1. **(20 pts) mathbioLibrary/setABiocLabs/Lab121_K5_tumor.pg**
Because of the accuracy of WebWork, you should use 5 or 6 significant figures on all problems.

In class we examined a growth curve for mouse mammary tumor cells. This question examines the rate of growth of Lewis lung carcinoma from a paper by L. Simpson-Herren et al. (1974) [1]. We will concentrate on their study of the growth of a primary tumor that is implanted in the subaxillary region of BDF mice. They collected data on the tumor weight (in g) as time passes (in days). Many studies have shown that the best model to fit tumors is the Gompertz growth model, while others use the standard logistic growth model that we studied in an earlier lab. In this lab, we will develop both the logistic and the Gompertz growth curves, then use these models to simulate the data in the paper.

Below we present a table that gives the time (shifted so $t = 0$ at the first data point), the weight of the tumor (in g), and the growth rate at each time. (The growth rate uses a 3-point method to approximate the derivative, which is not covered in this course.) We will fit the growth rate data to the logistic and Gompertz growth functions, then simulate each of these models to compare to the data presented in the paper. The table presents the weight of the tumor (p) in g at times (t) (days) with the growth rate given by $g(p)$ in g/day.

t	p	$g(p)$	t	p	$g(p)$
0	0.324	0.035	12	3.79	0.72
1	0.394	0.105	13	5.19	0.575
2	0.534	0.1905	14	4.94	0.32
3	0.775	0.3005	15	5.83	0.23
4	1.135	0.2375	16	5.4	0.12
5	1.25	0.1375	17	6.07	1.29
6	1.41	0.145	18	7.98	0.915
7	1.54	0.16	19	7.9	0.16
8	1.73	0.475	20	8.3	0.54
9	2.49	0.355	21	8.98	0.52
10	2.44	0.63	22	9.34	0.2
11	3.75	0.675			

a. You begin this laboratory exercise by finding the best logistic growth function for the growth of the tumor. In particular, you want to use Excel's trendline polynomial fit of order two with the y-intercept set to zero through the data for p and $g(p)$.

$$g(p) = a_2 p^2 + a_1 p.$$

Find the best fitting coefficients a_1 and a_2 for this model. Also, give the equation for the best fitting growth function, $g(p)$. (Note that you ignore the times listed in the table to find $g(p)$.) Include the sum of square errors between the logistic growth curve and the data.

$a_2 =$ _____
$a_1 =$ _____
$g(p) =$ _____
Sum of Square Errors = _____

Since $g(p)$ represents the growth rate of the tumor, then the tumor is at equilibrium when $g(p) = 0$. Find all equilibria according to this model (with $p_{1e} < p_{2e}$). The largest equilibrium is the maximum size that a particular tumor can reach due to limitations of blood supplies from angiogenesis (carrying capacity).

$p_{1e} =$ _____
$p_{2e} =$ _____

Find the derivative of the logistic growth function.

$g'(p) =$ _____

The maximum growth rate occurs at the vertex. Find the size p_{max} that produces the maximum growth rate, and determine the maximum growth rate at this size, $g(p_{max})$.

$p_{max} =$ _____
$g(p_{max}) =$ _____

b. The Gompertz growth curve satisfies the equation

$$G(p) = p(b - a\ln(p)).$$

In this part of the problem, you use the same data as you did in Part a, but you now fit the Gompertz growth curve $G(p)$ through the data. In this case, you want to find the least squares best fit of $G(p)$ to the data by varying a and b and using Excel's Solver routine. Write the Gompertz growth function and include the sum of square errors between the data and this function.
$a =$ _____
$b =$ _____
$G(p) =$ _____
Sum of Square Errors = _____

The Gompertz model has been shown to not hold well for small numbers of tumor cells, and the logarithm function isn't defined at 0. The function $G(p)$ gives another growth rate for the tumor, so the tumor is at equilibrium when $G(p) = 0$. Find the one equilibrium according to this model, and this equilibrium corresponds to the largest size that this model predicts for the tumor (carrying capacity).

$p_e =$ _____

Find the derivative of the Gompertz growth function.

$G'(p) =$ _____

Find the maximum growth rate according to the Gompertz model. Find the size p_{max} that produces the maximum growth rate, and determine the maximum growth rate at this size, $G(p_{max})$.

$p_{max} =$ _____
$G(p_{max}) =$ _____

c. In your Lab Report, create a graph that includes the data, the best fitting logistic growth curve, and the best fitting Gompertz growth curve. Describe how well the two models fit the data. Compare and contrast the shapes of these two growth models. Write a brief paragraph discussing the differences in the predicted maximum tumor size according to the logistic growth model and the Gompertz model. In addition, compare the maximum growth rates of the logistic growth model and the Gompertz model. Give at least two reasons why one would pick one of these models over the other.

d. In this part of the problem, we use the time series data given in the table, then show how our discrete dynamical models can reasonably simulate the data. The discrete logistic growth model is given by the equation:

$$p_{n+1} = p_n + g(p_n),$$

where $g(p_n)$ is the best quadratic function found in Part a. As an initial guess, start with your initial tumor weight as $p_0 = 0.324$. Then starting at $t = 0$, simulate the growth for 22 days. Use Excel's Solver to find the best possible p_0 value that minimizes the square error between the tumor weight in the data and the tumor weight given by the model. Give this best p_0 value and the least sum of square errors.

$p_0 =$ _____
Sum of Square Errors = _____

List the tumor weights at times $t = 5$, 10, 15, and 20. Give the percent error between the model and the data at these times (using the data as the more accurate value).

$p_5 =$ _____ Percent Error = _____
$p_{10} =$ _____ Percent Error = _____
$p_{15} =$ _____ Percent Error = _____
$p_{20} =$ _____ Percent Error = _____

e. The discrete Gompertz growth model is given by the equation:

$$p_{n+1} = p_n + G(p_n),$$

where $G(p_n)$ is the best Gompertz function found in Part b. As an initial guess, start with your initial tumor weight as $p_0 = 0.324$, starting at $t = 0$ and simulate the growth for 22 days. Use Excel's Solver to find the best possible p_0 value that minimizes the square error between the tumor weight in the data and the tumor weight given by the model. Give this best p_0 value and the least sum of square errors.

$p_0 =$ _____
Sum of Square Errors = _____

List the tumor weights at times $t = 5$, 10, 15, and 20. Give the percent error between the model and the data at these times (using the data as the more accurate value).

$p_5 =$ _____ Percent Error = _____
$p_{10} =$ _____ Percent Error = _____
$p_{15} =$ _____ Percent Error = _____
$p_{20} =$ _____ Percent Error = _____

f. In your Lab Report, plot the time series data from the table, your simulation of the logistic growth model, and your simulation of the Gompertz model. (Note that this time you need to use only the time data and the p data in the table.) Describe how well the two models fit the data. What are the similarities and differences between the two models? Write a short discussion that compares and contrasts the tumor progression based on the two models. Which model do you believe is better (if either) and why?

[1] L. Simpson-Herren, A. H. Sanford, and J. P. Holmquist.Cell population kinetics of transplanted and metastatic Lewis lung carcinoma, Cell Tissue Kinet. 7: 349-361, 1974.