Mathematical modelling applied to biology and medicine

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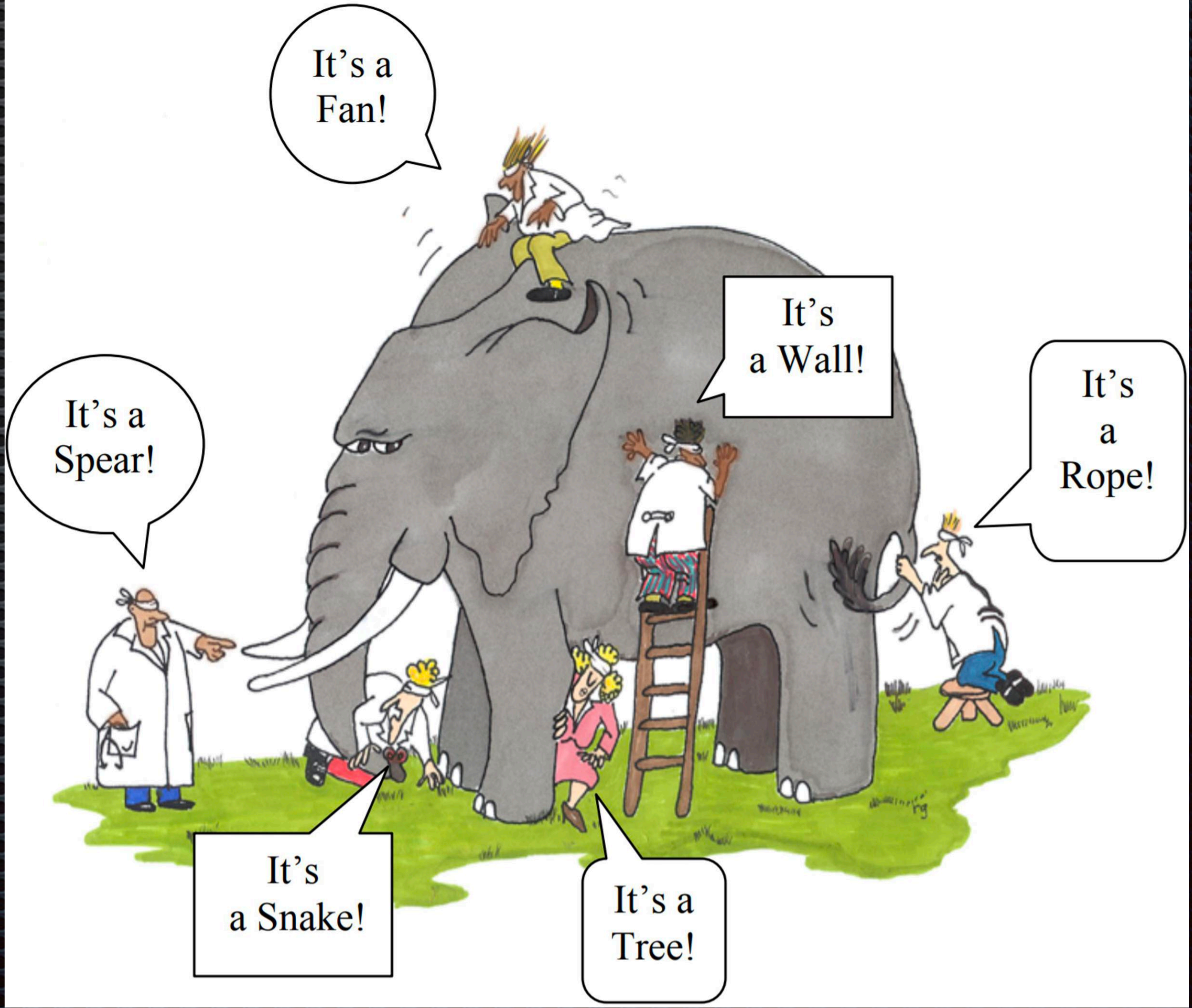
Mathematical modelling applied to biology and medicine

modelling *noun* [U] (MATHEMATICS, COMPUTING)

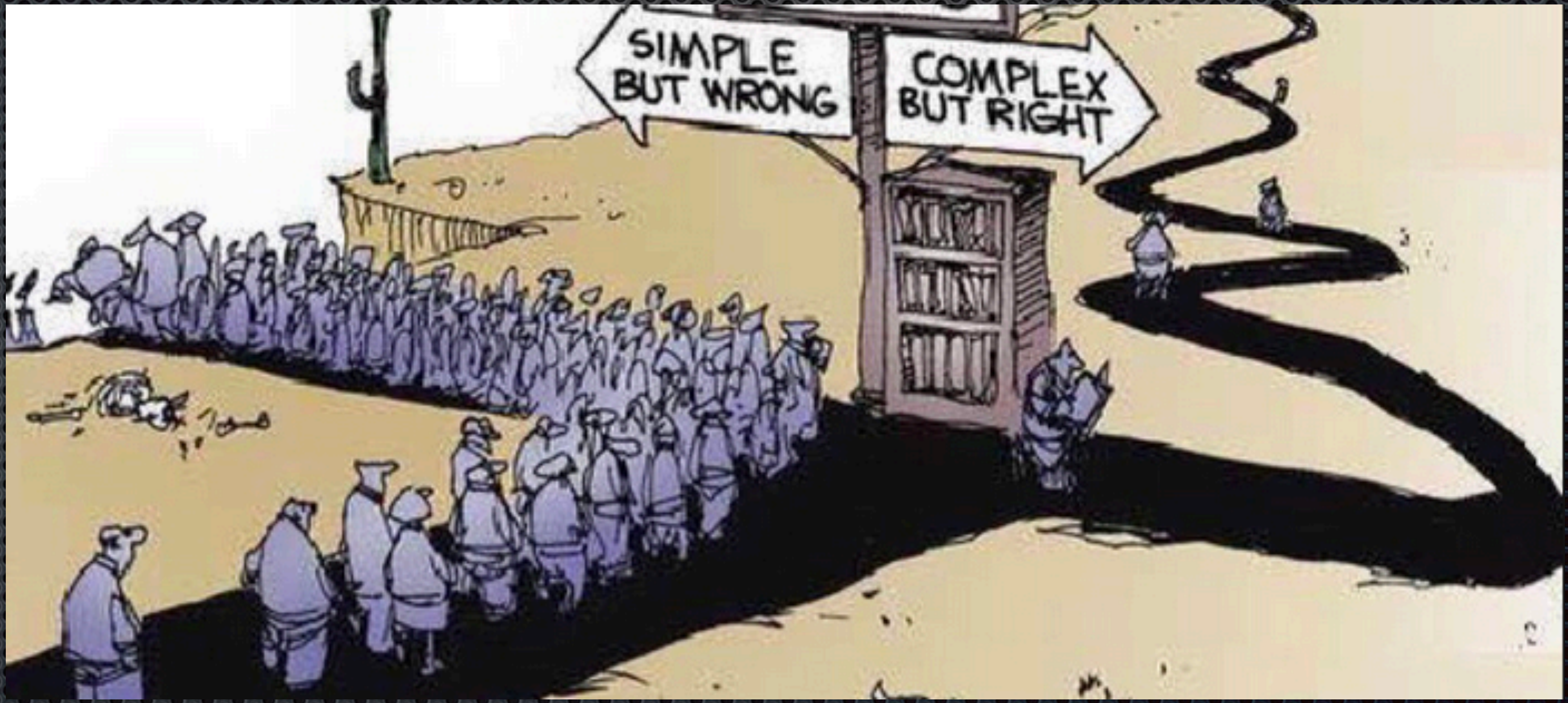
- the activity of using mathematical models (simple descriptions of a system or process) to make calculations or predict what might happen (*Cambridge dictionary*)

-the work of making a simple description of a system or a process that can be used to explain it, etc. (Oxford dictionary)



Modelling

- ✓ **Modelling** is a scientific approach that allows a model elaboration,
- ✓ the most known part of modelling is based on **mathematics**, and more particularly, on a part of mathematics that deals with variables and parameters taking values in the real numbers



In this lecture, we will only deal with mathematical modelling

Modelling and theorising

- ✓ we can theorise without modelling, and we can model without theorising. However, a model is often a precious tool in a theoretical approach,
- ✓ in practice: modelling may be useful in the 3 big steps of a scientific process:

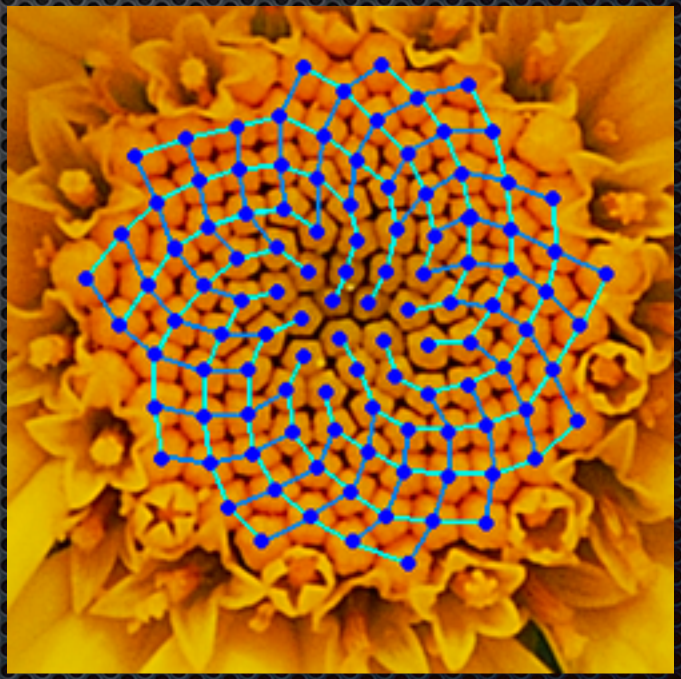
  1- detect and ask questions,
  2- set up the problem and collect data and knowledge,
  3- define actions and study the consequences

Modeler

- ✓ is the specialist of a strategy to design and use the models,
- ✓ knows how to efficiently model in a field in which he or his team has some expertise,
- ✓ knows a large variety of tools and methods,
- ✓ is inspired by the biological problem to propose a method and not the reverse,
- ✓ is involved in the biological knowledge improvement. In research project he would play a central role.

A model

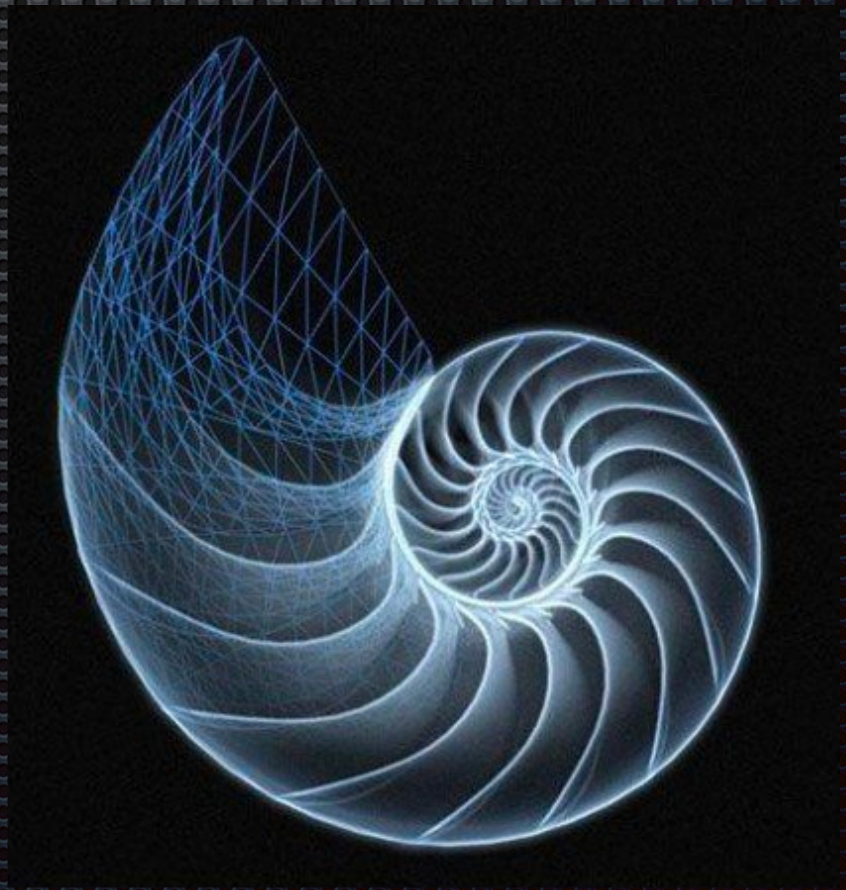
- ✓ is a symbolic representation of some aspects of an object, a phenomenon from the real world, in biology, ecology or medicine in our case,
- ✓ is not THE answer to a problem, but AN answer to the problem,
- ✓ is an instrument in the modeler toolbox,
- ✓ is strongly coupled with experiment and observation,
- ✓



A model

✓ is often integrated in a general framework dealing with the systems analysis

- even if the data are often right, in some cases, the model can validate them or not, it can be a control instrument,
- the model cannot be the excuse to a priori decisions, it can be used as a technical or political decisions

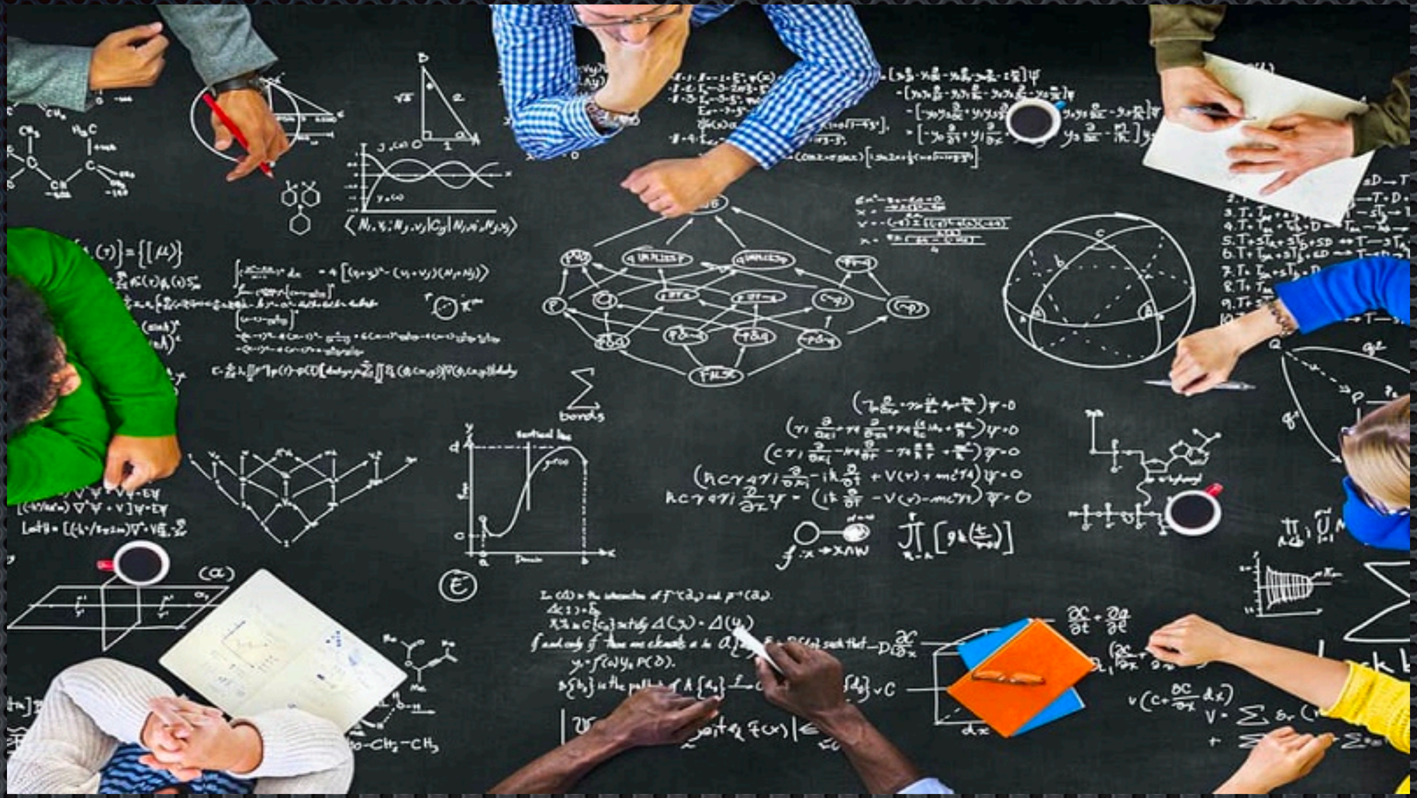


Characteristics of a model

To be efficient, a model needs to be operative, that is

- ✓answering the modelling goals,
- ✓be able to interpret in terms of biology,
- ✓be able to be translated into simple terms that everyone can understand,

Choice of the formalism



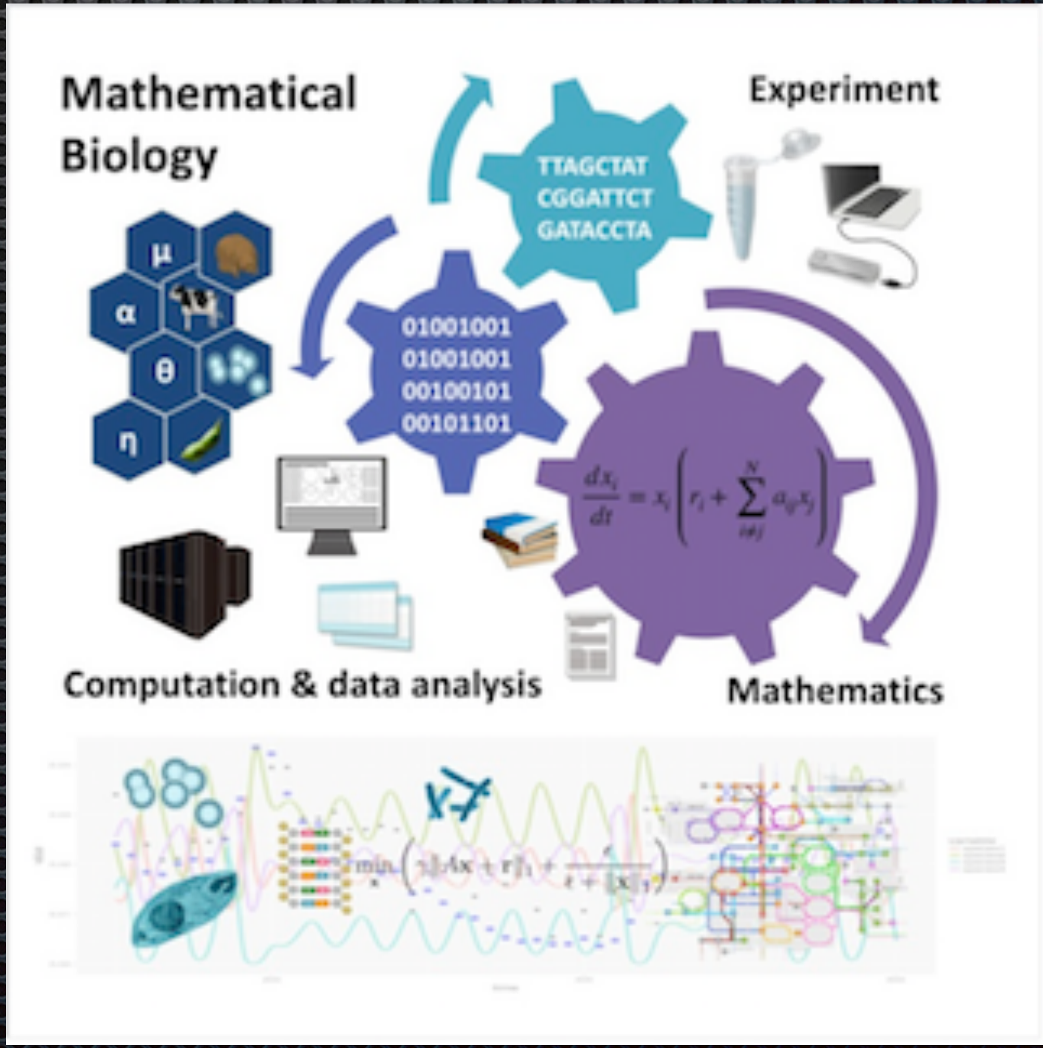
what kind of model should we choose?

- ✓ ode models,
- ✓logic models
- ✓simulations models (random number generators,…)
- ✓geometric models (curves, maps, surfaces,…)
- ✓data structured models (pde)
- ✓object centered models (agent based models, …)

Elaborating a model

to elaborate a model, we need to take into account:

✓ the object or the biological phenomenon to represent,
✓the formalism,
✓the goals (that is how we want to use the model)
✓data and a priori biological knowledge available or reachable by experiment or observation



Elaborating a model

the modeller should

- ✓ **formulate** the problem (that is write the model),
- ✓ **simplify** the model to be able to study its properties,
- ✓ **relate it** to other representations (graph, numerical code,)
- ✓ **interpret** the model and confront the obtained results with biological reality (most of the time seen throughout experimental data)

Some well known models

In biology and ecology

- ✓ enzymology: the Michaelis-Menten model,
- ✓ genetics: the Mendel laws,
- ✓ population genetics: Hardy-Weinberg law
- ✓ molecular biology: circadian clocks,…

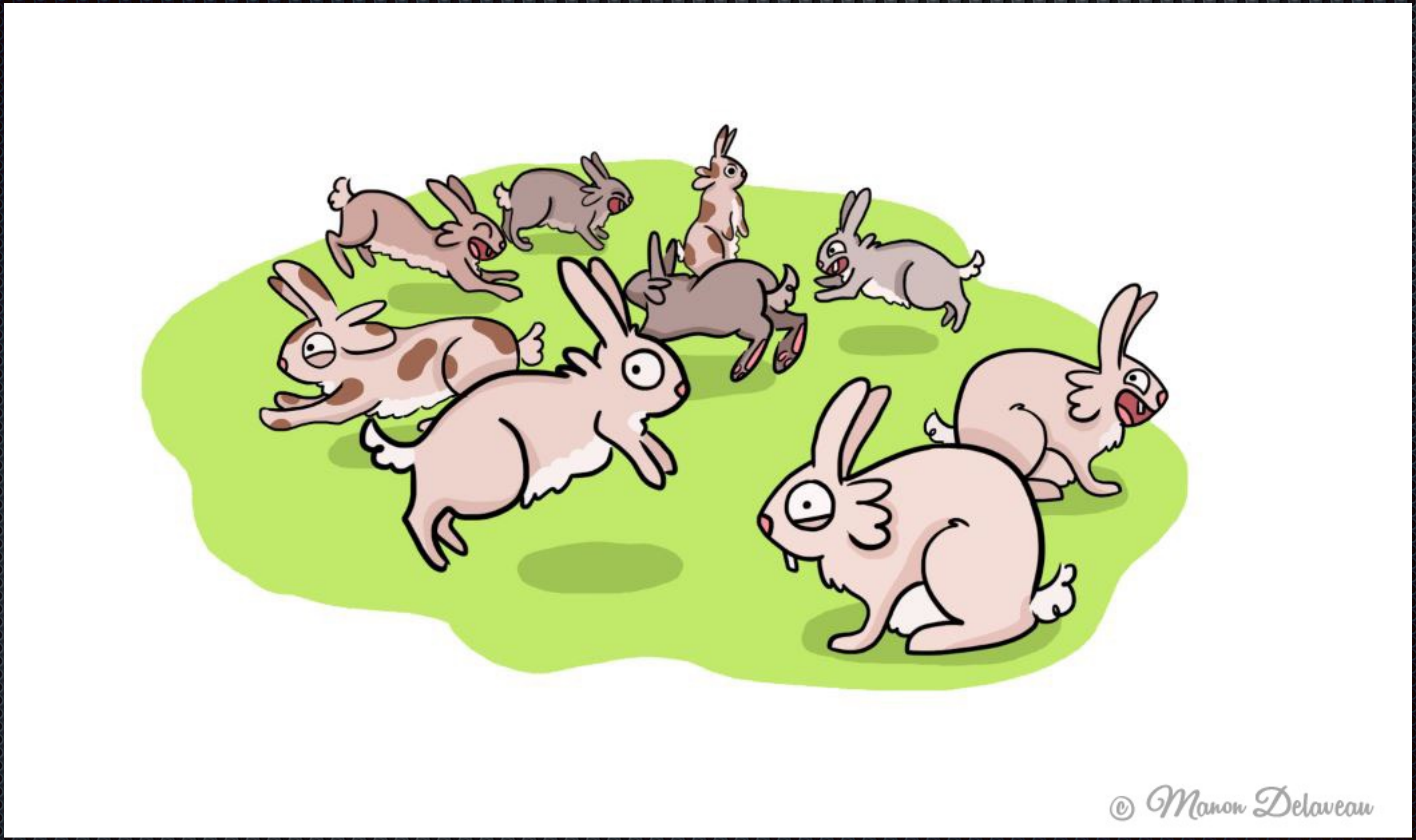
In medicine

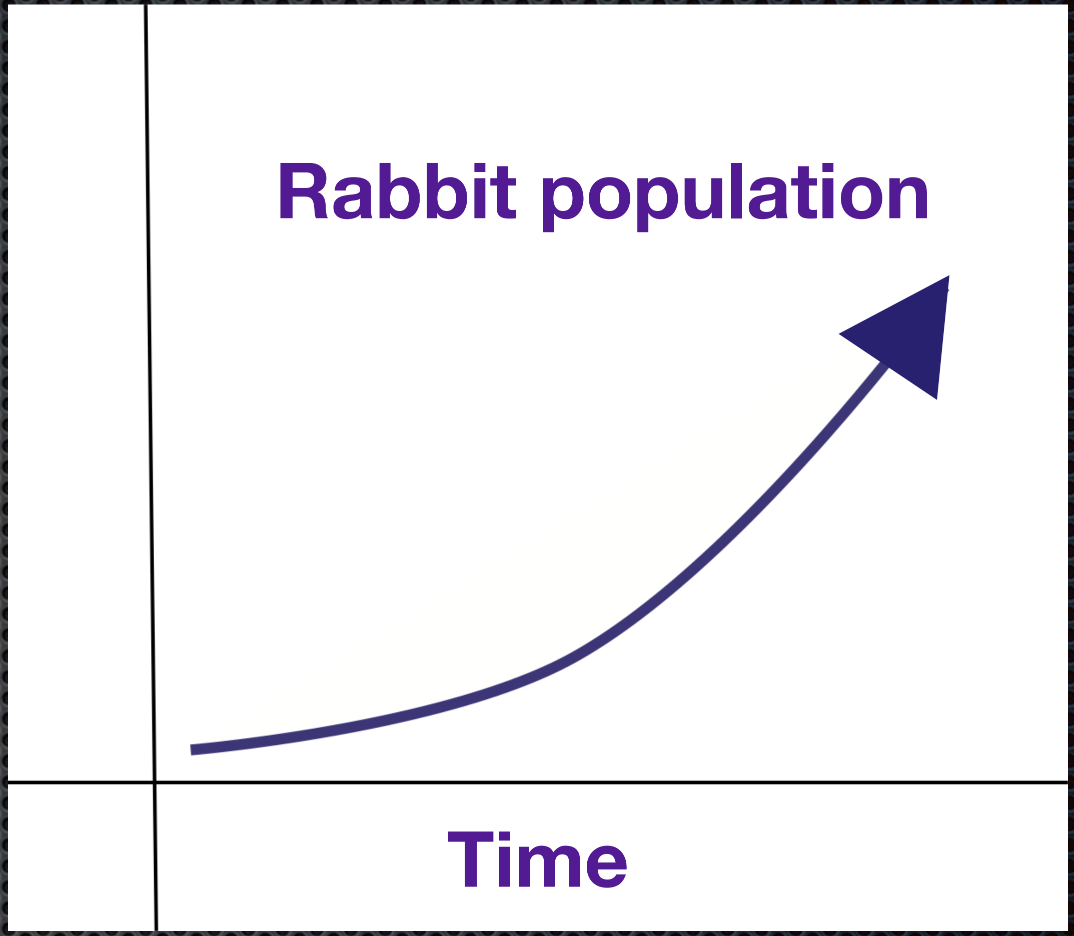
- ✓ epidemiology models,
- ✓ cancer development models,…

One of the simplest examples: population growth model

Thomas Robert Malthus (1766-1834)
British economist

Example of the rabbit population growth in Australia





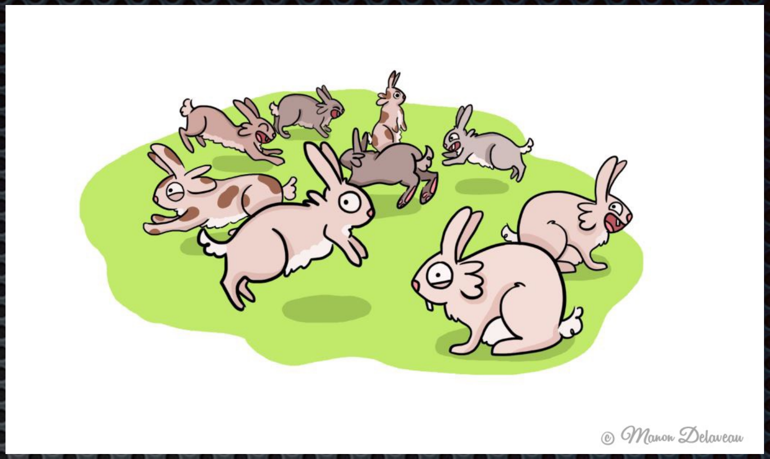
1850, Thomas Austin released 24 rabbits in the countryside of Australia.
1950 rabbit population was estimated to be 600 millions!

