Math in Microbiology

Hal L. Smith
PSA 631
halsmith@asu.edu

School of Mathematics and Statistics
Arizona State University

Outline

Where's the Math?

- quantify microbial growth
- population biology-mixed cultures
  - waste treatment
  - bio-remediation
  - biofilms, quorum sensing
  - mammalian gut microflora
  - food, beverage (beer,wine)
- gene regulatory networks
  - lac-operon
  - genetic engineering, synthetic biology
- disease modeling
  - Viral infections: HIV, HBV, Influenza
  - Bacterial infections: TB,
  - antibiotic treatment, antibiotic resistance

Malthusian Growth

N = biomass of bacteria
r = maximum growth rate

$$\text{per capita growth rate} = \frac{\triangle N}{N \triangle t} = r$$

or

$$\frac{dN}{dt} = rN$$

Solution is exponential growth

$$N(t) = N(0)e^{rt}$$

with doubling time: $N(T) = 2N(0)$

$$T = \ln(2)/r$$

Malthusian Growth

N = biomass of bacteria
r = maximum growth rate

$$\text{per capita growth rate} = \frac{\triangle N}{N\,\triangle t} = r$$

or

$$\frac{dN}{dt} = rN$$

Solution is exponential growth

$$N(t) = N(0)e^{rt}$$

with doubling time: $N(T) = 2N(0)$

$$T = \ln(2)/r$$

Malthusian Growth

N = biomass of bacteria
r = maximum growth rate

$$\text{per capita growth rate} = \frac{\triangle N}{N \triangle t} = r$$

or

$$\frac{dN}{dt} = rN$$

Solution is exponential growth

$$N(t) = N(0)e^{rt}$$

with doubling time: $N(T) = 2N(0)$

$$T = \ln(2)/r$$

Malthusian Growth

N = biomass of bacteria
r = maximum growth rate

$$\text{per capita growth rate} = \frac{\triangle N}{N \triangle t} = r$$

or

$$\frac{dN}{dt} = rN$$

Solution is exponential growth

$$N(t) = N(0)e^{rt}$$

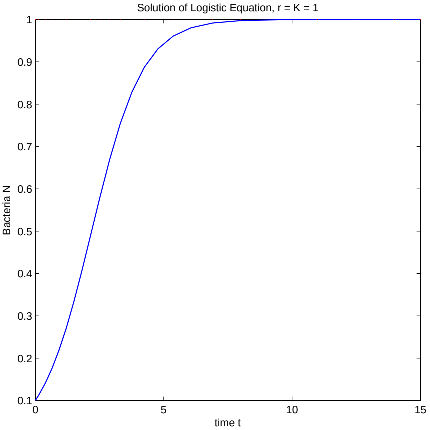
with doubling time: $N(T) = 2N(0)$

$$T = \ln(2)/r$$

The Logistic Equation

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right)$$

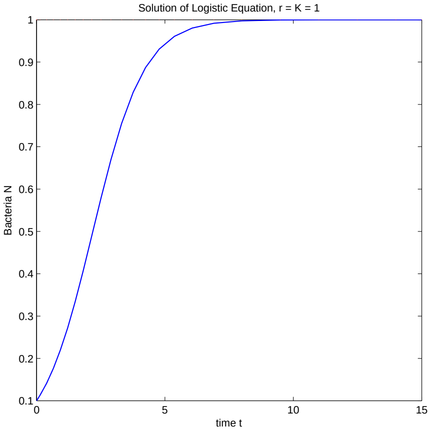
No change in N: $\frac{dN}{dt} = 0$ when $N = K$, equilibrium value of biomass.



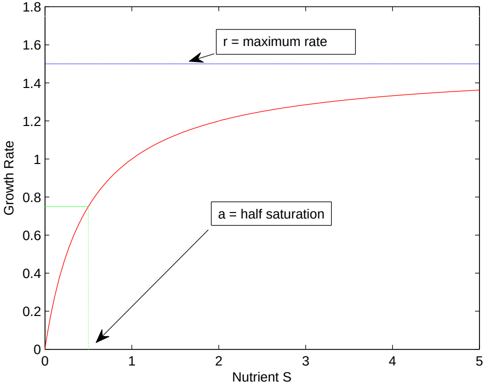
The Logistic Equation

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right)$$

No change in N: $\frac{dN}{dt} = 0$ when $N = K$, equilibrium value of biomass.



