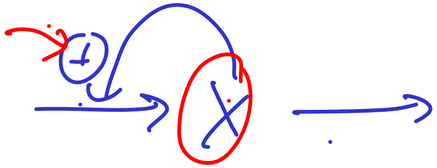
M4455: Synthetic Biology and Biotechnology

Model? $\rightarrow$ Simplified representation of a real system.



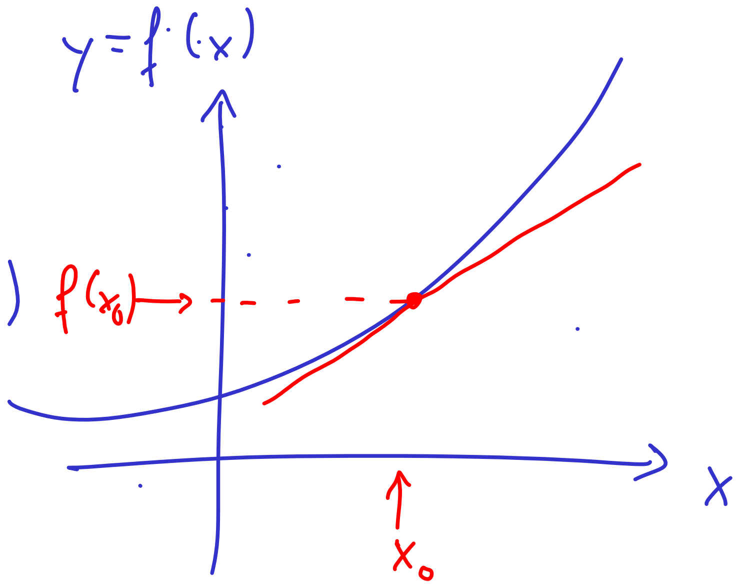
Mathematical Model: Quantitative & Mathematical description

