Glucose Utilization using Labeled Deoxyglucose

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Given Equations

$$\frac{dC_e}{dt} = k_1 C_p - \left(k_2 + k_3\right) C_e + k_4 C_m$$

$$\frac{dC_m}{dt} = k_3 C_e - k_4 C_m$$

Take the Laplace Transform of both

$$L\left[\frac{dC_e}{dt}\right] = L\left[k_1 C_p - \left(k_2 + k_3\right) C_e + k_4 C_m\right]$$

$$L\left[\frac{dC_m}{dt}\right] = L\left[k_3 C_e - k_4 C_m\right]$$

$$s * \bar{C}_e(s) = k_1 \bar{C}_p(s) - (k_2 + k_3)\bar{C}_e(s) + k_4 \bar{C}_m(s)$$

$$s * \bar{C}_m(s) = k_3 \bar{C}_e(s) - k_4 \bar{C}_m(s)$$

Rearrange the result

$$(s + k_2 + k_3)\bar{C}_e(s) - k_4 \bar{C}_m(s) = k_1 \bar{C}_p(s)$$

$$-k_3 \bar{C}_e(s) + (s + k_4)\bar{C}_m(s) = 0$$

$$\begin{bmatrix} s + k_2 + k_3 & -k_4 \\ -k_3 & s + k_4 \end{bmatrix} \begin{bmatrix} \bar{C}_e(s) \\ \bar{C}_m(s) \end{bmatrix} = \begin{bmatrix} k_1 \bar{C}_p(s) \\ 0 \end{bmatrix}$$

Use Cramer's Rule

$$\det\begin{bmatrix} s+k_2+k_3 & -k_4 \\ -k_3 & s+k_4 \end{bmatrix} = (s+k_2+k_3)(s+k_4)-k_3k_4 = s^2+sk_2+sk_3+sk_4+k_2k_4+k_3k_4-k_3k_4 =$$
$$s^2+(k_2+k_3+k_4)s+k_2k_4$$

$$\det_{C_e}\begin{bmatrix} k_1\bar{C}_p(s) & -k_4 \\ 0 & s+k_4 \end{bmatrix} = sk_1\bar{C}_p(s)+k_1k_4\bar{C}_p(s)$$

$$\det_{C_m}\begin{bmatrix} s+k_2+k_3 & k_1\bar{C}_p(s) \\ -k_3 & 0 \end{bmatrix} = k_1k_3\bar{C}_p(s)$$

$$\bar{C}_e(s)=\frac{sk_1\bar{C}_p(s)+k_1k_4\bar{C}_p(s)}{s^2+(k_2+k_3+k_4)s+k_2k_4}$$

$$\bar{C}_m(s)=\frac{k_1k_3\bar{C}_p(s)}{s^2+(k_2+k_3+k_4)s+k_2k_4}$$

Partial Fraction Decomposition

$$\alpha_{1,2}=\frac{1}{2}\left[(k_2+k_3+k_4)\mp\sqrt{(k_2+k_3+k_4)^2-4k_2k_4}\right]$$

Solve for A and B for

$$\bar{C}_e(s)=\bar{C}_p(s)\left[\frac{sk_1+k_1k_4}{s^2+(k_2+k_3+k_4)s+k_2k_4}\right] = \bar{C}_p(s)\left[\frac{sk_1+k_1k_4}{(s+\alpha_1)(s+\alpha_2)}\right] = \bar{C}_p(s)\left[\frac{A}{s+\alpha_1}+\frac{B}{s+\alpha_2}\right]$$
$$sk_1+k_1k_4=A(s+\alpha_2)+B(s+\alpha_1)=(A+B)s+A\alpha_2+B\alpha_1$$