Growth under nutrient limitation, Monod(1942)

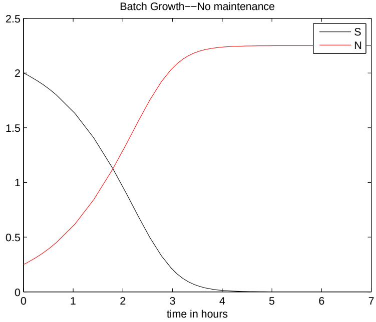


$$\frac{dN}{Ndt} = r\frac{S}{a+S}, \qquad \frac{dN}{-dS} = \text{yield constant} = \gamma$$

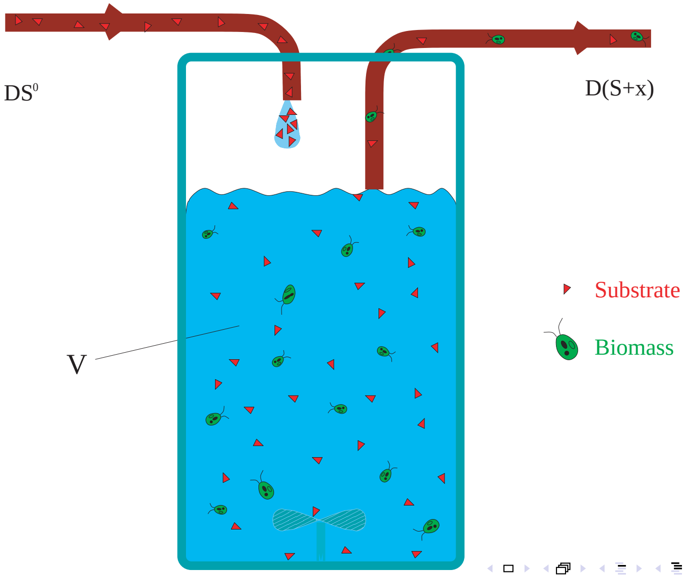
Growth in Batch Culture

$$\frac{dS}{dt} = -\frac{1}{\gamma}\frac{rSN}{a+S}, \quad S(0) = 2$$

$$\frac{dN}{dt} = \frac{rSN}{a+S}, \quad N(0) = 0.25$$



The Chemostat



The Old Tank Problem-No Bacteria

V = Volume of chemostat(ml)
F = Inflow = Outflow rate (ml/hr)
S^0 = Concentration of Substrate in Feed (gm/ml).
S = Concentration of Substrate in Chemostat (gm/ml).

Rate of change of Substrate (gm/hr)= INFLOW(gm/hr) - OUTFLOW(gm/hr)

$$\frac{d}{dt}(VS) = FS^0 - FS$$

Let $D = F/V$ be the Dilution Rate. Then

$$\frac{dS}{dt} = D(S^0 - S).$$

Mean Residence Time of chemostat is $\frac{1}{D} = \frac{V}{F}$.

The Old Tank Problem-No Bacteria

V = Volume of chemostat(ml)
F = Inflow = Outflow rate (ml/hr)
S^0 = Concentration of Substrate in Feed (gm/ml).
S = Concentration of Substrate in Chemostat (gm/ml).

Rate of change of Substrate (gm/hr)= INFLOW(gm/hr) - OUTFLOW(gm/hr)

$$\frac{d}{dt}(VS) = FS^0 - FS$$

Let $D = F/V$ be the Dilution Rate. Then

$$\frac{dS}{dt} = D(S^0 - S).$$

Mean Residence Time of chemostat is $\frac{1}{D} = \frac{V}{F}$.

The Old Tank Problem-No Bacteria

V = Volume of chemostat(ml)
F = Inflow = Outflow rate (ml/hr)
S^0 = Concentration of Substrate in Feed (gm/ml).
S = Concentration of Substrate in Chemostat (gm/ml).

