Global selection rule in chemical coupling

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Abstract

Coupling and decoupling of chemical reactions are explored through a modified heat balance equation. Reaction enthalpies are found to play crucial role; the sign of their product for a pair of consecutive chemical reactions determine whether they couple or not. The possibility of a coupling-uncoupling transition for such reactions is thus introduced for the first time. The present work resolves a paradox concerning negative efficiency of coupled consecutive chemical reactions. Enthalpy is also shown to be a "constant of motion" along the reaction coordinate as long as the mass action ratio varies little with temperature. The present analysis puts the observed difference between calorimetric and van’t Hoff enthalpies on a quantitative basis. A case study is presented with a third order reaction where the enthalpic criterion is useful in selecting the more probable of the alternative mechanisms.

PACS No. 82.60.-s 65.40.G
I. INTRODUCTION

The present work extends an earlier attempt \cite{1} to generalize the conventional phenomenology \cite{2,3} for describing thermodynamics of chemical reactions. The conventional approach, though based on the limiting assumption of near equilibrium, was applied to complex processes \cite{4} successfully. Coupling of chemical reactions, however was treated \cite{4} using a rather special example of a cyclic reaction system. For non-cyclic e.g. consecutive reaction schemes, the Onsager matrix is shown to be diagonal, ruling out phenomenological coupling. Conventional chemical wisdom, on the other hand, assumes a set of reactions to be coupled provided they have common intermediate(s). More importantly, the efficiency of coupling can be shown to be always negative for coupling schemes treated in the traditional way, whether in linear or non-linear domain. This renders the description of coupling itself as invalid in the established format. We show, on the contrary, how minor modifications in the balance equations lead to alteration in the definition of macroscopic fluxes and forces in chemical reaction systems \cite{6,7} permitting coupling. The reactions may now be coupled if enthalpy change in each is non-vanishing. Also, enthalpy remains a "constant of motion" along reaction coordinate provided the mass action ratio has a small variation with temperature. The recent debate on difference between van’t Hoff and calorimetric enthalpies \cite{8} are put on a more quantitative basis with our approach. A case study with a third order reaction having two possible mechanisms shows that our approach correctly identifies the more probable pathway.
II. THE BALANCE EQUATION REVISITED

Let us briefly recall the phenomenological equations for chemical coupling widely used in chemical literature. [4,7] For a set of reactions $\rho(=1,\ldots,r)$ in a fixed volume, the rates of change of entropy, concentration etc. are given by

\[
\frac{\partial s_v}{\partial t} = -\nabla J_s + \sigma \tag{1}
\]

\[
\frac{\partial c_i}{\partial t} = -\nabla J_i + \sum_{\rho} \nu_{i\rho} v_{\rho} \tag{2}
\]

\[
\frac{\partial q_v}{\partial t} = -\nabla J_q + \sum_{\rho} v_{\rho} \Delta H_{\rho} \tag{3}
\]

\[
T ds_v = dq_v - \sum_i \mu_i dc_i \tag{4}
\]

Here, $s_v$, $J_s$ are the density and flux terms for entropy, $c_i$, $J_i$ those for the $i$th chemical species and $q_v$, $J_q$ those for heat. $\nu_{i\rho}$ is the stoichiometric coefficient of the $i^{th}$ species in the $\rho^{th}$ chemical reaction for which the velocity is $v_{\rho}$. $\sigma$ is the entropy production term. While $\Delta H_{\rho}$ is the enthalpy change of the $\rho^{th}$ chemical reaction, the corresponding Gibbs free energy change, $\Delta G_{\rho}$, is given by the law of mass action as

\[
\Delta G_{\rho} = -RT \ln \left( \frac{v_{\rho}^+ / v_{\rho}^-}{v_{\rho}^+ - v_{\rho}^-} \right) \tag{5}
\]

where $v_{\rho}^+$ and $v_{\rho}^-$ are the forward and reverse reaction velocities of the $\rho^{th}$ reaction, and $v_{\rho} = v_{\rho}^+ - v_{\rho}^-$. From eqs. (1) - (4), equating non-gradient parts,

