Growth of Microorganisms

$N(t)$ = bacteria density at time t

K = reproduction rate per unit time

The meaning of K is the number of new bacteria that spawn from one bacteria in one unit of time

(1) $$N(t+\Delta t) - N(t) = K\, N(t)\, \Delta t$$

hence

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

Let $\Delta t \to 0$ in (2) to arrive at

(1) $$\boxed{\frac{dN}{dt} = K N}$$ Malthusian Growth.

When K is constant and the initial condition is $N(0) = N_0$ the solution of (1) is

(2) $$N(t) = N_0\, e^{Kt}$$

Many alternate assumptions can be made about the reproduction rate.

Notes on units

Throughout we will use the square bracket notation $[X]$ to denote the units of X

Additionally we shall let

$$L = \text{unit of length}$$

$$M = \text{unit of mass}$$

$$T = \text{unit of time}$$

Examples

v = velocity $\qquad [v] = LT^{-1}$

g = gravity constant $\qquad [g] = LT^{-2}$

F = force $\qquad [F] = MLT^{-2}$

E = energy $\qquad [E] = ML^2T^{-2}$

EXAMPLE Microorganism where N is bacteria density

$$\frac{dN}{dt} = KN \qquad [N] = \frac{\#}{L^3} \qquad [K] = T^{-1}$$

where # is "number of bacteria". Now suppose the bacteria are confined to a vat of volume V and let $n = NV$. Then

$$\frac{dn}{dt} = Kn \qquad [n] = \#$$

n = total number of bacteria.

Doubling time and experimental correspondence

$$\frac{dn}{dt} = \mathbb{K} n \qquad\qquad n(0) = n_0$$

has the solution

(1) $$n(t) = n_0 e^{+\mathbb{K} t}$$

The time τ it take for population doubling:

$$2n_0 = n_0 e^{+\mathbb{K}\tau}$$

soluing for τ

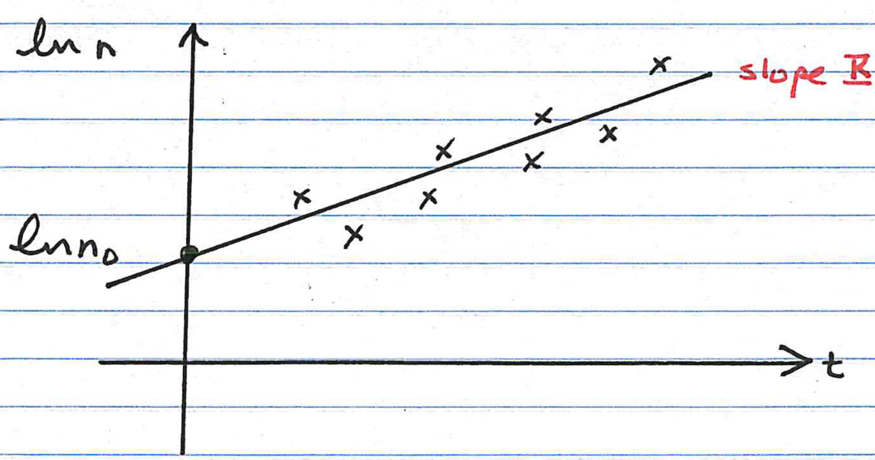
(2) $$\tau = \frac{\ln 2}{\mathbb{K}}$$

To find $\mathbb{K}$ from raw data first note taking log of (1) yields

slope

(3) $$\ln n = \ln n_0 + \mathbb{K} t$$

Measure many (t, n) pairs and find slope that best fits



Nutrient Dependent Growth

Reasonable to assume bacteria growth rate depends on the nutrient concentration C

$$C = \text{nutrient concentration}$$

$$[C] = M L^{-3}$$

Simplest assumption:

$$(1) \qquad \boxed{K(C) = \kappa C}$$

Next we introduce yield $Y = \alpha^{-1}$ where

α = mass of nutrient consumed in producing one new bacteria

$$[\alpha] = M/\#$$

So defined such that

$$(2) \qquad \boxed{\frac{dC}{dt} = -\alpha \frac{dN}{dt}}$$

In (2) the units of both sides must match:

$$\frac{M}{\cancel{T}\cancel{L^3}} = [\alpha] \frac{\#}{\cancel{T}\cancel{L^3}}$$

hence

$$[\alpha] = \frac{M}{\#} \qquad \frac{\text{mass}}{\text{bacteria}}$$

Given assumptions (1) - (2) we have

(3) $$\frac{dN}{dt} = B(C)N = \kappa CN$$

(4) $$\frac{dC}{dt} = -\alpha \frac{dN}{dt} = -\alpha\kappa CN$$

are two coupled ODE's for C and N.

We reduce the order of the system by first integrating (4)

$$\frac{dC}{dt} = -\alpha\frac{dN}{dt}$$

(5) $$\boxed{C(t) = C_0 - \alpha N(t)} \qquad C(0) = C_0$$

Consequently (3) becomes

(6) $$\boxed{\frac{dN}{dt} = \kappa \underbrace{(C_0 - \alpha N)}_{} N}$$

same as density dependent growth.

The separable lrst order ODE (6) can be solved via partial fractions, i.e integ. in N:

$$\frac{dN}{N(C_0 - \alpha N)} = \left(\frac{A}{N} + \frac{B}{C_0 - \alpha N}\right) dN$$

Solution of: $\boxed{\dfrac{dN}{dt} = \kappa (C_0 - \alpha N) N \qquad N(0) = N_0}$

$$(1) \qquad \frac{dN}{N(C_0 - \alpha N)} = \left(\frac{1}{C_0} \frac{1}{N} + \frac{\alpha}{C_0} \frac{1}{C_0 - \alpha N} \right) dN = \kappa \, dt$$

Integrate over $[N_0, N]$

$$(2) \qquad \ln N - \ln(\alpha N - C_0) \Big|_{N_0}^{N} = \underbrace{\kappa C_0}_{r} t$$

$$(3) \qquad \ln \left(\frac{N_0 (N\alpha - C_0)}{N (N_0 \alpha - C_0)} \right) = -rt$$

