Biochimica et Biophysica Acta, 657 (1981) 304—308

BBA Report

BBA 61385

A SEMI-ANALYTICAL EXPRESSION FOR THE CONCENTRATION DISTRIBUTION OF SUBSTRATE MOLECULES IN FAST, ENZYME-CATALYSED REACTION SYSTEMS

KUO-CHEN CHOU [a,*], TSE-TSAI LI [b,**] and GUO-QIANG ZHOU [c]

[a] *Physical Chemistry 2, Chemical Center, Lund (Sweden),* [b] *Shanghai Institute of Computer Technology and* [c] *Department of Automatic Engineering Control, Shanghai Jiaotong University, Shanghai (China)*

(Received July 24th, 1980)

Key words: Fast reaction; Concentration distribution; Enzyme catalysis; Theoretical mechanism

Summary

A semi-analytical expression for the concentration distribution of the substrate molecules in fast enzyme-catalysed reaction systems is presented. On this basis, the physical pictures of the reactions are discussed.

Although enzyme molecules can be regarded as spherical, the active site of an enzyme molecule usually occupies only a small part of its surface, or the entire active site is buried in a concave region, the so-called molecular crevice. Therefore, as we go more deeply into the fast enzyme-substrate reactions, we have to deal with non-spherically symmetric problems. In our previous work [1—2], taking the spatial factor, force field factor and activation energy factor into consideration, non-spherically symmetric equations have been set up. Unfortunately, it is not feasible to obtain an analytical solution from these equations, even in the case without force field (i.e., $U = 0$). The only approach is to find numerical solutions [3], from which, although some new results have been obtained, numerical solutions cannot provide us with a clear and concise picture of the concentration distribution of the reacting molecules. Thus, the following questions are naturally raised: (1) Can we find a semi-analytical expres-

* Visiting Professor at Cornell University, Baker Laboratory, Ithaca, NY 14853, U.S.A.
** Present address: Department of Biochemistry, Toronto University, Ontario, Canada.

sion for the concentration distribution in the fast enzyme-substrate reaction system? (2) Which kind of kinetic characters can be obtained from it? The present study was initiated in an attempt to discuss these problems.

First of all, we shall consider the following equation [1]

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial}{\partial r}c^*\right)+\frac{1}{r^2\sin\theta}\frac{\partial}{\partial\theta}\left(\sin\theta\frac{\partial}{\partial\theta}c^*\right)-\frac{1}{\mathbf{k}T}\left(\frac{\partial}{\partial r}c^*\right)\left(\frac{\partial U}{\partial r}\right)=0 \tag{1}$$

with the boundary conditions (Fig. 1):

$$\left.\begin{aligned}&c^*|_{r=R_0}=0\\&\text{(If we take Smoluchowski's boundary condition [1])}\\&\left(\frac{\partial c^*}{\partial r}\right)_{r=R_0}=\frac{1}{D}\sqrt{\frac{\mathbf{k}T}{2\pi m^*}}\,e^{-\epsilon_0/\mathbf{k}T}c^*\\&\text{(If we take Chou's boundary condition [2])}\end{aligned}\right\}\quad(0\leqslant\theta<\theta_a) \tag{2}$$

$$\left(\frac{\partial c^*}{\partial r}\right)_{r=R_0}=0\qquad(\theta_a<\theta\leqslant\pi) \tag{3}$$

$$c^*|_{r\to\infty}=c_0\qquad(0\leqslant\theta\leqslant\pi) \tag{4}$$

where U is the interaction potential between substrate (S) and enzyme (E) molecules, $\mathbf{k}$ the Boltzmann constant, T the absolute temperature, D the diffusion coefficient, $R_0 = R_E + R_S$ is the sum of the radii of an E molecule and an S molecule, ϵ_a the activation energy, $m^* = m_E m_S/(m_E + m_S)$ is the reduced mass

