Riassunto. È stata studiata la possibilità di seguire con un titolatore automatico impiegato come pH-stat l'andamento della respirazione e della glicolisi di cellule sopravviventi. I valori ottenuti sono in accordo con quelli descritti nella letteratura.

Rispetto al metodo manometrico sono segnalati alcuni vantaggi quali la rapidità delle determinazioni, la possibilità di variare più parametri sperimentali nel corso dell'esperienza nonchè la facilità di prelievo di materiale durante l'esperimento.

U. Ferrini and L. Bellelli

Istituto Regina Elena per lo Studio e la Cura dei Tumori, Roma (Italy), March 6, 1961.

STUDIORUM PROGRESSUS

An Approach to Molecular Dynamics of Chemical Reaction

According to the theory of transition state[1], the reaction rate constant can be expressed as

$$k = \varkappa(kT/h)\ \{Q_{(t)}/Q_{(i)}\}\ \exp\ (-\Delta U_i/kT), \qquad (1)$$

where $\varkappa$ is the transmission coefficient, kT the statistical temperature which is the absolute temperature T multiplied by Boltzmann's constant k, h Planck's constant, $Q_{(t)}$ the partition function of the so-called transition state, $Q_{(i)}$ the partition function of the initial molecular system, and ΔU_i is the activation energy. The chemical reaction has been classified by Horiuti into the two types, the one being an effusion-type and the other a diffusion-type, by the relations of the transmission coefficient $\varkappa \simeq 1$ and $\varkappa \ll 1$, respectively[2].

However, $\varkappa$ is a correction factor brought somewhat formally into the expression of rate constant. For the reaction of effusion-type ($\varkappa \simeq 1$), it can be considered that the transition state method of Eyring's is a good approach. But it must be supposed that the Eyring's theory is inapplicable to the reaction of diffusion-type, because the method is based on the equilibrium model of chemical reaction whose original concept can be found in the classical treatment of Arrhenius'[3]. Therefore, it will be desirable to deal with the problem from the more general point of view.

This paper describes an approach to the non-equilibrium model of chemical reaction from the molecular dynamical theory. One of our purposes in this work is to find the mutual relationships among the several theoretical treatments of reaction rate from a unified and general situation.

In the approach based on the non-equilibrium model, the problem is reduced to the diffusion problem of particles over a potential barrier from a potential-hollow corresponding to the initial configurations of reaction system to another hollow belonging to the final configurations of product system on the adiabatic potential energy surface[4]. If the degree of freedom of the reacting molecular system is given by f, the transition (hyper-) surface of the dimension $(f-1)$ can be defined in the vicinity of the 'watershed' of a potential barrier. A profile of the potential energy surface in the two dimensional case is shown diagrammatically in Figure 1. Our interest is focused upon the diffusion flux of the representative points of reaction system across the transition surface in phase space as a consequence of Brownian motion. It may be safely said that Brownian motion in the molecular level is responsible for diffusion process in the macroscopic level, in a broad sense. As shown in Figure 2, the behaviour of the flow of the representative points can be likened to the motion of Brownian particles as a whole. Such a Brownian particle-like motion results from the irregularly fluctuating forces due to the interaction between the reaction system and the surroundings. The reacting system is presumed to accept or lose energy through the fluctuating forces from the surroundings. Then the passage of the reacting system in the vicinity of the top of potential barrier to the final state taking the molecular configurations of product can be achieved by means of a large number of fluctuations.

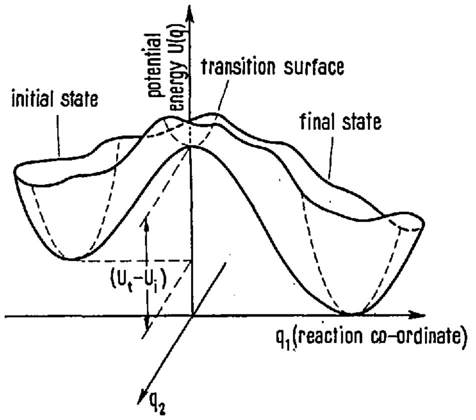

Fig. 1. A profile of two-dimensional potential energy surface.

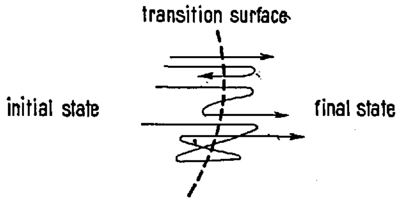

Fig. 2. Brownian particle-like motion of the representative points in the neighbourhood of the transition surface.

