My name, year in graduate school, college undergrad

<u>Mathematics of population growth</u> (generalize population, anything from humans to yeast)

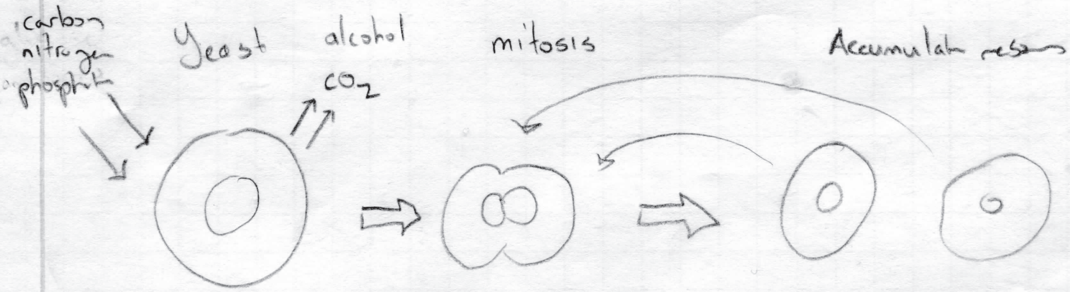
Why do we care about pop. growth?

prediction (human)
simulation
classification (strain)

Living things reproduce (but not everything that reproduces is living)

when they accumulate enough resources to create progeny

Resources can be space, food, number of competitors, etc.

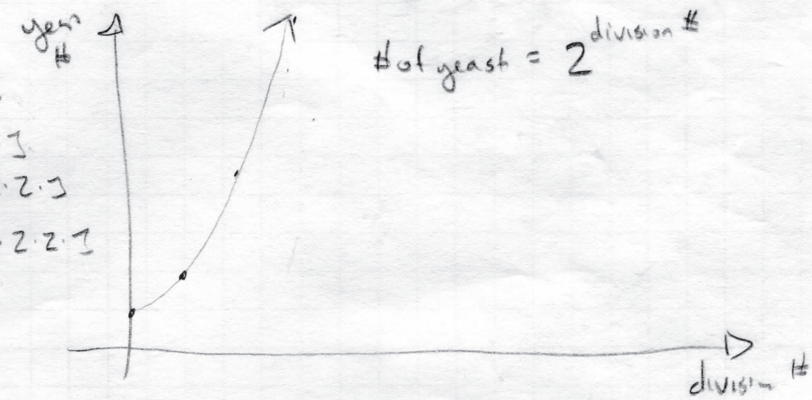


Yeast grows until it reaches a certain size, and then activates a new cycle: mitosis.

How many yeast will there be after 10 stages of division?

Division #	Yeast #
0	$1 = 1$
1	$2 = 2 \cdot 1$
2	$4 = 2 \cdot 2 \cdot 1$
3	$8 = 2 \cdot 2 \cdot 2 \cdot 1$
4	$16 = 2 \cdot 2 \cdot 2 \cdot 2 \cdot 1$
5	32
6	64

Let's plot this



$\#\text{ of yeast} = 2^{\text{division }\#}$

Change in yeast #

—
1
2
4
8

$$\frac{\Delta \text{Yeast}}{\Delta \text{division}} = \text{Yeast}$$

Lets convert this to time.

$$\frac{N(t+\Delta t) - N(t)}{\Delta t} = N(t)$$

As $\Delta t \to 0$ we have a derivative

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

What does $\frac{dN}{dt} = N$ mean?

$\frac{1}{N}\frac{dN}{dt} = 1$ The change of population per time per capita is one.
I.e. Each cell ~~split~~ has one daugther per unit time

This makes sense if we talk about divisions, but we want to talk about time.

So we say a cell has b daughters per unit time where b is birth rate.

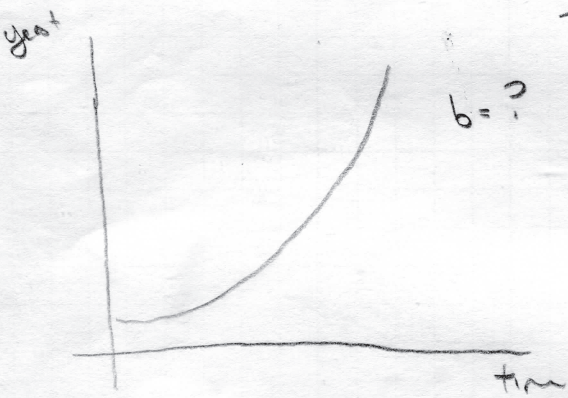
$\frac{1}{N}\frac{dN}{dt} = b \qquad \frac{dN}{dt} = bN$