\[
\sigma = J_q, \nabla (1/T) - \sum_i J_i, \nabla (\mu_i/T) + \sum_{\rho} v_{\rho} (\Delta H_{\rho} - \sum_i \mu_i \nu_{i\rho})/T \tag{6}
\]
For an isothermal chemical reaction system in a well-stirred (or homogeneous) medium we get,

\[ \sigma = \sum_{\rho} v_{\rho} \Delta S_{\rho} \quad (7) \]

from \( \Delta G_{\rho} = \Delta H_{\rho} - T \Delta S_{\rho} \) and the second law. Note that the rate of entropy production is obtained as a stoichiometric sum of entropy changes of reaction steps, \textit{without invoking any assumption of linearity of processes}.

Our eq. (7) can be compared with the standard one for \( \sigma \) found in chemical literature, \cite{4,7} viz.

\[ T \sigma = -\sum_{\rho} v_{\rho} \Delta G_{\rho} \quad (8) \]

Following standard phenomenological notations,

\[ v_{\rho} = -\sum_{\rho'} L_{\rho \rho'} \Delta G_{\rho'} \quad (9) \]

Linearising eq. (5), and using \( v_{\rho} = v_{\rho}^+ - v_{\rho}^- \) with eq. (9), we obtain

\[ L_{\rho \rho'} = \delta_{\rho \rho'} v_{\rho\text{(eq)}/RT} \quad (10) \]

where \( \delta_{\rho \rho'} \) is the Kronecker delta. Such a diagonal nature of \( L \) makes coupling between two different reactions impossible. Please note that coupling between
cyclic reactions can still emerge in this treatment, Onsager’s example \[4\] being the most famous one.

This impossibility does not occur in our treatment since unlike eq. (8), eq. (7) leads to a different phenomenological equation for the reaction velocity

$$v_{\rho} = -\sum_{\rho'} L_{\rho\rho'} \Delta S_{\rho'}$$

(11)

### III. PHENOMENOLOGICAL VS. CHEMICAL COUPLING

Coupling of chemical reactions, while gaining in popularity over the past few decades, have received little attention from theoreticians. The major contributors have been Prigogine and his coworkers \[4,9\]. Perhaps, the importance of coupled reactions is felt nowhere more than in treatments of biochemical cycles \[10\]. Glycolytic or the basic bioenergetic cycle (oxidative phosphorylation) are examples of intricate coupling of consecutive and cyclic reactions \[5\]. Yet, quantitative expression of reaction coupling is absent in existing literature in these fields.

According to Prigogine \[4\], a pair of reactions with affinities $A_i$ and $A_j$ and velocities $v_i$ and $v_j$ can couple if signs of $A_i v_j$ and $A_j v_j$ are different. This means that one reaction must drive another for the two reactions to couple. Based on this idea, Rottenberg \[5\] defined efficiency of coupling as

$$\eta = -A_1 v_1 / A_2 v_2$$

where the subscripts 1 and 2 denote the driven and the driving reactions re-
spectively. However, Hill [11] pointed out that

\[ A \times v \geq 0 \]

for individual reactions. Thus efficiency of coupling is negative and coupling of consecutive reactions at least is ruled out. This poses a far stronger challenge to the conventional theory describing coupling, as an objection to the problem posed by diagonal nature of the Onsager matrix, as shown in eq. (10), could be that the treatment there is strictly linear. Although Hill’s derivation is consistent with eq. (5), his conjecture that coupling of chemical reactions is only possible via common intermediates and has no phenomenological meaning otherwise, is hardly acceptable. In fact, Hill never sought to explain why a consecutive reaction pair always has a negative efficiency. The lacuna was in not appreciating a more fundamental problem, viz. the nature of the driving force behind reaction coupling. This impasse has been resolved by the present work, where the key steps in this regard were modification of eq. (8) to (7), and of eq. (9) to (11). From eq. (11) it is clear that in our theory the efficiency of coupling need not be always negative. Also, the Onsager matrix \( L_{\rho \rho'} \) is not necessarily diagonal. It can thus be used as a proper measure of the coupling strength between two reactions. The general approach is not only useful in resolving the paradox stated earlier, it also provides a simple thermodynamic criterion for coupling in simple reaction systems. For example, if the enthalpy of any reaction step \( \rho \) is zero, that reaction can not couple with any other reaction step \( \rho' \) as \( L_{\rho \rho'} \) again becomes diagonal.
IV. GIBBS RELATION ALONG REACTION TRAJECTORY: $\Delta H_{CAL}$ VS $\Delta H_{VH}$