In the f-dimensional phase space, the co-ordinates of position are called $(q_1, q_2, \ldots, q_f)$, the conjugate momenta are $(p_1, p_2, \ldots, p_f)$, and the reduced masses with regard to those degrees of freedom are $(M_1, M_2, \ldots, M_f)$, respectively. The co-ordinates are chosen so that these normalize each other in the neighbourhood of the transition surface, and q_1 is selected as the reaction co-ordinate.

The Hamiltonian H_r of the reaction system is given by

$$H_r = \sum_{\alpha=1}^{f} p_\alpha^2/2\,M_\alpha + U(q_1, q_2, \ldots, q_f), \qquad (2)$$

where $U(q_1, q_2, \ldots, q_f)$ is the potential energy of the system.

The potential energy of the system is developed in the power series of the displacements around the saddle-point in the transition surface, whose molecular configuration is specified by suffix t, as the following:

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[1] S. Glasstone, K. J. Laidler, and H. Eyring, *Theory of Rate Processes* (McGraw-Hill, New York 1941).

[2] J. Horiuti, Pap. Inst. Phys. Chem. Res. Tokyo *34*, 1174 (1938); Bull. Chem. Soc. Japan *13*, 210 (1939).

[3] S. Arrhenius, Z. phys. Chem. *4*, 226 (1889).

[4] H. A. Kramers, Physica *7*, 284 (1940).

$$U(q_1,q_2,\ldots,q_f) = U(q_{1t},q_{2t},\ldots,q_{ft}) + \sum_{\alpha,\beta=1}^{f} C_{\alpha\beta}\,\Delta q_\alpha\,\Delta q_\beta + \cdots \tag{3a}$$

where $\Delta q_\alpha \equiv (q_\alpha - q_{\alpha t})$. Since the position co-ordinates are normal in the vicinity of the transition surface, the $C_{\alpha\beta}$ matrix has only the diagonal element:

$$U(q_1, q_2, \ldots, q_f) = U(q_{1t}, q_{2t}, \ldots, q_{ft}) + \sum_{\alpha=1}^{f} C_{\alpha\alpha}(\Delta q_\alpha)^2 + \cdots \tag{3b}$$

All the elements but the C_{11} are positive, because of q_1 being the reaction co-ordinate. The C_{11} element can be put as

$$C_{11} \equiv -(^1/_2)\,(\partial^2 U/\partial q_1^2)_{\Delta q_1=0} = -(^1/_2)\,\omega_t^2 M_1, \tag{3c}$$

where ω_t has the dimension of frequency (multiplied by 2π). All the other terms are collectively called

$$\tilde{U}(q_2, q_3, \ldots, q_f) = \sum_{\alpha=2}^{f} C_{\alpha\alpha}(\Delta q_\alpha)^2. \tag{3d}$$

After all, Eq. (3b) becomes

$$U(q_1, q_2, \ldots, q_f) = U_t - (^1/_2)\,\omega_t^2 M_1 x^2 + \tilde{U}(q_2, q_3, \ldots, q_f) + \cdots, \tag{4}$$

where $U_t \equiv U(q_{1t}, q_{2t}, \ldots, q_{ft})$, and $x \equiv \Delta q_1 = (q_1 - q_{1t})$.

The KRAMERS-CHANDRASEKHAR's[4,5] equation governing the time variation of $W(q_1, q_2, \ldots, q_f, p_1, p_2, \ldots, p_f; t)$, which is the distribution function for the molecular system of f-degrees of freedom, is written as

$$\begin{aligned}\{\partial/\partial t + F_\alpha\,\partial/\partial p_\alpha + (p_\alpha/M_\alpha)\,\partial/\partial q_\alpha\}\,W &= \\ &= \partial/\partial p_\alpha\,\{kT\,\zeta_{\alpha\beta}\,\partial W/\partial p_\beta + \zeta_{\alpha\beta}(p_\beta/M_\beta)\,W\},\end{aligned} \tag{5}$$

where $F_\alpha = -\,\partial U/\partial q_\alpha$, and $\zeta_{\alpha\beta}$ is the friction tensor:

$$\zeta_{\alpha\beta} = (1/kT)\int_0^\infty \overline{A_\alpha(t)\,A_\beta(t+s)}\,\mathrm{d}s, \tag{6}$$

A_α is the component of the total fluctuating force owing to the interaction between the α-th degree of freedom of the reaction system and the surroundings, and the bar means an ensemble average with respect to the initial co-ordinates and momenta of all the other molecular systems.

