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Extended detailed balance for systems with irreversible reactions

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ABSTRACT

The principle of detailed balance states that in equilibrium each elementary process is equilibrated by its reverse process. For many real physico-chemical complex systems (e.g. homogeneous combustion, heterogeneous catalytic oxidation, most enzyme reactions, etc.), detailed mechanisms include both reversible and irreversible reactions. In this case, the principle of detailed balance cannot be applied directly. We represent irreversible reactions as limits of reversible steps and obtain the principle of detailed balance for complex mechanisms with some irreversible elementary processes. We prove two consequences of the detailed balance for these mechanisms: the structural condition and the algebraic condition that form together the *extended form of detailed balance*. The *algebraic condition* is the principle of detailed balance for the reversible part. The *structural condition* is the convex hull of the stoichiometric vectors of the irreversible reactions has empty intersection with the linear span of the stoichiometric vectors of the reversible reactions. Physically, this means that the irreversible reactions cannot be included in oriented cyclic pathways.

The systems with the extended form of detailed balance are also the limits of the reversible systems with detailed balance when some of the equilibrium concentrations (or activities) tend to zero. Surprisingly, the structure of the limit reaction mechanism crucially depends on the relative speeds of this tendency to zero.

1. Introduction

1.1. Detailed balance for systems with irreversible reactions: the grin of the vanishing cat

The principle of detailed balance was explicitly introduced and effectively used for collisions by Boltzmann (1964). In 1872, he proved his *H*-theorem using this principle. In its general form, this principle is formulated for kinetic systems which are decomposed into elementary processes (collisions, or steps, or elementary reactions). At equilibrium, each elementary process should be equilibrated by its reverse process. The arguments in favor of this property are founded upon microscopic reversibility. The microscopic "reversing of time" turns at the kinetic level into the "reversing of arrows": the elementary processes transform into their reverse processes. For example, the reaction $\sum_i \alpha_i A_i \to \sum_j \beta_j B_j$ transforms into $\sum_j \beta_j B_j \to \sum_i \alpha_i A_i$ and conversely. The equilibrium ensemble should be invariant with respect to this transformation because of microreversibility and the uniqueness of thermodynamic equilibrium. This leads us immediately to the concept of detailed balance: each process is equilibrated by its reverse process.

For a given equilibrium, the principle of detailed balance results in a system of *linear* conditions on kinetic constants (or collision kernels). On the contrary, if we postulate just the *existence* of an a priori unknown equilibrium state with the detailed balance property then a system of *nonlinear* conditions on kinetic constants appear. These conditions were introduced in by Wegscheider (1911) and used later by Onsager (1931). They are known now as the *Wegscheider conditions*.

For linear kinetics, the Wegscheider conditions have a very simple and transparent form: *for each oriented cycle of elementary processes the product of kinetic constants is equal to the product of kinetic constants of the reverse processes.*

However, many mechanisms of complex chemical and biochemical reactions, in particular mechanisms of combustion and enzyme reaction, include some irreversible (unidirectional) reactions. In many cases, complex mechanisms consist of some reversible and some irreversible reactions, equilibrium concentrations and rates of reactions become zeroes, and the standard forms of the detailed balance do not have a sense.

In physical chemistry, the feasibility of a reaction depends on the energies and entropies of system states, initial, final, and transition ones. Nevertheless, some combinations of irreversible reactions are impossible irrespective of the values of thermodynamic functions. Since Wegscheider's time it is known that the cyclic sequence of irreversible reactions (the completely irreversible cycle) is impossible. It is forbidden by the principle of

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detailed balance. In a similar way, the reaction mechanism $A \rightleftharpoons B$, $A \to C$, $C \to B$ is forbidden as well as $A \rightleftharpoons B$, $A \rightleftharpoons C$, $C \to B$.

Two fundamental problems can be posed:

(1) Which mechanisms with irreversible steps are allowed, and which such mechanisms are forbidden by the principle of detailed balance?

In accordance with our knowledge, this question was not answered rigorously and the general problem was not solved. Beside that, the procedure of determining the forbidden mechanisms was not described.

(2) Let a mechanism with some irreversible steps be not forbidden. Do we still have some relationships between kinetic constants of this mechanism?

In our paper, both problems are analyzed based on the same procedure. Substituting the zero kinetic constants by small, however not zero values we return to the fully 'reversible case', in which all steps of the reaction mechanism are reversible. Then, we analyze a limit case, in which small kinetic parameters tend to reach 0.

Such an idea was applied previously to several examples. In particular, Chu (1971) used this idea for a three-step mechanism, demonstrating that the mechanism $A \rightleftharpoons B$, $A \to C$, $B \to C$ can appear as a limit of reversible mechanisms which obey the principle of detailed balance, whereas the system $A \rightleftharpoons B$, $A \to C$, $C \to B$ cannot appear in such a limit. However, this approach was not applied to the general analysis of multi-step mechanisms, only to a few systems of low dimensions.

Since Lewis Carroll's "Alice's Adventures in Wonderland", the Cheshire Cat is well known, in particular its inscrutable grin. Finally this cat disappears gradually until nothing is left but its grin. Alice makes a remark she has often seen a cat without a grin but never a grin without a cat.

The detailed balance for systems with irreversible reactions can be compared with this grin of the Cheshire cat: the whole cat (the reversible system with detailed balance) vanishes but the grin persists.

1.2. Detailed balance: the classical relations

First, let us consider linear systems and write the general first order kinetic equations:

$$\dot{p}_i = \sum_j (k_{ij}p_j - k_{ji}p_i). \tag{1}$$

Here, p_i is the probability of a state A_i $(i=1,\ldots,n)$ (or, for monomolecular reactions, the concentration of a reagent A_i). The kinetic constant $k_{ij} \geq 0$ $(i \neq j)$ is the intensity of the transitions $A_j \to A_i$ (i.e., k_{ij} is $k_{i \leftarrow j}$). The rate of the elementary process $A_i \to A_j$ is $k_{ji}p_i$. The class of equations (1) includes the Kolmogorov equation for finite Markov chains, the Master equation in physical kinetics and the chemical kinetics equations for monomolecular reactions.

Let $p_i^{\mathrm{eq}} > 0$ be a positive equilibrium distribution. According to the principle of detailed balance, the rate of the elementary process $A_i \to A_j$ at equilibrium coincides with the rate of the reverse process $A_i \leftarrow A_j$:

$$k_{ij}p_j^{\mathrm{eq}} = k_{ji}p_i^{\mathrm{eq}}. \tag{2}$$

For a given equilibrium, p_i^{eq}, the principle of detailed balance is equivalent to this system (2) of linear equalities. To find the conditions of the *existence* of such a positive equilibrium that (2) holds, it is sufficient to write equations (2) in the logarithmic form, $\ln p_i^{\mathrm{eq}} - \ln p_j^{\mathrm{eq}} = \ln k_{ij} - \ln k_{ji}$, to consider this system as a system of linear equations with respect to the unknown $\ln p_i^{\mathrm{eq}}$, and to formulate the standard solvability condition.

After some elementary transformation this condition gives: a positive equilibrium with detailed balance (2) exists if and only if

1. If $k_{ij} > 0$ then $k_{ji} > 0$ (reversibility);
2. For each oriented cycle of elementary processes, $A_{i_1} \to A_{i_2} \to \ldots A_{i_q} \to A_{i_1}$, the product of the kinetic constants is equal to the product of the kinetic constants of the reverse processes:

$$\prod_{j=1}^{q} k_{i_{j+1}i_j} = \prod_{j=1}^{q} k_{i_j i_{j+1}} \tag{3}$$

where the cyclic numeration is used, $i_{q+1} = i_1$.

Of course, it is sufficient to use in (3) a basis of independent cycles (see, for example the review of Schnakenberg (1976)).

Let us introduce the more general Wegscheider conditions for nonlinear kinetics and the generalized mass action law. (For a more detailed exposition we refer to the textbook of Yablonskii et al., 1991.) The elementary reactions are given by the stoichiometric equations

$$\sum_i \alpha_{ri}A_i \to \sum_j \beta_{rj}A_j \quad (r=1,\ldots,m), \tag{4}$$

where A_i are the components and $\alpha_{ri} \geq 0$, $\beta_{rj} \geq 0$ are the stoichiometric coefficients. The reverse reactions with positive constants are included in the list (4) separately. We need this separation of direct and reverse reactions to apply later the general formalism to the systems with some irreversible reactions.

The *stoichiometric matrix* is $\mathbf{\Gamma} = (\gamma_{ri})$, $\gamma_{ri} = \beta_{ri} - \alpha_{ri}$ (gain minus loss). The *stoichiometric vector* γ_r is the rth row of $\mathbf{\Gamma}$ with coordinates $\gamma_{ri} = \beta_{ri} - \alpha_{ri}$.

According to the *generalized mass action law*, the reaction rate for an elementary reaction (4) is

$$w_r = k_r \prod_{i=1}^{n} a_i^{\alpha_{ri}}, \tag{5}$$

where $a_i \geq 0$ is the *activity* of A_i.

The list (4) includes reactions with the reaction rate constants $k_r > 0$. For each r we define $k_r^+ = k_r$, $w_r^+ = w_r$, k_r^- is the reaction rate constant for the reverse reaction if it is on the list (4) and 0 if it is not, w_r^- is the reaction rate for the reverse reaction if it is on the list (4) and 0 if it is not. For a reversible reaction, $K_r = k_r^+/k_r^-$.

The principle of detailed balance for the generalized mass action law is: For given values k_r there exists a positive equilibrium $a_i^{\mathrm{eq}} > 0$ with detailed balance, $w_r^+ = w_r^-$. This means that the system of linear equations

$$\sum_i \gamma_{ri}x_i = \ln k_r^+ - \ln k_r^- = \ln K_r \tag{6}$$

is solvable ($x_i = \ln a_i^{\mathrm{eq}}$). The following classical result gives the necessary and sufficient conditions for the existence of the positive equilibrium $a_i^{\mathrm{eq}} > 0$ with detailed balance (see, for example, the textbook of Yablonskii et al., 1991).

Proposition 1. *Two conditions are sufficient and necessary for solvability of* (6):

1. *If $k_r^+ > 0$ then $k_r^- > 0$ (reversibility);*
2. *For any solution $\boldsymbol{\lambda} = (\lambda_r)$ of the system*

$$\boldsymbol{\lambda}\mathbf{\Gamma} = 0 \left(\text{i.e. } \sum_r \lambda_r \gamma_{ri} = 0 \text{ for all } i \right) \tag{7}$$

the Wegscheider identity holds:

$$\prod_{r=1}^{m}(k_r^+)^{\lambda_r}=\prod_{r=1}^{m}(k_r^-)^{\lambda_r}. \tag{8}$$

Remark 1. It is sufficient to use in (8) a basis of solutions of the system (7): $\boldsymbol{\lambda}\in\{\boldsymbol{\lambda}^1,\ldots,\boldsymbol{\lambda}^g\}$.

Remark 2. The Wegscheider condition for the linear systems (3) is a particular case of the general Wegscheider identity (8). Therefore, the solutions $\boldsymbol{\lambda}$ of equation (7) are generalizations of the (non-oriented) cycles in the reaction networks. The basis of solutions corresponds to the basic cycles. This basis is, obviously, not unique.

