Abstract

The classical approaches to derivation of (generalized) Mass Action Law (MAL) assumes that the intermediate transition states (i) have short life time and (ii) are in partial equilibrium with the initial reagents of the elementary reaction. The partial equilibrium assumption (ii) means that the reverse decomposition of the intermediates is much faster than its transition through other channels to the products. In this work we demonstrate how avoiding of this partial equilibrium assumption modifies the reaction rates. It leads to effective ‘entanglement’ of reaction rates that become linear combinations of different MAL expressions.

Keywords: kinetic equation, mass action law, transition state, intermediate, non-equilibrium

1. Introduction: Backgrounds of generalized mass action law

The Mass Action Law (MAL) for chemical kinetics was postulated by Guldberg and Waage first for equilibrium (in 1864), and then for dynamics (in 1879). Boltzmann used the analogue of dynamical MAL (Stosszahlansatz) for collision in gases in 1872 and obtained the gas kinetics equation (Boltzmann’s equation). The physical assumptions behind MAL for complex chemical reactions were clarified later, in particular, in the transition state or the activated complex theories, 1935 (see review in [1]). From the kinetic point...
Fast equilibria
Small amounts

Figure 1: Schematic representation of the Michaelis–Menten–Stueckelberg (a), and Briggs–Haldane (b) asymptotic assumptions: an elementary process $\sum \alpha_{\rho i}A_i \rightarrow \sum \alpha_{\rho i}A_i$ goes through intermediate compounds $B^\pm_\rho$. The fast equilibria in the Michaelis–Menten case (a), $\sum \alpha_{\rho i}A_i \rightleftharpoons B^+_\rho$ and $\sum \beta_{\rho i}A_i \rightleftharpoons B^-_\rho$, can be described by conditional minima of the free energy. Concentrations of $B^\pm_\rho$ are small and transitions between them obey linear kinetic equation (Markov chains).

of view, the assumptions that lead to MAL can be summarized as follows (Fig. 1b):

1. The complex reaction is a combination of elementary reaction;
2. Elementary reactions go through intermediate states;
3. Intermediate states have a short lifetime and are present in very small concentrations compared to the main reagents;
4. There is a ‘fast equilibrium’ between the input reagents and the intermediate states for each elementary reaction and these fast partial equilibria can be described thermodynamically, by the conditional minimization of the free energy.

The kinetic assumptions used in the transition state theory were introduced much earlier. In 1913, Michaelis and Menten demonstrated for an enzyme reaction that under these assumptions the overall reaction follows MAL [2]. They used the term ‘compounds’ for the active intermediates. In 1952, Stueckelberg [3] used the same assumptions for the derivation of the Boltzmann equation from the Markovian microkinetics and demonstrated how the semidetailed balance conditions (called also the cyclic balance conditions [4] or the complex balance conditions [6, 7]) arose for the cases when the classical microreversibility conditions failed and the principle of detailed balance did not work. The semidetailed balance was invented by Boltzmann [5] as an answer to Lorentz’s critique of microreversibility. Boltzmann’s proof of sufficiency of semidetailed balance for $H$-theorem was straightforward.
The proof that the generalized MAL and semidetailed balance should hold for macroscopic kinetics is not so obvious. Watanabe [4] found that the Stueckelbeck work has “lack of proof” and declared direct connection between this condition and ergodicity of microscopic models. Detailed analysis of this asymptotic (Fig. 1b) was performed in 2011, the general Michaelis–Menten–Stueckelberg (MMS) theorem was formulated and proved for finite-dimensional systems [8], and extended further for general nonlinear Markov processes [9]. The physical assumptions that lead to generalized MAL with detailed or semidetailed (cyclic) balance were analyzed in [10].

Assumption 3 about the short lifetime of the transition states is the basis of the approach to microscopic theory of reaction rates. This constitutes the difference between the reagents and intermediates. Assumption 4 adds an additional time separation: equilibration between the input reagents and the intermediate states for every elementary reaction is much faster than other transitions of the intermediates. In this paper, we demonstrate a possible development of the reaction rate theory without assumption 4. Already in the first approximation, the reaction rate theory based on assumptions 1-3 produces the ‘entangled’ MAL: the reaction rates for elementary reactions become combinations of the MAL rates of different elementary reactions.