Provided that all the $\zeta_{\alpha\beta}$ except the ζ_{11} vanish, the component along the reaction co-ordinate of the friction tensor, and under the condition of Eq. (4), W becomes separable as the following:

$$\begin{aligned}W(q_1, q_2, \ldots, q_f, p_1, p_2, \ldots, p_f; t) &= \\ &= W_1(q_1, p_1; t)\cdot W'(q_2, q_3, \ldots, q_f, p_2, p_3, \ldots, p_f; t),\end{aligned} \tag{7}$$

where $W_1(q_1, p_1; t)$ is the solution of the equation

$$\begin{aligned}(\partial/\partial t + F_1\,\partial/\partial p_1 + p_1/M_1\,\partial/\partial q_1)\,W_1 &= \\ &= \partial/\partial p_1(kT\,\zeta_{11}\,\partial W_1/\partial p_1 + \zeta_{11}\,p_1/M_1\,W_1).\end{aligned} \tag{8}$$

In the neighbourhood of the transition surface, Eq. (8) is reduced to

$$\begin{aligned}(\partial/\partial t + \omega_t^2 M_1 x\,\partial/\partial p_1 + p_1/M_1\,\partial/\partial x)\,W_1 &= \\ &= \partial/\partial p_1(kT\,\zeta_{11}\,\partial W_1/\partial p_1 + \zeta_{11}\,p_1/M_1\,W_1).\end{aligned} \tag{9}$$

Here we have used Eq. (4) for F_1.

Admitting that the difference of the potential energies between the top of barrier and the bottom of the hollow of the initial state, $(U_t - U_i)$, is sufficiently larger than the thermal energy kT, we can consider the steady diffusion flux in the neighbourhood of the transition surface.

Eq. (9) becomes thereby

$$\begin{aligned}(\omega_t^2 M_1^2 x\,\partial/\partial p_1 + p_1\,\partial/\partial x)\,W_1 &= \\ &= \partial/\partial p_1\,(kT\,\zeta_{11} M_1\,\partial W_1/\partial p_1 + \zeta_{11}\,p_1 W_1).\end{aligned} \tag{10}$$

According to the treatment of CHANDRASEKHAR's[5], the solution of Eq. (10) can be obtained in the form of

$$W_1 = N_1\cdot f(s)\cdot\exp\left[-\{p_1^2/2M_1 - (^1/_2)\,\omega_t^2 M_1 x^2 + U_t\}/kT\right], \tag{11a}$$

$$\begin{aligned}f(s) = \{(a-\zeta_{11})/2\pi kT\zeta_{11}M_1\}^{1/2} &\times \\ \times \int_{-\infty}^{s} \exp\{-(a-\zeta_{11})\,s^2/2kT\,\zeta_{11}\,M_1\}\,ds&,\end{aligned} \tag{11b}$$

and

$$a = (\zeta_{11}/2) + \{(\zeta_{11}/2)^2 + (\omega_t M_1)^2\}^{1/2}, \tag{11c}$$

where N_1 is a normalization constant, and $s \equiv (p_1 - a\,x)$.

The boundary conditions are set up for Eq. (11a) as the following:

$$\left.\begin{array}{lll} f(s) \to 1 & \text{as} & s \to +\infty \\ f(s) \to 0 & \text{as} & s \to -\infty \end{array}\right\}, \tag{12}$$

these result from the initial condition that the system under consideration exists in the equilibrium initial state at first and not in the final state.

The steady diffusion flux $J_{st}^{(1)}$ across the transition surface, whose position is given by $x = (q_1 - q_{1t}) = 0$, can be calculated from

$$J_{st}^{(1)} = \int_{-\infty}^{+\infty} W_1(x=0, p_1)\,p_1/M_1\,dp_1. \tag{13}$$

By making use of Eqs. (11a, b), we obtain finally

$$\begin{aligned}J_{st}^{(1)} &= N_1\{(a-\zeta_{11})/2\pi kT\,\zeta_{11}\,M_1\}^{1/2}\exp(-U_t/kT)\,\times \\ &\times \int_{-\infty}^{+\infty} dp_1\,p_1/M_1\exp(-p_1^2/2kT\,M_1)\int_{-\infty}^{p_1} ds\,\exp\{-(a- \\ &-\zeta_{11})\,s^2/2kT\zeta_{11}M_1\} = kTN_1\,\{1-(\zeta_{11}/a)\}^{1/2}\exp(-U_t/kT).\end{aligned} \tag{14}$$