Remark 3. In equation (6) unknown $x_i=\ln a_i$ are independent variables and vector $\boldsymbol{x}$ can take any value in R^n. In practice, this is not always true. For example, for heterogeneous systems with solid components some activities may vary in a narrow interval or may be even constant (see the more detailed discussion below in Section 3.5). We do not study multiphase equilibiria in our paper.

Remark 4. All the closed chemical systems have linear conservation laws: conservation of mass, various sorts of atoms, electric charge and other conserved quantities. They are linear functions of the amounts N_i of chemical components A_i. There is a problem of uniqueness and existence of a positive equilibrium with detailed balance or without it for every set of values of the independent conservation laws. To solve this problem we need some properties of the connection between activities and concentrations, $(a_i)\leftrightarrow(c_i)$. We do not assume any hypothesis about this connection and study just existence of a positive equilibrium with detailed balance in the space of activities. The Wegscheider identity (8) gives a necessary and sufficient condition for this existence.

In practice, very often $k_r^-=0$ for some r, whereas $k_r^+>0$. In these cases, the standard forms of the detailed balance have no sense. Indeed, let us consider a linear reversible cycle with an irreversible buffer:

$$A_1\rightleftharpoons A_2\rightleftharpoons\ldots A_n\rightleftharpoons A_1\rightarrow A_0.$$

This system converges to the state where only $p_0>$ and $p_i=0$ for $i>0$. In this state, trivially, $w_r^+=w_r^-=0$ and it seems that the standard principle of detailed balance does not imply any restriction on the kinetic constants. Of course, this impression is wrong.

Let us consider this system as a limit of the system with a reversible buffer, $A_1\rightleftharpoons A_0$ (both reaction rate constants are positive), when the constant of the reverse reaction is positive but tends to zero: $k_{1\leftarrow 0}\to 0$, $k_{1\leftarrow 0}>0$. For each positive value $k_{1\leftarrow 0}>0$ the condition of detailed balance $w_r^+=w_r^-$ gives the Wegscheider identity (3) for the cycle $A_1\rightleftharpoons A_2\rightleftharpoons\ldots A_n\rightleftharpoons A_1$: The product of direct reaction rate constants is equal to the product of the reverse reaction rate constants. This condition holds also in the limit $k_{1\leftarrow 0}\to 0$. So, any practically negligible but positive value of the reverse kinetic constant implies the nontrivial Wegscheider condition for the other constants.

If we assume that the negligible values of the constants should not affect the kinetic systems then this Wegscheider condition should hold for the system with fully irreversible steps as well. Therefore, the following way for the formalization of the principle of detailed balance for irreversible reactions is proposed. We return to reversible reactions in which the principle of detailed balance is assumed by the introduction of small $k_r^->0$. Then we go to the limit $k_r^-\to 0$ ($k_r^->0$) for these reactions.

It is worth mentioning that the free energy has no limit when some of the reaction equilibrium constants tend to zero. For example, for the ideal gases $F=\sum_i N_i(RT\ln c_i+\mu_i^0-RT)$, where c_i is the concentration, N_i is the amount and μ_i^0 is the standard chemical potential of the component A_i. In the irreversible limit some $\mu_i^0\to\infty$. On the contrary, the activities

$$a_i=\exp\left(\frac{\mu_i-\mu_i^0}{RT}\right) \tag{9}$$

remain finite (for the ideal gases, for example, $a_i=c_i$) and the approach based on the generalized mass action law and the equations $w_r^+=w_r^-$ can be applied in the irreversible limit.

Below, we study systems with irreversible reactions as the limits of the systems with reversible reactions and detailed balance, when some reaction rate constants go to zero. We formulate the restrictions on the constants in this limit and find the finite number of conditions that is necessary and sufficient to check. First of all we have to discuss the necessary notion of cycles for general reaction networks.

1.3. Main results

We develop three approaches to the detailed balance conditions for the systems with some irreversible reactions. The first and the most physical idea is to consider an irreversible reaction as a limit of a reversible reaction when the reaction rate constant for a reverse reaction tends to zero. The limits of systems of reversible reactions with detailed balance conditions cannot be arbitrary systems with some irreversible reactions and we study the structural and algebraic restrictions for these systems.

The second approach is based on the technical idea to study the limits of the Wegscheider identities (8). Here, it is very useful to apply the concept of the general (nonlinear) irreversible cycles or pathways developed recently far enough for our purposes by Schuster et al. (2000), Gagneur and Klamt (2004) and other. Let us write all reactions separately (including direct and reverse reactions) (4). The general oriented cycle or pathway is a relation between vectors γ_r with non-negative coefficients: $\sum_r\lambda_r\gamma_r=0$, $\lambda_r\geq 0$ and $\sum_r\lambda_r>0$. For each system with all reversible reactions and detailed balance the Wegscheider identity (8) holds for any oriented cycle. Therefore, if an oriented cycle persists in the limit with some irreversible reactions, then, for $\lambda_r>0$, the rth reaction should remain reversible and for this cycle the Wegscheider condition persists.

This property motivates the definition of the extended (or weakened, Yablonsky et al. (2011)) form of detailed balance in Section 3.1 through the general oriented cycles and the Wegscheider conditions. Theorem 1 states that a system satisfies the extended form of detailed balance if and only if it is a limit of systems with all reversible reactions and detailed balance. One part of this theorem ("if") is proved immediately in Section 3.1, the proof of the second part ("only if") exploits the third approach and is postponed till Section 4.

The third idea is to study the limits when some equilibrium concentrations (or, more general, activities) tend to zero. For systems with all reversible reactions, we can explicitly express the constants of the reverse reactions through the constants of the direct reactions and the equilibrium activities: just use the detailed balance conditions, $w^+(a^{\mathrm{eq}})=w^-(a^{\mathrm{eq}})$. Here, instead of $2m$ parameters, $k_r^\pm$ (m is the number of reactions) we use $m+n$ parameters: m reaction rate constants k_r^+ and n equilibrium activities a_i^{eq}. In this description of the reversible reactions, the principle of detailed balance is trivially satisfied. Some reactions become irreversible in the limits when some of the equilibrium activities tends to zero. Surprisingly, the structure of the limit reaction mechanism crucially depends on the relative speeds of this tendency to zero.

In Section 4, we assume that $a_i^{\rm eq} = {\rm const}_i \times \varepsilon^{\delta_i}$ and study the limits $\varepsilon \to 0$. The n-dimensional space of exponents $\delta = (\delta_i)$ is split by m hyperplanes $(\gamma_r,\delta) = 0$ on convex cones. Each of these cones is given by a set of inequalities $(\gamma_r,\delta) \lesseqqgtr 0$ $(r = 1,\ldots,m)$. In every such a cone, the limit reaction mechanism for $\varepsilon \to 0$ is constant.

Using this approach, we prove the second part of Theorem 1 and even more: if a system satisfies the extended form of detailed balance then it may be obtained in the limit $\varepsilon \to 0$ from a system with all reversible reactions with given k_r^+ and $a_i^{\rm eq} = {\rm const}_i \times \varepsilon^{\delta_i}$ for some exponents δ_i (Theorem 4). So, all the three approaches to the consequences of the principle of detailed balance for the systems with some irreversible reactions are equivalent.

The computational problem associated with the extended form of detailed balance is nontrivial. For example, the oriented cycles (pathways) form a convex polyhedral cone and we have to formulate the structural condition of the extended form of detailed balance for all extreme rays (extreme pathways) of this cone (Theorem 2): if $\lambda_r > 0$ for a vector $\boldsymbol{\lambda}$ from an extreme ray then the rth reaction should remain reversible. Calculation of all these extreme rays is a well known and computational expensive problem (Fukuda and Prodon, 1996; Papin et al., 2003; Gagneur and Klamt, 2004). In Theorem 3, we significantly reduce the dimension of the problem.

Instead of the set of *all* stoichiometric vectors γ_r $(r = 1,\ldots,m)$ in the whole space of composition $\mathbb{R}^n$ (n is the number of components, m is the number of reactions) it is sufficient to consider the set of the stoichiometric vectors of the *irreversible* reactions in the quotient space $\mathbb{R}^n/S$, where S is spanned by the stoichiometric vectors of all *reversible* reactions. The simple exclusion of the linear conservation laws provides additional dimensionality reduction. The application of reduction methods is demonstrated in the case study in Section 3.5.

In Section 3.3, we formulate the main results for the simple case of linear (monomolecular) systems. Sections 3.4 and 3.5 are devoted to examples of nonlinear systems. In Section 3.4, the simple examples with obvious lists of the extreme pathways are collected. In Section 3.5, we analyze the possible irreversible limits for a complex reaction of methane reforming with CO_2.

2. Cycles and pathways in general reaction networks

There exist several graph representations of general reaction networks (Yablonskii et al., 1991; Temkin et al., 1996) and each of them implies the correspondent notion of a cycle. For example, each input and output formal sum in the reaction mechanism (4) can be considered as a vertex (a complex) and then a reaction with the positive rate constant is an oriented edge. This graph of the transformation of complexes is convenient for the analysis of the complex balance condition (Feinberg, 1972).

The bipartite graphs of reactions (Volpert and Khudyaev, 1985) gives us another example: it includes two types of vertices: components (correspond to A_i) and reactions (correspond to elementary reactions from (4)). There is an edge from the ith component to the sth reaction if $\alpha_{ri} > 0$ and from the sth reaction to the ith component if $\beta_{ri} > 0$. The correspondent stoichiometric coefficients are the weights of the edges. This graph is convenient for the analysis of the system stability, for calculation of Jacobians for the right hand sides of the kinetic equations and for analysis of their signs (Ivanova, 1979; Mincheva and Roussel, 2007). For nonlinear systems, these graphs do not give a simple representation of the detailed balance conditions.

We need a special notion of a cycle which corresponds to the algebraic relations between reactions. Let us recall that we include direct and inverse reactions in the reaction mechanism (4) separately. Each solution of (7) may be represented as follows:

$$\begin{array}{l|l}
 & \lambda_1 \times \left(\sum_i \alpha_{1i} A_i \to \sum_j \beta_{1j} A_j\right) \\
 & \lambda_2 \times \left(\sum_i \alpha_{2i} A_i \to \sum_j \beta_{2j} A_j\right) \\
+ & \vdots \\
 & \lambda_m \times \left(\sum_i \alpha_{mi} A_i \to \sum_j \beta_{mj} A_j\right) \\
\cline{2-2}
\end{array} = \sum_i a_i A_i \to \sum_j a_j A_j. \tag{10}$$

Here, $a_i = \sum_s \lambda_s \alpha_{si} \equiv \sum_s \lambda_s \beta_{si}$. Therefore, we need the following definition of a cycle.

Definition 1. An oriented cycle is a vector of coefficients $\boldsymbol{\lambda} \neq 0$ with all $\lambda_i \geq 0$ that satisfies (10).