2. The basic formalism

We use the following widely used notations borrowed from chemical kinetics [8, 11]. The list of the components (reagents) \( A_i \) is given. The mechanism of reaction is the list of the elementary reactions. Each reaction is represented by the stoichiometric equation:

\[
\sum_i \alpha_{\rho i} A_i \rightarrow \sum_i \beta_{\rho i} A_i,
\]

where \( \rho \) is the number of the elementary reaction and the stoichiometric coefficients \( \alpha_{\rho i}, \beta_{\rho i} \) are non-negative numbers; \( \alpha_\rho, \beta_\rho \) are vectors with components \( \alpha_{\rho i}, \beta_{\rho i}, \) correspondingly. The concentration of the component \( A_i \) is \( c_i \), the vector of concentrations is \( c \). The kinetic equations for \( (1) \) under isochoric isothermal conditions are (with obvious modifications for other conditions [8]):

\[
\frac{dc}{dt} = \sum_{\rho} (\beta_{\rho} - \alpha_{\rho}) r_{\rho},
\]

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where \( r_\rho \geq 0 \) is the reaction rate. The linear combinations \( \sum_i \alpha_\rho A_i \) and \( \sum_i \beta_\rho A_i \) are the *complexes*. Each complex can participate in various reactions. The list of coefficient vectors for complexes is \( \{\nu_j\} \). For each complex \( \sum_i \nu_{ji} A_i \) from the reaction mechanism we introduce an intermediate state, a *compound* (in Michaelis–Menten terminology) \( B_j \). Each elementary reaction is represented in the form of the “2n-tail scheme” with two intermediate compounds:

\[
\sum_i \alpha_\rho A_i \rightleftharpoons B^+_\rho \to B^-_\rho \rightleftharpoons \sum_i \beta_\rho A_i,
\]

where the compound \( B^+_\rho \) corresponds to the input complex \( \sum_i \alpha_\rho A_i \) of (1), and \( B^-_\rho \) corresponds to the output complex \( \sum_i \beta_\rho A_i \). The concentration of the compound \( B_j \) is \( \varsigma_j \), the vector of these concentrations is \( \varsigma \). Thermo-dynamical properties of the mixture is described by the free energy density (under the condition of small concentrations of compounds, \( \sum_i c_i \gg \sum_j \varsigma_j \), the free energy of the small admixture has the perfect form):

\[
f(c, \varsigma, T) = f_A(c, T) + RT \sum_{j=1}^q \varsigma_j \left( \ln \left( \frac{\varsigma_j}{\varsigma^*_j(c, T)} \right) - 1 \right)
\]

We assume that the standard equilibrium concentrations \( \varsigma^*_j \) are much smaller than the concentrations of \( A_i \), \( \sum_i c_i \gg \sum_j \varsigma^*_j \). The “fast equilibrium” reagents-compounds for a complex \( \sum_i \nu_{ji} A_i \) is described by the conditional minimisation of \( f(c, \varsigma, T) \) along the straight line \( c = c^\text{in} - \xi \nu_j, \varsigma_j = \varsigma^\text{in}_j + \xi \nu_j_j \), where superscript ‘in’ is used for the initial point for minimisation, and \( \xi \) is the coordinate along the line.

For the kinetics of compounds transformations, the smallness of concentrations of compounds leads to the linear (Markov) kinetics, where the rate constant \( \kappa_{lj} \) of transitions \( B_j \to B_l \) (or \( \kappa_{lj} \) if we need to stress the direction of transition) can depend on concentrations \( c \) and temperature \( T \).

According to the basic MMS asymptotics, there are two small parameters, \( \delta \) that evaluates the relative deviation of \( \varsigma \) from their conditional equilibrium approximation, and \( \varepsilon \) that evaluates the relative smallness of \( \varsigma \) comparing to \( c \). The compound rate constants should be rescaled when \( \varepsilon \to 0 \) as \( \frac{1}{\varepsilon} \kappa_{lj} \). In the asymptotic \( \delta, \varepsilon \to 0, \delta, \varepsilon > 0 \) kinetics of \( A_i \) may be described by the reaction mechanism (1) with the reaction rates

\[
r_\rho = \varphi_\rho \exp \left( \frac{\sum_i \alpha_\rho H_i}{RT} \right)
\]
where \( \mu_i = \frac{\partial f(c,T)}{\partial c_i} \) is the chemical potential of \( A_i \) and the kinetic factors \( \varphi_\rho \) satisfy the condition:

\[
\sum_{\rho, \alpha_\rho = y} \varphi_\rho \equiv \sum_{\rho, \beta_\rho = y} \varphi_\rho
\]

for any vector \( y \) from the set of all vectors \( \{\alpha_\rho, \beta_\rho\} \). This statement includes the generalized mass action law for \( r_\rho \) (5) and the semidetailed balance identity (6) for kinetic factors that is sufficient for the entropy growth. If the Markov chain of compound kinetics is reversible (i.e. satisfies the principle of detailed balance), then for the generalized MAL the principle of detailed balance holds in the form: \( \varphi_\rho^+ \equiv \varphi_\rho^- \).

