

## On thermodynamic and kinetic equivalence of chemical systems

CHITRA DUTTA, ANJAN DASGUPTA and JYOTIRMOY DAS\*

Biophysics Division, Indian Institute of Chemical Biology, 4 Raja S. C. Mullick Road, Calcutta 700 032, India

MS received 3 September 1983; revised 11 January 1984

**Abstract.** A composite reaction is represented by a number of elementary reactions describing its mechanisms. By a linear transformation, the chemical flow and flux can be changed and one might obtain a new mechanism. The present report works out the selection rule to be imposed on the transformation matrix if the two mechanisms are thermodynamically and/or, kinetically indistinguishable (or equivalent). The net free energy change, entropy production, Onsager symmetry, and the detailed balance condition are considered to be the invariants of the transformation for thermodynamic equivalence. The selection rule has to be slightly modified for cyclic reactions. Two cyclic reactions with equivalent mechanisms are also worked out. It is proposed that for biochemical systems predominated by cyclic reactions, the selection rule is more permissive, and occurrence of multiple mechanisms has a higher probability, resulting in an enhancement of the fidelity of the net reaction in the presence of random environmental 'error variables'.

**Keywords.** Composite reaction; selection rule; transformation matrix; Onsager symmetry; entropy; thermodynamic equivalence.

### 1. Introduction

A composite reaction can generally be represented by a set of elementary reactions. Each elementary reaction has a well-defined reaction velocity given by the law of mass-action (Shear 1967). The reaction-velocity expresses a single chemical flow-vector, the corresponding affinity being the chemical driving force (Prigogine 1967; Nicolis and Prigogine 1977). Often the mechanism of a composite reaction can be described by two or more sets of flow-force descriptions each leading to the same rate of entropy production (Prigogine 1967; Meixner 1942, 1943). These systems of elementary reactions, known as equivalent systems (Prigogine 1967) are related to one another by transformation matrices (Koenig *et al* 1961). However, such transformation matrices cannot be arbitrary, since the Onsager symmetry must be retained in any transformed descriptions (Coleman and Truesdell 1960). Koenig *et al* (1961) have demonstrated that a linear transformation essentially changes the reaction mechanism without affecting the overall kinetics. It is known that so long as the reactants, products and intermediates of a given composite reaction remain unchanged, the standard free-energy change does not depend on the mechanism of the reaction. Therefore, the transformation of chemical fluxes and forces must be such that the original and the transformed system give rise to an identical change in the standard free energy.

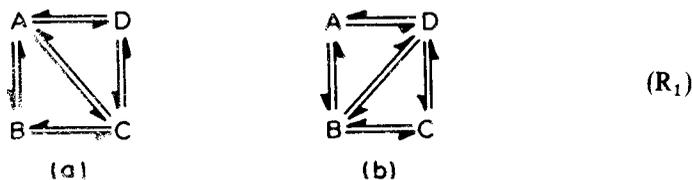
The present report describes that the mechanism independence of standard free-energy change can serve as an additional restriction on the transformation matrix. It

---

\* To whom all correspondence should be addressed.

has been shown that for most composite reactions (including the reactions described by Koenig *et al* 1961), the transformation matrix reduces to an identity matrix if this invariance of standard free energy change is considered.

Looped reactions seem to have a special status in this regard. Particularly the loops, which involve only isomerization reactions, are not associated with any change in the standard free energy. For such reactions, therefore, the transformation of chemical fluxes and flows seems to be more permissive. In other words, isomerization loops might involve kinetically and thermodynamically indistinguishable but mechanistically distinguishable chemical pathways. In a biological system most of the macromolecules are in states of dynamic conformational transitions. If a macromolecule can have four conformational status, say A, B, C and D, then the following two series of transitions are thermodynamically as well as kinetically indistinguishable. Now, if in mechanism (R<sub>1a</sub>) the transition  $C \rightleftharpoons A$  is affected due to any random or induced change, the thermodynamic and kinetic behaviour of the four conformers would still be unchanged. Qualitatively a multiple mechanism of a composite system increases the fidelity of the same. In contrast to looped reactions, non-cyclic chemical pathways generally lead to finite changes in standard free energy and hence the condition of invariance of free-energy-changes in indistinguishable mechanisms may be expected to be more restrictive for non-cyclic reactions than cyclic one.



## 2. Thermodynamic and kinetic indistinguishability of two reaction mechanisms

Any composite reaction  $C$  can be attributed to a particular mechanism  $(M_1) = \{E_\rho\}$ . For example, the composite reaction,



can have a mechanism expressible as



where  $E_1$ ,  $E_2$  and  $E_3$  are elementary reactions for which chemical affinity and reaction velocity can be explicitly defined, and  $X$  and  $Y$  are intermediates which do not appear in the overall reaction. Again, the composite reaction  $(R_2)$  can be attributed to an alternative mechanism,



which involves the same species as  $(M_1)$ .

