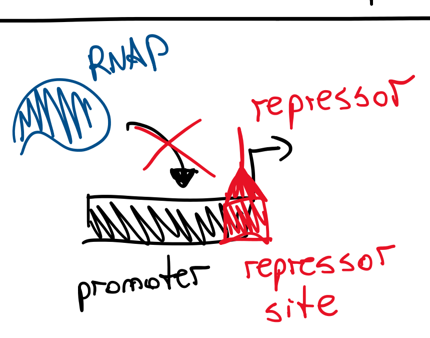
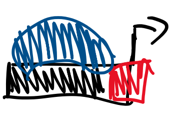
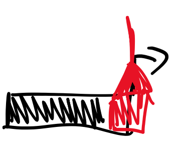
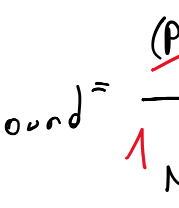
Cartoon model of simple repression



Follow the statistical mechanics protocol:

1. Identify the states the system can be found in
2. Assign energies to each state
3. Enumerate the # of ways each state can be realized
4. Compute the Boltzmann weights
5. Calculate prob. of state we're interested in by dividing its weight by the sum of all possible weights

STATES	ENERGY	MULTIPLICITY
	$P\varepsilon_{pd}^{NS} + R\varepsilon_{rd}^{NS}$ (P: RNAP #, R: repressor #)	$\frac{N_{NS}^{R+P}}{P!\,R!}$
	$(P-1)\varepsilon_{pd}^{NS} + R\varepsilon_{rd}^{NS} + \varepsilon_{pd}^{S}$ (one RNAP bound to promoter)	$\frac{N_{NS}^{R+P-1}}{(P-1)!\,R!}$
	$P\varepsilon_{pd}^{NS} + (R-1)\varepsilon_{rd}^{NS} + \varepsilon_{rd}^{S}$ (one repressor bound specifically)	$\frac{N_{NS}^{R-1+P}}{P!\,(R-1)!}$

STATES	BOLTZMANN WEIGHT
	$\frac{N_{NS}^{R+P}}{P!\,R!}\, e^{-\beta(P\varepsilon_{pd}^{NS} + R\varepsilon_{rd}^{NS})}$
	$\frac{N_{NS}^{R+P-1}}{(P-1)!\,R!}\, e^{-\beta((P-1)\varepsilon_{pd}^{NS} + \varepsilon_{pd}^{S} + R\varepsilon_{rd}^{NS})}$
	$\frac{N_{NS}^{R-1+P}}{P!\,(R-1)!}\, e^{-\beta(P\varepsilon_{pd}^{NS} + (R-1)\varepsilon_{rd}^{NS} + \varepsilon_{rd}^{S})}$

$$P_{bound} = \frac{\frac{N_{NS}^{R+P-1}}{(P-1)!\,R!}\, e^{-\beta((P-1)\varepsilon_{pd}^{NS} + \varepsilon_{pd}^{S} + R\varepsilon_{rd}^{NS})}}{\frac{N_{NS}^{R+P}}{P!\,R!}\, e^{-\beta(P\varepsilon_{pd}^{NS} + R\varepsilon_{rd}^{NS})} + \frac{N_{NS}^{R+P-1}}{(P-1)!\,R!}\, e^{-\beta((P-1)\varepsilon_{pd}^{NS} + \varepsilon_{pd}^{S} + R\varepsilon_{rd}^{NS})} + \frac{N_{NS}^{R-1+P}}{P!\,(R-1)!}\, e^{-\beta(P\varepsilon_{pd}^{NS} + (R-1)\varepsilon_{rd}^{NS} + \varepsilon_{rd}^{S})}}$$

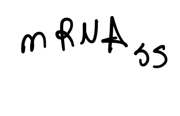
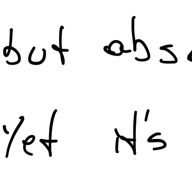
(multiply by $\frac{P!\,R!}{N_{NS}^{R+P}}\, e^{\beta(P\varepsilon_{pd}^{NS} + R\varepsilon_{rd}^{NS})}$; the first denominator term becomes 1)

$$= \frac{\frac{P}{N_{NS}}\, e^{-\beta(\varepsilon_{pd}^{S} - \varepsilon_{pd}^{NS})}}{1 + \frac{P}{N_{NS}}\, e^{-\beta(\varepsilon_{pd}^{S} - \varepsilon_{pd}^{NS})} + \frac{R}{N_{NS}}\, e^{-\beta(\varepsilon_{rd}^{S} - \varepsilon_{rd}^{NS})}}$$

($\Delta\varepsilon_{pd} = \varepsilon_{pd}^{S} - \varepsilon_{pd}^{NS}$, $\Delta\varepsilon_{rd} = \varepsilon_{rd}^{S} - \varepsilon_{rd}^{NS}$)

$$= \frac{\frac{P}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{pd}}}{1 + \frac{P}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{pd}} + \frac{R}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{rd}}} = P_{bound}$$

We just uncovered the "renormalized" statistical weights

STATES	RENORMALIZED WEIGHTS	SHORTHAND
	1	1
	$\frac{P}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{pd}}$	p
	$\frac{R}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{rd}}$	r

Remember that in steady state:

$$mRNA_{ss} = \frac{r}{\gamma} \cdot P_{bound}(P, R)$$

but absolute occupancies are hard to measure! Yet it's easy to measure gene expression. Since we don't know r or γ, calculate a

Fold-change (something I can measure)

$$\text{fold-change in gene expression} = \frac{mRNA_{ss}(P,R)}{mRNA_{ss}(P,R=0)} = \frac{\frac{r}{\gamma} P_{bound}(P,R)}{\frac{r}{\gamma} P_{bound}(P,R=0)}$$

$$= \frac{P_{bound}(P,R)}{P_{bound}(P,R=0)} = \text{fold-change in promoter occupancy}$$

(something I can calculate)

$$\text{Fold change} = \frac{\frac{p}{1+p+r}}{\frac{p}{1+p}} = \frac{p}{1+p+r} \cdot \frac{1+p}{p}$$

$$= \frac{1+p}{1+p+r}$$

Let's examine the relative values of p and r

$$p = \frac{P}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{pd}} = 0.02$$

($P \approx 5{,}000$, $N_{NS} \approx 5 \cdot 10^6$, $\Delta\varepsilon_{pd} \approx -3\,k_BT$)

$$\Rightarrow p \ll 1, \quad r \gg p$$

$$r = \frac{R}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{rd}} \simeq 970$$

($R \approx 10$, $\Delta\varepsilon_{rd} \approx -20\,k_BT$)

$$\text{Fold change} = \frac{1+p}{1+p+r} = \boxed{\frac{1}{1+r} = \text{Fold change}}$$

(weak promoter approximation)

$$\boxed{\text{Fold change} = \frac{1}{1 + \frac{R}{N_{NS}}\, e^{-\beta\Delta\varepsilon_{rd}}} = \frac{1}{\text{repression}}}$$