This is an interface between kinetics and thermodynamics of reaction processes [4]. For a reaction system the free energy change of the $\rho^{th}$ reaction away from equilibrium can be expressed by

$$\Delta G_\rho = \Delta G_0^\rho + RT \ln K_\rho$$

where the mass action ratio $K_\rho$ is given by

$$K_\rho = \prod_j c_j^{\nu_{ij}}$$

Writing the entropy change along the $\rho^{th}$ reaction as a stoichiometric sum of molal entropies, $S_i$

$$\Delta S_\rho = \sum_i \nu_{i\rho} S_i$$

From the relation $\Delta S_\rho = -\partial \Delta G_\rho / \partial T$, eq. (12) and $\Delta G_\rho = \Delta H_\rho - T \Delta S_\rho$,

$$\Delta S_\rho = \Delta S_0^\rho - R \ln K_\rho - R (\partial \ln K_\rho / \partial \ln T)$$

A simple consequence of eq. (15) is,
\[ \Delta H_\rho = \Delta H_\rho^0 - RT(\partial \ln K_\rho / \partial \ln T) \]  

(16)

Let us identify the two \( \Delta H \) terms appearing in eq. (16) clearly. At equilibrium, eq. (16) becomes

\[ \Delta H_{\rho}^{eq} = \Delta H_{\rho}^0 - RT[\partial \ln K_{\rho} / \partial \ln T]_{eq} \]  

(17)

If the second term on RHS becomes very small, we are left with

\[ \Delta H_{\rho} \simeq \Delta H_{\rho}^0 \]  

(18)

Eq. (18) may be stated as follows: the enthalpy remains approximately a constant of motion along the reaction co-ordinate for any reaction (the van’t Hoff approximation). Note that where it is not so, i.e. where \( \Delta H_{\rho} \) depends on the reaction coordinate and may even change its sign from \( \Delta H_{\rho}^0 \), a pair of coupled reactions may become decoupled or vice versa, as the coupling depends on sign of the product of the enthalpies of the respective reactions. A coupling-uncoupling transition is therefore possible for such a set of chemical reactions.

Much further work is needed in this area.

\( \Delta H_{\rho}^{eq} \) is clearly the experimentally measured enthalpy change in a reaction \( \text{viz. } \Delta H_{cal} \), which is conventionally measured at equilibrium (or near equilibrium) conditions. But the first term on RHS of eq. (16) or (17) can be identified with the van’t Hoff enthalpy of the reaction \( \text{viz. } \Delta H_{vH} \), defined as
\[ \Delta H_{vH} = \Delta H^0_p = RT(\partial \ln K_{eq}/\partial \ln T) \]  \hspace{1cm} (19)

Based on this discussion and the last two equations, we can write

\[ \Delta H_{cal} = \Delta H_{vH} - RT[\partial \ln K_p/\partial \ln T]_{eq} \]  \hspace{1cm} (20)

There is a large and growing body of evidence \cite{8,12,19} (including some unpublished work \cite{20}) of discrepancy between \( \Delta H_{cal} \) and \( \Delta H_{vH} \). There is also an awareness of the importance of the ratio of these two values, especially in interpreting biocalorimetric data \cite{21}. While for simple chemical reactions the ratio is close to unity, for reactions involving macromolecules e.g. in protein folding, there is clear departure of the ratio from unity. In biochemical literature, \cite{19,21} the numerical value of the ratio (which may vary from 0.5 to more than 4 \cite{13}, say) is taken to provide a measure of cooperativity of the biochemical reaction (e.g. folding). Our analysis gives a clear insight into the difference between the two enthalpy values. The origin of this difference stems from the difference in temperature dependence of equilibrium and non-equilibrium mass action ratios. Let us also recall that such difference between equilibrium and non-equilibrium values are accepted naturally for Gibbs free energy, for example, and the difference considered in terms of a mass action ratio.