Ordinary Differential Equations

- Universal
- Dynamic Systems
- Thorough Theory
- Numerics

Newton / Leibniz ~ 1700

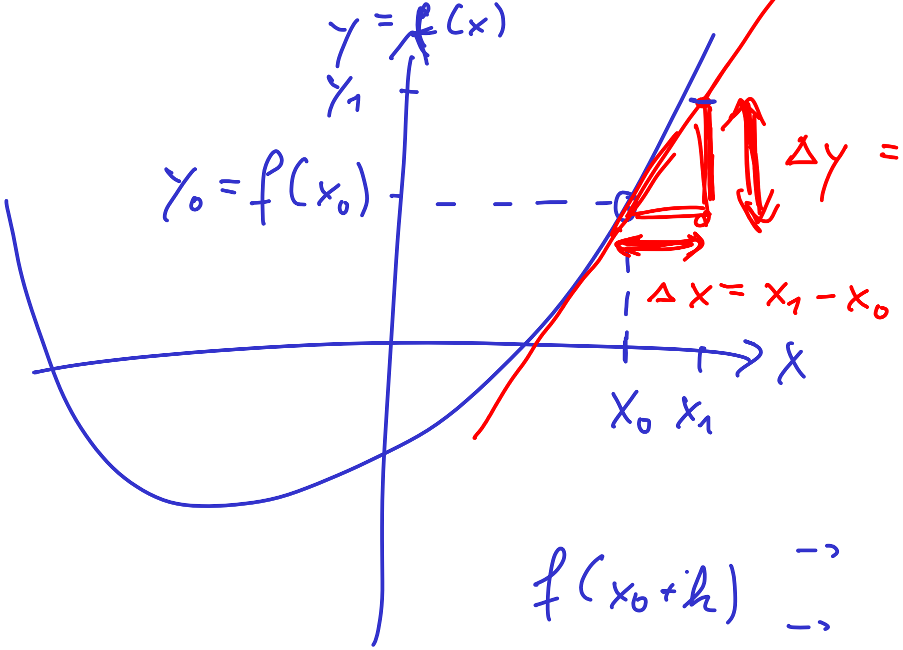
Recap: derivative Function $f(x)$



functions that change with time

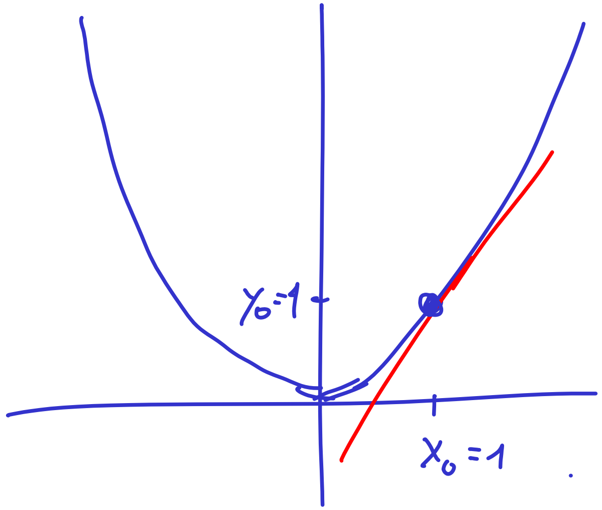
$x(t)$

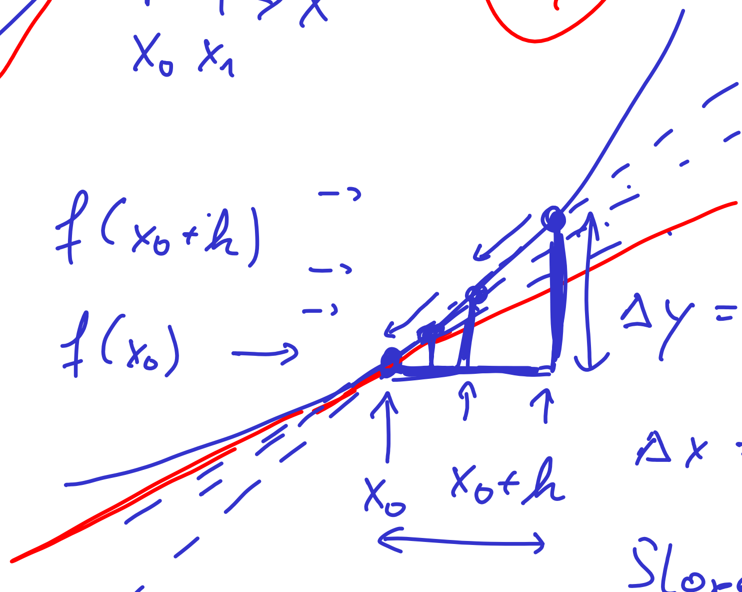
$x(t)$ unknown,
but $\frac{dx}{dt}$ is known!



$$\frac{\Delta y}{\Delta x}$$

Example $f(x) = x^2$





$$\Delta y = f(x_0+h) - f(x_0)$$

$$\Delta x = x_0 + h - x_0 = h$$

Slope: $$\frac{\Delta y}{\Delta x} = \frac{f(x_0+h) - f(x_0)}{h}$$

$$\frac{d f(x_0)}{dx} = \lim_{h \to 0} \frac{f(x_0+h) - f(x_0)}{h} = f'(x_0)$$

$f(x) = x^2$?

$$f(x+h) = (x+h)^2 = x^2 + 2xh + h^2$$

$$f'(x) = \lim_{h \to 0} \frac{f(x+h) - f(x)}{h} = \lim_{h \to 0} \frac{\cancel{x^2} + 2x\cancel{h} + \cancel{h^2} - \cancel{x^2}}{\cancel{h}} = \lim_{h \to 0} 2x + h = 2x$$

Definition

$x(\boxed{t}) = ?$

$\dot{x} = \frac{dx}{dt}$

Example

Growing bacteria

Observation: Every 20 minutes the population doubles

40 ×4

$\Rightarrow$ The population increase is proportional to the population

The growth rate is proportional to the population

$$\text{growth rate} = \frac{\text{increase in population}}{\text{time}} = v = \frac{dx}{dt}$$

x : bacterial population

$[x]$: number of bacteria

density (cells / volume)

$[v]: \frac{[x]}{\text{time}}$, e.g. $\frac{\text{number of bacteria}}{\text{minute}}$

Rule: growth rate is proportional to population (Hypothesis)

$$v = \frac{dx}{dt} = r \cdot x$$

proportionality constant

growth rate constant

$$[r] = \frac{1}{\text{time}}$$

Differential Equation:

$$\frac{dx}{dt} = \boxed{r} \cdot x$$

$$\boxed{\frac{dx(t)}{dt} = r \cdot x(t)} \quad (*)$$

Algebraic Equation

$$x^2 = 4 \qquad x^2 = -4$$

Solutions: $x = 2$ or $x = -2$

Numbers!

