

THERMAL DIFFUSION WITH CHEMICAL REACTION: A CARRIER SYSTEM

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The heat of transport of oxygen across a membrane mediated by hemoglobin (Hb) as a carrier is investigated by the method of irreversible thermodynamics. It is assumed that oxygen combines with hemoglobin molecules to form oxyhemoglobin according to the reaction $n\text{O}_2 + \text{Hb} = \text{HbO}_{2n}$. The oxyhemoglobin molecule HbO_{2n} then migrates to a new position and is reconverted to Hb by releasing oxygen.

It is shown that the heat of transport of oxygen consists of two contributions; one due to the reaction and the other from thermal diffusion of individual species present. Total oxygen flux across the membrane is also calculated in terms of temperature and the chemical potential difference of oxygen across the membrane. The use of the heat of transport as a measure of the efficiency of the heat pump for the carrier-mediated transport process is investigated.

In this report we discuss the calculation of the heat of transport of oxygen across membranes mediated by hemoglobin as a carrier. The purpose of this paper is two-fold. In the first place we wish to show how the subject of thermal diffusion in the presence of chemical reactions may be extended to apply to membrane transport processes. The heat of transport is the amount of heat associated with the diffusion flux under a vanishing temperature gradient (a limiting isothermal state). As such, the heat of transport is related to the transport of heat in a diffusion process. Therefore, our second purpose here is to explore the possibility of using the heat of transport as a measure of the efficiency of the heat pump for the transport of matter.

The problem of thermal diffusion in

the presence of chemical reactions has received considerable attention in the past. Shortly after Eastman¹⁾ introduced the concept of the heat of transport, Wagner²⁾ considered thermal diffusion of species which may exist as two different isomers, *i.e.*, thermal diffusion in the presence of an isomerization reaction. When the reaction was assumed to be in equilibrium, Wagner concluded that the heat of transport consists of two parts, a chemical part due to the reaction and a physical part due to thermal diffusion of the system where the reaction has effectively been frozen. The chemical part of the heat of transport may be written in terms of the heat of reaction ΔH and the difference in the self-diffusion coefficient of the two isomers. The chemical part vanishes when $\Delta H=0$, or when the diffusion coefficients of

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the isomers are identical. Wagner's treatment has been extended by Johnson and Beyerlein¹¹ to include the multiple equilibria reactions, $A_\nu \rightleftharpoons A_{\nu-1} + A$ ($\nu=2, 3, \dots$). The related problems have also been discussed by Walley¹², Brokaw¹³, Baranowski, Haring and deVries¹⁴ and Prigogine and Bues¹⁵.

Thermal diffusion processes may be discussed by the method of linear irreversible thermodynamics. Here fluxes J_i may be expressed in terms of the driving forces X_i and the phenomenological coefficients L_{ij} through the equation,

$$J_i = \sum L_{ij} X_j \quad (1)$$

According to the Onsager reciprocity relation, the L -matrix is symmetric, i.e.,

$$L_{ij} = L_{ji} \quad (2)$$

The coefficient L_{ij} ($i \neq j$) measures the strength of coupling between forces X_i and X_j . When coupling exists between material and heat transports, the heat of transport may be obtained through the coefficient L_{ij} .

In treating problems relating to thermal diffusion of a mixture in reaction equilibrium, one recognizes that the driving force for chemical reactions does not couple with either the driving force for diffusion or heat transport. This follows from the Curie theorem¹⁶ which prohibits coupling of forces where the tensorial characters differ by odd integers. Thus, the scalar force, chemical affinity, which gives rise to chemical reactions may not couple with the vectorial forces, the gradients of chemical potential and temperature which results in diffusion and the transport of heat, respectively. It is also important to notice, that at the state of reaction equilibrium, driving forces for diffusion are no longer independent, because the concentrations of each species is related to the equilibrium constant. Finally, the condition that diffusion fluxes for all species vanish may no longer define the thermal diffusion steady state due to the reaction stoichiometry.