Remark 5. Cycles in catalysis and, especially, in biochemistry are called pathways (Schuster et al., 2000; Papin et al., 2003). An oriented pathway is an oriented cycle from Definition 1. An extreme (oriented) pathway is a direction vector of an extreme ray of the cone Λ_+. A solution of equation (7) (a non-oriented cycle) is a non-oriented pathway.

Qualitatively these concepts have been introduced in the early 1940s by Horiuti who applied them to heterogeneous catalytic reactions (Horiuti, 1973). Horiuti used them to eliminate intermediates of the complex catalytic reaction by adding the steps of the detailed mechanism first multiplied by special coefficients. As result of such procedure, the chemical equation with no intermediates is obtained.

All oriented cycles form the cone Λ_+ (without the origin). *Extreme ray* of a convex cone is a face that is, at the same time, a ray. Each ray may be defined by a directional vector $\boldsymbol{\lambda}$ that is an arbitrary nonzero vector from this ray. The cone Λ_+ is defined by a finite system of linear equations (7) and inequalities $\lambda_r \geq 0$. Therefore, it has a finite set of extreme rays.

For integer stoichiometric coefficients, α_{si}, β_{si}, any extreme ray is defined by an uniform linear systems of equations with integer coefficients supplemented by the conditions $\lambda_i \geq 0$ and $\boldsymbol{\lambda} \neq 0$. Therefore, we can always select a direction vector with the integer coefficients. For each extreme ray, there exists a unique direction vector with minimal integer coefficients.

For monomolecular reaction networks, these cycles coincide with the oriented cycles in the graph of reactions (where vertices are reagents and edges are reactions).

There exists an oriented cycle of the length two for each pair of mutually reverse reactions. For these cycles the Wegscheider identities (8) hold trivially, for any positive values of $k^{\pm}$.

Remark 6. The systems without oriented cycles ($\Lambda_+ = \{0\}$) have a simple dynamic behavior. First of all, for such a system the convex hull of the stoichiometric vectors does not include zero: $0 \notin {\rm conv}\{\gamma_1,\ldots,\gamma_m\}$. Therefore, there exists a linear functional l that separates 0 from $\{\gamma_1,\ldots,\gamma_m\}$: $l(\gamma_s) > 0$ for all $s = 1,\ldots,m$. This linear function $l(c)$ increases monotonically due to any kinetic equation

$$\frac{{\rm d}c}{{\rm d}t} = \sum_s w_s \gamma_s$$

with reaction rates $w_s \geq 0$: ${\rm d}l(c)/{\rm d}t > 0$ if at least one reaction rate $w_s > 0$.

3. Extended form of detailed balance

3.1. Definition

A practically important reaction mechanism may include reversible and irreversible steps. However, some mechanisms with irreversible steps may be wrong because they cannot appear as the limits of reversible mechanisms with detailed balance. Therefore, the first question is about the mechanism structure: what is allowed?

The second question is about the constants: let the mechanism not be forbidden. If it is the limit of a system with detailed balance then the reaction rate constants may be connected by additional algebraic conditions like the Wegscheider conditions (3). We should describe all the necessary conditions. In this Section we answer both questions and formulate both conditions, structural and algebraic.

We have to study study the identities (8) in the limit when some $k_r^- \to 0$. First of all, let us consider reversible reactions: if $k_r^+ > 0$ then $k_r^- > 0$. It is sufficient to use in (8) only $\boldsymbol{\lambda}$ with nonnegative coordinates, $\lambda_r \geq 0$. Indeed, the direct and reverse reactions are included in the list (4) under different numbers. Assume that $\lambda_r < 0$ in an identity (8) for some r. Let the reverse reaction for this r have number r'. Let us substitute $(k_r^+)^{\lambda_r}$ in the left hand side of (8) by $(k_{r'}^+)^{-\lambda_r}$ and $(k_r^-)^{\lambda_r}$ in the right hand side by $(k_{r'}^-)^{-\lambda_r}$. The new condition is equivalent to the previous one. Let us iterate this operation for various r. In the finite number of steps all the powers $\lambda_r \geq 0$.

Let us use notation Λ for the linear space of solutions of (7) and Λ_+ for the cone of positive solutions $\boldsymbol{\lambda}$ $(\lambda_r \geq 0)$ of (7).

For reversible reactions, we proved the following proposition. Let the reactions are reversible and the direct and reverse reactions are included in the list (4) separately.

Proposition 2. *The Wegscheider identity* (8) *holds for all* $\boldsymbol{\lambda} \in \Lambda$ *if and only if it holds for all positive* $\boldsymbol{\lambda} \in \Lambda_+$.

Elementary linear algebra gives the following corollary for reversible reactions.

Corollary 1. *The solution of the system of linear equations for logarithms of equilibrium activities* (6) *exists if and only if for any positive solution* $\boldsymbol{\lambda}$ $(\lambda_r \geq 0)$ *of the system* $\boldsymbol{\lambda}\boldsymbol{\Gamma} = 0$ (7) *the condition* (8) *holds.*

Let us study identity (8) for a positive $\boldsymbol{\lambda}$ when some of $k_r \to 0$. In this limit, for every $\boldsymbol{\lambda} \in \Lambda_+$ Corollary 1 gives two conditions:

Corollary 2. *Let* $k_s > 0$, $k_s \to k_s^{\lim}$ *and the Wegscheider identity* (8) *holds for* k_s. *Then*

1. *If* $\lambda_s > 0$ *and* $k_s^+ \to 0$ *for some s then for some q* $\lambda_q > 0$ *and* $k_q^- \to 0$;
2. *If for all positive components* $\lambda_s > 0$ *the limit constants are positive,* $k_s^{\lim} \pm > 0$, *then the condition* (8) *holds for* $k_s^{\lim} \pm$.

We can interpret the positive solutions of (7) as oriented cycles (linear or nonlinear). The first condition means that if a cycle is cut by the limit $k_s^+ \to 0$ in one direction then it should be also cut by a limit $k_q^- \to 0$ in the opposite direction: the irreversible cycle is forbidden. This remark leads to the definition of the *structural condition* of the extended form of detailed balance.

Definition 2. A system of reactions (4) satisfies the structural condition of the extended form of detailed balance if for every $\boldsymbol{\lambda} \in \Lambda_+$ the reaction which satisfy $\lambda_s > 0$ are reversible: if $\lambda_s > 0$ then $k_s^{\pm} > 0$.

This condition means that all cycles should be reversible. The second condition means that for all cycles $\boldsymbol{\lambda} \in \Lambda_+$ which persist in the system with irreversible reactions the correspondent Wegscheider condition (8) holds. This is the *algebraic condition* of the extended form of detailed balance. Now, we are ready to formulate the definition of the extended form of detailed balance.

Definition 3. The subsystem satisfies the extended form of detailed balance if both the structural and the algebraic condition hold for all $\boldsymbol{\lambda} \in \Lambda_+$.

The following theorem gives the motivation to this definition.

Theorem 1. *A system with irreversible reactions is a limit of systems with reversible reactions and detailed balance if and only if it satisfies the extended form of detailed balance.*

Proof. Let us prove the direct statement: if a system is a limit of systems with reversible reactions and detailed balance then it satisfies the extended form of detailed balance. Indeed, let a system of reactions be a limit of systems with reversible reactions and detailed balance. This means that for each $j = 1,2,\ldots$ a set of reaction rate constants $k_{s,j}^{\pm} > 0$ is given, $k_{s,j}^{\pm} > 0$ satisfy the principle of detailed balance for all j and

$$k_s^{\pm} = \lim_{j\to\infty} k_{s,j}^{\pm}.$$

Assume that the structural condition is violated: there exists such a $\boldsymbol{\lambda} \in \Lambda_+$ that $\lambda_s > 0$ for an irreversible reaction $(k_s^+ > 0,\ k_s^- = 0)$. For all $j = 1,2,\ldots$ the principle of detailed balance gives:

$$\prod_{r,\lambda_r > 0} (k_{r,j}^+)^{\lambda_r} = \prod_{r,\lambda_r > 0} (k_{r,j}^-)^{\lambda_r}. \tag{11}$$

If $\lambda_r > 0$ then $k_r^+ > 0$. Therefore, for these r, sufficiently large j and some $\varepsilon,\delta > 0$, $\delta > k_{r,j}^{\pm} > \varepsilon > 0$. The left hand side of (11) is separated from zero. The right hand side of (11) tends to zero because all factors are bounded and at least one of them tends to zero, $k_{r,j}^- \to 0$. This contradiction proves the structural condition. To prove the algebraic condition, it is sufficient to notice that the Wegscheider identity for $k_{s,j}^{\pm} > 0$ holds for all j, hence, it holds in the limit $j \to \infty$.

We will prove the converse statement (if a system satisfies the extended form of detailed balance then it is a limit of systems with reversible reactions and detailed balance) in Section 4, in the proof of Theorem 4. □

3.2. Criteria

All $\boldsymbol{\lambda} \in \Lambda_+$ participate in the definition of the extended form of detailed balance. Nevertheless, it is sufficient to use a finite subset of this cone.

We can check directly that if for a set $\{\boldsymbol{\lambda}^s\}$ the structural and the algebraic conditions of the extended form of detailed balance hold then they hold for any conic combination of $\{\boldsymbol{\lambda}^s\}$, $\boldsymbol{\lambda} = \sum_s a_s \boldsymbol{\lambda}^s$, $a_s \geq 0$. Therefore, it is sufficient to check the conditions for the directional vectors of the extreme rays of Λ_+.

Let a reaction mechanism satisfy the extended principle of detailed balance. If we delete from this mechanisms any irreversible elementary reaction or any couple of mutually reverse elementary reactions, the resulting mechanism satisfies the extended principle of detailed balance as well.

A cone is pointed if the origin is its extreme point or, which is the same, this cone does not include a whole straight line. The cone Λ_+ is pointed because it belongs to the positive orthant $\{\boldsymbol{\lambda} \mid \boldsymbol{\lambda} \geq 0\}$.

It is a standard task of linear programming and computational convex geometry to find all the extreme rays of the polyhedral pointed cone Λ_+ (Bertsimas and Tsitsiklis, 1997; Motzkin et al., 1953;

Fukuda and Prodon, 1996). Let the directional vectors of these extreme rays be $\{\boldsymbol{\lambda}^s | s=1,\dots,q\}$.

Theorem 2. *The system satisfies the extended form of detailed balance if and only if the structural and algebraic conditions hold for the directional vectors* $\{\boldsymbol{\lambda}^s \mid s=1,\dots,q\}$ *of the extreme rays of the cone* Λ_+.

Theorem 2 follows just from the definition of extreme rays and the Minkowski theorem which states that every pointed cone given by linear inequalities admits a unique representation as a conic hull of a finite set of extreme rays.

This criterion can be simplified as well: it is necessary and sufficient to check the structural conditions for the extreme rays of Λ_+ and then the algebraic condition for a maximal linear independent subset of $\{\boldsymbol{\lambda}^s | s=1,\dots,q\}$.

Corollary 3. *The system satisfies the extended form of detailed balance if and only if the structural conditions hold for all directional vectors* $\{\boldsymbol{\lambda}^s | s=1,\dots,q\}$ *of the extreme rays of the cone* Λ_+ *and the algebraic conditions hold for a maximal linear independent subset of* $\{\boldsymbol{\lambda}^s | s=1,\dots,q\}$.

