1) Derive Expression For kinetic limit

$$G_j + R_x^o \rightleftharpoons (G_j : R_x)_c$$

$$(G_j : R_x)_c \rightarrow (G_j : R_x)_o$$

$$(G_j : R_x)_o \rightarrow R_x + G_j$$

$$(G_j : R_x)_o \rightarrow m_j + R_x + G_j$$

RNAP

$$R_{x,T} = R_x^o + (G_j : R_x)_c + (G_j : R_x)_o + \sum_{i=1,j}^{N} \left\{ (G_i : R_x)_c + (G_i : R_x)_o \right\}$$

$$K_{x,j}^{-1} \equiv \frac{k_{+j}}{k_{-j} + k_{I,j}} \quad ; \quad \tau_{xj}^{-1} = \frac{k_{I,j}}{(k_{A,j} + k_{E,j})}$$

a) Balances

$$\frac{d}{dt}((G_j : R_x)_c) = k_{+j} G_j R_x^o - k_{-j}(G_j : R_x)_c - k_{I,j}(G_j : R_x)_c$$

$$\frac{d}{dt}((G_j : R_x)_o) = k_{I,j}(G_j : R_x)_c - k_{A,j}(G_j : R_x)_o - k_{E,j}(G_j : R_x)_o$$

$\Rightarrow$

a) <u>Assuming Steady State</u>

all $\frac{d}{dt}$ Terms $\Rightarrow 0$

[1] $0 = K_{+J}(G_J : R_x^{\circ}) - K_{-J}(G_J : R_x)_C - K_{I,J}(G_J : R_x)_C$

[2] $0 = K_{I,J}(G_J : R_x)_C - K_{A,J}(G_J : R_x)_o - K_{E,J}(G_J : R_x)_o$

$\Rightarrow$ rearrange [1] and [2]

$$(G_J : R_x)_C = \left[\frac{K_{+J}}{K_{-J} + K_{I,J}}\right] G_J R_x^{\circ}$$

$$(G_J : R_x)_o = \left[\frac{K_{I,J}}{K_{A_J} + K_{E,J}}\right] (G_J : R_x)_C$$

$\Rightarrow$ Substitute in $\tau_{x,J}^{-1}$, $K_{x,J}^{-1}$

$$(G_J : R_x)_C = K_{x,J}^{-1} G_J R_x^{\circ}$$

$$(G_J : R_x)_o = \tau_{x,J}^{-1} (G_J : R_x)_C$$

substitute into [2]

$\Rightarrow$

$$(G_J : R_x)_o = \tau_{x,J}^{-1} K_{x,J}^{-1} G_J R_x^{\circ}$$

get This value from RNAP Balace

$\Longrightarrow$

a) RNAP

$$R_{x,T} = R_x^{\circ} + (G_j ; R_x)_c + (G_j ; R_x)_o + \underset{\sim}{\Sigma}$$

where $$\underset{\sim}{\Sigma} = \sum_{i=1,j}^{N} \{ (G_i ; R_x)_c + (G_i ; R_x)_o \}$$

=) ~~plug in eq [★]~~ from earlier
plug in eq [★★] from earlier

$$R_{x,T} = R_x^{\circ} + K_{x,j}^{-1} G_j R_x^{\circ} + \tau_{x,j}^{-1} K_{x,j}^{-1} G_j R_x^{\circ} + \underset{\sim}{\Sigma}$$

=) Modify $\underset{\sim}{\Sigma}$ for R_x°

$$\underset{\sim}{\Sigma} = \sum_{i=1,j}^{N} \{ (G_i ; R_x)_c + (G_i ; R_x)_o \}$$

$$\underset{\sim}{\Sigma}^{\star} = \sum_{i=1,j}^{N} \{ K_{x,i}^{-1} G_i \underbrace{R_x^{\circ}} + \tau_{x,i}^{-1} K_{x,i}^{-1} G_i \underbrace{R_x^{\circ}} \}$$

pull outside of summation

$$\underset{\sim}{\Sigma}^{\star\star} = \left[\sum_{i=1,j}^{N} \{ K_{x,i}^{-1} G_i + \tau_{x,i}^{-1} K_{x,i}^{-1} G_i \} \right]$$

=) So now

$$R_{x,T} = R_x^{\circ} + K_{x,j}^{-1} G_j R_x^{\circ} + \tau_{x,j}^{-1} K_{x,j}^{-1} G_j R_x^{\circ} + \underset{\sim}{\Sigma}^{\star\star} R_x^{\circ}$$

