin, and system (7) to

$$\dot{z}_i = \frac{1}{p_i} \exp(-z_i) \sum_{j=1}^{n} a_{ij}\mu_j \left(\exp\left(\sum_{k=1}^{n} m_{kj} z_k \right) - \exp\left(\sum_{k=1}^{n} m'_{kj} z_k \right) \right), \quad i = 1, \dots, n. \tag{8}$$

Introducing a (positive) function $\varphi(a, b)$ by $\mathrm{e}^a - \mathrm{e}^b = (a-b)\varphi(a, b)$ and functions $\psi_j(z) := \varphi(\sum_{k=1}^{n} m_{kj} z_k, \sum_{k=1}^{n} m'_{kj} z_k)$, $j = 1, \dots, n$, yields

$$\exp\left(\sum_{k=1}^{n} m_{kj} z_k \right) - \exp\left(\sum_{k=1}^{n} m'_{kj} z_k \right) = -\psi_j(z) \sum_{k=1}^{n} a_{kj} z_k,$$

where the $\psi_j(z)$ are positive.

Thus, (8) can be expressed as

$$\dot{z}_i = -\frac{1}{p_i} \exp(-z_i) \sum_{j=1}^{n} \sum_{k=1}^{n} a_{ij} a_{kj} \mu_j \psi_j(z) z_k, \quad i = 1, \dots, n. \tag{9}$$

The domain of this system is all of $\mathbb{R}^n$, and the only stationary point is the origin.

Now introduce the following Lyapunov function:

$$V(z) := \sum_{i=1}^{n} p_i \left(1 + (z_i - 1) \exp z_i \right). \tag{10}$$

$1 + (u-1)\mathrm{e}^u = \int_0^u t\mathrm{e}^t \, \mathrm{d}t$, so V is real analytic and positive definite with respect to the origin. $\operatorname{grad} V(z) = \sum_{i=1}^{n} p_i z_i (\exp z_i) e_i$, with the standard basis $(e_1, \dots, e_n)$ of $\mathbb{R}^n$. Thus, $V^*(z)$, the time derivative of the composition of V with a solution of (10) at z, is

$$V^*(z) = -\sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{k=1}^{n} z_i a_{ij} a_{kj} \mu_j \psi_j(z) z_k.$$

Define a matrix $B(z) = (b_{ij}(z))$ by

$$b_{ij}(z) := \sqrt{\mu_j \psi_j(z)}\, a_{ij}.$$

Then

$$V^*(z) = -\sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{k=1}^{n} z_i b_{ij}(z) b_{kj}(z) z_k = -z^{\mathrm{T}} B(z) B^{\mathrm{T}}(z) z = -\left\| B^{\mathrm{T}}(z) z \right\|^2,$$

where M^{T} is the transposed of a matrix or vector M and $\| \dots \|$ is the Euclidean norm. Now $\det(a_{ij}) \neq 0$ implies that $B(z)$ is nonsingular for any z. Therefore, V^* is negative definite with respect to the origin. By Lyapunov's second method [15, theorem 5.2], the origin is asymptotically stable in system (9). Hence, the same holds for $(1, \dots, 1)$ in (7) and for p in (3) or (2). This takes care of the second assertion of (iii).

To compute the linearization L of the vector field (8) at the origin one just has to collect the linear terms of the appropriate power series in the z_i. One has

$$\exp\left(\sum_{k=1}^{n} m_{kj} z_k\right) - \exp\left(\sum_{k=1}^{n} m'_{kj} z_k\right) = -\sum_{k=1}^{n} a_{kj} z_k + \cdots,$$

$$L_{ik} = -\frac{1}{p_i} \sum_{j=1}^{n} \mu_j a_{ij} a_{kj}, \qquad L = -P^{-1} G G^{\mathrm{T}},$$

where $P_{ik} := p_i \delta_{ik}$, $G_{ik} := a_{ik} \sqrt{\mu_k}$.