Rotor

__Activity #1.__ Solve $\frac{dN}{dt} = bN$

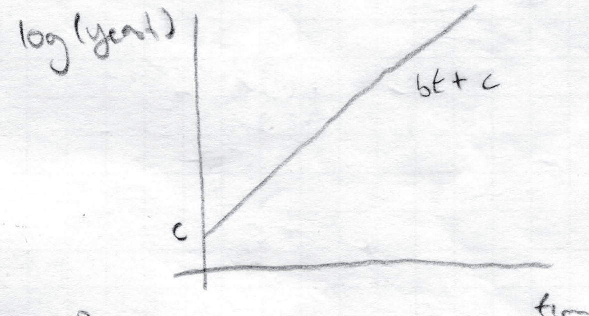
$\frac{dN}{N} = b \qquad \int \frac{dN}{N} = \int b\,dt \qquad \underline{\log N = bt + c} \qquad N(t) = e^{bt+c} = ae^{bt}$

This equation is useful



b = ?

$\Rightarrow$



This gives us b, the growth rate. (growth per time)

What do we do if we want doubling time?

__Activity #2:__ Determine doubling time given b

$N(0) = a$, double should be $2a$

$2a = ae^{bt}$, $\ln 2 = bt$

$2 = e^{bt}$, $t_{dbl} = \frac{\ln 2}{b}$

Or reparameterize in terms of doubling time, $b = \frac{\log 2}{t_{dbl}}$

$$N(t) = ae^{\frac{\log 2}{t_{dbl}} t} = a2^{\frac{t}{t_{dbl}}} = a2^{\#\text{ of doubling times}}$$

Activity #3

Assume yeast are cubic (they are spherical) with a length of $3\mu m$ and a doubling time of 2 hours. If yeast can survive off air (which they cannot) how long would it take one yeast cell to fill up a room with it's progeny?

Assume room is V

$$\frac{V\,m^3}{(3\times10^{-6}\,m)^3} = N(t) = e^{\frac{\log 2}{2}t}$$

$$t = \log\left(\frac{V\,(m^3)}{(3\times10^{-6}\,m)^3}\right)\frac{2}{\log 2} \text{ hours}$$

$V = 100 m^3$

$t = 124$ hours $\approx$ 5 days

Each

So if I leave a yeast cell in here we will be covered in yeast within 5 days....?

Why is this not true?

- Environment - nutrient depletion
- Cell death rate
- Variable cell growth rate
- Competition (ecology)

Exponential growth does not address these things. It also does not address

- Stochasticity
- Lag times
- Spatial / Temporal variability

Logistic equation

The first person to notice problems modeling with logistic equation was John Graunt (1620-1674), a haberdasher collected facts and founded demography (study of human population)

determined growth rate = # of christenings - # of deaths and used this to determine doubling time for London's population: 64 years

determined population of world $2^{(1662+3948)} \sim 2.5\times10^{26} \sim 200\times10^6/cm^2$

current year; date Adam and Eve appeared, BC

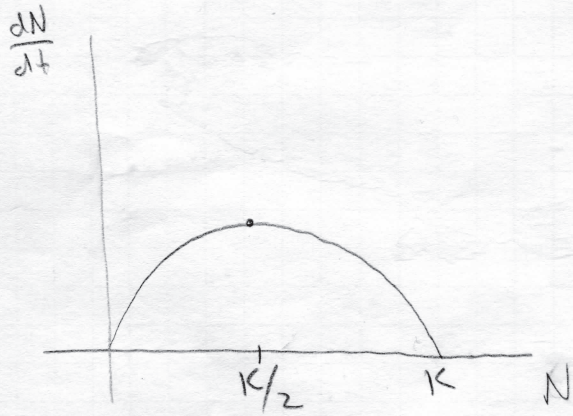
WAY too large, power of exponential growth.

Pierre-Francois Verhaulst (1800-1857)

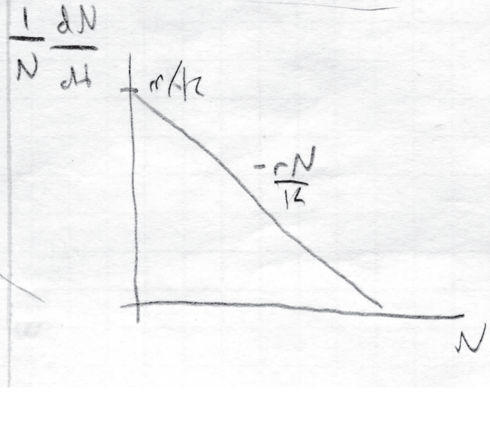
$$\frac{1}{N}\frac{dN}{dt} = (\text{birth rate} - \text{death rate})\left(1-\frac{N}{K}\right)$$

Added in parameter to say that change stops when $N=K$!

$$\frac{dN}{dt} = rN\left(1-\frac{N}{K}\right) = -\frac{rN^2}{K} + \frac{rN}{K}$$



Growth rate increases until it reaches max, and then slows down



The ability to reduce per individual gets harder and harder.