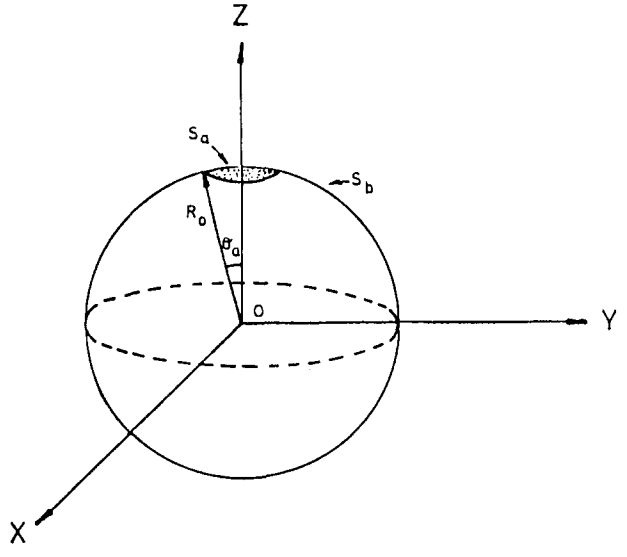

Fig. 1. S_a is the surface of the active site, and S_b is the surface of the remaining part of an enzyme molecule. $S_{R_0} = S_a + S_b$.

of the E and S molecules, θ_a the maximal derivation angle of the active site, c_0 the bulk concentration, and c^* has the following relation to c, the concentration of S molecules:

$$c = e^{-U/kT} c^* \tag{5}$$

Therefore, as soon as c^* is solved, the concentration distribution of S molecules is obtained, and so is the rate constant

$$k = \frac{D}{c_0} \iint_{S_r} e^{-U/kT} \frac{\partial c^*}{\partial r} \, dS \tag{6}$$

where S_r is any spherical surface with the radius $r \geqslant R_0$.

Now, let us define r^* as the maximal action radius between one E and one S molecule, i.e.,

$$U|_{r \geqslant r^*} = 0 \tag{7}$$

Thus, for those reaction systems in which $U = 0$ we should have $r^* = R_0$. If there is only the van der Waals short-range force, namely $U = U_v$, then r^* is just a few Å greater than R_0. In the space of $r \geqslant r^*$, Eqn. 1 will reduce to

$$\frac{1}{r^2} \frac{\partial}{\partial r}\left(r^2 \frac{\partial c^*}{\partial r}\right) + \frac{1}{r^2 \sin\theta} \frac{\partial}{\partial \theta}\left(\sin\theta \frac{\partial c^*}{\partial \theta}\right) = 0 \tag{8}$$

the solution of which can be expressed as [1]

$$c^* = c_0 + \sum_{l=0}^{\infty} \alpha_l \left(\frac{r^*}{r}\right)^{l+1} P_l(\cos\theta) , \qquad (r \geqslant r^*) \tag{9}$$

where $P_l(\cos\theta)$ is the Legendre polynominal. Actually, α_l will rapidly decrease with the increase of l, therefore, we have the following approximate expression:

$$c^* \approx c_0 + \sum_{l=0}^{L} \alpha_l \left(\frac{r^*}{r}\right)^{l+1} P_l(\cos\theta) , \qquad (r \geqslant r^*) \tag{10}$$

where the terms of $L > 5$ can usually be neglected. Consequently, it is very easy through the numerical solution to find the coefficients α_l that give the same results in Eqn. 10 the space of $r \geqslant r^*$ as those obtained through numerically solving Eqns. 1—4 directly.

Now, let us take the fast E-S reaction system in Ref. 1 as an example, where $R_0 = 20$ Å, $\theta_a = 20°$, $D = 7 \cdot 10^{-6}$ cm^2/s, $\epsilon_a = 0$, $m^* = 62$ daltons, $T = 298$ K, and $U = U_v$ the form of which is given in Ref. 3. For a reaction system like this, r^* is equal to 23 Å. If we take $L = 4$, the semi analytical solutions thus obtained have already arrived at the same precision as the numerical solutions given in Ref. 3. The results calculated when the van der Waals binding energy between the E and S molecules is -10 kT are as follows:

$$c \approx c_0 \left\{1 - 0.930\left(\frac{r^*}{r}\right) - 0.454 \cdot 10^{-2}\left(\frac{r^*}{r}\right)^2 \cos\theta - 0.216 \cdot 10^{-2}\left(\frac{r^*}{r}\right)^3 P_2(\cos\theta) - 0.196 \cdot 10^{-2}\left(\frac{r^*}{r}\right)^4 P_3(\cos\theta) + 0.439 \cdot 10^{-3}\left(\frac{r^*}{r}\right)^5 P_4(\cos\theta)\right\},$$

$$(r \geqslant r^* = 23\ \text{Å})$$

$$k = 1.133 \cdot 10^{10}/\text{M}^{-1} \cdot \text{s}^{-1} \qquad (11)$$

The concentration distribution calculated for the region of $R_0 \leqslant r < r^*$ is shown in Fig. 2.

