CHEME 7770 Prelim 1

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1. a) From the 4 proposed elementary reactions:

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

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

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

$$(G_j : R_x)_o \xrightarrow{k_{E,j}} m_j + R^o_x + G_j$$

Species balance on $(G_j : R_x)_o$ & $(G_j : R_x)_c$:

$$\frac{d(G_j : R_x)_o}{dt} = k_{I,j}(G_j : R_x)_c - (k_{A,j} + k_{E,j})(G_j : R_x)_o \quad (1)$$

$$\frac{d(G_j : R_x)_c}{dt} = k_{+,j} G_j R^o_x - (k_{-,j} + k_{I,j})(G_j : R_x)_c \quad (2)$$

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

$$k_{I,j}(G_j : R_x)_c = (k_{A,j} + k_{E,j})(G_j : R_x)_o \quad (3)$$

$$k_{+,j} G_j R^o_x = (k_{-,j} + k_{I,j})(G_j : R_x)_c \quad (4)$$

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

$$K^{-1}_{x,j} \equiv \frac{k_{+,j}}{k_{-,j} + k_{I,j}}$$

$$(G_j : R_x)_c = K^{-1}_{x,j} G_j R^o_x \quad (5)$$

Plug into Eq(3):

$$k_{I,j} K^{-1}_{x,j} G_j R^o_x = (k_{A,j} + k_{E,j})(G_j : R_x)_o$$

$$(G_j : R_x)_o = \frac{k_{I,j}}{k_{A,j} + k_{E,j}} K^{-1}_{x,j} G_j R^o_x$$

$$\tau^{-1}_{x,j} \equiv \frac{k_{I,j}}{k_{A,j} + k_{E,j}}$$

$$(G_j : R_x)_0 = \tau_{x,j}^{-1} K_{x,j}^{-1} G_j R_x^0 \quad (6)$$

Plug (5) & (6) into RNAP balance:

$$R_{x,T} = R_x^0 + K_{x,j}^{-1} G_j R_x^0 + \tau_{x,j}^{-1} K_{x,j}^{-1} G_j R_x^0 + \sum_{i=1,j}^{N} \left[K_{x,i}^{-1} G_i R_x^0 + \tau_{x,i}^{-1} K_{x,i}^{-1} G_i R_x^0 \right]$$

$$\tau_{x,j} K_{x,j} R_{x,T} = \tau_{x,j} K_{x,j} R_x^0 + \tau_{x,j} G_j R_x^0 + G_j R_x^0 + \sum_{i=1,j}^{N} \tau_{x,j} K_{x,j} \left[K_{x,i}^{-1} G_i R_x^0 + \tau_{x,i}^{-1} K_{x,i}^{-1} G_i R_x^0 \right]$$

$$\tau_{x,j} K_{x,j} R_{x,T} = R_x^0 \left(\tau_{x,j} K_{x,j} + \tau_{x,j} G_j + G_j \right) + R_x^0 \left[\sum_{i=1,j}^{N} \left(\frac{\tau_{x,j} K_{x,j}}{\tau_{x,i} K_{x,i}} (1 + \tau_{x,i}) G_i \right) \right]$$

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

$$\tau_{x,j} K_{x,j} R_{x,T} = R_x^0 \left[\tau_{x,j} K_{x,j} + G_j (\tau_{x,j} + 1) + \varepsilon_j \right]$$

$$R_x^0 = \frac{\tau_{x,j} K_{x,j}}{\tau_{x,j} K_{x,j} + G_j (1 + \tau_{x,j}) + \varepsilon_j} R_{x,T} \quad (7)$$

Plug (7) into (6):

$$(G_j : R_x)_0 = \frac{G_j}{\tau_{x,j} K_{x,j} + G_j (1 + \tau_{x,j}) + \varepsilon_j} R_{x,T} \quad (8)$$

Plug (8) into the kinetic limit of transcription:

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

b.) An N-gene system is approximately equal to a 1-gene system when $\varepsilon_i \approx 0$. This can occur when:

1: $\tau_{x,j} \to 0$ (very fast initiation for gene j)

2: $K_{x,j} \to 0$ (very high RNAP affinity for gene j)

3: $\tau_{x,i} \to \infty$ (very slow initiation for all genes $i \neq j$)

4: $K_{x,i} \to \infty$ (very low RNAP affinity for all genes $i \neq j$)

(2.) a)

State	Description	Weight	Activation?
0	no effector + no substrate	1	—
1	no effector + substrate	w_1	+
2	effector + substrate	$w_2 f_i$	++

control variable → $v(\ldots)_j$

$$v(\ldots)_j = \frac{\Sigma(\text{states leading to activation})}{\Sigma(\text{all possible states})}$$

$$v(\ldots)_j = \frac{w_1 + w_2 f_i}{1 + w_1 + w_2 f_i}$$

→ These weights come from the Boltzmann probabilities:

$P_0 \propto \exp(-\frac{\epsilon_0}{kT})$ → We set state 0 as the zero-energy state, making its weight = 1

$P_1 \propto \exp(-\frac{\epsilon_1}{kT})$

$P_2 \propto f_i \exp(-\frac{\epsilon_2}{kT})$

So the full overall rate becomes:

$$\hat{r}_j = K_{cat} E_1 \left(\frac{F6P}{K_{F6P} + F6P}\right)\left(\frac{ATP}{K_{ATP} + ATP}\right)\left(\frac{w_1 + w_2 f_i}{1 + w_1 + w_2 f_i}\right)$$

b) To estimate w_1, we look at the data to find the background level of activation. That is, where 3-5-AMP conc. = 0, which is when $f_i = 0$. Here, the overall rate becomes:

$$\hat{r}_j = r_j \left(\frac{w_1}{1 + w_1}\right)$$

Solving for w_1:

$$(1 + w_1)\hat{r}_j = r_j w_1$$

$$w_1(\hat{r}_j - r_j) = -\hat{r}_j$$

$$w_1 = \frac{\hat{r}_j}{r_j - \hat{r}_j}$$

→ Plug in overall rate data from dataset (see code)

To estimate w_2, we use the last data point, where the activation is closest to its asymptotic limit. Here, I made an approximation that $f_i \approx 1$ at equilibrium, though this is probably not true. Thus, the overall rate becomes:

$$\hat{r}_j = r_j \left(\frac{w_1 + w_2}{1 + w_1 + w_2} \right)$$

Solving for w_2:

$$\frac{\hat{r}_j}{r_j}(1 + w_1 + w_2) = w_1 + w_2$$

$$w_2 \left(1 - \frac{\hat{r}_j}{r_j}\right) = \frac{\hat{r}_j}{r_j} + w_1 \left(\frac{\hat{r}_j}{r_j} - 1\right)$$

$$w_2 = \frac{\frac{\hat{r}_j}{r_j} + w_1 \left(\frac{\hat{r}_j}{r_j} - 1\right)}{1 - \frac{\hat{r}_j}{r_j}}$$

→ plug in overall rate values from dataset (see code)

- See code for estimates of K_i & n_i