1. (a)

$$R_{x,T} = R_x^0 + (G_j:R_x)_c + (G_j:R_x)_o + \sum_{i=1,j}^{N}\left\{(G_i:R_x)_c + (G_i:R_x)_o\right\} \quad -(1)$$

$$\frac{d}{dt}(G_j:R_x)_c = k_+(G_j)(R_x) - k_-(G_j:R_x)_c - k_I(G_j:R_x)_c$$

$$\frac{d}{dt}(G_j:R_x)_o = k_I(G_j:R_x)_c - k_A(G_j:R_x)_o - k_{E,j}(G_j:R_x)_o$$

at s.s.

$$(G_j:R_x)_c \simeq \left(\frac{k_+}{k_-+k_I}\right)(G_j)(R_x) \quad -(2)$$

$$(G_j:R_x)_o \simeq \left(\frac{k_I}{k_A+k_E}\right)(G_j:R_x)_c = \underbrace{\left(\frac{k_I}{k_A+k_E}\right)}_{=\tau^{-1}_{x,j}}\underbrace{\left(\frac{k_+}{k_-+k_I}\right)}_{=K^{-1}_{x,j}}(G_j)(R_x) \quad -(3)$$

plug (2) & (3) into (1)

$$\Rightarrow R_{x,T} = R_x^0 + K^{-1}_{x,j}(G_j)(R_x) + \tau^{-1}_{x,j}K^{-1}_{x,j}(G_j)(R_x) + \sum_{i=1,j}^{N}\left\{(G_i:R_x)_c + (G_i:R_x)_o\right\} \quad -(4)$$

at s.s.

$$\sum_{i=1,j}^{N}(G_i:R_x)_c \simeq \sum_{i=1,j}^{N}\underbrace{\left(\frac{k_+}{k_-+k_I}\right)}G_i R_x$$

$$\sum_{i=1,j}^{N}(G_i:R_x)_o \simeq \left(\frac{k_I}{k_A+k_E}\right)\sum_{i=1,j}^{N}(G_i:R_x)_c = \sum_{i=1,j}^{N}\left(\frac{k_+}{k_-+k_I}\right)\left(\frac{k_I}{k_A+k_E}\right)G_i R_x$$

$$\Rightarrow (4) \Rightarrow R_{x,T} = R_x + K^{-1}_{x,j}(G_j)(R_x) + \tau^{-1}_{x,j}K^{-1}_{x,j}(G_j)(R_x) + \sum_{i=1,j}^{N}\left(K^{-1}_{x,i}G_iR_x + K^{-1}_{x,i}\tau^{-1}_{x,i}G_iR_x\right)$$

$$\therefore R_x = \frac{R_{x,T}}{1 + K^{-1}_{x,j}G_j + K^{-1}_{x,j}\tau^{-1}_{x,j}G_j + \sum_{i=1,j}^{N}\left[G_iK^{-1}_{x,i} + G_i\tau^{-1}_{x,i}K^{-1}_{x,i}\right]}$$

plug into $(G_j:R_x)_o$

$$\Rightarrow (G_j:R_x)_o = K^{-1}_{x,j}(\tau^{-1}_{x,j})G_jR_x \xRightarrow{\times\frac{K_{x,j}\tau_{x,j}}{K_{x,j}\tau_{x,j}}} \frac{R_{x,T}G_j}{K_{x,j}\tau_{x,j} + (\tau_{x,j}+1)G_j + K_{x,j}\tau_{x,j}\left[\sum_{i=1,j}^{N}\left(G_iK^{-1}_{x,i} + G_i\tau^{-1}_{x,i}K^{-1}_{x,i}\right)\right]}$$

$$= \frac{R_{X,T}\, G_j}{K_{X,j}\tau_{X,j} + (\tau_{X,j}+1)G_j + \sum_{i=1,j}^{N} \frac{K_{X,j}\tau_{X,j}}{K_{X,i}\tau_{X,i}} G_i(1+\tau_{X,i})}$$

$$= \frac{R_{X,T}\, G_j}{K_{X,j}\tau_{X,j} + (\tau_{X,j}+1)G_j + \varepsilon_j} \quad \text{where } \varepsilon_j = \sum_{i=1,j}^{N} \frac{K_{X,j}\tau_{X,j}}{K_{X,i}\tau_{X,i}} G_i(1+\tau_{X,i})$$

since $r_{X,j} = k_{E,j}(G_j : R_X)_0$

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

#.

(b)

if N-gene system can be approximately equivalent to the 1-gene system

$\Rightarrow$ means that ε_j should be very small that can be neglected

$\therefore$ ε_j should be relatively small then $(1+\tau_{X,j})G_j$ and $\tau_{X,j} K_{X,j}$

In this way, we can neglect ε_j and regard it as a 1-gene system.

3.

