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Modeling biological systems

A4 Santé-BIOTECH 1ST SEMESTER

1 DISCRETE-TIME MODELS

From J.Engelstädter, U. of Queensland, and Otto and Day 2007

SEQUENCES

Discrete-time models are sequences of numbers that follow certain rules.

Consider the following examples :

- *1 -2 4 -8 16 -32 …*
- *4 64 1024 16384 262144 …*
- *4 5 7 10 14 19 …*

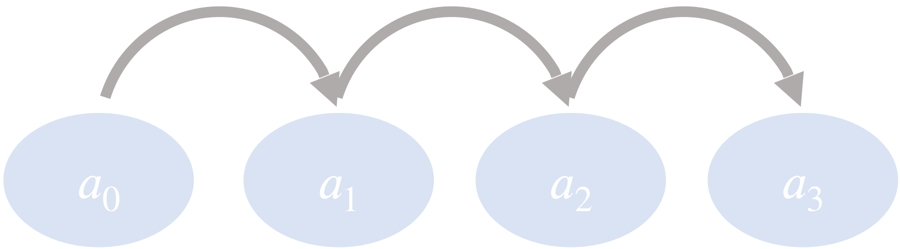
Explicit equations :

- $a_n = (-2)^n$
- $a_n = 4^{2n+1}$
- $a_n = 4 + \sum_{k=0}^{n} k$

Recursive equations :

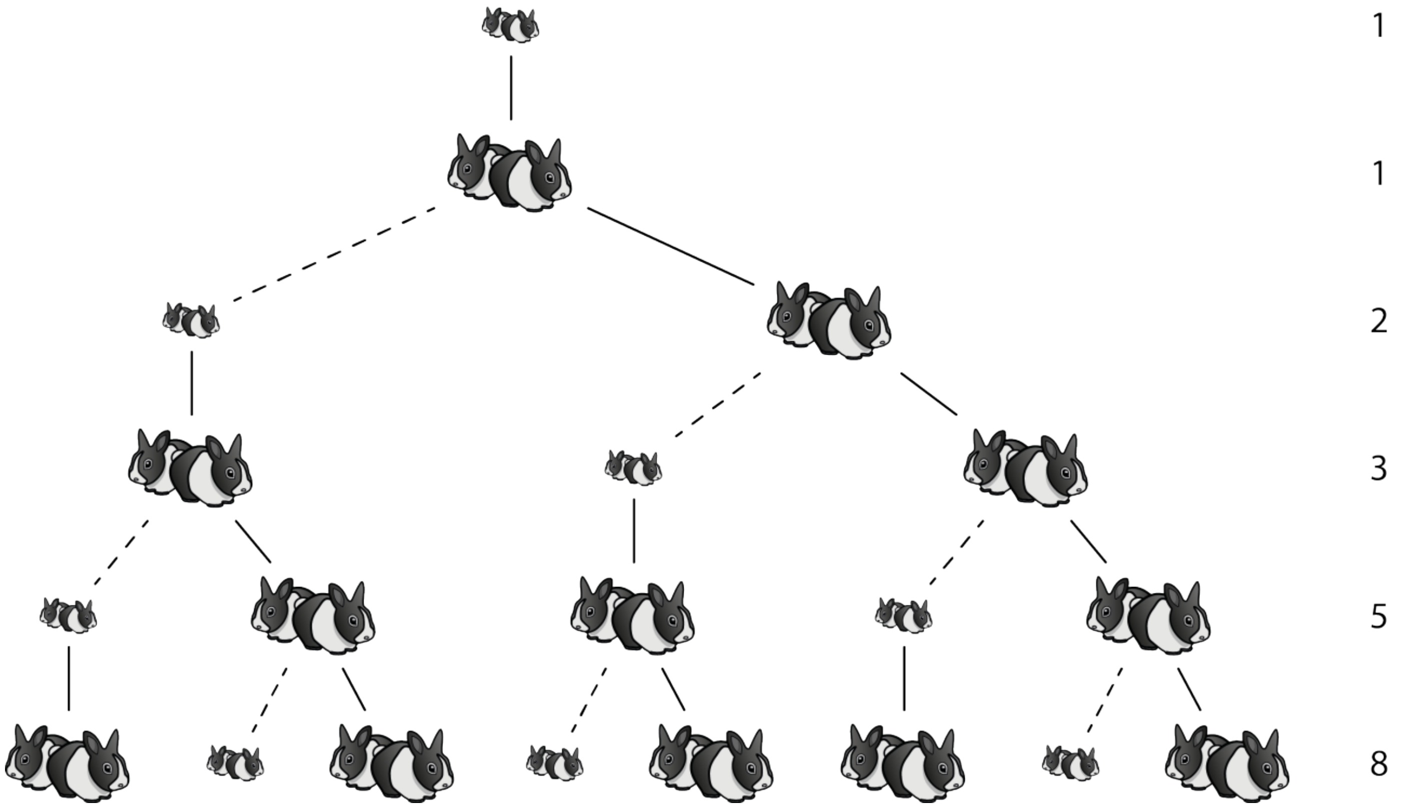
- $a_0 = 1;\ a_n = (-2)a_{n-1}$
- $a_0 = 4;\ a_n = 4^2 a_{n-1}$
- $a_0 = 4;\ a_n = a_{n-1} + n$

$$a_{n+1} = f(a_n)$$



FIBONACCI POPULATION GROWTH MODEL

- Fibonacci assumed pairs of rabbits that start mating after one month of growth and then indefinitely produce a new couple of baby rabbits each month



Fibonacci series :

1 1 2 3 5 8 13 21 34 55 89 …

EXPONENTIAL POPULATION GROWTH

Non-overlapping generations

Consider a population of asexually reproducing individuals.
In each generation, each individual produces on average a offspring individuals, following which the entire parental generation dies.

$$N_{t+1} = aN_t$$

Note that *a* is fixed value here

- $N_1 = aN_0$
- $N_2 = aN_1 = a(aN_0) = a^2 N_0$
- $N_3 = aN_2 = a(a^2 N_0) = a^3 N_0$
- $N_4 = aN_3 = a(a^3 N_0) = a^4 N_0$