By a result of Lyapunov (cf. [16, V. 5, theorem 3]), all eigenvalues of L have negative real parts. Consider the linear differential equation $\dot{x} = Lx$ for the moment; let X be the positive definite quadratic form $X(x) := x^{\mathrm{T}} P x$, then $X^*(x) = -2x^{\mathrm{T}} G G^{\mathrm{T}} x$ is negative definite, hence, Lyapunov's theorem confirms the claim above. In particular, the origin is a structurally stable stationary point of (8), and the proof of part (iii) of theorem 2.2 is complete. □

Proof of 2.2(iv)–(vi). We now turn to the statements in 2.2(iv)–(vi). By the invariance principle [15, lemma 5.5], V^* would be zero on a closed orbit of (9), contradicting $V^* < 0$ on $\mathbb{R}^n \backslash \{0\}$. So $\mathrm{int}(N)$ does not contain a closed orbit of (3), i.e., of (2).

To prove the somewhat stronger statement in (iv) transfer V to a Lyapunov function

$$W(y_1, \dots, y_n) := V(\ln y_1, \dots, \ln y_n)$$

for (7). Then

$$W(y) = \sum_{i=1}^{n} p_i (y_i \ln y_i + 1 - y_i). \tag{11}$$

We have $u \ln u + 1 - u = \int_1^u (\ln t)\, \mathrm{d}t$, which implies $\lim_{u \to 0+} (u \ln u + 1 - u) = 1$. So W has a continuous extension to all of N, also denoted W. In particular, $W(0) = \sum_{i=1}^{n} p_i$. To prove (iv)–(vi) of 2.2 we have to exploit this extended Lyapunov function W, defined also on the boundary $\mathrm{bd}(N)$ of N, where W^* is not defined.

Proposition 3.3. Let $\dot{y} = f(y)$ be a real analytic differential equation on N such that N is positively invariant. Let $W : N \to \mathbb{R}$ be continuous such that $W|_{\mathrm{int}(N)}$ is a Lyapunov function for $\dot{y} = f(y)$, with $W^* < 0$ on $\mathrm{int}(N)$ except on a finite set of points. Then $W \circ y$ is nonincreasing for any solution y of the differential equation.

Proof. The statement is trivial for a constant solution. Let $t_0 < t_1$ and $y : [t_0, t_1] \to N$ a nonconstant solution. If $y(]t_0, t_1[) \subset \mathrm{int}(N)$ then $W \circ y(t_1) < W \circ y(t_0)$ by Lyapunov theory; for $W \circ y$ is strictly decreasing on $]t_0, t_1[$, and, hence, on $[t_0, t_1]$, by $W^* < 0$ on $\mathrm{int}(N)$ outside finitely many points. If $y(]t_0, t_1[)$ is not contained in $\mathrm{int}(N)$ then

$$\left\{ t \in [t_0, t_1] \,\middle|\, \prod_{i=1}^{n} y_i(t) = 0 \right\}$$

is either a finite set or the whole interval $[t_0, t_1]$, because $y(t)$ is a real analytic function of t. In the first case, $y([t_0, t_1]) \cap \mathrm{bd}(N)$ is a finite set and $W \circ y$ is strictly decreasing by the argument given above. In the other case, $y([t_0, t_1]) \subset \mathrm{bd}(N)$. Assume that $W \circ y(t_1) > W \circ y(t_0)$. Let $\varepsilon := W \circ y(t_1) - W \circ y(t_0)$. By continuous dependence of solutions on initial conditions, one can choose a solution $\tilde{y} : [t_0, t_1] \to N$ such that $\tilde{y}(t_0) \in \mathrm{int}(N)$, $|W \circ \tilde{y}(t_0) - W \circ y(t_0)| < \varepsilon/2$ and $|W \circ \tilde{y}(t_1) - W \circ y(t_1)| < \varepsilon/2$. $W \circ \tilde{y}(t_1) < W \circ \tilde{y}(t_0)$ by the first case. Therefore,

$$\varepsilon < W \circ y(t_1) - W \circ \tilde{y}(t_1) + W \circ \tilde{y}(t_0) - W \circ y(t_0) < \frac{\varepsilon}{2} + \frac{\varepsilon}{2},$$

a contradiction. Thus, $W \circ y(t_1) \leqslant W \circ y(t_0)$, and the proof of 3.3 is complete. □

