Does an irreversible chemical cycle support equilibrium?

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Abstract

The impossibility of attaining equilibrium for cyclic chemical reaction networks with irreversible steps is apparently due to a divergent entropy production rate. A deeper reason seems to be the violation of the detailed balance condition. In this work, we discuss how the standard theoretical framework can be adapted to include irreversible cycles, avoiding the divergence. With properly redefined force terms, such systems are also seen to reach and sustain equilibria that are characterized by the vanishing of the entropy production rate, though detailed balance is not maintained. Equivalence of the present formulation with Onsager's original prescription is established for both reversible and irreversible cycles, with a few adjustments in the latter case. Further justification of the attainment of true equilibrium is provided with the help of the minimum entropy production principle. All the results are generalized for an irreversible cycle comprising of \( N \) number of species.

1 Introduction

Chemical reactions play a very important and interesting part in the theory and applications of non-equilibrium thermodynamics since inception \cite{1, 2, 3, 4, 5}. The irreversibility of processes in real systems \cite{6, 7, 8, 9} all around us and inside our bodies are almost always connected to chemical reactions \cite{10}. Thus, as was the case with equilibrium thermodynamics, major attention is paid towards chemical systems throughout the development of this discipline \cite{11, 12, 13, 14, 15}. The key concept of entropy production rate (EPR) \cite{16, 17, 18, 19, 20, 21, 22} to describe irreversible processes was connected with the reaction affinity since the very early days of irreversible thermodynamics by de Donder \cite{23}. In his seminal paper, Onsager \cite{1} introduced the reciprocal relations by considering a reversible triangular reaction network. He noted, however, that 'detailed balance' acts as an additional restriction to describe
chemical equilibrium, apart from the second law of thermodynamics. Since then, this ‘additional restriction’ of detailed balance became a rule of thumb, requiring each reaction to contain elementary steps in forward and reverse directions. Both these steps need to be considered in the formulation of EPR [24, 25, 26, 27, 28].

The above theoretical scheme fails to account for any equilibria in irreversible chemical cycles because setting of ‘backward’ rate constants equal to zero leads to divergence of the EPR. This is certainly unphysical. Unfortunately however, such an outcome has been used as an argument to eliminate the possibility of equilibrium being sustained by reaction cycles with irreversible steps, although the corresponding kinetic equations give fully consistent results. Recently, a few studies have addressed the issue. One bypass route is to coarse grain the system evolution at regular time intervals so that effective transition rates can be defined [29]. Another proposition is to perform an experiment over such a time span that the backward step, although present, has no chance to occur [30]. In this latter work [30], the authors rigorously derived a formula for EPR for irreversible transitions at the microscopic level, showing logarithmic dependence on the time span chosen and argued that the divergence of EPR for such processes is a theoretical artifact. This technique, however, is based on how accurately the setting of the finite time span approximates a real irreversible process, so as to avoid the divergence of EPR. Understandably, the backward rate constant is considered to be very small, but not exactly zero.

Having stated the background, here we study the EPR in cyclic chemical reaction networks with exactly irreversible steps, i.e., we set all the backward rate constants equal to zero. We show that the standard formulation of EPR in terms of the flux-force relations of individual reactions [4, 12, 13] can be applied to these systems as well, but only after proper modifications. Starting with the simplest example of a triangular network, the EPR is shown to vanish at the steady state of the irreversible cycle, justifying that the system reaches a true thermodynamic equilibrium. We further import the minimum entropy production principle [31, 32] that unequivocally ascertains the nature of a steady state. Finally, we generalize all the findings to an irreversible cycle containing \( N \) number of species to witness similar features.
2 Problem with irreversible cycles

We start the discussion with a reversible cycle consisting of three species, A, B, C as shown in Fig. 1. The time-dependent concentrations of species A, B, C, are denoted by \( a(t), b(t), c(t) \), respectively. The rate equations are given as

\[
\dot{a} = -(k_1 + k_{-3})a(t) + k_{-1}b(t) + k_3c(t),
\]
\[
\dot{b} = k_1a(t) - (k_{-1} + k_2)b(t) + k_{-2}c(t),
\]
\[
\dot{c} = k_{-3}a(t) + k_2b(t) - (k_{-2} + k_3)c(t),
\]

with \( \dot{a} + \dot{b} + \dot{c} = 0 \).