Katchalsky and Curran¹⁷ presented an interesting application of irreversible thermodynamics where they discussed the transport of oxygen across membranes mediated by hemoglobin under an isothermal condition. In this paper we extend their discussion to include a temperature gradient and calculate the heat of transport of oxygen across membranes. We follow Wagner's method. The system we consider is shown in Fig. 1 where the reaction



is confined within the membrane. The width of the membrane is h . To simplify the notation, O_2 will be referred to as component 1, Hb component 2 and HbO_{2n} component 3. In section II, we calculate the heat of transport of oxygen Q^* and in section III an expression for the total oxygen flux is derived. The Q^* obtained may be used to compute the heat flux J_q carrier by the flux of oxygen. We shall view the dissipation of heat through J_q as the input of useful power and diffusion (transport) of oxygen through the

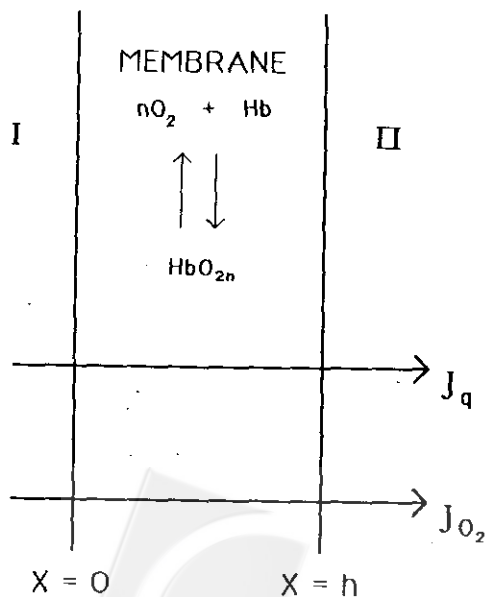


Fig. 1. Oxygen movement through membrane containing Hemoglobin.

membrane as the output. As such we shall define ϵ as the efficiency of the heat engine and calculate ϵ by equating

$$\epsilon = \frac{\text{work out-put due to the transport of oxygen}}{\text{total heat current associated with the oxygen flux}} \quad (4)$$

In section IV, we relate ϵ to Q^* and discuss how chemical reaction may influence ϵ . A brief summary of our result is given in section V.

THE HEAT OF TRANSPORT OF OXYGEN

In the derivation of the heat of transport, we shall assume that the solution is dilute so that the chemical potential of any given component i may be expressed in terms of its concentration C_i by the equation

$$\mu_i = \mu_i^0 + RT \ln C_i \quad (5)$$

Because of the dilute solution approximation we shall ignore coupling of various diffusion fluxes and set $L_{ij} = 0$ for $i \neq j$. Denoting

$$X_i = (-\nabla \mu_i)_{T,P} \quad (6)$$

and

$$X_q = -\nabla \ln T \quad (7)$$

fluxes and forces may be expressed in terms of the phenomenological coefficients as

$$\left. \begin{aligned} J_1 &= L_{11}X_1 + L_{1q}X_q \\ J_2 &= L_{21}X_1 + L_{2q}X_q \\ J_3 &= L_{31}X_1 + L_{3q}X_q \\ J_4 &= L_{41}X_1 + L_{42}X_2 + L_{43}X_3 + L_{4q}X_q \end{aligned} \right\} \quad (8)$$

where the relationship $L_{iq} = L_{qi}$ has been used. If one writes W_i as the mobility of the i th species and Q_i^* as the heat of transport of i as an independent species (i.e., when the reaction is "frozen") W_i and Q_i^* are related to the phenomenological coefficients by the equations

$$\left. \begin{aligned} L_i &= C_i W_i \\ L_{iq} &= C_i W_i Q_i^* \end{aligned} \right\} \quad (9)$$

Since the total oxygen concentration is given by $C_1 + nC_3$, Q^* , the total heat of transport of oxygen, may be written as,

$$Q^* = -RT \left\{ \frac{d \ln (C_1 + nC_3)}{d \ln T} \right\}_{st. st.} \quad (10)$$

where the subscript st. st. implies the stationary state. Let

$$\alpha_1 = C_1 / (C_1 + nC_3), \quad \alpha_3 = nC_3 / (C_1 + nC_3) \quad (11)$$

