Study on the Model for Regulation of the Allosteric Enzyme Activity

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The effects of activator molecule and repressive molecule on binding process between allosteric enzyme and substrate are discussed by considering the heterotropic effect of the regulating molecule that binds to allosteric enzyme. A model of allosteric enzyme with heterotropic effect is presented. The cooperativity and anticooperativity in the regulation process are studied.

Keywords allosteric enzyme, cooperativity and anticooperetivity, heterotropic effect, activator molecule, repressive molecule

Introduction

The kinetic feature of ligand interactions with macromolecule plays a significant role in biological regulation.[1,2] Multisubunit proteins such as human hemoglobin frequently exhibit cooperativity,[3-6] which arises from a coupling between the effects of ligand binding at the individual subunits and the interactions between subunits of the assembled quaternary structure.

One of the simplest and most popular models for allosteric proteins is the two-state (concerted) model (MWC model).[7,8] This model has been widely used as a first-order approximation to the behavior of hemoglobins and other allosteric proteins. Afterwards, some general allosteric enzyme models have been extensively developed by Koshland,[9] Hammes[10] and Ackers *et al*.[8] However, more complex parameters and conformational forms than those given in MWC model are involved in these general models of allosteric enzyme. So they are not so popular as MWC model.[11-13] However, people attempt to find the simplest scheme that will accommodate all observations. Data on allosteric proteins are still often interpreted using the MWC model, because of only a few parameters involved in it. One of the obvious limitations for MWC model is its inability to accommodate anticooperativity. In MWC model, a ligand always pulls the conformational equilibrium to the form which is preferentially binded by it, resulting in the enhancement of further binding of the same ligand. However apparent anticooperativity has been observed in some ligand bindings.[14-17] Anticooperativity means that the first binding of a ligand would induce a conformational change which weakens the next binding. Therefore, the MWC theory has been extended to a more general theory,[18,19] in which the binding affinity of a specific ligand depending on the conformational state of the allosteric protein and the occupancy of neighboring sites has been considered. It has been theoretically proved that MWC model is a special case of our theory. The extensive theory can explain not only the cooperativity, but also the anticooperativty in the regulation of allosteric protein. In this paper, by considering the heterotropic effect of the regulating molecule that binds to allosteric enzyme, the effects of activator molecule and repressive molecule on binding process between allosteric enzyme and substrate are discussed, and the cooperativity and anticooperativity in the regulation of allosteric enzyme are studied.

Model and theory

A protein composed of n protomers is considered. Each protomer contains two receptor sites (an active site

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and an allosteric site), and can exist in either of two reversibly equilibrating conformational states. These states are denoted by R (relaxed state) and T (taut state) forms. The activator molecules bind to conformational state R preferably, whereas repressive molecules bind to conformational state T preferably.

The conformational transformation of the allosteric protein and the equilibrium constants can be written as

$$R_{0,0} \rightleftharpoons T_{0,0} \tag{1}$$

$$L = T_{0,0}/R_{0,0}$$

Here the first subscript 0 of R and T indicates that the active sites of allosteric protein have not been occupied by substrate molecules; the second subscript 0 of R and T indicates that the allosteric sites of protein have not been occupied by activator molecule or repressive molecule.

The binding equilibria between the allosteric protein and activator molecule, repressive molecule as well as substrate molecules can be written as

$$R_{i,j} + A \rightleftharpoons R_{i,j+1} \tag{2}$$

$$R_{i,j} + S \rightleftharpoons R_{i+1,j} \tag{3}$$

$$T_{i,j} + I \rightleftharpoons T_{i,j+1} \tag{4}$$

$$T_{i,j} + S \rightleftharpoons T_{i+1,j} \tag{5}$$

$$(i, j = 1, 2, 3, \cdots n)$$

Here A denotes activator molecule, I denotes repressive molecule, and S denotes substrate molecule. The $R_{i,j}$ indicates the relaxed state bound by i substrate molecules and j activator molecules; the $T_{i,j}$ indicates taut state bound by i substrate molecules and j repressive molecule. $R_{i,j}$ and $T_{i,j}$ are defined by a set of all microscopic species of the R conformation and T conformation respectively. They have bound i substrate molecules and j regulative molecules (activator molecules or repressive molecule). From Eq. (2) to Eq. (4), the relations between macroscopic dissociation constants K and microscopic constants k for four kinds of reactions mentioned above can be deduced

