20.320 Exam #3

Problem 1

b. $$V\frac{dc_A}{dt} = Q\left(f_A C_{Tin} - C_A\right) + V k_g \frac{S}{k_m} C$$

$$V\frac{dc_N}{dt} = Q\left([1-f_A]C_{Tin} - C_N\right)$$

$$V\frac{dS}{dt} = VR_s - Vk_u(C_A + C_N)S - Q$$

c. $$0 = Q\left([1-f_A]C_{Tin} - C_N\right)$$

$$\Rightarrow C_N = (1-f_A)C_{Tin}$$

d. Assume $f_A <<< 1$.

Then $$0 = -\frac{Q}{V}C_A + k_g\frac{S}{K_m}C_A$$

$$\Rightarrow \frac{S}{K_m} = \frac{(Q/V)}{k_g}$$

So $$0 = R_s - k_u(C_A + C_N)\frac{(Q/V)K_m}{k_g} - (Q/V)^2\frac{K_m}{k_g}$$

$$\Rightarrow C_A = \frac{(R_s/K_m)k_g}{k_u(Q/V)} - \frac{(Q/V)}{k_u} - C_{Tin}$$

$$\therefore\ Q C_A = Q \left\{ \frac{(R_s/K_m) k_g}{k_u (Q/V)} - \frac{(Q/V)}{k_u} - C_{T in} \right\}$$

e. The general Monod equation for cell growth is

$$\mu(S) = \frac{k_g S}{K_m + S}$$

This reduces to the expression used here if $S < K_m$. Thus, we might surmise that the lymph node cytokine concentration is likely less than 10^{-9} M in order for this expression to be valid.

Problem 2

b. $$\frac{dR}{dt} = V_R - k_f L R - k_{eR} R$$

$$\frac{dC}{dt} = k_f L R - k_{eC} C$$

$$\frac{dm}{dt} = k_{t_1} g (1 + \beta C) - k_{h_1} m$$

now, since the rate of new receptor synthesis depends on translation of receptor mRNA, we can write $V_R = k_{t_2} m - k_{h_2} R$

Note: OR, the $-k_{h_2} R$ term can b neglected if it is assum that receptor degradation is mainly via endocytosis

c. $L = 0 \qquad 0 = V_R - k_{eR} R$

$$\Rightarrow \quad R = \frac{V_R}{k_{eR}}$$

now $V_R = k_{t_2} m - k_{h_2} R$

and $$m = \frac{k_{t_1} g}{k_{h_1}}$$

so $$V_R = \frac{k_{t_2} k_{t_1} g}{k_{h_1}} - k_{h_2} R$$

So, $$k_{eR} R = \frac{k_{t_2} k_{t_1} g}{k_{h_1}} - k_{h_2} R$$

$$\therefore \quad R = \frac{k_{t_2} k_{t_1} g}{k_{h_1}(k_{eR} + k_{h_2})} \equiv R_0$$

d. $L = L_0$

$$0 = V_R - k_f L_0 R - k_{eR} R$$

$$= \frac{k_{t_2} k_{t_1} g}{k_{h_1}} (1 + \beta C) - k_{h_2} R - k_f L_0 R - k_{eR} R$$

$$\Longrightarrow \frac{k_{t_2} k_{t_1} g}{k_{h_1}} (1 + \beta C) = (k_f L_0 + k_{eR} + k_{h_2}) R$$

Also, $0 = k_f L_0 R - k_{ec} C$

$$\Longrightarrow k_f L_0 R = k_{ec} C$$

So $\dfrac{k_{t_2} k_{t_1} g}{k_{h_1}} (1 + \beta C) = (k_f L_0 + k_{eR} + k_{h_2}) \dfrac{k_{ec}}{k_f L_0}$

$$\therefore \quad C = \frac{[k_{t_2} k_{t_1} g / k_{h_1}]}{(k_f L_0 + k_{eR} + k_{h_2}) \frac{k_{ec}}{k_f L_0} - \beta \left[\frac{k_{t_2} k_{t_1} g}{k_{h_1}} \right]}$$

So $\quad R + C = \left(1 + \frac{k_{ec}}{k_f L_0}\right) C$

$$= \frac{\left(1 + \frac{k_{ec}}{k_f L_0}\right)\left(\frac{k_{t_2} k_{t_1} g}{k_{h_1}}\right)}{\left(k_f L_0 + k_{eR} + k_{h_2}\right)\left(\frac{k_{eC}}{k_f L_0}\right) - \beta\left(\frac{k_{t_2} k_{t_1} g}{k_{h_1}}\right)} \equiv (R+C$$

$$\frac{(R+C)_{L_0}}{R_0} = \frac{\left(1 + \frac{k_{ec}}{k_f L_0}\right)\left(k_{eR} + k_{h_2}\right)}{\left(k_f L_0 + k_{eR} + k_{h_2}\right)\left(\frac{k_{ec}}{k_f L_0}\right) - \beta\left(\frac{k_{t_2} k_{t_1} g}{k_{h_1}}\right)}$$

< 1 for net down-regulation

> 1 for net upregulation

Note: if $k_{h_2} = 0$ is assumed (see Note on pg 3)

then

$$\frac{(R+C)_{L_0}}{R_0} = \frac{\left(1 + \frac{k_{ec}}{k_f L_0}\right) k_{eR}}{\left(k_f L_0 + k_{eR}\right)\left(\frac{k_{ec}}{k_f L_0}\right) - \beta\left(\frac{k_{t_2} k_{t_1}}{k_{h_1}}\right.}$$

If the $\beta = 0$ option was chosen, then

$$\frac{(R+C)_{L_0}}{R_0} = \frac{\left(1 + \frac{k_{ec}}{k_f L_0}\right) k_{eR}}{\left(k_f L_0 + k_{eR}\right)\left(\frac{k_{ec}}{k_f L_0}\right)} \quad \begin{matrix} < \\ \text{or} \\ > \end{matrix}$$

e. The receptor mRNA level can be increased by the R/L signaling, and if the net effect of the transcription and endocytotic processes is downregulation then the protein level would actually be decreased.