Now we are ready to prove 2.2(iv). Proposition (3.3) is applied to the extended Lyapunov function W for (7), defined on N. The invariance principle still implies that W is constant on any compact positive limit set [15, proof of lemma 5.5]. A closed orbit C in N is such a compact positive limit set (e.g., of itself). If C contains a point of $\mathrm{int}(N)$ then W is constant on C; but $V^* < 0$ on $\mathbb{R}^n \backslash \{0\}$ implies $W^* < 0$ on $C \cap \mathrm{int}(N)$, a contradiction. Passing from system (7) to (3) or (2), proves part (iv) of theorem 2.2.

For a proof of 2.2(v) and (vi), instead of (3) or (2), again we may consider (7), and show the following.

Proposition 3.4. Assume $t \mapsto y(t)$ is a nonzero solution of (3.9) in N, defined for all $t \in [0, \tau[$, $0 < \tau \leqslant \infty$, and not extendible on the right. Then there are $c_1, c_2 > 0$ such that $c_1 < \sum_{i=1}^{n} p_i y_i(t) < c_2$ for all $t \in [0, \tau[$.

The set $\{y \in N \mid c_1 < \sum_{i=1}^{n} p_i y_i < c_2\}$ is bounded and has positive distance from the origin (the p_i being positive by proof of 2.2(ii)). Hence, proposition 3.4 implies (v) and (vi) of theorem 2.2.

Proof of 3.4. We can once more apply proposition 3.3 to the system (7), with W the extended Lyapunov function of proof of 2.2(iv)–(vi), defined on N, which satisfies $W^* < 0$ in $\mathrm{int}(N) \backslash \{(1, \ldots, 1)\}$. Thus, for any increasing sequence $t_k \to \tau$, the sequence $(W \circ y(t_k))_{k \in \mathbb{N}}$ is nonincreasing.

If $\sum_{i=1}^n p_i y_i(t)$ is unbounded above for $t \to \tau$, then there is an increasing sequence $t_k \to \tau$ such that $\lim_{k\to\infty} \sum_{i=1}^n p_i y_i(t_k) = \infty$. So $\lim_{k\to\infty} y_{i_0}(t_k) = \infty$ for some i_0. The function $u \ln u + 1 - u$ is nonnegative with $\lim_{u\to\infty} u \ln u + 1 - u = \infty$. Therefore,

$$W \circ y(t_k) \geqslant p_{i_0}\big(y_{i_0}(t_k) \ln y_{i_0}(t_k) + 1 - y_{i_0}(t_k)\big),$$

hence, $\lim_{k\to\infty} W \circ y(t_k) = \infty$, which is impossible because the sequence is nonincreasing. Thus, $\sum_{i=0}^n p_i y_i(t) < c_2$ for some c_2.

If $\sum_{i=1}^n p_i y_i(t)$ is not bounded away from 0 for $t \to \tau$, then there exists an increasing sequence $t_k \to \tau$ such that $\lim_{k\to\infty} \sum_{i=1}^n p_i y_i(t_k) = 0$, i.e., $\lim_{k\to\infty} y(t_k) = 0$. We may assume $y(t_k) \neq 0$ for all k, as y is not the zero solution, and $0 \leqslant y_i(t_k) < 1$ for all i and k. By continuity, $\lim_{k\to\infty} W \circ y(t_k) = W(0)$. The function $u \ln u + 1 - u$ is strictly decreasing on $]0, 1[$ with $\lim_{u\to 0+} u \ln u + 1 - u = 1$. So W has a strict relative maximum at the origin. Thus, $W \circ y(t_k) < W(0)$. But $(W \circ y(t_k))_{k\in\mathbb{N}}$ is nonincreasing, a contradiction, and we conclude $\sum_{i=1}^n p_i y_i(t) > c_1$ for some positive c_1. □

As a preparation for the proof of 2.2(vii) we provide the following two simple propositions.