We shall proceed to make partial use of the concept of Eyring's, that is the equilibrium assumption with regard to the $(f-1)$ degrees of freedom except a single one of the reaction co-ordinate. Then, the total flux J_{st} is given by taking the equilibrium distribution function W'_{eq} for W' of Eq. (7):

$$\begin{aligned}J_{st} = J_{st}^{(1)}\int_{-\infty}^{+\infty}\!\cdots\!\int W'_{eq}\,(q_2, q_3, \ldots, q_f, p_2, p_3, \ldots, p_f)\,dq_2\,dq_3\ldots dq_f &\times \\ \times\, dp_2\,dp_3\ldots dp_f&,\end{aligned} \tag{15a}$$

$$\begin{aligned}\text{with}\quad W'_{eq} = N'\exp[-\{p_2^2/2M_2 + p_3^2/2M_3 + \cdots &+ \\ + p_f^2/2M_f + \hat{U}(q_2, q_3, \ldots, q_f)\}/kT]&,\end{aligned} \tag{15b}$$

where N' is a normalization constant.

The number of systems in the vicinity of the equilibrium initial state is

$$\begin{aligned}n_i = N_i \underset{(q;\ \text{initial configurations})}{\int\int\cdots\int}\ \underset{p;\ -\infty}{\int\cdots\int^{+\infty}} \exp[-\{\sum_{\alpha=1}^{f} p_\alpha^2/2M_\alpha &+ \\ + U(q_1, q_2, \ldots, q_f)\}/kT]\,dq_1\,dq_2\ldots dq_f\,dp_1\,dp_2\ldots dp_f&,\end{aligned} \tag{16}$$

whose range of integration with respect to the position co-ordinates is limited to the configurations in the initial state, and N_i is a normalization constant.

The rate constant k_i for the chemical reaction from the initial state to the final state can be expressed in the following form,

$$k_i = J_{st}/n_i = \varkappa(kT/h)\,\{Q_{(t)}/Q_{(i)}\}\exp(-U_t/kT), \tag{17a}$$

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[5] S. CHANDRASEKHAR, Rev. Mod. Phys. *15*, 1 (1943).

where the transmission coefficient is defined by

$$\varkappa = \{(\zeta_{11}/2\,\omega_t\,M_1)^2 + 1\}^{1/2} - (\zeta_{11}/2\,\omega_t\,M_1), \qquad (17\,\mathrm{b})$$

and the partition functions are defined classically by

$$Q_{(t)} = h^{-(f-1)} \int_{-\infty}^{+\infty}\!\!\cdots\!\int \exp\,[-\{p_2^2/2\,M_2 + p_3^2/2\,M_3 + \cdots + p_f^2/2\,M_f + \tilde{U}(q_2, q_3, \ldots, q_f)\}/kT]\; dq_2\,dq_3 \ldots dq_f\,dp_2\,dp_3 \ldots dp_f \qquad (17\,\mathrm{c})$$

for the molecular configurations in the neighbourhood of the transition surface, and

$$Q_{(i)} = h^{-f} \underset{\substack{(q:\ \text{initial}\\ \text{configurations})}}{\int\!\!\int} \cdots \underset{p;\ -\infty}{\overset{+\infty}{\int\!\!\int}} \exp\,[-\{\sum_{\alpha=1}^{f} p_\alpha^2/2\,M_\alpha + U(q_1, q_2, \ldots, q_f)\}/kT]\; dq_1\,dq_2 \ldots dq_f\,dp_1\,dp_2 \ldots dp_f \qquad (17\,\mathrm{d})$$

for the molecular configurations in the initial state, respectively. When the bottom of the potential hollow belonging to the initial state is chosen as the original level of the energy scale, Eq. (17a) can be transformed into

$$k_i = \varkappa(kT/h)\,\{Q_{(t)}/Q_{(i)}\}\exp(-\Delta U_i/kT), \qquad (17')$$

with $\Delta U_i = (U_t - U_i)$.

Here the value at the potential bottom of the initial state has been called U_i.

This expression can be compared with Eyring's one of rate constant. It must be remarked that the transmission coefficient is introduced inevitably to the expression of Eq. (17a), and has definite physical meaning.

For the case of large friction of

$$1/\tau_1 \equiv \zeta_{11}/M_1 \gg 2\,\omega_t, \qquad (18\,\mathrm{a})$$

where τ_1 is the time constant of the relaxation process of the momentum referring to the reaction co-ordinate, the transmission coefficient of Eq. (17b) is reduced to

$$\varkappa \simeq (M_1\,\omega_t/\zeta_{11}). \qquad (18\,\mathrm{b})$$

On the other hand, for the frictionless case of the limit of

$$\zeta_{11} \to 0, \qquad (19\,\mathrm{a})$$

the transmission coefficient approaches to unity,

$$\varkappa \to 1. \qquad (19\,\mathrm{b})$$

This last situation in the limit of Eq. (19a) corresponds correctly to Eyring's treatment.