Limiting resources

Density dependence

JMP

Activity #4 Solve $\frac{dN}{dt} = rN(1 - \frac{N}{K})$

$\frac{d}{dx} \log x = \frac{1}{x}$

Seperate variables (N's on one side, t's on other)

$$\int \frac{dN}{N(1-\frac{N}{K})} = \int r\,dt = rt + c_0$$

$$\Downarrow$$

$$\int \frac{K}{N(K-N)} dN = \int \frac{1}{N} dN + \int \frac{1}{K-N} dN = \log N - \log(K-N) + c = \log\left(\frac{N}{K-N}\right) + c_1$$

$$\frac{K}{N(K-N)} = \frac{A}{N} + \frac{B}{K-N} = \frac{1}{N} + \frac{1}{K-N}$$

$K = AK - AN + BN$

$A = 1$

$B = A = 1$

$\log\left(\frac{N}{K-N}\right) = rt + c_2$

Assume $K - N > 0$

$\frac{N}{K-N} = c_3 e^{rt}$

$N = Kc_3e^{rt} - Nc_3e^{rt}$

$N + Nc_3e^{rt} = Kc_3e^{rt}$

$N = \frac{Kc_3e^{rt}}{1+c_3e^{rt}}$

Plug in initial condition $N(0) = N_0$

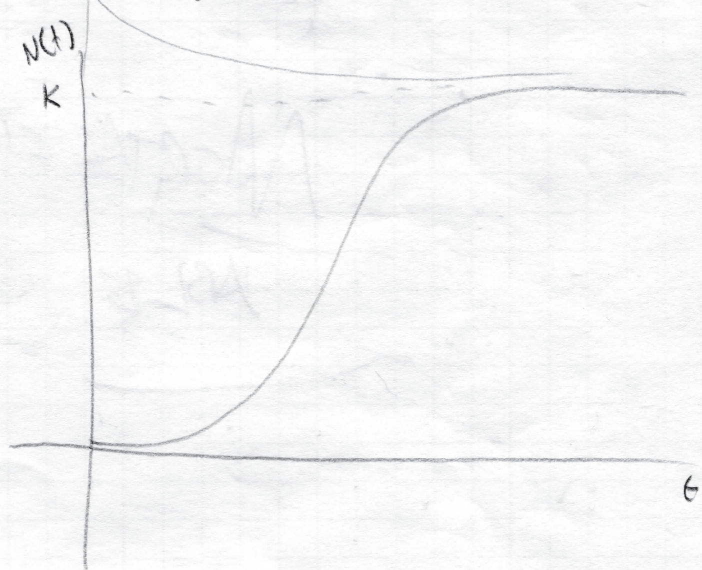
$N(0) = N_0 = \frac{Kc_3}{1+c_3}$

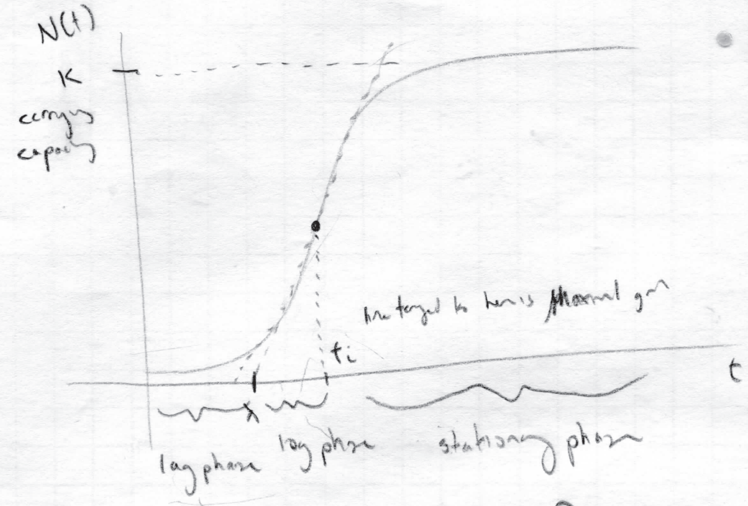
$N_0(1+c_3) = Kc_3$

$c_3 = \frac{N_0}{K-N_0}$

$$\Rightarrow N(t) = \frac{K\left(\frac{N_0}{K-N_0}\right)e^{rt}}{1+\left(\frac{N_0}{K-N_0}\right)e^{rt}} = \frac{KN_0e^{rt}}{K-N_0+N_0e^{rt}}$$

$$\times \frac{N_0e^{rt}}{N_0e^{rt}} = \frac{K}{(\frac{K}{N_0}-1)e^{-rt}+1}$$





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

$\approx rN$ at small N

Why is this a good model for yeast growth?