where $r = \kappa C_0$. Solve (3) for $N(t)$

$$(4) \qquad N(t) = \frac{N_0 B}{N_0 + (B - N_0) e^{-rt}}$$

where

$r = \kappa C_0$ growth parameter

$B = C_0 / \alpha$ carrying capacity $N' = 0$

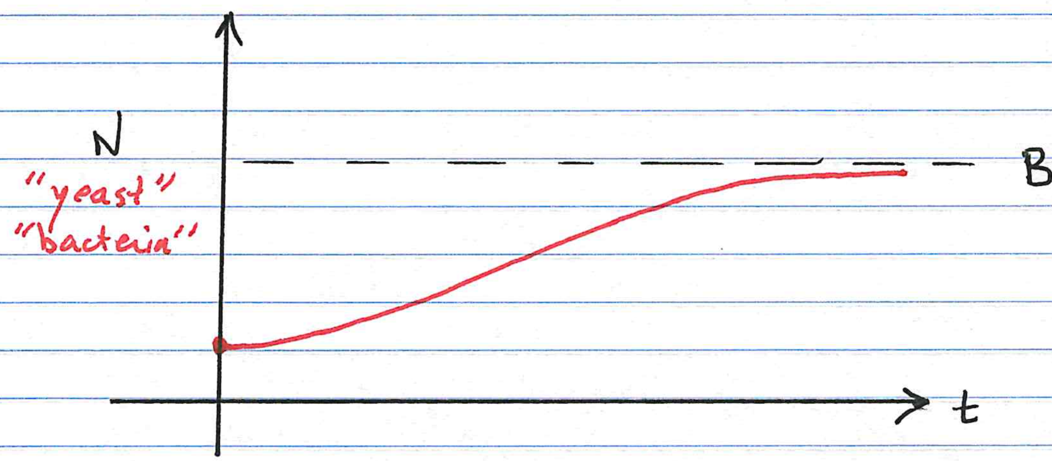
Population Density

$$\boxed{N(t) = \frac{N_0 B}{N_0 + (B - N_0)\, e^{-rt}}}$$

where $N_0 = N(0)$ and

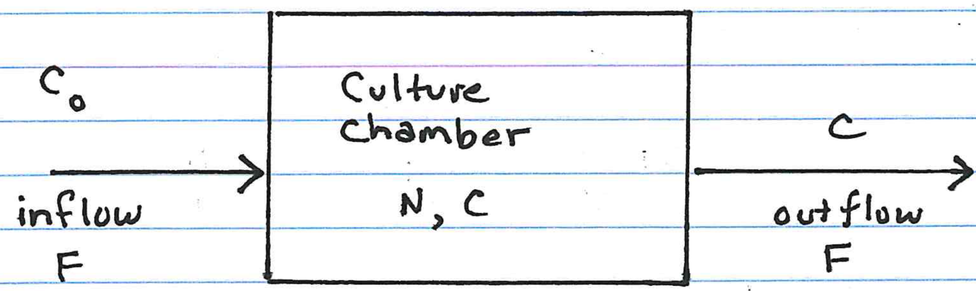
$r = K C_0$ = growth parameter

$B = C_0/\alpha$ = carrying capacity



* More realistic since population remains bounded

Chemostat Model



Bacteria of density N are in a culture chamber having nutrient concentration C. Nutrient of fixed concentration C_0 flows into the chamber at a constant flow rate F. The bacteria nutrient mix is pumped out at the same rate. Thus the volume V in the chamber is fixed.

$N(t)$	=	bacteria concentration	$\# L^{-3}$
$C(t)$	=	nutrient concentration	$M L^{-3}$
C_0	=	reservoir concentration	$M L^{-3}$
F	=	flow rate	$L^3 T^{-1}$
V	=	volume	L^3
Y	=	$\frac{1}{\alpha}$ yield constant	$\# M^{-1}$

Conservation of Bacteria

$$\frac{dN}{dt} = \text{reproduction} - \text{outflow}$$

Given $\underline{K}$ is the reproduction rate

$$(1) \qquad \frac{dN}{dt} = \underline{K} N - \frac{FN}{V}$$

Division by V is required for units to match:

$$\left[\frac{FN}{V}\right] = \frac{L^3}{T} \cdot \frac{1}{L^3} \cdot \frac{\#}{L^3} = \frac{\#}{T \cdot L^3}$$

which matches the other terms in (1)

Conservation of Nutrient

$$\frac{dc}{dt} = -\underset{\text{consumption}}{\text{bacteria}} - \text{outflow} + \text{inflow}$$

Given the same unit considerations

$$(2) \qquad \frac{dc}{dt} = -\alpha \underline{K} N - \frac{FC}{V} + \frac{FC_0}{V}$$

Again note the units

$$\left[\frac{FC}{V}\right] = \frac{L^3}{T} \cdot \frac{1}{L^3} \cdot \frac{M}{L^3} = \frac{M}{L^3 T}$$

Summary

One generally assumes the bacteria growth rate depends on the nutrient concentration

$$\mathbb{K} = \mathbb{K}(C)$$

for some function $\mathbb{K}$.

$$\boxed{\begin{aligned} \frac{dN}{dt} &= \mathbb{K}(C)N - \frac{FN}{V} \\ \frac{dC}{dt} &= -\alpha\mathbb{K}(C)N - \frac{FC}{V} + \frac{FC_0}{V} \end{aligned}}$$

