5440 Problem 3

a)

$$\frac{dm_i}{dt} = r_{x,i}\, u_i - (\mu + \theta_{m,i}) \bar{m}_i \quad (1)$$

$$\frac{d p_i}{dt} = r_{L,i}\, w_i - (\mu + \theta_{p,i}) p_i \quad (2)$$

@ s.s. $\frac{d}{dt} = 0$ ∴ from (1)

$$(\mu + \theta_{m_i}) m_i^* = r_{x_i} \bar{u}_i$$

$$m_i^* = \frac{r_{x_i}}{\mu + \theta_{m_i}} \bar{u}_i = K_x \bar{u}_i$$

and from (2)

$$p_i^* (\mu + \theta_{p,i}) = r_{L_i} w_i$$

$$r_{L_i} = K^L_{E,i} R_{LT} \left(\frac{m_i}{\nu \tau_{L,i} K_{L,i} + (\nu \tau_{L,i} + 1) m_i} \right)$$

∴ @ s.s.

$$r_{L_i} = K^L_{E,i} R_{LT} \left(\frac{K_x \bar{u}_i}{\nu \tau_{L_i} K_{L_i} + (\nu \tau_{L_i} + 1) K_x \bar{u}_i} \right)$$

∴

$$p_i^* = \frac{w_i}{\mu + \theta_{p_i}} \left(K^L_{E_i} R_{LT} \right) \left(\frac{K_x \bar{u}_i}{\nu \tau_{L_i} K_{L,i} + (\nu \tau_{L,i} + 1) K_x \bar{u}_i} \right)$$

$$p_i^* = \left[\left(\frac{K^L_{E_i} R_{LT}}{\mu + \theta_{p,i}} \right) \left(\frac{1}{\nu \tau_{L_i} K_{L_i} + (\nu \tau_{L,i} + 1) K_x \bar{u}_i} \right) \right] (K_x)(\bar{u}_i)(w_i)$$

↓

3 a) continued

$$p_i^* = \left[\left(\frac{K_{E_i}^L R_{LT}}{\mu + \theta_{p,i}}\right)\left(\frac{1}{\tau_{L,i} K_{L,i} + (\tau_{L,i}+1) K_X \bar{\mu}}\right)\right](K_X)(\bar{u}_i)(w_i)$$

by assumption #7 $\tau_{L,i} K_{L,i} \gg (\tau_{L,i}+1) K_X \bar{\mu}$

$\therefore$

$$\boxed{p_i^* = \underbrace{\left[\left(\frac{K_{E_i}^L R_{LT}}{\mu + \theta_{p,i}}\right)\left(\frac{1}{\tau_{L,i} K_{L,i}}\right)\right]}_{= K_L} (K_X)(\bar{u}_i)(w_i) \qquad p_i^* = K_L K_X \bar{u}_i w_i}$$

3B K_X from Prelim 1 solutions $= \dfrac{\left(93 \frac{mRNA}{cell}\right)\left(\frac{10^9 \text{ nmol/mol}}{6.022 \cdot 10^{23} \frac{mRNA}{mol}}\right)}{(1-70\%_{water})\left(4.3 \cdot 10^{-13} \frac{g}{cell}\right)} = 1.197 \frac{nmol}{gdw}$

given $w_i = 1$

$\bar{u}_i$ from Prelim 1 $= \dfrac{w_1 + w_2 f_I}{1 + w_1 + w_2 f_I}$, from Prelim 1 Solns. $w_1 = 0.25$, $w_2 = 98.75$

f_I from Prelim 1 $= \dfrac{I^n}{K_d^n + I^n}$, from Prelim 1 Solns. $n = 1.85$, $K_d = 9 \cdot 10^{-2}\ mM$ $\hookrightarrow K_d = 9 \cdot 10^{-5}\ nM$

$\therefore$

Translation Elongation — Translation Total Ribosomes

$$p_i^* = \left[\left(\frac{K_{E_i}^L R_{LT}}{\mu + \theta_{p,i}}\right)\left(\frac{1}{\tau_{L,i} K_{L,i}}\right)\right]\left(1.197 \frac{nmol}{gdw}\right)\left(\frac{0.25 + 98.75\left(\frac{I^{1.85}}{(9 \cdot 10^{-5}_{nM})^{1.85} + I^{1.85}}\right)}{1 + 0.25 + 98.75\left(\frac{I^{1.85}}{(9 \cdot 10^{-5}_{nM})^{1.85} + I^{1.85}}\right)}\right)(1)$$

dilution factor — Protein degradation — Translation time constant — Translation saturation constant

3 B continued

$$\text{Translation Elongation}: K_{E_i}^{L} = \left(\begin{matrix}\text{Translation}\\ \text{elongation}\\ \text{rate}\end{matrix}\right)\left(\frac{1}{\underbrace{\text{Protein length}}_{300aa}}\right) = \left(\overbrace{16.5\frac{aa}{sec}}^{\text{from PS2}}\right)\left(\overbrace{\frac{1}{300\ aa}}^{\text{from Part B}}\right) = 0.055\ sec^{-1}$$

$$\text{Translation TOTAL Ribosome?}: R_{LT} = (2.3\ \mu mol) \text{ - from PS2}$$

$$\text{dilution factor}: \mu = \frac{\log(2)}{\tau_D} = \frac{0.301}{\frac{40min}{60min/Hr}} = \underline{0.4515\ Hr^{-1}}$$