Hence  $(M_1)$  may be transformed into  $M_2 = \{E'_\rho\}$ , by considering the linear transformations of macroscopic flows and forces as

$$|V'\rangle = S|V\rangle, \quad (1)$$

and,

$$|A'\rangle = T|A\rangle, \quad (2)$$

where  $(A, V)$  and  $(A', V')$  are the affinity and velocity vectors in the reference and transformed systems and  $S$  and  $T$  are the transformation matrices. Such linear transformations are called "equivalent transformations" (Prigogine 1967) provided the original and transformed systems are thermodynamically as well as kinetically equivalent.

(i) Thermodynamic indistinguishability ( $\tau_1$ ) of two chemical systems requires:

(a) identical rate of entropy production ( $E$ ), i.e.

$$\sigma = \langle A|V\rangle = \langle A'|V'\rangle, \quad (3)$$

(b) preservation of Onsager symmetry relations ( $O$ ), i.e. in near equilibrium region the linear relations,

$$|V'\rangle = L'|A'\rangle,$$

and

$$|V\rangle = L|A\rangle.$$

Satisfy

$$L' = L', \quad (4a)$$

$$L = L'. \quad (4b)$$

(c) invariance of net change in free energy ( $G$ ), which means,

$$\Delta G = \Delta G', \quad (5)$$

$\Delta G$  and  $\Delta G'$  being net changes in free energy in reference and transformed systems. Since two mechanisms lead to the same overall reaction,  $\Delta G_{\text{overall}}$  being independent of path, must remain invariant. Hence (5) may be thought of as an exclusion principle for transformation matrix  $S$ , such that the matrices not satisfying ( $G$ ), i.e. (5), cannot describe equivalent transformation processes.

(d) invariance of solutions of detailed-balance conditions (Onsager 1931) at equilibrium (DB). Since the chemical system under consideration is assumed to be mass-closed, it would eventually reach a unique equilibrium point (Shear 1968, Gray 1970) in the limit of the ideal solution approximation (Nicolis and Prigogine 1977). Now two reaction routes will be indistinguishable if they both yield the same values of concentrations for each of the chemical species at equilibrium. Hence two sets of detailed-balance conditions must have the same set of solutions for equilibrium concentrations.

(ii) On the other hand, kinetic indistinguishability ( $\kappa_1$ ) of two mechanisms requires the time-evolution of the concentrations of reactants to be identical in both mechanisms, i.e.

$$dC_j/dt = (dC_j/dt)', \quad (6)$$

where  $C_j$  represents the concentration of the  $j$ th chemical species ( $j = 1, 2, \dots, n$ ,  $n$  being the total number of species involved). In fact ( $\kappa_1$ ) does not provide any additional constraint on the transformation matrix. The validity of ( $E$ ) is a sufficient condition for the validity of ( $\kappa_1$ ) provided chemical potential vectors are conserved. Chemical

potential vector  $|\mu\rangle$  being an explicit function of the activity coefficients only, remains unaltered during the transformation. We shall denote the invariance of  $|\mu\rangle$  by  $(M)$ , which requires

$$|\mu\rangle = |\mu'\rangle, \quad (7)$$

where  $|\mu\rangle$  and  $|\mu'\rangle$  are the chemical potential vectors in the reference and the transformed systems.

### 3. Equivalent transformations in non-cyclic reactions

Coleman and Truesdell (1960) showed that if the transformation matrices  $S$  and  $T$  defined in (1) and (2) satisfy the relation,

$$T = (S^{-1})^t = (S^t)^{-1}, \quad (8)$$

(E) and (O) [*i.e.* (3) and (4)] are satisfied trivially. Such a choice, however, requires the matrix  $S$  to be non-singular. The affinity vectors can be expressed as (Nicolis and Prigogine 1977)

$$|A\rangle = -v^t|\mu\rangle, \quad (9a)$$

and,

$$|A'\rangle = -v'^t|\mu'\rangle. \quad (9b)$$

where  $v = \|v_{j\rho}\|$  and  $v' = \|v'_{j\rho}\|$  are stoichiometric co-efficient matrices (Boyd 1977; Prigogine 1967) in the original and transformed descriptions respectively such that  $\rho = 1, 2, \dots, r$ ,  $r$  being the number of linearly independent simultaneous reactions. At this point, it should be mentioned that the present study deals only with those transformations which preserve the total number ( $r$ ) of elementary chemical pathways in original and transformed descriptions. Since concentration evolution vector  $|\dot{C}\rangle$  can be expressed as