3. The problem of fast non-equilibrium intermediates

The well founded combination of the generalized MAL with the complex or detailed balance conditions follows from the asymptotic assumptions presented in Fig. 1a. These assumptions seem quite realistic, except for one weak point. Fast equilibrium

\[
\sum_i \nu_{ji} A_i \rightleftharpoons B_j
\]

assumes that the inverse reaction there is much faster than the transitions between compounds and the lifetime of \( B_j \) is determined by its decomposition into \( \sum_i \nu_{ji} A_i \) (Fig. 2). In enzyme kinetics, such an assumption was abolished by Briggs and Haldane in 1925. They found the reaction rate for simple enzyme reaction on the basis of a single assumption: small concentrations of intermediates. Ironically, the Briggs–Hadane (BH) formula was called the Michaelis–Menten equation. Detailed analysis of the BH asymptotics was performed in [13]. In the generalized MAL, this analysis is still the open problem.

The MMS approach to exclusion of intermediates is very attractive because it needs no assumption about the rates of the non-linear reactions \( \sum_i \nu_{ji} A_i \rightarrow B_j \). These non-linear rates are excluded by the fast equilibrium condition and the resulting generalized MAL formulas are based on thermodynamics. The BH approach used the complete kinetic equations as a starting point and serves for the further simplification of existent MAL equations. But what can we do if the non-linear kinetic law is unknown and there is no fast equilibria between input reagents and intermediate (i.e. the assumption 4 can be wrong)? This is the problem.
Figure 2: A complex reaction can be decomposed in the groups of transitions associated with compounds $B_j$: $B_j$ is born and dies in a reaction (7) and can be transformed into several other compounds $B_i_k$. In the MMS asymptotics, the reverse reaction from (7) is much faster than the transitions $B_j \rightarrow B_i_k$. In our work, we avoid this assumption. (The reverse transitions $B_i_k \rightarrow B_j$ are also possible but belong to the schemes associated with $B_i_k$.)

4. Linearisation near partial equilibria

The first step can be very natural. Let us linearise the kinetic equation for the elementary reaction $\sum_i \nu_{ji} A_i \Leftrightarrow B_j$ near its equilibrium. Because the motion in this reaction is one-dimensional, the linearised equations will have the form of the relaxation time approximation for all non-linear kinetic laws. Therefore, this type of approximation near equilibrium has the same absolute validity as non-equilibrium thermodynamics.

If the concentration $\varsigma_j$ and $\varsigma_j^*$ are small and we neglect in the minimization the second order quantities $\varsigma_j \partial \varsigma_j^*(c, T)/\partial c_i$ then the partial equilibrium concentrations of $B_i$ has a simple form

$$\varsigma_j^{\text{peq}}(c, T) = \varsigma_j^*(c, T) \exp \left( \frac{\sum_i \nu_{ji} \mu_i(c, T)}{RT} \right),$$

where superscript ‘peq’ means partial equilibrium. The linearized reaction rate for (7) is

$$w_j(c, T) = \frac{1}{\tau_j} (\varsigma_j^{\text{peq}}(c, T) - \varsigma_j).$$
\[
\frac{dc_i}{dt} = -\sum_j v_{ji} w_j, \\
\frac{d\varsigma_j}{dt} = w_j + \sum_{l, l \neq j} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j).
\] (10)

The \(H\)-theorem for these equations (10) follows from the general results [14]: If (i) the density of reagents’ free energy \(f_A(c, T)\) (see (4)) is a convex function of \(c\), (ii) the partial equilibria in (9) are defined by conditional minimization of \(f(c, \varsigma, T)\) (4), and (iii) the standard equilibrium \(\varsigma^*\) is an equilibrium point of the Markovian kinetics of compounds, then the free energy density \(f(c, \varsigma, T)\) does not increase in time on solutions of (10).

5. Small parameter and quasi steady state asymptotics

Let us introduce explicitly a formal small parameter \(\varepsilon\) in (8), (9), and (10):

\[
\varsigma^\text{peq}_j = \varepsilon \varsigma^* \exp \left( \frac{\sum_i v_{ji} \mu_i}{RT} \right); \\
w_j = \frac{1}{\varepsilon \tau_j} \left( \varsigma^\text{peq}_j - \varsigma_j \right), \\
\frac{dc_i}{dt} = -\sum_j v_{ji} \frac{1}{\varepsilon \tau_j} \left( \varsigma^\text{peq}_j - \varsigma_j \right), \\
\frac{d\varsigma_j}{dt} = \frac{1}{\varepsilon \tau_j} \left( \varsigma^\text{peq}_j - \varsigma_j \right) + \frac{1}{\varepsilon} \sum_{l, l \neq j} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j).
\] (11) (12) (13)