$\therefore A+B=k_1$ and $A\alpha_2+B\alpha_1=k_1k_4$

$A=\dfrac{k_1k_4-k_1\alpha_1}{\alpha_2-\alpha_1}$ and $B=\dfrac{k_1\alpha_2-k_1k_4}{\alpha_2-\alpha_1}$

$$\bar{C}_e(s)=\bar{C}_p(s)\left[\frac{\dfrac{k_1k_4-k_1\alpha_1}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\dfrac{k_1\alpha_2-k_1k_4}{\alpha_2-\alpha_1}}{s+\alpha_2}\right]$$

Solve for A and B

$$\bar{C}_m(s) = \bar{C}_p(s)\left[\frac{k_1k_3}{s^2+(k_2+k_3+k_4)s+k_2k_4}\right] = \bar{C}_p(s)\left[\frac{k_1k_3}{(s+\alpha_1)(s+\alpha_2)}\right] = \bar{C}_p(s)\left[\frac{A}{s+\alpha_1}+\frac{B}{s+\alpha_2}\right]$$

$$k_1k_3 = A(s+\alpha_2)+B(s+\alpha_1) = (A+B)s + A\alpha_2 + B\alpha_1$$

$\therefore A+B=0$ and $A\alpha_2 + B\alpha_1 = k_1k_3$

$A = \dfrac{k_1k_3}{\alpha_2-\alpha_1}$ and $B = \dfrac{-k_1k_3}{\alpha_2-\alpha_1}$

$$\bar{C}_m(s) = \bar{C}_p(s)\left[\frac{\frac{k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\frac{-k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_2}\right]$$

Use $C_i = C_e + C_m$. Simplify and Combine Like Terms

$$\bar{C}_i(s) = \bar{C}_p(s)\left[\frac{\frac{k_1k_4-k_1\alpha_1}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\frac{k_1\alpha_2-k_1k_4}{\alpha_2-\alpha_1}}{s+\alpha_2}\right]+\bar{C}_p(s)\left[\frac{\frac{k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\frac{-k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_2}\right]$$

$$\bar{C}_i(s) = \bar{C}_p(s)\left[\frac{\frac{k_1k_4-k_1\alpha_1+k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\frac{k_1\alpha_2-k_1k_4-k_1k_3}{\alpha_2-\alpha_1}}{s+\alpha_2}\right] = \bar{C}_p(s)\left[\frac{\frac{k_1(k_3+k_4-\alpha_1)}{\alpha_2-\alpha_1}}{s+\alpha_1}+\frac{\frac{k_1(\alpha_2-k_3-k_4)}{\alpha_2-\alpha_1}}{s+\alpha_2}\right]$$

$\bar{C}_i(s) = \bar{C}_p(s)\left[\dfrac{A}{s+\alpha_1}+\dfrac{B}{s+\alpha_2}\right]$, where $A = \dfrac{k_1(k_3+k_4-\alpha_1)}{\alpha_2-\alpha_1}$ and $B = \dfrac{k_1(\alpha_2-k_3-k_4)}{\alpha_2-\alpha_1}$

Take the Inverse Laplace Transform

$$L^{-1}\left\{\bar{C}_i(s)\right\} = L^{-1}\left\{\bar{C}_p(s)\left[\frac{A}{s+\alpha_1}+\frac{B}{s+\alpha_2}\right]\right\} = AL^{-1}\left\{\bar{C}_p(s)\frac{1}{s+\alpha_1}\right\}+BL^{-1}\left\{\bar{C}_p(s)\frac{1}{s+\alpha_2}\right\}$$

Use the Convolution Theorem for Laplace Transforms

$$L^{-1}\{\bar{f}(s)\bar{g}(s)\} = \int_0^t f(u)g(t-u)du = f * g$$

$$\therefore C_i(t) = A\int_0^t e^{-\alpha_1(t-u)}C_p(u)du + B\int_0^t e^{-\alpha_2(t-u)}C_p(u)du = e^{-\alpha_1 t} * C_p(t) + e^{-\alpha_2 t} * C_p(t),$$

where $A = \dfrac{k_1(k_3+k_4-\alpha_1)}{\alpha_2-\alpha_1}$, $B = \dfrac{k_1(\alpha_2-k_3-k_4)}{\alpha_2-\alpha_1}$ and

$$\alpha_{1,2} = \frac{1}{2}\left[(k_2+k_3+k_4)\mp\sqrt{(k_2+k_3+k_4)^2-4k_2k_4}\right]$$