$$|\dot{C}\rangle = v|V\rangle.$$

From (1) and (6) the condition for  $(\kappa_1)$  is given by

$$v|V\rangle = v'|V'\rangle = -v^tS|V\rangle,$$

or

$$v' = v(S^{-1}). \quad (10)$$

It is now interesting to see that,

$$(i) \quad (E) \rightarrow (O). \quad (L_1)$$

*Proof:* (E) implies,

$$\langle A'|V'\rangle = \sigma = \langle A|V\rangle. \quad (11)$$

In near equilibrium region (Onsager 1931; Katchalsky and Curran 1967; Nicolis and Prigogine 1977), (11) yields

$$\langle A'|L|A'\rangle = \langle A|L|A\rangle. \quad (12)$$

From (2) and (12),

$$\langle A|T^tLT|A\rangle = \langle A|L|A\rangle,$$

or

$$\langle A|(T^tLT) - (L)|A\rangle = 0.$$

For non-cyclic reaction  $A_\rho$ 's ( $\rho = 1 \dots r$ ) are linearly independent. Hence

$$T'LT = L.$$

Thus in the transformation process defined by (1) and (2),  $L$ -matrix suffers a congruent transformation which retains its symmetry (Margenau and Murphy 1966; Coleman and Truesdell 1960).

Hence,

$$(L = L') \rightarrow (L' = L'').$$

Thus, (E) implies (O).

$$(ii) (E) \rightarrow (\kappa_1) \tag{L_2}$$

*Proof:* (E) requires,

$$\langle A' | V' \rangle = \langle A | V \rangle.$$

Using (9) and (7),

$$-\langle \mu | v' | V' \rangle = -\langle \mu | v | V \rangle.$$

Since  $\mu_j$ 's are linearly independent,

$$v' | V' \rangle = v | V \rangle,$$

or

$$|(\dot{C}') \rangle = |(\dot{C}) \rangle. \tag{13}$$

Equation (13) expresses nothing but  $(\kappa_1)$ .

$$(iii) (\kappa_1) \rightarrow (E) + (O) \tag{L_3}$$

*Proof:* Equation (11) shows that  $(\kappa_1)$  implies

$$v' = v(S^{-1}).$$

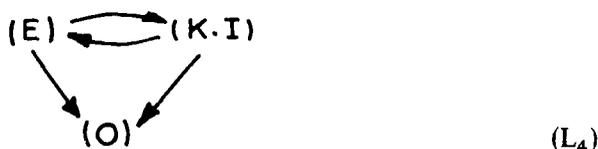
Then

$$\begin{aligned} |A' \rangle &= -v'^t |\mu' \rangle = -v'^t |\mu \rangle, \\ &= -[v(S^{-1})]^t |\mu \rangle, \\ &= -(S^{-1})^t v^t |\mu \rangle, \\ &= +(S^{-1})^t |A \rangle. \end{aligned} \tag{14}$$

Comparing equation (14) with (2), it follows that

$$T = (S^{-1})^t.$$

It has already been mentioned that the above relation [also expressed by (8)] implies the validity of both (E) and (O). Hence from the logical relations  $(L_1)$ ,  $(L_2)$  and  $(L_3)$ , one obtains the logical triangle,



So far the investigators (Coleman and Truesdell 1960; Koenig *et al* 1961) considered the validity of (E), (O) and ( $\kappa_1$ ) as sufficient criteria of thermodynamic and kinetic equivalence of two mechanisms, which may not be true, in general, since the validity of (E), (O) and ( $\kappa_1$ ) do not ensure the validity of (G) and (DB).

Equation (5) implies nothing but the invariance of the net equilibrium constant  $K$  since

$$K_{\text{eq}} = \exp[-(\Delta G/RT)].$$

Using the law of mass-action,  $K_{\text{eq}}$  can be expressed as

$$K_{\text{eq}} = \prod_{\rho=1}^r K_{\rho} = \prod_{\rho=1}^r \prod_{j=1}^n (C_j^{\text{eq}})^{\nu_{j\rho}}, \quad (15)$$

where  $K_{\rho}$  is the equilibrium constant for  $\rho$ th elementary reaction. ( $\kappa_1$ ) yields for a given set of initial conditions

$$(C_j^{\text{eq}}) = (C_j^{\text{eq}})', \quad (16)$$

where  $(C_j^{\text{eq}})$  and  $(C_j^{\text{eq}})'$  represents equilibrium values of  $C_j$  in the original and the transformed descriptions respectively. Then, from (5), (15) and (16), we get,

$$\sum_{j=1}^n \sum_{\rho=1}^r (\nu_{j\rho} - \nu'_{j\rho}) \ln C_j^{\text{eq}} = 0,$$

which, together with (10), yields

$$\sum_{j=1}^n \sum_{\rho=1}^r \left[ \nu_{j\rho} - \sum_{\rho'=1}^r \nu_{j\rho'} (S^{-1})_{\rho'\rho} \right] \ln C_j^{\text{eq}} = 0.$$