For explicit separation of slow and fast variables a simple linear transformation of concentrations \(c_i\) is needed [8]. This transformation excludes reaction rates \(w_j\) from the slow equations. The new variables are \(b_i = c_i + \sum_j v_{ji} \varsigma_j\). For them, the equations (10) have the form

\[
\frac{db_i}{dt} = \sum_{jl, l \neq j} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j) v_{ji}, \\
\frac{d\varsigma_j}{dt} = w_j + \sum_{l, l \neq j} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j).
\] (14)
With explicit small parameters these equations are

\[ \frac{db_i}{dt} = \frac{1}{\varepsilon} \sum_{jl, j \neq l} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j) \nu_{ji}, \]

\[ \frac{d\varsigma_j}{dt} = \frac{1}{\varepsilon \tau_j} (\varsigma_{j}^{\text{peq}} - \varsigma_j) + \frac{1}{\varepsilon} \sum_{l, l \neq j} (\kappa_{jl} \varsigma_l - \kappa_{lj} \varsigma_j). \]  

(15)

Here, the relaxation times for the equilibration reactions are \( \varepsilon \tau_j \) and \( \tau_j \) do not depend on \( \varepsilon \).

Let \( K \) be the matrix of kinetic coefficients for transitions between compounds: \( K_{jl} = \kappa_{jl} \) for \( j \neq l \) and \( K_{jj} = -\sum_l \kappa_{ji} \). This matrix has non-negative non-diagonal elements, non-positive diagonal and the sum of the elements in columns is zero. Therefore, according to Gershgorin’s circle theorem, all the eigenvalues have non-positive real parts. Let \( \text{diag}[d_i] \) be the diagonal matrix with diagonal elements \( d_i \). The matrix \( K - \text{diag}[1/\tau_i] \) has non-negative non-diagonal elements, non-positive diagonal and the sum of the elements in each column is strictly negative. Therefore, the eigenvalues of this matrix have negative real parts (Gershgorin’s theorem). In the vector form, the second equation in (15) is

\[ \frac{d\varsigma}{dt} = \frac{1}{\varepsilon} \text{diag} \left[ \frac{1}{\tau_i} \right] \varsigma^{\text{peq}} - \frac{1}{\varepsilon} \left( \text{diag} \left[ \frac{1}{\tau_i} \right] - K \right) \varsigma. \]

For given \( \mu_i, T \), the subsystem for concentration of compounds quickly converges to the quasi steady state (qss). (For detailed description of qss and pss approximations, their similarities and differences we refer to review [15].)

\[ \varsigma^{\text{qss}}(\mu, T) = \left( \text{diag} \left[ \frac{1}{\tau_i} \right] - K \right)^{-1} \text{diag} \left[ \frac{1}{\tau_i} \right] \varsigma^{\text{peq}}(\mu, T) \]

that is \( \varepsilon \)-small because \( \varsigma^{\text{eq}} \) is \( \varepsilon \)-small. Let us notice a simplification:

\[ \left( \text{diag} \left[ \frac{1}{\tau_i} \right] - K \right)^{-1} \text{diag} \left[ \frac{1}{\tau_i} \right] = (1 - \text{diag}[\tau_i] K)^{-1}. \]  

(16)

If \( \varsigma \) is \( \varepsilon \)-close to \( \varsigma^{\text{qss}}(\mu, T) \) then it is \( \varepsilon \)-small and the right-hand side of equations for \( b_i \) in (15) is not fast (in this case, it has zero or even higher order in \( \varepsilon \)). Thus, the Tikhonov theorem can be applied and the qss approximation
is valid for small $\varepsilon$. We can take into account that the difference $b_i - c_i$ is $\varepsilon$-small and write the resulting kinetic equation

$$\frac{dc_i}{dt} = \frac{1}{\varepsilon} \sum_{j,l,j \neq l} (\kappa_{jl}q_{ss}(\mu, T) - \kappa_{lj}q_{ss}(\mu, T)) \nu_{ji};$$

(17)

$$q_{ss}(\mu, T) = (1 - \text{diag}[\tau_i]K)^{-1}q_{\text{peq}}(\mu, T).$$

Equations for $c$ can be modified by changing the indexes in double summation:

$$\frac{dc_i}{dt} = \frac{1}{\varepsilon} \sum_{j,l,j \neq l} \kappa_{jl}q_{ss}(\mu, T)(\nu_{ji} - \nu_{li});$$

(18)

$$q_{ss}(\mu, T) = (1 - \text{diag}[\tau_i]K)^{-1}q_{\text{peq}}(\mu, T).$$

Each term in the right hand side of equations for $c$ in (18) can be represented in the standard form of the sums over reactions. For each pair $j, l$ consider elementary reaction (1) with $\alpha_{\rho_i} = \nu_{li}$ and $\beta_{\rho_i} = \nu_{ji}$. Then, according to (18), equation for $c$ is chemical kinetic equation with reaction rates

$$r_{\rho} = \frac{1}{\varepsilon} \kappa_{jl}q_{ss}(\mu, T).$$

(19)

The qss concentrations of compounds are linear combinations of the peq concentrations. Therefore, the reaction rate for each reaction (19) is combined from the same terms as the generalized MAL reaction rates. The matrix of coefficients of these combinations is $(1 - \text{diag}[\tau_i]K)^{-1}$. Let us call it the entanglement matrix.

