

# MAT 494/598----SYLLABUS----Fall, 2007

## Mathematical Models in Biosciences

If you are concerned with the exponential human population growth, scopes of the AIDS and diabetes epidemic, the alarming rate of species extinction and ultimately hopes for the future, you may find mathematical help in this course. The main objective of this course is to construct and study plausible mathematical models (difference and differential equation models) addressing current issues in biosciences. Computer simulation methods and programs will be introduced and emphasized.

**Instructor:** Prof. Yang KUANG    **E-mail:** [kuang@asu.edu](mailto:kuang@asu.edu) .

**Course Home page:** <http://math.asu.edu/~kuang/class/494MB.html>

**Section:** #80232/80277, PSA 309, 3:15pm-4:30pm, T, Th

**Office:** PSA 429, Phone: 965-6915    **Office hours:** 1:40pm-2:30pm, T, W, Th, and by appointment.

**PREREQUISITES:** Basic calculus and linear algebra

**TEXTBOOK:** **MATHEMATICAL MODELS IN BIOLOGY** by Leah Edelstein.

**SIAM Classics in Applied Mathematics 46** 2004 | 586 pages | Softcover \$50.

SIAM Member Price \$35.    <http://ec-securehost.com/SIAM/CL46.html>

The aim of this book is to present instances of interaction between two major disciplines, biology and mathematics. The goal has been that of addressing a wide audience. Biology students will find this text useful as a summary of mathematical methods used in modeling, and applied mathematics students may benefit from examples of applications of mathematics to real life problems. Undergraduate students, beginning graduate students, will find most of the material accessible and engaging.

### References:

**1: Mathematical Models in Population Biology and Epidemiology (Hardcover)**

by Fred Brauer, Carlos Castillo-Chavez. \$59.82 at Amazon & ships for FREE. [Details](#)

**3. Alexei Sharov, Quantitative Population Ecology** on-line lecture course at Virginia Tech.

**2:** David B. McDonald, (updated 2006) <http://www.uwyo.edu/dbmcd/popecol/>

### Grades are based on:

**Assignments:** 300 points (five set of assignments, each 40 points) **plus**

**One project:** 100 points (on a project) **or one final exam:** 100 points

If you are taking this course to satisfy qualifying exam requirement, you must take the final.

THE APPROXIMATE GRADING SCALE WILL BE:

A=85%-100%    B=70%-85%    C=60%-70%    D=45%-60%    E=less than 45%

Except in the case of a documentable emergency, late assignments will not be accepted.

If I cannot be reached, contact me by E-mail, or, a message can be left with the Mathematics Office (PSA 216, or phone 965-3951).

This course will cover most chapters of the first two parts of the textbook.

The **final exam** will be given in class (PSA 309) on Tuesday, Dec. 11, 2:40pm-4:30pm.

## Homework problems due on Thursday, Sept. 6

**Exercise 1.1:** Show that the solution of  $x' = re^{-at}x$ ,  $x(0)=1$  is the same as the solution of  $x' = rx - ax \ln x$  with  $x(0)=1$ .

**Exercise 1.2: True or false? Show your work in detail.** A single cell of the bacterium *E. coli* would, under ideal circumstances, divide every twenty minutes. ... it can be shown that in a single day, one cell of *E. coli* could produce a super-colony equal in size and weight to the entire planet earth.

**Exercise 1.3: Problem 5, page 152.**

**Exercise 1.4:** If this were a harvested population, where would you like to maintain the population size in order to manage for Maximum Sustained Yield (MSY)? (Hint: Assume that the population is harvested at the rate of  $C$ /unit of time, then the population grows according to  $dN/dt = rN(1-N/K) - C$ .)

**Exercise 1.5: Problem 2(a, c), page 29**

**Exercise 1.6: Problem 3, page 29**

**Exercise 1.7: Problem 9, page 31. Use Matlab to graph the solutions with  $n=20$ .**

**Exercise 1.8: Problem 15, page 33.**

**Exercise 1.9: Problem 16, page 33.**

**Exercise 1.10: Problem 19, page 34.**

**Exercise 1.11: Problem 20, page 35.**

**Lecture 1, Tuesday, Aug. 21.**

**Homework 1 is due on Thursday, Sept. 6.**

**Reading homework:** section 4.1, page 116-121.

## **Chapter 1: Introduction**

The purpose of science to society is to produce *useful models of reality*. While it is virtually impossible to make inferences from human senses which actually describe what “is,” we can form hypotheses based on *observations*. By analyzing a number of related hypotheses, scientists can form general theories. Specifically, scientists apply skeptical, methodical evaluation of the body of evidence that seeks to establish alternative working hypotheses, and then reject some hypotheses, while retaining others (the remainder are still subject to re-evaluation in the light of new data or theory). Such processes are the internal organs of sciences which are vital but usually not revealed in manuscripts, books, or presentations.