$$\begin{aligned}
K_{RAi,j} &= \frac{(R_{i,j-1})(A)}{(R_{i,j})} = \frac{\Omega_{n,j-1}}{\Omega_{n,j}} k_{RAi,j} \\
K_{TIi,j} &= \frac{(T_{i,j-1})(I)}{(T_{i,j})} = \frac{\Omega_{n,j-1}}{\Omega_{n,j}} k_{TIi,j} \\
K_{RSi,j} &= \frac{(R_{i-1,j})(S)}{(R_{i,j})} = \frac{\Omega_{n,i-1}}{\Omega_{n,i}} k_{RSi,j} \\
K_{TSi,j} &= \frac{(T_{i-1,j})(S)}{(T_{i,j})} = \frac{\Omega_{n,i-1}}{\Omega_{n,i}} k_{TSi,j}
\end{aligned} \tag{6}$$

Here $\Omega_{n,j} = n!/[(n-j)!j!]$. We easily obtain

$$\begin{aligned}
(R_{i,j}) &= \frac{(R_{i-1,j})(S)}{(K_{RSi,j})} = \frac{(R_{i-2,j})(S)^2}{K_{RSi,j}K_{RSi-1,j}} = \cdots \\
&= \frac{(R_{0,j})(S)^i}{\prod_{m=1}^{i} K_{RSm,j}} \\
(T_{i,j}) &= \frac{(T_{i-1,j})(S)}{(K_{TSi,j})} = \frac{(T_{i-2,j})(S)^2}{K_{TSi,j}K_{TSi-1,j}} = \cdots \\
&= \frac{(T_{0,j})(S)^i}{\prod_{m=1}^{i} K_{TSm,j}} \\
(T_{i,j}) &= \frac{(T_{i,j-1})(I)}{(K_{TIi,j})} = \frac{(T_{i,j-2})(I)^2}{K_{TIi,j}K_{TIi,j-1}} = \cdots \\
&= \frac{(T_{i,0})(I)^j}{\prod_{m=1}^{j} K_{TIi,m}} \\
(R_{i,j}) &= \frac{(R_{i,j-1})(A)}{(K_{RAi,j})} = \frac{(R_{i,j-2})(A)^2}{K_{RAi,j}K_{RAi,j-1}} = \cdots \\
&= \frac{(R_{i,0})(A)^j}{\prod_{m=1}^{j} K_{RAi,m}}
\end{aligned} \tag{7}$$

Because the binding between a ligand and an allosteric protein will generally affect the binding affinity between other ligand and allosteric protein, the microscopic dissociation constants in binding process of allosteric protein and ligands are different from one another. The binding affinity of a specific ligand generally depends not only on the conformational state of the allosteric protein, but also on the occupancy of other sites. For example, the experimental values of the microscopic dissocia-

tion constants (k_j) for human hemoglobin obtained at 25 ℃ in solution buffered to pH 7.4 in the presence and absence of NaCl (0.1 mol/L) show the progressive decrease in as oxygenation proceeds.[20] The $k_{RAi,j}$ ($k_{TIi,j}$) is assumed varying from $f_1 k_{RA}$ ($g_1 k_{TI}$) as $j = 1$ to k_{RA} (k_{TI}) as $j \to \infty$, and $k_{RSj,0}$ ($k_{TSj,0}$) varying from fk_{RS} (gk_{TS}) as $j = 1$ to k_{RS} (k_{TS}) as $j \to \infty$, namely

$$\begin{aligned} &k_{RAi,1} = f_1 k_{RA}, k_{RAi,2} = f_1^{1/2^m} k_{RA}, k_{RAi,3} \\ &= f_1^{1/3^m} k_{RA}, \cdots, k_{RAi,n} = f_1^{1/n^m} k_{RA} \\ &k_{TIi,1} = g_1 k_{TI}, k_{TIi,2} = g_1^{1/2^m} k_{TI}, k_{TIi,3} \\ &= g_1^{1/3^m} k_{TI}, \cdots, k_{TIi,n} = g_1^{1/n^m} k_{TI} \\ &k_{RS1,0} = fk_{RS}, k_{RS2,0} = f^{1/2^m} k_{RS}, k_{RS3,0} \\ &= f^{1/3^m} k_{RS}, \cdots, k_{RSn,0} = f^{1/n^m} k_{RS} \\ &k_{TS1,0} = gk_{TS}, k_{tS2,0} = g^{1/2^m} k_{TS}, k_{TS3,0} \\ &= g^{1/3^m} k_{TS}, \cdots, k_{TSn,0} = g^{1/n^m} k_{TS} \end{aligned} \tag{8}$$