$L(t)$ = number of rabbits at time t

b = birth rate

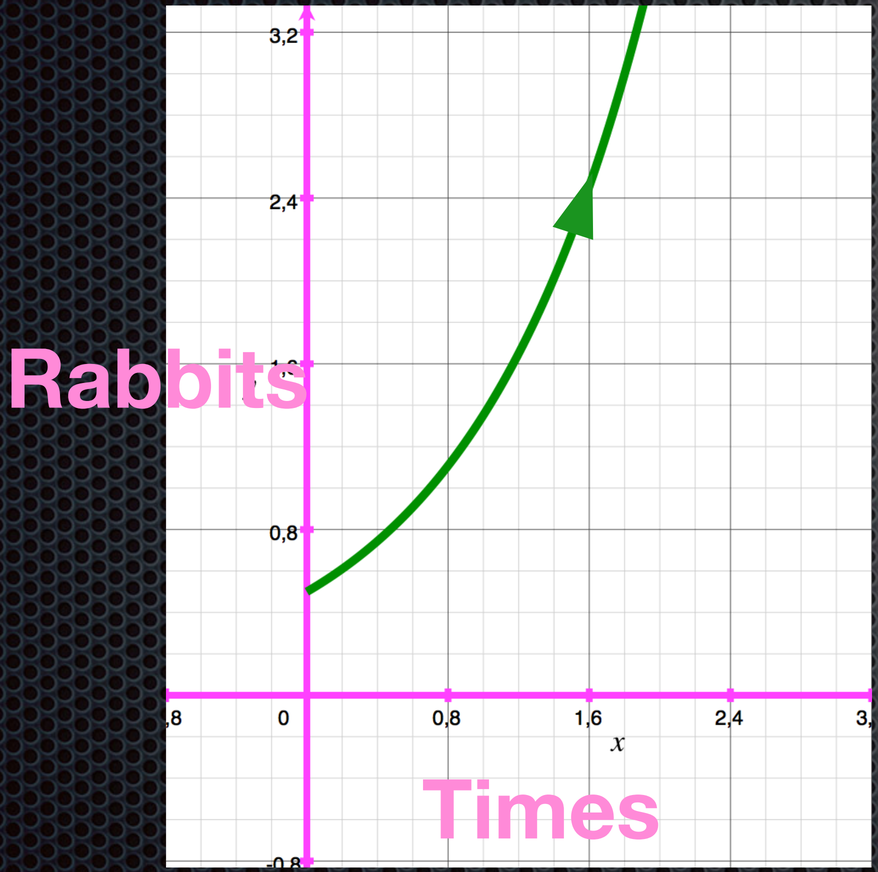
d = death rate

$L'(t)$ = rate of changes of population with time

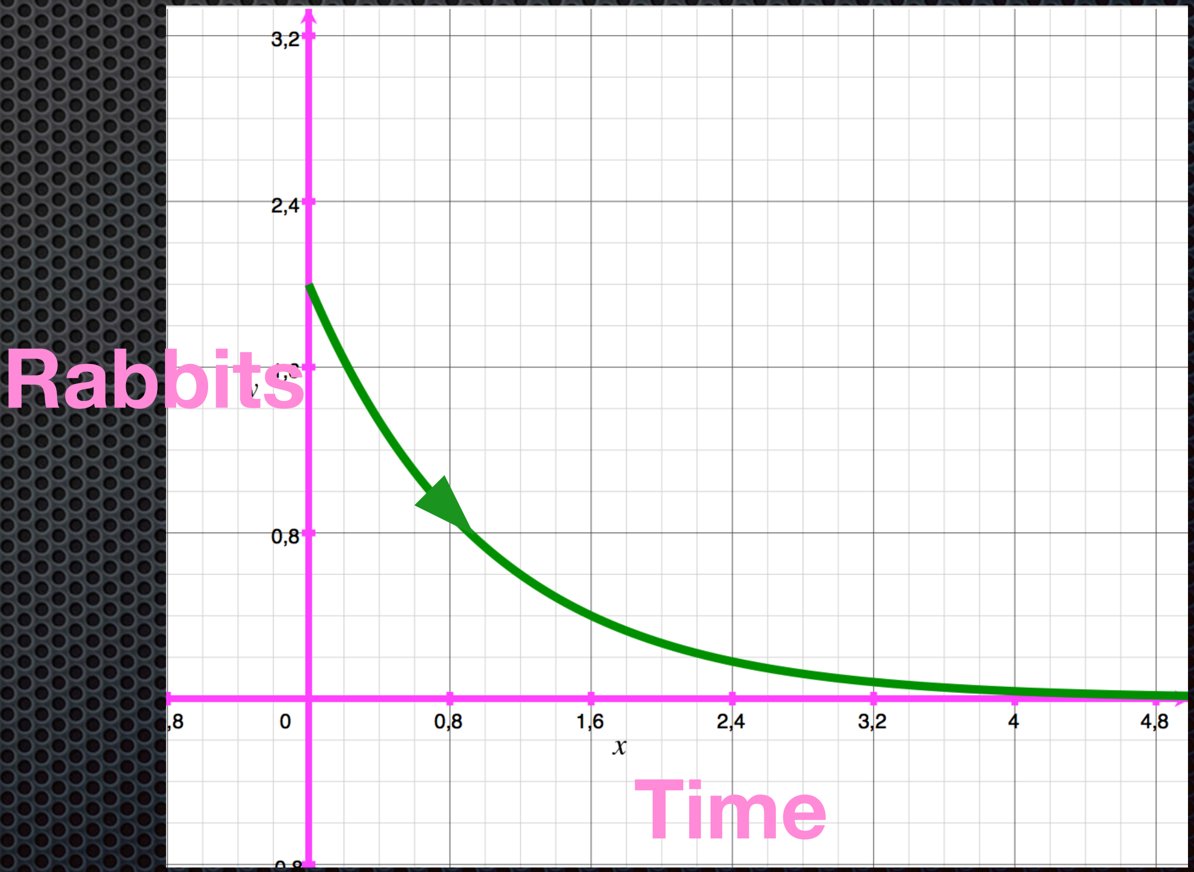


$$\boxed{L(t)' = b.L(t) - d.L(t)} \longrightarrow \boxed{L(t)' = a.L(t)}$$

$a = b - d$



$b > d$



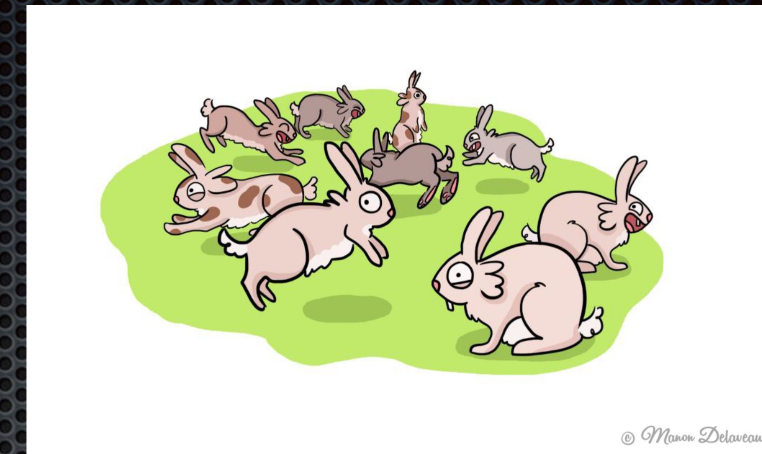
$b < d$

L(t) = number of rabbits at time t

b = birth rate

d = death rate

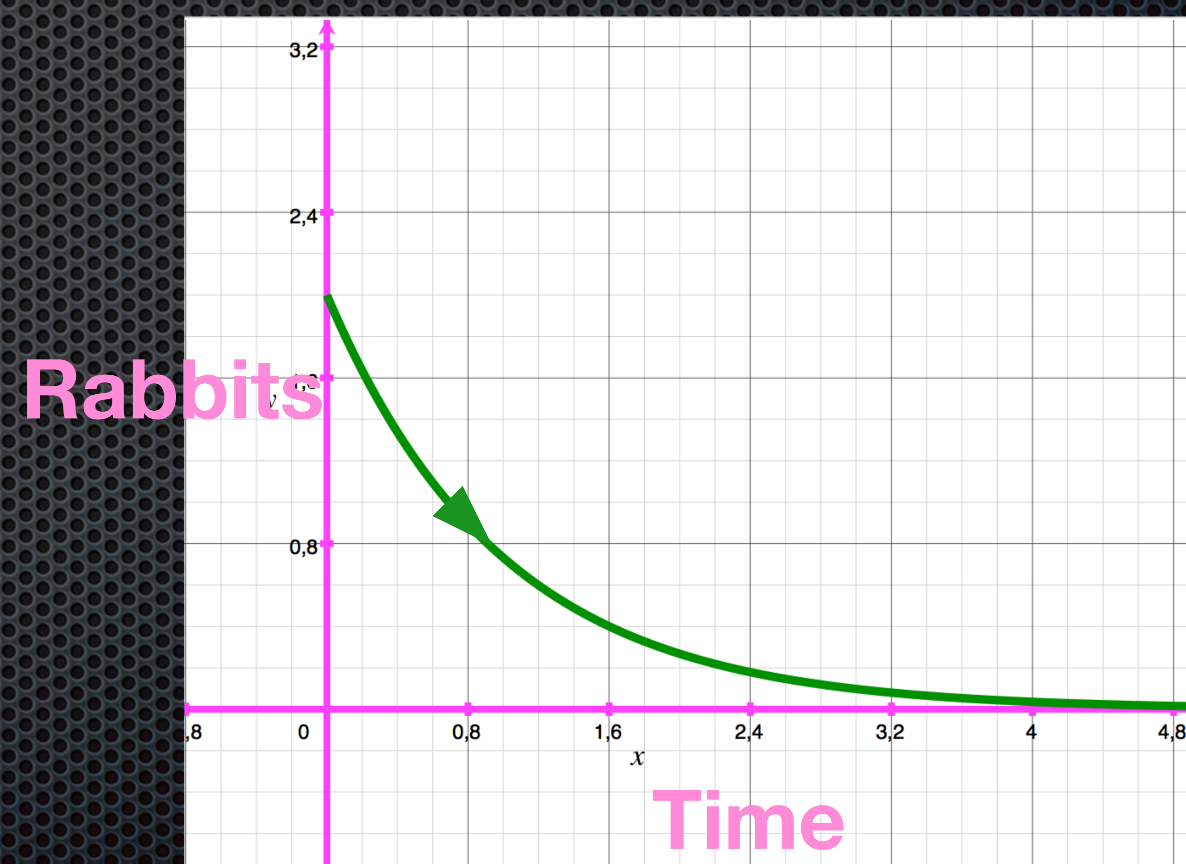
L'(t) = variation of population with time



$$L(t)' = 8.L(t) - 3.L(t) \longrightarrow L(t)' = 5.L(t)$$

5= 8-3

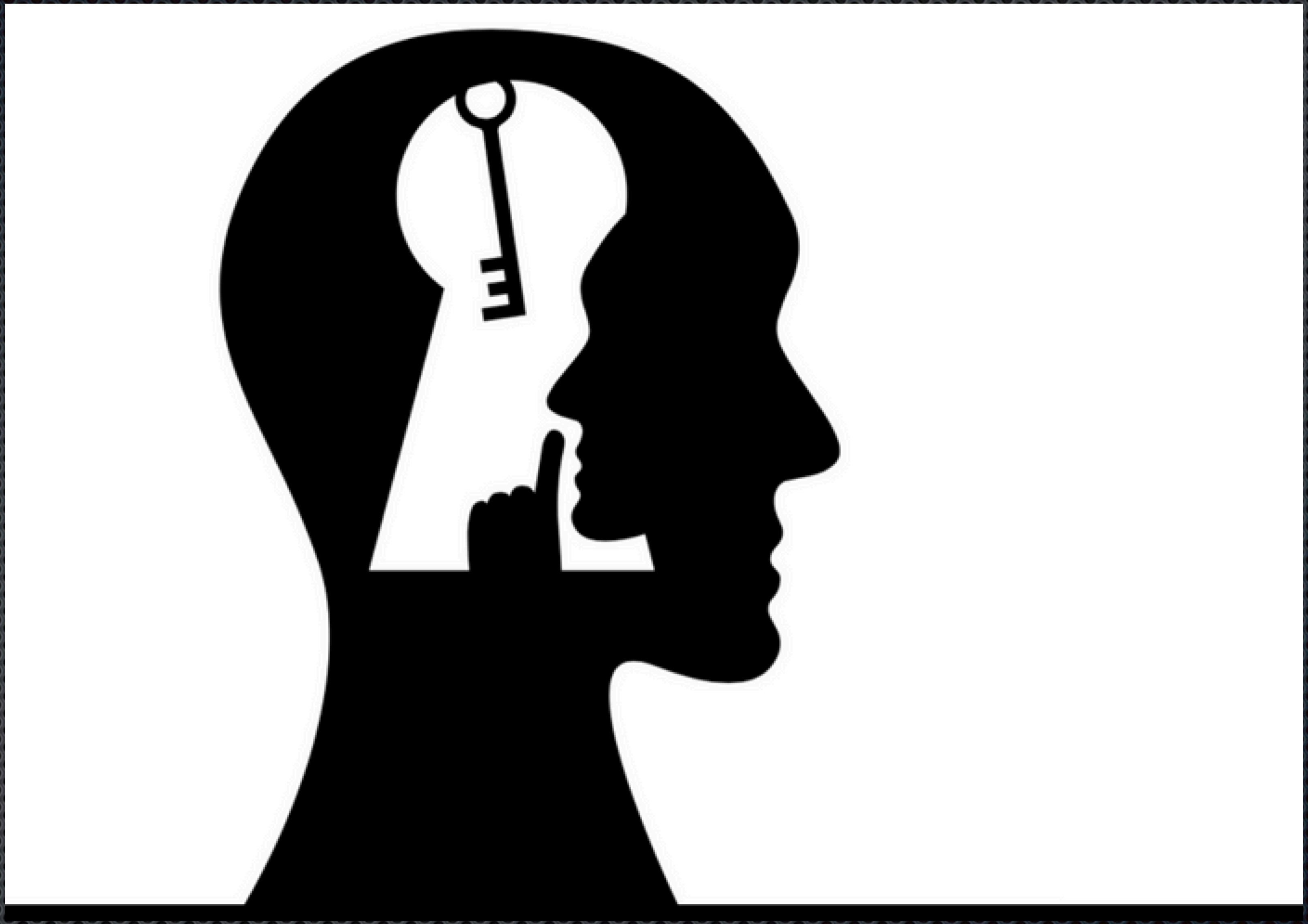
b>d



b<d

How do we study such a problem?

The secret?

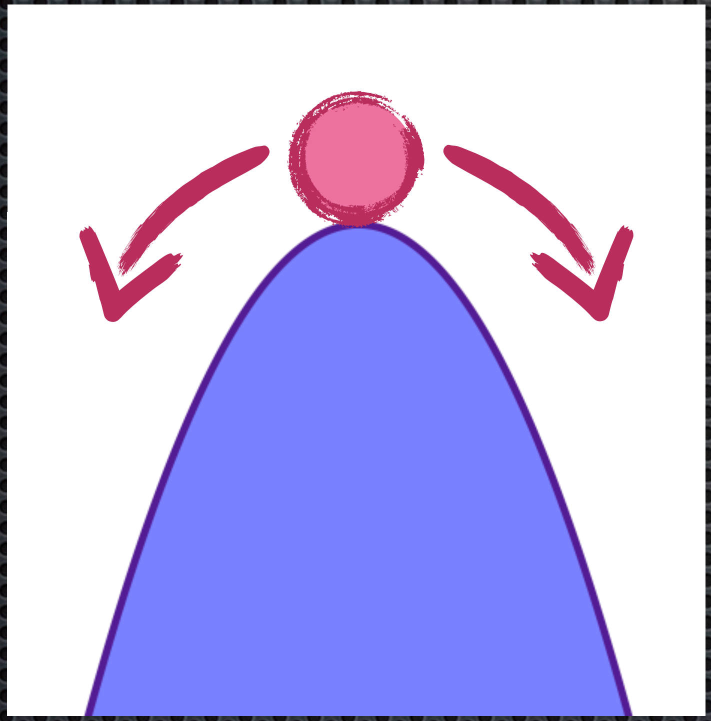


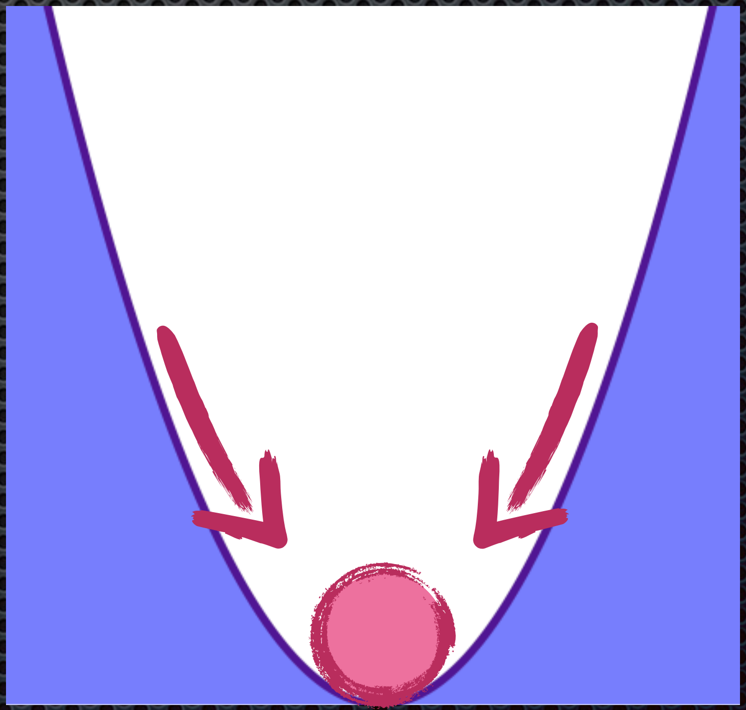
The secret?

Equilibria!

What is an equilibrium ?

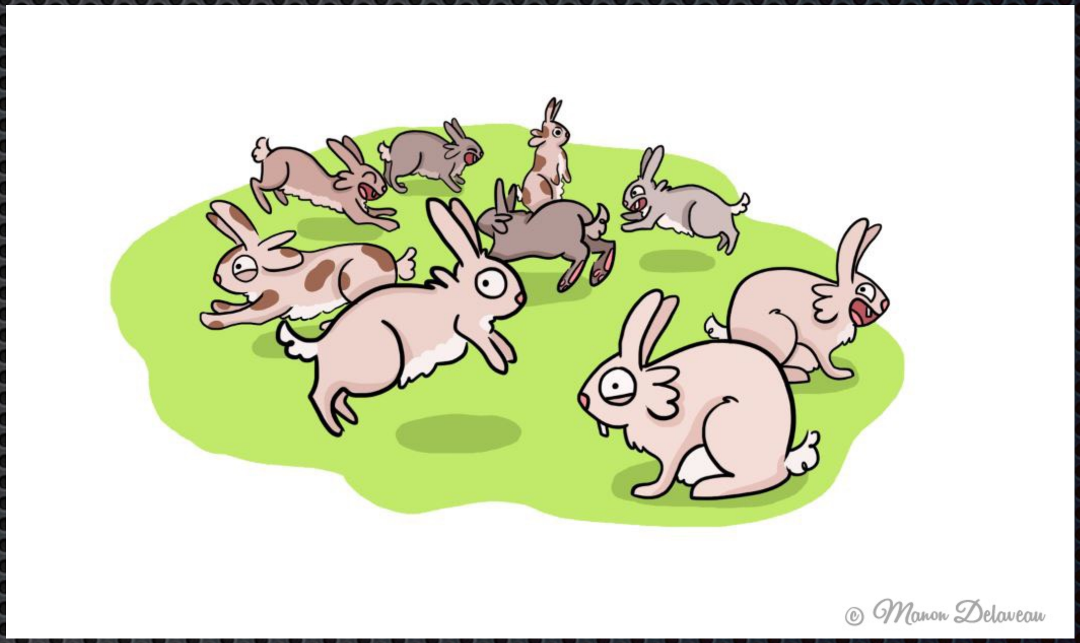
it is a steady state:
it does not vary with time!





Equilibrium: a point that does not vary in time!

Example with rabbits



$L(t)' = a.L(t)$

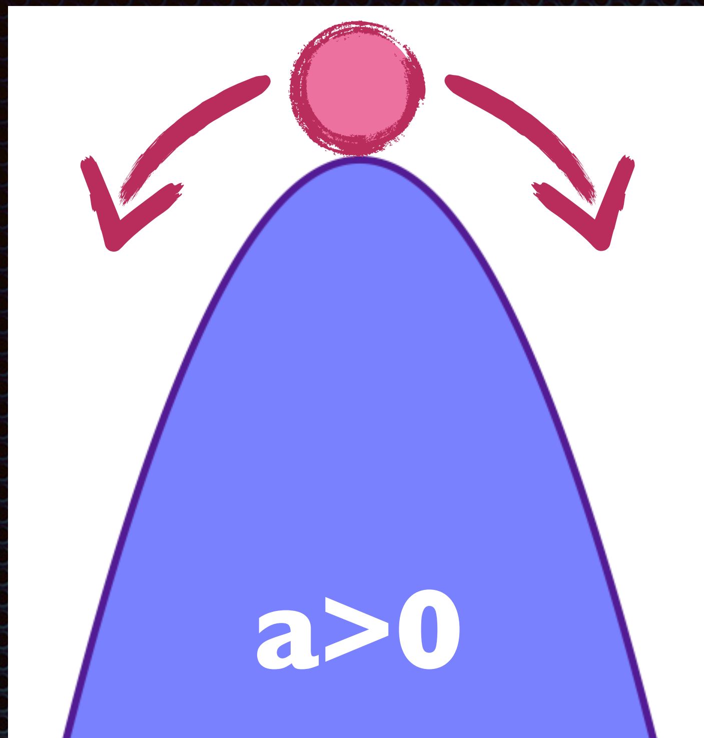
Equilibria? Denote them L^*

variation is null with time:

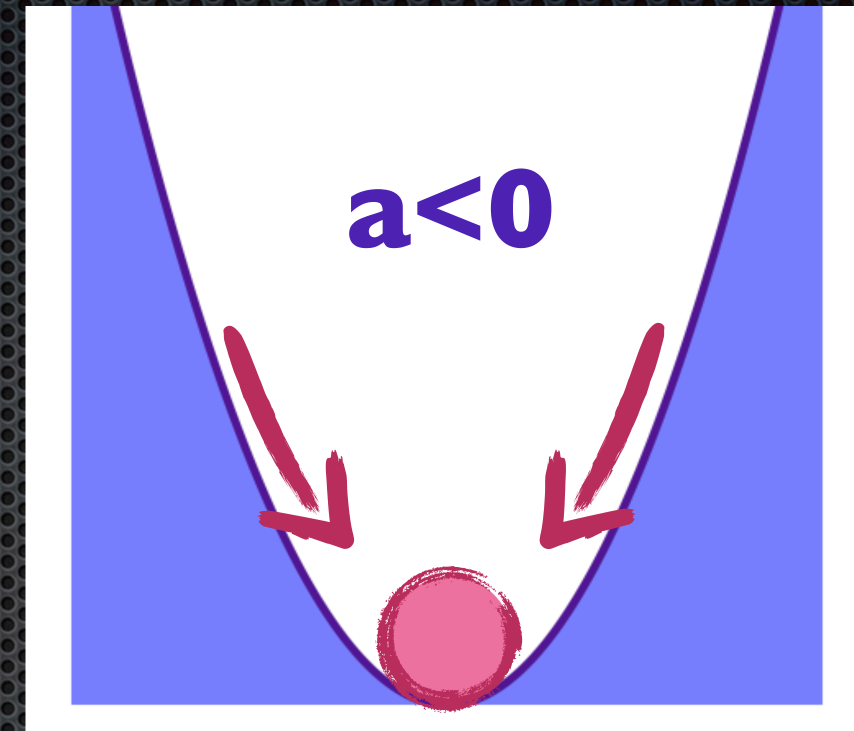
$L^{*\prime} = 0$ so $a.L^* = 0$ and if $a \neq 0$ then $L^* = 0$

One single equilibrium: $L^* = 0$!

