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Review

Chemical and biochemical thermodynamics: Is it time for a reunification?

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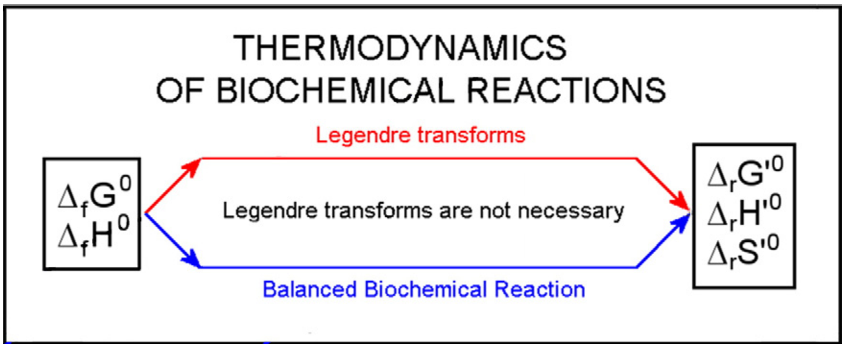
HIGHLIGHTS

- An overview on thermodynamics of biochemical and chemical reactions is proposed.
- A method which reunifies the “two separate worlds” of conventional thermodynamics and transformed thermodynamics is illustrated.
- The use of balanced biochemical reaction to avoid the Legendre transforms is described.

GRAPHICAL ABSTRACT



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ABSTRACT

The thermodynamics of chemical reactions in which all species are explicitly considered with atoms and charge balanced is compared with the transformed thermodynamics generally used to treat biochemical reactions where atoms and charges are not balanced. The transformed thermodynamic quantities suggested by Alberty are obtained by execution of Legendre transformation of the usual thermodynamic potentials. The present analysis demonstrates that the transformed values for $\Delta_r G'^0$ and $\Delta_r H'^0$can be obtained directly without performing Legendre transformations by simply writing the chemical reactions with all the pseudoisomers explicitly included and charges balanced. The appropriate procedures for computing the stoichiometric coefficients for the pseudoisomers are fully explained by means of an example calculation for the biochemical ATP hydrolysis reaction. It is concluded that the analysis has reunited the “two separate worlds” of conventional thermodynamics and transformed thermodynamics.

In addition, it is also shown that the value of the conditional Gibbs energy of reaction, $\Delta_r G'$, for a biochemical reaction is the same of the value of $\Delta_r G$ for any chemical reaction involving pseudoisomers of the biochemical reagents.

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Contents

1. Introduction

The IUPAC-IUBMB Joint Commission on Biochemical Nomenclature (JCBN) [1–3] states: “chemical equations are written in terms of specific ionic and elemental species and balance elements and charge, whereas biochemical equations are written in terms of reactants that often consist of species in equilibrium with each other and do not balance elements that are assumed fixed, such as hydrogen at constant pH. Both kinds of reaction equations are needed in biochemistry”.

Homeostasis has the effect of keeping the conditions at which biochemical reactions occur within a narrow range. As a consequence in a biochemical reaction the concentration of reactants, including H^+ and Mg^{2+} ions, remains essentially constant. The same Commission [2] also asserts: “…when pH and pMg are specified, a whole new set of transformed thermodynamic properties come into play. These properties are different from the usual Gibbs energy G, enthalpy H, and entropy S and they are referred to as the transformed Gibbs energy G', transformed enthalpy H', transformed entropy S'.” As a consequence, two categories of thermodynamics based on different concepts and different formalisms have been established: i) chemical thermodynamics that employs conventional thermodynamic potentials to deal with chemical reactions; ii) biochemical thermodynamics that employs Legendre-transformed thermodynamic potentials to deal with biochemical reactions.

However, it has been recently demonstrated [4] that, by balancing the biochemical reactions, it is possible to treat the biochemical reactions as chemical reactions thereby obviating the need for complicated, transformed thermodynamic potentials. This approach permits $\Delta_r G'^0$, $\Delta_r H'^0$, and $\Delta_r S'^0$ to be obtained directly from $\Delta_f G^0$, $\Delta_f H^0$, and $\Delta_f S^0$ at various T, pH, pMg, and ionic strength I. The method has general applicability. This article presents the general theory underlying the method and provides illustrative examples of its application. The development and use of these methods allow the two worlds of chemical and biochemical thermodynamics, which so far have been treated separately, to be reunified within the same thermodynamic framework.