If, for a given reaction mechanism, the set $\{\boldsymbol{\lambda}^s \mid s=1,\dots,q\}$ of directional vectors of the extreme rays of Λ_+ is known, then it is easy to check, whether this mechanism satisfies the structural conditions of the extended form of detailed balance. It is sufficient to examine for each $\lambda_r^s > 0$, whether $k_r^- > 0$.

After these conditions are examined, it is a simple task to extract the independent set of the Wegscheider identities that should be valid: just select a maximal linear independent subset from the set of $\boldsymbol{\lambda}^s$ and write the correspondent Wegscheider identities.

It is convenient to use all the extreme pathways especially if we would like to study all the subsystems of the given system, which satisfy the extended form of detailed balance. On the other hand, it is computationally expensive to find the set $\{\boldsymbol{\lambda}^s | s=1,\dots,q\}$ (see, for example, the paper by Gagneur and Klamt, 2004). The amount of computation could be significantly reduced because it is not necessary to use all the extreme pathways.

Let us consider a reaction mechanism, which includes both reversible and irreversible reactions. For the reversible reactions, let us join the direct and reverse reactions. Let $\gamma_1,\dots,\gamma_r$ be the stoichiometric vectors of the reversible reactions and $v_1,\dots,v_s$ be the stoichiometric vectors of the irreversible reactions. We use $\boldsymbol{\Gamma}_r$ for the stoichiometric matrix of the reversible reactions and Λ_r for the solutions of the equations $\boldsymbol{\lambda}\boldsymbol{\Gamma}_r = 0$.

The linear subspace $S=\mathrm{span}\{\gamma_1,\dots,\gamma_r\}\subset\mathbb{R}^n$ consists of all linear combinations of the stoichiometric vectors of the reversible reactions. Let us consider the quotient space $\mathbb{R}^n/S$. We use notation $\overline{v}_j$ for the images of v_j in $\mathbb{R}^n/S$.

The following theorem gives the criteria of the extended form of detailed balance, which are more efficient for computations.

Theorem 3. *The system satisfies the extended form of detailed balance if and only if*

1. *The convex hull of the stoichiometric vectors of irreversible reactions does not intersect S, i.e.*
   $$0 \notin \mathrm{conv}\{\overline{v}_1,\dots,\overline{v}_s\}, \tag{12}$$
2. *The reversible reactions satisfy the principle of detailed balance.*

Proof. Let the condition 1 be violated, i.e. $0 \in \mathrm{conv}\{\overline{v}_1,\dots,\overline{v}_s\}$. In this case, there exist such a nonnegative $\theta_i \geq 0$ that $\sum_{j=1}^s \theta_j = 1$ and $\sum_{j=1}^s \theta_j v_j \in S$. This means that $\sum_{j=1}^s \theta_j v_j + \sum_{i=1}^r \lambda_i\gamma_i = 0$. We can transform the sum $\sum_{i=1}^r \lambda_i\gamma_i$ in a combination with positive coefficients if for any negative λ_i we substitute γ_i by the stoichiometric vector of the reverse reaction, that is, $-\gamma_i$. As a result, we get the element of Λ_+, a combination of the stoichiometric vectors with nonnegative coefficients, which is equal to zero and includes some stoichiometric vectors of the irreversible reactions with nonzero coefficients. Therefore, the structural condition of the extended form of detailed balance is violated.

Let the structural condition be violated. Then there exist a combination $\sum_{j=1}^s \theta_j v_j + \sum_{i=1}^r \lambda_i\gamma_i = 0$ with $\theta_j \geq 0$ and $\sum_{j=1}^s \theta_j > 0$. Let us notice that

$$\sum_{j=1}^s \frac{\theta_j}{\sum_{j=1}^s \theta_j} v_j = -\sum_{i=1}^r \frac{\lambda_i}{\sum_{j=1}^s \theta_j}\gamma_i,$$

and, therefore, $0 \in \mathrm{conv}\{\overline{v}_1,\dots,\overline{v}_s\}$. The condition 1 is violated.

We proved that the condition 1 is equivalent to the structural condition of the extended form of detailed balance.

If the condition 1 holds then the condition 2 is, exactly, the algebraic condition of the extended form of detailed balance. □

Remark 7. The first condition of Theorem, $0 \notin \mathrm{conv}\{\overline{v}_1,\dots,\overline{v}_s\}$, is equivalent to the existence of such a linear functional l on $\mathbb{R}^n$ that $l(v_j) > 0$ for all $j=1,\dots,s$ and $l(\gamma_j) = 0$ for all $j=1,\dots,r$.

3.3. Linear systems

The results of previous sections for a linear system (1) have a geometrically clear form (see also the paper by Yablonsky et al., 2011).

Proposition 3. *The necessary and sufficient condition for the extended form of detailed balance is: In any cycle* $A_{i_1} \to A_{i_2} \to \dots \to A_{i_q} \to A_{i_1}$ *with the strictly positive constants* $k_{i_{j+1}i_j} > 0$ *(here* $i_{q+1} = i_1$*) all the reactions are reversible (*$k_{i_j i_{j+1}} > 0$*) and the identity (3) holds.*

The states (reagents) A_q and A_r ($q \neq r$) are *strongly connected* if there exist oriented paths both from A_q to A_r and from A_r to A_q (each oriented edge corresponds to a reaction with the nonzero reaction rate constant). From Proposition 3 we get the following statement.

Corollary 4. *Let a linear system satisfy the extended form of detailed balance. Then all reactions in any directed path between strongly connected states are reversible.*

In brief, a linear system with the extended form of detailed balance can be described as follows: (i) the oriented cycles are reversible and satisfy the classical condition (3), (ii) the system consists of the reversible parts and the irreversible transitions between these parts and (iii) the system of these irreversible transitions is acyclic.

For example, let us analyze subsystems of the simple cycle, $A_1 \rightleftharpoons A_2 \rightleftharpoons A_3 \rightleftharpoons A_1$:

$$\boldsymbol{\Gamma}^{\mathrm{T}} = \begin{bmatrix} -1 & 0 & 1 & 1 & 0 & -1 \\ 1 & -1 & 0 & -1 & 1 & 0 \\ 0 & 1 & -1 & 0 & -1 & 1 \end{bmatrix} \tag{13}$$

The cone of nonnegative solutions Λ_+ to the equation $\boldsymbol{\lambda}\boldsymbol{\Gamma} = 0$ has extreme rays with the following direction vectors: $\boldsymbol{\lambda}^1 = (1,1,1,0,0,0)$, $\boldsymbol{\lambda}^2 = (0,0,0,1,1,1)$, $\boldsymbol{\lambda}^3 = (1,0,0,1,0,0)$, $\boldsymbol{\lambda}^4 = (0,1,0,0,1,0)$, and $\boldsymbol{\lambda}^5 = (0,0,1,0,0,1)$. Vectors $\boldsymbol{\lambda}^{3-5}$ give trivial identities (8) $k_i^+ k_i^- = k_i^- k_i^+$ ($i=1,2,3$) and vectors $\boldsymbol{\lambda}^{1,2}$ give the same identity: $k_1^+ k_2^+ k_3^+ = k_1^- k_2^- k_3^-$.

If we delete one elementary reaction from the simple cycle (i.e. one column from $\boldsymbol{\Gamma}^{\mathrm{T}}$ (13)) then one of the nonnegative solutions

$\boldsymbol{\lambda}^{1,2}$ persists and, due to the extended detailed balance principle, all the reactions should be reversible. This means that the structural condition of extended detailed balance is not satisfied for the simple reversible cycle without one direct or reverse reaction. If two reactions are reversible then the third should be reversible or completely vanish. If we delete one direct reaction (with number 1, 2 or 3) and one reverse reaction (with number 4, 5 or 6) then there remain no non-trivial solutions in Λ_+ and, therefore, no non-trivial relations between the constants persist after deletion of these two reactions.

For the linear systems, the oriented cycles in the graph of reactions (where vertices are the components and edges are the reactions) give the positive solutions to the equation (7): for a linear oriented cycle C the sum of the stoichiometric vectors of its reactions is zero. Moreover, any positive solution of (7) is a convex combination of such cyclic solutions and, therefore, the directed vectors of the extreme rays of Λ_+ can be selected in this form.

3.4. *Simple examples of nonlinear systems*

In this section, we present several elementary examples. For these examples, the sets of the extreme pathways are obvious.

Let us examine a reaction mechanism with irreversible reactions $A \overset{k_1}{\to} B$ and $2B \overset{k_2}{\to} 2A$:

$$\mathbf{\Gamma}^{\mathrm{T}} = \begin{bmatrix} -1 & 2 \\ 1 & -2 \end{bmatrix}. \tag{14}$$

The cone Λ_+ is a ray with the directional vector $\boldsymbol{\lambda} = (2,1)$. Both $\lambda_{1,2} > 0$, hence, both reactions should be reversible and the condition holds: $(k_1^+)^2 k_2^+ = (k_1^-)^2 k_2^-$.

Let us slightly modify this example: $2\mathrm{H} \to \mathrm{H}_2$, $\mathrm{H} + \mathrm{H}_2 \to 3\mathrm{H}$:

$$\mathbf{\Gamma}^{\mathrm{T}} = \begin{bmatrix} -2 & 2 \\ 1 & -1 \end{bmatrix}. \tag{15}$$

The cone Λ_+ is a ray with the directional vector $\boldsymbol{\lambda} = (1,1)$. Both $\lambda_{1,2} > 0$, hence, both reactions should be reversible and the condition holds: $k_1^+ k_2^+ = k_1^- k_2^-$.

If we change the direction of one reaction in the previous example then the new irreversible systems satisfies the extended form of detailed balance: $2\mathrm{H} \to \mathrm{H}_2$, $3\mathrm{H} \to \mathrm{H} + \mathrm{H}_2$:

$$\mathbf{\Gamma}^{\mathrm{T}} = \begin{bmatrix} -2 & -2 \\ 1 & 1 \end{bmatrix}. \tag{16}$$

The cone Λ_+ is trivial (it includes no rays, just the origin), hence, the structural condition holds. The algebraic condition trivially holds, because there is no reversible reaction.