Then Q^* may be rewritten as

$$\begin{aligned} Q^* &= -RT \left(\alpha_1 \frac{d \ln C_1}{d \ln T} + \alpha_3 \frac{d \ln C_3}{d \ln T} \right) \\ &= -(\alpha_1 X_1 + \alpha_3 X_3) X_q^{-1} \end{aligned} \quad (12)$$

in view of Eqs. (5) and (6). To compute Q^* we notice first that at the state of reaction equilibrium

$$n\mu_1 + \mu_2 = \mu_3 \quad (13)$$

and since

$$(d\mu_i)_p = (d\mu_i)_{T,p} - S_i dT \quad (14)$$

one obtains

$$nX_1 + X_2 - X_3 = -\Delta H X_q \quad (15)$$

where ΔH is the heat of reaction ($\Delta H = T\Delta S$ at constant P). Also, one notices that

$$J_2 + J_3 = 0 \quad (16)$$

because hemoglobin must be confined inside the membrane and there is no external flow of hemoglobin. Equation (16) implies that the flows of Hb and HbO₂ are equal in magnitude but opposite in direction, that is Eq. (16) describes the circulation of hemoglobin inside the membrane. Combining Eqs. (16), (8) and (9) the driving forces X_2 and X_3 may be related to the thermal force X_q by the equation,

$$C_2 W_2 X_2 + C_3 W_3 X_3 = -(C_2 W_2 Q_2^* + C_3 W_3 Q_3^*) X_q \quad (17)$$

Finally, there is no net transfer of mass

at the steady state. Therefore, if one denotes m_i as the mass of the species i ,

$$m_1 J_1 + m_2 J_2 + m_3 J_3 = 0 \quad (18)$$

Since $m_3 = m_2 + n m_1$, Eq. (18) is reduced to

$$J_1 + n J_2 = 0 \quad (19)$$

Eq. (19) is a consequence of the conservation of the oxygen flux, *i.e.*, at the stationary state the flow of oxygen in and out of the membrane must be equal. Eq. (19) enables one to write X_1 and X_2 in terms of X_3 ,

$$C_1 W_1 X_1 + n C_2 W_2 X_2 = -(C_1 W_1 Q_1^* + n C_2 W_2 Q_2^*) X_3 \quad (20)$$

By substituting Eqs. (15), (17) and (20) into Eq. (12) Q^* may be calculated. The result is,

$$\begin{aligned} Q^* = & (n^2 C_2 W_2 C_3 W_3 + C_3 W_3 C_1 W_1 \\ & + C_1 W_1 C_2 W_2)^{-1} \{ (n \alpha_1 C_2 W_2 C_3 W_3 \\ & - \alpha_3 C_1 W_1 C_2 W_2) \Delta H + C_1 W_1 Q_1 (\alpha_1 C_2 W_2 \\ & + \alpha_1 C_3 W_3 + n \alpha_2 C_2 W_2) \\ & + \alpha_3 C_1 W_1 C_2 W_2 Q_2^* \\ & + n C_2 W_2 C_3 W_3 (Q_3^* - Q_2^*) \alpha_1 \\ & + \alpha_3 C_2 W_2 Q_3^* (n^2 C_2 W_2 C_1 W_1) \} \end{aligned} \quad (21)$$

The first term in Eq. (21) represents the contribution from the chemical reaction. It may be rewritten as,

$$\begin{aligned} Q^*(\text{Chem}) = & (n^2 C_2 W_2 C_3 W_3 + C_3 W_3 C_1 W_1 \\ & + C_1 W_1 C_2 W_2)^{-1} \\ & \cdot \{ C C_2 W_2 \alpha_1 \alpha_3 (W_3 - W_1) \Delta H \} \end{aligned} \quad (22)$$

where we have used Eq. (11) and denoted C for $C_1 + n C_2$.

Eq. (22) indicates, that when $\Delta H = 0$, $Q^*(\text{chem})$ vanishes. This is also true when $W_2 = 0$ or $W_3 = W_1$. In the case where $W_2 = 0$, it implies no circulation of hemoglobin. When $W_1 = W_3$, oxygen and oxyhemoglobin move with an equal mobility and the heat of reaction can only contribute to the heat of transport of hemoglobin, Q_H^* , which is given by

$$\begin{aligned} Q_H^* = & -RT \left\{ \frac{d \ln (C_2 + C_3)}{d \ln T} \right\}_{\text{st. st.}} \\ = & (n^2 C_2 W_2 C_3 W_3 + C_3 W_3 C_1 W_1 \\ & + C_1 W_1 C_2 W_2)^{-1} \{ C_1 W_1 \beta_2 C_3 (W_3 \\ & - W_1) \Delta H + \beta_3 C_1 W_1 C_2 W_2 (n Q_1^* + Q_2^*) \\ & + (n^2 \beta_2 C_3 W_3 + \beta_3 C_1 W_1) (C_2 W_2 Q_2^* \\ & + C_3 W_3 Q_3^*) - \beta_2 C_3 W_3 (C_1 W_1 Q_1^* \\ & + n C_2 W_2 Q_2^*) + \beta_3 C_2 W_2 Q_3^* (n^2 C_2 W_2 \\ & + C_1 W_1) \} \end{aligned} \quad (23)$$

where in Eq. (23), $\beta_2 = C_2 / (C_2 + C_3)$ and $\beta_3 = C_3 / (C_2 + C_3)$.