The EPR \( \sigma(t) \) of the network is expressed in terms of fluxes \( J_i \) and the corresponding forces \( X_i \) as \([4]\)

\[
\sigma(t) = \frac{1}{T} \sum_{i=1}^{3} J_i(t)X_i(t).
\]

The fluxes are defined as \([4, 24, 26]\):

\[
J_1(t) = k_{-1}b(t) - k_1a(t),
\]
\[
J_2(t) = k_{-2}c(t) - k_2b(t),
\]
\[
J_3(t) = k_{-3}a(t) - k_3c(t).
\]
The corresponding forces are

\[ X_1(t) = \mu_B - \mu_A = T \ln \frac{k_{-1}b(t)}{k_1a(t)}, \quad (8) \]

\[ X_2(t) = \mu_C - \mu_B = T \ln \frac{k_{-2}c(t)}{k_2b(t)}, \quad (9) \]

\[ X_3(t) = \mu_A - \mu_C = T \ln \frac{k_{-3}a(t)}{k_3c(t)}, \quad (10) \]

Here and throughout the paper, we have set the Boltzmann constant \( k_B = 1 \).

The condition of detailed balance \([3, 4]\) requires the fluxes of each individual reaction to vanish at steady state, i.e.,

\[ J_1^* = J_2^* = J_3^* = 0. \quad (11) \]

When this condition is satisfied, the reaction system reaches equilibrium.

Note that, if the steps are irreversible, we must set \( k_{-1} = k_{-2} = k_{-3} = 0 \). Then, the forces given by right sides in Eqs (8-10), and hence the EPR, diverge. This necessitates a different approach where, obviously, the forces need to be redefined to avoid any disaster. So, the basic problem is to have a divergence-free expression for the EPR in an irreversible cycle.

However, before proceeding further, we make some comments on the prevailing notion that equilibrium can not be maintained by an irreversible cycle due to (i) divergent nature of EPR and (ii) violation of the detailed balance condition. Indeed, Onsager himself considered detailed balance as an additional assumption. He wrote \([1]\): “..., however, the chemists are accustomed to impose a very interesting additional restriction, namely: when the equilibrium is reached each individual reaction must balance itself.” This point is also discussed at length by Denbigh, clearly stating that the above system can reach equilibrium following the laws of thermodynamics without requiring the condition of detailed balance \([3]\). Indeed, if we investigate the role of the backward step in each individual reaction, we see that it provides a pathway that produces the opposite effect of that due to the forward step on the concentrations of the species involved. Now, the beauty of the cyclic network is that, even with irreversible steps, there exists a ‘feedback’ for each species, although not in the sense of detailed balance. Thus, all the species in the irreversible cycle have finite, non-zero concentrations and well-defined chemical potentials during the time evolution as well as in the long-time limit.
In our opinion, this provides enough justification to search for a consistent non-equilibrium thermodynamic description of such systems. In this context, we may also mention the work of Xiao et al. \cite{33} on the entropy production in a Brusselator model with irreversible steps where the state changes in the population space become reversible.

3 The remedy

The kinetic scheme of the ABC irreversible cycle is shown in Fig. 2. At first, we determine the equilibrium concentrations of the species. They are

![Figure 2: Schematic diagram of the ABC cyclic irreversible reaction network](image)

obtained from Eqs (1)-(3) by setting $\dot{a} = \dot{b} = \dot{c} = 0$ with $k_{-1} = k_{-2} = k_{-3} = 0$, as

$$a^e = k_2 k_3 / K, \quad (12)$$
$$b^e = k_1 k_3 / K, \quad (13)$$
$$c^e = k_1 k_2 / K, \quad (14)$$

with $K = k_1 k_2 + k_2 k_3 + k_1 k_3$. By equilibrium, we mean the true thermodynamic equilibrium only with

$$\mu_A^e = \mu_B^e = \mu_C^e. \quad (15)$$
Then, using the above equilibrium concentrations and Eq. (15), we obtain the expressions of the forces in the irreversible cycle as

\[ X_1 = (\mu_B - \mu_A) = \Delta \mu_{BA}^q + T \ln \frac{b}{a} = -T \ln \frac{b^e}{a^e} + T \ln \frac{b}{a} = T \ln \frac{k_2 b}{k_1 a}. \] (16)

Similarly,

\[ X_2 = (\mu_C - \mu_B) = T \ln \frac{k_3 c}{k_2 b}, \] (17)

\[ X_3 = (\mu_A - \mu_C) = T \ln \frac{k_1 a}{k_3 c}. \] (18)