We realize that further simplification of eq. (20) may be difficult. Instead, we use certain experimental data to show that the mass action ratio, \( K_p \), may have a scaling dependence on the experimental temperature. Holtzer \cite{12} estimates that the difference between the calorimetric and van’t Hoff enthalpies
may be of the order of 45 calories per stoichiometric unit for simple chemical reactions. From eq. (20), this leads to

\[
\frac{\partial \ln K_\rho}{\partial \ln T} \simeq \frac{-45}{(300 \times 1.98)} = -0.075
\]  

(21)

at room temperature (300°K). We immediately obtain

\[
K_\rho \simeq \text{const} \times T^{-\alpha}
\]  

(22)

where \( \alpha \simeq 0.075 \) for simple chemical reactions.

V. COUPLING COEFFICIENTS IN TWO STEP REACTION - KINETIC APPROXIMATION

Using the dissipation eq. (7), we may express the phenomenological relation of a pair of reactions by

\[
\Delta S_2 = R_{21} v_1 + R_{22} v_2
\]

where \( v_1 \) and \( v_2 \) are velocities of the two reactions and \( R_{ij} \) are the coupling terms. The pre-equilibrium condition [22] is given by

\[
\Delta G_1 \rightarrow 0 \quad \text{and} \quad v_1 \rightarrow 0
\]  

(23)

If we use the approximate linear relation in such cases
\[
\Delta S_1 = R_{11} v_1 + R_{12} v_2 \simeq R_{12} v_2 
\]  
(24)

\(\Delta G_1 \simeq 0\) implies \(\Delta H_1 \simeq T \Delta S_1\). Using the arguments of eq. (24), the entropy change in the first reaction is given as

\[
\Delta S_1 \simeq \Delta H_1^0 / T 
\]  
(25)

Using eq. (24), eq. (25) assumes the form

\[
\Delta H_1^0 = R_{12}' v_2 
\]  
(26)

where \(R_{12}' = T R_{12}\). The approximate form of the dissipation equation can be expressed as

\[
\sigma = \Delta S_1 v_1 + \Delta S_2 v_2 \simeq \Delta S_2 v_2 \geq 0 
\]  
(27)

As \(v_2\), velocity of the rate-determining step, is positive both for positive and negative coupling, the pre-equilibrium approximation should satisfy

\[
\Delta S_2 \geq 0 
\]  
(28)

Eqs. (25) - (28) express the nature of thermodynamic coupling that may
exist for kinetic schemes satisfying the pre-equilibrium condition. Eq. (26) implies that velocity of the rate determining step will be proportional to the enthalpy change in the pre-equilibrium step. It may be interesting to note that for positive coupling, the pre-equilibrium step must be endothermic and vice versa. If on the other hand the coupling is negative the relation $\Delta H_1^0 \leq 0$ must be satisfied. The negative coupling implies that one of the reactions among the pair has a negative dissipative component and is therefore driven by the other.

VI. A CASE STUDY WITH IN A SIMPLE REACTION

Let us consider a typical chemical reaction

$$2NO + O_2 \rightarrow 2NO_2$$

Using reported molar enthalpy values [23] the overall $\Delta H_0$ of this reaction is approximately 27.02 Kcal/mole. The standard mechanism (henceforth referred to as mechanism I) cited [24] is the following one:

$$2NO = N_2O_2$$

$$N_2O_2 + O_2 \rightarrow 2NO_2$$

This mechanism is able to explain the accepted rate law for the overall reaction \textit{viz.}
\[ \text{Rate} = k[\text{NO}]^2[\text{O}_2] \]

as also the negative sign of the activation energy of the overall reaction. \[25\]

Recently, \[26\] an alternative mechanism (referred to as mechanism II), has been proposed, namely

\[ \text{NO} + \text{O}_2 = \text{OONO} \]

\[ \text{OONO} + \text{NO} \rightarrow 2\text{NO}_2 \]

which agrees with the rate law given above. According to Plambeck, \[26\] spectroscopic evidence admits of simultaneous existence of both these mechanisms in the overall reaction, although concentration of OONO may be larger than \(N_2O_2\). Both the intermediates are short lived species, and although there is speculation about the structure of \(N_2O_2\), \[27\] nothing is known about OONO.

