TAKE HOME PROJECT 1 Biomedical Engineering

Background: Many years ago I was involved in human experiments that involved PET scanning. Link:
(https://en.wikipedia.org/wiki/Positron_emission_tomography .

This project uses data from one of those experiments. In this case we are injecting fludeoxyglucose (FDG) that has been tagged with F^{18}. Here is its link:
https://en.wikipedia.org/wiki/Fludeoxyglucose_(18F))

FDG travels through the arterial system, where we measure its concentration (C_p), and crosses the blood brain barrier. It's metabolized in the brain according to the compartment model displayed in the diagram.
The governing equations for this are given along with the rate constants for this model. (Note: I have taken care of unit normalization and all numerical values should be used as given.) At the time I was working with Rodney Brooks, a physicist who had built a PET scanner for NIH. He published a paper for the model given in this paper (you will have it available for this project). In it he solved the set of coupled differential equations you see below (not using Laplace transforms). However the easiest way to solve this problem is by the method of Laplace transforms. That is what I am asking you to do! And more!

(a) In the model shown in Figure 1 the rates of change of C_e (free), F^{18}DG in brain tissue and C_m (trapped) , F^{18}DG-6-P in brain tissue are equal to the net transport of FDG and FDG-6-P into their compartments. That is

$$(1)\quad \frac{dC_e}{dt} = k_1 C_p - (k_2 + k_3) C_e + k_4 C_m$$

$$(2)\quad \frac{dC_m}{dt} = k_3 C_e - k_4 C_m$$

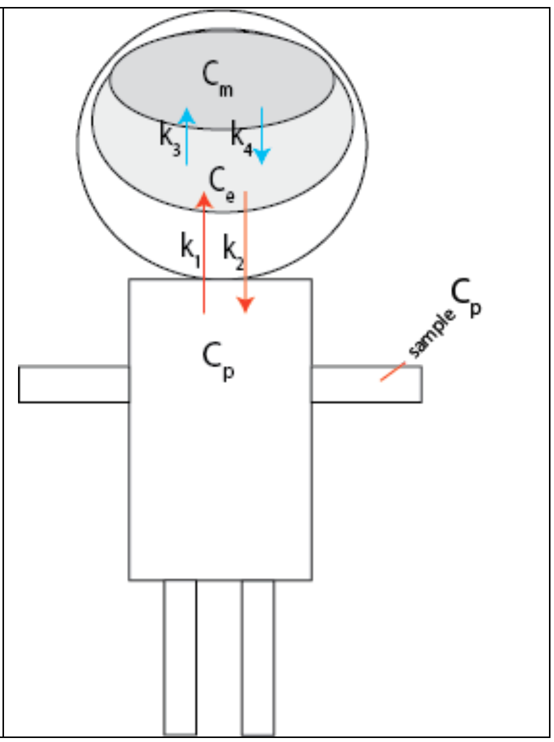

Figure 1

where initial concentrations are assumed to be zero. Note that C_p the concentration of FDG in the blood, as a function of time, is an experimentally acquired function. Then the total brain tissue concentration, C_i is given by

(3) $C_i = C_e + C_m$

Solve for C_i using the method of Laplace transforms starting with the coupled differential equations given above. **Show every detail of the calculation and reproduce formula (4) in the associated paper by Brooks (Answer #1).** However instead of presenting this in the form given in the paper present it in terms of convolutions (those integrals in the paper are in fact convolutions – do you recognize that – its also a hint). A few other hints follow:

1. $C_p(t)$ is not given as an analytic function it is in fact tabulated data below. When solving this system of equations simple carry it as this symbol or its Laplace transform quantity $\tilde{C}_p(s)$ when appropriate.
2. I would use Cramer's rule to solve for $C_e(s)$, $C_m(s)$
3. You may also want to use the quadratic formula to get some factors for a quadratic expression you get.
4. Remember how the convolution arises when applying the Laplace transform methodology, that is when you have a product of functions in s-space!!

(b) Next, having solved for $C_i(t)$ analytically in terms of convolution functions (equation 4 from paper where your version is written in terms of convolutions) use the following values for the rate constants:

$k_1 = .102$ $k_2 = .130$ $k_3 = .062$ $k_4 = .0068$

and the values for C_p :

Time (minutes)	Concentration
0.0	0.0
1.08	84.9
1.78	230.0
2.30	233.0
2.75	220.0
3.30	236.4
3.82	245.1
4.32	230.0
4.80	227.8
5.28	261.9
5.95	311.7
6.32	321.0
6.98	316.6
9.83	220.7
16.30	231.7
20.25	199.4
29.67	211.1
39.93	190.8

58.00	155.2
74.00	140.1
94.00	144.2

Note you will need to extrapolate the values pass 94 minutes to get a good feel for the behavior of $C_i(t)$ over time. I recommend taking the last few points starting with 58 min and eye balling an average line through them that goes to zero at some later time (we know that this goes to zero at some later time because the FDG in the blood is ultimately voided by urination). Then pick off a number of times and concentrations from this line to extend the table above. Note the calculation you will use the values in is relatively insensitive to the values extrapolated, they just need to be reasonable.

Use a method of numerical integration to compute the concentration, $C_i(t)$ (Answer #2).

Hints follow:

> One of the easiest ways is to do the integration involved with the convolutions using the trapezoid rule (basic calculus) for integration with the intervals given in our extended table above. Note the convolution integrals involve the "running" or integration variable τ and the time t. t is not a variable but it is involved in the calculation, both in the integrand and bounds. To apply the trapezoid rule to calculate the convolutions you can code this in Matlab in terms of nested **FOR** loops. The outer loop one setting t and the inner over τ (I will give other hints on this in the next few weeks if requested). Note you are welcome to do the convolution calculation anyway you want (but try to do the numerical evaluations using Matlab).

(c) Plot C_p and C_i versus time. Make sure your plots show the major shape of the curve by plotting values pass 94 minutes! What does this tell you about how long you should wait to scan after the injection of an isotope tagged version of FDG in this PET imaging experiment $C_i(t)$ (**Answer #3**)?