The above equations are naturally adjusted to avoid the divergence experienced in case of their counterparts in the reversible cycle, given in Eqs (8)-(10). In the derivation of Eqs (16)-(18), the major modification is in the definition of equilibrium constants appearing in the standard-state chemical potential differences. Conventionally, the equilibrium constant is taken equal to the ratio of forward and reverse rate constants. When the reactions are irreversible, there are no reverse rate constants and hence, one needs to generalize the concept. In Eqs (16)-(18), the ratio of the concentrations of the species, constant at equilibrium, plays the role of an equilibrium constant. In this context, we mention that the equality of equilibrium constant to the ratio of forward and backward rate constants is often misunderstood as a consequence of thermodynamics. As stated by Denbigh [3]: “The point made by Onsager is that this equality can be proved from the second law only in the special case where there is a single independent reaction taking place in the system.” Thus, for multiple reactions, the conventional definition of equilibrium constant requires detailed balance to hold at equilibrium. This stands as an extra principle not contained in thermodynamics. Hence, in an irreversible cycle where detailed balance is violated, it is not surprising that the equilibrium constant should be modified accordingly. Now, from Eqs (5)-(7), the fluxes in the irreversible cycle become

\[ J_1(t) = -k_1 a(t), \] (19)

\[ J_2(t) = -k_2 b(t), \] (20)

\[ J_3(t) = -k_3 c(t). \] (21)

Then, from Eq. (4), we obtain the EPR of the irreversible cycle as

\[ \sigma(t) = k_1 a(t) \ln \frac{k_1 a(t)}{k_2 b(t)} + k_2 b(t) \ln \frac{k_2 b(t)}{k_3 c(t)} + k_3 c(t) \ln \frac{k_3 c(t)}{k_1 a(t)}, \] (22)
which obviously remains finite. Still, the acid test for any expression of EPR is its positivity. In the next paragraph, we will show that \( \sigma(t) \), as given in Eq.(22), is always positive and becomes zero at equilibrium.

We define
\[
k_1 a(t) + k_2 b(t) + k_3 c(t) = N(t) > 0.\tag{23}
\]

Then dividing Eq.(22) by \( N(t) \), we get
\[
\frac{1}{N(t)} \sigma(t) = x \ln \frac{x}{y} + y \ln \frac{y}{z} + z \ln \frac{z}{x}, \tag{24}
\]
where
\[
x = \frac{k_1 a(t)}{N(t)},
\]
\[
y = \frac{k_2 b(t)}{N(t)},
\]
\[
z = \frac{k_3 c(t)}{N(t)},
\]
with
\[
x + y + z = 1,
\]
from Eq.(23). Now, we define two normalized probability distributions, \( P(= \{ p_i \}, i = 1, 2, 3) \) and \( Q(= \{ q_i \}, i = 1, 2, 3) \), with
\[
p_1 = x, p_2 = y, p_3 = z, \tag{25}
\]
and
\[
q_1 = y, q_2 = z, q_3 = x. \tag{26}
\]
Then we can rewrite Eq.(24) in a more revealing form of the Kullback-Leibler distance of two normalized distributions \[34\] and using the positivity of the latter \[35\], the proof is complete by virtue of the expression
\[
\sigma(t) = N(t) \sum_{i=1}^{3} p_i \ln \frac{p_i}{q_i} \geq 0. \tag{27}
\]
The equality in Eq.(27) will be valid for \( p_i = q_i, \forall i. \) This implies \( x = y = z \), which in turn leads to \( k_1 a = k_2 b = k_3 c. \) It is easy to see from Eqs (1)-(3) with \( k_{-1} = k_{-2} = k_{-3} = 0 \) that this condition will be satisfied when \( \dot{a} = \dot{b} = \dot{c} = 0. \) So EPR becomes zero as the concentrations of all the species become fixed. Then we can say that the irreversible cycle reaches equilibrium, characterized by the vanishing of EPR, as desired. Hence, the expression of
EPR for the irreversible cycle in Eq. (22) satisfies all the basic requirements to be thermodynamically consistent and physically meaningful.

For further support of the result that such an irreversible cycle reaches equilibrium as obtained above, we explore the minimum entropy production principle (MEPP) [5, 7]. To this end, we temporarily call the equilibrium to be a steady state. MEPP tells that EPR has its minimum at a steady state that lies close enough to equilibrium with approximately linear relation between fluxes and forces [7]. However, recently it has been rigorously shown by Ross and coauthors [31, 32], that this principle is true if and only if the steady state is the state of thermodynamic equilibrium. Here we investigate this fact by using the expression EPR of the irreversible cycle. From Eq. (22), we get

\[
\left( \frac{\partial \sigma'}{\partial a} \right) = k_1 \ln \frac{k_1 a}{k_2 b} + \frac{k_1 a - k_3 c}{a}.
\]

At steady state, \( \dot{a} = \dot{b} = \dot{c} = 0 \) and from Eqs (1)-(3) one gets \( k_1 a_s = k_2 b_s = k_3 c_s \) for the irreversible cycle. Then, of course, we have

\[
\left( \frac{\partial \sigma}{\partial a} \right)_{s} = 0.
\] (28)

Following a similar procedure, one easily obtains

\[
\left( \frac{\partial \sigma}{\partial b} \right)_{s} = 0 = \left( \frac{\partial \sigma}{\partial c} \right)_{s}.
\] (29)

However, according to Eq. (22), \( \sigma(t) \geq 0 \). So, the extremum at the steady state is the minimum and therefore, the steady state reached by the irreversible cycle is indeed the state of equilibrium.