Two images to illustrate this: a marble and love

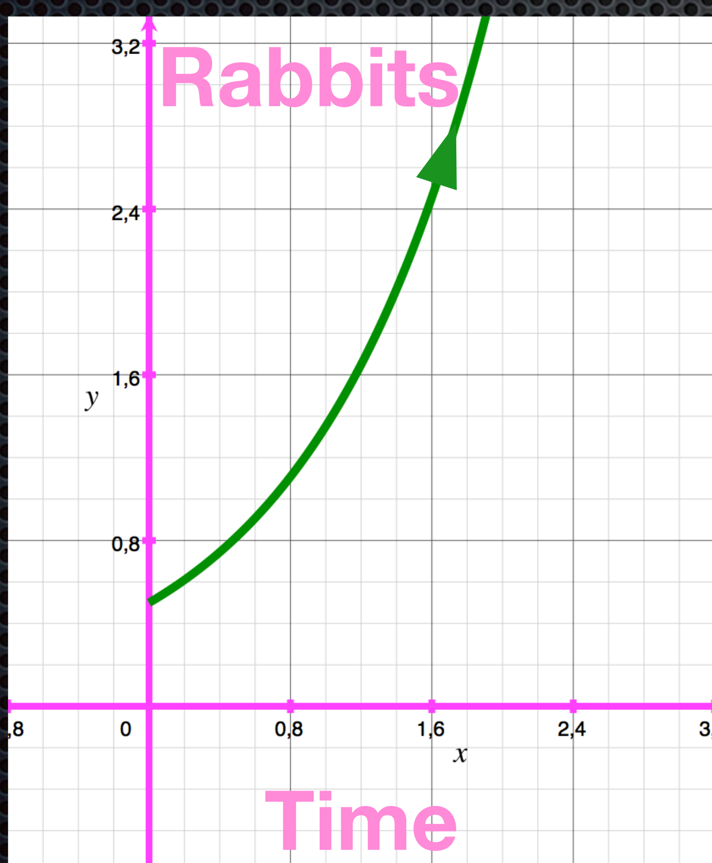


$$A(t)' = a.A(t)$$



a>0, A’(t)>0, A increasing

a<0, A’(t)<0, L decreasing



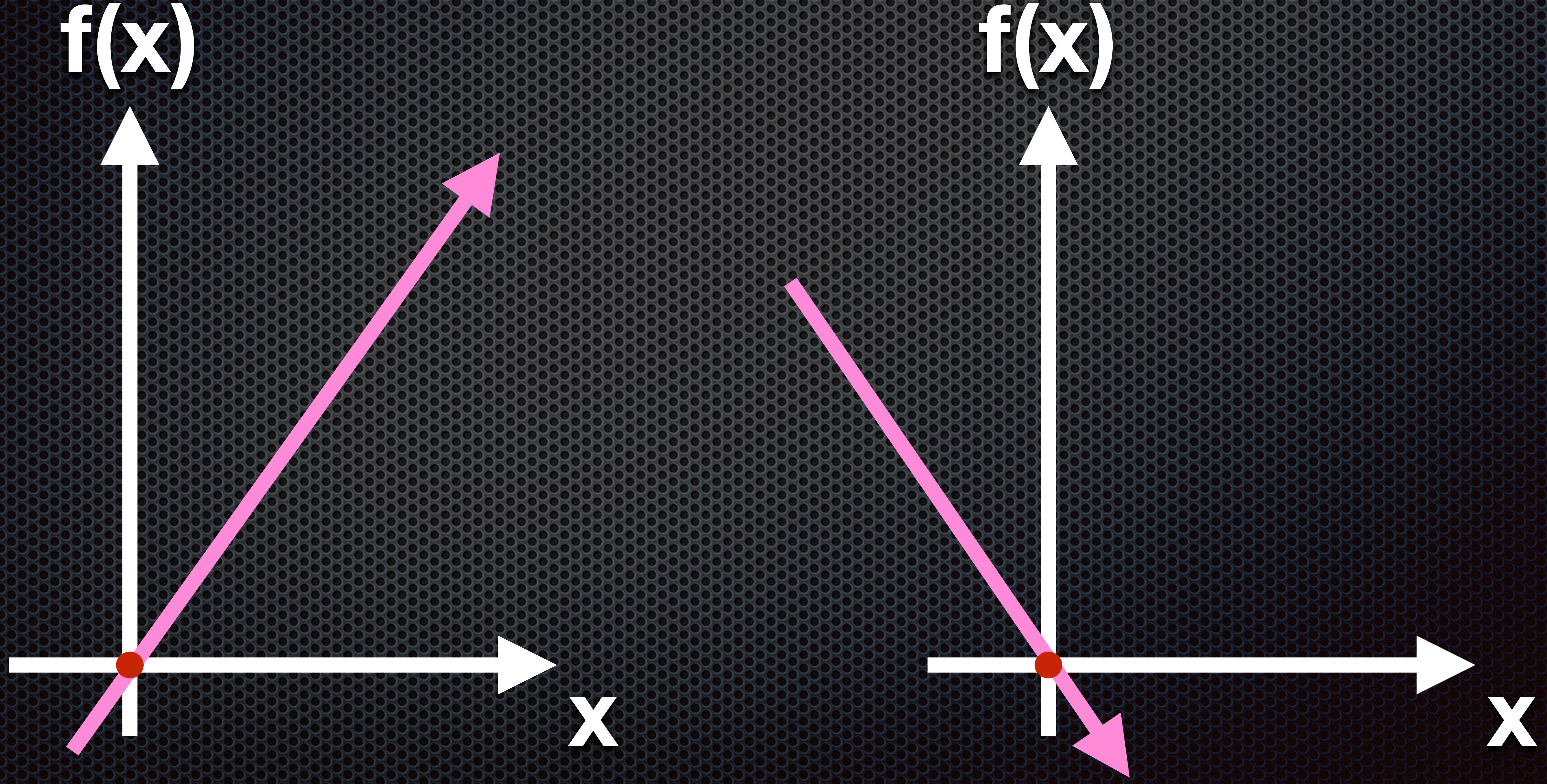
A*=0 unstable

A*=0 stable

$x' = a.x = f(x)$

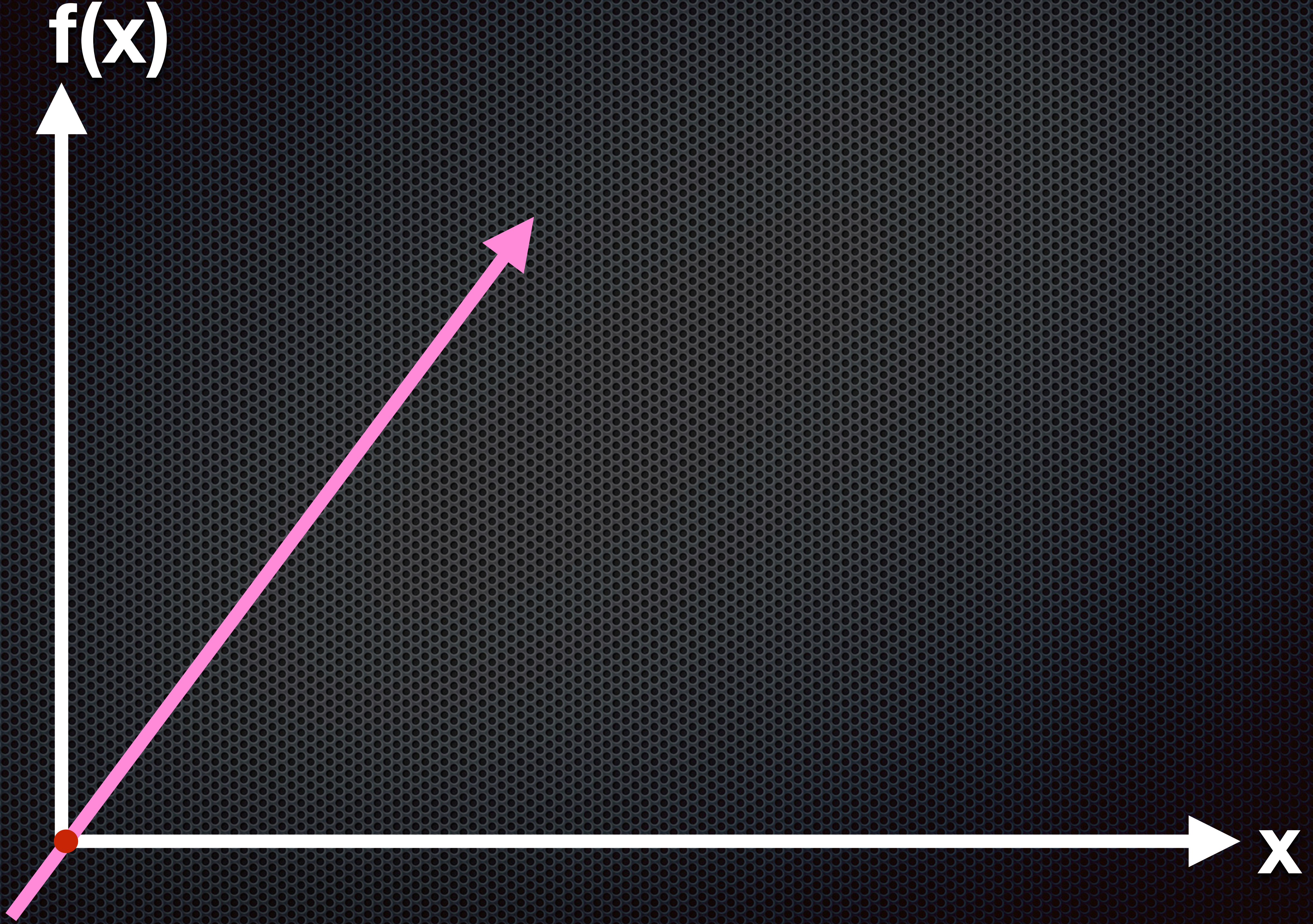
x^*=equilibrium

$x^{*\prime} = 0 = ax^*$ so $x^* = 0$

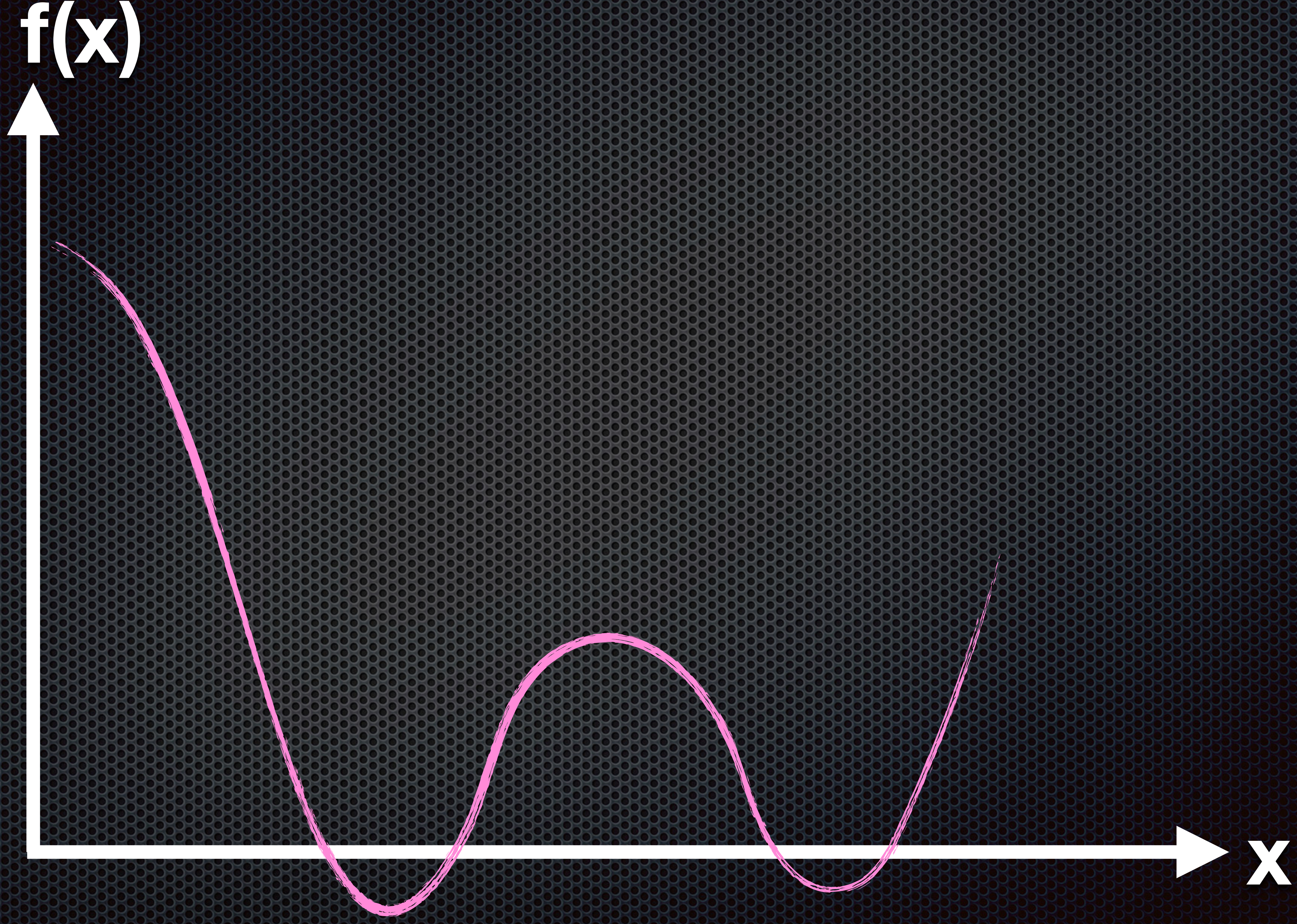


More generally

$x' = a.x$



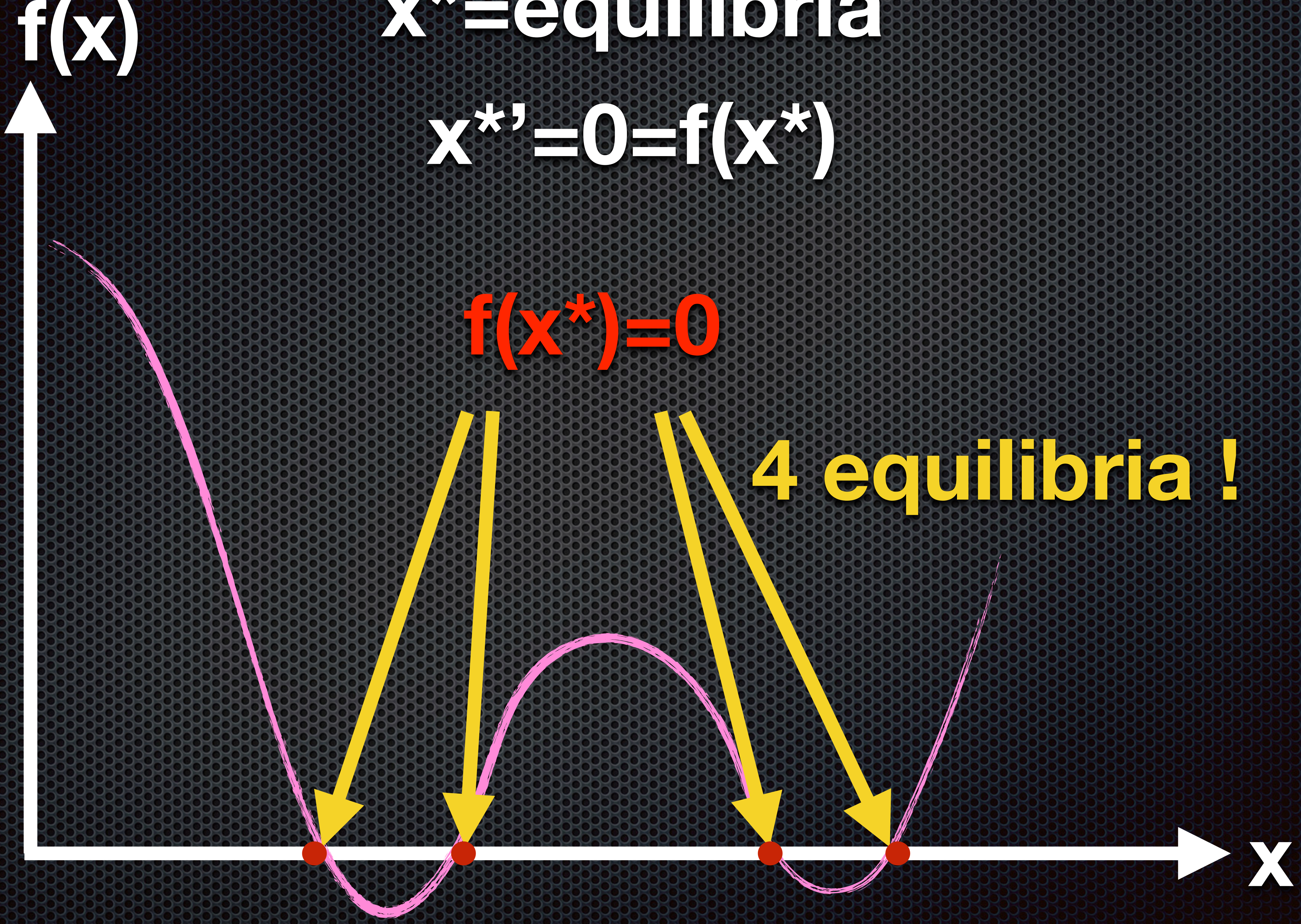
$x' = f(x)$



$$x' = f(x)$$

$$x^* = \text{equilibria}$$

$$x^{*\prime} = 0 = f(x^*)$$



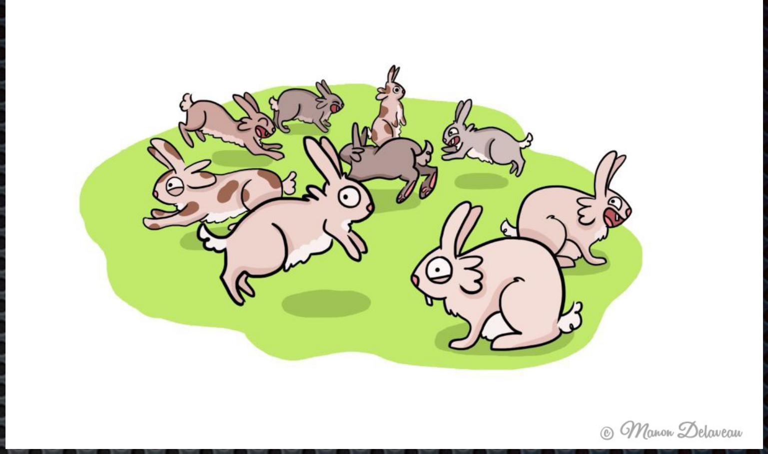
Problem with the Malthus model

$L(t)$ = number of rabbits at time t

b = birth rate

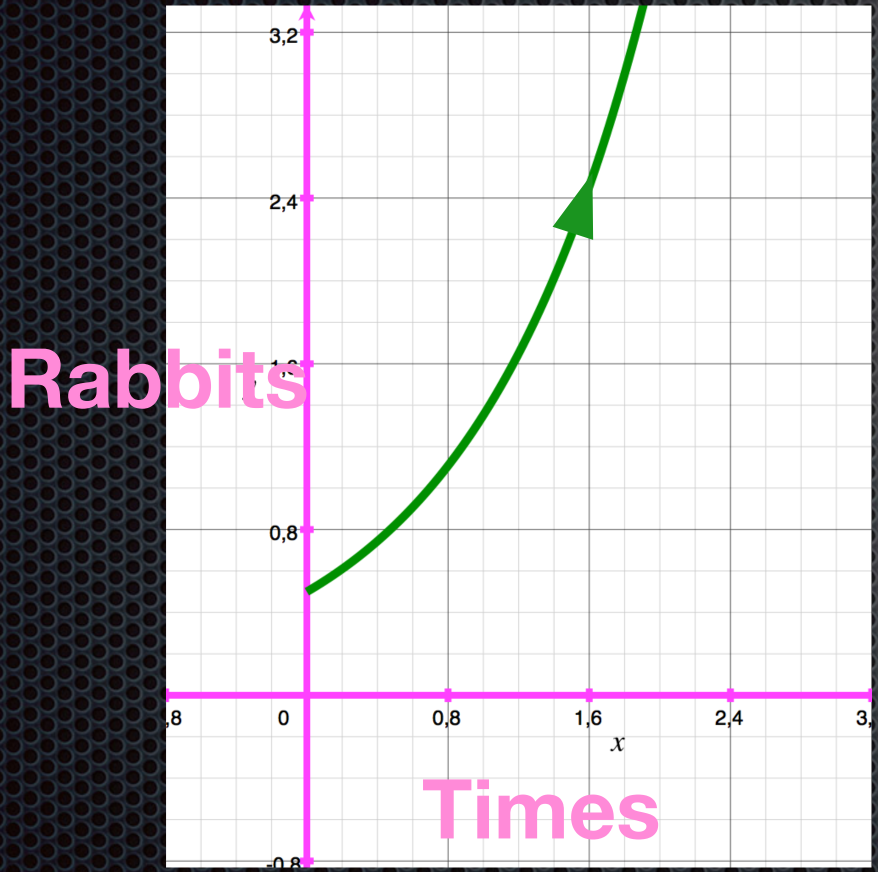
d = death rate

$L'(t)$ = rate of changes of population with time

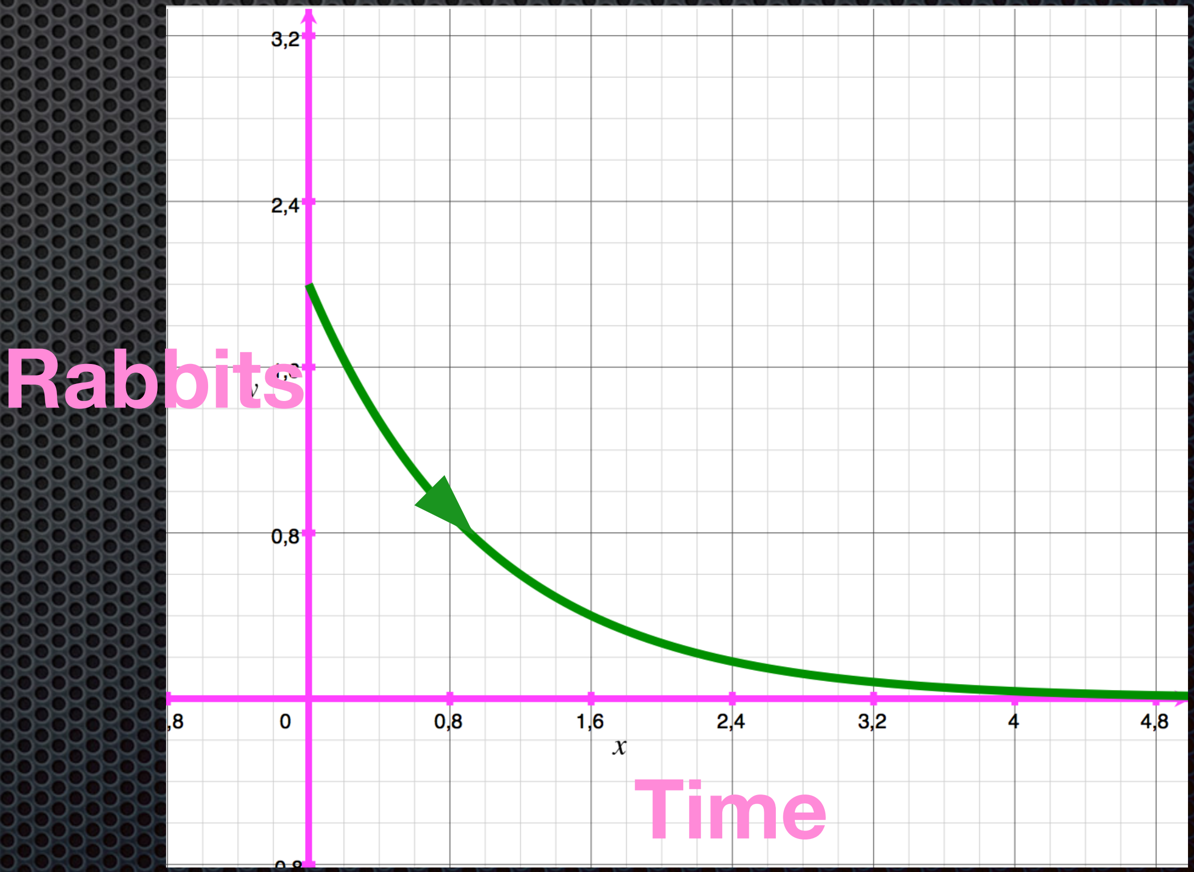


$$\boxed{L(t)' = b.L(t) - d.L(t)} \longrightarrow \boxed{L(t)' = a.L(t)}$$

$a = b - d$



b>d

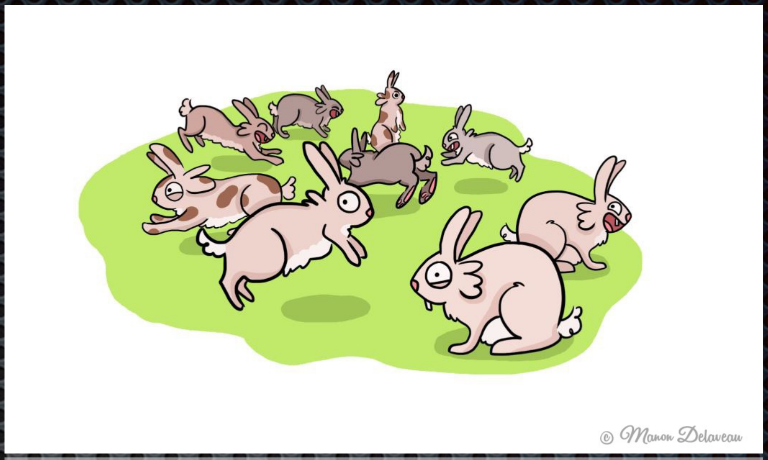


b<d

A too simple model...

Pierre François Verhulst (1804-1849)
Belgian mathematician

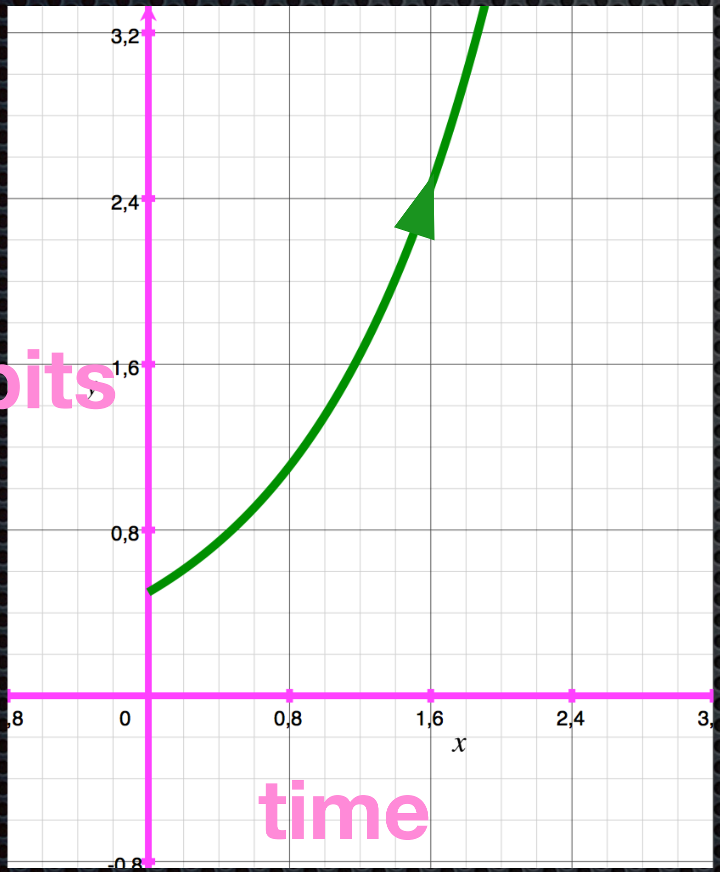
$L(t)$ = number of rabbits at time t
b = birth rate
d = death rate
$L'(t)$ = rate of changes of population with time



$$\boxed{L(t)' = a.L(t)}$$

Malthus

Verhulst suggests that **a** is not a constant!

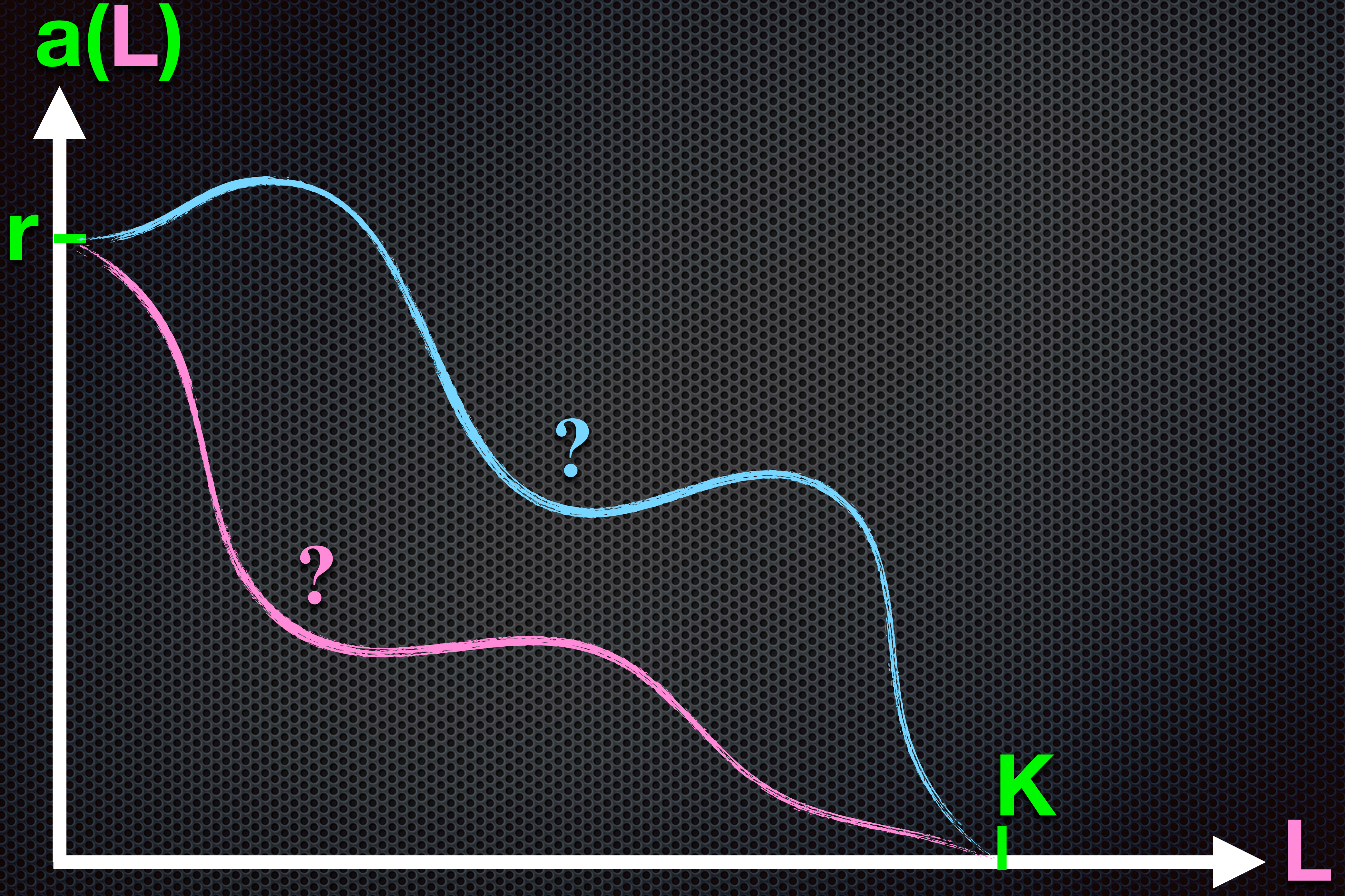


a>0

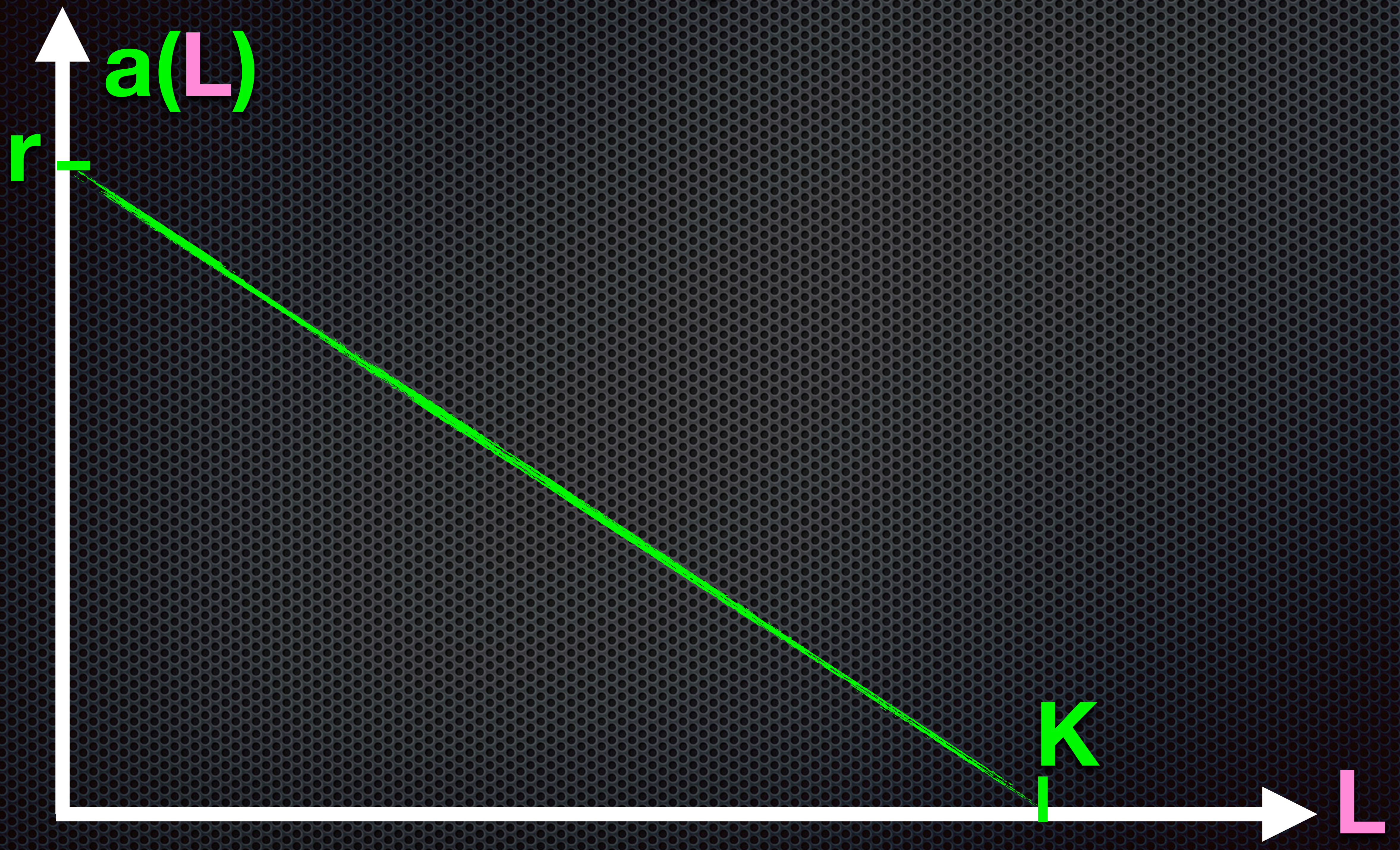
Growth (or decay)
would depend on the L population itself
1-maximal growth rate **r** for small populations L,
2-null growth rate when the population is too large (reaching a value K called the carrying capacity)

We would then change **a** to **a(L)** ...