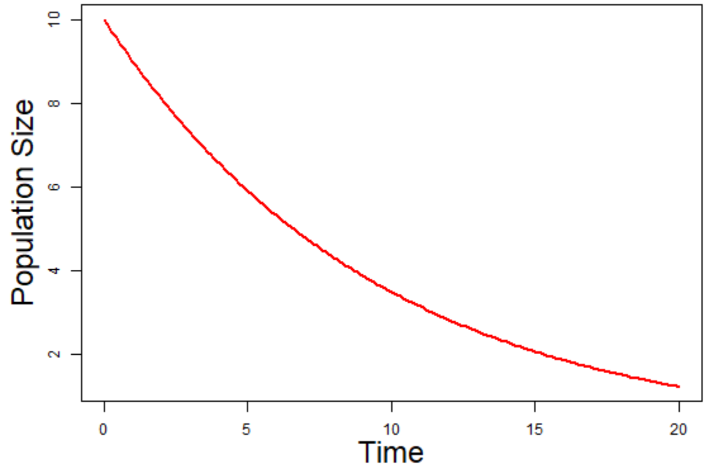
$$N_t = a^t N_0$$

Let's set 3 different values of *a*

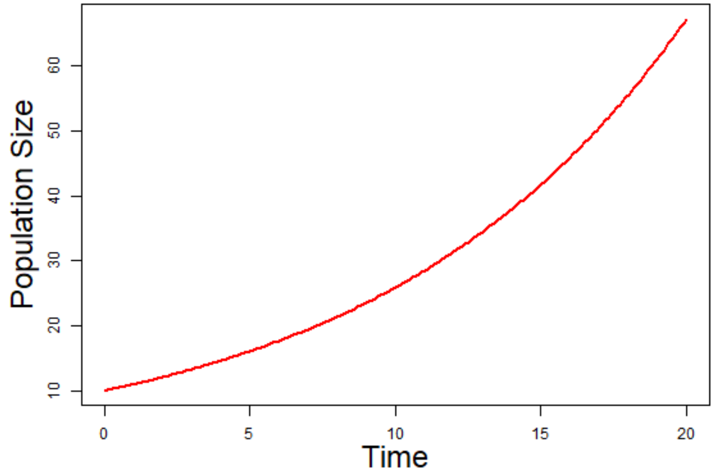
EXPONENTIAL POPULATION GROWTH

Non-overlapping generations

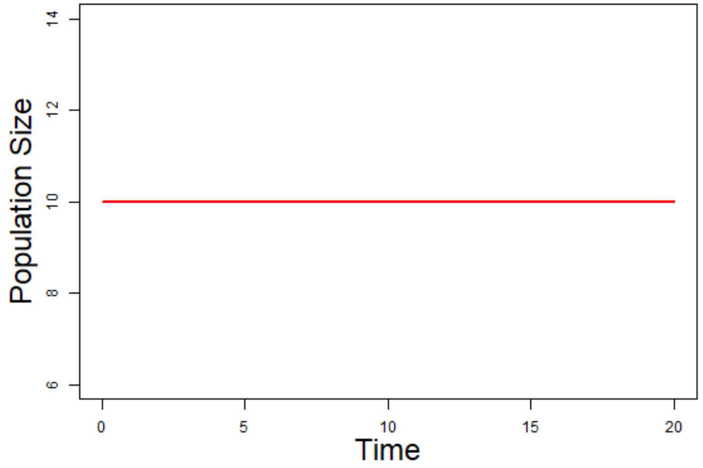
$$a < 1$$
$$ex: N_t = 0{,}9^t N_0$$



$$a > 1$$
$$ex: N_t = 1{,}1^t N_0$$



$$a = 1$$
$$N_t = N_0$$



LOGISTIC POPULATION GROWTH

Assume that the number of surviving offspring that an individual produces isn't constant but instead decreases with increasing population size

- N is the size of the population
- M is the maximum population size
- b is the maximum number of offspring an individual can produce

Note that *a* is not a fixed value anymore since it depends on N

- $N_{t+1} = a(N)N_t$

$$a = a(N) = b(1 - \frac{N}{M})$$

$$\Rightarrow N_{t+1} = b(1 - \frac{N_t}{M})N_t$$

LOGISTIC POPULATION GROWTH

Assume that the number of surviving offspring that an individual produces isn't constant but instead decreases with increasing population size

- N is the size of the population
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Let’s redefine the population size with :

- x as the population size relative to the maximum population

$$x := \frac{N}{M}$$

LOGISTIC POPULATION GROWTH

Assume that the number of surviving offspring that an individual produces isn't constant but instead decreases with increasing population size

- N is the size of the population
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- b is the maximum number of offspring an individual can produce

Let's redefine the population size with :

- x as the population size relative to the maximum population

$$x := \frac{N}{M}$$

$$N_{t+1} = b(1 - \frac{N_t}{M})N_t$$

$$x_{t+1} = b(1 - x_t)x_t$$

LOGISTIC POPULATION GROWTH

- N is the size of the population
- M is the maximum population size
- b is the maximum number of offspring an individual can produce

- x is defined as the population size relative to the maximum population

$$x := \frac{N}{M}$$

Let
- $b = 5$
- $x_t = 0,5$ (which means the current population is half the maximum)

$$x_{t+1} = b(1 - x_t)x_t$$

$$x_{t+1} = (b - b * x_t)x_t$$

$$x_{t+1} = bx_t - bx_t^2$$

$$x_{t+1} = 5 * 0,5 - 5 * 0,5 * 0,5 = 1,25$$

LOGISTIC POPULATION GROWTH

- N is the size of the population
- M is the maximum population size
- b is the maximum number of offspring an individual can produce

- x is defined as the population size relative to the maximum population

$$x := \frac{N}{M}$$

Let

- $b = 5$
- $x_t = 0{,}5$ (which means the current population is half the maximum)
- $x_{t+1} = 1{,}25$