(a) From Table 1 in the reference,

$S =$

	v_1	v_2	v_3	v_4	v_5	v_6	b_1	b_2	b_3	b_4	b_5	b_6	b_7	b_8	b_9
G	-1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
RNAP	-1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
G^*	1	-1	0	0	0	0	0	0	0	0	0	0	0	0	0
NTP	0	-n	0	0	0	0	0	1	0	0	0	0	0	0	0
mRNA	0	1	-1	-1	1	0	0	0	0	0	0	0	0	0	0
Pi	0	2n	0	0	2a	2	0	0	0	0	0	0	0	0	-1
NMP	0	0	n	0	0	0	0	0	0	-1	0	0	0	0	0
rib	0	0	0	-1	1	0	0	0	0	0	0	0	0	0	0
rib^*	0	0	0	1	-1	0	0	0	0	0	0	0	0	0	0
AAtRNA	0	0	0	0	a	1	0	0	0	0	0	0	0	0	0
GTP	0	0	0	0	-2a	0	0	0	0	0	0	0	1	0	0
tRNA	0	0	0	0	a	-1	0	0	0	0	0	0	0	0	0
GDP	0	0	0	0	2a	0	0	0	0	0	0	0	0	-1	0
protein	0	0	0	0	1	0	0	0	-1	0	0	0	0	0	0
AA	0	0	0	0	0	-1	1	0	0	0	0	0	0	0	0
ATP	0	0	0	0	0	-1	0	0	0	0	1	0	0	0	0
AMP	0	0	0	0	0	1	0	0	0	0	0	-1	0	0	0

$$r_{x,j} = \underbrace{k_E}_{=\frac{\dot v_x}{l_G} = \frac{60}{924}} \overset{0.15\,\mu M}{R_X} \left(\frac{\overset{5nM = 5\times10^{-3}\,\mu M}{G_j}}{\underbrace{I_x}_{2.7} \underbrace{K_X}_{0.3\,\mu M} + (I_x+1)G_j} \right) = 5.87\times10^{-5}\ \frac{\mu M}{s}$$

$$\hat r_{x,j} = r_{x,j}\, u_j = r_{x,j} \frac{W_1 + W_2 f_I}{1 + W_1 + W_2 f_I}, \quad \text{where } f_I = \frac{I^n}{K^n + I^n}$$

$$r_{L,j} = \underbrace{\frac{\dot{V}_L}{\ell_p}}_{\frac{16.5}{308}\,s^{-1}} \underbrace{R_L}_{1.6\,\mu M} \left(\frac{m_j}{\underbrace{\tau_L}_{0.8} \underbrace{K_L}_{57} + (\tau_L + 1)\, m_j} \right)$$

mRNA conc.

from s.s of transcription:

$$\cancel{\frac{dm_j}{dt}}^{\,0} = r_{x,j}\, u_j - \underbrace{k^d_{x,j}}_{8.35/60\,s^{-1}} m_j - \cancel{m_j B^{-1} \dot{B}}$$

neglect dilution ∵ small

$$m_j = \frac{5.87 \times 10^{-5}\, u}{8.35/60} = 4.223 \times 10^{-4}\, u\, \mu M$$

$$\Rightarrow \therefore r_{L,j} = 0.08571 \times \left(\frac{4.223 \times 10^{-4}\, u}{45.6 + 1.8 \times 4.223 \times 10^{-4}\, u} \right) \frac{\mu M}{s}$$

$$\hat{r}_{L,j} = r_{L,j} \cdot w_j = r_{L,j} \quad (w_j = 1 \text{ at kinetic limit})$$

(b) protein balance:

$$\cancel{\frac{dp_j}{dt}}^{\,0\ (\because s.s.)} = \underbrace{r_{L,j}\, w_j}_{\text{from (a)}} - \underbrace{k^d_{L,j}}_{9.9 \times 10^{-3}/60\ s^{-1}} p_j - \cancel{p_j B^{-1} \dot{B}}$$

neglect

$$\Rightarrow p_j = \frac{0.08571 \times \left(\frac{4.223 \times 10^{-4}\, u}{45.6 + 1.8 \times 4.223 \times 10^{-4}\, u} \right)}{9.9 \times 10^{-3}/60} \quad \mu M$$

continue on matlab for the plot.

(c)

The concept of shadow price:

How much more profit you would get by increasing the amount of that resource by one unit.

⇒ By changing the bound of exchange flux, which one of the fluxes will affect the translation rate most?

⇒ sensitivity

∴ if I increase 1 unit of exchange fluxes,

for GTP, it'll cause an increase of $1/2a$ for translation rate.

for GPP, and Pi, there's also an increase of $1/2a$

but for protein, there's an increase of 1,

which is higher than others.

⇒ ∴ Protein exchange flux is the translation rate most sensitive to.