Rate of change of Substrate (gm/hr)= INFLOW(gm/hr) - OUTFLOW(gm/hr)

$$\frac{d}{dt}(VS) = FS^0 - FS$$

Let $D = F/V$ be the Dilution Rate. Then

$$\frac{dS}{dt} = D(S^0 - S).$$

Mean Residence Time of chemostat is $\frac{1}{D} = \frac{V}{F}$.

The Old Tank Problem-No Bacteria

V = Volume of chemostat(ml)
F = Inflow = Outflow rate (ml/hr)
S^0 = Concentration of Substrate in Feed (gm/ml).
S = Concentration of Substrate in Chemostat (gm/ml).

Rate of change of Substrate (gm/hr)= INFLOW(gm/hr) - OUTFLOW(gm/hr)

$$\frac{d}{dt}(VS) = FS^0 - FS$$

Let $D = F/V$ be the Dilution Rate. Then

$$\frac{dS}{dt} = D(S^0 - S).$$

Mean Residence Time of chemostat is $\frac{1}{D} = \frac{V}{F}$.

Classical Chemostat Model

Novick & Szilard, 1950.

$$\frac{dS}{dt} = D(S^0 - S) - \frac{1}{\gamma}\frac{rSN}{a+S}$$
$$\frac{dN}{dt} = \frac{rSN}{a+S} - DN$$

Environmental parameters: $D = F/V,\ S^0$

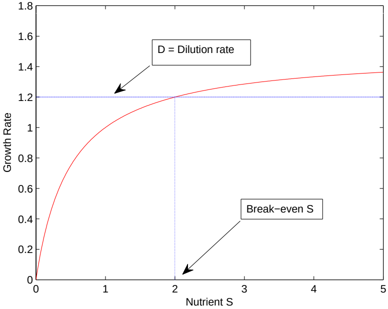
Biological parameters: $r,\ a,\ \gamma$

Break-even nutrient level

$$\frac{dN}{Ndt} = \frac{rS}{a+S} - D = 0$$

when

$$S = \lambda = \frac{aD}{r-D}$$



Survival or Washout

If flow rate is not too large:

$$D = \frac{F}{V} < r$$

and if the nutrient supply exceeds the break-even level:

$$\lambda < S^0$$

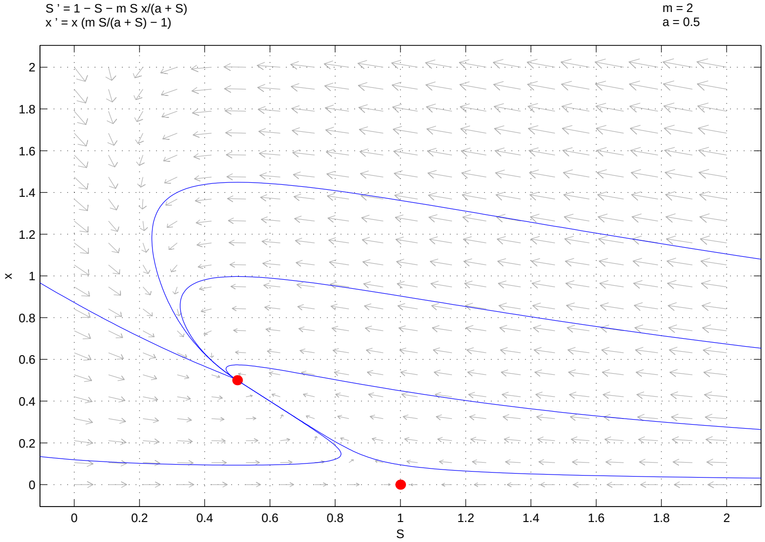
then bacteria survive:

$$N(t) \to \gamma(S^0 - \lambda)$$

Otherwise, they are washed out:

$$N(t) \to 0$$

Phase Plane

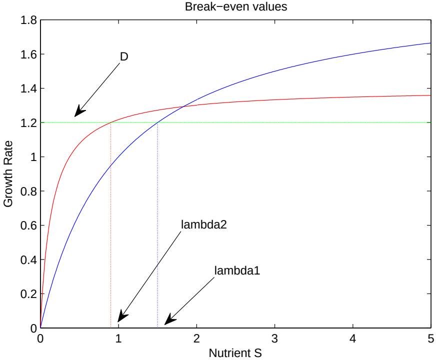


Competing Strains of Bacteria

$$
\begin{aligned}
\frac{dS}{dt} &= D(S^0 - S) - \frac{1}{\gamma_1}\frac{r_1 N_1 S}{a_1 + S} - \frac{1}{\gamma_2}\frac{r_2 N_2 S}{a_2 + S} \\
\frac{dN_1}{dt} &= \left(\frac{r_1 S}{a_1 + S} - D\right) N_1 \\
\frac{dN_2}{dt} &= \left(\frac{r_2 S}{a_2 + S} - D\right) N_2
\end{aligned}
$$