$$x_{t+2} = b(1 - x_{t+1})x_{t+1}$$

$$x_{t+2} = (b - b * x_{t+1})x_{t+1}$$

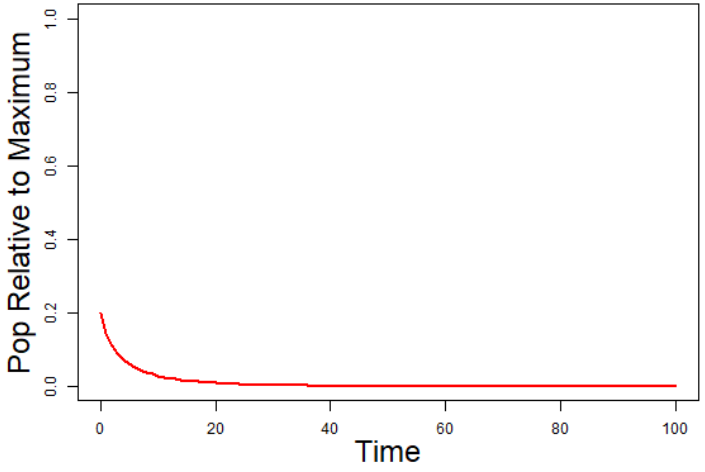
$$x_{t+2} = bx_{t+1} - bx_{t+1}^2$$

$$x_{t+2} = 5 * 1{,}25 - 5 * 1{,}25 * 1{,}25 = -1{,}5625$$

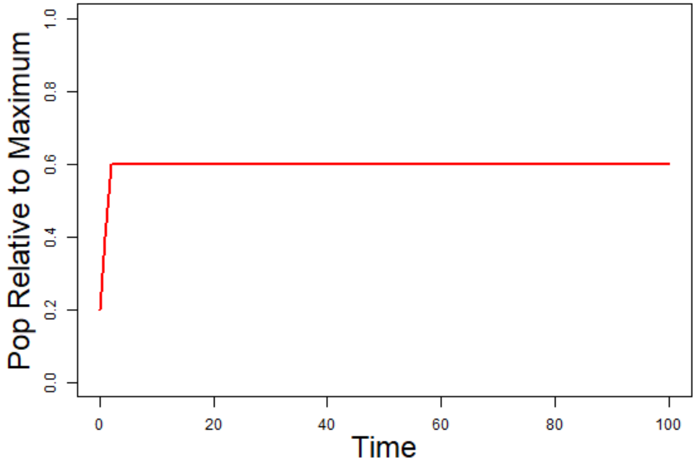
LOGISTIC POPULATION GROWTH

For $N = 10$ and $\mathrm{M} = 50$

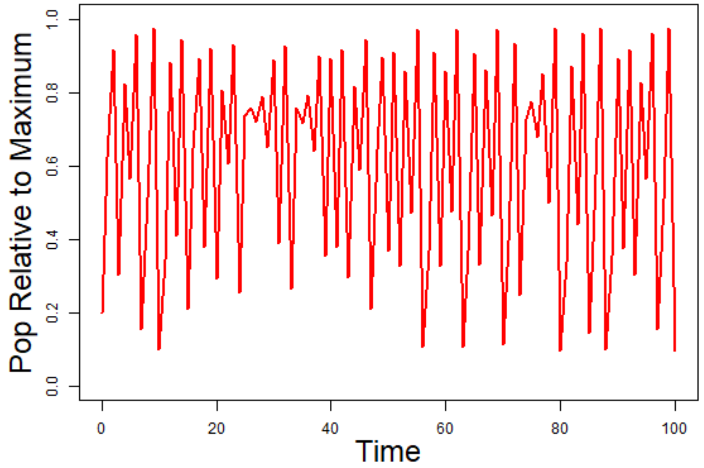
$b = 0{,}9$



$b = 2{,}5$



$b = 3{,}9$



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For $N = 10$ and $\mathrm{M} = 50$

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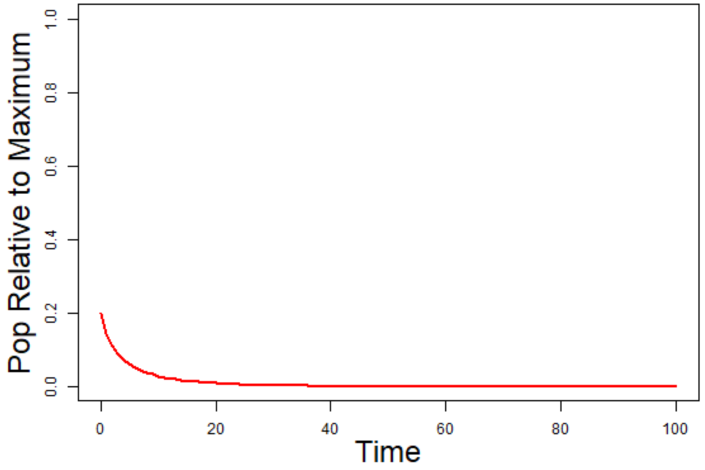

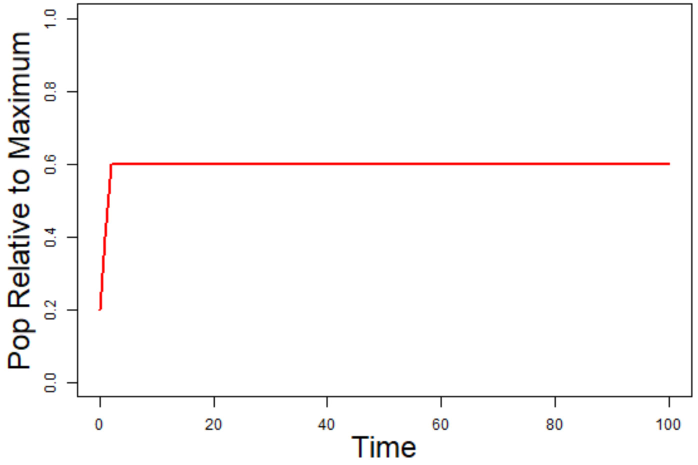

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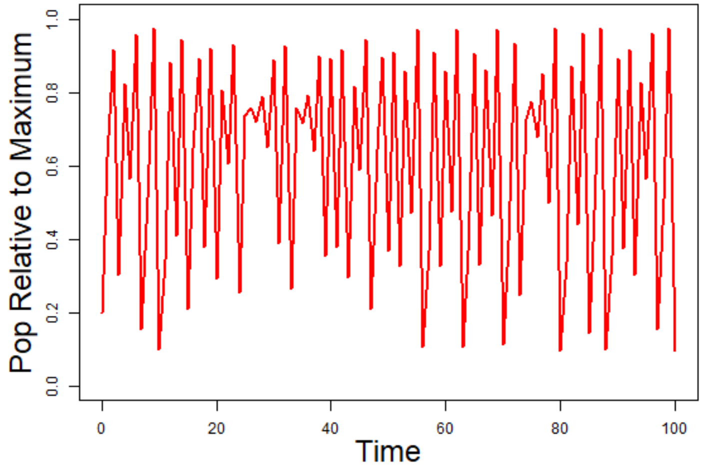


How to know if there will be a threshold ? Is it even stable ?

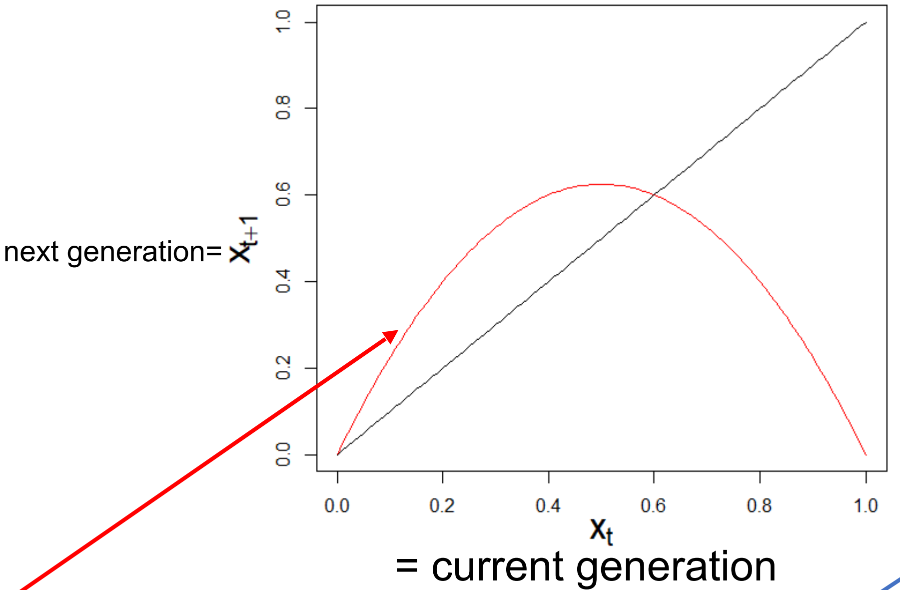
METHOD : FROM THE GRAPHIC

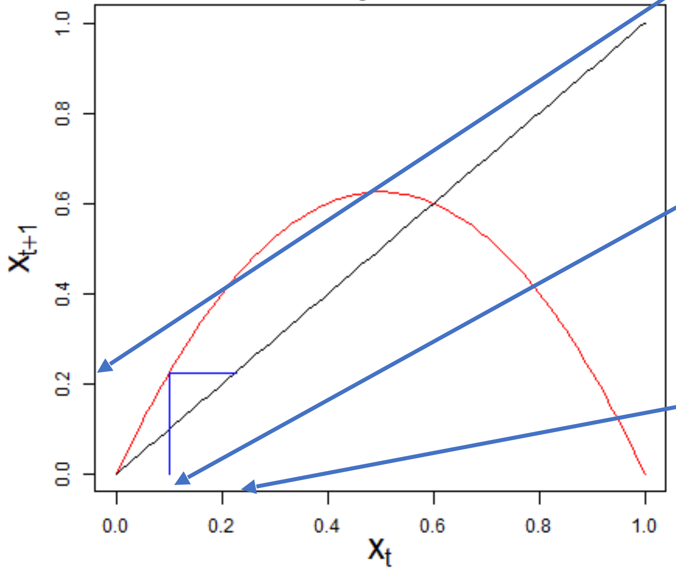
The graphical method is a great way of intuitively grasping discrete-time models with one variable, such as the logistic growth model.