Let us add the forth reversible and nonlinear elementary reaction $A_1 + A_2 \rightleftharpoons 2A_3$ (with the constants $k_4^{\pm}$) to a linear reversible cycle. We should add to $\mathbf{\Gamma}^{\mathrm{T}}$ (13) two new columns:

$$\mathbf{\Gamma}^{\mathrm{T}} = \begin{bmatrix} -1 & 0 & 1 & -1 & 1 & 0 & -1 & 1 \\ 1 & -1 & 0 & -1 & -1 & 1 & 0 & 1 \\ 0 & 1 & -1 & 2 & 0 & -1 & 1 & -2 \end{bmatrix}. \tag{17}$$

The extreme rays of Λ_+ include four rays that correspond to pairs of mutually reverse reactions ($\boldsymbol{\lambda}^{1-4}$), two rays that correspond to the linear cycle ($\boldsymbol{\lambda}^{5,6}$) and six rays for three nonlinear cycles ($\boldsymbol{\lambda}^{7-12}$): (i) $A_1 + A_2 \to 2A_3$, $A_3 \to A_2$, $A_3 \to A_1$; (ii) $A_1 + A_2 \to 2A_3$, $A_3 \to A_1$, $A_1 \to A_2$ and (iii) $A_1 + A_2 \to 2A_3$, $A_3 \to A_2$, $A_2 \to A_1$:

$$\boldsymbol{\lambda}^5 = (1,1,1,0,0,0,0,0), \quad \boldsymbol{\lambda}^6 = (0,0,0,0,1,1,1,0),$$

$$\boldsymbol{\lambda}^7 = (0,0,1,1,0,1,0,0), \quad \boldsymbol{\lambda}^8 = (0,1,0,0,0,0,1,1),$$

$$\boldsymbol{\lambda}^9 = (1,0,2,1,0,0,0,0), \quad \boldsymbol{\lambda}^{10} = (0,0,0,0,1,0,2,1),$$

$$\boldsymbol{\lambda}^{11} = (0,0,0,1,1,2,0,0), \quad \boldsymbol{\lambda}^{12} = (1,2,0,0,0,0,0,1).$$

We omit $\boldsymbol{\lambda}^{1-4}$ which do not produce nontrivial conditions. For the reversible reaction mechanism (when $k_{1-4}^{\pm} > 0$), there are two independent Wegscheider identities (8) that formalize the classical principle of detailed balance: $k_1^+ k_2^+ k_3^+ = k_1^- k_2^- k_3^-$ and $k_3^+ k_4^+ k_2^- = k_3^- k_4^- k_2^+$. If some of the elementary reactions are irreversible then the direction vectors $\boldsymbol{\lambda}^{5-12}$ produce eight conditions. For $\boldsymbol{\lambda}^{5,7,9,11}$ these conditions are as follows:

- ($\boldsymbol{\lambda}^5$) If $k_{1,2,3}^+ > 0$ then $k_{1,2,3}^- > 0$ and $k_1^+ k_2^+ k_3^+ = k_1^- k_2^- k_3^-$;
- ($\boldsymbol{\lambda}^7$) If $k_{3,4}^+, k_2^- > 0$ then $k_{3,4}^-, k_2^+ > 0$ and $k_3^+ k_4^+ k_2^- = k_3^- k_4^- k_2^+$;
- ($\boldsymbol{\lambda}^9$) If $k_{1,3,4}^+ > 0$ then $k_{1,3,4}^- > 0$ and $k_1^+ (k_3^+)^2 k_4^+ = k_1^- (k_3^-)^2 k_4^-$;
- ($\boldsymbol{\lambda}^{11}$) If $k_4^+, k_{1,2}^- > 0$ then $k_4^-, k_{1,2}^+ > 0$ and $k_4^+ k_1^- (k_2^-)^2 = k_4^- k_1^+ (k_2^+)^2$.

To obtain the conditions for $\boldsymbol{\lambda}^{6,8,10,12}$ it is sufficient to change the superscripts $^+$ to $^-$ and inverse. These eight conditions represent the extended form of detailed balance for a given mechanism. To check, whether a subsystem of this mechanism satisfies the extended form of detailed balance, it is necessary and sufficient to check these conditions.

3.5. *Methane reforming processes: a case study*

3.5.1. *The system*

Methane reforming with CO_2 is a complex reaction network (Benson, 1981). The main reactions in the methane reforming are:

1. $\mathrm{CO}_2 + \mathrm{H}_2 \rightleftharpoons \mathrm{CO} + \mathrm{H}_2\mathrm{O}$ (RWGS, Reverse water-gas shift),
2. $\mathrm{CH}_4 + \mathrm{CO}_2 \rightleftharpoons 2\mathrm{CO} + 2\mathrm{H}_2$ (Dry reforming),
3. $\mathrm{CO}_2 + 4\mathrm{H}_2 \rightleftharpoons \mathrm{CH}_4 + 2\mathrm{H}_2\mathrm{O}$ (Methanation),
4. $\mathrm{CH}_4 + \mathrm{H}_2\mathrm{O} \rightleftharpoons \mathrm{CO} + 3\mathrm{H}_2$ (Steam reforming),
5. $\mathrm{CH}_4 \rightleftharpoons 2\mathrm{H}_2 + \mathrm{C}$ (Methane decomposition),
6. $2\mathrm{CO} \rightleftharpoons \mathrm{CO}_2 + \mathrm{C}$ (Boudouard reaction),
7. $\mathrm{C} + \mathrm{H}_2\mathrm{O} \rightleftharpoons \mathrm{CO} + \mathrm{H}_2$ (Coal gasification).

For the reagents, we use the notations $A_1 = \mathrm{CH}_4$, $A_2 = \mathrm{CO}_2$, $A_3 = \mathrm{CO}$, $A_4 = \mathrm{H}_2$, $A_5 = \mathrm{H}_2\mathrm{O}$, $A_6 = \mathrm{C}$. Amount of A_i is N_i. There exist three independent linear conservation laws: $b_{\mathrm{C}} = N_1 + N_2 + N_3 + N_6$; $b_{\mathrm{H}} = 4N_1 + 2N_4 + 2N_5$; $b_{\mathrm{O}} = 2N_2 + N_3 + N_5$. The number of degrees of freedom in the closed system is three (six components minus three independent conservation laws).

This example enriches our discussion because it deviates from the nice abstract scheme discussed above. First of all, the reactions 1–7 are not elementary steps. We consider them as overall reactions which have their own intrinsic and complicated reaction mechanism. This does not cause a serious problem because the generalized mass action law describes the equilibria of the complex overall reactions as well as the equilibria of the elementary ones. Therefore, we can apply the concept of the extended form of detailed balance and our Theorems 1–3 to the process network 1–7 build from the complex reactions. Rigorously speaking, we deal not with the elementary reaction steps but with the main equilibria and may discuss, for example, not the “Boudouard reaction” but the “Boudouard equilibrium”.

The second problem is the heterogeneity of the system: $A_1, \ldots, A_5$ are gases and $A_6 = \mathrm{C}$ is solid. Some of the reactions go on the surface of the solid.

If a multiphase system is ideal and the solid components are stoichiometric ones (i.e. they have a fixed composition) then the free energy has the form

$$F = \sum_{A_i-\mathrm{gas}} N_i (RT \ln c_i + \mu_i^0 - RT) + \sum_{A_i-\mathrm{solid}} N_i \mu_i^0. \tag{18}$$

Here, the free energy of solid components differs from the free energy of gases by the absence of the term $RTN \ln c$. This term corresponds to the ideal gas pressure $PV = NRT$. In our case,

$$F = \sum_{i=1}^{5} N_i (RT \ln c_i + \mu_i^0 - RT) + N_6 \mu_6^0. \tag{19}$$

To define the activities, we follow (9). For the ideal gases $a_i = c_i$ and for the stoichiometric solids $a_i \equiv 1$.

In Section 1.2, we studied homogeneous systems and considered $x_i = \ln a_i$ as independent unknowns in the detailed balance equations (6):

$$\sum_i \gamma_{ri} x_i = \ln K_r \ (x_i = \ln a_i^{\mathrm{eq}}). \tag{20}$$

Therefore, for any solution of this system, the activities $a_i = \exp x_i$ represented a positive equilibrium.

In a heterogeneous system with the free energy (18) the activities for the solid components are constant, the correspondent $x_i \equiv 0$. Let $\boldsymbol{x} = (x_i)$ be a solution to Eqs. (20), $\boldsymbol{\Gamma x} = \boldsymbol{K}$, where $\boldsymbol{K}$ is the vector of the equilibrium constants. The vector $\boldsymbol{a} = (a_i)$, $a_i = \ln x_i$ is a vector of equilibrium activities if and only if $x_i = 0$ for all the solid components A_i. Instead of analyzing the solvability of the detailed balance equations (20) we have to study its solvability under additional condition: $x_i = 0$ for all the solid components A_i.

Let us postpone the discussion of the extended principle of detailed balance in multiphase systems and consider the system "gaseous mixture + one stoichiometric solid". Let A_n be solid.

If there is the only solid component then the solvability conditions for the system (20) and for this system with additional condition $x_n = 0$ coincide. Indeed, there exist a positive stoichiometric linear conservation law:

$$\sum_{i=1}^{n} \gamma_{ri} b_i = 0 \quad \text{for all } r \text{ and } b_i > 0 \text{ for all } i.$$

For example, this may be conservation of mass or of the amount of atoms. Let $\boldsymbol{b} = (b_i)$. For any solution of the detailed balance conditions (20) $\boldsymbol{x} = (x_i)$, the vector

$$\boldsymbol{x}' = \boldsymbol{x} - \frac{x_n}{b_n} \boldsymbol{b}$$

is also a solution to (20) with the condition $x'_n = 0$.

So, for our example with seven equilibria 1–7 the conditions of the extended principle of detailed balance for the heterogeneous system with solid $A_6 = C$ are described by the Theorems 1–3 and wee can use the results of the preceding sections.

3.5.2. The classical Wegscheider conditions

To formulate the classical Wegscheider identities, we have to join the direct and inverse reactions and to find the basic solutions of the system of linear equations $\boldsymbol{\lambda \Gamma} = 0$. The stoichiometric matrix for this example is:

$$\boldsymbol{\Gamma}^{\mathrm{T}} = \begin{bmatrix} 0 & -1 & 1 & -1 & -1 & 0 & 0 \\ -1 & -1 & -1 & 0 & 0 & 1 & 0 \\ 1 & 2 & 0 & 1 & 0 & -2 & 1 \\ -1 & 2 & -4 & 3 & 2 & 0 & 1 \\ 1 & 0 & 2 & -1 & 0 & 0 & -1 \\ 0 & 0 & 0 & 0 & 1 & 1 & -1 \end{bmatrix}. \tag{21}$$

The system of seven equations $\boldsymbol{\lambda \Gamma} = 0$) is redundant. There are only three independent equations (one equation for every degree of freedom). It is sufficient to take the components of stoichiometric vectors that correspond to the components A_2, A_4, A_6. Other components satisfy the same linear relations as the selected ones. The reduced matrix $\boldsymbol{\Gamma}_{\mathrm{r}}^{\mathrm{T}}$ is

$$\boldsymbol{\Gamma}_{\mathrm{r}}^{\mathrm{T}} = \begin{bmatrix} -1 & -1 & -1 & 0 & 0 & 1 & 0 \\ -1 & 2 & -4 & 3 & 2 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 & -1 \end{bmatrix}. \tag{22}$$

There are four independent solutions of the equations $\boldsymbol{\lambda \Gamma} = 0$ (seven variables minus three independent equations). For example, we can take the following basis of solutions: (−1,1,0,−1, 0,0,0), (0,0,0,−1,1,0,1), (1, 0,0,0,0,1,1), (1,0,−1,−1,0,0,0).

The correspondent Wegscheider identities are: $K_2 = K_1 K_4$, $K_5 K_7 = K_4$, $K_1 K_6 K_7 = 1$, $K_1 = K_3 K_4$.