Answer #1

$$C_i(t) = A\int_0^t e^{-\alpha_1(t-u)}C_p(u)du + B\int_0^t e^{-\alpha_2(t-u)}C_p(u)du = e^{-\alpha_1 t} * C_p(t) + e^{-\alpha_2 t} * C_p(t),$$

where $A = \dfrac{k_1(k_3+k_4-\alpha_1)}{\alpha_2-\alpha_1}$, $B = \dfrac{k_1(\alpha_2-k_3-k_4)}{\alpha_2-\alpha_1}$ and

$$\alpha_{1,2} = \frac{1}{2}\left[(k_2+k_3+k_4)\mp\sqrt{(k_2+k_3+k_4)^2-4k_2k_4}\right]$$

Answer #2

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clear

%Define Variables
k_1 = .102;
k_2 = .13;
k_3 = .062;
k_4 = .0068;

b = k_2 + k_3 + k_4;
four_ac = 4 * k_2 * k_4;
alpha_1 = (1/2) * (b + sqrt(b^2 - four_ac));
alpha_2 = (1/2) * (b - sqrt(b^2 - four_ac));

A = (k_1 * ((k_3 + k_4 - alpha_1))/(alpha_2 - alpha_1));
B = (k_1 * ((alpha_2 - k_3 - k_4))/(alpha_2 - alpha_1));

time_min = [0, 1.08, 1.78, 2.3, 2.75, 3.3, 3.82, 4.32, 4.8,
5.28, 5.95, 6.32, 6.98, 9.83, 16.3, 20.25, 29.67, 39.93, 58, 74,
94];
Cp = [0, 84.9, 230, 233, 220, 236.4, 245.1, 230, 227.8, 261.9,
311.7, 321, 316.6, 220.7, 231.7, 199.4, 211.1, 190.8, 155.2,
140.1, 144.2];

%Linear Regression using Last 5 Points
time_min_last5 = time_min(length(time_min)-5+1:end);
Cp_last5 = Cp(length(Cp)-5+1:end);
linear_regression = polyfit(time_min_last5, Cp_last5, 1);
x_regression = linspace(58,200);
y_regression = polyval(linear_regression, x_regression);
time_min_with_regression = [time_min, x_regression(27:end)];
Cp_with_regression = [Cp, y_regression(27:end)];
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Ci_A = zeros(1,length(time_min_with_regression));
Ci_B = zeros(1,length(time_min_with_regression));

%Outer loop for Ci(t)
%Inner loop for Convolution integral
for t = 1:length(time_min_with_regression)
    for tau = 2:t
        delta_t = time_min_with_regression(tau)-
time_min_with_regression(tau-1);

        n_1 = exp(alpha_1 * time_min_with_regression(tau)) *
Cp_with_regression(tau);
        n_2 = exp(alpha_1 * time_min_with_regression(tau-1)) *
Cp_with_regression(tau-1);
        Ci_A(t) = Ci_A(t) + (1/2)*delta_t*(n_1 + n_2);

        n_11 = exp(alpha_2 * time_min_with_regression(tau)) *
Cp_with_regression(tau);
        n_22 = exp(alpha_2 * time_min_with_regression(tau-1)) *
Cp_with_regression(tau-1);
        Ci_B(t) = Ci_B(t) + (1/2)*delta_t*(n_11 + n_22);
    end

    Ci_A(t) = Ci_A(t) * exp(-
alpha_1*time_min_with_regression(t));
    Ci_B(t) = Ci_B(t) * exp(-
alpha_2*time_min_with_regression(t));

end

Ci = (A.*Ci_A) + (B.*Ci_B);