Frequently, the goal of a mathematical bioscience effort is to obtain an **integrative understanding** of some biological issues with the help of mathematical tools (often models). **In most of such cases, models are our purposes and our products.** The models shall be biologically well motivated, mathematically carefully (painfully) formulated and numerically thoroughly tested (they shall produce plausible dynamics when parameters are plausible). *Models must be built on the basis of a solid and preferably a comprehensive understanding of the relevant existing biology literature/knowledge.* This often requires the collaboration of bio-scientists. Lack of such solid understanding contributed to the proliferation of many imaginary and absurdly formulated ad hoc models in the literature. To succeed in a modeling effort is very much like to succeed in an experimental effort: learn from failures and keep improving on the model at hand.

Once a model is satisfactorily formulated, mathematicians may devote substantial effort to systematically study the fine, insightful and often rich dynamics of the model, such effort often calls for advanced training in mathematics and is often labeled as biomathematical research. Hence biomathematics is an important and integral part of the broadly defined area of mathematical biosciences.

As biosciences continue to strengthen their dominance of sciences, mathematical biosciences are doing the same in the broad areas of applied mathematics and applications of mathematics. In addition, mathematical biosciences’ reaches are expanding rapidly into the hearts of all areas of biosciences. Many of us may aware the fundamental importance of an advanced calculus course in undergraduate mathematics education. Arguably, mathematical ecology occupies a similar position in mathematical biosciences training. In this sense, this course seeks to lay a basic foundation for mathematical biosciences research.

**Science as simplification:** Observation, modeling and experiment can each be seen as a way of organizing, ordering and simplifying our understanding of the natural world.

Observations can simplify by focusing on critical components and highlighting similarities and differences among phenomena. Modeling simplifies by exposing the effects of a few model parameters, ignoring many or most of the complexities of the real world. Experiment simplifies by holding all but a few factors constant (by the use of replicates and controls).

## Why use mathematical models or mathematical approaches?

1) To expose faulty assumptions.

Consider the Malthus (<http://www.marxists.org/reference/subject/economics/malthus/>) exponential growth ( $x' = ax$ ) as an example. The assumption there is that growth is independent of population size/density. According to Malthus, "...Population, when unchecked, increases in a geometrical ratio. Subsistence increases only in an arithmetical ratio. A slight acquaintance with numbers will show the immensity of the first power in comparison of the second. By that law of our nature which makes food necessary to the life of man, the effects of these two unequal powers must be kept equal. This implies a strong and constantly operating check on population from the difficulty of subsistence. This difficulty must fall somewhere and must necessarily be severely felt by a large portion of mankind...." In truth, Malthus model, while useful in some physical applications, it almost never applies to natural populations except for a short time following introductions or invasions. We are forced to incorporate density dependence, leading to many density dependent growth models, including the logistic equation ( $x' = rx(1-x/K)$ ), regrowth model ( $x' = b-ax$ , for perennials) and Gompertz model ( $x' = r_0 e^{-at} x$ , or  $x' = rx - ax \ln(x/d)$ ,  $r = r_0 + a \ln x_0$ ). A more mechanistic approach involves the employment of Droop

(growth rate) model ( $\mu = \mu_{\max} \left(1 - \frac{q}{Q}\right)$ ).

logistic.m

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```
function [Ydot] = LogisticCont(t,Y, r, K)
r=1; K=1.4;
Ydot(1) = r*Y(1)*(1-Y(1)/K);
Ydot=Ydot';
```

regrowth.m

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```
function [Ydot] = regrowth(t,Y, r, K)
r=1; K=1.4;
Ydot(1) = r*(1-Y(1)/K);
Ydot=Ydot';
```