Proposition 3.5. Let $q \in \mathrm{bd}(N)$ and $i \in \{1, \ldots, n\}$ such that $q_i = 0, q_k > 0$ for $k \neq i$. Let $a_{ij} \neq 0$ for at least one $j \in \{1, \ldots, m\}$. Then q has a neighborhood U in N such that for system (2.2) or (3.1), $\dot{x}_i > 0$ in $U \cap \mathrm{int}(N)$.

Proof. If j is such that $a_{ij} = 0$ then the jth summand of $\dot{x}_i$ in (3) is zero. So let j be any index such that $a_{ij} \neq 0$.

Case 1. $a_{ij} > 0$, i.e., $m_{ij} < m'_{ij}$. The jth summand of $\dot{x}_i$ is

$$a_{ij} x_i^{m_{ij}} \big(k_j x_1^{m_{1j}} \cdots x_i^0 \cdots x_n^{m_{nj}} - k'_j x_1^{m'_{1j}} \cdots x_i^{a_{ij}} \cdots x_n^{m'_{nj}}\big)$$

which is positive for x sufficiently close to q and x_i positive, because then $x_i^0 = 1$ and $x_i^{a_{ij}}$ can be chosen arbitrarily close to 0.

Case 2. $a_{ij} < 0$, i.e., $m_{ij} > m'_{ij}$. In this case, the jth summand of $\dot{x}_i$ is

$$a_{ij} x_i^{m'_{ij}} \big(k_j x_1^{m_{1j}} \cdots x_i^{-a_{ij}} \cdots x_n^{m_{nj}} - k'_j x_1^{m'_{1j}} \cdots x_i^0 \cdots x_n^{m'_{nj}}\big) > 0$$

for x close to q and x_i positive.

As at least one a_{ij} is nonzero, $\dot{x}_i$ is positive at all points x with $x_i > 0$, in a neighborhood of q. □

Proposition 3.6. Let $q \in \mathrm{bd}(N)$ and $i \in \{1, \ldots, n\}$ such that $q_i = 0, q_k > 0$ for $k \neq i$. For system (2) or (3), let $\dot{x}_i = 0$ at q. Then $\dot{x}_i = 0$ at every x satisfying $x_i = 0$, i.e., $\dot{x}_i = 0$ on the closure of the face F_i containing q. In particular, $\overline{F_i}$ is invariant.

Proof. If $a_{ij} = 0$ for every j then clearly $\dot{x}_i = 0$ anywhere. If j is such that $a_{ij} \neq 0$ then $m_{ij} \neq m'_{ij}$ and at least one of $x_i^{m_{ij}}, x_i^{m'_{ij}}$ is zero for $x_i = 0$. The nonzero one (if any)

is of the form x_i^0, which is 1 for $x_i = 0$ and makes the jth summand and, hence, all of $\dot{x}_i$ positive for all x with $x_k > 0$ for $k \neq i$. As $\dot{x}_i = 0$ at q, both of $x_i^{m_{ij}}, x_i^{m'_{ij}}$ must be zero for $x_i = 0$. Thus, $\dot{x}_i = 0$ for all x with $x_i = 0$. In particular, if the ith coordinate of a point is zero then the whole orbit of that point lies in the set given by $x_i = 0$, i.e., in $\overline{F_i}$. □