Here f and g are constants that give a measure of how the binding affinity of active site depends on the occupancy number of active site. f_1 and g_1 are constants which give a measure of how the binding affinity of allosteric site depends on the occupancy number of allosteric site. The m is a positive integer ($m = 1, 2, 3$ *etc.*). From Eq. (6) to Eq. (8), the analytic expression may be obtained as:

$$\begin{aligned} \sum_{i,j}^{n} (R_{i,j}) &= (R_{0,0}) \left\{ 1 + \frac{1}{f_1^{C_m}} \left[\left(1 + \frac{(A)}{k_{RA}} \right)^n - 1 \right] \right\} \cdot \\ &\left\{ 1 + \frac{1}{f^{C_m}} \left[\left(1 + \frac{(S)}{k_{RS}} \right)^n - 1 \right] \right\} \end{aligned} \tag{9}$$

$$\begin{aligned} \sum_{i,j}^{n} (T_{i,j}) &= (T_{0,0}) \left\{ 1 + \frac{1}{g_1^{C_m}} \left[\left(1 + \frac{(I)}{k_{TI}} \right)^n - 1 \right] \right\} \cdot \\ &\left\{ 1 + \frac{1}{g^{C_m}} \left[\left(1 + \frac{(S)}{k_{RS}} \right)^n - 1 \right] \right\} \end{aligned}$$

Here $C_m = \pi^{2m} 2^{2m-1} B_m / (2m)!$, B_m is constant ($B_1 = 1/6$, $B_2 = 1/30$, $B_3 = 1/42$); C_m is also constant.

By using the binomial expansion relations

$$\left[1 + \frac{(F)}{k} \right]^n = 1 + \sum_{i=1}^{n} \frac{n!}{(n-i)!\,i!} \left[\frac{(F)}{k} \right]^i$$

and

$$n \left(1 + \frac{(F)}{k} \right)^{n-1} \left(\frac{(F)}{k} \right) = \sum_{i=1}^{n} \frac{i(n!)}{(n-i)!\,i!} \left[\frac{(F)}{k} \right]^i$$

(Here $(F) = (A)$, (I), (S), *etc.*), the following relations may be further gotten

$$\begin{aligned} &\sum_{i,j=0}^{n} i(R_{i,j}) \\ &= \sum_{i=1}^{n} i \sum_{j=0}^{n} (R_{i,j}) \\ &= \left\{ 1 + \frac{1}{f_1^{C_m}} \left[\left(1 + \frac{(A)}{k_{RA}} \right)^n - 1 \right] \right\} \sum_{i=1}^{n} i(R_{i,0}) \\ &= \frac{(R_{0,0})}{f^{C_m}} n \left(1 + \frac{(S)}{k_{RS}} \right)^{n-1} \frac{(S)}{k_{RS}} \left[1 - \frac{1}{f_1^{C_m}} + \frac{1}{f_1^{C_m}} \cdot \right. \\ &\left. \left(1 + \frac{(A)}{k_{RA}} \right)^n \right] \end{aligned} \tag{10}$$

$$\begin{aligned} &\sum_{i,j=0}^{n} i(T_{i,j}) \\ &= \sum_{i=1}^{n} \sum_{j=0}^{n} (T_{i,j}) \\ &= \left\{ 1 + \frac{1}{g_1^{C_m}} \left[\left(1 + \frac{(I)}{k_{TI}} \right)^n - 1 \right] \right\} \sum_{i=1}^{n} i(T_{i,0}) \\ &= \frac{(T_{0,0})}{g^{C_m}} n \left(1 + \frac{(S)}{k_{TS}} \right)^{n-1} \frac{(S)}{k_{TS}} \cdot \\ &\left[1 - \frac{1}{g_1^{C_m}} + \frac{1}{g_1^{C_m}} \left(1 + \frac{(I)}{k_{TI}} \right)^n \right] \end{aligned} \tag{11}$$

By using of Eq. (9) to Eq. (11), the equilibrium fractional saturation θ_s with respect to substrate S may be derived to Eq. (12).