Gompertz.m

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```
function [Ydot] = Gompertz(t,Y)
Ydot(1) = Y(1)*Y(2);
Ydot(2) = -Y(2);
Ydot=Ydot';
```

OneSpeciesPlot.m

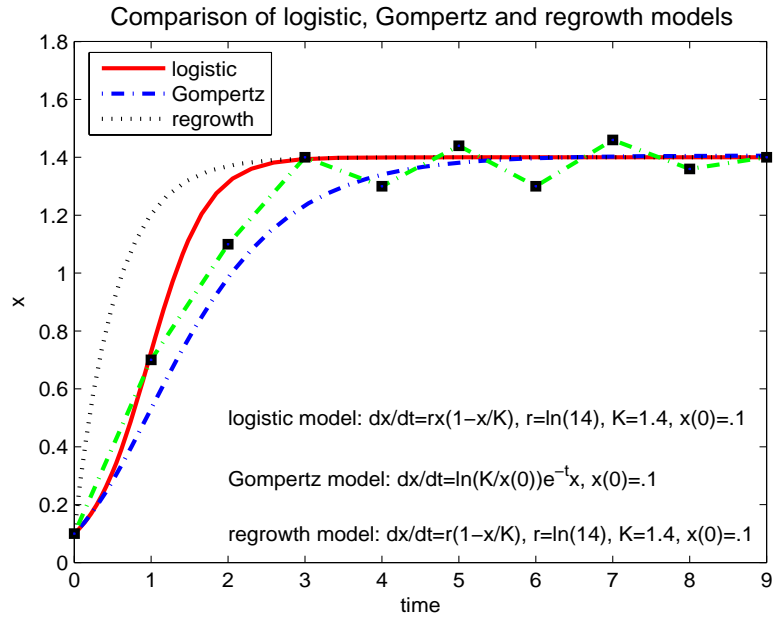
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```
figure
time=9; fs=10;
[T1,Y1] = ode23s('logisticCon',[0 time],[.1]);
[T2,Y2] = ode23s('Gompertz',[0 time],[.1, log(14)]);
[T3,Y3] = ode23s('regrowth',[0 time],[.1]);
x = 0:1:9;
y = 0.2*[0.5 3.5 5.5 7 6.5 7.2 6.5 7.3 6.8 7]';
option=odeset('AbsTol',1e-9,'RelTol',1e-9);
plot(T1(:,1),Y1(:,1),'r',T2(:,1),Y2(:,1),'b-',T3(:,1),Y3(:,1),'k',x,y,'-gs','LineWidth',2,...
'MarkerEdgeColor','k','MarkerFaceColor','b','MarkerSize',4);
text(2,0.5,'logistic model: dx/dt=rx(1-x/K), r=ln(14), K=1.4, x(0)=.1','FontSize',fs);
text(2,0.3,'Gompertz model: dx/dt=ln(K/x(0))e^{-t}x, x(0)=.1','FontSize',fs);
```