6. The MMS limit and the classical generalized MAL

To obtain the MMS asymptotic formulas, we may assume that $\tau_i$ are also small. That is, there exists an additional small parameter $\delta > 0$ and the relaxation times for the equilibration $\sum \nu_{ji}A_i \Rightarrow B_j$ is $\delta \varepsilon \tau_j$.

The MMS asymptotics with $\delta \to 0$ gives the generalized MAL reaction rates in the assumption of partial equilibria between compounds $B_j$ and the corresponding complexes $\sum \nu_{ji}A_i$:

$$r_{\rho}^{\text{peq}} = \frac{1}{\varepsilon} \kappa_{jl}q_{\text{ss}}^{\text{peq}}(\mu, T) =$$

(20)

$$= \frac{1}{\varepsilon} \kappa_{jl}q_{ss}^{\text{peq}}(\mu, T) \exp \left( \frac{\sum \nu_{ji}\mu_i(c, T)}{RT} \right).$$

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If we use the notation $\varphi_{\rho} = \frac{1}{2}\kappa_{j}\varsigma_{l}^{*}(c, T)$ then we obtain the standard generalized MAL factorization of reaction rate onto kinetic and thermodynamic factors (5). The semidetailed balance condition (6) is a straightforward consequence of the assumption that the standard thermodynamic equilibrium $\varsigma^{*}$ is also the equilibrium of the Markov kinetics of compounds: for all $j$

$$\sum_{l}(\kappa_{jl}\varsigma_{l}^{*} - \kappa_{lj}\varsigma_{j}^{*}) = 0. \quad (21)$$

This balance condition means that the microscopic parameters $\kappa_{jl}$ and $\varsigma^{*}$ are not independent and the constraints (21) are nonlinear (bilinear). Happily, in the macroscopic expressions for generalized MAL, like (20), these parameters participate together, in a product $\xi_{jl} = \kappa_{jl}\varsigma_{l}^{*}$. Parameters $\xi_{jl}$ ($\xi_{jl} \geq 0, j \neq l$) have much simpler linear a priory constraints: for all $j$

$$\sum_{l}(\xi_{jl} - \xi_{lj}) = 0. \quad (22)$$

For the generalized MAL, the values of $\xi_{jl}$ can be extracted from the macroscopic reaction rates $r_{\rho}$ (20) and the thermodynamic data about reagents $A_{i}$.

It is impossible to extract the all the microscopic data about $\kappa_{jl}$ and $\varsigma$ from the observation of the macroscopic reaction rates $r_{\rho}$. Nevertheless, the ratio of some microscopic constants can be found. If two elementary reactions have the same input complex with the coefficients $\nu_{li}$ and the output complexes have the coefficients $\nu_{ji}$ and $n_{qi}$ the ratio of the corresponding reaction rates coincides with the ratio of the compounds reaction rate constants $\kappa_{jl}/\kappa_{qi}$. According to (19) and (20), this is true both for the peq and qss reaction rates.

7. A simple example of entangled MAL

The structure of the entanglement matrix is closely connected to the representation of the macroscopic reaction mechanism as transformation of complexes. Let us introduce this formalism [6] with the corresponding notations. Each formal sum in the elementary reactions (1) is called a complex: $\Theta_{i} = \sum_{i}\nu_{li}A_{i}$. The same complex can participate in several reactions. A complex reaction can be represented as a oriented graph of transition between complexes.
Let us consider a simple example following [16, 8]: 18 elementary reactions (9 pairs of mutually reverse reactions) from the hydrogen combustion mechanism.

\[
\begin{align*}
H + O_2 & \rightleftharpoons O + OH; & O + H_2 & \rightleftharpoons H + OH; \\
OH + H_2 & \rightleftharpoons H + H_2O; & O + H_2O & \rightleftharpoons 2OH; \\
HO_2 + H & \rightleftharpoons H_2 + O_2; & HO_2 + H & \rightleftharpoons 2OH; \\
H + OH + M & \rightleftharpoons H_2O + M; & H + O_2 + M & \rightleftharpoons HO_2 + M; \\
H_2O_2 + H & \rightleftharpoons H_2 + HO_2
\end{align*}
\]