- N is the size of the population
- M is the maximum population size
- b is the maximum number of offspring an individual can produce

$$f(x) = b(1-x)x$$

$$x := \frac{N}{M} \quad b = 2{,}5 \quad N = 5 \quad M = 50$$





x_{0+1} at the next generation

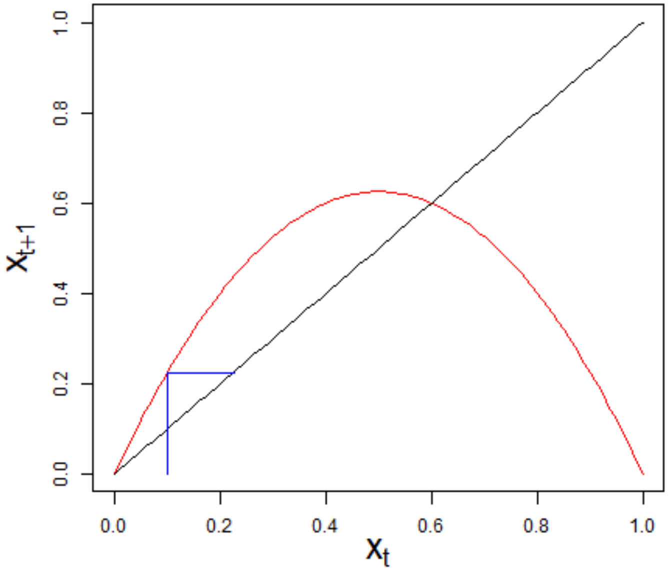
x_0 at the current generation is

$$= \frac{N}{M} = 5/50 = 0{,}1$$

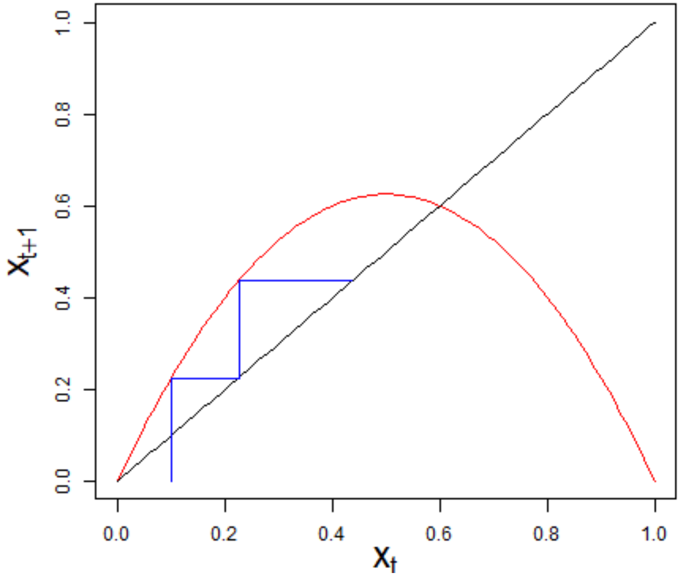
x_1 at the new current generation

METHOD : FROM THE GRAPHIC

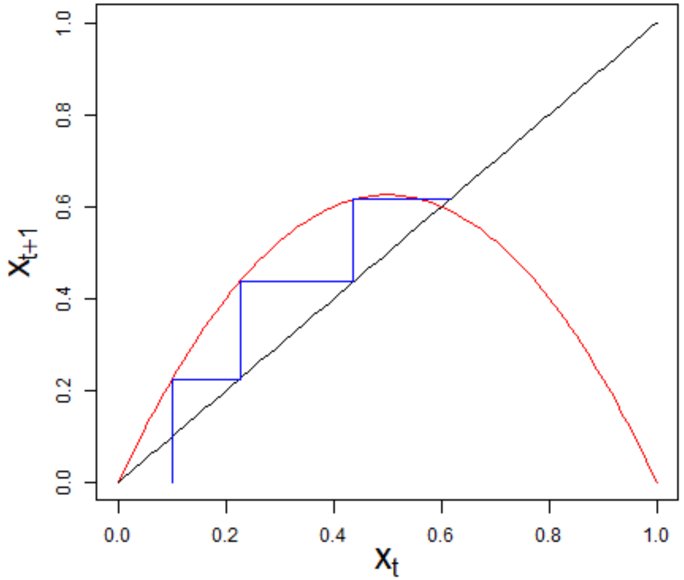
1st generation



2nd generation

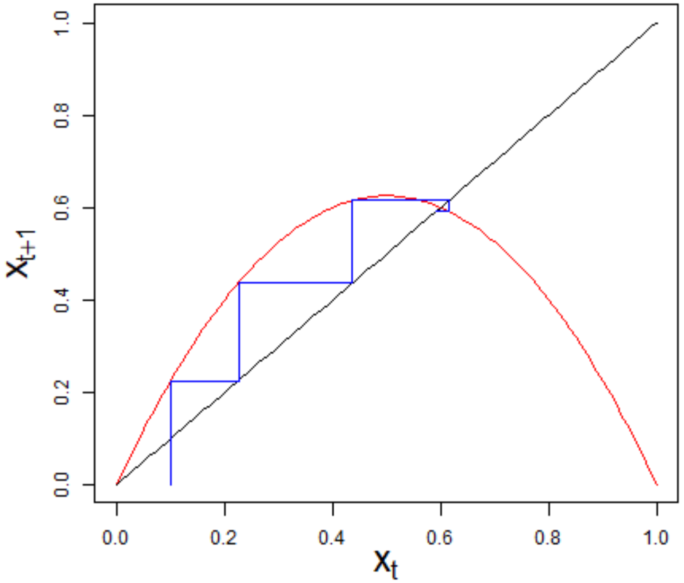


3rd generation



4th generation

Almost convergence



METHOD : FROM THE GRAPHIC

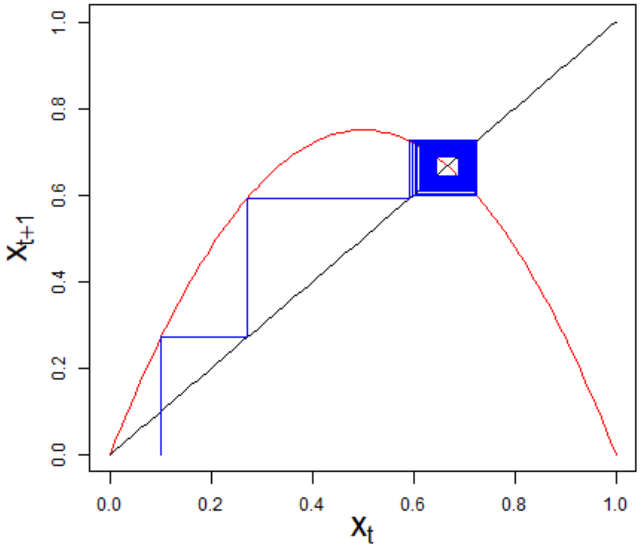
Convergence will usually require an virtually infinite number of generations, as we observe a cyclic behavior