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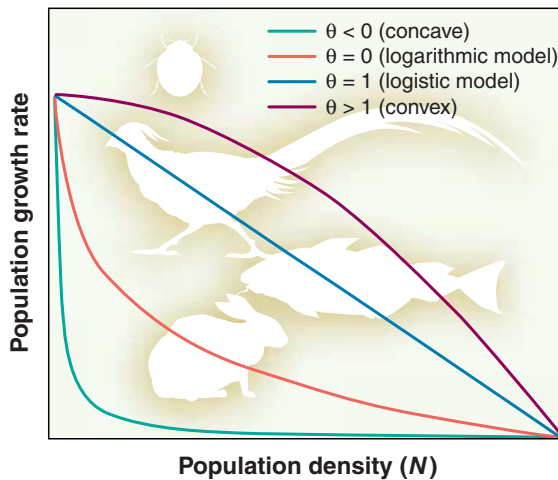
text(2,0.1,'regrowth model: dx/dt=r(1-x/K), r=ln(14), K=1.4, x(0)=.1','FontSize',fs);
legend('logistic','Gompertz','regrowth',2)
title('Comparison of logistic, Gompertz and regrowth models','FontSize',12)
xlabel('time'); ylabel('x'); xlim([0 time]); ylim([0 1.8]);

```



**Different shapes for the relationship between population growth rate and density.**

The growth rate–density relationship can be modeled by the  $a$ -logistic equation per capita growth rate (pgr) =  $r_1[1 - (N/K)^a]$ :  $r_1$  is the rate of population growth at density 0 [ $r_1 = r_0/(1 - K^{-a})$ ], where  $r_0$  is the maximal rate of population growth from low density];  $K$  is the carrying capacity of the environment, or equilibrium;  $a$  controls the shape of the relationship and depends on the ways that members of a population interact at different densities. Sibly *et al.* (Science, 2005) find that mammals, birds, fish, and insects do not generally grow exponentially to carrying capacity, as had been widely thought due to logistic model. Instead, population growth decelerates well before carrying capacity is achieved, as illustrated by the concave

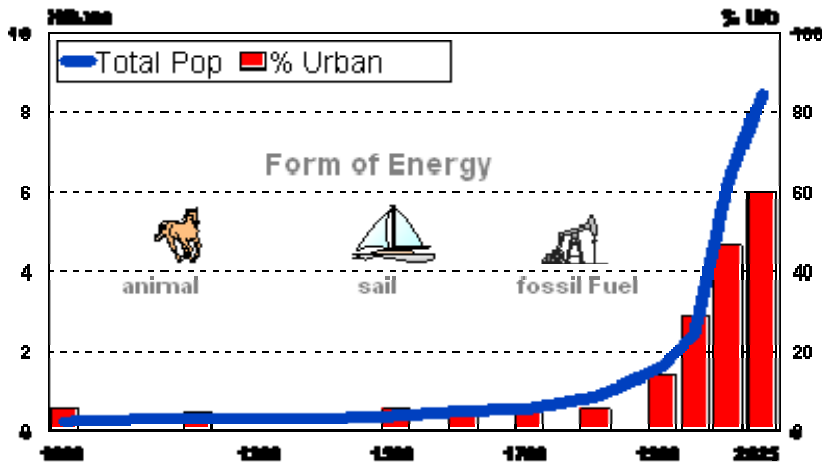


curve.

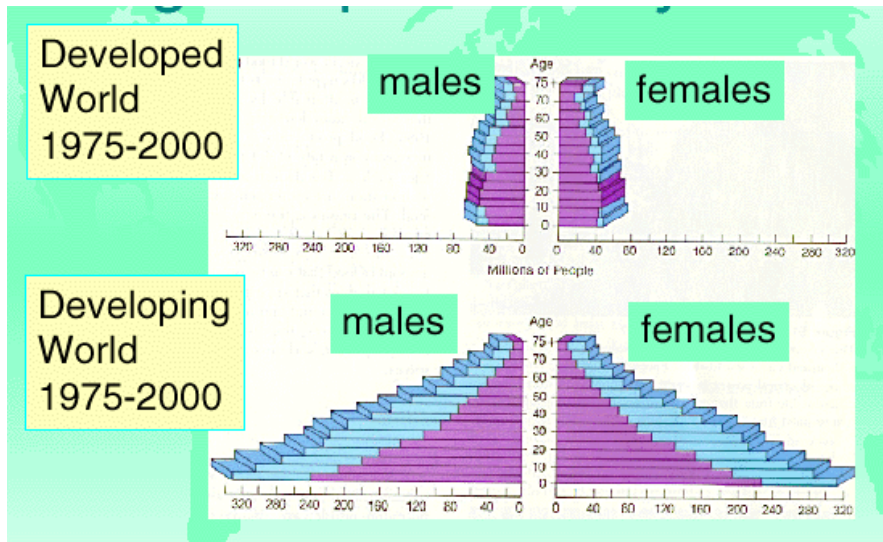
**Exercise 1.1:** Show that the solution of  $x' = r_0 e^{-at} x$ ,  $x(0) = x_0$  is the same as the solution of  $x' = rx - ax \ln x$  with  $x(0) = x_0$ .

2) To provide testable statement or new insights.

Models can guide our thinking, provide the basis for critical tests or experiments and clarify our thinking about a problem. Consider again the logistic equation. The maximum growth rate shall occur at  $x = K/2$ . This statement can be tested by some specific population growth experiments. For example, by inspecting the following figure, one may estimate the earth's carrying capacity for human is 9-10 billions. **DO NOT BELIEVE THIS.**



Age structure is a very important aspect of population dynamics.



Science is progressive, and subject to test and falsification. We seek a better, more comprehensive view of interrelationships. In the arts, no one can improve on Shakespeare or Beethoven -- a new artist may be revolutionary, perhaps, but not progressive in the same sense.

## Lecture 2, Thursday, Aug. 23.

*Population ecology* is a major subfield of [ecology](#)—one that deals with the dynamics of [species populations](#) and how these populations interact with [the environment](#).

[http://en.wikipedia.org/wiki/Population\\_ecology](http://en.wikipedia.org/wiki/Population_ecology)

A single cell of the bacterium *E. coli* would, under ideal circumstances, divide every twenty minutes. ... it can be shown that in a single day, one cell of *E. coli* could produce a super-colony equal in size and weight to the entire planet earth. (**Exercise 1.2**). M. Crichton (1969), *The Andromeda Strain* (Dell, New York, p. 247).