Proof of 2.2(vii). Fix $i \in \{1, \ldots, n\}$. If $a_{ij} = 0$ for all j then $\dot{x}_i = 0$ for (3) everywhere. So x_i is constant on any solution, which takes care of (vii) in that case. Assume $a_{ij} \neq 0$ for at least one $j \in \{1, \ldots, m\}$. Then by proposition 3.5, any compact subset S of F_i has a neighborhood U in N such that $\dot{x}_i > 0$ in $U \cap \text{int}(N)$. So, the only way a solution could approach S would be via F_i itself. But by proposition 3.6 $\overline{F_i}$ is invariant. Therefore, a point with ω-limit set S is not in int(N). □

Proof of corollary 2.3. Instead of (2) we study (7), for $n = m = 2$, with a nonsingular balance matrix and the stationary point $(1, \ldots, 1)$. The positive limit set S of an arbitrary point in int(N) is forward bounded, and forward bounded away from 0, by 2.2(v) and (vi). So S is a connected compact nonempty invariant set in N [17, chapter 16, theorem 1.1 and proof], not containing the origin, on which the extended Lyapunov function W of proof of 2.2(iv)–(vi) is constant. As $W^* < 0$ on int$(N)\backslash\{(1, \ldots, 1)\}$, the set S equals $\{(1, \ldots, 1)\}$ or is contained in one of the open axes. But the latter is excluded by 2.2(vii). Therefore, $S = \{(1, \ldots, 1)\}$. Together with 2.2(iii) this shows that the stationary point is globally asymptotically stable in int(N). □

Proof of corollary 2.4. Consider system (2), or equivalently, (3), under the hypothesis $n \geqslant m$. Assume the existence of a structurally stable closed orbit C in int(N). If $n > m$ we can add $n - m$ trivial reaction steps in (1), which amounts to adding $n - m$ columns of zeros to the matrices (m_{ij}), (m'_{ij}), (a_{ij}) and does not change the solutions of (2) and (3). So we still have C as a structurally stable closed orbit in int(N), but the balance matrix now has square form. By an appropriate small perturbation of the m_{ij}, m'_{ij} as nonnegative real numbers, all m_{ij}, m'_{ij} become positive; a subsequent even smaller perturbation makes the balance matrix nonsingular, while the m_{ij}, m'_{ij} stay positive. Choosing these perturbations small enough will keep the existence of a structurally stable closed orbit in int(N). Though the m_{ij}, m'_{ij} are not necessarily integers any more, the arguments of proof of 2.2(ii) and (iii) remain valid, and the new system on int(N) has a unique stationary point and can be transformed to (8) on $\mathbb{R}^n$, with a positive definite Lyapunov function V satisfying $V^* < 0$ outside the origin, which excludes the existence of any closed orbit. This leads to a contradiction, so the original system does not have a structurally stable closed orbit. □

We finally give an example with two reactants and three reaction steps, having at least three equilibria in the interior of the positive quadrant.

Example 3.7. The three stoichiometric equations $X \leftrightarrow Y$, $X \leftrightarrow 2Y$, $4X + 2Y \leftrightarrow 2X + 4Y$, with the rate constants $k_i = 1$, $k_i' = 0.1$ for $i = 1, 2, 3$ lead to the differential system:

$$\dot{x} = -2x + 0.1y + 0.1y^2 - 2x^4y^2 + 0.2x^2y^4,$$
$$\dot{y} = 3x - 0.1y - 0.2y^2 + 2x^4y^2 - 0.2x^2y^4.$$

Adding the two equations leads to the condition $x = 0.1y^2$ for a stationary point, subsequent substitution into the first equation gives a polynomial equation $P(y) = 0$, where $P(y)$ has alternating signs for $y = 0.5$, 1.5, 2.5 and 3.5. So, P has at least three real zeros, and the system has at least three equilibria.

Whether this behavior occurs in cases meaningful from the chemical point of view, remains to be investigated.

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