3.5.3. Allowed and forbidden mechanisms

In general, all the seven reactions can be considered as reversible but under various conditions some of them are almost irreversible. Let us study which combinations of irreversible reactions are possible in accordance with the extended form of detailed balance.

For example, existence of the positive solution $(0,1,0,0,0,1,1) \in \Lambda$ guarantees that the irreversible system $CO_2 + H_2 \to CO + H_2O$, $CH_4 + CO_2 \to 2CO + 2H_2$, $CO_2 + 4H_2 \to CH_4 + 2H_2O$, $CH_4 + H_2O \to CO + 3H_2$, $CH_4 \to 2H_2 + C$, $2CO \to CO_2 + C$, $C + H_2O \to CO + H_2$ is forbidden by the extended form of detailed balance. This conclusion is also obvious from the correspondent Wegscheider condition $K_2 K_6 K_7 = 1$. Indeed, if all the $k_i^- \to 0$ for bounded from below $k_i^+ > \varepsilon > 0$ then all $K_i \to \infty$ and $K_2 K_6 K_7 \to \infty$. This contradicts the Wegscheider condition.

The first reaction (RWGS, Reverse water–gas shift) is reversible in the wide interval of conditions (Moe, 1962). Let us first study all the reaction mechanisms with the reversible first reaction and the irreversible reactions 2-7. We find the combinations of the directions of the irreversible reactions that satisfy the extended form of detailed balance. As a criterion of the extended form of detailed balance we use Theorem 3. After that, we consider other reactions as the reversible ones (in addition to RWGS) and study the corresponding reaction mechanisms.

The space S is a straight line with the directional vector γ_1 with coordinates (−1,−1,0) in the coordinate system (N_2, N_4, N_6) that corresponds to the components A_2, A_4, A_6. Let us represent the quotient space $\mathbb{R}^3/S$ in the coordinate system (N_2, N_6) that corresponds to the components A_2, A_6. For this purpose, we have to eliminate the coordinate N_4 using vector γ_1. As a result, we get the following vectors:

$$\overline{\gamma}_2 = \begin{pmatrix} -3 \\ 0 \end{pmatrix}, \quad \overline{\gamma}_3 = \begin{pmatrix} 3 \\ 0 \end{pmatrix}, \quad \overline{\gamma}_4 = \begin{pmatrix} -3 \\ 0 \end{pmatrix},$$

$$\overline{\gamma}_5 = \begin{pmatrix} -2 \\ 1 \end{pmatrix}, \quad \overline{\gamma}_6 = \begin{pmatrix} 1 \\ 1 \end{pmatrix}, \quad \overline{\gamma}_7 = \begin{pmatrix} -1 \\ -1 \end{pmatrix}. \tag{23}$$

For example, to find $\overline{\gamma}_2$, we take γ_2 (the second column in (22)) and exclude the coordinate N_4 by adding $2\gamma_1$. The result is a vector $\gamma_2 + 2\gamma_1$. In coordinates (N_2, N_6), this vector gives us $\overline{\gamma}_2$.

The stoichiometric vectors of irreversible reactions are $+\gamma_j$ or $-\gamma_j$ $(j = 2, \ldots, 7)$. Their images in the quotient space $\mathbb{R}^3/S$ are $+\overline{\gamma}_j$ or $-\overline{\gamma}_j$. The extended form of detailed balance requires that the convex envelope of these vectors should not include zero. We have to arrange signs in $\pm\gamma_j$ to provide this property. First of all, we see immediately from (23) that the second and the forth reaction should have the same directions and the third reaction should have the opposite direction. The directions of the sixth and the seventh reactions should be opposite. Therefore, we have to analyze eight possible reaction mechanisms. Let us represent them by the directions of reactions:

$$\begin{bmatrix}(a)\\ \rightleftharpoons\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \rightarrow\\ \rightarrow\\ \leftarrow\end{bmatrix},\quad \begin{bmatrix}(b)\\ \rightleftharpoons\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \rightarrow\\ \leftarrow\end{bmatrix},\quad \begin{bmatrix}(c)\\ \rightleftharpoons\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \leftarrow\end{bmatrix},\quad \begin{bmatrix}(d)\\ \rightleftharpoons\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \leftarrow\\ \rightarrow\\ \leftarrow\end{bmatrix},\quad \begin{bmatrix}(e)\\ \rightleftharpoons\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \rightarrow\\ \leftarrow\\ \rightarrow\end{bmatrix},\quad \begin{bmatrix}(f)\\ \rightleftharpoons\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \rightarrow\end{bmatrix},\quad \begin{bmatrix}(g)\\ \rightleftharpoons\\ \rightarrow\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \leftarrow\\ \rightarrow\end{bmatrix},\quad \begin{bmatrix}(h)\\ \rightleftharpoons\\ \leftarrow\\ \rightarrow\\ \leftarrow\\ \leftarrow\\ \leftarrow\\ \rightarrow\end{bmatrix}. \tag{24}$$

Arrows here correspond to the directions of reactions. For example, the case (a) corresponds to the reaction mechanism

1. $CO_2+H_2 \rightleftharpoons CO+H_2O$,
2. $CH_4+CO_2 \rightarrow 2CO+2H_2$,
3. $CO_2+4H_2 \leftarrow CH_4+2H_2O$,
4. $CH_4+H_2O \rightarrow CO+3H_2$,
5. $CH_4 \rightarrow 2H_2+C$,
6. $2CO \rightarrow CO_2+C$,
7. $C+H_2O \leftarrow CO+H_2$.

Combinations (c) and (f) contradict the condition 1 from Theorem 3: the origin belongs to the convex envelope of the vectors $\overline{\nu}_j$ of irreversible reactions (see Fig. 1). Hence, only six combinations of directions of irreversible reactions satisfy the extended form of detailed balance (from $2^6=64$ possible combinations of directions): (a), (b), (d), (e), (g) and (h).

Let us extend the list of reversible reactions. If we assume that the second reaction (dry reforming), is reversible together with the first one (RWGS) then the third and the forth reactions should be also reversible because $\gamma_3=2\gamma_1-\gamma_2$ and $\gamma_4=\gamma_2-\gamma_1$, hence, $\gamma_{3,4} \in \mathrm{span}\{\gamma_1,\gamma_2\}$. According to the condition 1 from Theorem 3, this contradicts to the extended form of detailed balance if the first and the second reactions are reversible and the third and the forth are not.

Analogously, in addition to the reversible reaction RWGS, the Boudouard equilibrium 6 and coal gasification 7 can be reversible only together because $\gamma_7=-\gamma_1-\gamma_6$.

We have to consider three possible sets of reversible reactions:

1. 1, 2, 3 and 4,
2. 1 and 5,
3. 1, 6 and 7.

For all three cases, $\dim S=2$ and $\dim(\mathbb{R}^3/S)=1$. We will use for the quotient space the coordinate N_6 which corresponds to $A_6=\mathrm{C}$.

In the first case, let us exclude the coordinate N_4 from $\overline{\gamma}_{5,6,7}$ (23) using vector $\overline{\gamma}_2$. We get one-dimensional vectors

$$\overline{\gamma}_5=1, \quad \overline{\gamma}_6=1, \quad \overline{\gamma}_7=-1.$$

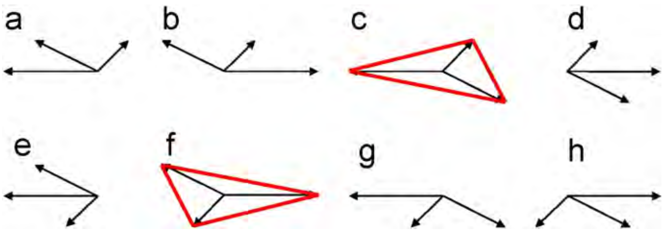

Fig. 1. Images of the stoichiometric vectors of irreversible reactions $\overline{\nu}_j=\pm\overline{\gamma}_j$ in $\mathbb{R}^3/S$ for various combinations of directions of reactions (24) in coordinates N_2 (abscissa), N_6. The configurations with $0 \in \mathrm{conv}\{\overline{\nu}_2,\ldots,\overline{\nu}_7\}$ are outlined. Vectors $\overline{\nu}_2$, $\overline{\nu}_3$ and $\overline{\nu}_4$ coincide as well as vectors $\overline{\nu}_6$ and $\overline{\nu}_7$.

To satisfy the extended form of detailed balance the directions of the fifth and the sixth reaction should coincide and the direction of the seventh reaction should be opposite: there are two possible combinations of arrows in irreversible reactions 5, 6 and 7 if reactions 1, 2, 3 and 4 are reversible: 5→,6→,7← and 5←,6←,7→.

In the second case, let us exclude the coordinate N_4 from $\overline{\gamma}_{2,3,4,6,7}$ (23) using vector $\overline{\gamma}_5$. We get one-dimensional vectors

$$\overline{\gamma}_2=-2/3, \quad \overline{\gamma}_3=2/3, \quad \overline{\gamma}_4=-2/3, \quad \overline{\gamma}_6=1/2, \quad \overline{\gamma}_7=-1/2.$$

Again, according to the extended form of detailed balance, here are two possibilities of directions of irreversible reactions 2, 3, 4, 6 and 7 if reactions 1 and 5 are reversible: 2→,3←,4→,6←,7→ and 2←,3→,4←,6→,7←.

In the third case, let us exclude the coordinate N_4 from $\overline{\gamma}_{2,3,4,5}$ (23) using vector $\overline{\gamma}_6$. We get one-dimensional vectors

$$\overline{\gamma}_2=3, \quad \overline{\gamma}_3=-3, \quad \overline{\gamma}_4=3, \quad \overline{\gamma}_5=3.$$

According to the extended form of detailed balance, here are two possibilities of directions of irreversible reactions 2, 3, 4, and 5 if reactions 1, 6 and 7 are reversible: 2→,3←,4→,5→ and 2←,3→,4←,5←.

In the first and the third cases, there are nontrivial Wegscheider identities for the reaction equilibrium constants of reversible reactions. If reactions 1, 2, 3 and 4 are reversible (case 1) then $\dim \Lambda=2$ and the basis of Λ is, for example, $\boldsymbol{\lambda}^1=(2,-1,-1,0)$ $(2\gamma_1-\gamma_2-\gamma_3=0)$ and $\boldsymbol{\lambda}^2=(1,-1,0,1)$ $(\gamma_1-\gamma_2+\gamma_4=0)$. The two correspondent Wegscheider identities are: $K_1^2=K_2K_3$ and $K_1K_4=K_2$ (where $K_i=k_i^+/k_i^-$).

If the reactions 1, 6 and 7 are reversible then $\dim \Lambda=1$ and the basis of Λ consists of one vector $\boldsymbol{\lambda}=(1,1,1)$ $(\gamma_1+\gamma_6+\gamma_7=0)$. The correspondent Wegscheider identity is: $K_1K_6K_7=1$.

If we add one more reversible reaction in cases 1–3 then all the reactions 1–7 should be reversible in according to the extended form of detailed balance.

In this case study, we demonstrated also how it is possible to organize computations and reduce the dimension of the computational problems.