Since  $C_j^{\text{eq}}$  depends to some extent on the initial conditions two different descriptions will yield identical changes in the net free energy irrespective of the initial conditions imposed on the system provided

$$\sum_{\rho=1}^r \sum_{\rho'=1}^r \nu_{j\rho'} [\delta_{\rho\rho'} - (S^{-1})_{\rho'\rho}] = 0. \quad (17)$$

Equation (17) provides a selection rule to the transformation matrix  $S$  for (G) to be satisfied.

At equilibrium, the forward ( $v_{\rho}^{+}$ ) and reverse ( $v_{\rho}^{-}$ ) velocities are equal and the detailed balance condition is given by (Gray 1970)

$$v_{\rho}^{+} = v_{\rho}^{-}$$

or,

$$k_{\rho}^{+} \prod_{j=1}^n (C_j^{\text{eq}})^{\nu_{j\rho}^{+}} = k_{\rho}^{-} \prod_{j=1}^n (C_j^{\text{eq}})^{\nu_{j\rho}^{-}}, \quad (18a)$$

where,  $(v_{\rho})^{\pm}$ ,  $k_{\rho}^{\pm}$  and  $\nu_{j\rho}^{\pm}$  are reaction velocities, kinetic constants and stoichiometric coefficient of  $j$ th species in  $\rho$ th forward and backward reactions respectively in original description. Similarly, using primed notations for transformed descriptions we get the detailed-balance conditions,

$$(k_{\rho}^{+})' \prod_{j=1}^n (C_j^{\text{eq}})^{\nu_{j\rho}^{+}} = (k_{\rho}^{-})' \prod_{j=1}^n (C_j^{\text{eq}})^{\nu_{j\rho}^{-}} \quad (18b)$$

Equation (16) shows that (18a) and (18b) must have identical sets of solutions for  $C_j^{eq}$ . Equations (18a) and (18b) can be written in the form

$$\sum_{j=1}^n v_{j\rho} \ln C_j^{eq} = \ln \frac{k_\rho^+}{k_\rho^-} = \ln K_\rho, \tag{18c}$$

and

$$\sum_{j=1}^n v'_{j\rho} \ln C_j^{eq} = \ln \frac{(k_\rho^+)'}{(k_\rho^-)'} = \ln K'_\rho. \tag{18d}$$

Equation (18), together with (DB), yields

$$\sum_{j=1}^n (v_{j\rho} - v'_{j\rho}) \ln C_j^{eq} = \ln \frac{K_\rho}{K'_\rho} \tag{19}$$

where,  $K_\rho = k_\rho^+ / k_\rho^-$  and  $v_{j\rho} = v_{j\rho}^- - v_{j\rho}^+$  have already been defined in (15) and (9) respectively. Equations (19) and (10), together give,

$$\sum_{j=1}^n \left[ v_{j\rho} - \sum_{\rho'=1}^r v_{j\rho'} (S^{-1})_{\rho'\rho} \right] \ln C_j^{eq} = \ln \frac{K_\rho}{K'_\rho}. \tag{20}$$

Equation (20) provides another set of selection rules comprising of  $r$  number of simultaneous relations which must be satisfied by the transformation matrix  $S$  in order to satisfy (DB). Hence, two mechanisms of any composite reaction can be said to be indistinguishable, if the transformation matrix  $S$  in (1) satisfies simultaneously (3), (17) and (20), i.e. the conditions (E) [and also (O) and ( $\kappa_1$ )], (G) and (DB) respectively. Any transformation matrix satisfying only (E), (O) and ( $\kappa_1$ ), may not represent indistinguishable transformations as can easily be seen from the following illustration,

$$S = \begin{pmatrix} 1 & 0 & 0 & \dots & 0 & -\alpha_1 \\ 0 & 1 & 0 & \dots & 0 & -\alpha_2 \\ 0 & 0 & 1 & \dots & 0 & -\alpha_3 \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ \vdots & \vdots & \vdots & & \vdots & \vdots \\ 0 & 0 & 0 & \dots & 1 & -\alpha_{r-1} \\ 0 & 0 & 0 & \dots & 0 & 1 \end{pmatrix} \tag{21}$$

satisfying (1), (2) and (8) where  $\alpha_1, \dots, \dots, \alpha_{r-1}$  are arbitrary real constants.