2. Biochemical reactions and conditional equilibrium constants

Biochemical reactions are expressed in terms of reagents where each of them represents the sum of several chemical species named pseudoisomers. A typical example is the hydrolysis reaction of adenosine triphosphate (ATP), with formation of adenosine diphosphate (ADP) and phosphate (Pi),

$$\mathrm{ATP} + \mathrm{H_2O} = \mathrm{ADP} + \mathrm{Pi} \tag{1}$$

where ATP, ADP and Pi represent all pseudoisomers constituting the biochemical reagent. For example, in a 1 M solution of ATP at pH = 7 and pMg = 2, the chemical species of ATP present at significant concentration (>10^{-3} M) are ATP^{4-}, $HATP^{3-}$, $MgATP^{2-}$, $MgHATP^-$ and Mg_2ATP. Following Alberty [5,6], the species formed by a given biochemical reagent constitute a pseudoisomer group.

The equilibrium constant K' of biochemical reaction (Eq. (1)), usually named apparent equilibrium constant or conditional equilibrium constant, is given by the equation:

$$K' = \frac{([\mathrm{ADP}]/c^0)([\mathrm{Pi}]/c^0)}{[\mathrm{ATP}]/c^0} = \frac{[\mathrm{ADP}][\mathrm{Pi}]}{[\mathrm{ATP}]c^0} \tag{2}$$

where [ADP], [Pi] and [ATP] are the total concentrations of all pseudoisomers of ADP, Pi, and ATP respectively with $c^0 = 1$ M. This apparent (or conditional) equilibrium constant is function of T, p, pH, pMg and ionic strength I.

The active species in enzyme binding and the energy-producing form in active transport and muscular contraction is $MgATP^{2-}$ [7–12]. The actual chemical reaction is therefore:

$$\mathrm{MgATP^{2-}} + \mathrm{H_2O} = \mathrm{MgADP^-} + \mathrm{H_2PO_4^-} \tag{3}$$

with an equilibrium constant given by

$$K_c = \frac{([\mathrm{MgADP^-}]/c^0)([\mathrm{H_2PO_4^-}]/c^0)}{[\mathrm{MgATP^{2-}}]/c^0} = \frac{[\mathrm{MgADP^-}][\mathrm{H_2PO_4^-}]}{[\mathrm{MgATP^{2-}}]c^0} \tag{4}$$

which is function of T, p and I.

The equilibria among the species of a pseudoisomer group are assumed to be much faster than that of the biochemical reaction. Therefore the chemical species constituting a pseudoisomer group are always at equilibrium throughout the course of the biochemical reaction.

Let us choose the biochemical reaction (Eq. (1)) of hydrolysis of ATP as paradigm of a biochemical reaction. The adducts formed by ATP^{4-}, ADP^{3-} and HPO_4^{2-} with H^+ and Mg^{2+} ions are shown in Fig. 1. The pseudoisomers of the biochemical reagents of reaction (Eq. (1)) are here reported:

ATP: ATP^{4-}, $HATP^{3-}$, H_2ATP^{2-}, $MgATP^{2-}$, $MgHATP^-$ and Mg_2ATP (6 pseudoisomers);

ADP: ADP^{3-}, $HADP^{2-}$, H_2ADP^-, $MgADP^-$ and MgHADP (5 pseudoisomers);

Pi: HPO_4^{2-}, $H_2PO_4^-$ and $MgHPO_4$ (3 pseudoisomers).

As shown in Fig. 1, it is assumed that the pseudoisomers of each biochemical reagent are always in equilibrium as reaction (3) proceeds.

Eqs. (2) and (4) imply that the equilibria in question are for a “dilute-ideal” solution, in which the activity coefficients of all reactants and products are independent of concentration over the concentration range under consideration and that the activity of the solvent is near unity. Although these conditions cannot be expected to hold rigorously in any actual system, in practice K' and K_c are frequently found to be constant within the experimental error of the measurements in biochemical systems. It is also to be noted that K' and K_c must be dimensionless. For concentration equilibrium constants, this can be achieved by using “relative concentrations”, that is, concentration divided by a standard concentration equal to one. In this work all concentrations are implicitly considered relative concentrations and the equilibrium