It will be easily seen that the case of Eq. (18a) is equivalent to the treatment on the basis of the diffusion model of chemical reaction in a narrow sense. It has been known that KRAMERS-CHANDRASEKHAR's equation being the diffusion equation in phase space is transformed into Smoluchowski's diffusion equation in position space only, if we ignore all effects which occur in intervals of the order $\tau = M/\zeta$. In the present problem, by making use of the local equilibrium for the momentum distribution

$$W_1(q_1, p_1; t) \simeq w_1(q_1; t)\,(2\,\pi\,M_1\,kT)^{-1/2}\exp(-p_1^2/2\,M_1\,kT), \qquad (20)$$

and integrating suitably Eq. (8) with respect to p_1, we obtain the following diffusion equation of Smoluchowski's,

$$\left.\begin{aligned} \partial w_1/\partial t &= -\,\partial/\partial q_1\,J_s^{(1)} \\ J_s^{(1)} &= -\,D^{(1)}\,\partial w_1/\partial q_1 + (F_1/\zeta_{11})\,w_1 \end{aligned}\right\}, \qquad (21)$$

where $J_s^{(1)}$ denotes to be Smoluchowski's diffusion flux along the reaction co-ordinate q_1, and the diffusion constant is defined by $D^{(1)} \equiv kT/\zeta_{11}$.

If the equilibrium condition is valid in the position space too, we obtain

$$w_1 = \text{constant} \times \exp\,\{-\,U(q_1, q_2, \ldots, q_f)/D^{(1)}\zeta_{11}\} \qquad (22\,\mathrm{a})$$

by the integration of Eq. (21) under the condition of $J_s^{(1)} = 0$.

Combining Eq. (22a) with Eq. (20), the following equilibrium distribution function can be obtained,

$$W_{1,eq} = N_{eq}\exp[-\{p_1^2/2\,M_1 + U\}/kT], \qquad (22\,\mathrm{b})$$

where N_{eq} is a normalization constant.

The expression of the rate constant on the basis of Eq. (21) under the steady condition is given by [6,7]

$$k_i^{(1)} = (kT/\zeta_{11})\{\underset{\substack{\text{range of}\\ \text{potential barrier}}}{\int} \exp\,(U/kT)\,dq_1 \underset{\substack{\text{initial}\\ \text{configurations}}}{\int} \exp\,(-U/kT)\,dq_1\}^{-1}. \qquad (23)$$

By making use of Eq. (4) for the potential energy in the neighbourhood of the transition surface, and supplementing the integration with regard to the space of momenta and the other co-ordinates, Eq. (23) becomes

$$k_i = (kT/\zeta_{11}\,h) \left\{ \frac{\int_{-\infty}^{+\infty} \exp\,(-\,p_1^2/2\,M_1\,kT)\,dp_1}{\int_{-\infty}^{+\infty} \exp\,(-\,\omega_t^2\,M_1\,x^2/2\,kT)\,dx} \right\} \times$$

$$\times\ \{Q_{(t)}/Q_{(i)}\}\exp\,(-\,\Delta U_i/kT) = $$

$$= (M_1\,\omega_t/\zeta_{11})\,(kT/h)\,\{Q_{(t)}/Q_{(i)}\}\exp(-\,\Delta U_i/kT), \qquad (24)$$

where $Q_{(t)}$, $Q_{(i)}$, and ΔU_i have the same forms and meanings as before. It has been found that Eq. (24) is just identical with Eq. (17′) under the condition of Eq. (18a), and the transmission coefficient is given by

$$\varkappa = M_1\,\omega_t/\zeta_{11}.$$

Therefore, it is concluded that the rate constant of Eq. (17′), derived from the application of KRAMERS-CHANDRASEKHAR's equation to the motion of a single degree of freedom along the reaction co-ordinate, serves as a general expression which unifies the two types of effusion and diffusion of chemical reaction.

Zusammenfassung. Der bei Ablauf einer chemischen Reaktion stattfindende Elementarvorgang wird mit Hilfe des Diffusionsmodells untersucht. Der hierbei für die Geschwindigkeitskonstante gewonnene Ausdruck [Gl. (17′)] stimmt in dem Grenzfalle, dass der Reibungskoeffizient verschwindet, mit dem Ergebnis nach der Eyringschen Übergangsmethode und im Grenzfalle grosser Reibungskoeffizienten mit der Darstellung Gleichung (24) für den Smoluchowskischen Diffusionsfluss im Lagekoordinatenraume überein.

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[8] The author takes great pleasure in acknowledging the encouragement of Prof. K. OOMORI.