There are 16 different complexes here:

\[
\begin{align*}
\Theta_1 & = H + O_2, & \Theta_2 & = O + OH, \\
\Theta_3 & = O + H_2, & \Theta_4 & = H + OH, \\
\Theta_5 & = OH + H_2, & \Theta_6 & = H + H_2O, \\
\Theta_7 & = O + H_2O, & \Theta_8 & = 2OH, \\
\Theta_9 & = HO_2 + H, & \Theta_{10} & = H_2 + O_2, \\
\Theta_{11} & = H + OH + M, & \Theta_{12} & = H_2O + M, \\
\Theta_{13} & = H + O_2 + M, & \Theta_{14} & = HO_2 + M, \\
\Theta_{15} & = H_2O_2 + H, & \Theta_{16} & = H_2 + HO_2.
\end{align*}
\]

The reaction mechanism can be represented as

\[
\begin{align*}
\Theta_1 & \rightleftharpoons \Theta_2, & \Theta_3 & \rightleftharpoons \Theta_4, & \Theta_5 & \rightleftharpoons \Theta_6, \\
\Theta_7 & \rightleftharpoons \Theta_8, & \Theta_9 & \rightleftharpoons \Theta_{10}, \\
\Theta_{11} & \rightleftharpoons \Theta_{12}, & \Theta_{13} & \rightleftharpoons \Theta_{14}, & \Theta_{15} & \rightleftharpoons \Theta_{16}
\end{align*}
\]

This graph of transformation of complexes has a very simple structure: There are five isolated pairs of complexes and one connected group of four complexes.

Let us rewrite the basic formulas in these notations. For each reaction \(\Theta_l \rightarrow \Theta_j\) consider the generalized MAL reaction rate (5)

\[
r_{jl} = \varphi_{jl} \exp \left( \frac{\sum_i \nu_{ji} \mu_i(c,T)}{RT} \right).
\]

(The standard order of indexes is used, \(r_{j\rightarrow i}\) ) For the perfect systems the free energy density is

\[
f(c,T) = RT \sum_i c_i \left( \ln \left( \frac{c_i}{c_i^*} \right) - 1 \right),
\]

11
where $c_i^*$ is a standard equilibrium (an equilibrium point for a priori selected values of linear balances).

The Boltzmann factor for the perfect system is:

$$
\exp \left( \frac{\sum_{i} \nu_{ji} \mu_i(c, T)}{RT} \right) = \prod_i \left( \frac{c_i}{c_i^*} \right)^{\nu_{ji}}
$$

under the standard assumption that $c^\alpha = 1$ if $\alpha = 0$ and $c \geq 0$. Then the generalized MAL turns into the classical MAL

$$
\phi_{jl} = \varphi_{jl} \prod_i \left( \frac{c_i}{c_i^*} \right)^{\nu_{ji}}
$$

Under assumption (6): for all $j$

$$
\sum_{j} \varphi_{jl} \equiv \sum_{l} \varphi_{lj},
$$

or, with the systems with microreversibility (the most common case in physics and chemistry [10]): for pairs all $j, l$ ($j \neq l$)

$$
\varphi_{jl} \equiv \varphi_{lj}.
$$

The non-negative quantities $\varphi_{jl}$ are not compulsory constant. Their detailed dependence on the concentrations, temperature, or other conditions is beyond the scope of this work.

For the entanglement example, we select a system with five components $A_1-5$, three complexes, $\Theta_1 = A_1 + A_2$, $\Theta_2 = 2A_3$, $\Theta_3 = A_4 + A_5$, and two reversible reactions:

$$
\Theta_1 \rightleftharpoons \Theta_2 \rightleftharpoons \Theta_3.
$$

We can find such fragments in many complex reactions, for example, in the hydrogen combustion mechanism mentioned above.

According to the transient state modeling (Figs. 1, 2), there is one compound for each complex, $B_i$ ($i = 1, 2, 3$). The complete scheme of reactions with compounds consists of five reversible reactions: $\Theta_i \rightleftharpoons B_i$ ($i = 1, 2, 3$) and $B_1 \rightleftharpoons B_2 \rightleftharpoons B_3$.

For kinetic model we need the following data: five standard equilibrium concentrations for reagents, $c_i^*$, three standard equilibrium concentrations
for compounds, $ς^*$, four reaction rate constants for transitions between compounds, $\kappa_{21}, \kappa_{12}, \kappa_{32},$ and $\kappa_{23},$ and three relaxation times for the equilibration between the complexes and compounds, $\tau_{1-3}$ (9). These data are not independent and the balance conditions should hold (21). We assume even stronger physical conditions, detailed balance:

$$\kappa_{21}ς^*_1 = \kappa_{12}ς^*_2 (= w^*_1) \text{ and } \kappa_{32}ς^*_2 = \kappa_{23}ς^*_3 (= w^*_2),$$

(24)

where $w^*_1, 2$ are the equilibrium fluxes between the corresponding compounds.