How should we choose a(L)?



How should we choose a(L)? One solution: the simplest curve: the straight line !



Malthus $\boxed{L(t)' = a.L(t)}$

$$a(L) = -rL/K + r$$

$$= r(1-L/K)$$

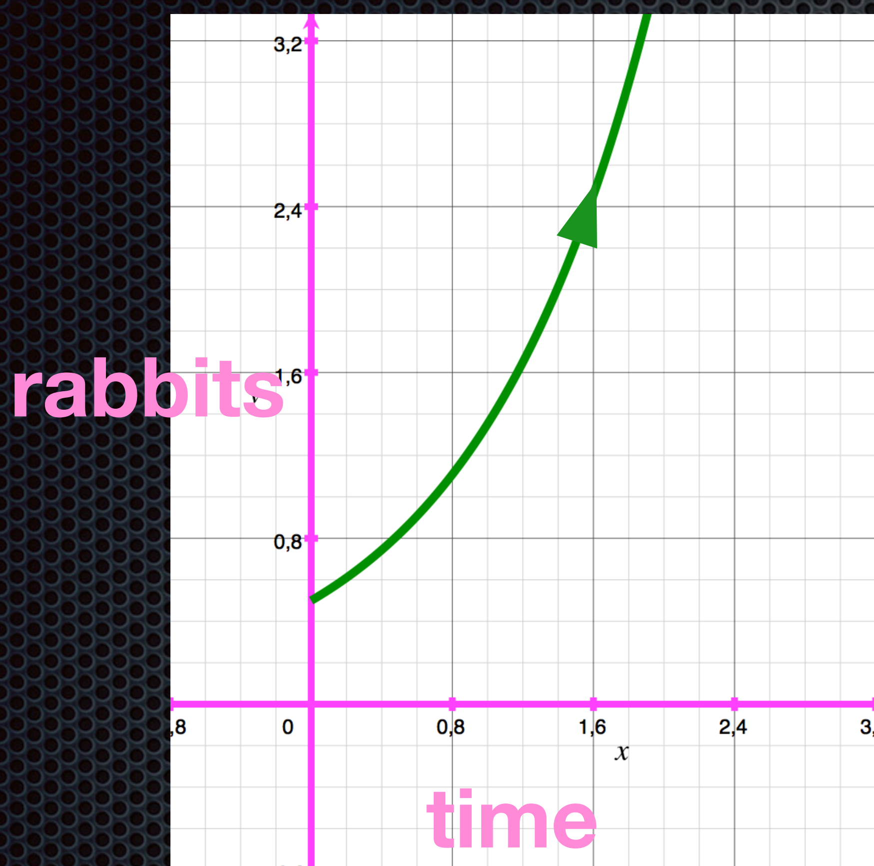
Verhulst $\boxed{L(t)' = r(1-L/K).L(t)}$

r: maximal growth rate

K: carrying capacity

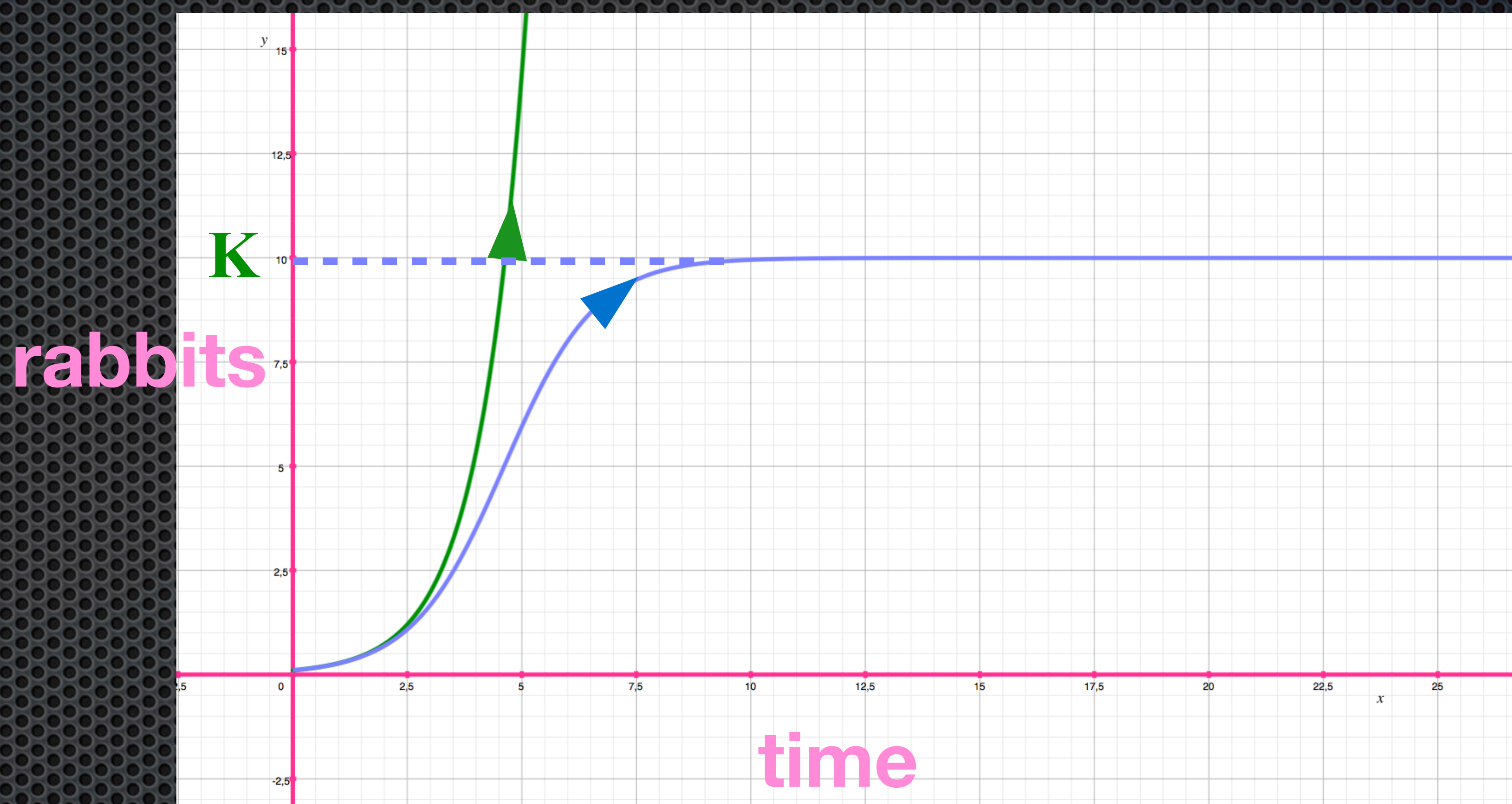
Difference between the two models

Malthus
exponential curve



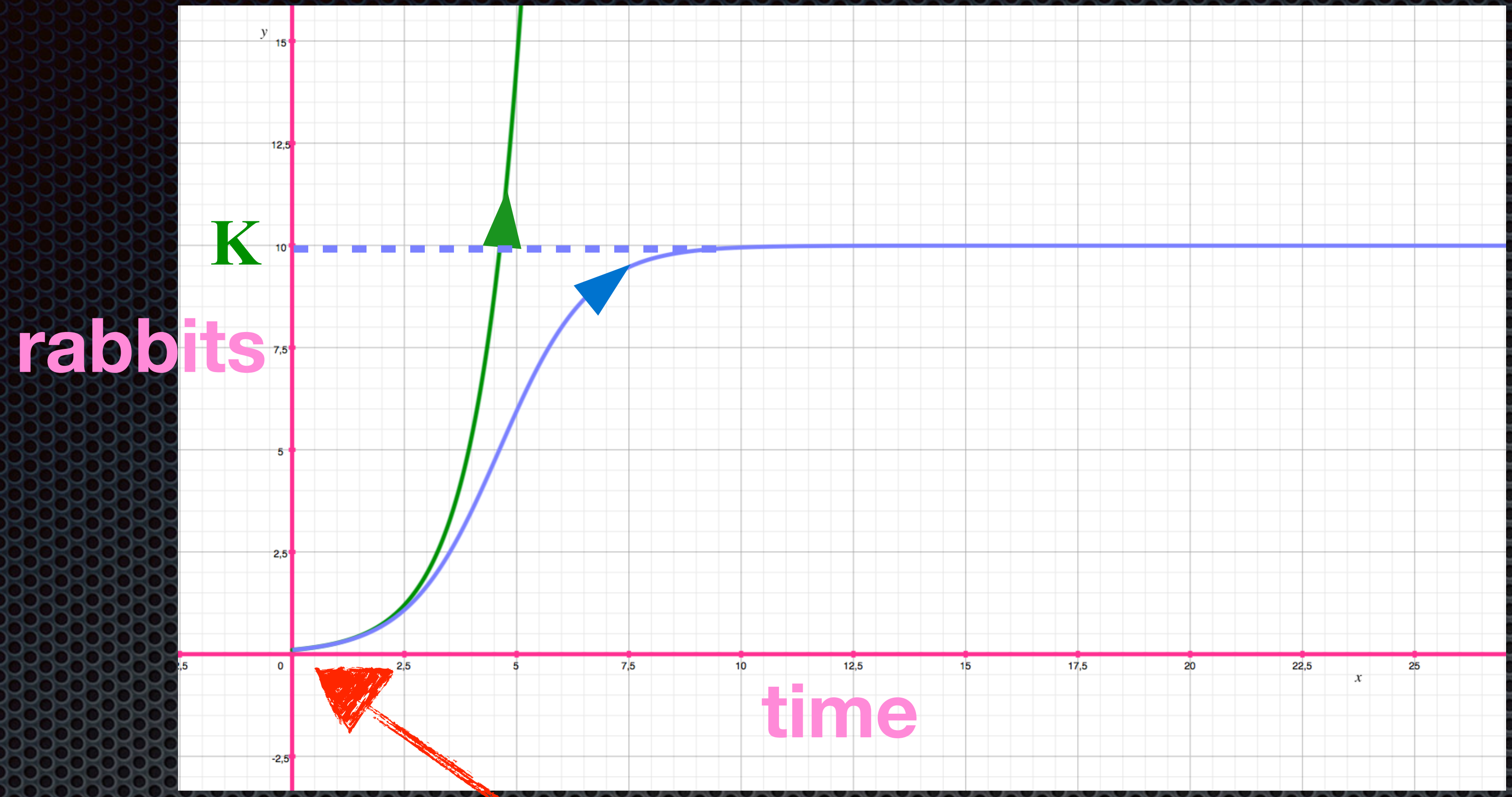
a>0

Verhulst
logistic curve



Even if more realistic,

Verhulst model is still not appropriate…



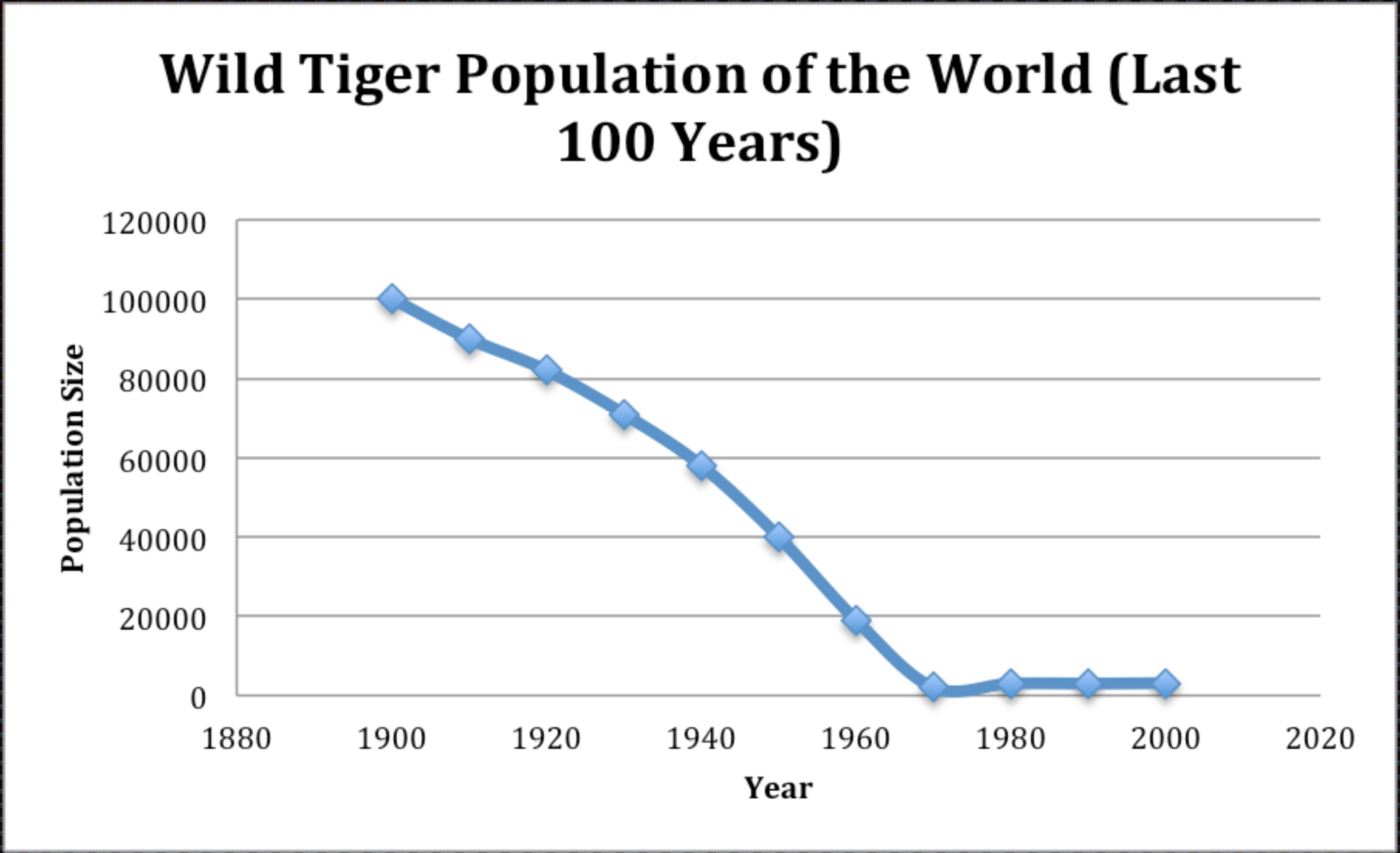
Even if initial population is close to 0, repopulating the species is not a problem…

this seemed a big issue...

Suppose that 2 wild tigers remain in the world,

one male and one female…

one in India, the other one in China


Wild Tiger Population of the World (Last 100 Years)
120000
100000
80000
60000
40000
20000
0
Population Size
1880
1900
1920
1940
1960
1980
2000
2020
Year

2013

SCIENCES ET AVENIR

Nature

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TEMPS FORTS ▸ COP21 "Coywolf" Empreinte de l'eau L'arbre transexuel Risques industr

À LA UNE

Sciences > Nature & environnement > Les tigres sont proches de l'extinction

Les tigres sont proches de l'extinction

Par Erwan Lecomte
Voir tous ses articles

Publié le 29-07-2013 à 18h40

A+ A-

La journée internationale du tigre est l'occasion de rappeler les menaces qui pèsent sur cette espèce.

Des tigres sibériens dans un zoo au Danemark BAGGER HENNING/SCANPIX SUEDE/SIPA

Repopulating the species is almost impossible…

Verhulst model is not exact in this case

How should we solve it ?

Warder Clyde Allee (1885-1955)
American zoologist et ecologist

Allee effect

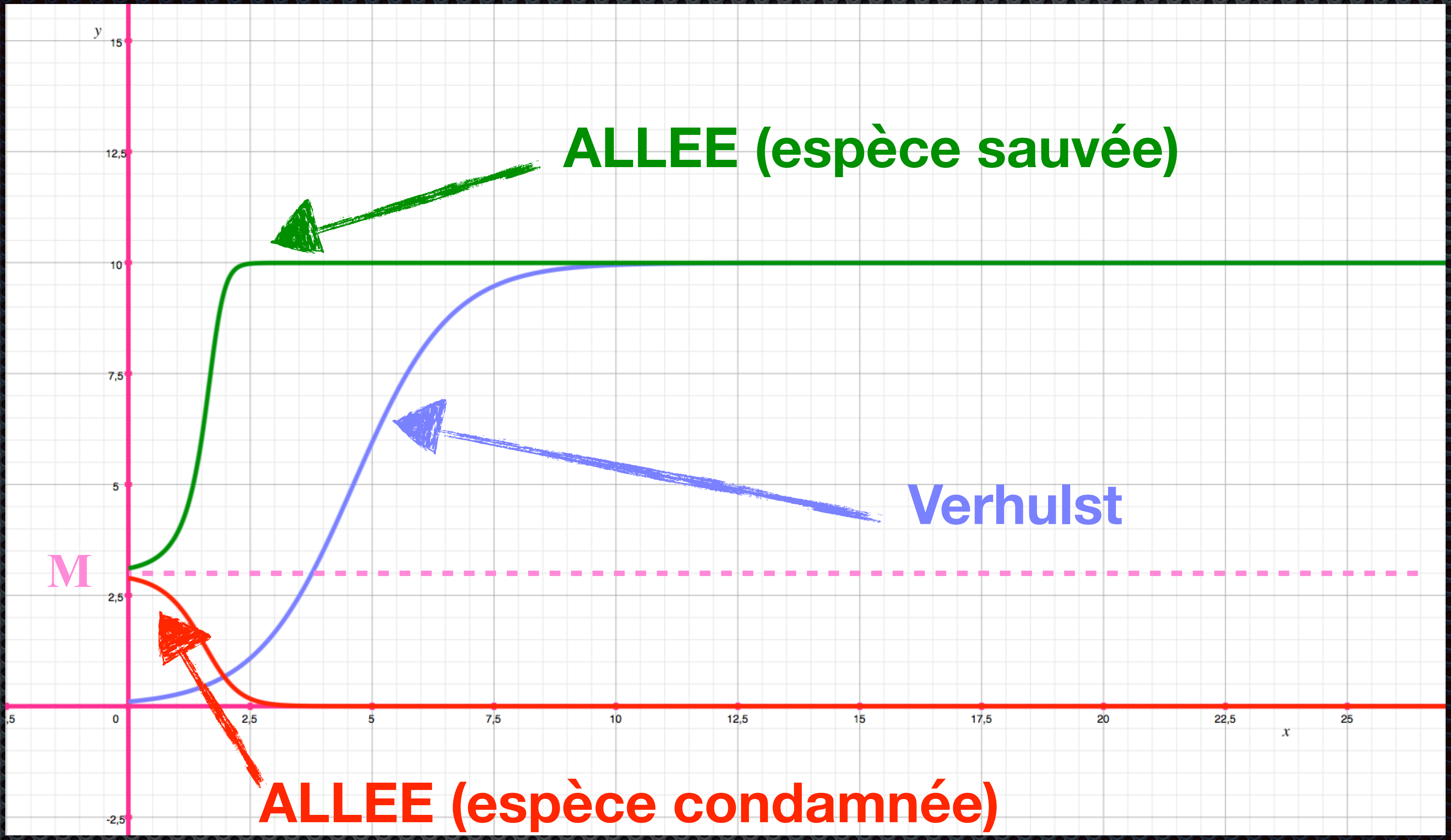
Allee effect

Malthus $\boxed{L(t)' = a.L(t)}$

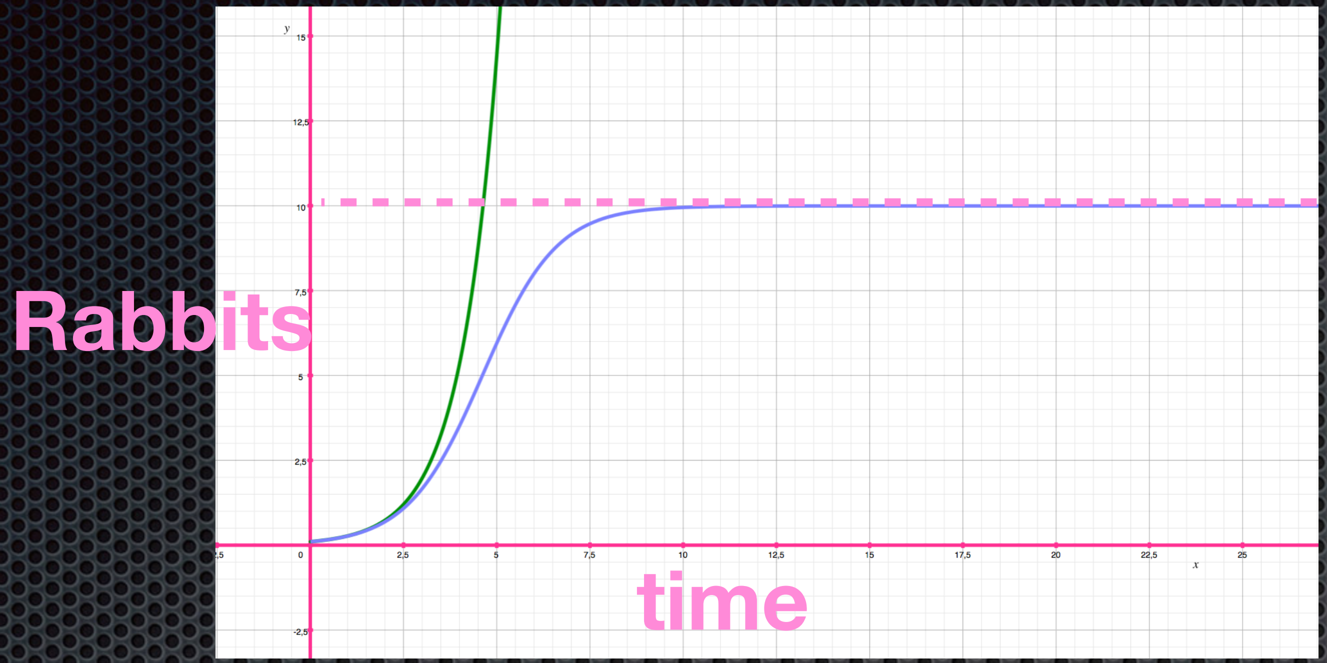
Verhulst $\boxed{L(t)' = r(1-L/K).L(t)}$

Allee $\boxed{L(t)' = r(1-L/K).L(t).(M-L)}$

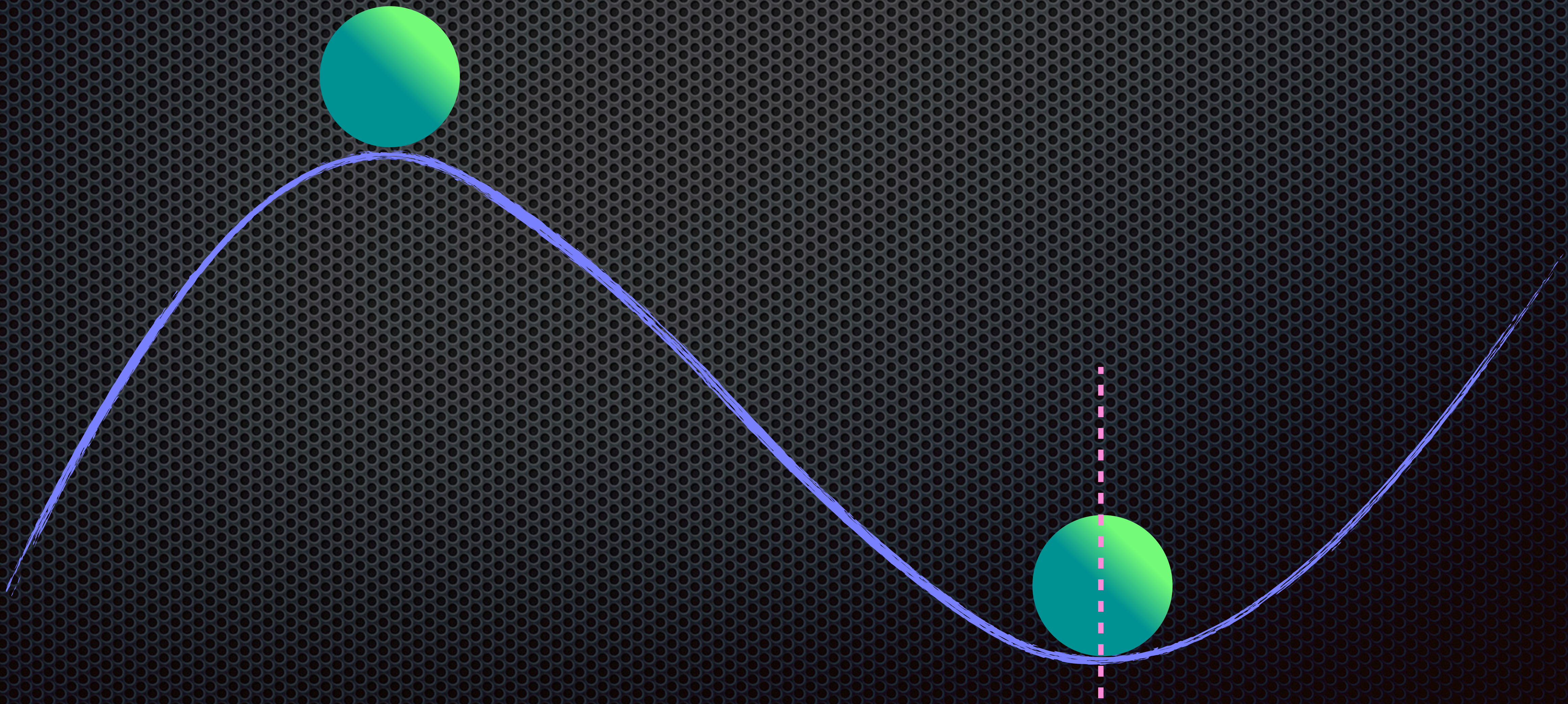
L'effet Allee



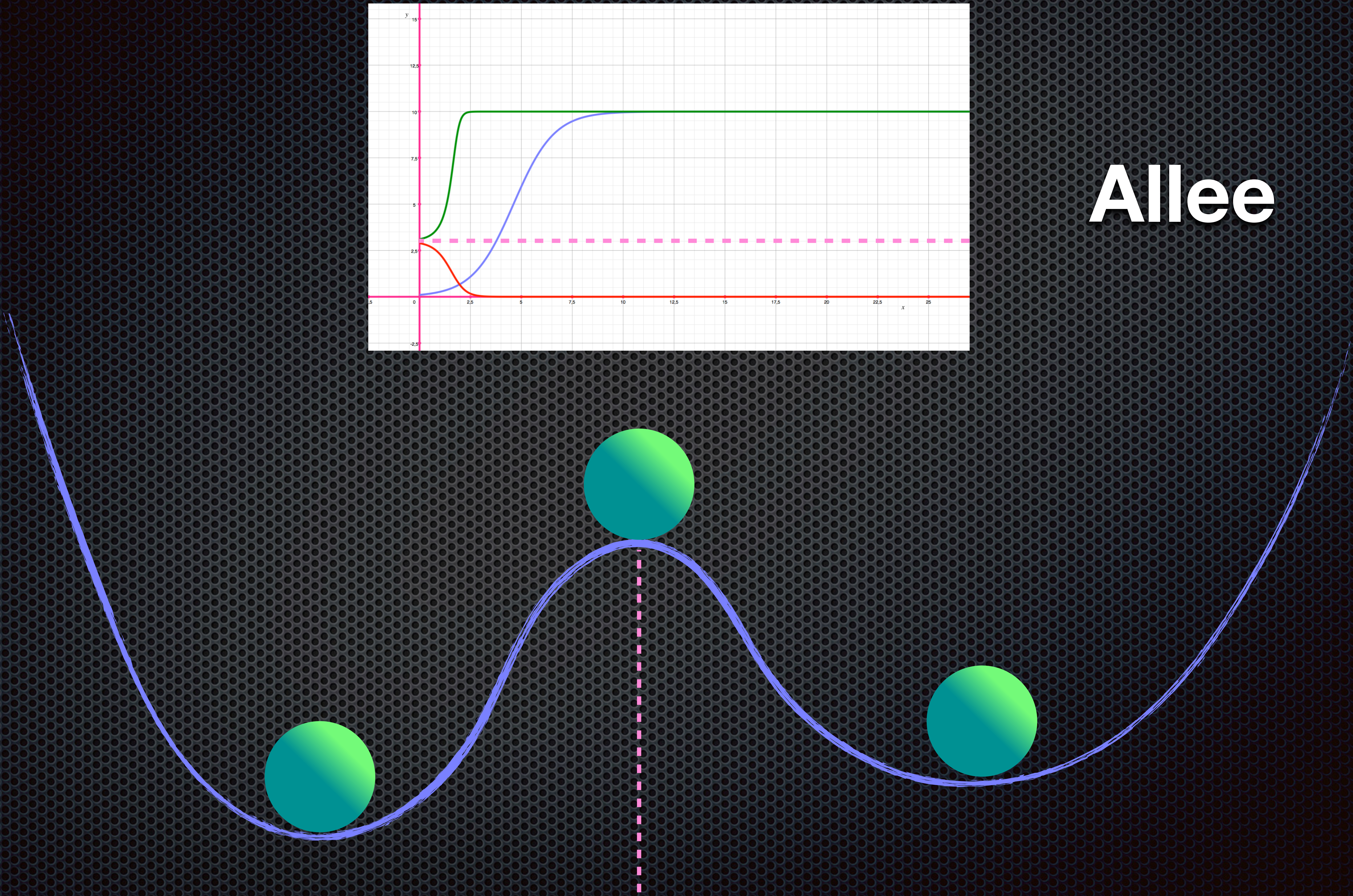
Interpretation



Verhulst



Interpretation



Allee

Everything may not be totally lost for tigers ?