Break-even concentrations

$$\frac{dN_1}{N_1 dt} = \frac{r_1 S}{a_1 + S} - D = 0 \Leftrightarrow S = \lambda_1 = \frac{a_1 D}{r_1 - D}$$
$$\frac{dN_2}{N_2 dt} = \frac{r_2 S}{a_2 + S} - D = 0 \Leftrightarrow S = \lambda_2 = \frac{a_2 D}{r_2 - D}$$



Competitive Exclusion Principle

Hsu,Hubbell,Waltman (1977); Aris, Humphrey (1977), Powell(1958), Stewart,Levin(1973), Tilman (1982)

Assume that both species can survive in the absence of competition. If

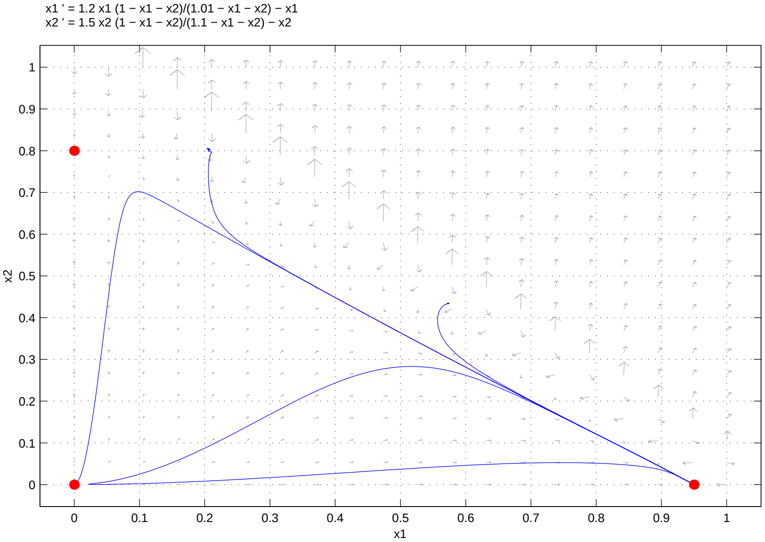
$$\lambda_1 < \lambda_2 < S^0$$

Then N_1 wins:

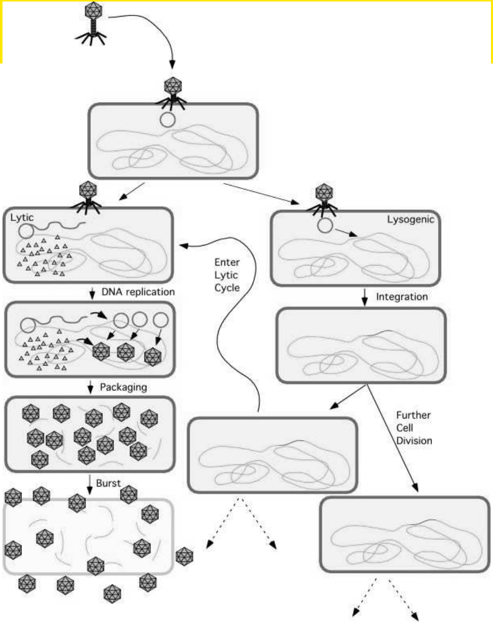
$$N_1(t) \to \gamma_1(S^0 - \lambda_1), \quad N_2(t) \to 0$$

Winner is the organism that can grow at the lowest nutrient level.