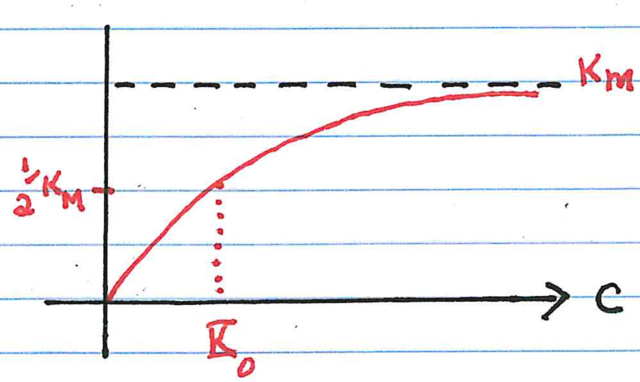
Two coupled nonlinear differential equations.

Michaelis Menten Kinetics

$$\boxed{\mathbb{K}(C) = \frac{K_M C}{\mathbb{K}_0 + C}}$$

Common assumed form. Derivation later

This reproduct rate has a saturation:



Graph of $\mathbb{K}(C)$. Saturates at maximal rate of $\mathbb{K}_M$.

Dimensional Analysis

Is a process by which dependent and independent variables are scaled by constants of like units in a manner which simplifies the model equations. Here

(1) $n = \dfrac{N}{N^*}$ $\qquad c = \dfrac{C}{C^*}$ $\qquad \tau = \dfrac{t}{t^*}$.

Here N^*, C^* and t^* are constants having units of $[N], [C], [t]$. We get to chose these constants. And note that (n, c, τ) are now <u>dimensionless</u>!

Substitute (1) into the model equations:

$$\frac{d(nN^*)}{d(\tau t^*)} = \left(\frac{K_M C^* c}{K_0 + C^* c}\right)(nN^*) - \frac{F}{V}(nN^*)$$

$$\underbrace{\frac{dn}{d\tau}}_{\text{isolate}} \cdot \frac{N^*}{t^*} = \frac{K_M \; N^* c}{K_0/C^* + c} \cdot n - \left(\frac{FN^*}{V}\right) n$$

Ultimately for N-equation we get the dimensionless form

$$\frac{dn}{d\tau} = (K_M t^*) \frac{cn}{K_0/C^* + c} - \left(\frac{Ft^*}{V}\right) n$$

Non-arrowed terms are constants.

Pre-dimensionless scaled equations:

$$\text{(2)} \quad \frac{dn}{d\tau} = (K_M t^*)\left(\frac{c}{\underset{\substack{\uparrow\\ 2}}{K_0/C^*} + c}\right) n - \left(\underset{\substack{\uparrow\\ 1}}{\frac{Ft^*}{V}}\right) n$$

$$\text{(3)} \quad \frac{dc}{d\tau} = \left(\underset{\substack{\uparrow\\ 3}}{\frac{\alpha t^* K_M N^*}{C^*}}\right)\left(\frac{c}{K_0/C^* + c}\right) - \left(\frac{Ft^*}{V}\right) c + \left(\frac{t^* F C_0}{V C^*}\right)$$

Pick t^* so term 1 equals one

$$\text{(4)} \quad t^* = \frac{V}{F}$$

Pick C^* so term 2 equals one

$$\text{(5)} \quad C^* = K_0$$

Pick N^* so term 3 equals one

$$\text{(6)} \quad N^* = \frac{K_0}{\alpha t^* K_M}$$

With these choices (2)-(3) <u>greatly</u> simplify!

$$\boxed{\begin{aligned} \frac{dn}{d\tau} &= \alpha_1 \frac{nc}{1+c} - n \\ \frac{dc}{d\tau} &= -\frac{nc}{1+c} - c + \alpha_2 \end{aligned}}$$

Dimensionless Model

Has only two parameters

$$\alpha_1 = \frac{V K_M}{F}$$

$$\alpha_2 = \frac{C_0}{K_0}$$

Much better than original dimensional model

$$F, V, \alpha, C_0, K_M, K_0$$

six parameters!!