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2016

Big News: Wild Tiger Populations are Increasing for the First Time in a Century

The number of wild tigers has risen to nearly 3,900, thanks to enhanced protections and conservation commitments

By John R. Platt on April 10, 2016 1

Photo: Roderick Elme. Used under Creative Commons license

M Biodiversité

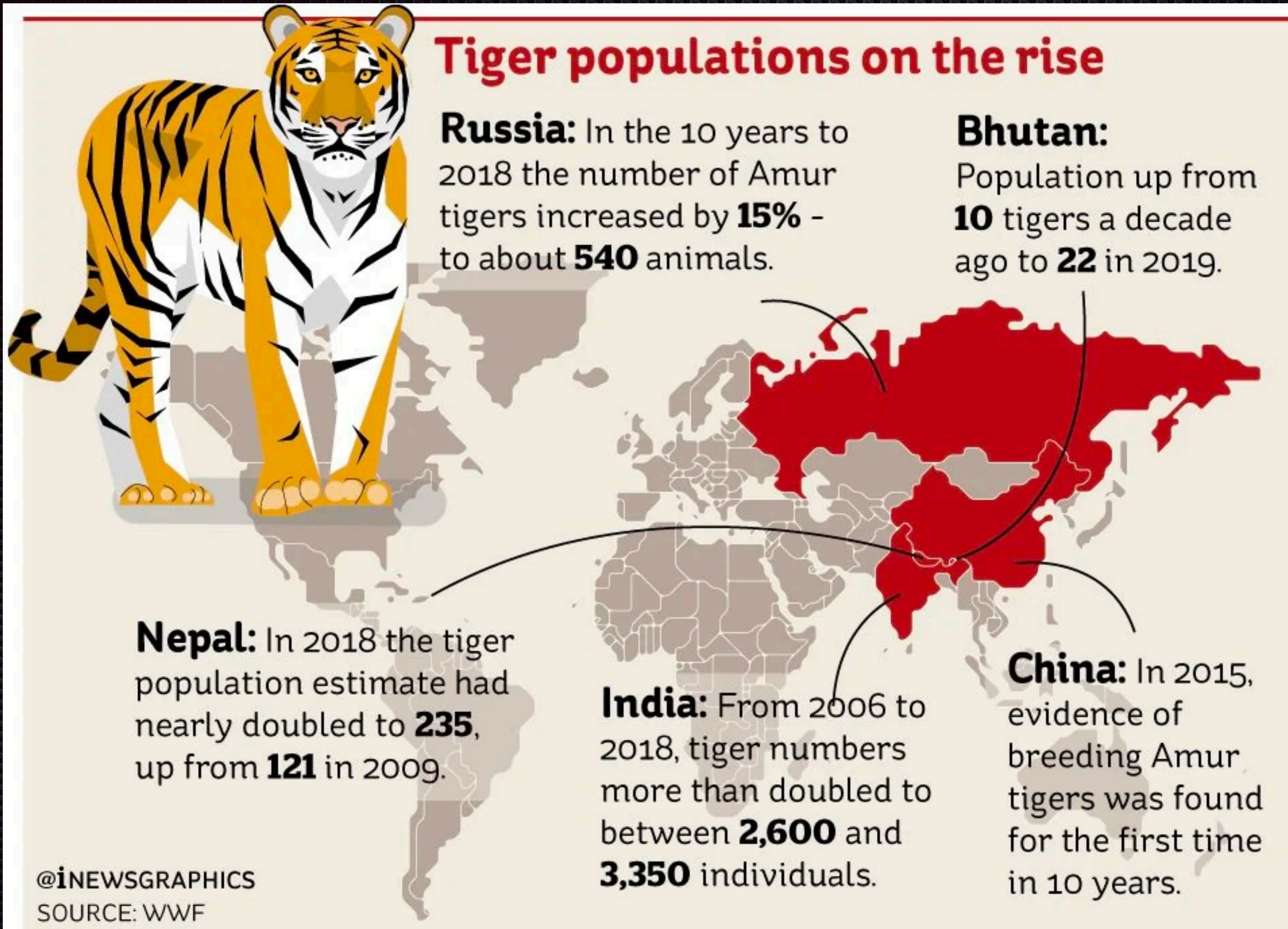
PLANÈTE BIODIVERSITÉ

ARTICLE SÉLECTIONNÉ DANS LA MATINALE DU 12/04/2016 > Découvrir l'application

Le nombre de tigres sauvages augmente pour la première fois en 100 ans

Le Monde | 11.04.2016 à 17h36 • Mis à jour le 12.04.2016 à 16h19 |

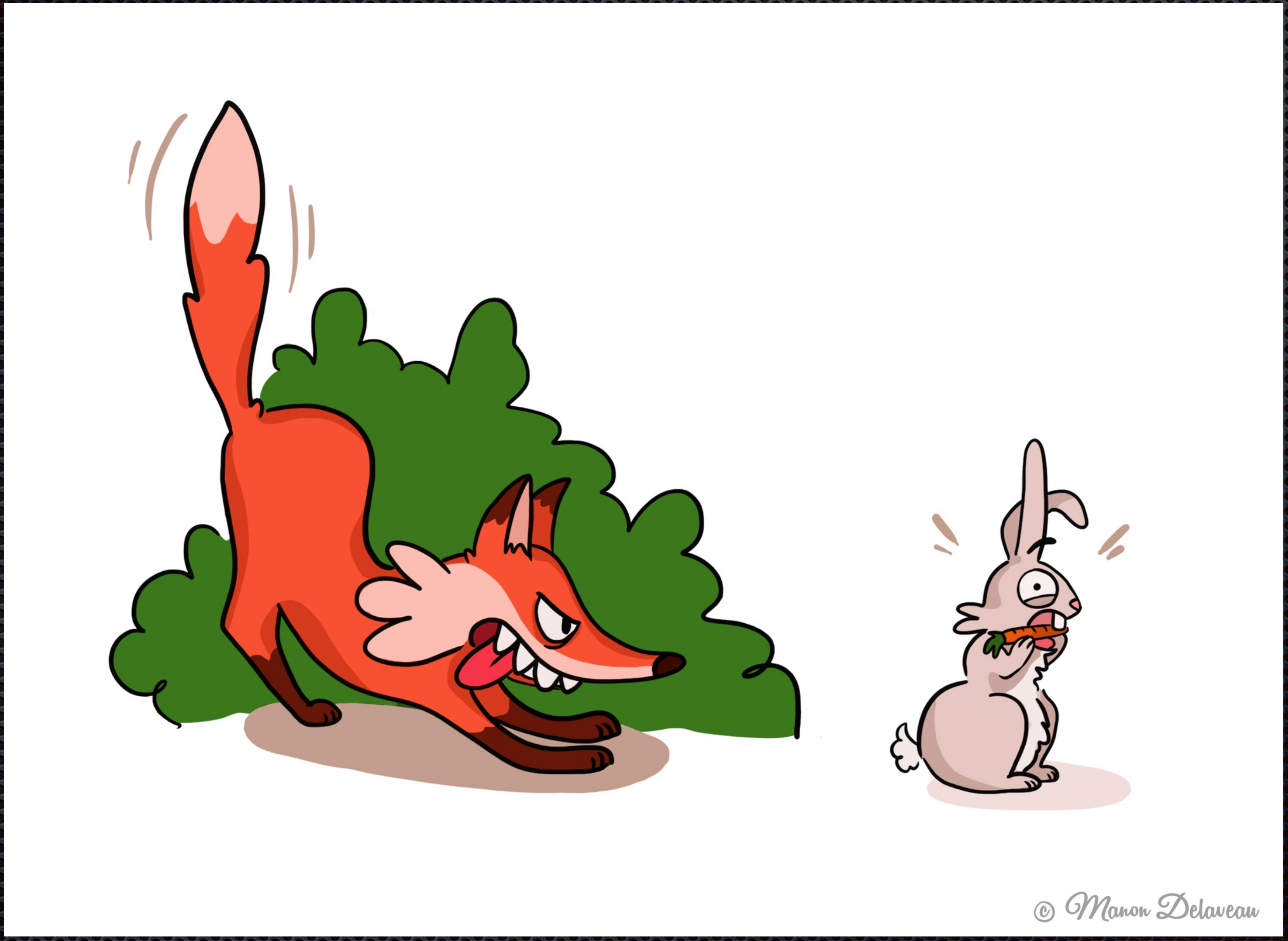
Par Aurélie Sipos


Tiger populations on the rise
Russia: In the 10 years to 2018 the number of Amur tigers increased by 15% - to about 540 animals.
Bhutan: Population up from 10 tigers a decade ago to 22 in 2019.
Nepal: In 2018 the tiger population estimate had nearly doubled to 235, up from 121 in 2009.
India: From 2006 to 2018, tiger numbers more than doubled to between 2,600 and 3,350 individuals.
China: In 2015, evidence of breeding Amur tigers was found for the first time in 10 years.
@iNEWSGRAPHICS
SOURCE: WWF

More complex models

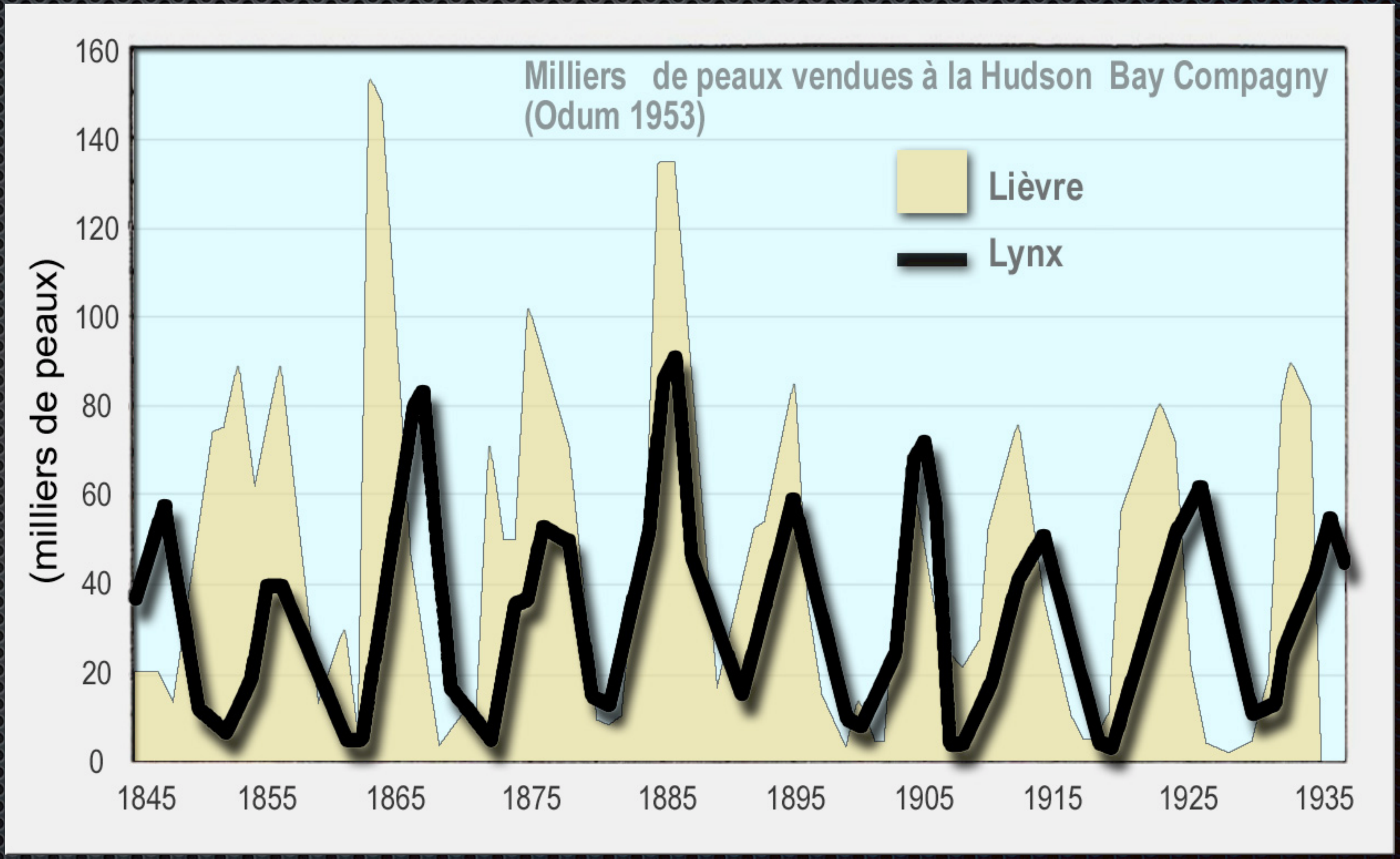
Prey predator models

A model with data



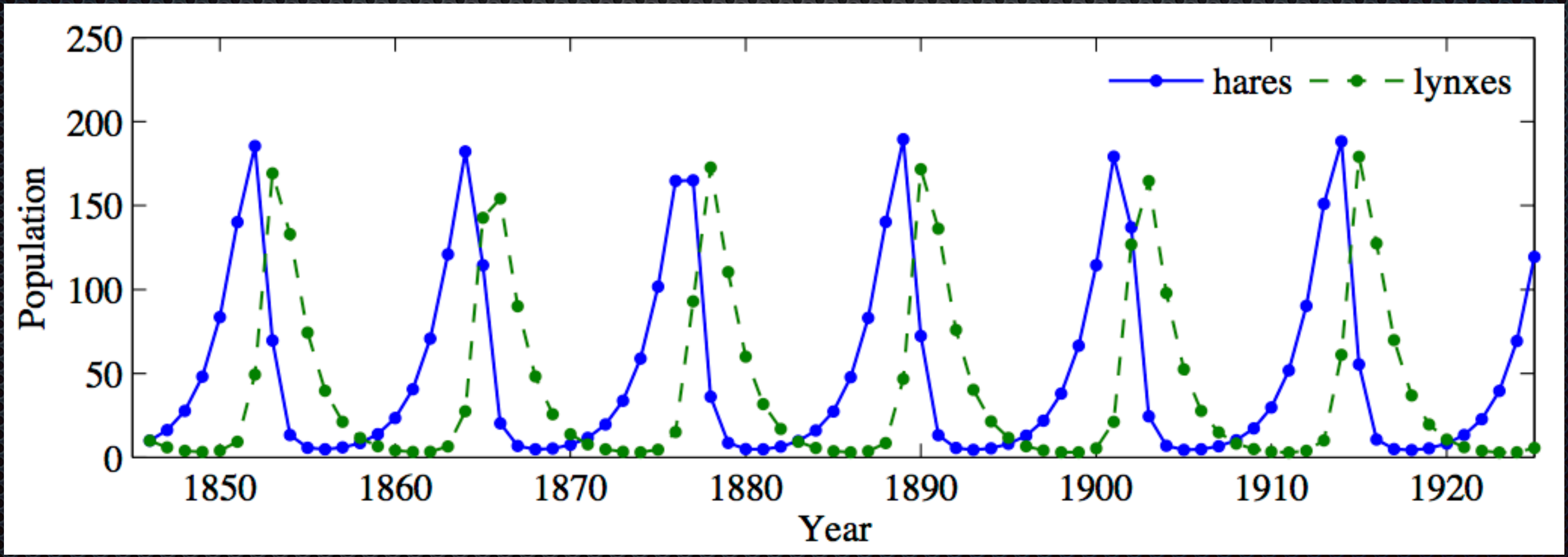
Snow shoe hares versus Lynxes

Snow shoe hares versus Lynxes



$L(t)$ = Lynxes
$H(t)$ = Hares

$$L(t)' = -L(t)(a - b.H(t))$$
$$H(t)' = H(t)(c - d.L(t))$$

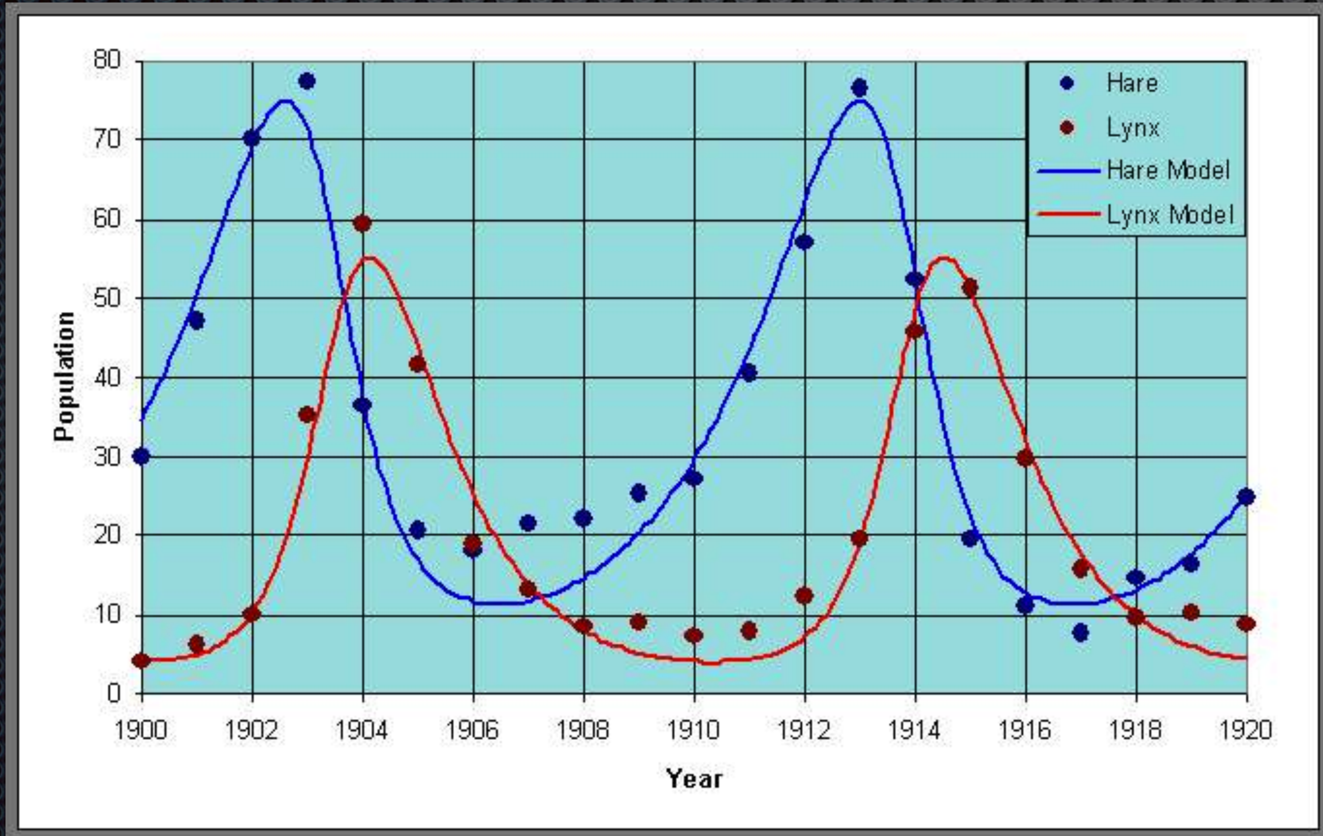


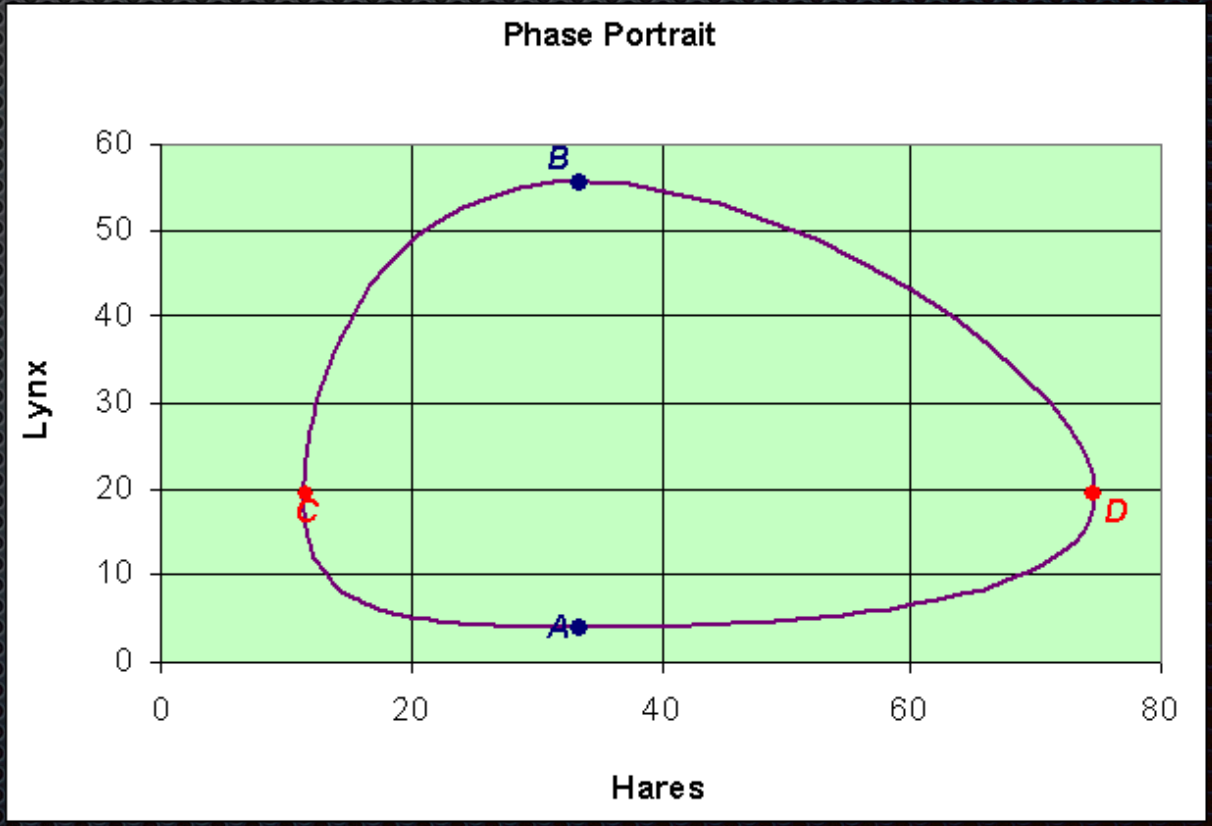
Lotka-Volterra (1925 - 1926)