The transformation equations for stoichiometric coefficients in two descriptions then can be expressed as

$$v'_{j\rho} = v_{j\rho}, \quad (\rho = 1, 2, \dots, r-1).$$

$$v'_{jr} = v_{jr} + \sum_{\rho=1}^{r-1} \alpha_\rho v_{j\rho}.$$

The selection rule given by (G), i.e. (17) now implies

$$\sum_{\rho=1}^{r-1} \alpha_\rho v_{j\rho} = 0, \quad (j = 1, \dots, n) \tag{22}$$

Equation (22) represents  $n$  number of simultaneous homogeneous linear equations

(since  $j = 1 \dots n$ ) for  $(r-1)$  number of variables ( $\alpha_\rho$ 's). Thus, for  $r < n$ , the only possible solution for (22) is  $\alpha_\rho = 0$ , for  $\rho = 1, 2 \dots (r-1)$ , i.e.  $S = I$ , an identity matrix.

So, for non-cyclic reactions i.e., for  $r < n$ , Koenig's transformation matrix (21) cannot provide two or more mechanisms which will be thermodynamically indistinguishable for arbitrary set of initial conditions. However, for a specified set of initial conditions, i.e. for a given set of equilibrium concentration, Koenig's transformation matrix given by (21) can transform a reaction mechanism thermodynamically and kinetically equivalent provided selection rule given by (17) is satisfied, i.e.,

$$\sum_{j=1}^n \sum_{\rho=1}^r \alpha_\rho v_{j\rho} \ln C_j^{\text{eq}} = 0. \quad (23)$$

It can be easily verified that transformation matrix  $S$  given by (21) will satisfy (DB), i.e. (20), provided

$$K_\rho = K'_\rho \quad (\text{for } \rho = 1 \dots r-1), \quad (24a)$$

and

$$\sum_{j=1}^n \sum_{\rho=1}^{r-1} \alpha_\rho v_{j\rho} \ln C_j^{\text{eq}} = \ln \frac{K_r}{K'_r}. \quad (24b)$$

But (23) implying (G) shows that left side of (24b) vanishes, so that we can write

$$K_r = K'_r. \quad (24c)$$

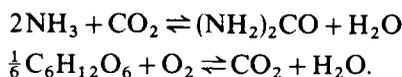
It is to be noted that even these selection rules cannot be satisfied for  $r \leq 2$ , since (23) takes the form

$$\alpha_1 \sum_{j=1}^n v_{j1} \ln C_j^{\text{eq}} = \alpha_1 \ln K_1 = 0, \quad (24d)$$

or

$$\alpha_1 \Delta G_1 = 0.$$

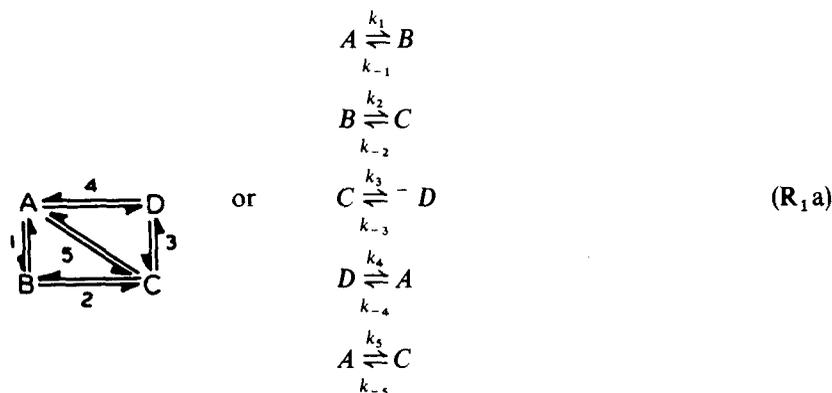
In general, the  $\Delta G_1$ , the free energy change associated with the first elementary reaction, is non-zero and has a negative sign (Keizer 1975). Thus the (24d) implies  $\alpha_1 = 0$ , which indicates that Koenig's transformation matrix fails to describe any other equivalent mechanism for the example cited in their work, i.e. the synthesis of urea in liver,



#### 4. Example of equivalent mechanisms for monomolecular looped reactions in isolated systems

It is worth mentioning that the selection rule (17) imposed by invariance of free energy change may be trivial for looped reactions in isolated systems. To illustrate this point the reaction scheme  $R_1(a)$  and  $(b)$  can be considered. As already mentioned in these schemes,  $A, B, C, D$  might be considered as four structurally interchangeable conformations of a given macromolecule (or monomolecular isomers), original

mechanism is expressed as (assuming isomerization reactions involved are elementary).