Yeast undergo three phases of growth which can be extrapolated

lagphase: yeast start up machinery, begin responding to environment

"waking up"

lagtime

log phase or exponential phase: yeast are happy as could be! In anaerobic state, consuming as much sugar as possible & producing CO_2 & alcohol byproducts.

sidenote: why does yeast produce alcohol?

maximal growth rate

stationary phase: yeast are still growing, but <u>much</u> slower since all of the glucose is gone. Switch to aerobic growth, & metabolize alcohol

carrying capacity

diauxic shift

lots of sugar makes yeast grow in fermentation, using glucose to produce alcohol & CO_2

when sugar is gone the yeast use alcohol to continue growing

Equation of logistic growth $N(t) = \dfrac{K}{1 + \left(\frac{K}{N_0} - 1\right)e^{-rt}}$

can be generalized to $N(t) = \dfrac{a}{1 + e^{b-ct}}$

There ~~three~~ are <u>3</u> parameters & 3 things we are interested in:

lag time

maximal growth rate

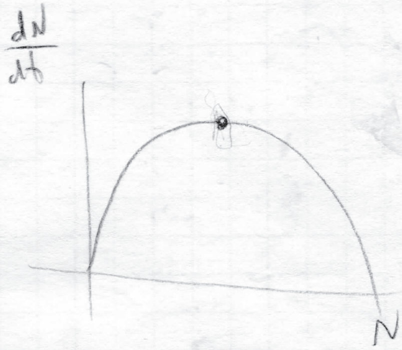
carrying capacity

Activity #5 Reparameterize general equation

Carrying capacity

$$\lim_{t \to \infty} N(t) = \lim_{n \to \infty} \frac{a}{1+e^{b-ct}} = \boxed{a = K}$$

Maximal growth rate occurs when $\frac{dN}{dt}$ is maximum



which occurs when $\frac{d^2N}{dt^2} = 0$

$$\frac{dN}{dt} = \frac{d}{dt}\left(\frac{a}{1+e^{b-ct}}\right) = \frac{-a(-ce^{b-ct})}{(1+e^{b-ct})^2} = \frac{ace^{b-ct}}{(1+e^{b-ct})^2}$$

$$\frac{d^2N}{dt^2} = \frac{d}{dt}\left(\frac{ace^{b-ct}}{(1+e^{b-ct})^2}\right)$$

Quotient Rule

$$\frac{d}{dt}\left(\frac{f(t)}{g(t)}\right) = \frac{f'g - g'f}{|g|^2}$$

$$= \frac{ac(-c)e^{b-ct}(1+e^{b-ct})^2 - 2(-c)(1+e^{b-ct})ace^{b-ct}}{(1+e^{b-ct})^4}$$

$$= \frac{-ac^2e^{b-ct}(1+e^{b-ct})^2 + 2ac^2e^{b-ct}(1+e^{b-ct})}{(1+e^{b-ct})^4} = 0 \text{ when } t_{max} = \frac{b}{c}$$

Growth rate at $t_{max} = \frac{dN}{dt}(t_{max}) = \frac{ace^{b-c(\frac{b}{c})}}{(1+e^{b-c(\frac{b}{c})})^2} = \boxed{\frac{ac}{4} = \mu_m}$ $\boxed{c = \frac{4\mu_m}{a}}$

Lag time occurs when tangent line from maximal growth rate hits x-axis

Tangent line $y = \mu_m t + d$ $\quad y = N\left(\frac{b}{c}\right) = \frac{a}{2}$ $\quad t = \frac{b}{c}$

$$\frac{a}{2} = \mu_m\left(\frac{b}{c}\right) + d \qquad d = \frac{a}{2} - \mu_m\frac{b}{c}$$

$$y = \mu_m t + \frac{a}{2} - \mu_m\frac{b}{c}$$

$$0 = \mu_m t_\lambda + \frac{a}{2} - \mu_m\frac{b}{c}$$

$$\frac{\mu_m\frac{b}{c} - \frac{a}{2}}{\mu} = t_\lambda$$

$$\frac{\frac{ac}{4}\frac{b}{c} - \frac{a}{2}}{\frac{ac}{4}} = t_\lambda$$

$$t_\lambda = \frac{\frac{ab}{4} - \frac{a}{2}}{\frac{ac}{4}} = \frac{b}{c} - \frac{2}{c}$$

$$\boxed{t_{lag} = \frac{b-2}{c}} \qquad \boxed{b = ct_{lag} + 2 = \frac{4\mu_m}{a}t_{lag} + 2}$$