%Plot Ci and Cp
figure
hold on
plot(time_min_with_regression, Ci)
plot(time_min_with_regression, Cp_with_regression)
xlabel('Time(minutes)')
ylabel('C_{i}')
title('C_{i} and C_{p} vs Time')
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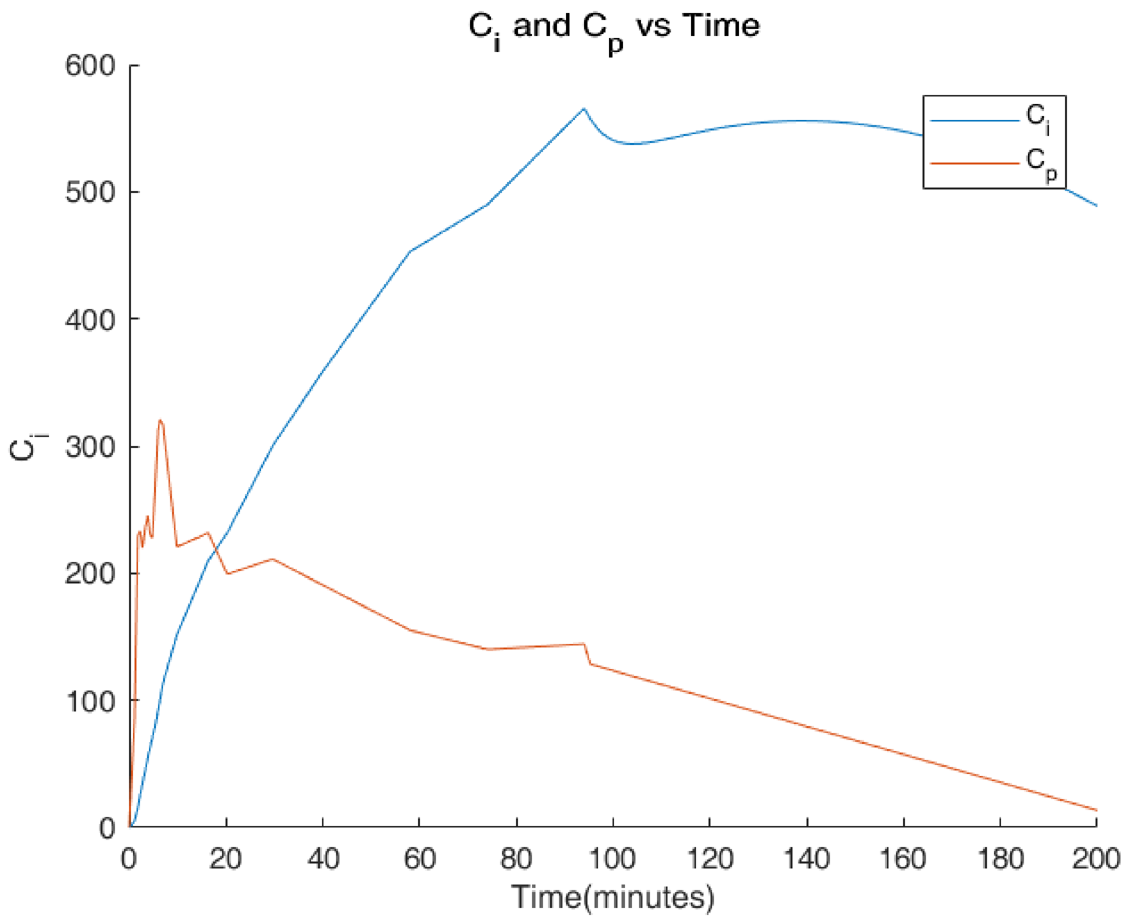
Answer #3



According to the figure above, C_i reaches a peak at around 94 minutes and begins to level off. Therefore, one should wait around the same time for FDG to travel from the capillaries to the tissues, where it would be metabolized.