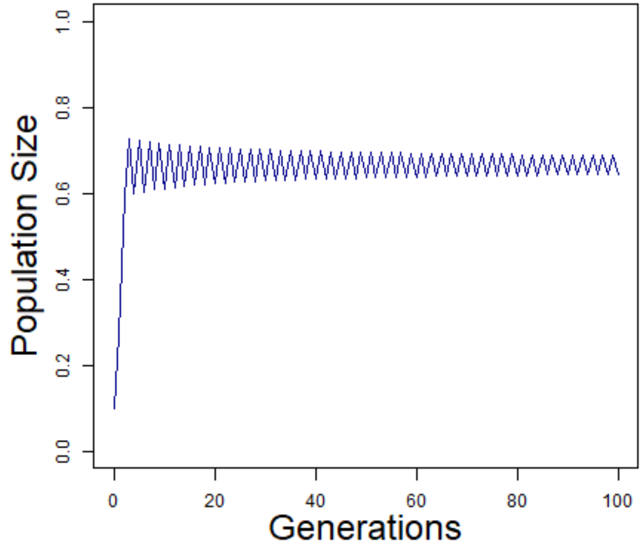
- N is the size of the population
- M is the maximum population size
- b is the maximum number of offspring an individual can produce

$$f(x) = b(1-x)x$$

$$x := \frac{N}{M} \quad b = 3 \quad N = 5 \quad M = 50$$

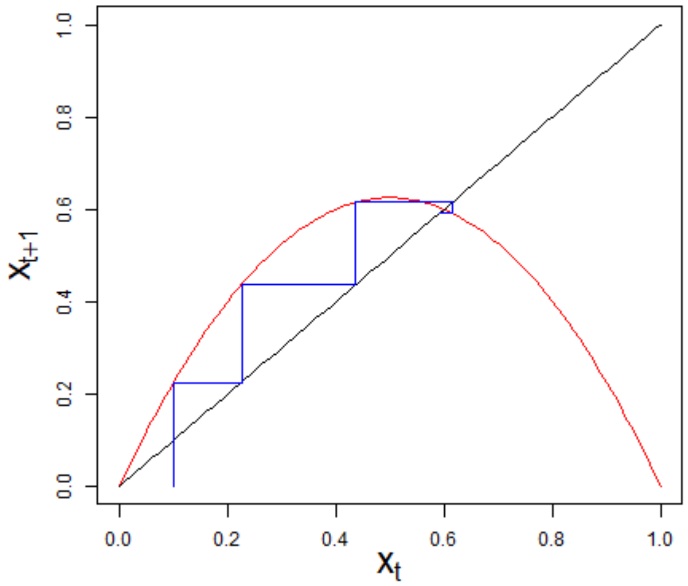
100th generation





EQUILIBRIA

The points where the function defining the model and the diagonal intersect represent equilibria



We can define an equilibrium point $\hat{x}$ as one where applying our model function doesn't have any effect, i.e. where :

$$f(\hat{x}) = \hat{x}$$

In our example of the logistic growth model, we can find the equilibria by solving the equation for $\hat{x}$

$$b(1 - \hat{x})\hat{x} = \hat{x}$$

EQUILIBRIA

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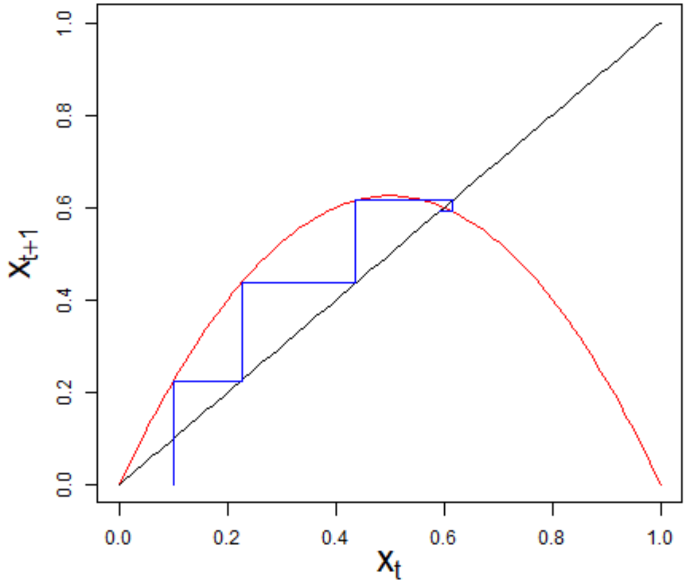