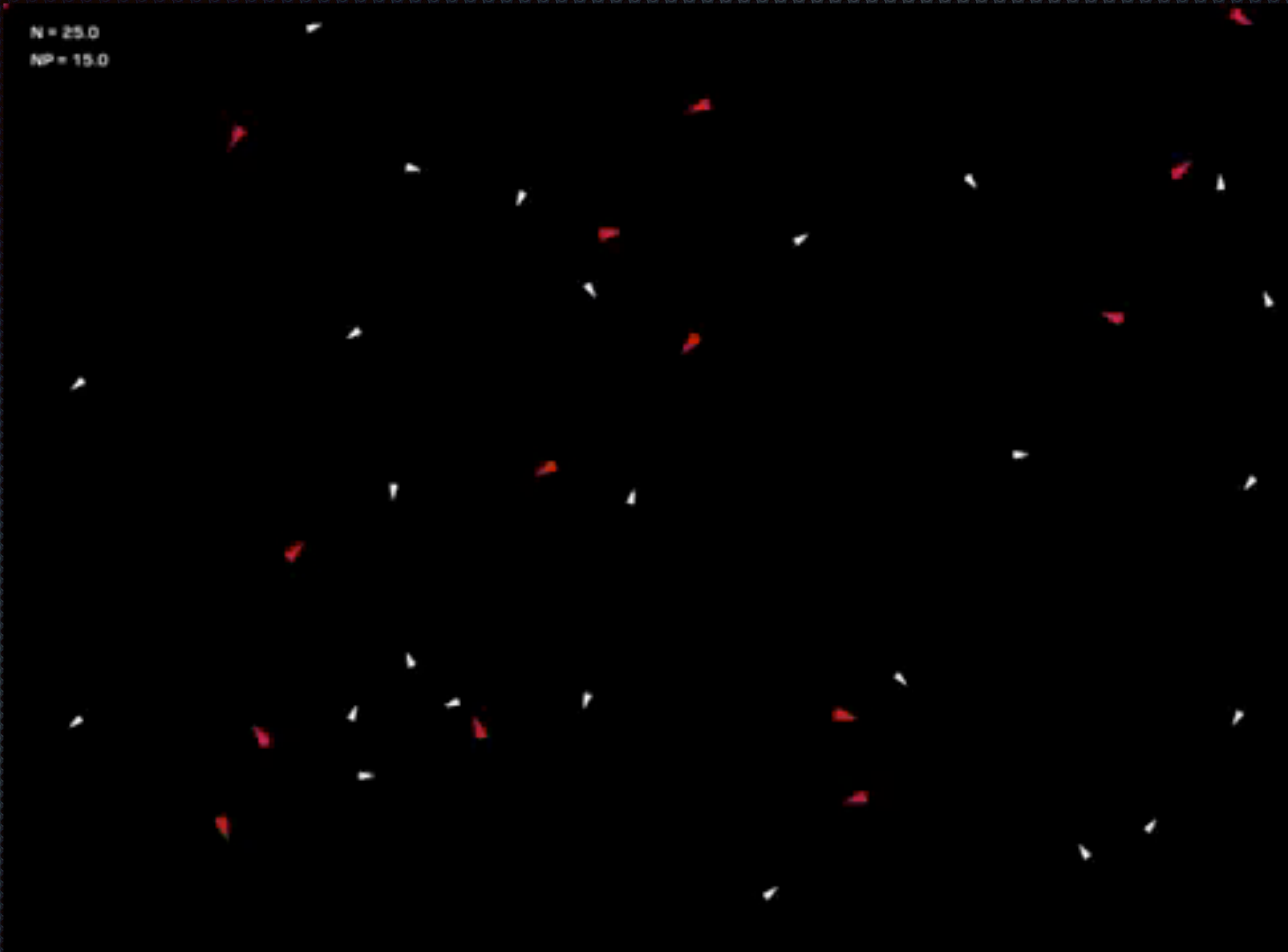
Alfred Lotka
(american)
1880-1949

$$L(t)' = -L(t)(a-b.H(t))$$
$$H(t)' = H(t)(c - d.L(t))$$

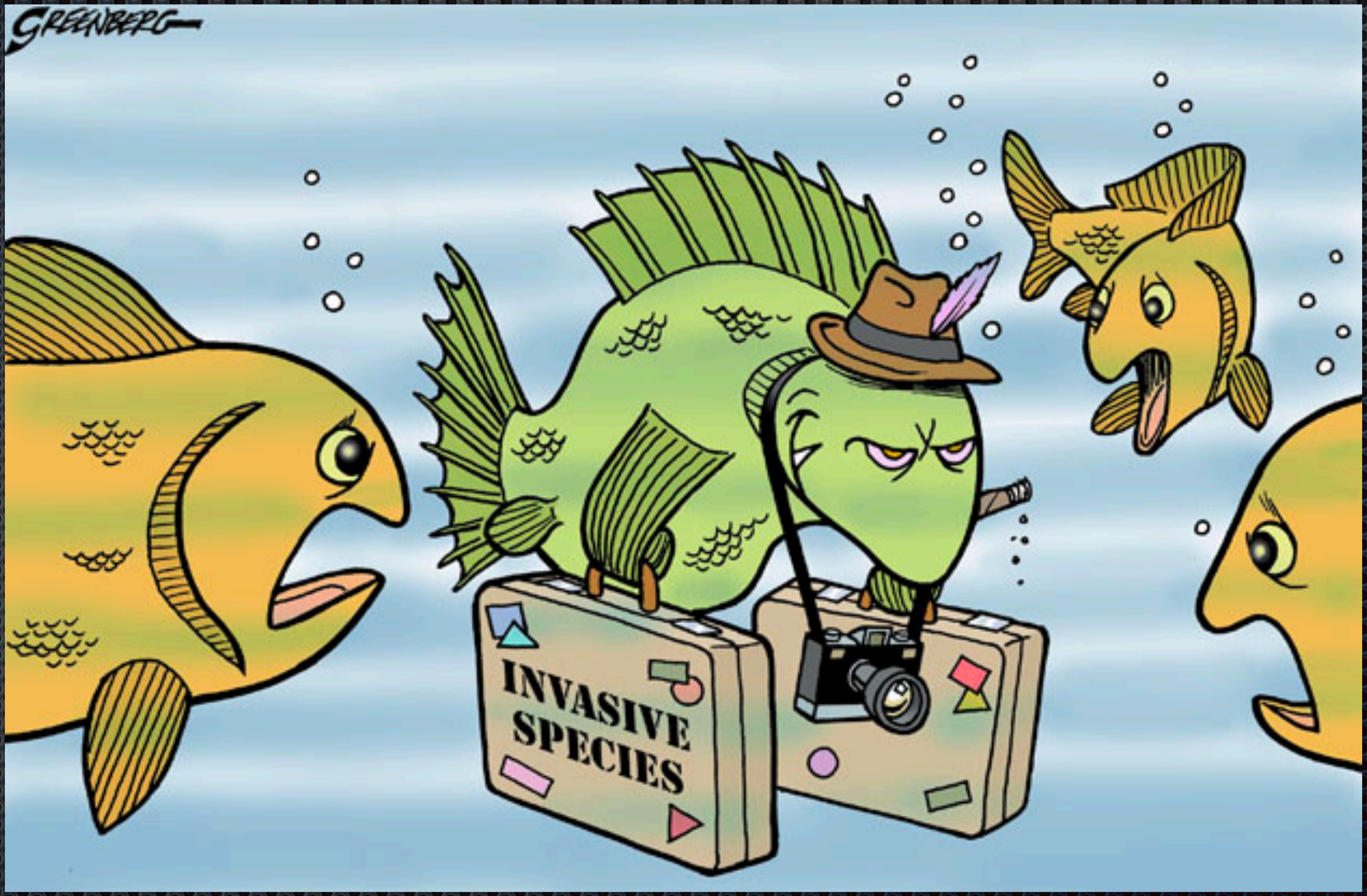
Vito Volterra
(italian)
1860-1940






N = 25.0
NP = 15.0

Models
of species invasion

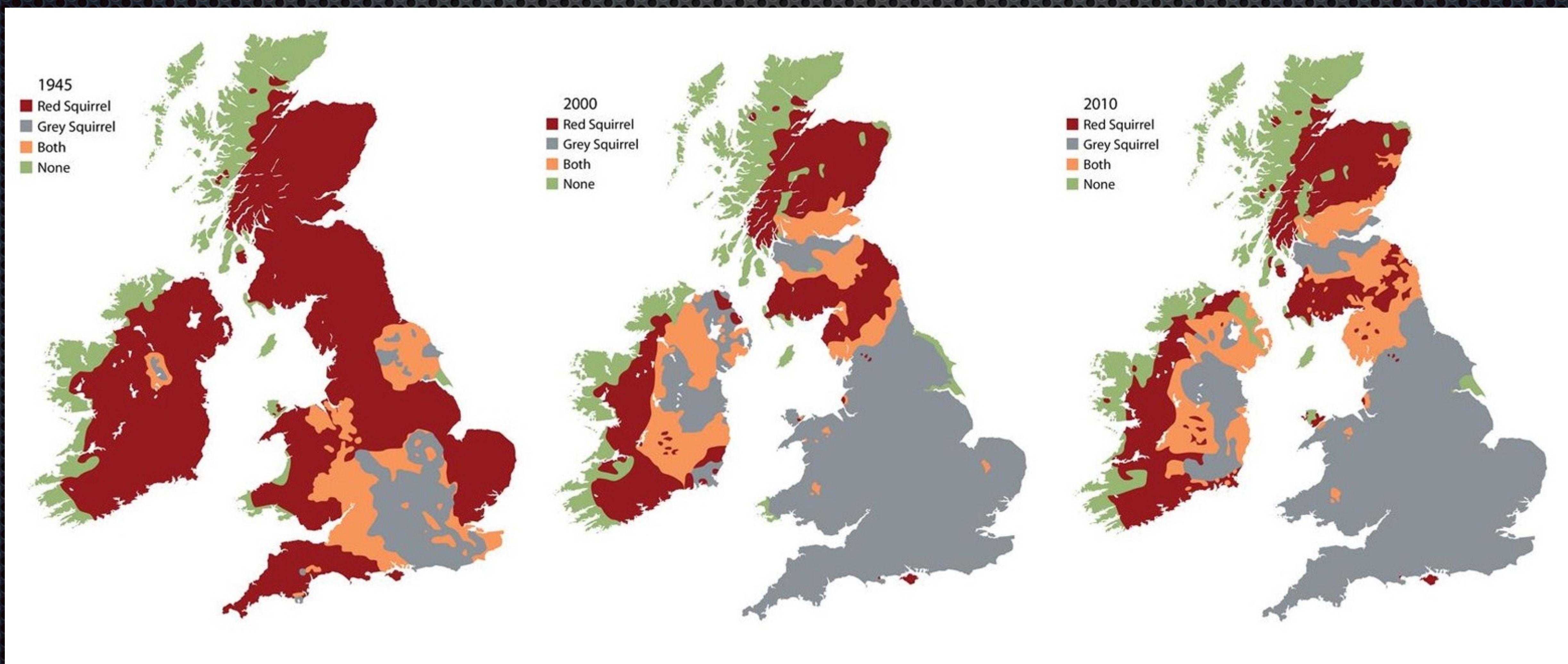


Red squirrels versus grey squirrels


TALKING POINT

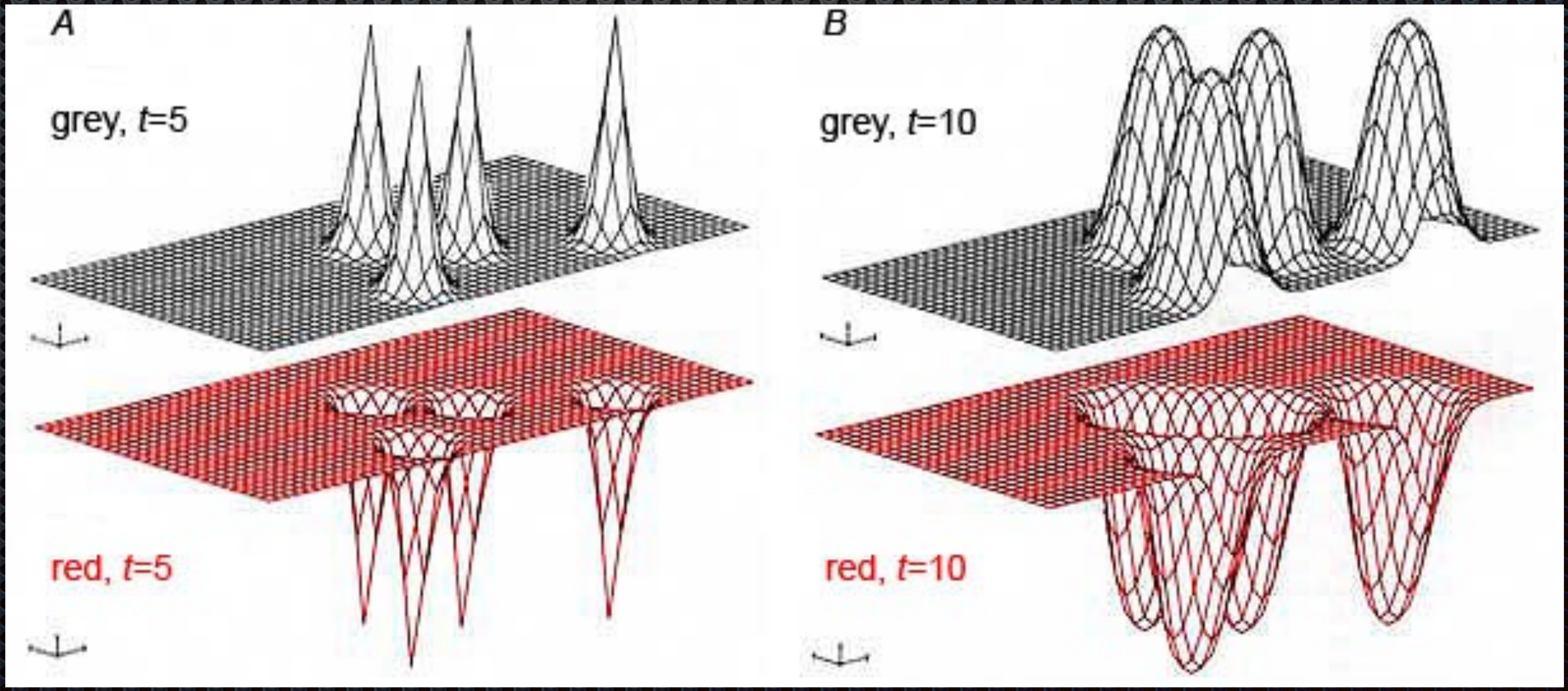
THE RED HAS LOST – SO ACCEPT THE GREY

STEPHEN HARRIS believes that the vast sums spent on saving the red squirrel and eradicating its nemesis, the grey, are a waste of money. Here, he offers a rational solution to a thorny issue.



Even more complex models
Reaction diffusion models

$$
\begin{cases}
\dfrac{\partial S_1}{\partial T} = D_1 \nabla_X^2 S_1 + a_1 S_1 (1 - b_1 S_1) - c_1 S_2 S_1, \\[2ex]
\dfrac{\partial S_2}{\partial T} = D_2 \nabla_X^2 S_2 + a_2 S_2 (1 - b_2 S_2) - c_2 S_1 S_2.
\end{cases}
$$



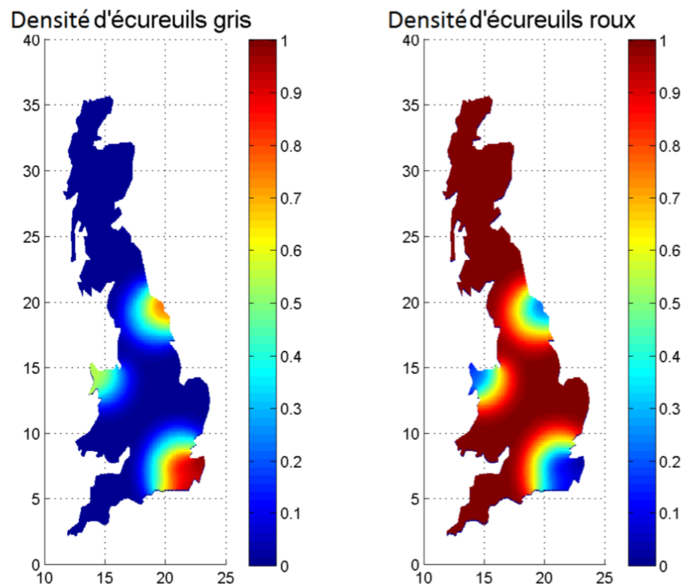


FIGURE 5.15 – Répartition des écureuils au Royaume-Uni en 1930

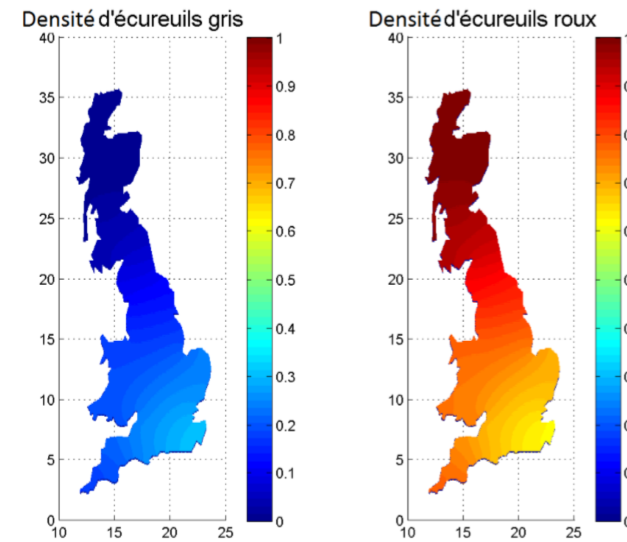


FIGURE 5.16 – Répartition des écureuils au Royaume-Uni en 1950.

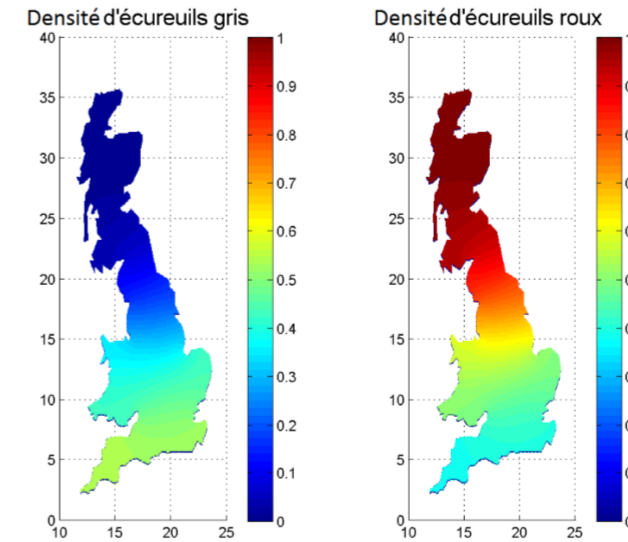


FIGURE 5.17 – Répartition des écureuils au Royaume-Uni en 1970.

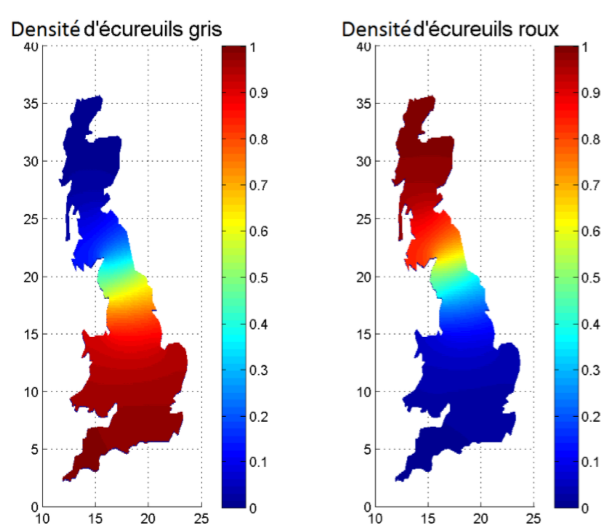


FIGURE 5.18 – Répartition des écureuils au Royaume-Uni en 1990.

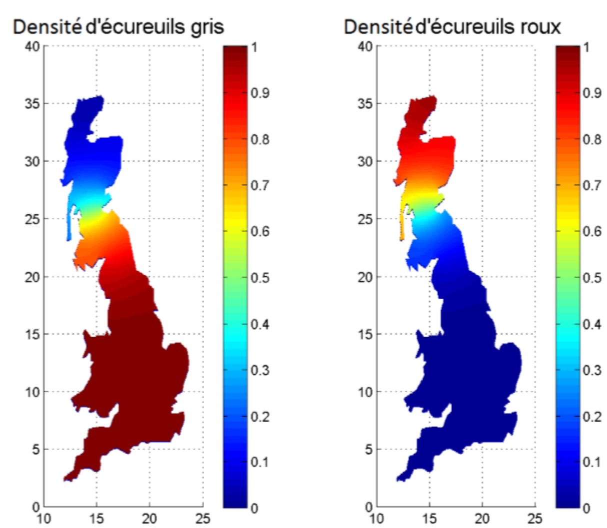


FIGURE 5.19 – Répartition des écureuils au Royaume-Uni en 2014.

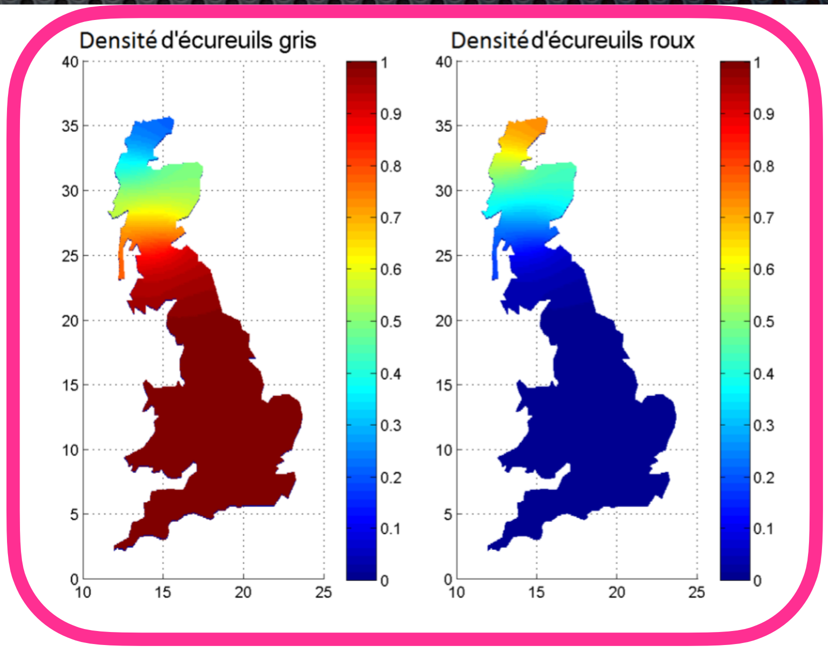
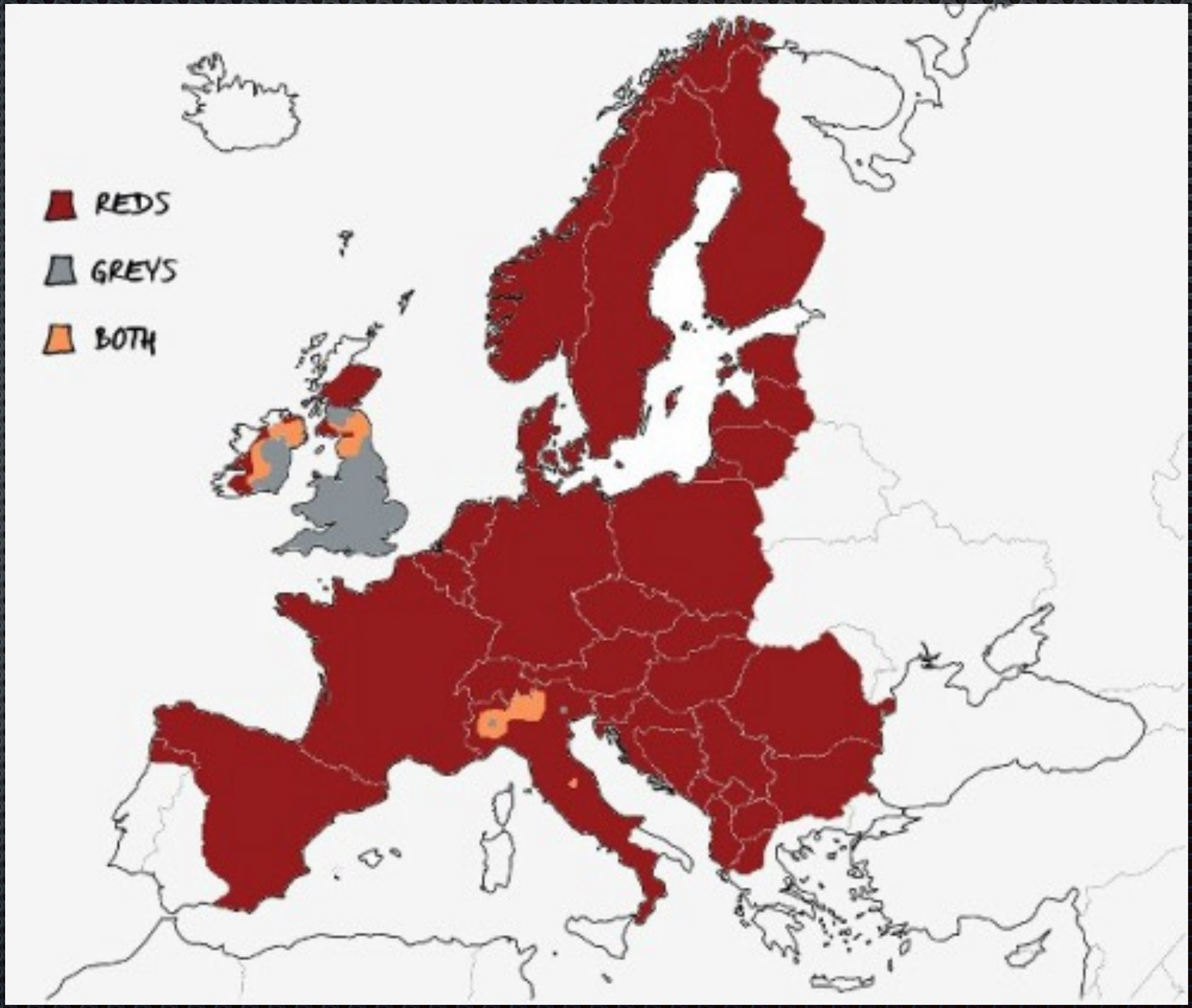


FIGURE 5.20 – Prévision de la répartition des écureuils au Royaume-Uni en 2030

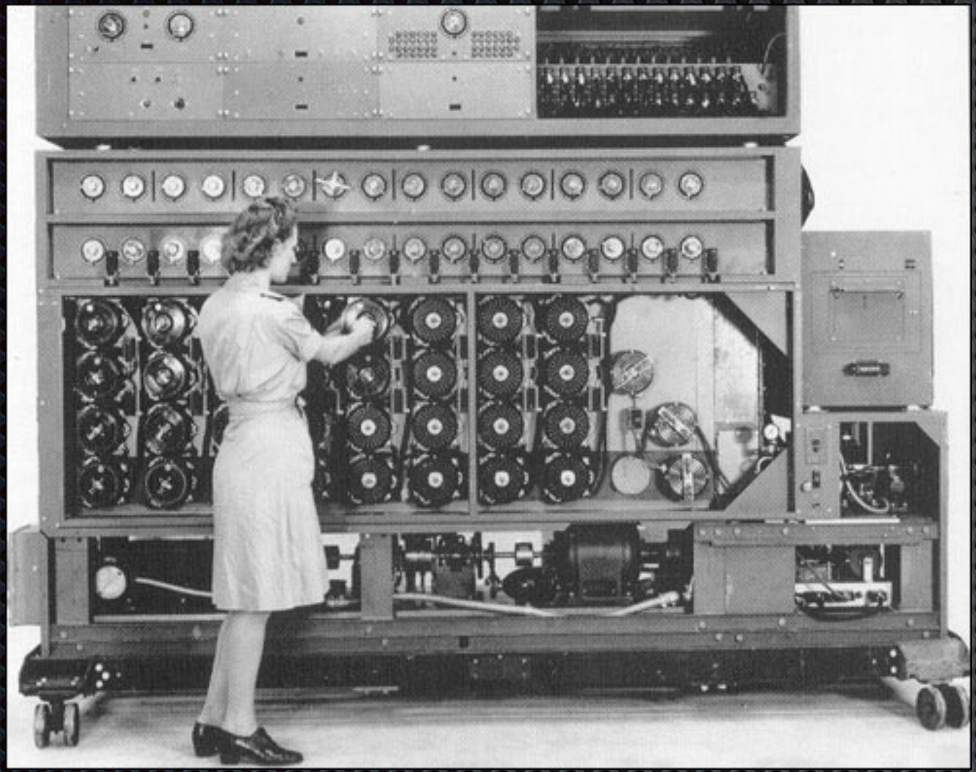
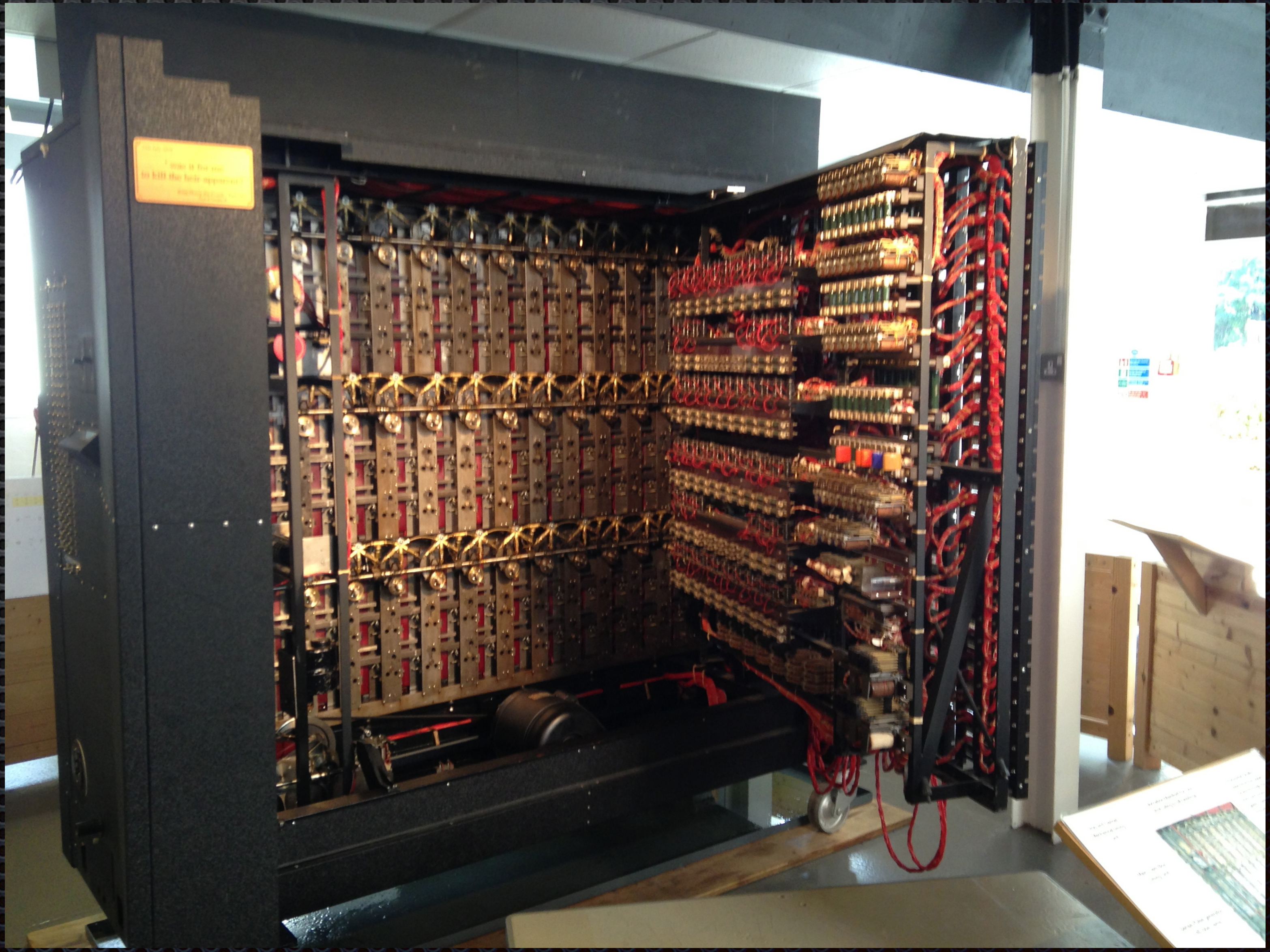