The partial equilibrium concentrations of compounds are (8):

$$ς_{\text{peq}}^j = \frac{ς^*_j}{\prod_i (c_i \cdot c^*_i)^{\nu_{ji}}},$$

(25)

in particular,

$$ς_{\text{peq}}^1 = \frac{ς^*_1}{c_1 \cdot c^*_1}, \quad ς_{\text{peq}}^2 = \left(\frac{c_3}{c^*_3}\right)^2, \quad ς_{\text{peq}}^3 = \frac{ς^*_3}{c_4 \cdot c^*_4}. $$

The entanglement matrix is $E = (1 - \text{diag}[\tau_i]K)^{-1}$:

$$E = \begin{pmatrix}
1 + \tau_1\kappa_{21} & -\tau_1\kappa_{12} & 0 \\
-\tau_2\kappa_{21} & 1 + \tau_2(\kappa_{12} + \kappa_{32}) & -\tau_2\kappa_{23} \\
-\tau_3\kappa_{32} & 1 + \tau_3\kappa_{23} & 1
\end{pmatrix}^{-1}.
$$

The vector of qss concentrations of compounds is $ς^{\text{qss}} = Eς^{\text{peq}}$. The qss reaction rates are: $r_{jl}^{\text{qss}} = \kappa_{jl}ς^{\text{qss}}$. It is straightforward to get explicit formulas for reaction rates, but they are quite cumbersome, so we will limit ourselves to a numerical example. Let $c^*_1 = 1, \quad ς^*_1-3 = 1, \quad \kappa_{ij} = 1,$ and $\tau_{1-3} = 1$ (here we omit the small parameter, since it is vanished in microscopic quantities).

For these data, $w^*_1 = w^*_2 = w^*_3 = 1,$

$$ς_{\text{peq}}^1 = c_1c_2, \quad ς_{\text{peq}}^2 = c_3^2, \quad ς_{\text{peq}}^3 = c_4c_5.$$
\[
E = \begin{bmatrix}
2 & -1 & 0 \\
-1 & 3 & -1 \\
0 & -1 & 2
\end{bmatrix}
^{-1} = \frac{1}{8}
\begin{bmatrix}
5 & 2 & 1 \\
2 & 4 & 2 \\
1 & 2 & 5
\end{bmatrix};
\]

\[
\varsigma^{\text{qss}} = \frac{1}{8}
\begin{bmatrix}
5c_1c_2 + 2c_3^2 + c_4c_5 \\
2c_1c_2 + 4c_3^2 + 2c_4c_5 \\
c_1c_2 + 2c_3^2 + 5c_4c_5
\end{bmatrix};
\]

\[
r_{21}^{\text{qss}} = \frac{1}{8}(5c_1c_2 + 2c_3^2 + c_4c_5),

r_{12}^{\text{qss}} = \frac{1}{8}(2c_1c_2 + 4c_3^2 + 2c_4c_5),

r_{32}^{\text{qss}} = \frac{1}{8}(2c_1c_2 + 4c_3^2 + 2c_4c_5),

r_{23}^{\text{qss}} = \frac{1}{8}(c_1c_2 + 2c_3^2 + 5c_4c_5).
\]

If we decipher this system according to the standard (textbook [11]) MAL kinetics then we find three reversible elementary reactions

\[
\Theta_1 \rightleftharpoons \Theta_2 \rightleftharpoons \Theta_3 \rightleftharpoons \Theta_1.
\]

Initial two reversible elementary reactions turned into three ones. The reaction rate constants also changed. In the stoichiometric form, these reactions with the new reaction rates are listed below

1. \(A_1 + A_2 \rightleftharpoons 2A_3, k_1^+ = \frac{1}{3}, k_1^- = \frac{1}{4};\)
2. \(2A_3 \rightleftharpoons A_4 + A_5, k_2^+ = \frac{1}{4}, k_2^- = \frac{1}{4};\)
3. \(A_4 + A_5 \rightleftharpoons A_1 + A_2, k_3^+ = \frac{1}{8}, k_3^- = \frac{1}{8}.\)

We see that the connected component of the complex transition graph turned into the complete digraph. This is the universal effect of the entanglement matrix. The equilibrium did not change.
8. Entanglement matrix in the first approximation

The MMS asymptotics (Fig. 1a) assumes that equilibration of fast equilibria is infinitely much faster than other transitions between compounds (the products $\tau_k k_{ji} \to 0$ for all $i, j, k$). We rejected this assumption (Fig. 1b) and, in combination with linearisation near partial equilibria, obtained the entanglement matrix (16), (18). Let us analyze an intermediate assumption that equilibration of fast equilibria is faster than other transitions between compounds but not infinitely faster. Introduce a formal small parameter $\delta$.