One obvious solution : $\hat{x}_1 = 0$

This equilibrium is called a **trivial** solution

$$b(1-\hat{x}) = 1$$

$$\left(1-\hat{x}\right) = \frac{1}{b}$$

$$\hat{x} = 1 - \frac{1}{b}$$

A second solution : $\hat{x}_2 = 1 - \frac{1}{b}$

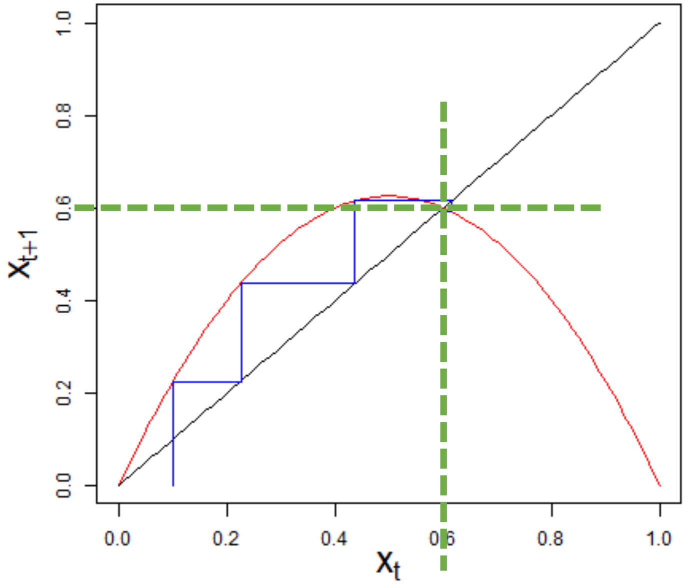
EQUILIBRIA

$$b = 2{,}5$$

$$\hat{x}_2 = 1 - \frac{1}{b}$$

$$\hat{x}_2 = 1 - \frac{1}{2{,}5}$$

$$\hat{x}_2 = 1 - 0{,}4 = 0{,}6$$

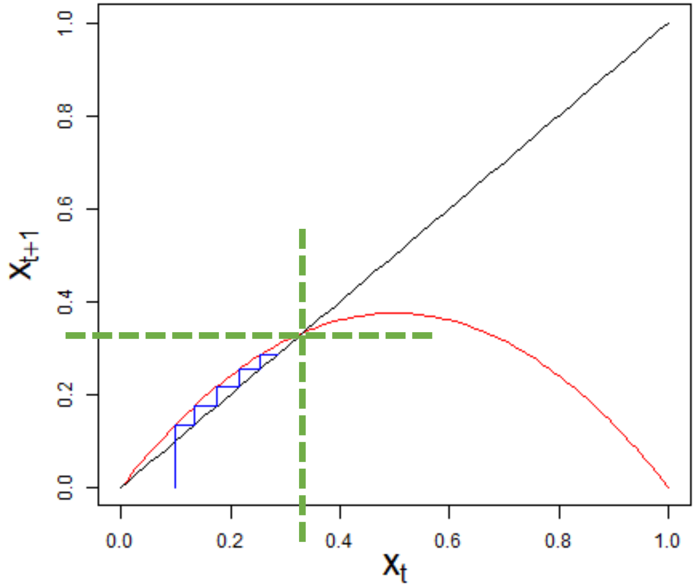


$$b = 1{,}5$$

$$\hat{x}_2 = 1 - \frac{1}{b}$$

$$\hat{x}_2 = 1 - \frac{1}{1{,}5}$$

$$\hat{x}_2 = 1 - 0{,}667 = 0{,}333$$



EQUILIBRIA AND STABILITY

An equilibrium is called **locally stable** if the system converges to the equilibrium when starting from sufficiently close by.

An equilibrium is called **locally unstable** if small perturbations away from the equilibrium result in the system moving entirely away from it.

So how to determine if an equilibrium is stable in a **Discrete-Time Model** ?

1. Obtain the derivative f' of the function f that defines the recursion equation.

2. Insert equilibrium values $\hat{x}$ in the derivative function (e.g., $f'(\hat{x})$) and simplify.

3. If the absolute value of this expression is :
< 1, the equilibrium is locally stable,
> 1, the equilibrium is unstable.

If this expression is negative, there will be oscillations around this equilibrium.

EQUILIBRIA AND STABILITY

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So here is our function:
$f(x) = b(1-x)x$

And its derivative:
$f'(x) = b(1-x) + bx(-1)$

$f'(x) = b(1-2x)$

First equilibrium : $\hat{x}_1 = 0$

$f'(\hat{x}_1) = (1 - 2 \times 0) \times b = b$

So :
The equilibrium is stable for $b < 1$
The equilibrium is unstable for $b > 1$

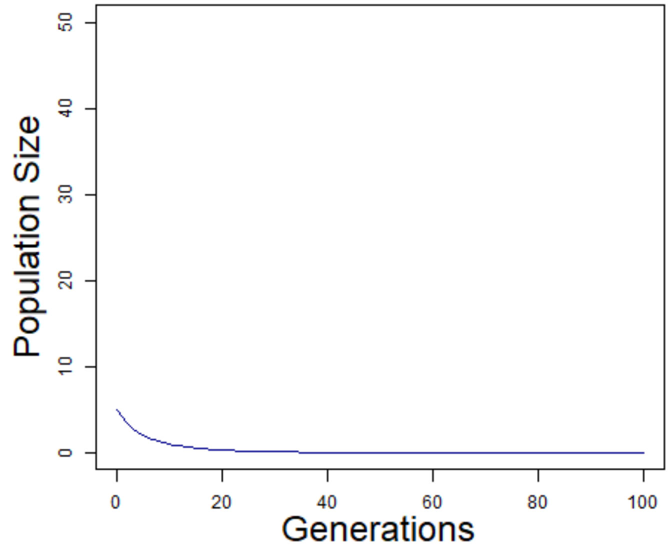
EQUILIBRIA AND STABILITY

First equilibrium : $\hat{x}_1 = 0$

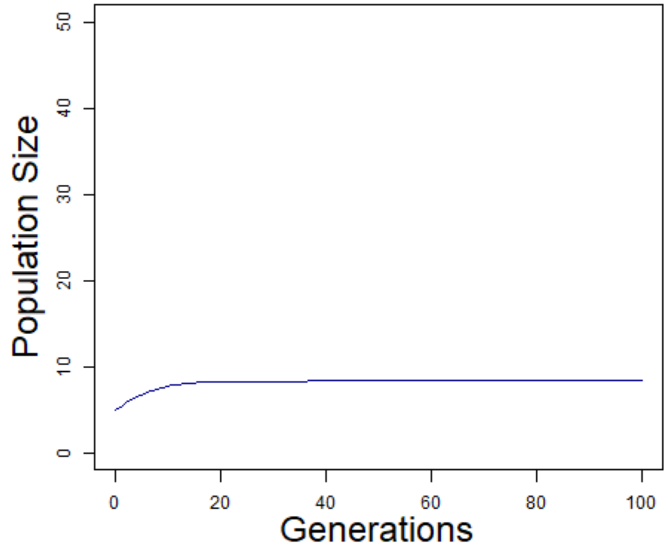
The equilibrium is stable for $b < 1$

The equilibrium is unstable for $b > 1$

$b = 0{,}9$



$b = 1{,}2$



EQUILIBRIA AND STABILITY

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If this expression is negative, there will be oscillations around this equilibrium.

So here is our derivative :
$f'(x) = b(1 - 2x)$

Second equilibrium : $\hat{x}_2 = 1 - \dfrac{1}{b}$

$$f'(x) = b(1 - 2 * \left(1 - \frac{1}{b}\right))$$

$$f'(x) = b(1 - 2 + \frac{2}{b})$$

$$f'(x) = b(- 1 + \frac{2}{b})$$

$$f'(x) = 2 - b$$

The equilibrium is stable for $1 < b < 3$

The equilibrium is unstable for $b > 3 \text{ } or \text{ } b < 1$

The model will show oscillations for $b > 2$

EQUILIBRIA AND STABILITY

Second equilibrium : $\hat{x}_2 = 1 - \frac{1}{b}$

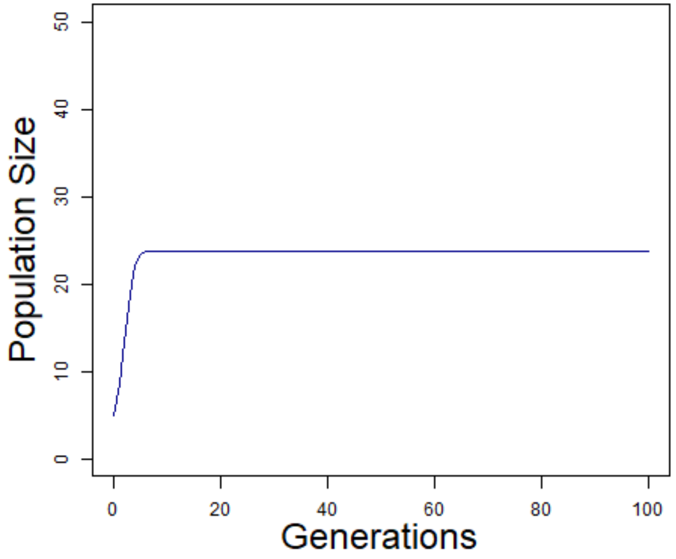
The equilibrium is stable for $1 < b < 3$