It is convenient to express the concentration as dimensionless parameters: $\beta = \frac{(I)}{k_{TI}}$, $\gamma = \frac{(A)}{k_{RA}}$ and $\alpha = \frac{(S)}{k_{RS}}$, where $k_{TS} = \frac{k_{RS}}{c}$, $\frac{(S)}{k_{TS}} = c\alpha$. Eq. (12) can be rewritten as Eq. (13).

$$\theta_s=\frac{f(A)\frac{(S)}{k_{RS}f^{C_m}}\left[1+\frac{(S)}{k_{RS}}\right]^{n-1}+g(I)L\frac{(S)}{k_{TS}g^{C_m}}\left[1+\frac{(S)}{k_{TS}}\right]^{n-1}}{f(A)\left[1-\frac{1}{f^{C_m}}+\frac{1}{f^{C_m}}\left[1+\frac{(S)}{k_{RS}}\right]^{n}\right]+g(I)L\left[1-\frac{1}{g^{C_m}}+\frac{1}{g^{C_m}}\left(1+\frac{(S)}{k_{TS}}\right)^{n}\right]} \tag{12}$$

Here

$$L=(T_{0,0})/(R_{0,0}),\ f(A)=1-\frac{1}{f_1^{C_m}}+\frac{1}{f_1^{C_m}}\left(1+\frac{(A)}{k_{RA}}\right)^n$$

and

$$g(I)=1-\frac{1}{g_1^{C_m}}+\frac{1}{g_1^{C_m}}\left(1+\frac{(I)}{k_{TI}}\right)^n$$

$$\theta_s=\frac{f(\gamma)\frac{\alpha}{f^{C_m}}(1+\alpha)^{n-1}+g(\beta)L\frac{c\alpha}{g^{C_m}}(1+c\alpha)^{n-1}}{f(\gamma)\left[1-\frac{1}{f^{C_m}}+\frac{1}{f^{C_m}}(1+\alpha)^n\right]+g(\beta)L\left[1-\frac{1}{g^{C_m}}+\frac{1}{g^{C_m}}(1+c\alpha)^n\right]} \tag{13}$$

Here

$$f(\gamma)=1-\frac{1}{f_1^{C_m}}+\frac{1}{f_1^{C_m}}(1+\gamma)^n,\ g(\beta)=1-\frac{1}{g_1^{C_m}}+\frac{1}{g_1^{C_m}}(1+\beta)^n.$$

Eq. (13) is an important result in present work, which depends on c, L, α, β, γ (the five parameters as in MWC model), f and g (just as in our previous work), f_1 and g_1.

Results and discussion

The curves of θ_s versus α and the parameter R_s shall be calculated by use of Eq. (13) under different conditions. Then the cooperativity (anticooperativity) and the effects of activator molecule and repressive molecule on binding process between allosteric enzyme and substrate will be discussed. Here R_s is defined as[8]

R_s = (the ligand concentration of 90% saturation)/(the ligand concentration of 10% saturation)

Let $L'=\frac{g(\beta)}{f(\gamma)}L$, Eq. (13) is converted into Eq. (14).

No activator agent and repressor agent

If $(A)=(I)=0$, that is $\beta=\gamma=0$, then $L'=L$, Eq. (14) is converted into Eq. (15).

$$\theta_s=\frac{g^{C_m}\alpha(1+\alpha)^{n-1}+f^{C_m}L'c\alpha(1+c\alpha)^{n-1}}{(1+L')(fg)^{C_m}+g^{C_m}[(1+\alpha)^n-1]+L'f^{C_m}[(1+c\alpha)^n-1]} \tag{14}$$

$$\theta_s=\frac{g^{C_m}\alpha(1+\alpha)^{n-1}+f^{C_m}Lc\alpha(1+c\alpha)^{n-1}}{(1+L)(fg)^{C_m}+g^{C_m}[(1+\alpha)^n-1]+Lf^{C_m}[(1+c\alpha)^n-1]} \tag{15}$$

Case (1): If $f=g=1$, Eq. (15) is converted into

$$\theta_s=\frac{\alpha(1+\alpha)^{n-1}+Lc\alpha(1+c\alpha)^{n-1}}{(1+\alpha)^n+L(1+c\alpha)^n} \tag{16}$$

This is just the result of well-known MWC model.[7,18] All the observations which have been interpreted by MWC model on allosteric proteins can be explained in the general model.