From Eqn. 11 we can see that the rate constant k attains the magnitude as high as $10^{10}/\text{M}^{-1} \cdot \text{s}^{-1}$, however the concentration distribution in the space of $r \geqslant r^* = 23$ Å is quite close to spherical symmetry. Only within the spherical shell of $R_0 \leqslant r < r^*$, the thickness of which is merely 3 Å, does the concentration distribution deviate significantly from spherical symmetry and possess a very high concentration gradient as indicated in Fig. 2. These results provide us with a clear picture: inside the spherical shell of $R_0 \leqslant r < r^*$ there is a very strong flow of S molecules around the protein surface of an E molecule to its active site, whereas outside the region the flow of S molecules is moderate and quasi-spherically symmetric.

However, the situation is quite different if the van der Waals binding energy

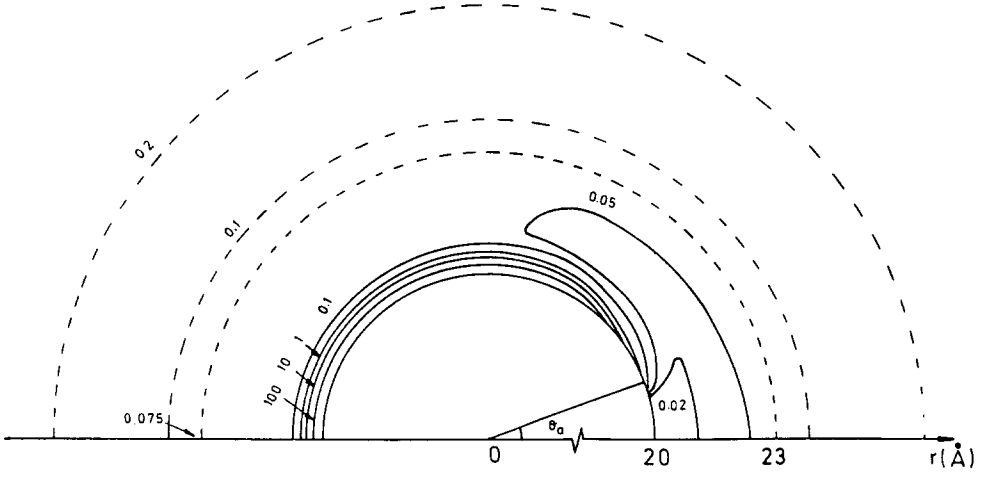

Fig. 2. The contour map of the concentrations of the substrate molecules in the region of $R_0 \leqslant r < r^*$ for the reaction system concerned (see text). The unit of the numbers indicated at the contour lines is c_0, the bulk concentration. The dotted lines are the corresponding contour lines outside the region, which are given by Eqn. 11.

is equal to zero; in that case, we have

$$\left.\begin{aligned} c \approx c_0 \Big\{1 - 0.141\left(\frac{r^*}{r}\right) - 0.175\left(\frac{r^*}{r}\right)^2 \cos\theta - 0.155\left(\frac{r^*}{r}\right)^3 P_2(\cos\theta) \\ - 0.122\left(\frac{r^*}{r}\right)^4 P_3(\cos\theta) - 0.903 \cdot 10^{-1}\left(\frac{r^*}{r}\right)^5 P_4(\cos\theta)\Big\} \\ k = 1.730 \cdot 10^9/\mathrm{M}^{-1} \cdot \mathrm{s}^{-1} \end{aligned}\right\} \quad (12)$$

which indicates that the concentration distribution is far from spherical symmetry in quite an extensive region.

This work was supported by Shanghai Jiaotong University, Shanghai Institute of Computer Technology and the Chemical Center of Lund. The authors are also much indebted to Dr. Torbjörn Drakenberg, Professor Sven Larsson and Professor Björn Lindman for illuminating discussions. K.-C.C. was a visiting Professor in the Chemical Centre of Lund, Sweden.

References

1 Chou, K.C. and Jiang, S.P. (1974) Sci. Sin. 17, 664—680
2 Chou, K.C. (1976) Sci. Sin. 19, 505—528
3 Li, T.T. and Chou, K.C. (1976) Sci. Sin. 19, 117—136