The equilibrium is unstable for $b > 3 \ or \ b < 1$

The model will show oscillations for $b > 2$

$b = 1{,}9$

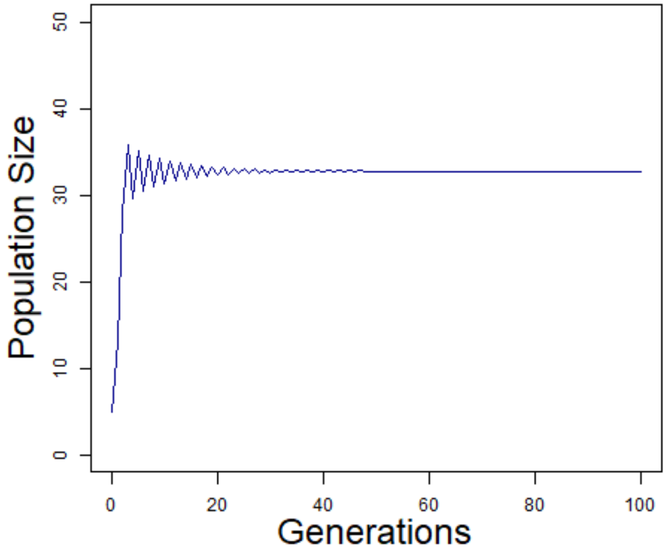
Stable equilibrium



$b = 2{,}9$

Stable equilibrium

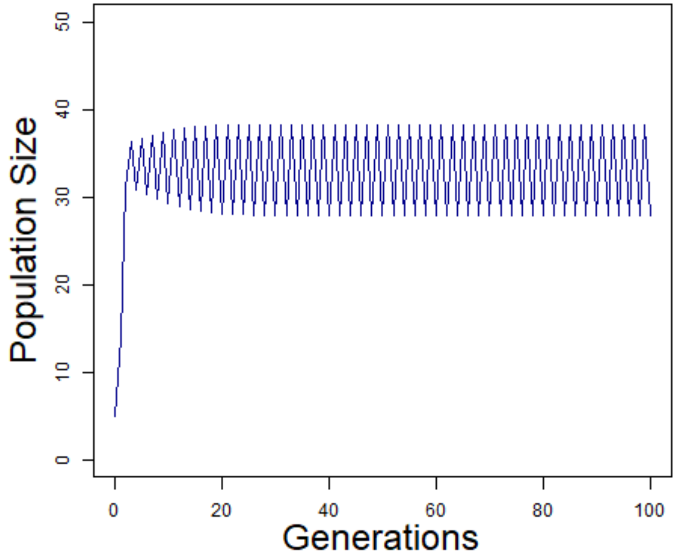
Oscillations



$b = 3{,}1$

Unstable equilibrium

Oscillations



NATURAL SELECTION IN A CLONAL POPULATION

Let us consider how selection operates in a simple, **clonal population**

We assume that there is only a single round of reproduction following which the parental generation dies

- N is the size of the population, now constant
- Two genotypes :
  - Type A produces k offspring individuals per round of reproduction
  - Type B produces $(1 + s)k$ offspring individuals
- s is called the selection coefficient

$$\begin{cases} n_A^0(t) = kn_A(t) \\ n_B^0(t) = (1 + s)kn_B(t) \end{cases}$$

NATURAL SELECTION IN A CLONAL POPULATION

Reminder :

- N is the size of the population, is constant
- Two genotypes :
  - Type A produce k offspring individual per round of reproduction
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$$\begin{cases} n_A^0(t) = k n_A(t) \\ n_B^0(t) = (1 + s) k n_B(t) \end{cases}$$

$$\begin{cases} n_A(t+1) = \dfrac{N}{n_A^0(t) + n_B^0(t)} n_A^0(t) \\ n_B(t+1) = \dfrac{N}{n_A^0(t) + n_B^0(t)} n_B^0(t) \end{cases}$$

$$\begin{cases} n_A(t+1) = \dfrac{N}{n_A^0(t) + n_B^0(t)} k n_A(t) \\ n_B(t+1) = \dfrac{N}{n_A^0(t) + n_B^0(t)} (1 + s) k n_B(t) \end{cases}$$

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$$\begin{cases} n_A(t+1) = \dfrac{n_A(t)N}{n_A(t) + (1+s)n_B(t)} \\ n_B(t+1) = \dfrac{(1+s)n_B(t)N}{n_A(t) + (1+s)n_B(t)} \end{cases}$$

We introduce a new variable: $p(t) = \dfrac{n_B(t)}{N}$

NATURAL SELECTION IN A CLONAL POPULATION

We introduce a new variable: $p(t) = \dfrac{n_B(t)}{N}$

So we have:

$$n_B(t+1) = \frac{(1+s)n_B(t)N}{n_A(t) + (1+s)n_B(t)}$$

And:

$$p(t+1) = \frac{n_B(t+1)}{N}$$

$$p(t+1) = \frac{(1+s)n_B(t)}{n_A(t) + (1+s)n_B(t)}$$

Or our total population N is :

$$n_A(t) + n_B(t) = N$$

Thus:

$$p(t+1) = \frac{(1+s)n_B(t)}{N + sn_B(t)}$$

$$p(t+1) = \frac{(1+s)Np(t)}{N + sNp(t)}$$

$$p(t+1) = \frac{(1+s)p(t)}{1 + sp(t)}$$

NATURAL SELECTION IN A CLONAL POPULATION

Exercise: give the equilibria of the equation

$$\hat{p} = \frac{(1+s)\hat{p}}{1+s\hat{p}}$$

Reminder:
You can mathematically find the equilibria by solving the equation for the variable (in this case $\hat{p}$)

NB: assume that $s \neq 0$

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NATURAL SELECTION IN A CLONAL POPULATION

- N is the size of the population, is constant
- Two genotypes :
  - Type A produce k offspring individual per round of reproduction
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- s is called the selection coefficient

$$p(t) = \frac{n_B(t)}{N}$$

$$\hat{p} = \frac{(1+s)\hat{p}}{1+s\hat{p}}$$

Again, a simple solution : $\hat{p}_1 = 0$

$$\frac{(1+s)}{1+s\hat{p}} = 1$$

$$1+s = 1+s\hat{p}$$

$$\hat{p} = \frac{s}{s}$$

A second solution : $\hat{p}_2 = 1$

NATURAL SELECTION IN A CLONAL POPULATION

Exercise: give the stability of the model, for both equilibria (find $f'\left(\hat{p}_1\right)$ and $f'(\hat{p}_2)$)

So how to determine if an equilibrium is stable?

1. Obtain the derivative f' of the function f that defines the recursion equation.

2. Insert the formula for the equilibrium (e.g., $f'(\hat{x})$) and simplify.

3. If the absolute value of this expression is :
< 1, the equilibrium is locally stable,
> 1, the equilibrium is unstable.