Unknown: $x(t)$

Try: $x(t) = e^{r \cdot t}$

Test: $\frac{dx}{dt} = r \cdot e^{r \cdot t}$ ⇐ this solves $(*)$,

because $\boxed{\frac{dx}{dt} = r \cdot x}$

$x(t) = x_0 \, e^{r \cdot t}$

$\frac{dx}{dt} = x_0 \cdot r \cdot e^{rt}$, also solves $(*)$

Infinite number of solutions! $x(t) = x_0 \cdot e^{rt}$

Initial value problem

Differential Equation + Initial Condition

has exactly one solution!

Initial conditions: x at time 0

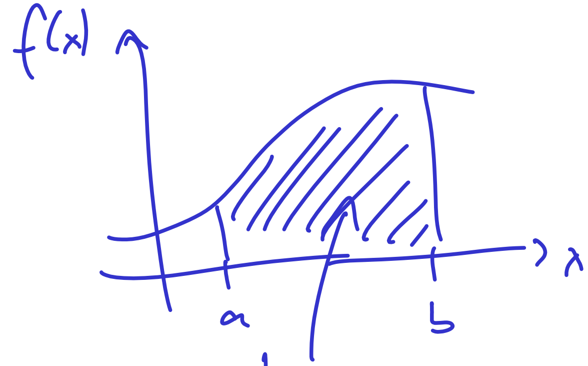
$x(0) = x_0$

" $\frac{dx}{dt} = r \cdot x \quad \Big| \cdot dt$ " Simplest differential equation

Separation of variables

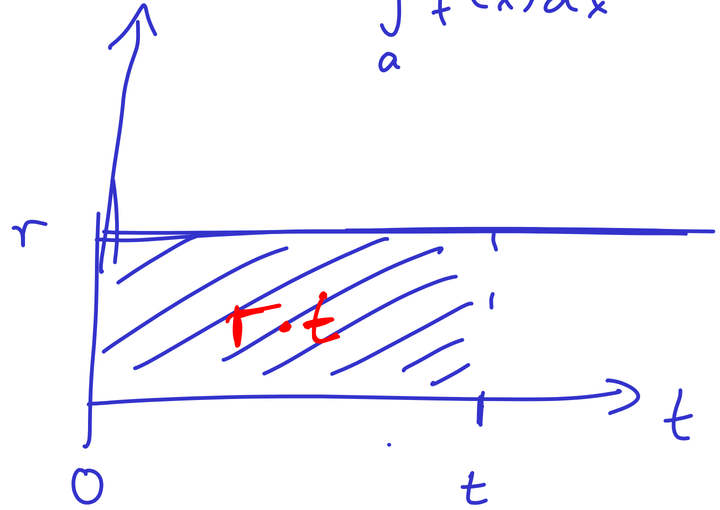
$$dx = r \cdot x \cdot dt \quad \Big| : x$$

$$\frac{dx}{x} = r \cdot dt \quad \leftarrow \quad \text{separated } x \text{ and } t$$



$$\int_a^b f(x)\,dx$$

$f(t) = r$



$$\int_{x(0)}^{x(t)} \frac{dx}{x} = \int_0^t r \cdot dt = r \cdot t$$

derivation $\frac{d}{dt}$

$$\int \frac{1}{x}\,dx = \ln x$$

$$\frac{d}{dx}$$

$$x^{-2} \xrightarrow{\frac{d}{dx}} -2x^{-3}$$

$$x^n \longrightarrow n \cdot x^{\underline{n-1}} \leftarrow$$

$$\ln x(t) - \ln x(0) = r \cdot t$$

$$\ln a - \ln b = \ln \frac{a}{b}$$

$$\Leftrightarrow \ln \frac{x(t)}{x(0)} = r \cdot t \Leftrightarrow \frac{x(t)}{x(0)} = e^{r \cdot t} \Leftrightarrow \boxed{x(t) = x(0) \cdot e^{rt}}$$

Observations

↓

Model

↓

Prediction

agreement → confirmation of model assumptions

<u>disagreement</u>

↓

identify missing components

question model assumption

Model assumption for exponential growth:

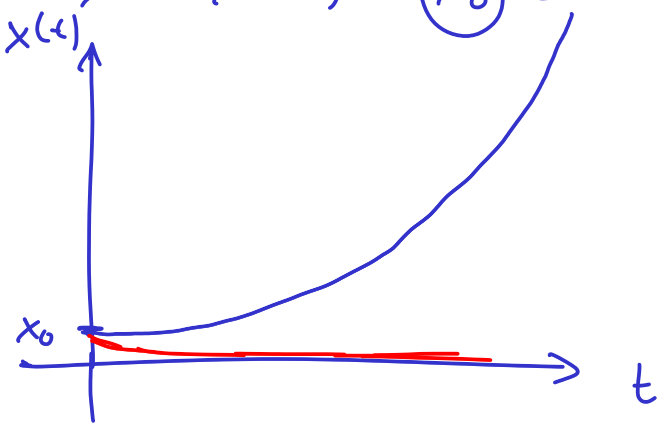
growth rate is proportional to population

x: population

r: constant (growth rate const.)

$$\rightarrow \quad \frac{dx}{dt} = r \cdot x \quad \longrightarrow \quad x(t) = x_0 e^{rt}$$

$x_0 = x(0)$: initial population



$r > 0$

$r < 0$

$$\lim_{t \to \infty} x(t) \rightarrow \infty$$

$$24\ \text{hrs} = 72 \cdot 20\ \text{min}$$

$$2^{10} = 1024 \approx 1000 = 10^3$$

$$1\ \text{bacterium} \longrightarrow 2^{72}\ \text{bacteria}$$

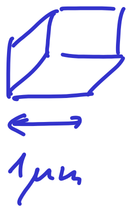
$$2^{70} \approx 10^{21}$$

$$2^{72} \approx 4 \cdot 10^{21}$$

$$V_{E.coli} = 1\ fl$$

$$2^{72} \cdot V_{E.coli} = 4 \cdot 10^{21} \cdot 10^{-18}\ m^3 = \underline{\underline{4000\ m^3}}$$

$$20m \times 20m \times 10m$$



$$(\underbrace{1\mu m}_{10^{-6}\,m})^3 = 10^{-18}\ \underbrace{m^3}_{1000\ l} = 10^{-15}\ l = 1\ fl$$

Prediction: After 1 day, the lecture hall is full of E.coli biomass

<u>Obviously wrong!</u>

- Unlimited resources
- Transport?

→ Improve model to become more realistic

Verhulst (1838): logistic growth

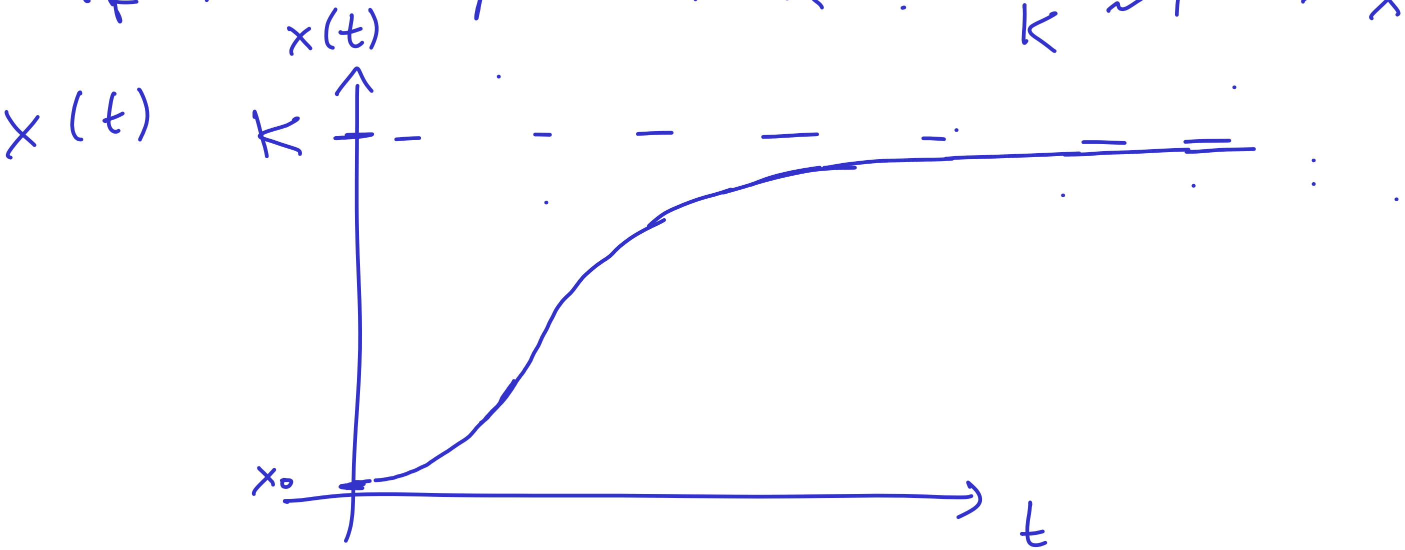
Additional term reflecting limitation of resources

$$\left(\frac{dx}{dt}\right) = \dot{x} = r \cdot x \cdot \left(1 - \frac{x}{K}\right)$$