The reaction-velocities are given by

$$|V\rangle = K|C\rangle, \tag{25}$$

where

$$K = \begin{pmatrix} k_1 & -k_{-1} & 0 & 0 \\ 0 & k_2 & k_{-2} & 0 \\ 0 & 0 & k_3 & k_{-3} \\ k_{-4} & 0 & 0 & k_4 \\ k_5 & 0 & k_{-5} & 0 \end{pmatrix} \tag{26}$$

$$|V\rangle = (V_1 \ V_2 \ V_3 \ V_4 \ V_5)^t, \tag{27a}$$

and

$$|C\rangle = (A \ B \ C \ D)^t. \tag{27b}$$

$K_{\pm\rho}$ 's in (26) are kinetic constants for  $\rho$ th forward and backward reactions and  $A, B, C, D$  in (27) are the concentrations of reactants.

The affinities  $A_\rho$ 's ( $\rho = 1 \dots 5$ ) are no longer independent since they satisfy the conservation equations

$$A_1 + A_2 + A_3 + A_4 = 0, \tag{28a}$$

$$A_1 + A_2 = A_5. \tag{28b}$$

So, choosing  $A_1, A_2$  and  $A_3$  as independent affinities  $A^1, A^2$  and  $A^3$ , we get,

$$|A^i\rangle = M|A\rangle, \tag{29}$$

where,

$$M = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \end{pmatrix}. \tag{30}$$

Then, the rate of entropy production  $\sigma$  is given by

$$\sigma = \langle A^i | V^i \rangle, \tag{31}$$

where,

$$|V^i\rangle = N|V\rangle, \tag{32}$$

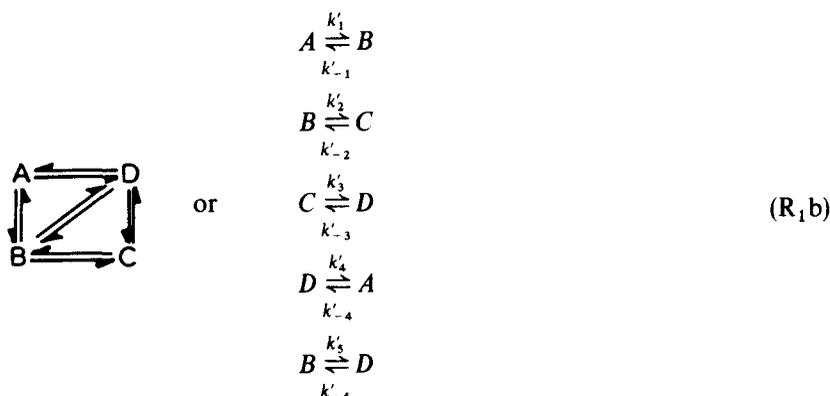
matrix  $N$  being given by

$$N = \begin{pmatrix} 1 & 0 & 0 & -1 & 1 \\ 0 & 1 & 0 & -1 & 1 \\ 0 & 0 & 1 & -1 & 0 \end{pmatrix} \quad (33)$$

In near equilibrium region, the phenomenological velocity-affinity relation takes the form (Katchalsky and Curran 1967)

$$|V'\rangle = L|A'\rangle, \quad (34)$$

$L$  being the symmetric Onsager matrix for mechanism  $R_1(a)$ . If we now consider a linear transformation of reaction rates and affinities as given by (1) and (2), where  $S$  and  $T$  are such transformation matrices that  $V'$  and  $A'_\rho$  represent the variable mechanism  $R_1(b)$ ,



The rate of entropy production given by (31) and the symmetry of  $L$ -matrix in equation (34) will be preserved if transformations (1) and (2) result in linear transformations of independent flows and fluxes as

$$|(V')\rangle = R|V'\rangle, \quad (35a)$$

$$|(A')\rangle = (R^T)^{-1}|A'\rangle. \quad (35b)$$

where  $R$  is the transformation matrix for independent flows. For mechanism  $R_1(b)$ , the reaction velocity vector can be expressed as,

$$|V'\rangle = K'|C\rangle, \quad (36)$$

where

$$K' = \begin{pmatrix} k'_1 & -k'_{-1} & 0 & 0 \\ 0 & k'_2 & -k'_{-2} & 0 \\ 0 & 0 & k'_3 & k'_{-3} \\ -k'_{-4} & 0 & 0 & k'_4 \\ 0 & k'_5 & 0 & k'_{-5} \end{pmatrix} \quad (37)$$

where  $k'_{\pm\rho}$  are kinetic constants of  $\rho$ th forward and backward reactions in mechanism  $R_1(b)$ .