If this expression is negative, there will be oscillations around this equilibrium

$$\hat{p} = \frac{(1+s)\hat{p}}{1+s\hat{p}}$$

$$\hat{p}_1 = 0$$

$$\hat{p}_2 = 1$$

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NATURAL SELECTION IN A CLONAL POPULATION

- N is the size of the population, is constant
- Two genotypes :
  - Type A produce k offspring individual per round of reproduction
  - Type B produce $(1+s)k$ offspring individuals
- s is called the selection coefficient

$$p(t) = \frac{n_B(t)}{N}$$

$$\hat{p} = \frac{(1+s)\hat{p}}{1+s\hat{p}}$$

Start with the derivative:

$$f'(p) = \frac{(1+s) * \left(1+sp\right) - (1+s)p * s}{(1+sp)^2}$$

$$f'(p) = \frac{(1+s)}{(1+sp)^2}$$

Inserting the first equilibrium:

$$f'(0) = 1+s$$

And the second equilibrium:

$$f'(1) = \frac{1}{1+s}$$

NATURAL SELECTION IN A CLONAL POPULATION

Exercise: give the stability of the model

So how to determine how is the stability?

1. Obtain the derivative f' of the f function that defines the recursion equation.

2. Insert the formula for the equilibrium (e.g., $f'(\hat{x})$) and simplify.

3. If the absolute value of this expression is :
< 1, the equilibrium is locally stable,
> 1, the equilibrium is unstable.

If this expression is negative, there will be oscillations around this equilibrium

$$\hat{p} = \frac{(1+s)\hat{p}}{1+s\hat{p}}$$

$$f'(0) = 1 + s$$

$$f'(1) = \frac{1}{1+s}$$

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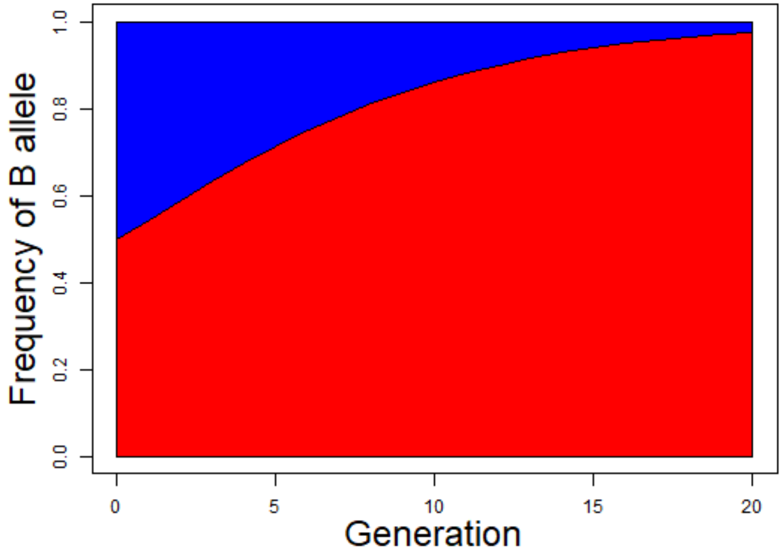
EQUILIBRIA AND STABILITY

First equilibrium : $\hat{p}_1 = 0$

$$f'(0) = 1 + s$$

$s = 0,2$



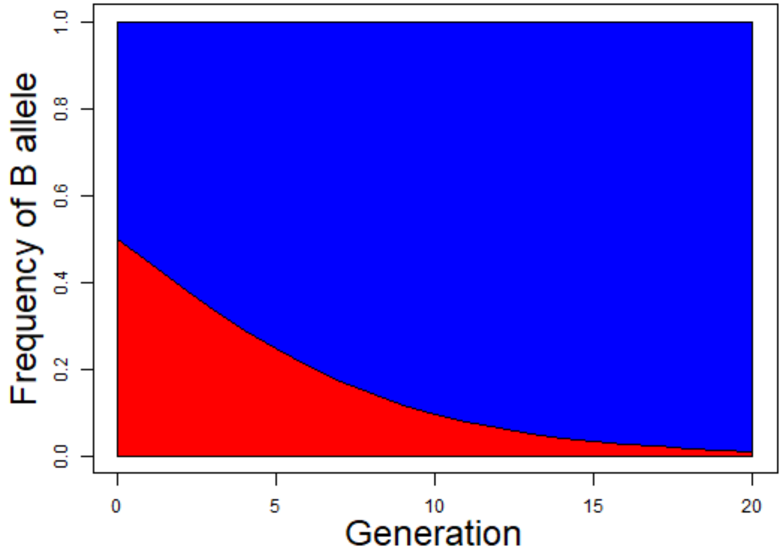
The equilibrium is stable for $s < 0$

The equilibrium is unstable for $s > 0$

Second equilibrium : $\hat{p}_2 = 1$

$$f'(1) = \frac{1}{1 + s}$$

$s = -0,2$



The equilibrium is stable for $s > 0$

The equilibrium is unstable for $s < 0$

2 CONTINUOUS-TIME MODELS (part I)

ÉCOLE D'INGÉNIEURS PARIS-LA DÉFENSE

From J.Engelstädter, U. of Queensland, and Otto and Day 2007

REMINDER ON DIFFERENTIAL EQUATIONS

Regular equations look like this :

$$x + x^2 = 6$$

This equation has two solutions :

$$x_1 = 2$$
$$x_2 = -3$$

- In equations like this, we are looking for numbers that, when inserted for a variable (in this case x), turn the equation into a true statement
- There may be :
  - one solution,
  - several solutions (as in the example),
  - an infinity of solutions or
  - no solution at all.

REMINDER ON DIFFERENTIAL EQUATIONS

Differential equations are equations in which the unknown object is not a number, but a function. Moreover, these equations involve not only the function, but also derivatives of that function.

Consider the following example:

$$y(t)(1-2t) = ty'(t)$$

In this differential equation, we want to solve for y, which is an unknown function of the variable t. The equation involves the function $y(t)$ itself, its first derivative $y'(t)$, and the variable t.

REMINDER ON DIFFERENTIAL EQUATIONS

Let's continue on this example:

$y(t)(1-2t) = ty'(t)$

A solution of the above ODE is

$y(t) = te^{-2t}$

Here is its derivative:

$y'(t) = e^{-2t} - 2te^{-2t}$

so :

$y'(t) = e^{-2t}(1-2t)$

We can verify that solution by inserting y and its derivative into the differential equation and see if the equality is respected:

$$y(t)(1-2t) - ty'(t) = te^{-2t}(1-2t) - t[e^{-2t}(1-2t)]$$
$$= te^{-2t} - 2t^2e^{-2t} - te^{-2t} + 2t^2e^{-2t}$$
$$= 0$$

The equality is verified, this was a valid solution.

Actually, we can verify that any function following this pattern is a solution:

$y(t) = Kte^{-2t}$with $K \in \mathbb{R}$

TERMINOLOGY

- This example, and the differential equation we will be dealing with in this course, are **ordinary differential equations**, or **ODE**.
- This simply means that the unknown function is a **function of only a single variable** (here (t), usually used for time).

Differential equations having more than one variable are called **partial differential equations**, or **PDE**. For example, the one-dimensional wave equation below:

$$\frac{\partial^2 y}{\partial t^2} = a^2 \frac{\partial^2 y}{\partial x^2}$$

This PDE is said to be of **second order**, meaning that the second derivatives of the y function shows up in the equation. y depends on 2 variables : x and t ; and each partial derivative of each variables occurs in the equation above.

Finally, it is a **linear** differential equation because it represents a linear relationship between $y(t)$ and its derivatives. (In other words, no nonlinear terms such as $y(t)^2$ or $\cos(y(t))$ occur).