Case (2): If $L\to 0$, Eq. (15) is converted into

$$\theta_s=\frac{\alpha(1+\alpha)^{n-1}}{f^{C_m}+[(1+\alpha)^n-1]} \tag{17}$$

For the sake of simplicity, $n=4$, $m=2$ are arbitrarily assumed (for $m>2$, the same results may be obtained). The corresponding values of R_s under different

parameter choices are calculated (see first line of Table 1). The results show that: when $f < 1$, one has $R_s > 81$, and the behavior of anticooperation is manifested; when $f = 1$, one has $R_s = 81$, and the curve is of Michaelis-Menten type (no cooperativity); when $f > 1$, one has $R_s < 81$, and the sigmoidal feature of curve indicates the cooperativity.

Case (3): When $c = 1$, the corresponding values of R_s are calculated by Eq. (15) (see second line of Table 1). The results show that: if f, $g < 1$, one has $R_s > 81$, and the behavior of anticooperation is manifested. if $f = g = 1$, one has $R_s = 81$, and the curve is of Michaelis-Menten type (no cooperativity). if f, $g > 1$, one has $R_s < 81$, and the sigmoidal feature of curve indicates the cooperativity.

Case (4): If $L = 1000$, $f = g = 100$ or $f = g = 0.1$, the values of R_s are calculated by Eq. (15) (see third line of Table 1). The results show that: when $f = g = 100$, one has R_s decreasing and cooperativity increasing as c decreases; when $f = g = 0.1$, one has R_s and anticooperativity increasing as c increases.

Case (5): If $c = 0$, Eq. (15) is converted into

$$\theta_s = \frac{\alpha(1+\alpha)^{n-1}}{f^m(1+L)+[(1+\alpha)^n-1]} \tag{18}$$

The values of R_s are calculated by Eq. (18) (see fourth line of Table 1). The results show that: when $f = 100$, one has R_s decreasing and cooperativity increasing as L increases; when $f = 0.01$, one has R_s and anticooperativity increasing as L decreases.

Summary

1. In MWC model there are only three parameters, L, c and α. This is just the $f = g = 1$ limit of our generalized model. In this case, no cooperativity occurs as $c = 1$ or $L = 0$. The cooperativity takes place when c decreases and L increases. But no anticooperativity occurs for all parameter choices.

2. From cases (2) and (3), it can be found that both the cooperativity and anticooperativty occur at $L = 0$ or $c = 1$. It means that the cooperativity does not require two states R and T definitely as in MWC model.

3. By inspection of cases (2) to (5), it can be easily found that the cooperativity occurs at f and g larger than 1 and the anticooperativity occurs at f and g smaller than 1. The former means the first binding of ligand favourable to the follow-up binding, while the latter means the first binding of ligand harmful to the follow-up binding. From cases (4) and (5), it can be found that the parameters c and L do influence the cooperativity (anticooperativity). But the determinating factor of cooperativity and anticooperativity is the value of f and g.

4. $L = 0$ and $c = 0$ are special cases in which the parameter g disappears and only parameter f appears in the equilibrium fractional saturation. This is what expected since the two states model has degenerated to one state essentially.

Activator agent and repressor agent existing

So far the effect of parameters L, f, g and c on the

Table 1 Calculation of parameter R_s under different parameter choices ($n = 4$, $m = 2$)

$L = 0$		$L = 1000$, $c = 1$			$L = 1000$			$c = 0$		
f	R_s	f	g	R_s	$f = g$	c	R_s	f	L	R_s
0.1	692	0.1	0.01	8173	0.1	0	24	100	1	6
1	81	0.01	0.1	692	0.1	1	8173	100	10	5
10	19	1	1	81	100	0	3	100	100	4
100	7	100	10	19	100	0.1	4	100	1000	3
		1000	10	19	100	1	7	0.01	1	4495
		10	100	7				0.01	10	749
		10	1000	5				0.01	100	113
								0.01	1000	24

cooperativity and the anticooperativity have been discussed. In the next part, the effect of the activator agent and repressor agent on the curves of θ_s—α will be mainly discussed. The influence of f_1 and g_1 on R_s under fixed $f = g = 1$ will be discussed at first. For the sake of simplicity, $L = 1000$, $n = 4$, and $m = 2$ are also assumed.

