Give all answers to at least **4 significant figures**.

1. An experimental drug is being tested to see the response of the immune system in a drug trial for cancer chemotherapy. Below is a table of the readings of the drug in the blood as time passes after an injection of the drug at $t = 0$ days.

Day	Drug (μg/dl)
0	8
1	7.5
2	6.2
4	5.3
6	3.7
10	2.2
15	1.8
20	0.9

a. The drug is metabolized in the liver and eliminated through the urine. It is assumed that the decay of this drug is exponential, so fits the model

$$D(t) = A\,e^{-kt}.$$

Use Excel's Trendline with an Exponential fit to the data. Give the best values of A and k that you find (to 4 significant figures). Also, give the sum of square errors between the data and the model.

b. The drug stimulates a cytokine response in the blood. Over the next 20 days the blood is measured to determine the response of the body to this new experimental drug. Below are the data for the level of cytokine in the blood.

Day	Cytokine (ng/dl)
0	0
1	8.5
2	15.9
4	25.4
6	33.1
10	38.2
15	35.7
20	30.6

The researchers use the standard model in pharmakinetics of exponential release and decay of the cytokine in the body. This model is given by

$$C(t) = B(e^{-qt} - e^{-kt}),$$

where the decay k matches the drug decay from Part a. Use Excel's solver to find the least squares best fit to the parameters B and q. As an initial guess use $B = 200$ and $q = 0.05$. Write the model with the best parameters, then state the sum of square errors between this model and the data. Give the percent error at $t = 10$ and $t = 20$ days. Find the derivative of this model ($C'(t)$). Use the techniques from class to find the time that this model predicts a maximum concentration of the cytokine and when this occurs. (Give your answers to 4 significant figures.)

c. Another researcher suggests that since the cytokines are being released by the white blood cells that a population model might be more appropriate. She suggests that the data might be better fit by a Ricker's model of the form

$$R(t) = Kt\,e^{-rt}.$$

Use Excel's solver to find the least squares best fit to the parameters K and r. As an initial guess use $K = 10$ and $r = 0.1$. Write the model with the best parameters, then state the sum of square errors between this model and the data. Which model gives the smaller sum of square errors. Give the percent error at $t = 10$ and $t = 20$ days. Find the derivative of this model ($R'(t)$). Use the techniques from class to find the time that this model predicts a maximum concentration of the cytokine and when this occurs. (Give your answers to 4 significant figures.)

2. Type 1 or juvenile diabetes is a very dangerous disease caused by an autoimmune response to the β-cells in the pancreas. The earlier the diagnosis of the disease, the better the chances of controlling it with insulin and helping the subject live longer. One simple test for diagnosis is the glucose tolerance test (GTT), where the subject ingests a large amount of glucose (1.75 mg/kg body wt) then has his or her blood monitored for about 6 hours following the glucose administration. Ackerman *et al* [1] created a simple mathematical model for glucose and insulin regulation that is given by the equation

$$G(t) = G_0 + Ae^{-\alpha t}\cos(\omega(t - \delta)).$$

where $G(t)$ is the blood glucose level (in mg/dl of blood). The GTT allows the fitting the parameters G_0, A, α, ω, and δ.

a. Consider the data below from a couple of patients. Find the best fitting parameters, G_0, A, α, ω, and δ in the equation for $G(t)$. Write the sum of square errors between the data and the model.

t (min)	$G_1(t)$ mg/dl	$G_2(t)$ mg/dl
0	75	105
0.5	160	190
0.75	180	205
1	155	225
1.5	95	200
2	75	185
2.5	65	110
3	80	100
4	85	85
5	80	90

b. Graph the best fitting solution for each of these patients. Using the model, find the absolute maximum and absolute minimum for each of these patients giving both the time, t, and glucose level, G, at the extrema in the 5 hour range of the data.

c. Experimental testing of this model has shown that the parameter α varied from subject to subject, so was not a good predictor of diabetes. However, the parameter $\omega_0 = \sqrt{\omega^2 + \alpha^2}$ was quite robust and proved a good indicator of diabetes. In particular, healthy individuals satisfied $2\pi/\omega_0 < 4$, while the reverse inequality indicated diabetes. Use this information to determine if the data above come from a normal or a diabetic patient.

[1] Ackerman, E., Rosevear, J. W., and McGuckin, W. F. (1964). A mathematical model of the glucose tolerance test, *Phys. Med. Biol.*, **9**, 202-213.