1. A model of a promoter in phage lambda that is regulated by lambda repressor comprises four chemical reactions.

   Lambda repressor is a dimer so that

$$\mathrm{R} + \mathrm{R} \underset{}{\overset{K_d}{\rightleftharpoons}} \mathrm{R}_2$$

   and binds to two binding sites on the promoter, D, when it is a dimer, but not as a monomer.

   The dimer is able to bind to either binding site when the other site is empty

$$\mathrm{D}_{00} + \mathrm{R}_2 \overset{K_{01}}{\rightleftharpoons} \mathrm{D}_{01}$$

   and

$$\mathrm{D}_{00} + \mathrm{R}_2 \overset{K_{10}}{\rightleftharpoons} \mathrm{D}_{10}$$

   but if a dimer is already bound then a second dimer can only bind if the first binding site is free:

$$\mathrm{D}_{01} + \mathrm{R}_2 \overset{\tilde{K}_{10}}{\rightleftharpoons} \mathrm{D}_{11}$$

   RNA polymerase binds to the promoter when a single dimer is bound, but not to either the free promoter or the promoter with two bound dimers.

   Write down an equation for the transcription rate as a function of monomers R assuming that all binding reactions are at equilibrium and that a bound RNA polymerase is always able to initiate transcription.

   Compare your result to Eq 6 in Hasty, Pradines, Dolnik, and Collins, Proc Nat Acad Sci USA 97: 2075 (2000).

   [Solution on the next page]

Solution

1. There are five states of the DNA:

   (a) free – corresponding to the number 1 in the equation for the rate of transcription

   (b) a dimer of repressor bound to the right-hand site – corresponding to $K_{01}R_2$

   (c) a dimer of repressor bound to the left-hand site – corresponding to $K_{10}R_2$

   (d) two bound dimers – corresponding to $\tilde{K}_{10}K_{01}R_2^2$

   (e) RNA polymerase and a repressor bound to the right-hand site – corresponding to $K_{01}R_2K_QQ$

   (f) RNA polymerase and a repressor bound to the left-hand site – corresponding to $K_{10}R_2K_QQ$.

   Only the two states with bound RNA polymerase initiate transcription with, say, rate u. If there are n copies of the promoter, the rate of transcription is therefore

$$\frac{nu(K_{01}K_QQR_2 + K_{10}K_QQR_2)}{1 + K_{01}R_2 + K_{10}R_2 + \tilde{K}_{10}K_{01}R_2^2 + K_{01}K_QQR_2 + K_{10}K_QQR_2}$$

   Further, we know that $R_2 = K_dR^2$ and Hasty et al write $K_{10} = \sigma K_{01}$ so that

$$\frac{nuK_{01}(1+\sigma)K_QQK_dR^2}{1 + K_{01}(1+\sigma)(1+K_QQ)K_dR^2 + \tilde{K}_{10}K_{01}K_d^2R^4}$$

   which for the dependence on $R - x$ in their notation – has a similar but not identical form to the transcription term in their Eq 6, providing Q is constant.