Q^* derived in Eq. (21) has one interesting limiting expression. When $W_2 = \infty$, component 2 (Hb) may be regarded effectively homogeneous. Under this circumstance $Q_2^* = 0$. This is because Q_2^* is the heat of transport of hemoglobin and is given by the heat flux divided by the flux of Hb which is infinite. This conclusion may also be looked at from the point of view of the Soret experiment. Here $Q_2^* = L_{22} / L_2$. Since the rate of entropy creation must be positive, $|L_{22}| \leq \sqrt{L_2 L_{22}}$. Therefore

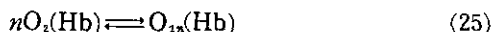
$$\text{Limit}_{L_2 \rightarrow \infty} |Q_2^*| \leq (L_1 / L_2)^{1/2} = 0$$

which is equivalent to say that no heat of transport exists when the flow has no "resistance".

By setting $W_2 = \infty$ and $Q_2^* = 0$, Eq. (21) is reduced to

$$\begin{aligned} Q^* = & (C_1 W_1 + C_3 W_3)^{-1} \{ \alpha_1 \alpha_3 (W_3 - W_1) \Delta H \\ & + (C_1 W_1 Q_1^* + C_3 W_3 Q_3^*) \} \end{aligned} \quad (24)$$

When hemoglobin is homogeneous it may be regarded as a part of the solvent and we may write Eq. (3) as



Equation (25) is identical to the isomerization reaction considered by Wagner. The heat of transport obtain in Eq. (24) agrees with Wagner's result.

THE FLOW OF OXYGEN ACROSS THE MEMBRANE

In this section we investigate the total

outgoing flux of oxygen J_{O_2} , which is given by the equation

$$J_{O_2} = h^{-1} \int_0^h (J_1 + nJ_2) dx \quad (26)$$

J_{O_2} in Eq. (26) may be evaluated under the state of reaction equilibrium and the boundary condition that both Hb and HbO₂ be confined in the membrane. Thus conditions given in both Eq. (15) and (17) are applicable and lead to

$$J_{O_2} = \left\{ D_1 + \frac{n^2}{\bar{C}_1} \left(\frac{1}{\bar{C}_2 D_2} + \frac{1}{\bar{C}_3 D_3} \right)^{-1} \right\} \Delta C_1 + \left\{ \frac{\bar{C}_1 D_1 Q_1^*}{RT^2} + \frac{n}{RT^2} \left(\frac{1}{\bar{C}_2 D_2} + \frac{1}{\bar{C}_3 D_3} \right)^{-1} (\Delta H - Q_2^* + Q_3^*) \right\} \Delta T \quad (27)$$

where D_i ($=W_i RT$) is the diffusion coefficient of the species i , \bar{T} is the average temperature and \bar{C}_i is the average concentration of the species i . \bar{C}_i 's are related through the equation $k = \bar{C}_3 / (\bar{C}_1 \bar{C}_2)$, where k is the equilibrium constant for the reaction (3). ΔC_1 and ΔT are respectively, the average concentration and temperature gradients across the membrane and are given by

$$\Delta C_1 = (C_1^0 - C_1^h) h^{-1}, \quad \Delta T = (T^0 - T^h) h^{-1} \quad (28)$$

where C_1^0 and T^0 are respectively, the concentration of oxygen and temperature at $x=0$. The first term in Eq. (27) represents the transport of oxygen due to diffusion. The second term is the contribution of the temperature gradient to the flow of oxygen. Since $\bar{C}_2 + \bar{C}_3 = \bar{C}_{Hb}$ is the (average) total concentration of hemoglobin, one denotes the average diffusion coefficient for the hemoglobin as D_{Hb} and writes

$$\bar{C}_{Hb} D_{Hb} = \left(\frac{1}{\bar{C}_2 D_2} + \frac{1}{\bar{C}_3 D_3} \right)^{-1} \quad (29)$$