$$E = (1 - \delta \text{diag}[\tau_i] K)^{-1}.$$  

For sufficiently small $\delta$ the following series for $E$ converges:

$$E = 1 + \delta \text{diag}[\tau_i] K + \delta^2 (\text{diag}[\tau_i] K)^2 + \ldots.$$  

In the first approximation,

$$E = 1 + \delta \text{diag}[\tau_i] K + o(\delta).$$  

If we introduce such small parameter into the simple example from the previous section then we obtain:

$$E = 1 + \delta \begin{bmatrix} 1 & -1 & 0 \\ -1 & 2 & -1 \\ 0 & -1 & 1 \end{bmatrix} + o(\delta);$$

$$\varsigma^{qss} = \begin{bmatrix} (1 + \delta)c_1 c_2 - \delta c_3^2, \\ -\delta c_1 c_2 + (1 + 2\delta)c_3^2 - \delta c_4 c_5 \\ -\delta c_3^2 + (1 + \delta)c_4 c_5 \end{bmatrix};$$

$$r^{qss}_{21} = (1 + \delta)c_1 c_2 - \delta c_3^2, \quad r^{qss}_{12} = -\delta c_1 c_2 + (1 + 2\delta)c_3^2 - \delta c_4 c_5, \quad r^{qss}_{32} = -\delta c_1 c_2 + (1 + 2\delta)c_3^2 - \delta c_4 c_5, \quad r^{qss}_{23} = -\delta c_3^2 + (1 + \delta)c_4 c_5.$$  

Again, the reaction rates become linear combinations of known MAL dependencies. The approximate formulas for small $\delta$ can lead to the positivity loss when some of macroscopic concentrations $c_i$ become $\delta$-small.
9. Conclusion

The century old classical MMS asymptotic approach to derivation of (generalized) Mass Action Law (MAL) implies two properties of intermediate transition states:

**Quasi steady state.** The intermediate states have short life time and are present in much smaller concentrations than the main reagents.

**Fast equilibrium.** The intermediate states are in partial equilibrium with the initial reagents of the elementary reaction. This means that the reverse decomposition of the intermediates is much faster than its transition through other channels to the products.

The transition state (activation complex) theory also relies on these assumptions. The intermediate states are named differently by different groups of researchers: the transition states, the activation complexes or just compounds. We called them ‘compounds’ employing the Michaelis-Menten terminology.

The classical approaches have an important advantage: there is no need to postulate a kinetic law for the birth of the transition state (compounds) from the reagents in no-linear reactions. This non-linear kinetic law follows from the thermodynamic description of the partial equilibrium and then the transformations of transition states is described by the linear kinetics (Markov chains). The kinetic constants for this linear kinetics can be evaluated (the transition state or activation complex theory) or extracted from combination of experimental data and theoretic estimates. The structure of the kinetic law will be the same: the generalized MAL.

It is possible to relax the assumption of fast equilibrium without postulating a kinetic law for the birth of the transition state (compounds) from the reagents in no-linear reactions. For this purpose, we can just linearize the still unknown equation of the birth of compounds from combinations of initial reagents. The single elementary reaction goes along one stoichiometric vector, therefore, the linearized kinetics can be described by one constant – the relaxation time. Of course this relaxation time may be different for different compounds and also depend on the conditions.

We demonstrate how substituting of the partial equilibrium assumption by the weaker assumption of the linear kinetics near partial equilibria modifies the reaction rates. In this approach, the asymptotic quasi steady state expressions for reaction rates were produced. The final reaction rates are combinations of the generalized MAL expressions but for different reactions. We called this effect the ‘entanglement’ of MAL.
In particular, any connected component of the digraph of the transitions between complexes is transformed into a complete digraph of reactions. Thus, the set of reactions \( \text{O} + \text{H}_2\text{O} \rightleftharpoons \text{2OH} \rightleftharpoons \text{HO}_2 + \text{H} \rightleftharpoons \text{H}_2 + \text{O}_2 \) should be compulsory supplemented to the complete digraph by three reversible reactions \( \text{O} + \text{H}_2\text{O} \rightleftharpoons \text{HO}_2 + \text{H} \), \( \text{O} + \text{H}_2\text{O} \rightleftharpoons \text{H}_2 + \text{O}_2 \), and \( \text{2OH} \rightleftharpoons \text{H}_2 + \text{O}_2 \).

The approach based on the quasi steady state assumption that the intermediates have short life time and are present in small concentrations works well if the microkinetic equations are linearized near partial equilibrium. In this approximation, the kinetic law is the ‘entangled MAL’ combined from the same terms. This approach can be incorporated in modern advances framework of multiscale non-equilibrium thermodynamics [17, 18]. The next step beyond this approximation requires the analysis of microscopic models of elementary reaction phenomena, depends on the details of the interaction of particles, and goes beyond the scope of universal phenomenological theory.

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