At equilibrium, the detailed-balance conditions satisfied by the equilibrium concentrations  $A_0$ ,  $B_0$ ,  $C_0$  and  $D_0$  are given by

$$\begin{aligned}
 k_1 A_0 = k_{-1} B_0; & \quad k_2 B_0 = k_{-2} C_0; & \quad k_3 C_0 = k_{-3} D_0; \\
 k_4 D_0 = k_{-4} A_0; & \quad k_5 A_0 = k_{-5} C_0. &
 \end{aligned}
 \quad (38)$$

For mechanism  $R_1$  (a), and,

$$\begin{aligned} k'_1 A_0 &= k'_{-1} B_0; & k'_2 B_0 &= k'_{-2} C_0; & k'_3 C_0 &= k'_{-3} D_0; \\ k'_4 D_0 &= k'_{-4} A_0; & k'_5 B_0 &= k'_{-5} D_0 \end{aligned} \quad (39)$$

for mechanism  $R_1$  (b).

Elimination of  $A_0$ ,  $B_0$  etc from (38) and (39) will yield

$$k'_i = (k_i/k_{-i})k'_{-i} \quad (40a)$$

for  $i = 1, 2, 3$  and  $4$ , and,

$$k'_5 = (k_2 k_3/k_{-2} k_{-3})k'_{-5} \quad (40b)$$

Then, from equations (24)–(27), (37) and (40), we can write

$$k' = Uk, \quad (41)$$

where

$$U = \begin{pmatrix} k'_{-1}/k_{-1} & 0 & 0 & 0 & 0 \\ 0 & k'_{-2}/k_{-2} & 0 & 0 & 0 \\ 0 & 0 & k'_{-3}/k_{-3} & 0 & 0 \\ 0 & 0 & 0 & k'_{-4}/k_{-4} & 0 \\ 0 & (k_3/k_{-2} k_{-3})k'_{-5} & k_{-5}/k_{-3} & 0 & 0 \end{pmatrix}. \quad (42)$$

Now from equations (25)–(27), (33), (36) and (41), we get,

$$SK|C\rangle = UK|C\rangle. \quad (43)$$

Since in looped reactions all the concentrations of the reactants cannot evolve independently (43) will be satisfied for arbitrary values of  $C_j$ 's only if,

$$\det|S - U| = 0, \quad (44)$$

which, together with (42) yields

$$\det|S| = \det|U| = 0. \quad (45)$$

The transformation (34) results in a transformation in stoichiometric coefficient matrix as given by (11), *i.e.*

$$v'^t|\mu\rangle = Tv|\mu\rangle, \quad (46)$$

where, the stoichiometric coefficient matrices in two mechanisms  $R_1$  (a) and  $R_1$  (b) are respectively given by

$$v = \begin{pmatrix} -1 & 0 & 0 & +1 & -1 \\ +1 & -1 & 0 & 0 & 0 \\ 0 & +1 & -1 & 0 & +1 \\ 0 & 0 & +1 & -1 & 0 \end{pmatrix} \quad (47)$$

and,

$$v' = \begin{pmatrix} -1 & 0 & 0 & +1 & 0 \\ +1 & -1 & 0 & 0 & -1 \\ 0 & +1 & -1 & 0 & 0 \\ 0 & 0 & +1 & -1 & +1 \end{pmatrix} \quad (48)$$

so that  $v_{j\rho}$  and  $v'_{j\rho}$  represent stoichiometric coefficient of  $j$ th species in  $\rho$ th reaction in mechanism  $R_1(a)$ ,  $R_1(b)$  and chemical potential vector  $|\mu\rangle$  being given by

$$|\mu\rangle = \begin{pmatrix} \mu_A \\ \mu_B \\ \mu_C \\ \mu_D \end{pmatrix} \quad (49)$$

in either description.

Since all the concentrations  $A$ ,  $B$ ,  $C$  and  $D$  are not independent, all  $\mu_j$ 's no longer remain independent. Hence, (46) will be satisfied if,

$$\det |T'(v)^t - v^t| = 0. \quad (50)$$

Transformed affinities  $A'_\rho$ 's also satisfy conservation equations of the form

$$A'_1 + A'_2 + A'_3 + A'_4 = 0, \quad (51a)$$

and

$$A'_2 + A'_3 = A'_5. \quad (51b)$$

Choosing  $A_1$ ,  $A_2$  and  $A_3$  as independent affinities we can write,

$$|(A^t)\rangle = M'|A^t\rangle, \quad (52)$$

where  $M'$  is of identical form as  $M$  given by (30). Similarly, independent velocities  $V^t$  will now be given by

$$|(V^t)\rangle = N'|V^t\rangle \quad (53)$$

where,

$$N' = \begin{pmatrix} +1 & 0 & 0 & -1 & 0 \\ 0 & +1 & 0 & -1 & +1 \\ 0 & 0 & +1 & -1 & +1 \end{pmatrix} \quad (54)$$

So that rate of entropy production is given by

$$\sigma = \langle A^t | V^t \rangle \quad (55)$$

With the help of (31), (35) and (55),  $\sigma$  can be easily shown to be invariant.