(a) If $f_1 = g_1 = 1$ and $c = 0$, the values of R_s under different parameter choices are calculated by use of Eq. (14) and shown in Table 2.

Table 2 Values of R_s changing with β and γ for $f_1 = g_1 = 1$ and $c = 0$

β	3	1	0	0	0
γ	0	0	0	5	100
R_s	3.3	3.7	4.9	53.6	76.3

The results show that: as growing of the concentration of repressor agent β, the value of R_s decreases and the cooperativity increases; as growing of the concentration of active agent γ, the value of R_s increases and the cooperativity decreases. No anticooperativity occurs in this case.

(b) If repressor agent exists only, $\gamma = 0$, the equilibrium fractional saturation θ_s does not depend on parameter f_1. When $c = 0$, the binding ability of T conformation on substrate is far inferior to the R conformation. The values of R_s depending on the concentration of repressor agent β and parameter g_1 are calculated by use of Eq. (14) and shown in Table 3.

Table 3 Values of R_s changing with β and g_1 for $\gamma = 0$ and $c = 0$

β	0	2.5	5	1	2
g_1	-	10	10	0.1	0.1
R_s	4.9	3.8	3.4	3.3	3.2

The results show that: as growing of the concentration of repressor agent β, the value of R_s decreases and the cooperativity increases; as growing of parameter g_1, the value of R_s increases and the cooperativity decreases.

(c) If activator agent exists only, $\beta = 0$, the equilibrium fractional saturation θ_s does not depend on parameter g_1. When $c = 0.1$, the binding ability of T conformation on substrate is inferior to the R conformation. The values of R_s depending on the concentration of activator agent and parameter f_1 are calculated by use of Eq. (14) and shown in Table 4.

Table 4 Values of R_s changing with γ and f_1 for $\beta = 0$ and $c = 0.1$

γ	10	5	10	5	0
f_1	0.1	0.1	10	10	10
R_s	79.0	76.3	54.5	24.2	23.6

The results show that: as growing of the concentration of activator agent γ, the value of R_s increases and the cooperativity decreases; as growing of parameter f_1, the value of R_s decreases and the cooperativity increases.

Next the influence of f and g on R_s is discussed under fixed $f_1 = g_1 = 1$. For the sake of simplicity, $L = 1$, $n = 4$ *and* $m = 2$ are also assumed. According to the definition of R_s, the curves of R_s versus the repressor agent concentration β and the activator agent concentration γ can be calculated.

(a) For fixed γ, if $f > g > 1$, as growing of repressor concentration β, the value of R_s increases and the cooperativity decreases; if $g > f > 1$, as growing of repressor concentration β, the value of R_s decreases and the cooperativity increases. The results are shown in Fig. 1 (for $\gamma = 5$). If $g < f < 1$, as growing of repressor concentration β, the value of R_s decreases and the anticooperativity decreases; if $f < g < 1$, as growing of repressor concentration β, the value of R_s increases and the anticooperativity increases. The results are shown in Fig. 2 (for $\gamma = 5$).

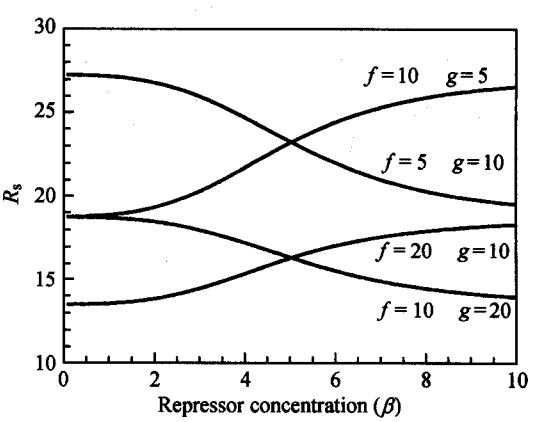

Fig. 1 Curves of R_s with repressor concentration for different f and g.