4. Multiscale degenerated equilibria

Let in a system of reversible reactions with detailed balance some $k_s^- \to 0$, when the correspondent k_s^+ remains constant and separated from zero. In this case, some equilibrium activities also tend to zero. Indeed, at equilibrium $w_s^+=w_s^-$, $w_s^- \to 0$ because $k_s^- \to 0$, hence, $w_s^+ \to 0$ and some of a_i^{eq} with $\alpha_{si}>0$ also tend to zero due to the generalized mass action law (5). Therefore, the irreversible limits of the reactions with detailed balance are closely related to the limits when some equilibrium activities tend to zero. (For the usual mass action law is sufficient to replace the "activity a_i" by the "concentration c_i".)

In this section we study asymptotics $a_i^{\mathrm{eq}}=\mathrm{const}\times\varepsilon^{\delta_i}$, $\varepsilon\to 0$ for various values of non-negative exponents $\delta_i \geq 0$ $(i=1,\ldots,n)$.

There exists a well known way to satisfy the principle of detailed balance: just write $k_r^-=k_r^+/K_r$ where K_r is the equilibrium constant:

$$K_r=\frac{\prod_{i=1}^n (a_i^{\mathrm{eq}})^{\beta_{ri}}}{\prod_{i=1}^n (a_i^{\mathrm{eq}})^{\alpha_{ri}}}.$$

We can define the equilibrium constant through the equilibrium thermodynamics as well (see, for example, the classical book by Prigogine and Defay, 1962). In this case, the principle of detailed balance is also satisfied for the mass action law.

In this approach, we have to group the direct and reverse reactions together. Therefore, m is here the number of pairs of reactions, direct + inverse ones. We deal with $m+n$ constants (m rate constants k_r^+ for direct reactions and n equilibrium data for individual reagents: equilibrium concentrations or activities) instead of 2 m constants $k_r^{\pm}$. For these $m+n$ constants, the principle of detailed balance produces no restrictions (Gorban et al., 1989; Yang et al., 2006). It holds "by the construction" for any positive values of these constants if $k_r^- = k_r^+/K_r$ and the equilibrium constants are calculated in accordance with the equilibrium data.

To transform the conditions of $a_i^{\rm eq} \to 0$ into irreversibility of some reactions, it is not sufficient to know which $a_i^{\rm eq} \to 0$. We have to take into account the rates of these convergence to zero for different i. In the simple example, $A_1 \rightleftharpoons A_2 \rightleftharpoons A_3 \rightleftharpoons A_1$, if $a_{1,2}^{\rm eq} \to 0$, $a_1/a_2 \to 0$ then in the limit we get the system $A_1 \to A_2$ (because the A_1/A_2 equilibrium is shifted to A_2), $A_1 \to A_3$, $A_2 \to A_3$. For the inverse relations between a_1 and a_2, $a_2/a_1 \to 0$, the limit system is $A_2 \to A_1$ (the A_1/A_2 equilibrium is shifted to A_1), $A_1 \to A_3$, $A_2 \to A_3$. For the both limit systems, the equilibrium activities of A_1, A_2 are zero but the directions of reaction are different.

The limit structure of the reaction mechanism when some of $a_i^{\rm eq} \to 0$ depends on the behavior of the ratios $a_i^{\rm eq}/a_i^{\rm eq}$. To formalize this dependence, let us introduce a parameter $\varepsilon > 0$ and take $a_i^{\rm eq} = {\rm const} \times \varepsilon^{\delta_i}$. At equilibrium, each monomial in the generalized mass action law is proportional to a power of ε:

$$w_r^{\rm eq+} = k_r^+ {\rm const} \times \varepsilon^{\sum_i \alpha_{ri}\delta_i}, \quad w_r^{\rm eq-} = k_r^- {\rm const} \times \varepsilon^{\sum_i \beta_{ri}\delta_i}.$$

The principle of detailed balance gives: $w_r^{\rm eq+} = w_r^{\rm eq-}$. Therefore,

$$\frac{k_r^+}{k_r^-} = {\rm const} \times \varepsilon^{(\gamma_r,\delta)}, \tag{25}$$

where δ is the vector with coordinates δ_i.

There are three possibilities for the reversibility of an elementary reaction in asymptotic $\varepsilon \to 0$:

1. If $(\gamma_r,\delta) = 0$ then the reaction remains reversible in asymptotic $\varepsilon \to 0$. This means that $0 < \lim(k_s^+/k_s^-) < \infty$. Therefore, if one of the reactions persists in the limit then the reverse reaction also persists.
2. If $(\gamma_r,\delta) < 0$ then in asymptotic $\varepsilon \to 0$ can remain only direct reaction. This means that $\lim(k_s^-/k_s^+) = 0$.
3. If $(\gamma_r,\delta) > 0$ then in asymptotic $\varepsilon \to 0$ can remain only reverse reaction. This means that $\lim(k_s^+/k_s^-) = 0$.

It is possible that $(\gamma_r,\delta) = 0$ but both $k_r^{\lim \pm} = 0$ just because $k_r^+ = 0$ and $k_r^- = 0$ and not because of the equilibrium degeneration. If we delete some irreversible reactions or several pairs of mutually reverse reaction then the extended form of detailed balance persists. Therefore, we do not consider these cases separately and always discuss the limit reaction mechanisms with the maximal sets of nonzero rate constants.

For each stoichiometric vector γ_r the n-dimensional space of vectors δ is split in three sets: hyperplane $(\gamma_r,\delta) = 0$ (reaction remains reversible), hemispace $(\gamma_r,\delta) < 0$ (only direct reaction remains) and hemispace $(\gamma_r,\delta) > 0$ (only reverse reaction remains). For the reaction mechanism, intersections of these sets for all γ_r ($r = 1,\ldots,m$) form a tiling of the n-dimensional space of vectors δ. The intersection of all hyperplanes $(\gamma_r,\delta) = 0$ corresponds to the initial reversible reaction mechanism. Other sets from this tiling correspond to the reaction mechanisms that are limits of the initial reaction mechanism when some of the reaction rate constants tend to zero but the principle of detailed balance is valid. In our study, the exponents δ_j should be nonnegative, hence, we have to study the tiling of the positive orthant $\delta_j \geq 0$ in $\mathbb{R}^n$ Description of the tiling produced by a system of hyperplanes $(\gamma_r,\delta) = 0$ is a classical problem of combinatorial geometry.

In the usual linear triangle $A_1 \rightleftharpoons A_2 \rightleftharpoons A_3 \rightleftharpoons A_1$ we have to consider three hyperplanes in the space of exponents $\delta = (\delta_1,\delta_2,\delta_3)$: $\delta_1 = \delta_2$ ($(\gamma_1,\delta) = 0$), $\delta_2 = \delta_3$ ($(\gamma_2,\delta) = 0$) and $\delta_3 = \delta_1$ ($(\gamma_3,\delta) = 0$). At least one of the exponents should take zero value to keep the overall concentration in equilibrium neither zero nor infinite. Let us take $\delta_1 = 0$. The hyperplanes turn in the straight lines on the plane (δ_2,δ_3): $0 = \delta_2$ ($(\gamma_1,\delta) = 0$), $\delta_2 = \delta_3$ ($(\gamma_2,\delta) = 0$) and $\delta_3 = 0$ ($(\gamma_3,\delta) = 0$). The positive octant on the plane (δ_2,δ_3) is split in five sets (A)–(E), that correspond to the limits with some irreversible reactions, and the origin:

- (A) $\delta_2 = 0$, $\delta_3 > 0$, $A_1 \rightleftharpoons A_2$, $A_3 \to A_1$, $A_3 \to A_2$,
- (B) $\delta_3 > \delta_2 > 0$, $A_3 \to A_2 \to A_1$, $A_3 \to A_1$,
- (C) $\delta_3 = \delta_2 > 0$, $A_3 \rightleftharpoons A_2$, $A_2 \to A_1$, $A_3 \to A_1$,
- (D) $\delta_2 > \delta_3 > 0$, $A_2 \to A_3 \to A_1$, $A_2 \to A_1$ (this case differs from (B) by the transposition $2 \leftrightarrow 3$),
- (E) $\delta_2 > 0$, $\delta_3 = 0$ $A_1 \rightleftharpoons A_3$, $A_2 \to A_1$, $A_2 \to A_3$ (this case differs from (A) by the transposition $2 \leftrightarrow 3$).
- The origin corresponds to the fully reversible mechanism.

For a less trivial example, let us analyze the reaction mechanism from Section 3.4: $A_1 \rightleftharpoons A_2 \rightleftharpoons A_3 \rightleftharpoons A_1$, $A_1 + A_2 \rightleftharpoons 2A_3$. This is a reversible cycle supplemented by a nonlinear step.

We join the direct and reverse elementary reactions and, therefore,

$$\boldsymbol{\Gamma}^{\rm T} = \begin{bmatrix} -1 & 0 & 1 & -1 \\ 1 & -1 & 0 & -1 \\ 0 & 1 & -1 & 2 \end{bmatrix}. \tag{26}$$

The columns of this matrix are the stoichiometric vectors γ_r.

Let us study the tiling of the positive orthant in $\mathbb{R}^3$ by the planes $(\gamma_r,\delta) = 0$ ($r = 1,\ldots,4$). First of all, it is necessary and sufficient to study this tiling of the positive octants in three planes: $\delta_1 = 0$, or $\delta_2 = 0$, or $\delta_3 = 0$ because at least one equilibrium concentration should not tend to zero and, therefore, has zero exponent. The symmetry between A_1 and A_2 allows us to study two planes: $\delta_1 = 0$ or $\delta_3 = 0$.

On the plane $\delta_1 = 0$ with coordinates δ_2, δ_3 we have four straight lines: $(\gamma_1,\delta) = 0$ ($\delta_2 = 0$), $(\gamma_2,\delta) = 0$, ($\delta_2 = \delta_3$), $(\gamma_3,\delta) = 0$ ($\delta_3 = 0$) and $(\gamma_4,\delta) = 0$ ($\delta_2 = 2\delta_3$). These lines divide the positive octant ($\delta_{2,3} \geq 0$) into seven parts (Fig. 2) and the origin:

1. (A) $\delta_2 = 0$, $\delta_3 > 0$, $A_1 \rightleftharpoons A_2$, $A_3 \to A_1$, $A_3 \to A_2$, $2A_3 \to A_1 + A_2$,
2. (B) $\delta_2 > 0$, $\delta_3 > \delta_2$, $A_2 \to A_1$, $A_3 \to A_1$, $A_3 \to A_2$, $2A_3 \to A_1 + A_2$,
3. (C) $\delta_2 = \delta_3 > 0$, $A_2 \to A_1$, $A_3 \to A_1$, $A_3 \rightleftharpoons A_2$, $2A_3 \to A_1 + A_2$,

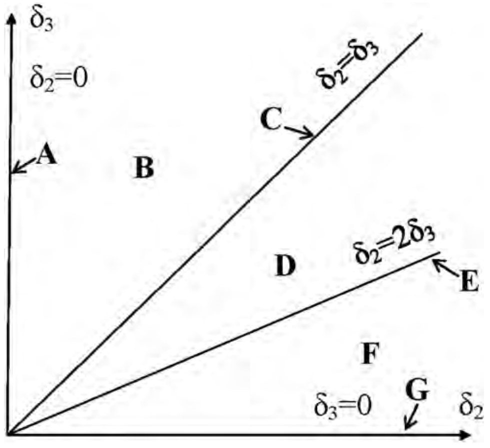

Fig. 2. Tiling of the positive octant of the plane (δ_2,δ_3) $(\delta_1 = 1)$ that corresponds to seven irreversible limits of the reaction mechanism.

