Problem set 8 Solutions

BE.320 Spring 2006

(1) x = luciferase mRNA $\frac{dx}{dt} = k_1\sigma g - k_2 x$

y = luciferase protein $\frac{dy}{dt} = k_3 x - k_4 y$

$k_1$ ≡ transcription rate constant
$k_2$ ≡ message degradation rate
$k_3$ ≡ translation rate constant
$k_4$ ≡ protein degradation rate

$\sigma$ = promoter strength coefficient  g = luciferase gene copy number

steady state at t = 8 hours:

$$\frac{dx}{dt} = 0 = k_1\sigma g - k_2 x \Rightarrow x_{ss} = \frac{k\sigma g}{k_2} = 100 \text{ messages per cell}, \; g = 8$$

$$\frac{k_1\sigma}{k_2} = 12.5$$

$$\frac{dy}{dt} = 0 = k_3 x - k_4 y \Rightarrow \frac{k_3}{k_4} = \frac{y_{ss}}{x_{ss}} = \frac{10{,}000}{100} = 100 \Rightarrow y_{ss} = \frac{k_3}{k_4} x_{ss}$$

To find $k_1, k_2, k_3, k_4, \sigma$: Approach: integrate to get expressions for x(t) and y(t), then use our initial conditions and 8hr/24hr steady state values as boundary conditions to hopefully solve for those 5 parameters

solve for x(t) first: $\frac{dx}{dt} = k_1\sigma g - k_2 x$

take derivative: $\frac{d^2x}{dt^2} = -k_2\frac{dx}{dt} \rightarrow \frac{d^2x}{dt^2} + k_2\frac{dx}{dt} = 0$

characteristic roots: $r^2 + k_2 r = 0 \Rightarrow r(r + k_2) = 0 \Rightarrow r = 0, -k_2$

solution: $x(t) = A + Be^{-k_2 t}$

Initial condition: $x(0) = 0 \Rightarrow A + B = 0$

Boundary condition: at steady state, $x = \frac{k_1\sigma g}{k_2}$ $\left(\frac{dx}{dt} = 0\right)$

steady state is when $t \to \infty$, meaning $Be^{-k_2 t} \to 0$

$$x(t \to \infty) = \frac{k_1\sigma g}{k_2} \Rightarrow A = \frac{k_1\sigma g}{k_2}$$

$$A + B = 0 \Rightarrow B = \frac{-k_1\sigma g}{k_2}$$

solution: $$x(t) = \frac{k_1\sigma g}{k_2} - \frac{k_1\sigma g}{k_2} e^{-k_2 t} = x_{ss} - x_{ss}e^{-k_2 t} = x_{ss}\left(1 - e^{-k_2 t}\right)$$

Now solve for y:

$$\frac{dy}{dt} = \frac{k_3 k_1\sigma g}{k_2} - \frac{k_3 k_1 \sigma g}{k_2} e^{-k_2 t} - k_4 y$$

$$\frac{dy}{dt} + k_4 y = \frac{k_3 k_1 \sigma g}{k_2} - \frac{k_3 k_1 \sigma g}{k_2} e^{-k_2 t} \qquad P(t) = k_4$$
$$Q(t) = \frac{k_3 k_1 \sigma g}{k_2} - \frac{k_3 k_1 \sigma g}{k_2} e^{-k_1 t}$$

integrating factor: $u(t) = e^{\int P(t)dt} = e^{\int k_4 dt} = e^{k_4 t}$

$$u(t) y = \int u(t) Q(t) \Rightarrow \quad e^{k_4 t} y = \int e^{k_4 t} \left( \frac{k_3 k_1 \sigma g}{k_2} - \frac{k_3 k_1 \sigma g}{k_2} e^{-k_2 t} \right) dt$$

$$e^{k_4 t} y = \frac{k_3 k_1 \sigma g}{k_2} \int (e^{k_4 t} - e^{k_4 t} e^{-k_2 t}) dt$$

$$e^{k_4 t} y = \frac{k_3 k_1 \sigma g}{k_2} \left( \frac{1}{k_4} e^{k_4 t} - \frac{1}{k_4 - k_2} e^{(k_4 - k_2)t} + C \right)$$

$$y = \frac{k_3 k_1 \sigma g}{k_2 k_4} - \frac{k_3 k_1 \sigma g}{k_2 (k_4 - k_2)} e^{-k_2 t} + C e^{-k_4 t}$$

find C: initial conditions: $y(0) = 0 \Rightarrow \quad \frac{k_3 k_1 \sigma g}{k_2 k_4} - \frac{k_3 k_1 \sigma g}{(k_4 - k_2) k_2} + C = 0$

$$C = \frac{k_3 k_1 \sigma g}{(k_4 - k_2) k_2} - \frac{k_3 k_1 \sigma g}{k_2 k_4}$$

final solution: $y = \frac{k_3 k_1 \sigma g}{k_2 k_4} - \frac{k_3 k_1 \sigma g}{k_2 (k_4 - k_2)} e^{-k_2 t} + \left( \frac{k_3 k_1 \sigma g}{k_2 (k_4 - k_2)} - \frac{k_3 k_1 \sigma g}{k_2 k_4} \right) e^{-k_4 t}$

$$y = \frac{k_3 k_1 \sigma g}{k_2 k_4} (1 - e^{-k_4 t}) + \frac{k_3 k_1 \sigma g}{k_2 (k_4 - k_2)} (e^{-k_4 t} - e^{-k_2 t})$$

