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**Power of nature**  
**Power of human craft**



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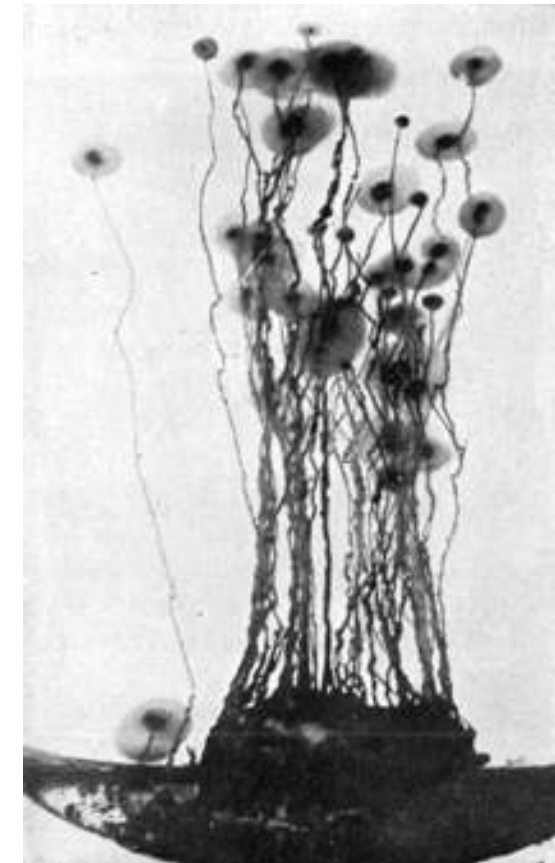
## Nature's shapes: Distinct from Physics' shapes?

Jacques Monod's *Chance and Necessity*:

The shape of a fossil animal



Yet, many shapes in the mineral world are  
reminiscent of biological shapes



Osmotic growth, photographed by  
transparency, showing the « nuclei » of  
end « organs »



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## Outline

- State of the art: from genetic engineering to synthetic biology
- A key to life: information is physical
- The power of Nature: recruiting contextual information
- The power of human craft: *Homo sapiens* is an invasive species
- A way for the future: keep natural information available



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## From the domestication of plants and animals...