REDS
GREYS
BOTH

These reaction diffusion models describe

many biological phenomena

Alan Turing (1912-1954)
British mathematician

5 NOMINATIONS GOLDEN GLOBES
DONT MEILLEUR FILM
MEILLEUR ACTEUR
MEILLEURE ACTRICE DANS UN SECOND RÔLE
“L’UN DES MEILLEURS FILMS DE L’ANNÉE”
THE NEW YORK OBSERVER
“BENEDICT CUMBERBATCH TRIOMPHE”
VARIETY
★★★★
“UN THRILLER MAGNIFIQUE”
EMPIRE
VOUS NE CONNAISSEZ PAS CET HOMME. POURTANT, IL A CHANGÉ NOS VIES.
BENEDICT CUMBERBATCH
KEIRA KNIGHTLEY
IMITATION GAME
UN FILM DE
MORTEN TYLDUM
BLACK BEAR PICTURES PRÉSENTE EN ASSOCIATION AVEC FILMNATION ENTERTAINMENT UNE PRODUCTION BLACK BEAR PICTURES
UNE PRODUCTION BRISTOL AUTOMOTIVE "THE IMITATION GAME" BENEDICT CUMBERBATCH KEIRA KNIGHTLEY
MATTHEW GOODE RORY KINNEAR AVEC CHARLES DANCE ET MARK STRONG CASTING NINA GOLD COIFFURE ET MAQUILLAGE IVANA PRIMORAC
COSTUMES SAMMY SHELDON DIFFER DÉCORS MARIA DJURKOVIC MUSIQUE ALEXANDRE DESPLAT MONTAGE WILLIAM GOLDENBERG, A.C.E.
DIRECTEUR DE LA PHOTOGRAPHIE ÓSCAR FAURA COPRODUCTEUR PETER HESLOP PRODUCTEUR DÉLÉGUÉ GRAHAM MOORE PRODUIT PAR NORA GROSSMAN P.G.A.
IDO OSTROWSKY P.G.A. TEDDY SCHWARZMAN P.G.A. ÉCRIT PAR GRAHAM MOORE RÉALISÉ PAR MORTEN TYLDUM
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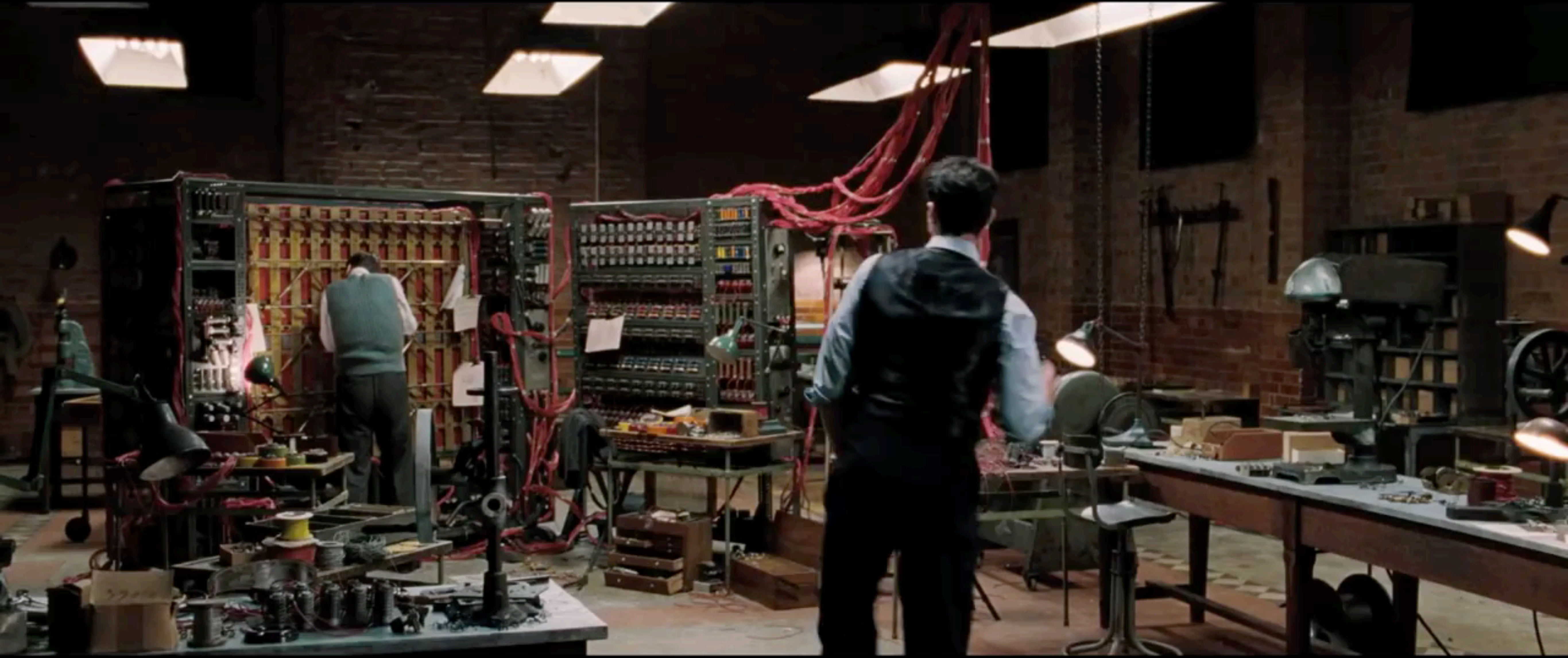
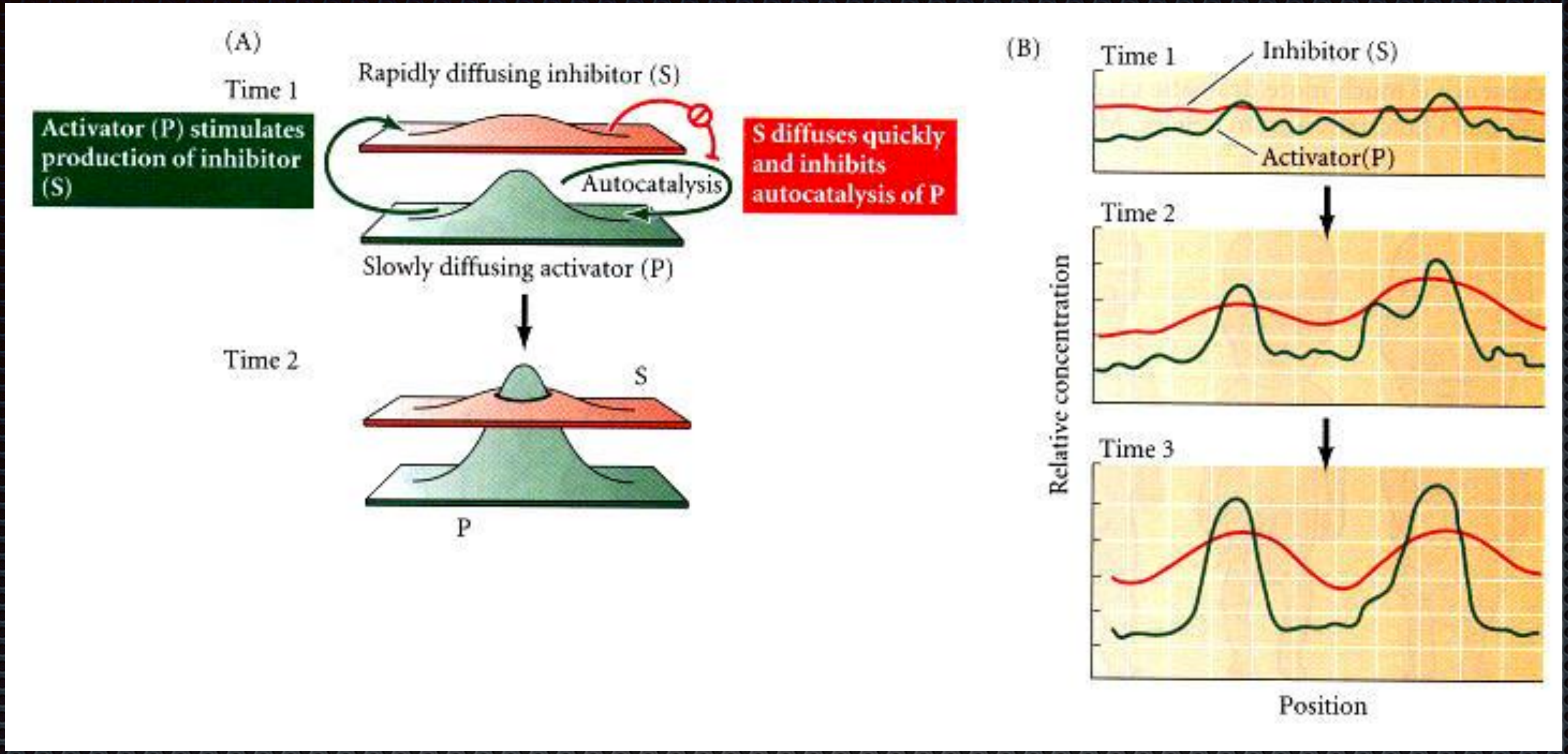
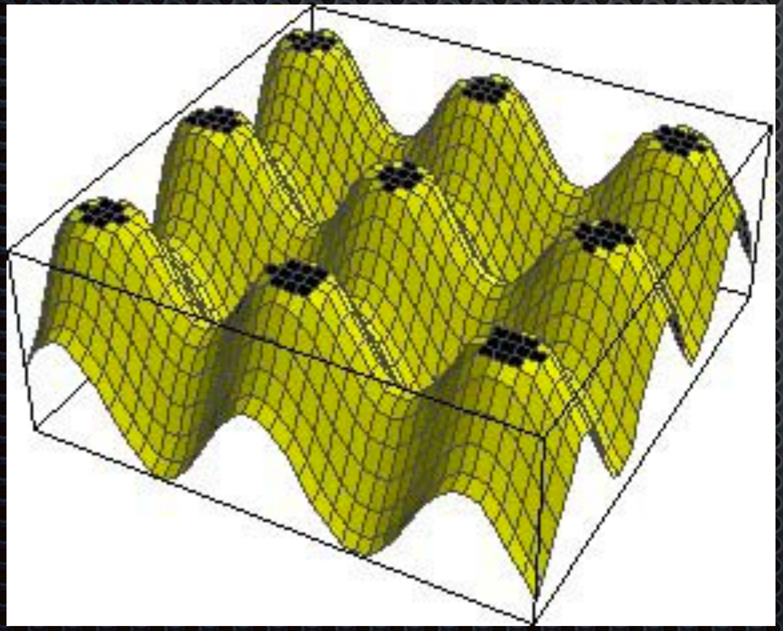
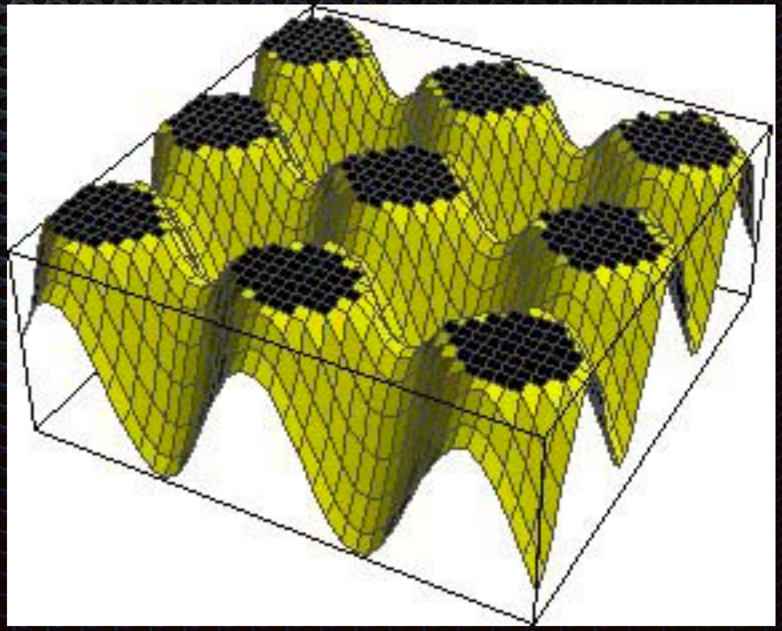
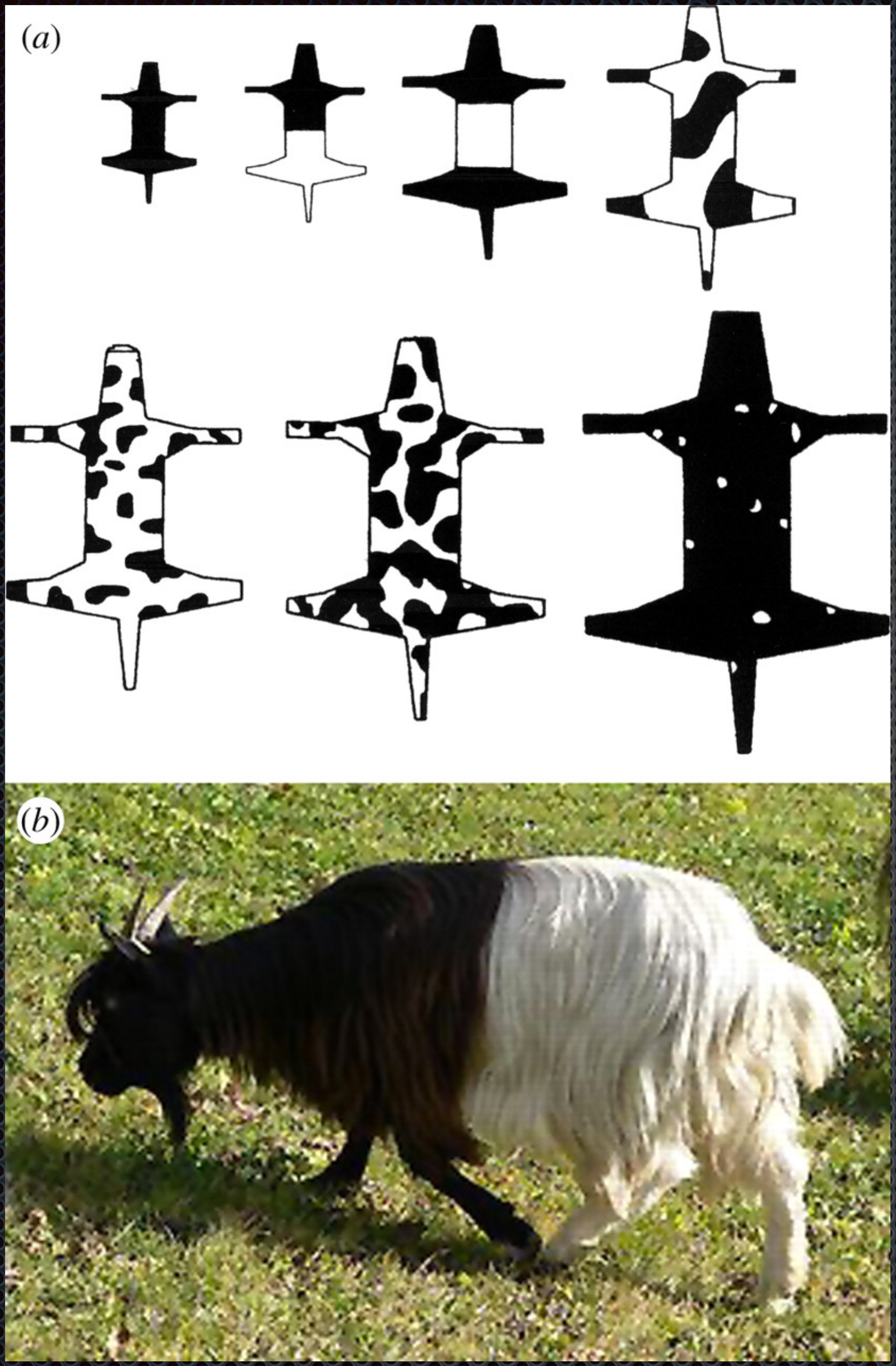


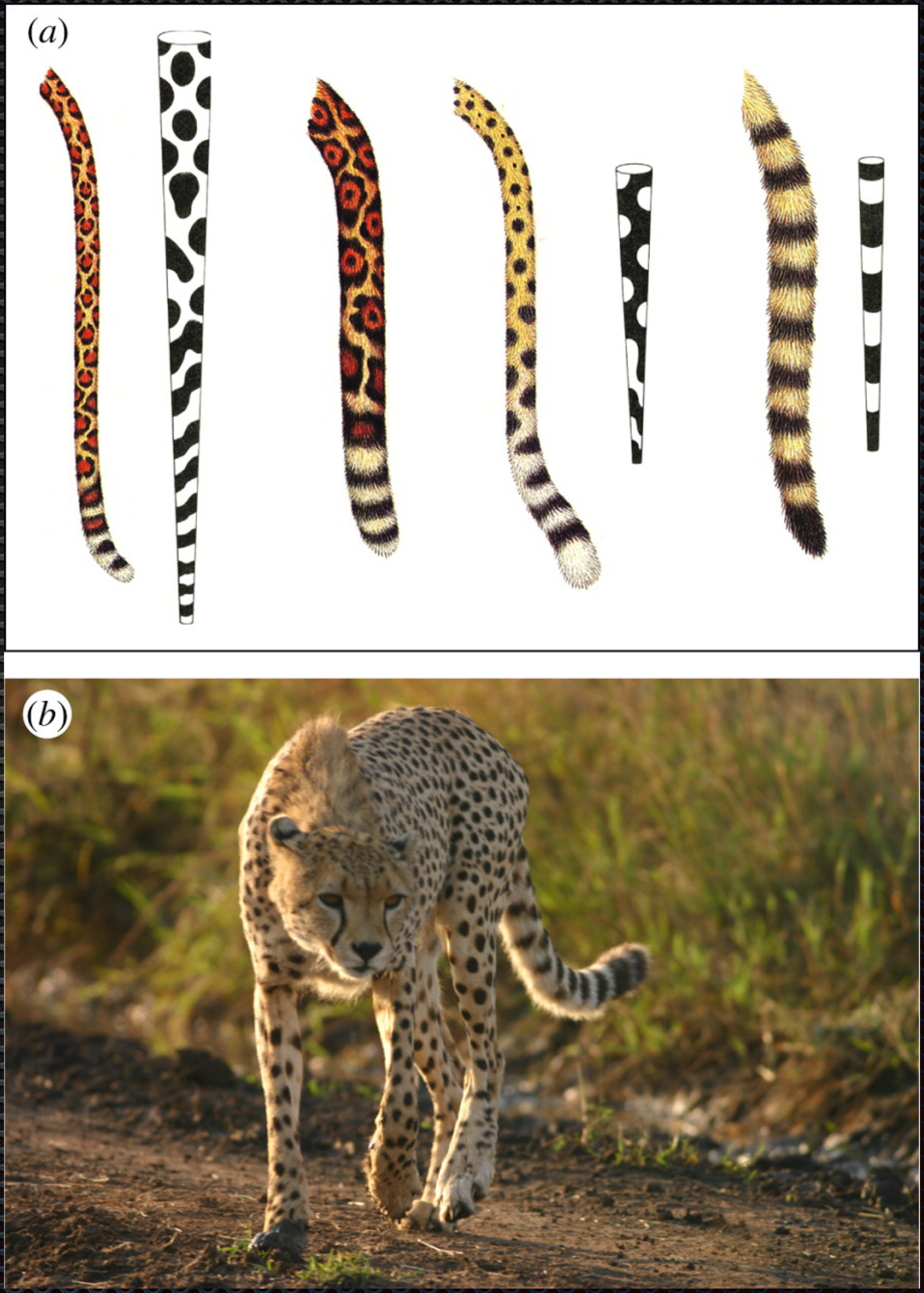


$$\begin{cases} \dfrac{\partial u_1}{\partial t} = r_1(u_1, u_2) + D_1 \nabla^2 u_1 \\ \dfrac{\partial u_2}{\partial t} = r_2(u_1, u_2) + D_2 \nabla^2 u_2 \end{cases}$$





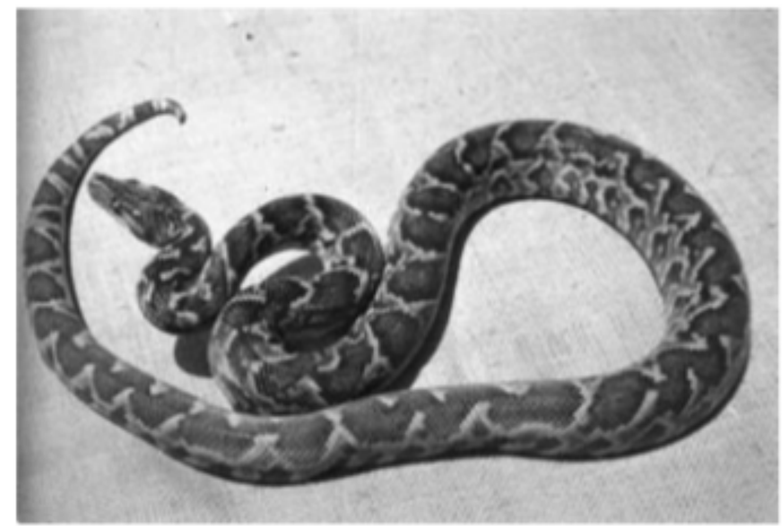

(a)
(b)


(a)
(b)

(a)

(b)

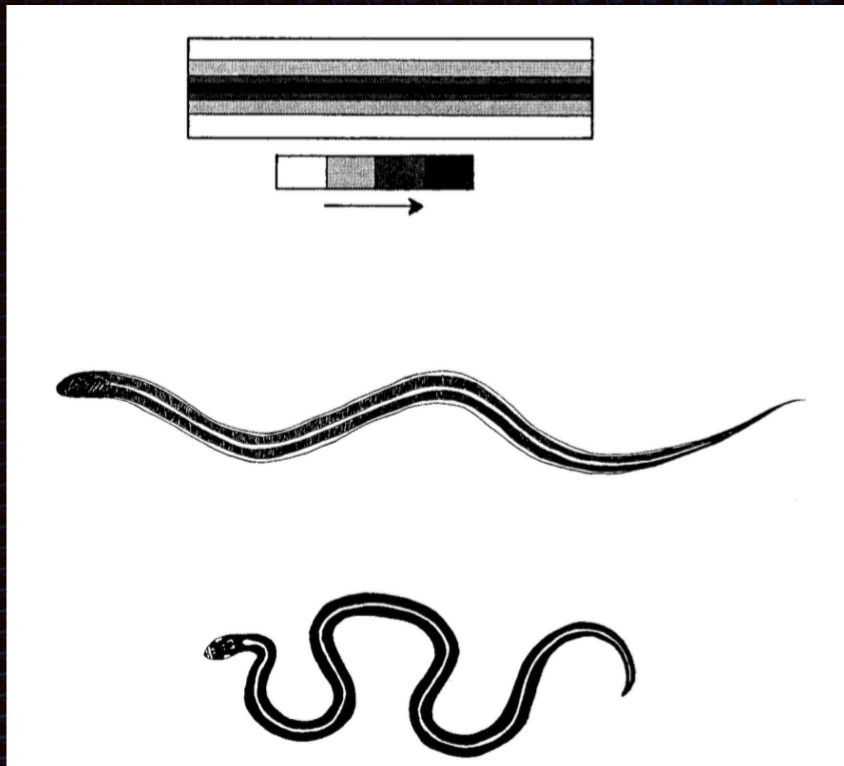
(c)

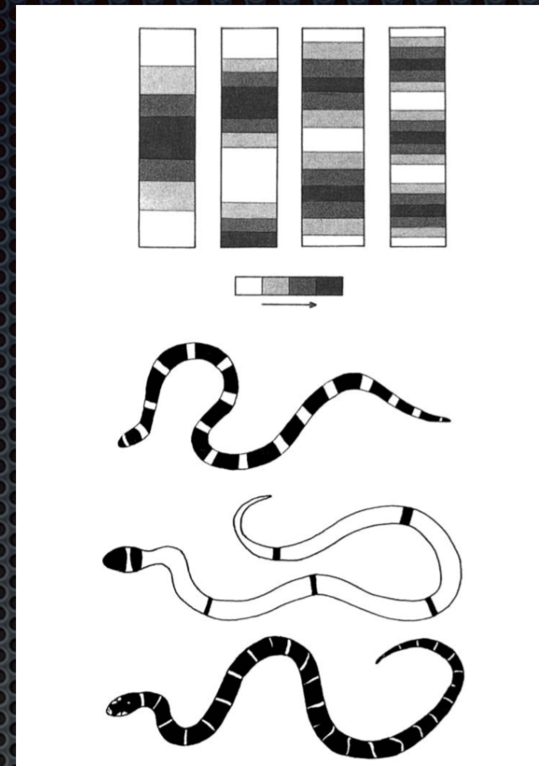


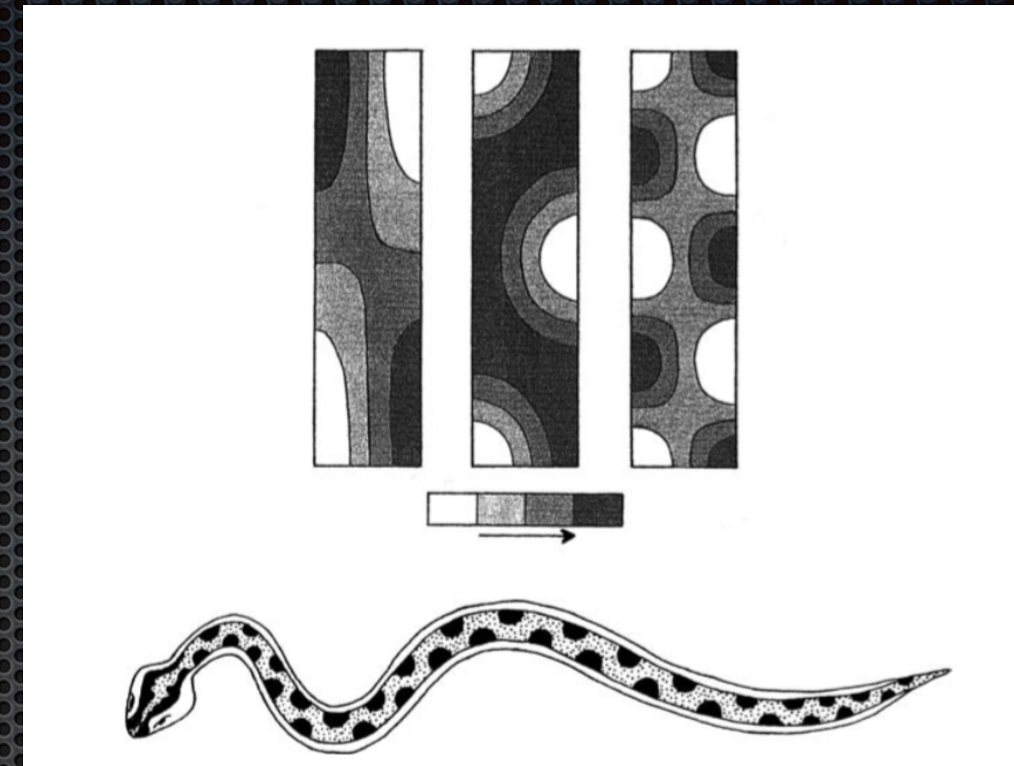
(d)

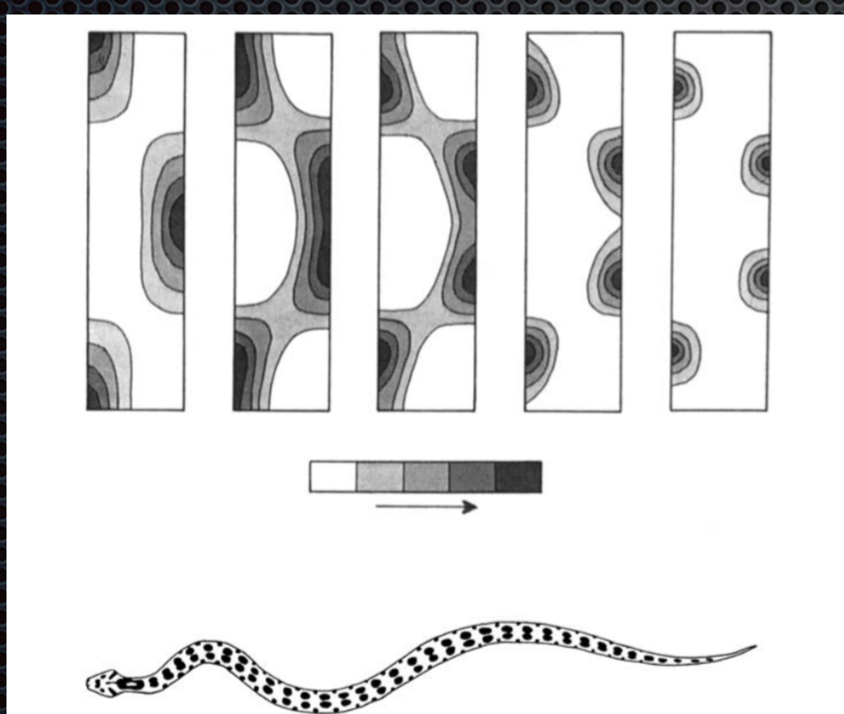
(e)

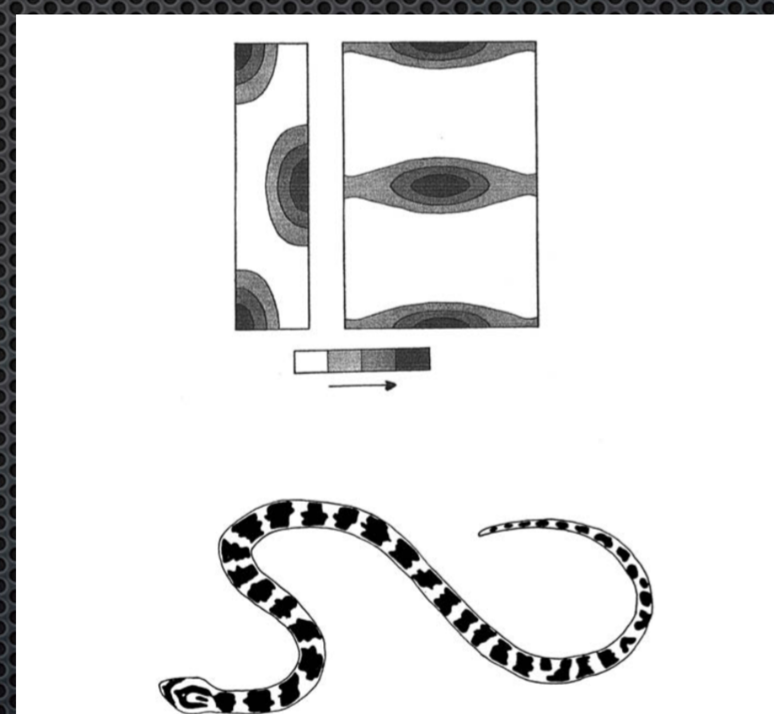
(f)