$x_{ss} = \frac{k_1 \sigma g}{k_2} = 100 \qquad y(t) = \frac{k_3}{k_4} x_{ss} (1 - e^{-k_4 t}) + \frac{k_3}{k_4 - k_2} x_{ss} (e^{-k_4 t} - e^{-k_2 t})$

$\frac{k_3}{k_4} = 100 \Rightarrow \frac{k_3}{k_4} = \frac{y_{ss}}{x_{ss}} \Rightarrow x_{ss} = y_{ss} \frac{k_4}{k_3}$

$$y(t) = y_{ss} (1 - e^{-k_4 t}) + \frac{k_4}{k_4 - k_2} y_{ss} (e^{-k_4 t} - e^{-k_2 t})$$

$$x(t) = x_{ss} (1 - e^{-k_2 t})$$

steady state $x(t)$ at 8 hours, assume $\frac{x(t)}{x_{ss}} = 0.99 = 1 - e^{-k_2 t} \Rightarrow \boxed{k_2 = 0.58 \text{ hours}^{-1}}$

$$k_1 \sigma = 12.5 k_2 \Rightarrow \boxed{k_1 \sigma = 7.25 \text{ hours}^{-1}}$$

steady state ~~x~~ $y(t)$ at 24 hours, assume $\frac{y(t)}{y_{ss}} = 0.01$ (almost gone)

$$\frac{y(t)}{y_{ss}} = 1 - e^{-k_4 t} + \frac{k_4}{k_4 - k_2} e^{-k_4 t} - \frac{k_4}{k_4 - k_2} e^{-k_2 t} = 0.01$$

at $t=24$: $$\frac{y(24)}{y_{ss}} = 1 - e^{-k_4 24} + \frac{k_4}{k_4 - 0.58} e^{-k_4 24} - \frac{k_4}{k_4 - 0.58} e^{-0.58t} = 0.01$$

solve for $k_4$ by trial and error:

if $k_4 \simeq k_2$, $\therefore k_4 = 0.5 \Rightarrow \frac{y(24)}{y_{ss}} = 0.999$

$k_4 < k_2$, $\therefore k_4 = 0.01 \Rightarrow \frac{y(24)}{y_{ss}} = 0.1996$

$k_4 \ll k_2$, $\therefore k_4 = 1e^{-3} \Rightarrow \frac{y(24)}{y_{ss}} = 0.022$

$k_4 = 5e^{-4} \Rightarrow \frac{y(24)}{y_{ss}} = 0.011$

$\boxed{k_4 = 5 \times 10^{-4} \text{ hours}^{-1}}$, $\frac{k_3}{k_4} = 100 \Rightarrow \boxed{k_3 = 5 \times 10^{-2} \text{ hours}^{-1}}$

Not possible to determine $k_1$, or separately. We would need an experiment to determine one of these parameters in order to get the other

2. $a C_{16}H_{34} + bO_2 + cNH_3 \longrightarrow C_{4.4}H_{7.3}N_{0.86}O_{2.2} + dCO_2 + eH_2O$

carbon: $16a = 4.4 + d$

hydrogen: $34a + 3c = 7.3 + 2e$ $\qquad RQ = \frac{d}{b} = 0.63 \Rightarrow d = 0.63b$

oxygen: $2b = 2.2 + 2d + e$

nitrogen: $c = 0.86$

$34a + 2.58 = 7.3 + 2e \Rightarrow 34a = 4.72 + 2e$

$2b = 2.2 + 2d + e \Rightarrow 2b = 2.2 + 2(0.63b) + e = 0.74b = 2.2 + e$

$\Rightarrow e = 0.74b - 2.2$

$34a = 4.72 + 2(0.74b - 2.2)$

$34a = 0.32 + 1.48b \Rightarrow 34a = 0.32 + 1.48b$

$16a = 4.4 + 0.63b \Rightarrow 34a = 9.35 + 1.338756$

Final stoichiometries:

$b = 63.93, \; a = 2.79$

$d = 0.63b = 40.27$

$e = 45.1076$

$$\boxed{2.79 C_{16}H_{34} + 63.93O_2 + 0.86 NH_3 \longrightarrow C_{4.4}H_{7.3}N_{0.86}O_{2.2} + 40.27CO_2 + 45.1H_2O}$$

$$Y_S = \frac{\text{cell mass}}{\text{substrate mass}} = \frac{4.4\times12 + 7.3\times1 + 0.86\times14 + 2.2\times16}{2.79(16\times12 + 34\times1)} = \frac{107.34 \text{ g}_{cell}/\text{mol}}{2.79 \text{ mol}(226 \text{ g}_{sub}/\text{mol})} = \boxed{0.17 \frac{\text{g cell}}{\text{g sub}}}$$

$$\frac{1}{Y_H} = \frac{\Delta H_S}{Y_S} - \Delta H_c, \quad \Delta H_c = 6 \frac{\text{kcal}}{\text{g}} \qquad \Delta H_S = 11.3 \frac{\text{kcal}}{\text{g}}$$ (used website for hexadecane)

$$\frac{1}{Y_H} = \frac{11.3 \frac{\text{kcal}}{\text{g sub}}}{0.17 \frac{\text{g cell}}{\text{g sub}}} - 6\frac{\text{kcal}}{\text{g cell}} \quad 60.47 \frac{\text{kcal}}{\text{g cell}} \Rightarrow \boxed{Y_H = 0.0165 \frac{\text{g cell}}{\text{kcal}}} \Rightarrow \frac{Y_H}{Y_S} = 10.3 \frac{\text{kcal}}{\text{g sub}}$$

Per ton of $C_{16}H_{34}$:

$$1 \text{ metric ton} = 1\times10^6 \text{ g} \Rightarrow 1\times10^6 \text{ g } C_{16}H_{34} \times \frac{10.3 \text{ kcal}}{\text{g}} = \boxed{1.03\times10^7 \text{ kcal of heat}}$$

How much cooling water would need to be evaporated:

$H_2O$'s latent heat of evaporation = $-2270$ kJ/kg

$$1.03\times10^7 \text{ kcal} \times \frac{4.184 \text{ kJ}}{1 \text{ kcal}} \times \frac{1 \text{ kg}}{2270 \text{ kJ}} \times \frac{1 \text{ L}}{1 \text{ kg}} = \boxed{1.90\times10^4 \text{ L of water}}$$

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%pset8_matlab_solution

rho = 10^10;
Nav = 6.022e23;

Rs0=2e3; Cs0=3e3; Ri0=3e3; Ci0=3e3; Li0=3e-9;
%if you want to convert Li0 from M to #/cell:
Li0 = (Nav/rho) * 3e-9;
%but this is not really necessary since this is an inital GUESS not an initial condition
%and since we know that even a bad initial guess will be okay in this problem,
%the units are not too important.

%initial guess
Y0=[Rs0 Cs0 Ri0 Ci0 Li0];

solution = fsolve(@trafficking_dynamics,Y0);

'part a'
Rs=solution(1)
Cs=solution(2)
Ri=solution(3)
Ci=solution(4)
Li=solution(5)

Y0 = ones(1,5);
solution = fsolve(@trafficking_dynamics,Y0);

'part b'
Rs=solution(1)
Cs=solution(2)
Ri=solution(3)
Ci=solution(4)
Li=solution(5)
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%function to solve
function F = trafficking_dynamics(X)
%we will return the steady-state values of Rs, Cs, Ri, Ci, Li

%X is the initial guess:
Rs = X(1);
Cs = X(2);
Ri = X(3);
Ci = X(4);
Li = X(5);

%these are mostly from L&L chapter 3
L = 1e-9; %M , constant
rho = 10^10; %cells/L, constant
Nav = 6.022e23; %#/mol, constant
%all of these rates are also per cell
kf = 7.2e7; %M^-1 min^-1
kr = 3.4e-1; %min^-1
VR = 1.3e2; %#/min
keR = 3.0e-2; %min^-1
keC = 1e-1; %min^-1
kxR = 5.8e-2; %min^-1
kxC = 5.3e-2; %min^-1
kh = 1e-1; %min^-1
kfprime = 2e6; %M^-1 min^-1
krprime = 1.2e-2; %min^-1
kxL = 1e-2; %min^-1
kfp = 4e-14; %min^-1

L = (Nav/rho) * 1e-9;

%dRs/dt = 0 (#/cell*time), same for all further rates
F(1) = VR - (kf*L*Rs*(rho/Nav) - kr*Cs) - keR*Rs + kxR*Ri;
%dCs/dt = 0
F(2) = kf*L*Rs*(rho/Nav) - kr*Cs - keC*Cs + keC*Ci;
%dRi/dt = 0
F(3) = keR*Rs - kxR*Ri - kh*Ri - (kfprime*Li*Ri*(rho/Nav) - krprime*Ci);
%dCi/dt = 0
F(4) = keC*Cs - kxC*Ci - kh*Ci + kfprime*Li*Ri*(rho/Nav) - krprime*Ci;
%dLi/dt = 0
F(5) = krprime*Ci - kfprime*Li*Ri*(rho/Nav) - kh*Li - kxL*Li + kfp*L;
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