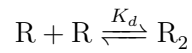


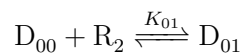
1. A model of a promoter in phage lambda that is regulated by lambda repressor comprises four chemical reactions.

Lambda repressor is a dimer so that

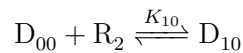


and binds to two binding sites on the promoter,  $D$ , when it is a dimer, but not as a monomer.

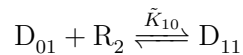
The dimer is able to bind to either binding site when the other site is empty



and



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



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.