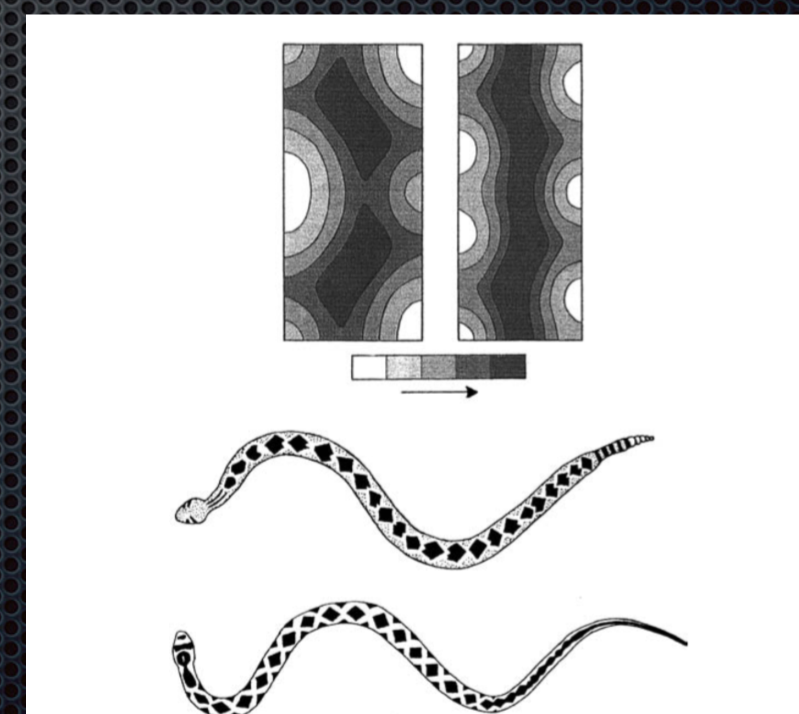


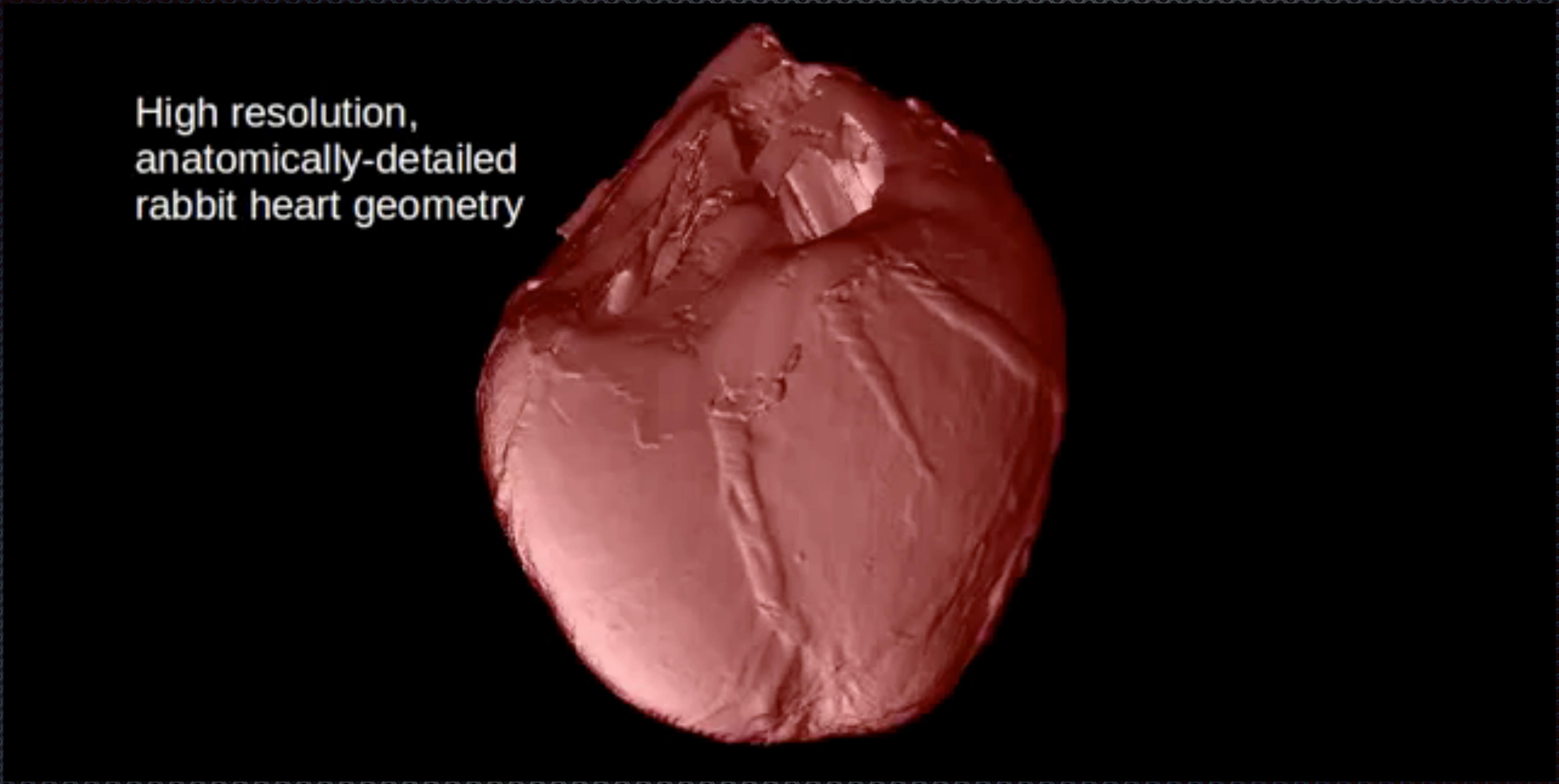








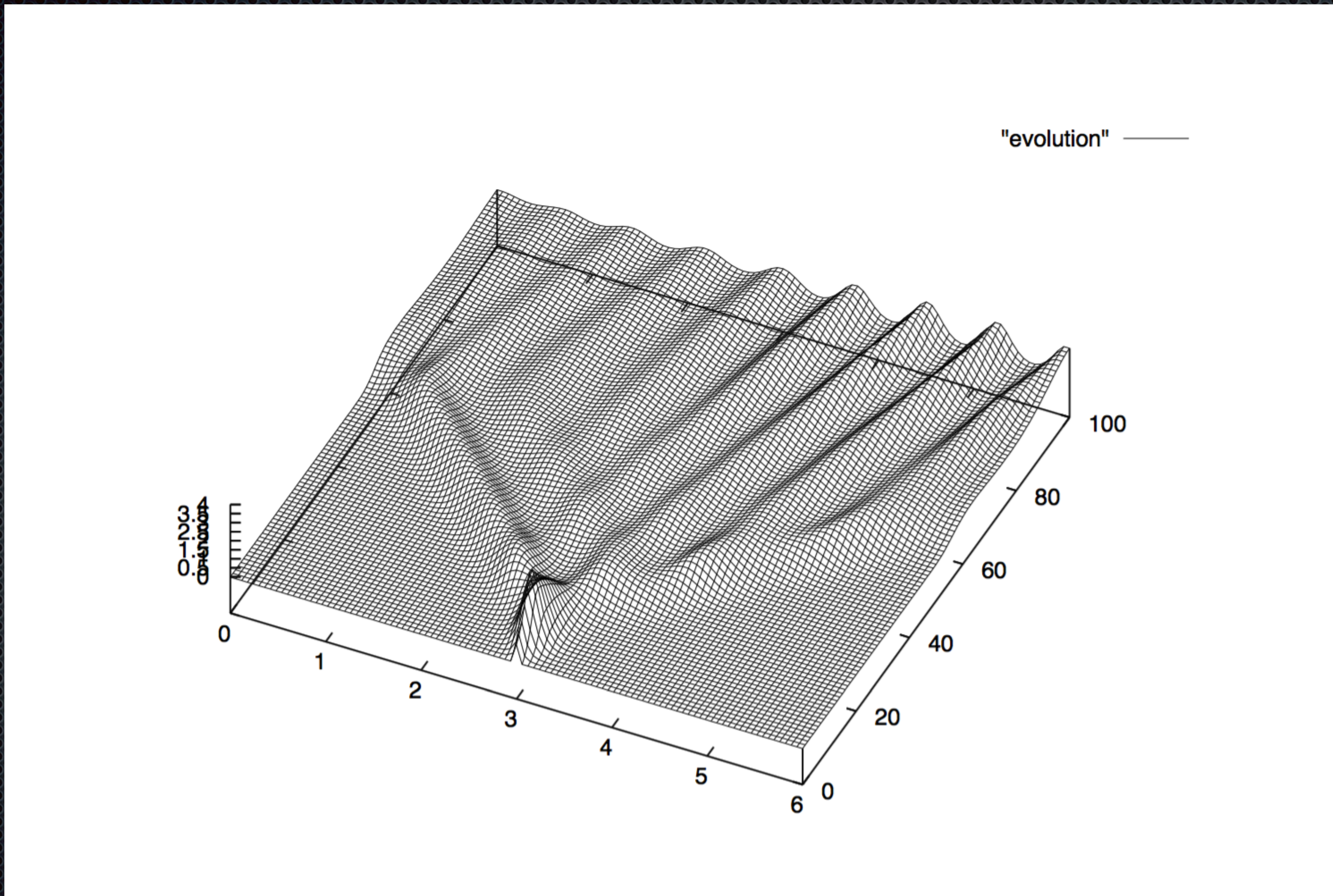


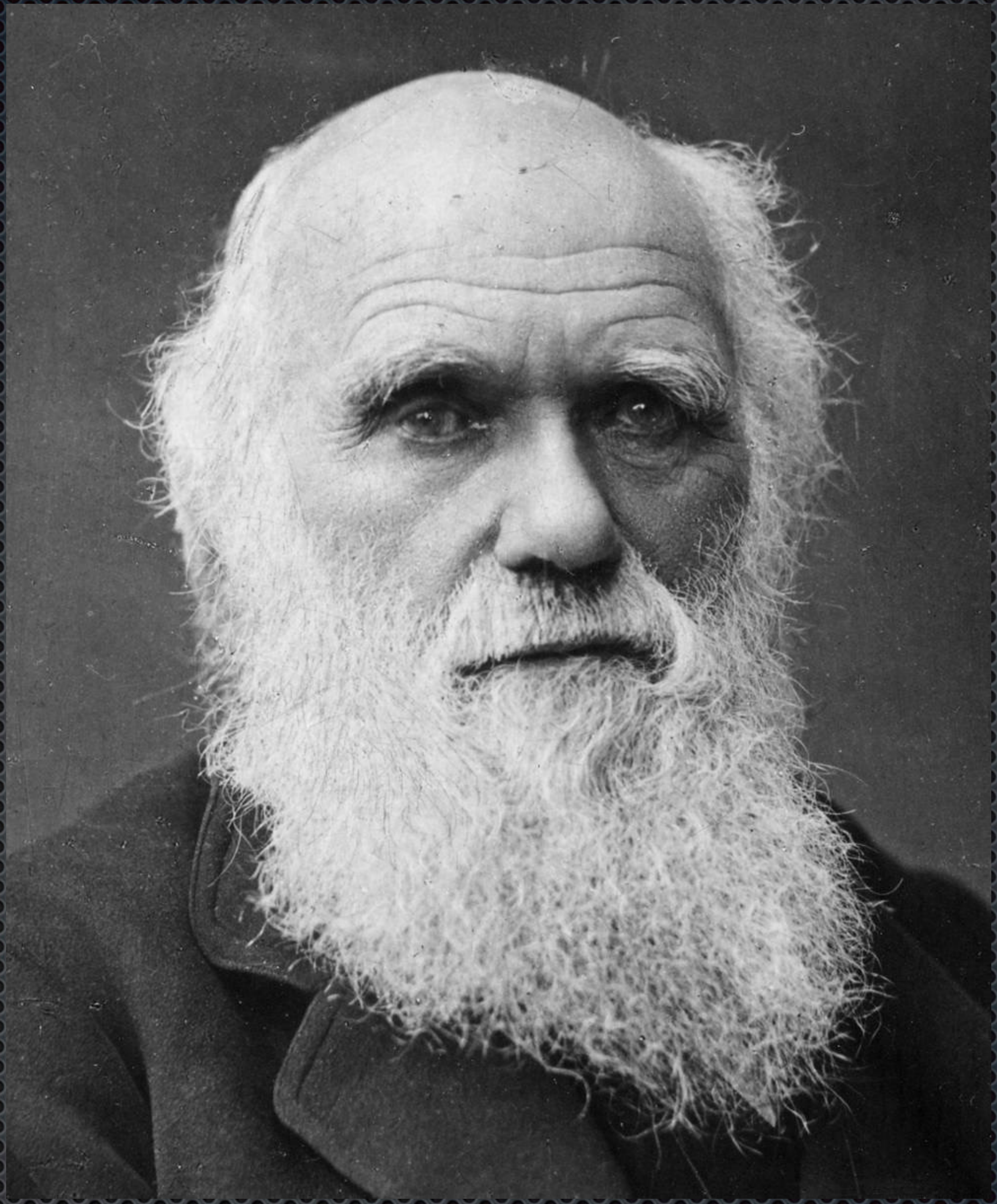

High resolution,
anatomically-detailed
rabbit heart geometry

Even evolution theory

Adaptative dynamics

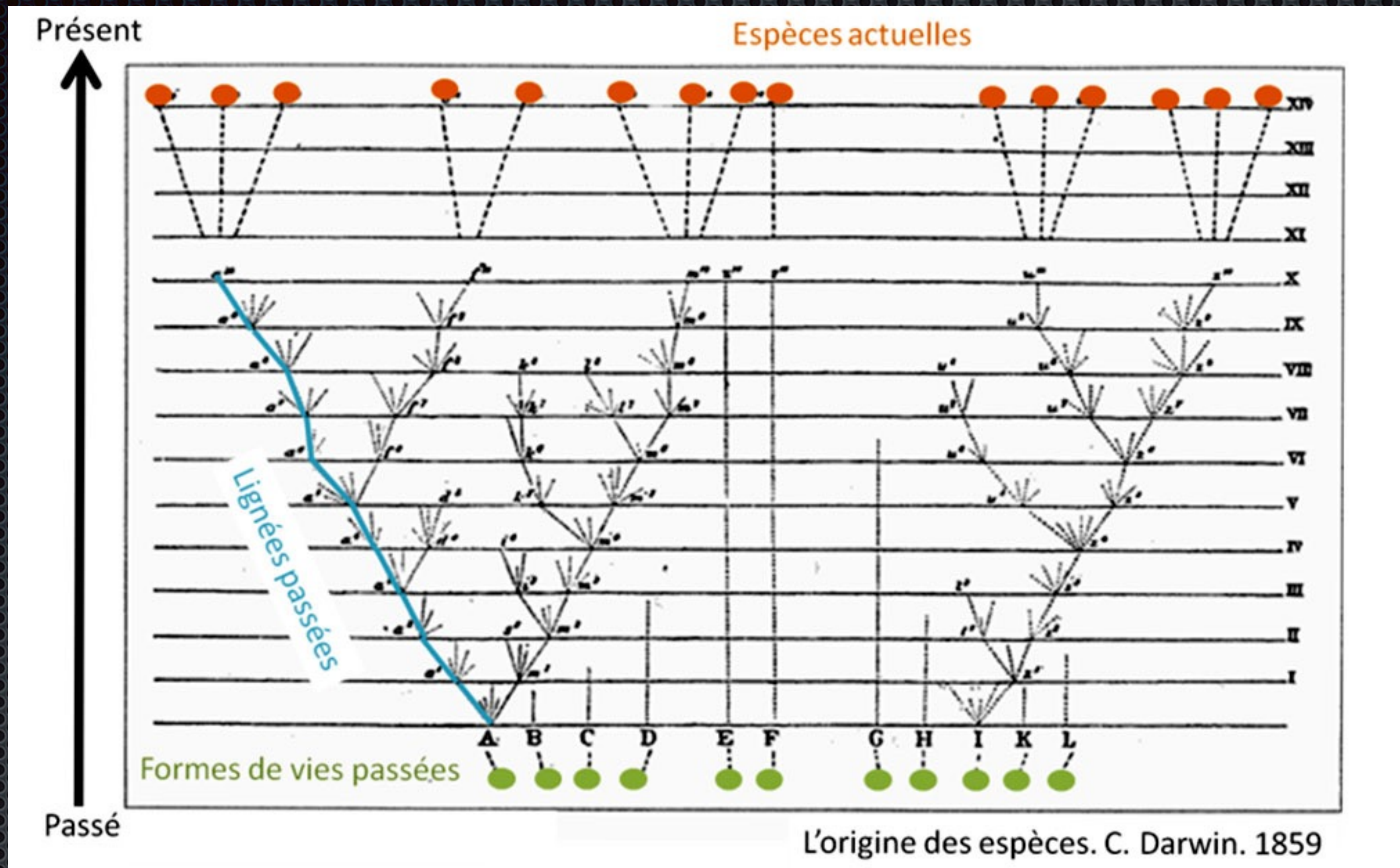
$$
\begin{aligned}
\frac{\partial u}{\partial t}(t,x) &= \alpha u(t,x)\left(\kappa - \int_\Omega \varphi(x-y)u(t,y)dy\right) + d\Delta u(t,x)\\
&= \alpha u(t,x)\left(\kappa - (\varphi * u)(t,x)\right) + d\Delta u(t,x),
\end{aligned}
$$



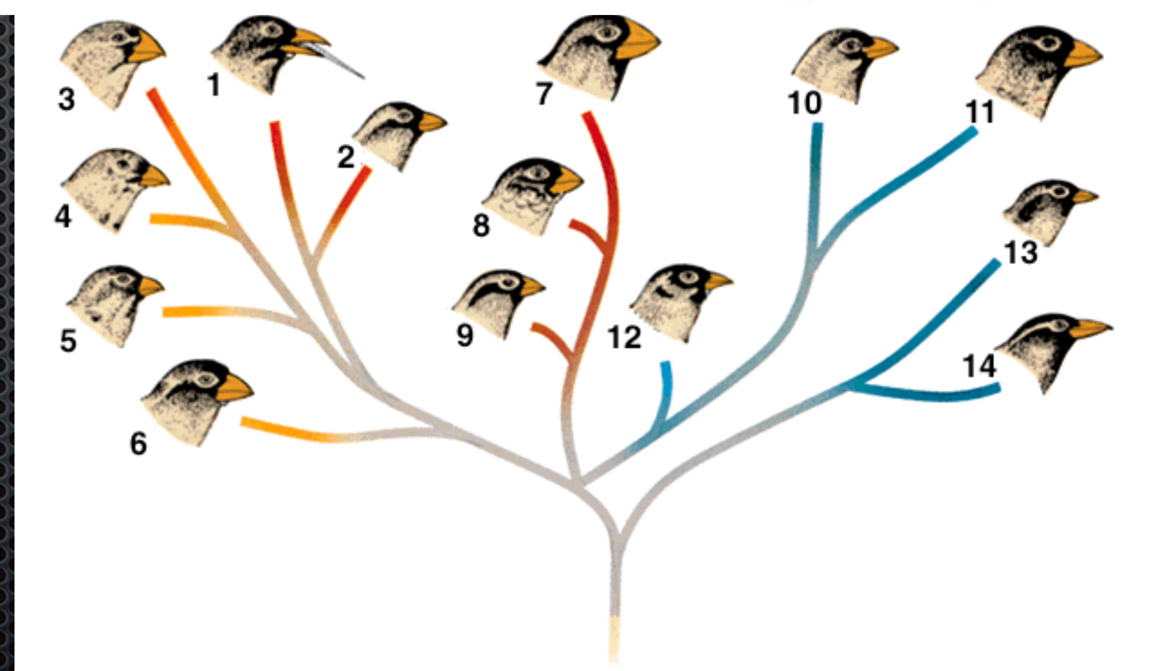


Charles Robert Darwin (1809-1882)
British Naturalist

Darwin's notebooks



L'origine des espèces. C. Darwin. 1859



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Populational adaptive evolution, chemotherapeutic resistance and multiple anti-cancer therapies

Alexander Lorz, Tommaso Lorenzi, Michael E. Hochberg, Jean Clairambault, Benoît Perthame

UPEC
UNIVERSITÉ PARIS-EST CRÉTEIL VAL DE MARNE
Connaissance - Action

Thèse présentée pour l'obtention du grade
de Docteur de l'université Paris Est-Créteil

Spécialité : Virologie

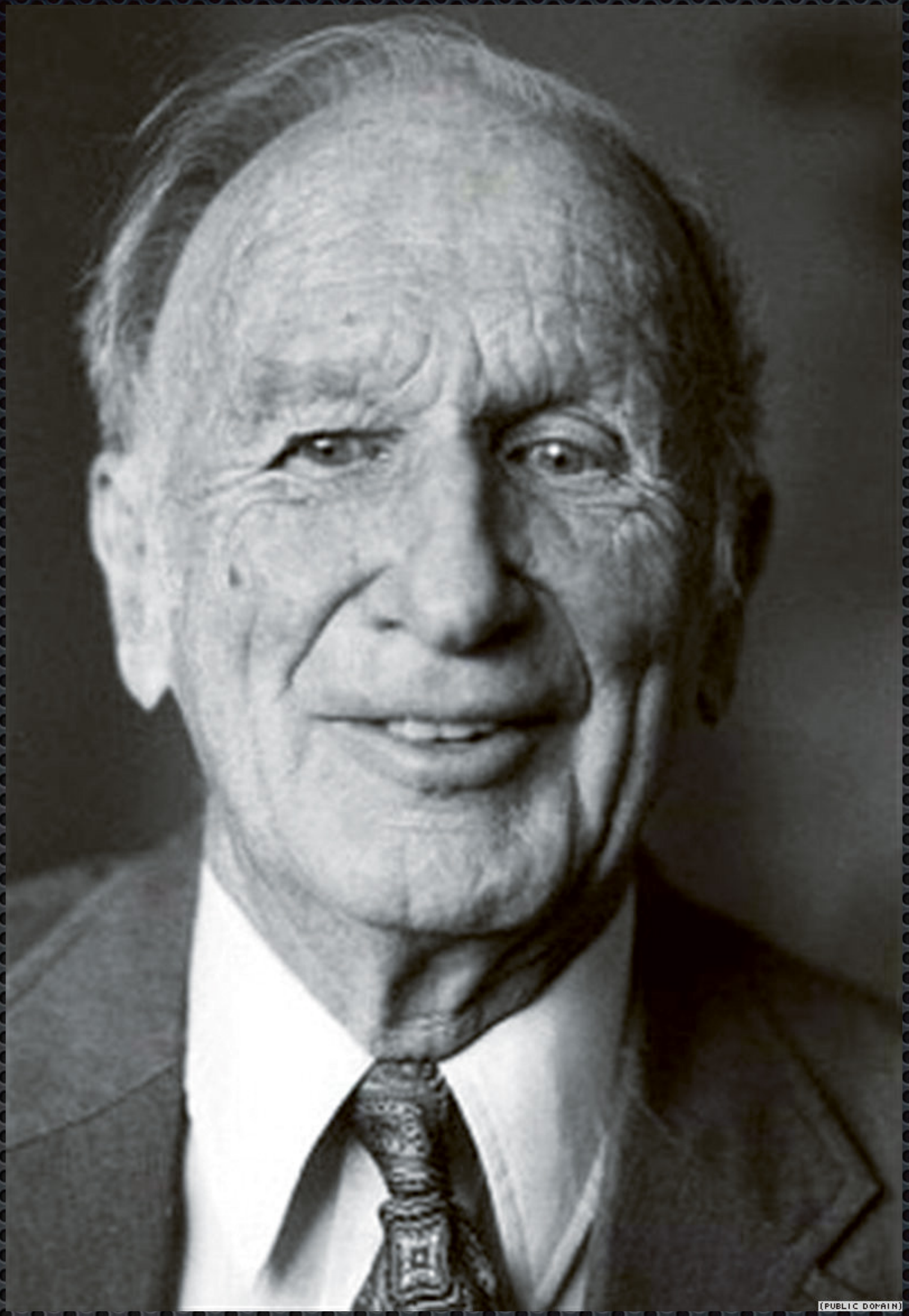
Par Christophe RODRIGUEZ

Dynamique adaptative des virus hautement variables à un nouvel environnement réplicatif

Adaptive dynamics of highly variable viruses to new replicative environment

Présentée et soutenue publiquement le 23 octobre 2012

And so many other models

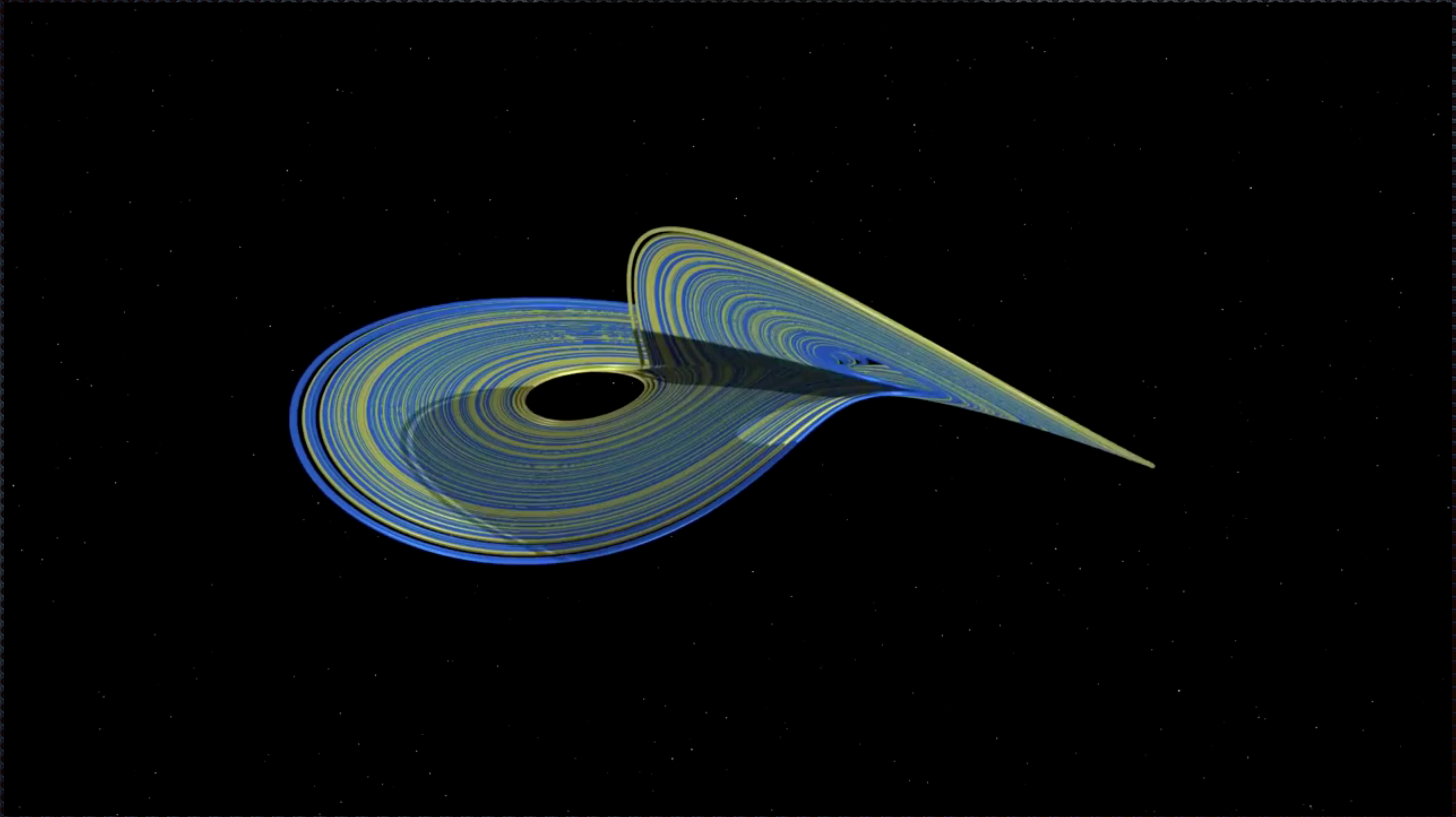


Edward Norton Lorenz (1917-2008)
American meteorologist

$$\frac{\mathrm{d}x}{\mathrm{d}t} = \sigma(y - x),$$

$$\frac{\mathrm{d}y}{\mathrm{d}t} = x(\rho - z) - y,$$

$$\frac{\mathrm{d}z}{\mathrm{d}t} = xy - \beta z.$$

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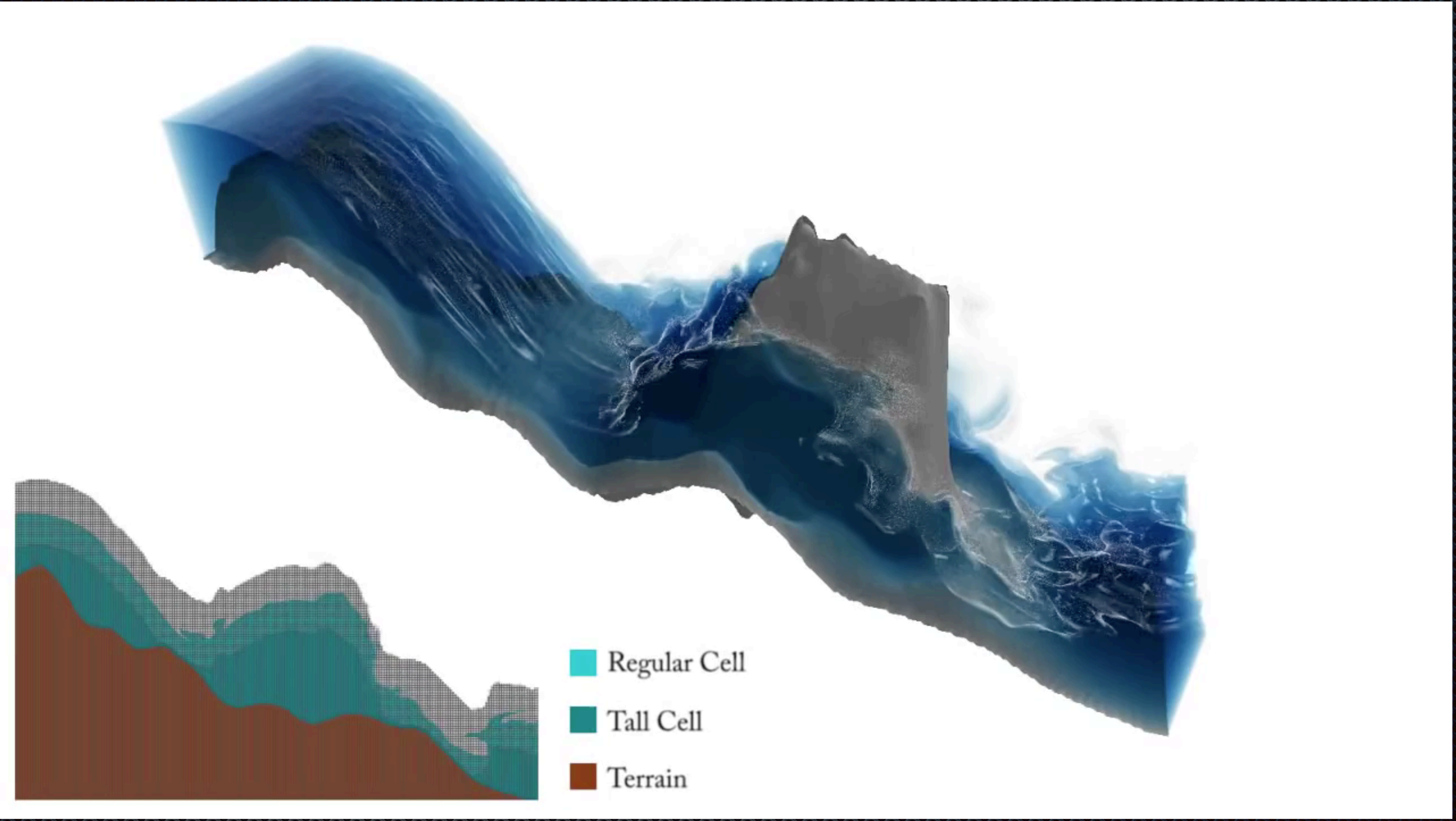
Regular Cell
Tall Cell
Terrain


19/20 RHONE-ALPES
SCIENCES
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