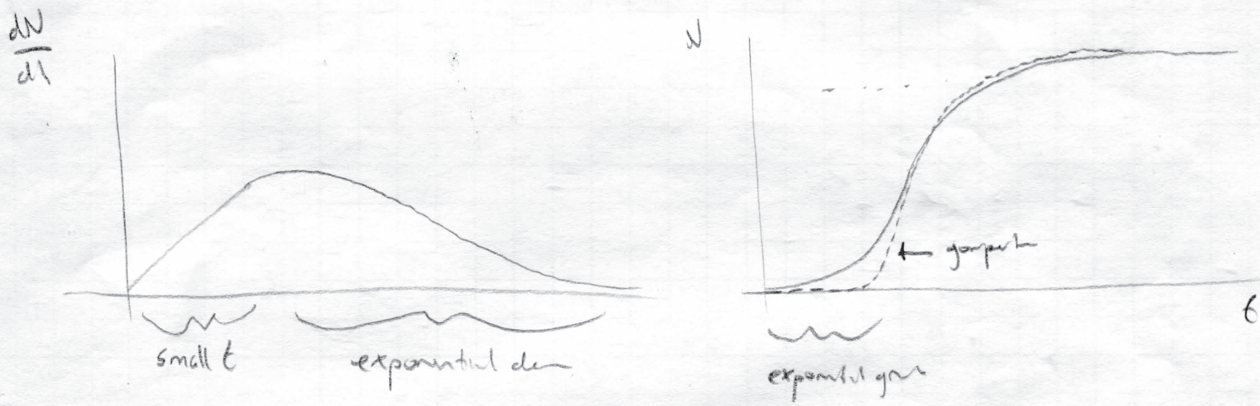
Plug it in

$$N(t) = \frac{K}{1 + e^{\frac{4\mu m}{K} t_{lag} + 2 - \frac{4\mu m}{K} t}} = \frac{K}{1 + e^{\left(-\frac{4\mu m}{K}(t - t_{lag}) + 2\right)}}$$

Gompertz, developed in 1825

Instead of carrying capacity, what if we assume cells divide slower as time goes on and the number increases. Why does this make sense? (resources)

$$\frac{dN}{dt} = q e^{-\alpha t} N$$ sketch this



Activity #6

Solve $\frac{dN}{dt} = q e^{-\alpha t} N$

$$\int \frac{1}{N} dN = \int q e^{-\alpha t} dt$$

$$\log N = -q\alpha e^{-\alpha t} + c$$

$$N(t) = m e^{-q\alpha e^{-\alpha t}} = a e^{-e^{b-ct}}$$

$$y = K e^{-e^{\left(\frac{\mu m e}{K}(t_{lag} - t) + 1\right)}}$$ Reparameterized in the same way

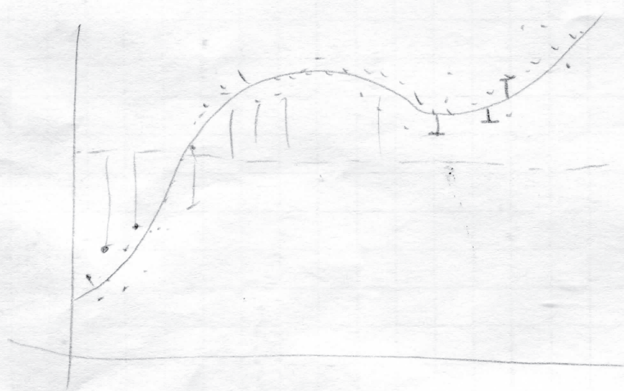
Regression Fitting curves to data

Sum of squared error $= \sum_{i=1} (y_i - f_i)^2$ $\quad y_i$ = data, f_i = model

Sample variance proportional $\sum_{i=1} (y_i - \bar{y})^2$

Fraction of unexplained variance (variance that we can not determine from model) $= \frac{SSE}{SST}$ $\quad$ Explained variance $= 1 - \frac{SSE}{SST} = R^2$

Maximize R^2, minimize



← mean

$\frac{SSE}{SST} = 1$ then you are doing no better than drawing the average

$\frac{SSE}{SST} = 0$ then you explain it perfectly

$1 - \frac{SSE}{SST}$

Activity #7 Fitting real data