(a) Sneha Kabaria

$$G_p + R_x \underset{k_-}{\overset{k_+}{\rightleftharpoons}} (G_p : R_x)_C$$

$$(G_p : R_x)_C \xrightarrow{k_I} (G_p : R_x)_O$$

$$(G_p : R_x)_O \xrightarrow{k_A} R_x + G_p$$

$$(G_p : R_x)_O \xrightarrow{k_{E,j}} m_p + R_x + G_p$$

$r_{x,j} = k_{E,j} (G_j : R_x)_O$, $\hat{r}_{x,j} = r_{x,j} \cdot u(I)$

Material Balances

(closed complex) $\frac{d}{dt}(G_j : R_x)_C = k_+ (G_j)(R_x) - k_- (G_p : R_x)_C - k_I (G_j : R_x)_C = 0$ (1)

(open complex) $\frac{d}{dt}(G_j : R_x)_O = k_I (G_j : R_x)_C - k_A (G_j : R_x)_O - k_{E,j} (G_j : R_x)_O = 0$ (2)

↑ Assume steady-state

RNAP $R_{x,T} = R_x + (G_j : R_x)_C + (G_j : R_x)_O$ (3)

Solve (1) and (2)

$$(G_j : R_x)_C \simeq \left(\frac{k_+}{k_- + k_I}\right)(G_j)(R_x) \quad (4)$$

$$(G_j : R_x)_O \simeq \left(\frac{k_I}{k_A + k_E}\right)(G_j : R_x)_C \quad (5)$$

$$K_{x,j}^{-1} = \left(\frac{k_+}{k_- + k_I}\right)$$

$$\tau_{x,j}^{-1} = \left(\frac{k_I}{k_A + k_E}\right)$$

$$(G_j : R_x)_O = \left(K_{x,j}^{-1}\right)(G_j)(R_x)(\tau_{x,j})$$

$$R_x = \frac{R_{x,T}(\tau_{x,j} K_{x,j})}{\tau_{x,j} K_{x,j} + (\tau_{x,j} + 1) G_j}$$

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

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

gives:

a. Constants

(see constants pdf for citations)

$k_{E,j} = e_x L^{-1} = \frac{42 \text{ nt/s}}{3075 \text{ nt}} = .0135 \ s^{-1}$

$R_{x,T} = 30 \times 10^{-6} \ mM$

$G_j = \frac{2500 \text{ copies}}{\text{cell}} \times \frac{\text{mol}}{6.02 \times 10^{23} \text{ copies}} \times \frac{\text{cell}}{6.7 \times 10^{-13} L} = 3093.3 \ mM$

$k_I = .024 \ s^{-1}$

$K_{E,j} = \left(\frac{k_- + k_I}{k_+} \right) = k_I \underbrace{\left(\frac{k_- + k_I}{k_I \ k_+} \right)}_{\text{McClure}} = 2.49 \times 10^{-5} \ mM$ (Julia)

$\tau_{x,j} = \frac{t_{E,j}}{k_I + k_A} = \frac{k_{E,j}}{k_I} \overset{\text{slope}}{=} .569 \ s$ (Julia)

Assume $k_A << k_{E,j}$

$k_A << k_I$

Now that we have R_x we can get the

(b) $\tau = .5691$

since $\tau = \frac{k_{E,I}}{k_I} < 1$

$\tau \Rightarrow$ **elongation limited**

(c) $\frac{dm_j}{dt} = \sum_{k=1}^{R} \sigma_{jk} r_k - m_j \beta^{-1} \dot{\beta}$

$\sigma_{jk} r_k$: rates of production and degradation

$m_j \beta^{-1} \dot{\beta}$: dilution volume change

mRNA balance $\frac{dm_j}{dt} = r_{x,j} u_j - k^d_{x,j} m_j - m_j \beta^{-1} \dot{\beta} = 0$ @ steady state

($r_{x,j} u_j$: transcription; $k^d_{x,j} m_j$: degradation; $m_j \beta^{-1} \dot{\beta}$: dilution)

[mRNA] $m_j = \frac{r_{x,j} u_j}{k^d_{x,j} + \beta^{-1} \dot{\beta}}$

u(I) $u_j(I) = \frac{w_1 + w_2 f_I}{1 + w_1 + w_2 f_I}$

fraction $f_I = \frac{I^n}{K + I^n}$

dilution $\beta^{-1} \dot{\beta} = \frac{1}{30 \text{ min}} \cdot \left(\frac{\text{min}}{60 \text{ s}}\right) = .005 s^{-1}$

($\beta^{-1} \dot{\beta}$: specific growth rate)

$k^d_{x,j} = \frac{.693}{\text{half-life}} = \frac{.693}{5(60s)} = .0023 s^{-1}$ (assuming 1st order)

all in Julia (constants given in problem) or constants document