## Chapter 2: Single species growth models

### 2.1. Malthusian and logistic growth models

**Required Reading:** section 4.1, page 116-121.

**Suggested Reading:** Thomas Malthus: *An Essay on the Principles of Population Growth*, 1798. <http://www.marxists.org/reference/subject/economics/malthus/>

**Suggested Reading:** Georgyi Frantsevitch Gause: *The Struggle for Existence*, 1934. Free online <http://www.ggause.com/Contgau.htm>. Buy for \$35 at Amazon.com.

<http://www.amazon.com/gp/product/0486495205/102-6000505-7050558?v=glance&n=283155>

The four major processes that regulate population growths are: birth ( $B$ , +), death ( $D$ , -), immigration ( $I$ , +) and emigration ( $E$ , -) (where  $B$  is the number of births,  $D$  is the number of deaths,  $I$  is the number of immigrants and  $E$  is number of emigrants). We assume first that the population grows in a closed environment. Hence we will ignore both the immigration and emigration processes.

There are many other factors that keep populations in check such as intra- and inter-specific competition, predation, and diseases. These factors often reduce birth rate and/or increase death rate. Hence we may decompose their effects on population growth into the birth and death processes. We assume that the population change occur **continuously**.

$$dN/dt=B-D. \quad (\text{Eqn 4.1})$$

The alternative is to use **difference** equations -- with that technique, time changes **discretely**. An example of a difference equation for population growth is  $N_t = 2 * N_{t-1}$ .

If we assume that birth rate and death rate are constant  $b$  and  $d$ , respectively, in equation 4.1, then we obtain ( $r=b-d$ )

$$dN/dt=bN-dN=(b-d)N=rN. \quad (\text{Eqn 4.2})$$

Equation describes an exponentially growing population. This equation is also referred as *Malthusian growth model*.  $N(t)$  in terms of our starting population,  $N(0)=N_0$ , and the growth rate  $r$  takes the form of

$$N(t) = N_0 e^{rt}. \quad (\text{Eqn 4.3})$$

A quantity that is sometimes of interest is the **doubling time** — the time it takes a population to double in size under positive exponential growth.

$$2N_0 = N_0 e^{rt}. \quad (\text{Eqn 4.4})$$

We can cancel the  $N_0$ , then take the log of both sides, giving us  $\ln(2) = rt$  or

$$t = \ln(2)/r. \quad (\text{Eqn 4.5})$$

$r$  is sometimes called the **intrinsic or instantaneous rate of increase**. It expresses the balance between birth and death processes. Here are some conditions under which populations **may** grow exponentially for a short period of time.

- 1) **Invasive** species when they first arrive.
- 2) Species **colonizing** a new habitat (e.g., an isolated island).
- 3) Species that are **rebounding** from a population crash.
- 4) When they develop **novel adaptations** to cope with the environment (cancer cells).

It can be shown that in a single day, one cell of *E. coli* could produce a super-colony equal in size and weight to the entire planet earth. Why this never took place? The hidden and false assumption here is that the birth and death rates are constant -- that is, we implicitly assumed that the birth and death rates were independent of the population size and wouldn't change over time. The simplest (ad hoc) way to correct these assumptions is to assume these rates are linearly dependent on population density:

