Prelim 1

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$$\mathcal{G}_j + R_X^o \rightleftharpoons (\mathcal{G}_j : \mathrm{R_X})_C \quad k_+, k_-$$
$$(\mathcal{G}_j : \mathrm{R_X})_C \longrightarrow (\mathcal{G}_j : \mathrm{R_X})_O \quad k_I$$
$$(\mathcal{G}_j : \mathrm{R_X})_O \longrightarrow R_X + \mathcal{G}_j \quad k_A$$
$$(\mathcal{G}_j : \mathrm{R_X})_O \longrightarrow m_j + R_X + \mathcal{G}_j \quad k_{E,j}$$

$$r_{X,j} = k_{E,j}\,(\mathcal{G}_j : \mathrm{R_X})_O$$

$$R_{X,T} = R_X^o + (\mathcal{G}_j : \mathrm{R_X})_C + (\mathcal{G}_j : \mathrm{R_X})_O + \sum_{i=1,j}^{\mathcal{N}} \left\{ (\mathcal{G}_i : \mathrm{R_X})_C + (\mathcal{G}_i : \mathrm{R_X})_O \right\}$$

Part a

$$r_{X,j} = k_{E,j}^X\,(\mathcal{G}_j : \mathrm{R_X})_O$$

Solve for $(G_j : R_X)_O$ in terms of R_X

Assume steady-state for closed and open conformations

closed conformation equation:

$$\frac{d}{dt}(G_j : R_X)_C = k_+(G_j)(R_X) - k_-(G_j : R_X)_C - k_I (G_j : R_X)_C = 0$$

solve for $(G_j : R_X)_C$:

$$\xrightarrow{\text{rearrange}} (G_j : R_X)_C (k_- + k_I) = k_+ (G_j)(R_X) \longrightarrow (G_j : R_X)_C = \frac{k_+}{k_- + k_I}(G_j)(R_X) \xrightarrow[K^{-1}]{\text{apply definition}} \boxed{(G_j : R_X)_C = K_{X,j}^{-1}(G_j)(R_X)}$$

Open conformation equation:

$$\frac{d}{dt}(G_j : R_X)_O = k_I (G_j : R_X)_C - k_A (G_j : R_X)_O - k_{E,j}(G_j : R_X)_O = 0$$

solve for $(G_j : R_X)_O$:

$$\xrightarrow{\text{rearrange}} (G_j : R_X)_O (k_A + k_{E,j}) = k_I (G_j : R_X)_C \longrightarrow (G_j : R_X)_O = \frac{k_I}{k_A + k_{E,j}}(G_j : R_X)_C \xrightarrow[\tau_{X,j}^{-1}]{\text{apply definition}} \boxed{(G_j : R_X)_O = \tau_{X,j}^{-1}(G_j : R_X)_C}$$

plug in $(G_j : R_X)_C$ solution into $(G_j : R_X)_O$ equation:

$$\boxed{(G_j : R_X)_O = K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j)(R_X)}$$

$$R_{X,T} = R_X^o + (\mathcal{G}_j : \mathrm{R_X})_C + (\mathcal{G}_j : \mathrm{R_X})_O + \sum_{i=1,j}^{\mathcal{N}} \left\{ (\mathcal{G}_i : \mathrm{R_X})_C + (\mathcal{G}_i : \mathrm{R_X})_O \right\}$$

Apply RNAP balance to solve for $(G_j : R_X)_O$ in terms of $R_{X,T}$

$$R_X = R_{X,T} - \left((G_j : R_X)_C + (G_j : R_X)_O + \sum_{i=1,j}^{\mathcal{N}} \left((G_i : R_X)_C + (G_i : R_X)_O \right) \right)$$

plug in above equations of $(G_j : R_X)_C$ and $(G_j : R_X)_O$:

$$R_X = R_{X,T} - \left(K_{X,j}^{-1}(G_j)(R_X) + K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j)(R_X) + \sum_{i=1,j}^{\mathcal{N}} \left[K_{X,i}^{-1}(G_i)(R_X) + K_{X,i}^{-1}\tau_{X,i}^{-1}(G_i)(R_X) \right] \right)$$

$$\xrightarrow{\text{rearrange}} R_X \left(1 + K_{X,j}^{-1}(G_j) + K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j) + \sum_{i=1,j}^{\mathcal{N}} \left[K_{X,i}^{-1}(G_i) + K_{X,i}^{-1}\tau_{X,i}^{-1}(G_i) \right] \right) = R_{X,T}$$

$$\xrightarrow{\text{solve for } R_X} \boxed{R_X = R_{X,T} \left[1 + K_{X,j}^{-1}(G_j) + K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j) + \sum_{i=1,j}^{\mathcal{N}} \left[K_{X,i}^{-1}(G_i) + K_{X,i}^{-1}\tau_{X,i}^{-1}(G_i) \right] \right]^{-1}}$$

Solve for the rate of transcription of gene j, $r_{X,j}$

$$r_{X,j} = k_{E,j}^X (G_j : R_X)_O = k_{E,j}^X K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j)(R_X) = \frac{k_{E,j}^X K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j)\,R_{X,T}}{\left[1 + K_{X,j}^{-1}(G_j) + K_{X,j}^{-1}\tau_{X,j}^{-1}(G_j) + \sum_{i=1,j}^{\mathcal{N}} \left[K_{X,i}^{-1}(G_i) + K_{X,i}^{-1}\tau_{X,i}^{-1}(G_i) \right] \right]}$$

$$\xrightarrow[K_j^{-1}\tau_j^{-1}]{\text{rearrange}} r_{X,j} = k_{E,j}^X R_{X,T} \left[\frac{G_j}{K_{X,j}\tau_{X,j} + \tau_{X,j}(G_j) + G_j + \underbrace{\sum_{i=1,j}^{\mathcal{N}} \left[\frac{\tau_{X,j}K_{X,j}}{K_{X,i}} G_i + \frac{\tau_{X,j}K_{X,j}}{\tau_{X,i}K_{X,i}} G_i \right]}} \right]$$

$\hookrightarrow$ summation term $= \sum_{i=1,j}^{\mathcal{N}} \left[\frac{\tau_{X,j}K_{X,j}}{K_{X,i}\tau_{X,i}} G_i (\tau_{X,i} + 1) \right]$

rearrange, apply definition of ε $\longrightarrow$

$$\left[\frac{G_j}{\ } \right]$$

$\hookrightarrow$ summation term $= \sum_{i=1,j} \left[\frac{\tau_{x,j} K_{x,j}}{K_{x,i} \tau_{x,i}} G_i (\tau_{x,i} + 1) \right]$

$\xrightarrow{\text{rearrange, apply definition of } \mathcal{E}}$ $$\boxed{r_{x,j} = k^{x}_{E,j} R_{x,T} \left[\frac{G_j}{K_{x,j}\tau_{x,j} + G_j(\tau_{x,j}+1) + \mathcal{E}_j} \right]}$$ Q.E.D.

Part 6

Expression of gene j in an N gene system approaches the single-gene model when $K_{x,j}\tau_{x,j} + G_j(\tau_{x,j}+1) + \mathcal{E}_j \longrightarrow K_{x,j}\tau_{x,j} + G_j(\tau_{x,j}+1)$, which occurs when:

- $G_j >> G_i$ for all $i \neq j$, This is true if gene j is expressed on a high copy number plasmid and genes i have only individual genomic copies.

- $\tau_{x,j} K_{x,j} << K_{x,i} \tau_{x,i}$ for all $i \neq j$. $\tau_{x,j}$ is small when $k_{I,j}$ is high (conversion from closed to open conformation is fast), and $K_{x,j}$ is small when $k_{+,j}$ is high (polymerase binding gene j is fast). This could occur if RNA polymerase binds the gene j promoter much more strongly than the promoters of genes i.