We performed \textit{ab-initio} calculations on \(N_2O_2\) and OONO. The GAMESS software package \[28\] was used with the ccpVTZ basis set, \[29\] augmented by a d and diffuse s, p type polarization functions. We present only thermochemical data in Kcal/mol (for \(\Delta H^0\) or \(\Delta G^0\)) or cal/mol-K (for \(\Delta S^0\)). Subscripts 1 and 2 represent the two steps in the overall reaction. Along with standard data \[23\] \[27\] our results are (with an estimated error limit of \(\pm 10\) percent) For mechanism I:

\[
\begin{align*}
\Delta S_1^0 &= -40.68 \text{ cal/mol-K} & \Delta S_2^0 &= 5.93 \text{ cal/mol-K} \\
\Delta H_1^0 &= -30.2 \text{ Kcal/mol} & \Delta H_2^0 &= 3.18 \text{ Kcal/mol} \\
\Delta G_1^0 &= -17.9 \text{ Kcal/mol} & \Delta G_2^0 &= 1.4 \text{ Kcal/mol}
\end{align*}
\]
Corresponding values for Mechanism II are

\[ \Delta S_1^0 = -34.34 \text{ cal/mol-K} \quad \Delta S_2^0 = -0.39 \text{ cal/mol-k} \]
\[ \Delta H_1^0 = -11.60 \text{ Kcal/mol} \quad \Delta H_2^0 = -15 \text{ Kcal/mol} \]
\[ \Delta G_1^0 = -1.29 \text{ Kcal/mol} \quad \Delta G_2^0 = -15.29 \text{ Kcal/mol} \]

It is clear that in both the mechanisms the enthalpy change in the pre-equilibrium step has a negative sign. Eq. (26) implies that one reaction must drive the other. From eq. (28) it follows that for both the mechanisms, 
\[ \Delta S_2 = \Delta S_2^0 - R \ln K_2 > 0, \]
where \( K_2 \) is the mass action ratio for the second step of the reaction. Therefore,

for Mechanism I

\[ \Delta S_2^0 \geq R \ln [NO_2]^2 / ([N_2O_2][O_2]) \]  \hspace{1cm} (29)

and for Mechanism II

\[ \Delta S_2^0 \geq R \ln [NO_2]^2 / ([NO]^2[OONO]) \]  \hspace{1cm} (30)

If the intermediate concentration is small, \( \Delta S_2^0 \) must be greater than a positive quantity. This need not be the case if the intermediate has a higher concentration, since then the right hand side of inequality (30) shifts towards more negative value. Incidentally, the first mechanism has a positive \( \Delta S_2^0 \). In the second mechanism \( \Delta S_2^0 \) has a value approaching zero. In this case, (30)
can hold good provided the intermediate concentration has a higher value. As pointed out by Plambeck, [26] both the mechanisms are known to exist, but higher concentration is seen for OONO. The observation is thus in accordance with the thermodynamic arguments presented above.

VII. CONCLUDING REMARKS

The present paper shows that coupling of chemical reactions should not be described in vague qualitative terms e.g. existence of common chemical intermediates. A pair of reactions remain decoupled as long as the product of their reaction enthalpies is non-negative. Coupling can only occur if they have enthalpies of opposite signs. An interesting corollary is that the same pair of reactions can undergo a transition from coupled to decoupled state (or vice versa), provided the mass action ratio of one or both the reactions change appreciably with progress of the reaction(s). An important modification brought forward by the present work is that the rate of internal entropy change near equilibrium is a weighted sum of the entropies (and not free energies or chemical affinities, as the form in which it is usually expressed) of the participating reactions. The observed deviation of calorimetric (measured) enthalpy from the van’t Hoff value for a reaction has also been explained, the origin of which is shown to be in the difference in the temperature dependence of equilibrium and non-equilibrium mass action ratios. For a class of simple chemical reactions, where the deviation is small, the enthalpy remains a constant of motion along the reaction coordinate. Finally, our treatment is shown to identify the more probable of alternate pathways for a typical third order chemical reaction.
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