τ_D - doubling time; from assumption 1

$$\text{Protein degradation}: \theta_{P_i} = \frac{\log(\frac{1}{2})}{P_i\ \text{half life}} = \frac{\log(\frac{1}{2})}{24\ Hrs} = \underline{-0.012543\ Hr^{-1}}$$

from assumption 6

$$\text{Translation time constant}: \tau_{L,i} \approx \frac{K_E^L}{K_I} = \frac{0.055\ sec^{-1}}{\left(\frac{1}{1.5sec}\right)} = 0.0825 \quad \underline{\text{unitless}}$$

assumes $K_A << K_I, K_E^L$

translation initiation time from assumption 8.

$$\text{Translation saturation constant}: K_{L,i} = 200\ \mu M$$

from assumption 10

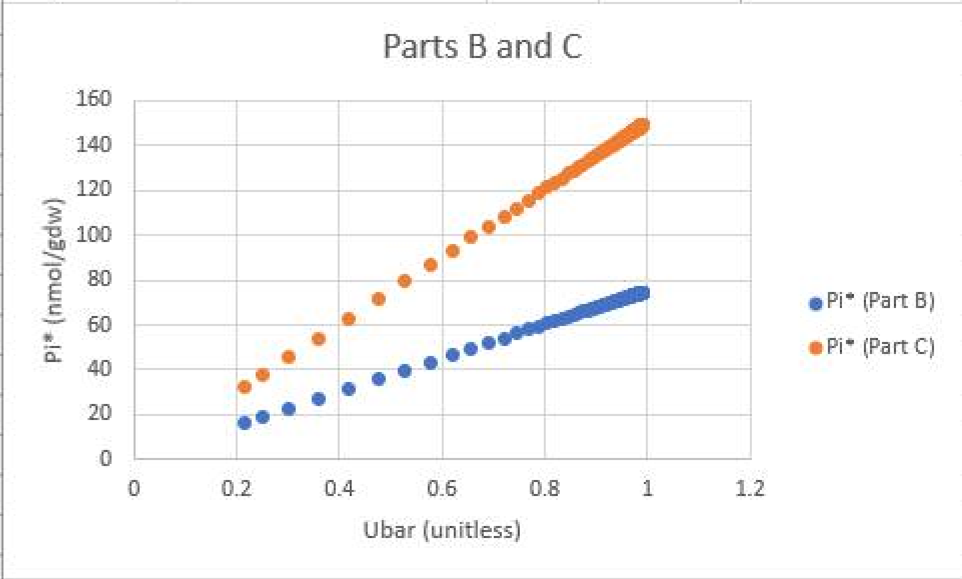
$$V_i^{max} = \left(\frac{\text{Translation elongation rate}}{\text{Protein length}}\right)\left(\begin{matrix}\text{ribosome}\\ \text{concentration}\end{matrix}\right)$$

$\therefore$

$$K_L = \left[\left(\frac{\left(\frac{16.5}{300}\ sec^{-1}\right)\left(\frac{3600\ sec}{Hr}\right)(2.3\ \mu mol)}{0.4515\ Hr^{-1} + (-0.012543\ Hr^{-1})}\right)\left(\frac{1}{(\underbrace{0.0825}_{\text{unitless}})(200\ \mu M)}\right)\right]$$

$$\therefore \boxed{K_L = 62.88\ \text{unitless}}$$

Parameter Table	Value	Units	Source
Kl	62.88	unitless	Calculated on paper in my written part of 3B of this problem
Kx	1.197	nmol/gdw	gain from prelim Q1
Wi	1	unitless	Given in problem statement
n	1.85	unitless	Parameter from Prelim Q1
Kd	0.09	mmol	Parameter from Prelim Q1
W1	0.25	unitless	Parameter from Prelim Q1
W2	98.75	unitless	Parameter from Prelim Q1
KEL (Translation elongation constant)	0.055	sec^-1	From PS2/ and the problem statement of part B
RLT	2.3	micro-M	From PS2
mu (dilution factor)	0.301	hours^-1	From assumption 1 and some math shown on paper
Protein degregation thetaP	-0.0125	hours^-1	From assumption 6 and some math shown on paper
Translation time constant TauL	0.0825	unitless	From assumption 8 and using KEL
Translation saturation constant KLi	200	micro-M	from assumption 10
Polysome amplification constant	2		



Thus, it is clear to see when the polysome amplification constant is greater than 1 the curve moves up as a function of Ubar.

Explanation:
Mathematically: the polysomal constant simply multiplies the slope by its value, thus if it is greater than 1 the slope increases and the value of every point increases.

Physically: I would guess that a polysomal amplification constant greater than one means that more than 1 ribosome is working on translation at any one point, thus the sequence is read faster and the protein produced faster, ergo steeper slope.