(b) For fixed β, if $f > g > 1$, as growing of activator concentration γ, the value of R_s decreases and the cooperativity increases; if $g > f > 1$, as growing of activator concentration γ, the value of R_s increases and the

cooperativity decreases. The results are shown in Fig. 3 (for $\beta = 5$). If $1 > f > g$, as growing of activator concentration β, the value of R_s increases and the anticooperativity increases; if $1 > g > f$, as growing of activator concentration β, the value of R_s decreases and the anticooperativity decreases. The results are shown in Fig. 4 (for $\beta = 5$).

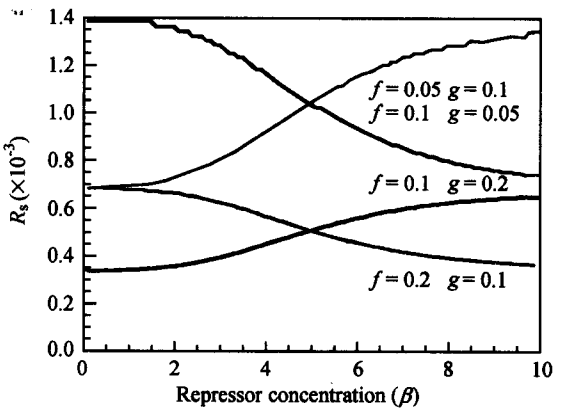

Fig. 2 Curves of R_s with repressor concentration for different f and g.

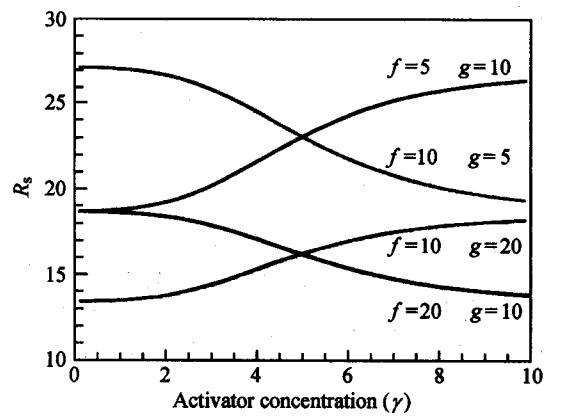

Fig. 3 Curves of R_s with activator concentration for different f and g.

Summary

1. In MWC model, there are only five parameters, c, L, α, β and γ in the existence of activator agents and repressor agents. This should be extreme case ($f = g = 1$, $f_1 = g_1 = 1$) of our generalized model. In this case, no anticooperativity occurs for all parameter choices.

2. The activator molecule and repressor molecules play opposite roles in the regulation of enzyme activity.

3. The effect of parameters f and g on the cooperativity and anticooperativity is larger than that of f_1 and g_1 in regulation of allosteric enzyme by comparing calculations of R_s under the different $f(g)$ and $f_1(g_1)$. Above discussion shows that the new model provides more possibilities for the studies of interaction between substrate (activator, repressor) and allosteric enzyme.

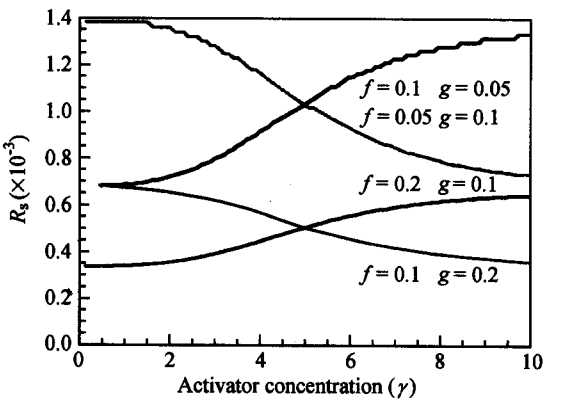

Fig. 4 Curves of R_s with activator concentration for different f and g.

Conclusion

The effects of activator agent molecule and repressor molecule on binding process between allosteric enzyme and substrate are discussed. The results show that the proposed model can explain not only cooperativity but also anticooperativity in the regulation of allosteric enzyme. The theory provides more possibilities for the studies of interaction between many ligands and allosteric proteins, which are helpful to understand the variability in the regulations of allosteric enzyme activities.

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