4. (D) $0<\delta_3<\delta_2<2\delta_3$, $A_2\to A_1$, $A_3\to A_1$, $A_2\to A_3$, $2A_3\to A_1+A_2$,
5. (E) $0<\delta_2=2\delta_3$, $A_2\to A_1$, $A_3\to A_1$, $A_2\to A_3$, $2A_3\rightleftharpoons A_1+A_2$,
6. (F) $\delta_2>2\delta_3>0$, $A_2\to A_1$, $A_3\to A_1$, $A_2\to A_3$, $A_1+A_2\to 2A_3$,
7. (G) $\delta_3=0$, $\delta_2>0$, $A_2\to A_1$, $A_1\rightleftharpoons A_3$, $A_2\to A_3$, $A_1+A_2\to 2A_3$,
8. The origin corresponds to the fully reversible mechanism.

The same picture gives us the plane $\delta_2=0$ with coordinates δ_1, δ_3: we need just to transpose the indexes, $1\leftrightarrow 2$.

On the plane $\delta_3=0$ with coordinates δ_1, δ_2 the positive octant is divided into five parts and the origin:

1. $\delta_1=0$, $\delta_2>0$, $A_2\to A_1$, $A_1\rightleftharpoons A_3$, $A_2\to A_3$, $A_1+A_2\to 2A_3$ (this is exactly the case (G) from Fig. 2),
2. $0<\delta_1<\delta_2$, $A_2\to A_1$, $A_1\to A_3$, $A_2\to A_3$, $A_1+A_2\to 2A_3$,
3. $0<\delta_1=\delta_2$, $A_1\rightleftharpoons A_2$, $A_1\to A_3$, $A_2\to A_3$, $A_1+A_2\to 2A_3$,
4. $\delta_1>\delta_2>0$, $A_1\to A_2$, $A_1\to A_3$, $A_2\to A_3$, $A_1+A_2\to 2A_3$,
5. $\delta_2=0$, $\delta_1>0$, $A_1\to A_2$, $A_1\to A_3$, $A_2\rightleftharpoons A_3$, $A_1+A_2\to 2A_3$,
6. The origin corresponds to the fully reversible mechanism.

This approach is equivalent to the previous definition of the extended form of detailed balance based on the pathway analysis. Indeed, if the reaction mechanism with some irreversible reactions is a limit of the reversible mechanism with detailed balance then it satisfies the conditions of the extended form of detailed balance. (This is the direct statement of Theorem 1 proved in Section 3.2.) To prove the converse statement, we have to take a system that satisfies the extended form of detailed balance and to find such a set of exponents $\delta_i\geq 0$ $(i=1,\dots,n)$ that the system appears in the limit of a reversible system with detailed balance when $\varepsilon\to 0$ and $a_i^{\rm eq}={\rm const}\times\varepsilon^{\delta_i}$.

Let a system with some irreversible reactions satisfy the extended form of detailed balance. We follow the notations of Theorem 3: γ_j $(j=1,\dots,r)$ are the stoichiometric vectors of the reversible reactions and $\nu_1,\dots,\nu_s$ are the stoichiometric vectors of the irreversible reactions. The linear subspace $S={\rm span}\{\gamma_1,\dots,\gamma_r\}\subset\mathbb{R}^n$ consists of all linear combinations of the stoichiometric vectors of the reversible reactions. We use notation $\overline{\nu}_j$ for the images of ν_j in $\mathbb{R}^n/S$.

Let $k_j^{\pm}>0$ $(j=1,\dots,r)$ be the reaction rate constants for the reversible reactions and $q_j=q_j^+>0$ $(j=1,\dots,s)$ be the reaction rate constants for the irreversible reactions. We extend the system by adding the reverse reactions with the constants $q_j^->0$. If the extended system satisfies the principle of detailed balance then

$$\frac{k_j^+}{k_j^-}=\prod_{i=1}^{n}(a_i^{\rm eq})^{\gamma_{ri}}\quad\text{and}\quad\frac{q_j^+}{q_j^-}=\prod_{i=1}^{n}(a_i^{\rm eq})^{\nu_{ri}},\tag{27}$$

where $a_i^{\rm eq}$ is a point of detailed balance.

Theorem 4. *Let the system satisfy the extended form of detailed balance. Then there exists a vector of nonnegative exponents* $\delta=(\delta_i)$ $(i=1,\dots,n)$ *and the family of extended systems with equilibria* $a_i^{\rm eq}=a_i^*\varepsilon^{\delta_i}$ *such that condition* (27) *hold,* $k_j^{\pm}$ $(j=1,\dots,r)$ *and* $q_j=q_j^+$ $(j=1,\dots,s)$ *do not depend on* ε, *and* $q_j^-\to 0$ *when* $\varepsilon\to 0$.

Proof. If the system satisfies the extended form of detailed balance then the reversible part satisfies the principle of detailed balance and, hence, there exists a positive point of detailed balance for the reversible part of the system (Theorem 3): $a_i^*>0$ and

$$k_j^+\prod_{i=1}^{n}(a_i^*)^{\alpha_{ri}}=k_j^+\prod_{i=1}^{n}(a_i^*)^{\beta_{ri}}.$$

Let us take $a_i^{\rm eq}=a_i^*\varepsilon^{\delta_i}$. Due to (27), $k_j^+/k_j^-={\rm const}\times\varepsilon^{(\gamma_j,\delta)}$. To keep the $k_i^{\pm}$ independent of ε, we have to provide $(\gamma_j,\delta)=0$. Analogously, $q_j^+/q_j^-={\rm const}\times\varepsilon^{(\nu_j,\delta)}$. The rate constant q_j^+ should not depend on ε and $q_j^-\to 0$ when $\varepsilon\to 0$. Therefore, $(\nu_j,\delta)<0$. We came to the system of linear equations and inequalities with respect to exponents δ_i:

$$(\gamma_j,\delta)=0\ (j=1,\dots,r),\quad(\nu_j,\delta)<0\ (j=1,\dots,s).\tag{28}$$

The solvability of this system is equivalent to the condition 1 of Theorem 3 (see Remark 7). To prove the existence of nonnegative exponents $\delta_i\geq 0$, we have to use existence of positive conservation law: $b_i>0$, $(\gamma_j,b)=0$, $(\nu_j,b)=0$. For every solution δ of (28) and any number d, the vector $\delta+db$ is also a solution of (28). Therefore, the nonnegative solution exists. We proved the theorem and the converse statement of Theorem 1. □

Proposition 4. *Let a system with the stoichiometric vectors* γ_s *and the extended detailed balance be obtained from the reversible systems with detailed balance in the limit* $a_i^{\rm eq}={\rm const}\times\varepsilon^{\delta_i}$, $\varepsilon\to 0$. *For this system, the linear function* (δ,c) *of the concentrations* c *monotonically decreases in time due to the kinetic equations* $dc/dt=\sum_s w_s\gamma_s$.

Proof. Indeed, $d(\delta,c)/dt=\sum_s w_s(\gamma_s,\delta)$ (compare to Remark 6). For the reversible reactions, the sign of w_s is indefinite but $(\gamma_s,\delta)=0$. For the irreversible reactions, we always can take $w_s=w_s^+\geq 0$ just by the selection of notations. In this case, only k_s^+ survived in the limit $\varepsilon\to 0$, this means that $(\gamma_s,\delta)<0$. Therefore, $d(\delta,c)/dt\leq 0$ and it is zero if and only if all the reaction rates of the irreversible reactions vanish. □

So, the vector of exponents δ defines the (partially) irreversible limit of the reaction mechanism and, at the same time, gives the explicit construction of the special Lyapunov function for the kinetic equations of the limit system.

In this Section, we developed the approach to the systems with some irreversible reactions based on multiscale degeneration of equilibria, when some $a_i\to 0$ as ε^{δ_i}. We proved in Theorem 4 that this approach is equivalent to the extended form of detailed balance based on the pathways analysis or on the limits of the systems with detailed balance when some of the reaction rate constants tend to zero.

5. Conclusion

The classical principle of detailed balance operates with mechanisms, which consist of fully reversible elementary processes (reactions). If such mechanisms have cycles of reactions, each cycle is characterized by one Wegscheider relationship (8) between its rate constants. The number of functionally independent relationships is equal to the number of linearly independent cycles, linear or nonlinear.

In difference from this classical case, we analyzed mechanisms, which may include irreversible reactions as well. For such mechanisms we proved an *extended form of detailed balance* considering the irreversible reactions as limits of reversible steps, when the rate constants of the corresponding reverse reactions approach zero. The novelty of this form is that the extended detailed balance now is presented as a necessary combination of two constituents:

- Structural conditions in accordance to which the irreversible reactions cannot be included in oriented cyclic pathways.
- Algebraic conditions which are written for the “reversible part” of the complex mechanism taken separately, without irreversible reactions, using the classical Wegscheider relationships.

The computational tools combine linear algebra (some standard tools for chemical kinetics) with methods of linear programming. The most expensive computational problem appears when we check the structural condition of the extended form of detailed balance.

Let n be the number of components, and let $\mathbb{R}^n$ be the composition space. We consider a system with r reversible and s irreversible reactions. Let us use $\gamma_1,\ldots,\gamma_r$ for the stoichiometric vectors of the reversible reactions, $v_1,\ldots,v_s$ for the stoichiometric vectors of the irreversible reactions and $\overline{v}_j$ for the images of v_j in the quotient space $\mathbb{R}^n/S$, where S is spanned by the stoichiometric vectors of all reversible reaction, $S=\mathrm{span}\{\gamma_1,\ldots,\gamma_r\}\subset\mathbb{R}^n$. The reaction mechanism satisfies the structural condition of the extended form of detailed balance if and only if

$$0\notin\mathrm{conv}\{\overline{v}_1,\ldots,\overline{v}_s\}.$$

We have to check whether the origin belongs to the convex hull of the vectors $\overline{v}_1,\ldots,\overline{v}_s$. In practice, we can always assume that these vectors have exactly known rational (or even integer) coordinates.

We combined three approaches to study the restrictions implied by the principle of detailed balance in the systems with some irreversible reactions:

1. Analysis of limits of the systems with all reversible reactions and detailed balance when some of the reaction rate constants tend to zero.
2. Analysis of the Wegscheider identities for elementary pathways when some of the reaction rate constants turn into zero.
3. Analysis of limits of the systems when some equilibrium concentrations (or, more general, activities) tend to zero.

We proved that these three approaches are equivalent if we take into account not only which equilibrium concentrations tend to zero, but the speed of this tendency as well. The various partially or fully irreversible limits of the reaction mechanisms are, in this sense, multiscale asymptotics of the reaction networks when some equilibrium concentration tend to zero with different speed.

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