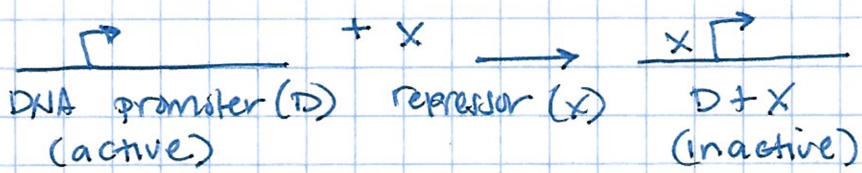
THE INPUT FUNCTIONS OF GENES
MICHAELIS-MENTEN & HILL EQUATIONS

- REFERENCE: URI ALON - INTRO TO SYSTEMS BIOLOGY



CONSERVATION OF DNA SITE = SITE BOUND + SITE UNBOUND = TOTAL

$$D_{TOTAL} = D + XD$$

FOR 1 SITE IN BACTERIA, $D_T = 1/\text{CELL VOLUME} \sim 1/\mu m^3 \sim 1\,nM$

FOR EUKARYOTIC CELLS, NUCLEUS VOLUME $\sim 10\text{-}100\ \mu m^3$

$$D_T \sim 10-100\ pM$$

RATE OF CHANGE OF XD:

$$\frac{dX}{dt} = k_{on} X \cdot D - k_{off}[XD]$$

DIFFUSION-LIMIT → $k_{on} \sim 10^8 - 10^9\ 1/M\text{-sec}$

$k_{off} \sim$ widely varies $\sim 1/\text{sec}$ by bond strength

@ SS

$$k_D\ \text{[=] DISSOCIATION CONSTANT} = \frac{k_{off}}{k_{on}} \overset{SS}{\approx} \frac{[X][D]}{[XD]}$$

→ WE WANT TO ELIMINATE [XD]

$$k_D = \frac{[X][D]}{[XD]} \qquad D_T = [D] + [XD]$$

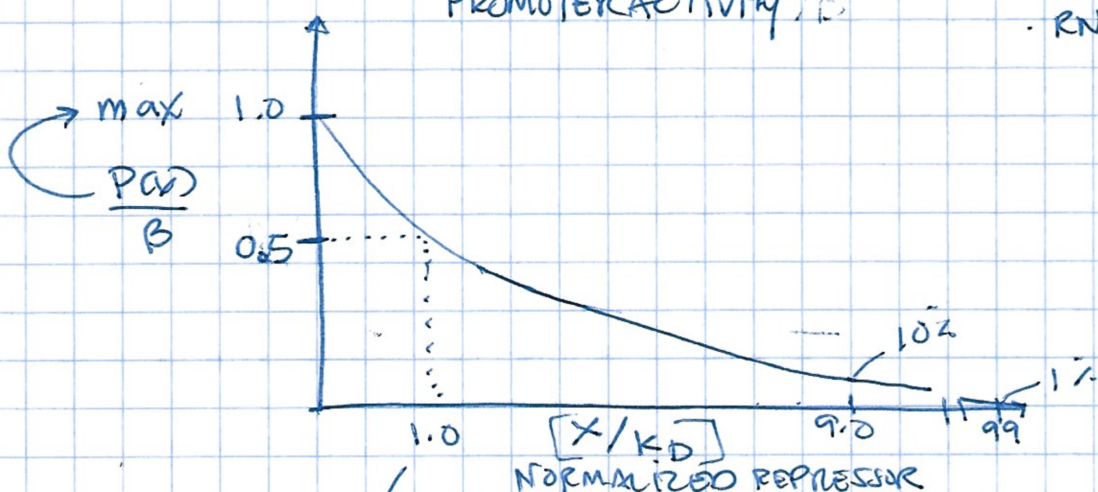
$$[XD] = \frac{[X][D]}{k_D} \Rightarrow D_T = [D] + \frac{[X][D]}{k_D}$$

$$D_T = D(1 + X/k_D)$$

NOW WE KNOW THE FRACTION OF DNA UNBOUND $\Rightarrow \frac{D}{D_T} = \frac{1}{(1 + X/k_D)} \Rightarrow$ PROMOTER ACTIVITY $\propto \frac{D}{D_T}$

SINCE PROMOTER ACTIVITY $\propto \frac{D}{D_T}$ WE WRITE

PROMOTER ACTIVITY: $P(X) = \frac{\beta}{1 + X/K_D}$ where β = maximal transcription rate
- SET BY SEQUENCE
- RNAP,



when $X = K_D$, ACTIVITY = ½ MAX

REFLECTIONS

1. IF YOU START AT HALF ACTIVITY (X=0.5), HOW MANY FOLD DO YOU HAVE TO INCREASE X/K_D TO GET 90% REPRESSION? HOW MUCH TO GET 99%.

2. IF YOU NEEDED VERY TIGHT REPRESSION ($P/\beta \ll 0.01$) WHICH PARAMETERS WOULD YOU EXPERIMENTALLY OR BY DESIGN BE ABLE TO CHANGE?