Assignment: PET Analysis
Due Monday, 10/16/2019 by 11:59 pm
Complete the deliverables listed below and upload to Canvas.
Please upload each file separately (i.e., don't compress them or make a .zip file)

- Matlab m-file with code to answer the following questions
- A report (saved as a pdf) of answers and figures (if necessary) to support your answer
- Make sure each plot/figure has a title, labeled axes, and is displayed in the correct aspect ratio.

NOTE: I will be traveling 10/14 to 10/18. Therefore, I will not be holding office hours that week. Please send me an email or attend office hours on 10/10.

For problem (1) use control_dX and treated_dx. Control_dx and treated_dx are both structures with the following pieces of information;
control_dx.SUV: SUV image (128 x 128 x 159 slices);
control_dx.roi_tumor: ROI over tumor
control_dx.roi_muscle: ROI over muscle;
d0,d1,d2,d3,d4,d7 correspond to the number of days following treatment. Day 0 is a pre-treatment image (baseline).

(1) (25 pts) We have two mice that were imaged with ^{18}F-MISO PET. ^{18}F-MISO is a PET tracer (i.e. contrast agent) that accumulates (and is retained) in hypoxic cells. Mice with HER2+ breast cancer received injections of either saline (control group) or trastuzumab (treated group). Tratsuzumab primarily inhibits cell proliferation, however, it also has been known to suppress angiogenesis. Tumors tend to overexpress angiogeneic factors resulting in abnormal vasculature (poor perfusion and delivery, leaky). Suppressing angiogenic factors results in the "normalization" of tumor vasculature and potentially improving tissue perfusion.

a. How is tumor hypoxia related to tumor vasculature?

b. (2 Plots) Calculate the SUV in muscle at each time point for the control and treated mouse.
- **i.** (1st plot) Plot the mean and 95% confidence interval.
- **ii.** (2nd plot) Plot the mean and 95% confidence interval normalize the means to day 0's value.

c. (2 Plots) Calculate the SUV in tumor at each time point for the control and treated mouse.
- **i.** (1st plot) Plot the mean and 95% confidence interval.
- **ii.** (2nd plot) Plot the mean and 95% confidence interval. Normalize the means to day 0's value.

d. What does the SUV tell us about the mice (or the drug they are receiving)? Why would we normalize our measurements to a muscle measurement? Based off of these two mice, do these imaging measures support our hypothesis on what Tratsuzumab is doing to the tumor?

(2) (25 pts) PET kinetic modeling & curve fitting: Expand the ODE45/curvefit code we developed in class to estimate model parameters from this digital reference object (DRO). DROs are used to evaluate the new code and to test out image acquisition settings.

a. DRO1 is a 4D (2 in space, 2 in time) array where model parameters (k_1, k_2, and k_3) are varied spatially (in x-y plane) throughout the domain. DRO(y,x,:,1) = the [C_T] time course, DRO (y,x,:,2) = the [C_{IC}] time course for position (y,x). Extend the code from class to fit each k_1, k_2, and k_3 at each location. Use the *imagesc* command to display the estimated k_1, k_2, and k_3. Label your plots, an add colorbars.
   Hint: For debugging purposes $k_1 = k_2 = k_3 = 0.01$ at position y = 1, x = 1. So make sure your code can actually match that curve when you use those parameters before trying to fit the entire domain.
   Also, C_p is provided as an inline function. So to grab the value of the AIF at time t just simply type "Cp(t)" . so Cp(5) = 76.7898. The time vector for these simulations is saved as "time".

b. DRO2 consists of 3 different concentration time courses collected with different SNRs. Extend the code from class to fit for k_1, k_2, and k_3 from each time course. What is the effect on SNR on parameter estimates. Calculate the percent error between the estimated and true parameters for each SNR scenario

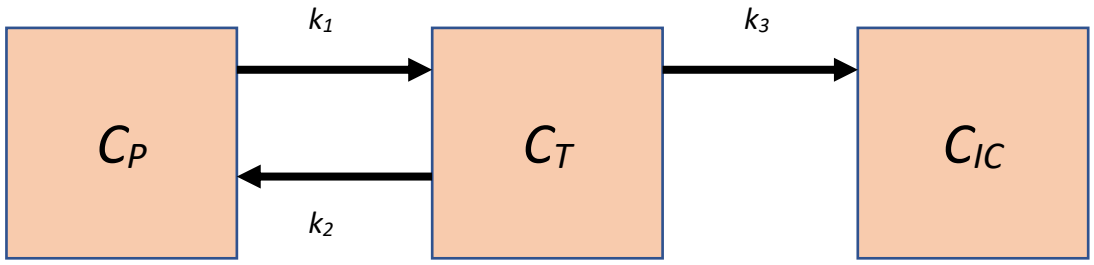
(Assume $k_1 = .1$, $k_2 = .2$, and $k_3 = 0.05$). Provide 3 plots of the model fit (use lines) plotted with the measurement (use dots).

DRO2(1,:,1) = the [C_T] time course for noiseless scenario
DRO2(1,:,2) = the [C_p] time course for noiseless scenario
DRO2(2,:,1) = the [C_T] time course for the medium noise scenario
DRO2(2,:,2) = the [C_p] time course for the medium noise scenario
DRO2(3,:,1) = the [C_T] time course for the high noise scenario
DRO2(3,:,2) = the [C_p] time course for the high noise scenario

c. DRO 3 consist of 1 set of concentration time courses (DRO3(:,1) = [C_T] time course, DRO3(:,2) = [C_p] time course). Sample DRO3 using the following commands:

```
DRO3_high_tr = DRO3(:,:);
DRO3_medium_tr = DRO3(1:10:end,:);
DRO3_low_tr = DRO3(1:40:end,:);
```

Extend the code from class to fit for k_1, k_2, and k_3. How does temporal resolution effect our ability to estimate model parameters? Calculate the percent error between the estimated and true parameters for each SNR scenario (Assume $k_1 = .8$, $k_2 = .2$, and $k_3 = 0.1$). Provide 3 plots of the model fit (use lines) plotted with the measurement (use dots).



C_P = [Tracer] in plasma, C_T = [Tracer] in tissue, C_{IC} = [Tracer] in cells
k_1 to k_3 are all bounded between 0 and 1.
Hints for solving with ODE 45:

(1) Write out the system of ODEs describing the compartment model above
(2) The dC_p/dt equation is not needed as we are provided with the time course of C_p. Thus, within your function you will only have 2 equations.
(3) You will only need the initial conditions for C_T and C_{IC}, but will need to provide C_p(t)