1. The *lac* repressor has four symmetric units each of which is able to bind lactose, and the repressor as a whole has two conformational states – one that is able to bind DNA and the other that cannot. Given that intracellular lactose causes the repressor to unbind DNA, write down an equation for how the fraction of repressor that is able to bind DNA changes with the concentration of lactose.

   [Solution on the next page]

2. By considering the individual binding sites for ligand of an allosteric molecule that has two binding sites for ligand in total, derive using a differential equation that the overall association constant for moving from the T_1 to the T_2 state is $K_T/2$.

Solution

1. If the T-state is the one able to bind DNA and because the repressor has four units, the appropriate formula for the fraction of activated receptor is

$$f_{\text{DNA}} = \frac{(1 + K_T\ell)^4}{(1 + K_T\ell)^4 + L(1 + K_R\ell)^4}$$

where ℓ is the concentration of lactose.

The repressor should unbind from the DNA when lactose enters the cell. We therefore want $K_R \gg K_T$. Writing the bias as $c = K_T/K_R$ so that $c \ll 1$, we have

$$f_{\text{DNA}} = \frac{(1 + cK_R\ell)^4}{(1 + cK_R\ell)^4 + L(1 + K_R\ell)^4}$$

and so if c is small

$$f_{\text{DNA}} \simeq \frac{1}{1 + L(1 + K_R\ell)^4}.$$

The fraction of repressor that binds DNA therefore goes to zero as ℓ increases.