$$b = b(N) = b_0 - b_1 N, \quad d = d(N) = d_0 + d_1 N. \quad (\text{Eqn 4.6})$$

This yields the following logistic growth model (where  $K = r / (b_1 + d_1)$ ,  $r = b_0 - d_0$ ):

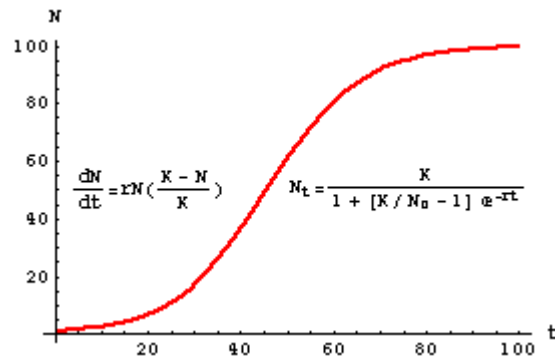
$$dN/dt = b_0 - b_1 N - d_0 - d_1 N = rN(1 - N/K). \quad (\text{Eqn 4.7})$$

The solution of the logistic equation takes the form of:

$$N_t = \frac{N_0 e^{rt}}{1 + (e^{rt} - 1) \frac{N_0}{K}}. \quad (\text{Eqn 4.8})$$

Below is a typical solution of the logistic population growth ( $K=100$ ). We observe that at population size of  $K/2$ , the growth rate begins to decline and eventually reaches an asymptote at

the carrying capacity,  $K$ . Changing the value of  $r$  will affect the steepness of the ascending portion.



**Figure 2.1.** A typical solution of the logistic population growth ( $K=100$ ).

**Questions to ponder:** 1) What happens when  $N > K$ ? 2) At what point is the population growing most rapidly? How would you find that mathematically?

**Exercise 1.3:** Problem 5, page 152.

**Exercise 1.4:** If this were a harvested population, where would you like to maintain the population size in order to manage for Maximum Sustained Yield (MSY)? (Hint: Assume that the population is harvested at the rate of  $C$ /unit of time, then the population grows according to  $dN/dt = rN(1-N/K) - C$ .)

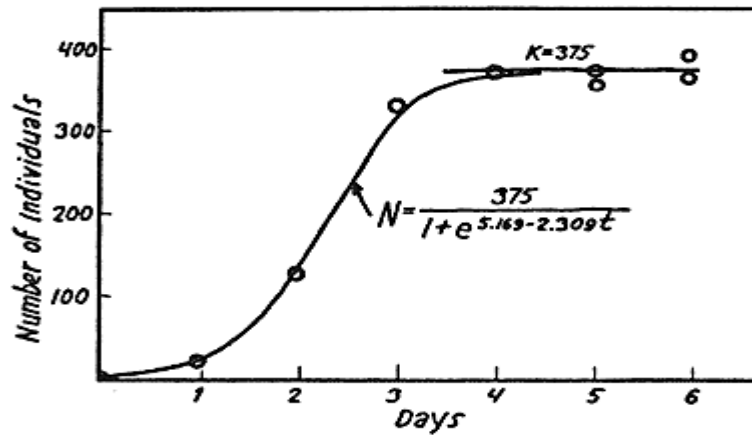
Many observed population growth dynamics can not be appropriately modeled by logistic model (Eqn 4.7). **Other models are needed.**

**How we obtain  $r$  and  $K$  from real-world data on observed population sizes over time?** With an observed set of measurements of population size against time, we can estimate  $r$  by plotting the data with  $X$ -axis,  $t$  and  $Y$ -axis, population sizes at various times  $t$ , and then: 1) eyeballing an estimate of  $K$  (the asymptote or place where the curve flattens out); 2) since we now have an estimate of  $K$  (and already knew  $N_0$  and  $N_t$ ), we can solve the log transformed logistic equation:

$$\ln \frac{K - N_t}{N_t} = -rt + \ln \frac{K - N_0}{N_0} \quad (\text{Eqn 4.9})$$

for  $r$ ; 3) or, we can estimate  $r$  graphically, as (the negative of) the slope of the plot of Eqn 4.9.

For example, Gause fit his experiment data on the growth of *Paramecium caudatum* to logistic model and yielded the saturating population level at  $K = 375$  individuals. The coefficient of multiplication or the biotic potential of one *Paramecium* ( $r$ ) was found to be 2.309. This means that per unit of time (one day) under his experiment conditions of cultivation, every *Paramecium* can potentially give 2.309 new *Paramecia*.



**Fig. 2.2.** The growth of population of *Paramecium caudatum* (Fig. 4 in Gause).

Regrowth equation  $N' = rN - rN^2/K$  is a preferred choice when modeling tree and perennial plant growth. Recently, it is often used to model immune cell growth and late stage resource (such as space and some limiting nutrient) limited growth.