4 Equivalence of the approach with Onsager’s original formulation

There is an alternative way of defining the forces and the fluxes for a chemical reaction system than those given in Eqs (5)-(10). Actually, this formalism was originally considered by Onsager [1] to construct the EPR of a reversible triangular reaction network [3]. In this method, the flux is defined as the rate of change of concentration of a species and the corresponding force is
the deviation of the chemical potential of that species from its equilibrium value. The fluxes are then written as

\[ J_a = \dot{a}, \quad J_b = \dot{b}, \quad J_c = \dot{c}, \]  

with \( \dot{a} + \dot{b} + \dot{c} = 0 \). The corresponding forces are

\[ X_a = \mu_{eA} - \mu_A(t) = T \ln \frac{a^e}{a(t)}, \]
\[ X_b = \mu_{eB} - \mu_B(t) = T \ln \frac{b^e}{b(t)}, \]
\[ X_c = \mu_{eC} - \mu_C(t) = T \ln \frac{c^e}{c(t)}. \]

It is evident that defined this way, they are equally eligible to construct the expression of EPR in reversible as well as in irreversible chemical cycles. The EPR then becomes

\[ \sigma'(t) = \frac{1}{T} \sum_{i=a,b,c} J_i(t) X_i(t). \]  

As already mentioned, the concentrations of the species remain finite throughout the evolution of the reaction system with irreversible steps. Thus, a distinct advantage of Eq.(36) is that the EPR does not diverge in the irreversible cycle. At equilibrium, the forces in Eqs (33)-(35) (and the corresponding fluxes) vanish and hence, the EPR becomes zero.

For the reversible cycle in Fig.1, we can show the equality of Eq.(1) and Eq.(36) straightforwardly. Starting from Eq.(1) and using Eqs (30)-(35) along with Eqs (1)-(2) and \( \dot{c} = -(\dot{a} + \dot{b}) \), we obtain

\[ T \sigma'(t) = \dot{a}(X_a - X_c) + \dot{b}(X_b - X_c) \]
\[ = \dot{a}(\mu_C - \mu_A) + \dot{b}(\mu_C - \mu_B) \]
\[ = (k_{-1}b(t) - k_1a(t))(\mu_B - \mu_A) + (k_{-2}c(t) - k_2b(t))(\mu_C - \mu_B) \]
\[ + (k_{-3}a(t) - k_3c(t))(\mu_A - \mu_C) \]
\[ = \sum_{i=1}^{3} J_i(t) X_i(t) = T \sigma(t). \]  

(37)
The only ‘condition’ used in the above derivation is that of thermodynamic equilibrium, \( i.e., \) Eq.(15). To be also valid for the irreversible cycle in Fig.2, the fluxes \( J_i \) and the forces \( X_i \) in Eq.(37) should be defined as given in Eqs (16)-(21). This equivalence further strengthens the approach to formulate the EPR in an irreversible chemical cycle where both the forms can be used interchangeably. To convince ourselves further, in the next section, we will generalize the problem to an irreversible N-cycle by using fluxes and forces of the forms of Eqs (30)-(35).

5 EPR in an irreversible N-cycle

In this section, we derive an expression of EPR in an irreversible cycle containing \( N \) number of species, shown in Fig.3 as a generalization of Eq.(36). We denote the species by \( A_i \) and their concentrations by \( c_i(t) \), \( i = 1, 2, \cdots, N \).

![Figure 3: Schematic diagram of a cyclic irreversible reaction network containing \( N \) number of species](image)

The rate equations are given as

\[
\dot{c}_i = -k_i c_i(t) + k_{i-1} c_{i-1}(t), \quad i = 1, 2, \cdots, N
\]  

(38)

with the boundary conditions \( k_0 = k_N \), \( c_0(t) = c_N(t) \) and the constraint

\[
\sum_{i=1}^{N} \dot{c}_i = 0.
\]  

(39)
The fluxes are defined as
\[ J_i = \dot{c}_i, \ i = 1, 2, \cdots, N \] (40)
and the corresponding forces are
\[ X_i = (\mu_i^e - \mu_i(t)), \ i = 1, 2, \cdots, N. \] (41)

