Q1

$$G_j + R_x^\circ \underset{k_{-,j}}{\overset{k_{+,j}}{\rightleftharpoons}} (G_j : R_x)_c$$

$$(G_j : R_x)_c \xrightarrow[k_{I,j}]{} (G_j : R_x)_o$$

$$(G_j : R_x)_o \xrightarrow[k_{A,j}]{} R_x + G_j$$

$$(G_j : R_x)_o \xrightarrow[k_{E,j}]{} m_j + R_x + G_j$$

Assume

$$r_{x,j} = k_{E,j}(G_j : R_x)_o$$

Goal: Get an expression for $(G_j : R_x)_o$ in terms of measurable concentrations

$\text{conc}^{-1}t^{-1}$ on rate constant; off rate const. for RNAP @ promoter for gene j

$$\Rightarrow \frac{d}{dt}(G_j : R_x)_c = k_{+,j}(G_j)(R_x^\circ) - k_{-,j}(G_j : R_x)_c - k_{I,j}(G_j : R_x)_c \quad \text{—— (I)}$$

t^{-1}; t^{-1} rate constant for open complex formation

and,

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

t^{-1} rate const. for abortive initiation; $t^{-1} \Rightarrow$ r.c. for elongation of gene j.

Assume steady state $\Rightarrow \frac{d}{dt}(G_j : R_x)_c = 0 = \frac{d}{dt}(G_j : R_x)_o$

(I) becomes:-

$$(k_{I,j} + k_{-,j})(G_j : R_x)_c = k_+(G_j)(R_x^\circ)$$

$$\therefore (G_j : R_x)_c = \frac{k_{+,j}(G_j)(R_x^\circ)}{k_{I,j} + k_{-,j}} = \left(\frac{k_{+,j}}{k_{I,j} + k_{-,j}}\right)(G_j)(R_x^\circ) \quad \text{—— (Ia)}$$

(II) becomes:-

$$k_I(G_j : R_x)_c = (k_{A,j} + k_{E,j})(G_j : R_x)_o$$

$$\therefore (G_j : R_x)_c = \left(\frac{k_{A,j} + k_{E,j}}{k_{I,j}}\right)(G_j : R_x)_o \quad \text{—— (IIa)}$$

Equate (Ia) and (IIa)

$$\left(\frac{k_{+,j}}{k_{I,j} + k_{-,j}}\right)(G_j)(R_x^\circ) = \left(\frac{k_{A,j} + k_{E,j}}{k_{I,j}}\right)(G_j : R_x)_o$$

So, $$(G_j : R_x)_o = \left(\frac{k_{+,j}}{k_{I,j} + k_{-,j}}\right)\left(\frac{k_{I,j}}{k_{A,j} + k_{E,j}}\right)(G_j)(R_x^\circ)$$

[=] conc. — saturation const. for gene j; time const. for gene j

Define $\bar{K}_{x,j}^{-1} \equiv \left(\frac{k_{+,j}}{k_{I,j} + k_{-,j}}\right)$; $\tau_{x,j}^{-1} \equiv \left(\frac{k_{I,j}}{k_{A,j} + k_{E,j}}\right)$

$$\boxed{\therefore (G_j : R_x)_o = \bar{K}_{x,j}^{-1}\,\tau_{x,j}^{-1}\,(G_j)(R_x^\circ)} \quad \text{—— (III)}$$

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

$$\text{or, } R_x^\circ = R_{x,T} - \frac{(G_j)(R_x^\circ)}{K_{x,j}} - \frac{(G_j)(R_x^\circ)}{K_{x,j}\,\tau_{x,j}} - \sum_{i=1,j}^{N} \left\{ \frac{(G_i)(R_x^\circ)}{K_{x,i}} + \frac{(G_i)(R_x^\circ)}{K_{x,i}\,\tau_{x,i}} \right\}$$

$$\text{or, } R_x^\circ = R_{x,T} - R_x^\circ \left[\frac{G_j}{K_{x,j}} + \frac{G_j}{K_{x,j}\,\tau_{x,j}} + \left\{ \sum_{i=1,j}^{N} \frac{G_i}{K_{x,i}} + \frac{G_i}{K_{x,i}\,\tau_{x,i}} \right\} \right]$$

$$\therefore R_x^\circ = \frac{R_{x,T}}{1 + \frac{G_j}{K_{x,j}} + \frac{G_j}{K_{x,j}\,\tau_{x,j}} + \sum_{i=1,j}^{N} \frac{G_i}{K_{x,i}} + \frac{G_i}{K_{x,i}\,\tau_{x,i}}}$$

$$\boxed{\therefore R_x^\circ = \frac{R_{x,T}}{\dfrac{K_{x,j}\,\tau_{x,j} + G_j\tau_{x,j} + G_j + \sum_{i=1,j}^{N} \left(\dfrac{G_i\tau_{x,i} + G_i}{K_{x,i}\,\tau_{x,i}} \right) K_{x,j}\,\tau_{x,j}}{K_{x,j}\,\tau_{x,j}}}}$$

Now,

$$r_{x,j} = k_{E,j}(G_j : R_x)_o$$

$$= \frac{k_{E,j}(G_j)(R_x^\circ)}{K_{x,j}\,\tau_{x,j}}$$

$$= k_{E,j}\, R_{x,T} \left[\frac{G_j}{\cancel{K_{x,j}\tau_{x,j}}} \left\{ \frac{1}{\dfrac{K_{x,j}\tau_{x,j} + G_j\tau_{x,j} + G_j + \varepsilon_j}{\cancel{K_{x,j}\tau_{x,j}}}} \right\} \right]$$

where $\varepsilon_j = \sum_{i=1,j}^{N} \frac{K_{x,j}\,\tau_{x,j}\,(1+\tau_{x,i})\,G_i}{K_{x,i}\,\tau_{x,i}}$.

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

b) To be equivalent to the 1-gene system talked in class, $\varepsilon_j = 0$

We know:

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

There are several ways $\varepsilon_j = 0$

- G_i is very small
- $\tau_{x,j}$ is very small. $\tau_{x,j} = \dfrac{k_{A,j} + k_{E,j}}{k_{I,j}}$

  so, $k_{I,j} << k_{A,j} + k_{E,j}$

  If we assume $k_{A,j} << k_{E,j}$, then $k_{I,j} << k_{E,j}$

  So, the system is initiation limited.
- $K_{x,j}$ is very small
- $K_{x,i}$ is very large.