Combining Eq. (27) and (29), one obtains

$$J_{O_2} = (\bar{C}_1 D_1 + n^2 \bar{C}_{Hb} D_{Hb}) \Delta \ln \bar{C}_1 + \left\{ \frac{\bar{C}_1 D_1 Q_1^*}{RT} + \frac{n \bar{C}_{Hb} D_{Hb}}{RT} (\Delta H - Q_2^* + Q_3^*) \right\} \Delta T \quad (30)$$

where

$$\Delta \ln \bar{C} = \bar{C}_1^{-1} \Delta C_1 \quad \text{and} \quad \Delta \ln \bar{T} = \bar{T}^{-1} \Delta T.$$

It is seen in Eq. (30) that contributions to the total oxygen flux from thermal diffusion process may be divided into two parts. The first part is due to the migration of free oxygen as represented by the term with D_1 . Then, there is also a contribution from the chemical reaction. Here hemoglobin and oxyhemoglobin have opposite effects. This seems reasonable since they migrate against each other. In the limiting situation where $Q_2^* \sim Q_3^*$, contribution from the reaction to the oxygen flux is dependent on the magnitude of the heat of reaction. Exothermicity favors the transport of oxygen in the direction of the temperature gradient ($T^h > T^0$ and $\Delta \ln \bar{T} < 0$) whereas endothermic reactions will favor the transport of oxygen against the temperature gradient.

THE SYSTEM AS A HEAT PUMP

In an interesting article exploiting the concept of entropy as time's speed regulator, Odum and Pinkerton¹⁰ noted that many coupled processes in biological systems may be viewed as a coupling of the input and output of an engine. In one direction there is a release of stored energy, a decrease in free energy, and the creation of entropy. In the other direction, there is the storing of energy, the increase of free energy and an entropy decrease due to this coupling. The entire process consists, therefore, of a coupling of input power consumption and output power production. In the case of thermal diffusion, the coupling of diffusion to the transport of heat is much like a heat engine or its reverse, the heat pump.

When a thermal gradient exists across the membrane, the transport of heat couples to the transport of oxygen. The consumption of thermal power leads to the transport of species, a production of chemical work. Following Odum and Pinkerton, we define an efficiency of the

process ϵ as

$$\epsilon = \frac{J_{O_2} \{ -(\mu_1^0 - \mu_1^A) \}}{J_{O_2} Q^*} \quad (31)$$

In Eq. (31) the numerator represents the dissipation due to the transport of oxygen and the denominator is the heat flux associated with the transport. For a heat engine, a smaller Q^* represents a better efficiency; that is, when the chemical part of Q^* is opposite to the diffusion part, the cancellation effect would make Q^* smaller. Equation (31) also indicates that ϵ is larger, the greater the difference of the chemical potential difference across the membrane.

Most biological systems are isothermal, and thermal diffusion processes may be viewed effectively as heat pumps. The coefficient of performance (COP) of the heat pump may be written as

$$COP = \epsilon^{-1} \quad (32)$$

From Eq. (32) it is seen that the performance would be more effective the larger the value of Q^* . Here a large heat of reaction would also help the dissipation of metabolic heat.

SUMMARY

We have derived the heat of transport of oxygen, Q^* , across the membrane mediated by a carrier. The derivation is based on the assumption that cross diffusion fluxes may be ignored and the solution is ideal. Our result indicates that Q^* consists of chemical and diffusional parts. The chemical part is due to the reaction which gives rise to the carrier-mediated transport, and is proportional to the heat of the reaction. The carrier-mediated transport of oxygen considered in this paper has been discussed in Katchalsky and Curran⁹ when the system is isothermal. Including a temperature gradient enables us to investigate the transport of heat. This should be of some significance in the discussion of the transport of heat in biological system.

This is because many biochemical reactions involving the production and consumption of heat are localized and may lead to local temperature gradients. Such local temperature gradients might play some role in the transport of materials. From the point of view of optimum performance of this "molecular" heat pump, a large ΔH which leads to a large value of Q^* will be beneficial. On the other hand ΔG should be small and not much different from zero, otherwise the equilibrium would be "stiff" and can hardly be shifted. From the present analysis it is clear that a system efficient for the transport of heat, must incorporate chemical reactions that have large ΔH and ΔS but mutually compensating to yield a small ΔG . For biological polymers, this can be achieved by ligand binding and a large conformational change.

Finally, we have computed the total outgoing oxygen flow in the presence of a temperature gradient. Its effect is dependent on the heat of reaction, diffusion coefficients and the "bare" heat of transport of species involved.

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