Equations (2), (29), (35b) and (52) altogether yield

$$MT|A\rangle = (R')^{-1}M|A\rangle, \quad (56)$$

which will be satisfied if,

$$\det |MT - (R')^{-1}M| = 0. \quad (57)$$

Similarly, (1), (32) (35a) and (52) give

$$RN|V\rangle = N'S|V\rangle, \quad (58)$$

which will be satisfied provided

$$\det |RN - N'S| = 0. \quad (59)$$

Thus, the elements of  $(5 \times 5)$  matrices  $S$  or  $T$ , and  $(3 \times 3)$  matrix  $R$  should satisfy only four simultaneous homogeneous equations (45), (49), (57) and (59) which can always give non-trivial solutions for  $S_{jK}$  (or  $T_{iK}$ ) and  $R_{iK}$ 's.

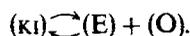
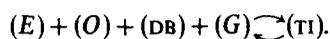
Apparently it seems that  $R_1(a)$  and  $R_1(b)$  cannot be kinetically equivalent since time derivative of any particular species, for example,  $\dot{A}$  in  $R_1(a)$  depends explicitly on  $C$ , while in  $R_1(b)$ , it does not. But, as long as, we are considering closed systems, the changes in concentrations are not absolutely independent and an increase in  $C$  causing changes in  $A, B$  and  $D$ , will cause equal changes in  $\dot{A}$  in both  $R_1(a)$  and  $R_1(b)$ , since  $|\dot{C}\rangle$  remains invariant and the logical relation ( $L_2$ ) shows that

$$\dot{A} |_{R_1(a)} = \dot{A} |_{R_1(b)}$$

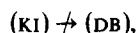
for any particular set of values for  $(A, B, C, D)$  at any given instant.

## 5. Discussion

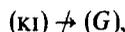
Present report emphasizes that for a given set of thermodynamic and kinetic parameters multiple indistinguishable mechanisms can exist, though the conditions of invariance of net change in free-energy and detailed-balance conditions restrict the choice of such 'equivalent' mechanisms. It is interesting to note that if two mechanisms are thermodynamically indistinguishable they will automatically be kinetically indistinguishable. However, that the reverse may not be true, is apparent from the following logical relations:



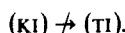
But



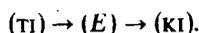
and,



Hence,



and



For cyclic reactions the role played by  $(G)$  has to be modified. In unimolecular cyclic reaction, for example, the free energy changes are zero in the original and transformed descriptions. Thus, no additional selection rule can be obtained from the invariance of net free energy change. The other logical statements are still applicable.

One of the intriguing results of the present analysis is that the existence of equivalent transformations is more restrictive for non-cyclic reactions, compared to cyclic reactions, for which the net free energy change is always zero. Hence, the probability of existence of multiple indistinguishable mechanisms is higher for cyclic relative to non-cyclic reactions. It should be emphasized here that biochemical pathways often involve closed reaction cycles, for example, any autocatalytic reaction must involve closed loop (Eigen 1971). Hence, the present observation appears significant considering that cyclic reaction besides facilitating the self-organization process, might enhance the fidelity of the system with respect to environmental perturbation.

This work was supported by CSIR, India.

## References

- Boyd R K 1977 *Chem. Rev.* 77 93  
 Coleman B D and Truesdell C 1960 *J. Chem. Phys.* 33 28

Eigen M 1971 *Naturwissenschaften*. **58** 465

Gray B F 1970 *Trans. Faraday Soc.* **66** 363

Katchalsky A and Curran P F 1967 in *Non-equilibrium thermodynamics in biophysics*, (Harvard: University Press)

Keizer J 1975 *J. Theor. Biol.* **49** 323

Koenig F O, Horne F H and Mchilner D M 1961 *J. Am. Chem. Soc.* **83** 1029

Margenau H and Murphy G M 1956 in *The mathematics of physics and chemistry* (Van Nostrand Reinhold Company)

Meixner J 1942 *Ann. Phys.* **41** 409 (see Prigogine 1967)

Meixner J 1943 *Ann. Phys.* **43** 244 (see Prigogine 1967)

Nicolis G and Prigogine I 1977 in *Self-organization in non-equilibrium systems*, (New York: Wiley Interscience)

Onsager L 1931 *Phys. Rev.* **37** 405 **38** 2265

Prigogine I 1967 in *Introduction to thermodynamics of irreversible processes* (New York: Interscience Publishers)

Shear D 1967 *J. Theor. Biol.* **16** 212

Shear D 1968 *J. Chem. Phys.* **48** 4144