K: capacity (carrying capacity)

If x is small: $\frac{x}{K} \approx 0$, $\dot{x} = r \cdot x$ $\rightarrow$ exponential growth

If x is comparable to K: $\frac{x}{K} \approx 1 \Rightarrow \dot{x} \approx 0$



Stationary states

$$\boxed{\dot{x} = 0}$$

Logistic growth

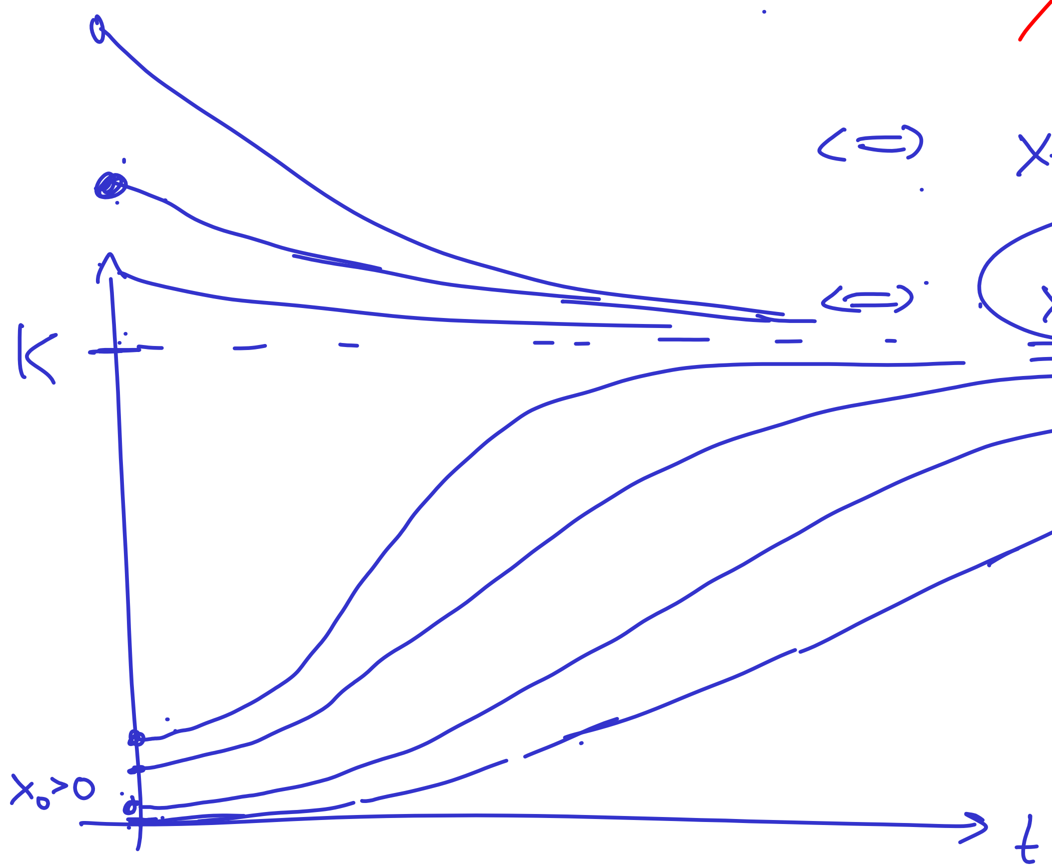
$$\dot{x} = r \cdot x \left(1 - \frac{x}{K}\right) \longleftarrow$$

To identify stationary states, we have to solve

$$\dot{x} = 0 \iff \cancel{r} \cdot x \cdot \left(1 - \frac{x}{K}\right) = 0$$

$$\iff x = 0 \quad \underline{\text{or}} \quad 1 - \frac{x}{K} = 0$$

$$\iff x = 0 \quad \text{or} \quad \underline{x = K}$$



$x > K$: $\frac{x}{K} > 1$

$\Rightarrow \left(1 - \frac{x}{K}\right) < 0$

$\Rightarrow \dot{x} < 0$

$x = K$: stable state

$x = 0$: unstable state

$$\lim_{t \to \infty} x(t) = K \quad \text{, as long as } x(0) > 0$$