Winner grows at lowest substrate level



Life Cycle of Phage



Stewart, Levin, Chao, The American Naturalist (1977)

S = glucose, N = E. coli, P = T4 Phage, N_I = infected E. coli
$\tau = 0.6hrs$ phage latent period, $b = 80$ burst size

$$\frac{dS}{dt} = D(S^0 - S) - \frac{1}{\gamma}\frac{rSN}{a+S}$$

$$\frac{dN}{dt} = \left(\frac{rS}{a+S} - D\right)N - kNP$$

$$\frac{dN_I}{dt} = kNP - e^{-D\tau}kN(t-\tau)P(t-\tau) - DN_I$$

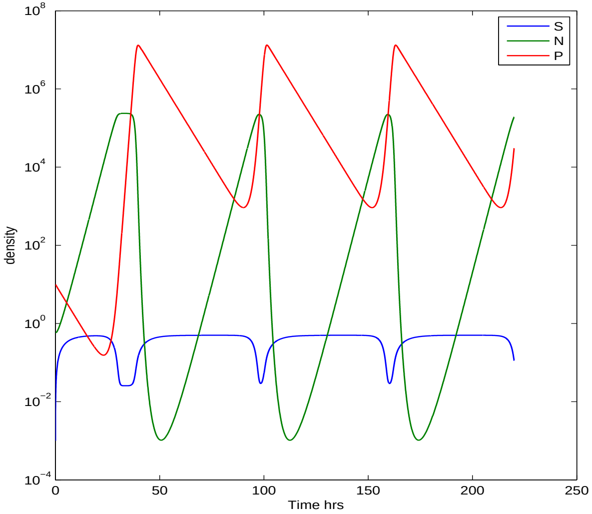
$$\frac{dP}{dt} = be^{-D\tau}kN(t-\tau)P(t-\tau) - kN(t)P(t) - DP(t)$$

Stewart, Levin, Chao, The American Naturalist (1977)

S = glucose, N = E. coli, P = T4 Phage, N_I = infected E. coli
$\tau = 0.6hrs$ phage latent period, $b = 80$ burst size

$$\begin{aligned}
\frac{dS}{dt} &= D(S^0 - S) - \frac{1}{\gamma}\frac{rSN}{a+S} \\
\frac{dN}{dt} &= \left(\frac{rS}{a+S} - D\right)N - kNP \\
\frac{dN_I}{dt} &= kNP - e^{-D\tau}kN(t-\tau)P(t-\tau) - DN_I \\
\frac{dP}{dt} &= be^{-D\tau}kN(t-\tau)P(t-\tau) - kN(t)P(t) - DP(t)
\end{aligned}$$

Phage-Bacteria cycles



Food Chain: Z eats Y eats X

$$
\begin{aligned}
\frac{dX}{dt} &= X(1-X) - \frac{r_1 XY}{a_1 + X} \\
\frac{dY}{dt} &= \frac{r_1 XY}{a_1 + X} - d_1 Y - \frac{r_2 YZ}{a_2 + Y} \\
\frac{dZ}{dt} &= \frac{r_2 YZ}{a_2 + Y} - d_2 Z
\end{aligned}
$$

A. Hastings, Chaos in a 3-species food chain, Ecol. Soc. Amer. 72 (1991)

Food Chain: Z eats Y eats X

$$\frac{dX}{dt} = X(1-X) - \frac{r_1XY}{a_1+X}$$
$$\frac{dY}{dt} = \frac{r_1XY}{a_1+X} - d_1Y - \frac{r_2YZ}{a_2+Y}$$
$$\frac{dZ}{dt} = \frac{r_2YZ}{a_2+Y} - d_2Z$$

A. Hastings, Chaos in a 3-species food chain, Ecol. Soc. Amer. 72 (1991)

Food Chain: Z eats Y eats X

$$
\begin{aligned}
\frac{dX}{dt} &= X(1-X) - \frac{r_1 XY}{a_1 + X} \\
\frac{dY}{dt} &= \frac{r_1 XY}{a_1 + X} - d_1 Y - \frac{r_2 YZ}{a_2 + Y} \\
\frac{dZ}{dt} &= \frac{r_2 YZ}{a_2 + Y} - d_2 Z
\end{aligned}
$$

A. Hastings, Chaos in a 3-species food chain, Ecol. Soc. Amer. 72 (1991)

Teacup attractor for Food Chain