$\Rightarrow$

a) Divide through to get just R_x^o

$$\frac{R_{x,T}}{K_{x,j}^{-1} G_j + \tau_{x,j}^{-1} K_{x,j}^{-1} G_j + \underset{\sim}{\Sigma}^{**}} = R_x^o$$

$\Rightarrow$ Multiply top and bottom by $(\tau_{x,j} K_{x,j})$

$$R_x^o = \frac{R_{x,T}\, \tau_{x,j}\, K_{x,j}}{\underbrace{G_j \tau_{x,j} + G_j + K_{x,j} \tau_{x,j}}_{\text{looks like PS I}} + \underbrace{K_{x,j} \tau_{x,j} \underset{\sim}{\Sigma}^{**}}_{\text{New Term}}}$$

$\Rightarrow$ Modify New Term

$$\Rightarrow \quad K_{x,j} \tau_{x,j} \sum_{i=1,j}^{N} \left\{ K_{x,i}^{-1} G_i \left(1 + \tau_{x,i}^{-1}\right) \right\}$$

$$= \sum_{i=1,j}^{N} \left\{ \frac{K_{x,j} \tau_{x,j}}{K_{x,i}} \left(1 + \tau_{x,i}^{-1}\right) G_i \right\}$$

$\Rightarrow$ Multiply through by $\frac{\tau_{x,i}^{-1}}{\tau_{x,i}^{-1}}$ $\Rightarrow$

$\Rightarrow$

$$\frac{\tau_{x,i}^{-1}}{\tau_{x,i}^{-1}} \left(1 + \tau_{x,i}^{-1}\right) = \frac{1}{\tau_{x,i}} \left(\tau_{x,i} + 1\right) = \frac{1}{\tau_{x,i}} \left(1 + \tau_{x,i}\right)$$

R) So now

$$= \sum_{i=1,j}^{N} \left\{ \frac{k_{x,j}\, \tau_{x,j}}{k_{x,i}} \left(\frac{\tau_{x,i}^{-1}}{\tau_{x,i}^{-1}} (1 + \tau_{x,i}^{-1}) \right) G_i \right\}$$

$$= \underbrace{\sum_{i=1,j}^{N} \left\{ \frac{k_{x,j}\, \tau_{x,j}}{k_{x,i}\, \tau_{x,i}} (1 + \tau_{x,j}) G_i \right\}}_{}$$

$$= \mathcal{E}_j$$

$\Rightarrow$ put back into R_x^o equation from pg 4

Now

$$R_x^o = \frac{R_{x,T}\, \tau_{x,j}\, k_{x,j}}{G_j(\tau_{x,j} + 1) + \tau_{x,j}\, k_{x,j} + \mathcal{E}_j} \qquad [\phi]$$

from first order

$$\Rightarrow r_{x,j} = k_{E,j} (G_j \cdot R_x)_o$$

$$= k_{E,j}\, \tau_{x,j}^{-1}\, k_{x,j}^{-1}\, G_j\, R_x^o$$

$\Rightarrow$ substitute in R_x^o from $[\phi]$

$\Longrightarrow$

$$r_{x,j} = \frac{k_{E,j}\, \cancel{\tau_{x,j}^{-1}\, k_{x,j}^{-1}}\, G_j\, R_{x,T}\, \cancel{\tau_{x,j}\, k_{x,j}}}{G_j(1+\tau_{x,j}) + \tau_{x,j}\, k_{x,j} + \varepsilon_j}$$

Thus

$$\boxed{r_{x,j} = k_{E,j}\, R_{x,T} \left(\frac{G_j}{G_j(1+\tau_{x,j}) + \tau_{x,j}\, k_{x,j} + \varepsilon_j} \right)}$$

where

$$\varepsilon_j = \sum_{i=1,\neq j}^{N} \left\{ \frac{k_{x,j}\, \tau_{x,j}}{k_{x,i}\, \tau_{x,i}} (1+\tau_{x,i})\, G_i \right\}$$

b) Under what circumstances does a N-gene system reduce to the 1-gene system

- To reduce, ε_j would need to be zero, as in class there was no ε_j value
To drive this to happen there should be an elongation limiting system
under this, $\varepsilon_j \approx 0$, and $(1+\tau_{x,j}) \approx 1$
So the $r_{x,j}$ in class in elongation limiting would equal the value derived here.