Then, using Eq.(39) and the equality of chemical potentials of all the species at equilibrium, the EPR in the irreversible N-cycle can be written as
\[ \sigma'_N(t) = \frac{1}{T} \sum_{i=1}^{N} J_i X_i = \frac{1}{T} \sum_{i=1}^{N-1} \dot{c}_i (\mu_N - \mu_i). \] (42)

Now at equilibrium with \( \dot{c}_i = 0, \ \forall i \), we have
\[ \frac{c_i^e}{c_i} = k_i \frac{c_i}{k_N}, \ i = 1, 2, \cdots, N-1. \] (43)

Using Eq.(43), one can write
\[ \mu_N - \mu_i = \Delta \mu_{Ni}^0 + T \ln \frac{c_N}{c_i} = -T \ln \frac{c_i^e}{c_i} + T \ln \frac{c_N}{c_i} = T \ln \frac{k_N c_N}{k_i c_i}. \] (44)

Then from Eqs (38), (40) and (44), we can write Eq.(42) as
\[ \sigma'_N(t) = (k_N c_N(t) - k_1 c_1(t)) \ln \frac{k_N c_N(t)}{k_1 c_1(t)} + (k_1 c_1(t) - k_2 c_2(t)) \ln \frac{k_N c_N(t)}{k_2 c_2(t)} + \cdots \]
\[ + (k_{N-3} c_{N-3}(t) - k_{N-2} c_{N-2}(t)) \ln \frac{k_N c_N(t)}{k_{N-2} c_{N-2}(t)} + (k_{N-2} c_{N-2}(t) - k_{N-1} c_{N-1}(t)) \ln \frac{k_N c_N(t)}{k_{N-1} c_{N-1}(t)} \]
\[ = k_1 c_1(t) \ln \frac{k_1 c_1(t)}{k_2 c_2(t)} + k_2 c_2(t) \ln \frac{k_2 c_2(t)}{k_3 c_3(t)} + \cdots + k_{N-1} c_{N-1}(t) \ln \frac{k_{N-1} c_{N-1}(t)}{k_N c_N(t)}. \] (45)

Eq.(45) is obviously the generalized form of Eq.(22). Therefore, one can justify that \( \sigma'_N(t) \geq 0 \), following the similar procedure as outlined earlier. It is also evident that \( \sigma'_N(t) = 0 \) corresponds to the state of equilibrium, with \( \dot{c}_i = 0, \ \forall i \).

Now we test whether the MEPP holds for the irreversible N-cycle. From Eq.(42), we can write
\[ \left( \frac{\partial \sigma'_N}{\partial c_n} \right) = \frac{\partial}{\partial c_n} \left( \dot{c}_n \ln \frac{c_n^e}{c_n} + \dot{c}_{n+1} \ln \frac{c_{n+1}^e}{c_{n+1}} \right) \]
\[ = -k_n \ln \frac{c_n}{c_n} - \dot{c}_n + k_n \ln \frac{c_{n+1}}{c_{n+1}}. \quad (46) \]

Then, at equilibrium, we get
\[
\left( \frac{\partial \sigma'_N}{\partial c_n} \right)_e = 0, \quad (47)
\]
as required by the MEPP.

Before concluding, we clarify that a linear irreversible network cannot be treated using either formalism [Eq.(1) and Eq.(36)]. The reason is that, in the long-time limit, the amounts of all the species, except the terminal one, become zero, resulting in undefined chemical potentials.

6 Conclusion

In this work, we have discussed on the feasibility of an irreversible chemical cycle reaching equilibrium. The kinetic equations assert that the concentrations, and hence the chemical potentials, of all the constituents remain well-defined throughout the system evolution. This justifies a non-equilibrium thermodynamic study of such systems, where, in principle, nothing should diverge. The standard scheme fails in this respect, revealing a catastrophic behavior. We have established that, with appropriate redefinitions of forces, the divergence of EPR can be avoided. Using the formulation presented here, it is shown that any cyclic irreversible chemical network reaches a state of true thermodynamic equilibrium, indicated by zero EPR, though detailed balance is not satisfied. The equivalence of this approach with Onsager’s original formulation of EPR confirms its authenticity. For the reversible cycle, the proof is straightforward whereas, for the irreversible one, a modified description of force is required. The positivity of the expression of EPR in the irreversible cycle is established to show that the outcomes are thermodynamically consistent. Analysis of the MEPP further acknowledges that the EPR in the irreversible network has its minimum at the equilibrium sought. Therefore, we affirm that any irreversible chemical cycle does indeed reach and sustain equilibrium.
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