Teosinte



Corn

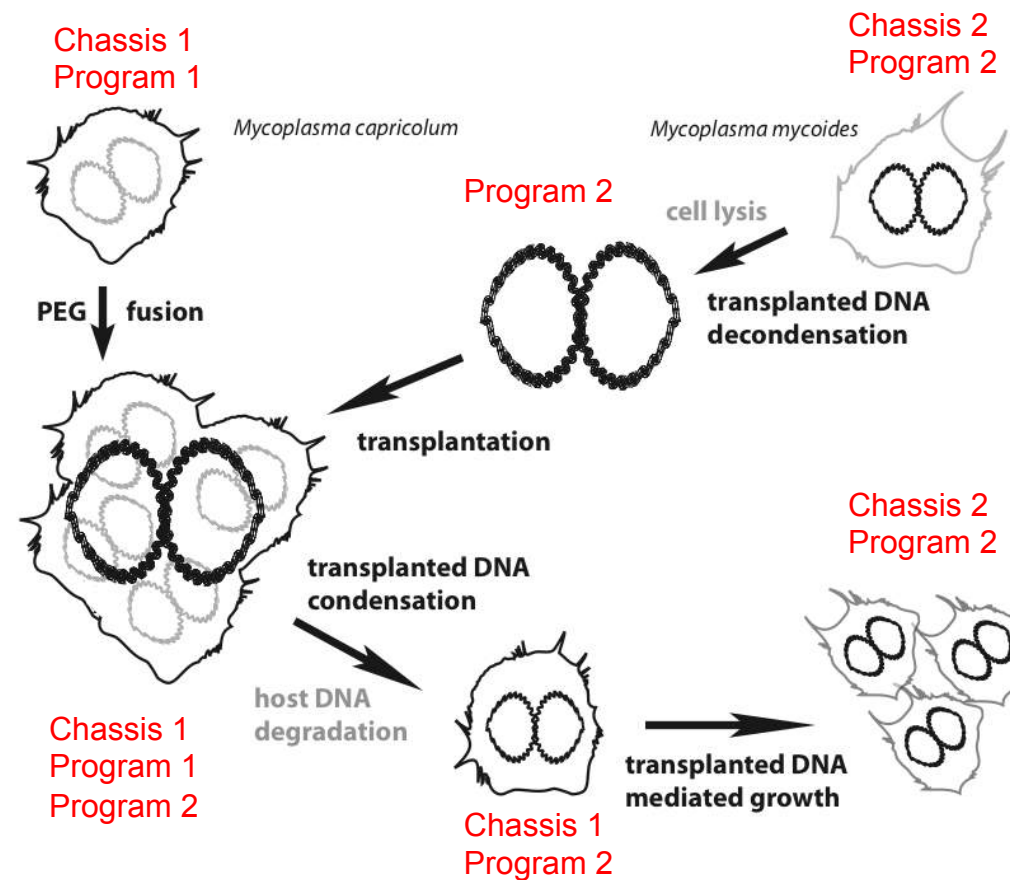




## ...combining genes to make a living organism...

- Domestication
  - Discovery of characters/genes
  - Combinatorial gene shuffling
- Genetic engineering
  - Restriction enzymes
  - Meganucleases
  - Zinc fingers
  - CRISPR / Cas
  - NgAgo?

- Synthetic Biology
  - Program
  - Chassis





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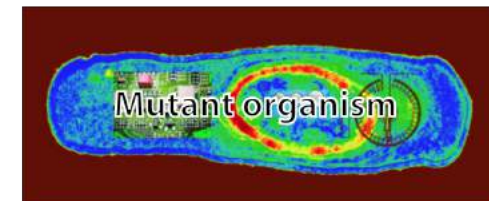
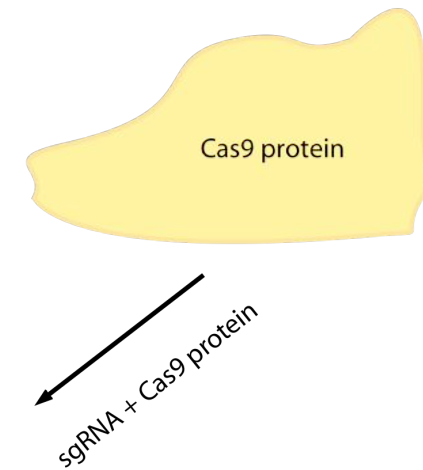
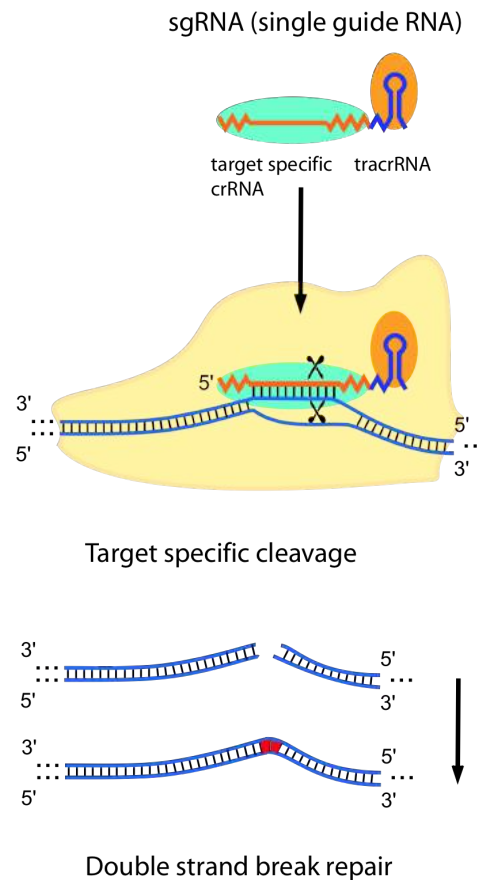
### Nature:

The CRISPR-Cas system has evolved as an antiviral immune system propagated in a acquired hereditary change

### Human craft:

It has been recruited by scientists as a tool for genetic engineering with exquisite precision and ease

## ...to the CRISPR revolution





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## The first CRISPR modified food



### Not a GMO for the FDA:

« APHIS has concluded that your CRISPR/Cas9-edited white button mushrooms as described in your letter do not contain any introduced genetic material. APHIS has no reason to believe that CRISPR/Cas9-edited white button mushrooms are plant pests »

[https://www.technologyreview.com/s/601285/  
here-come-the-unregulated-gmos/](https://www.technologyreview.com/s/601285/here-come-the-unregulated-gmos/)



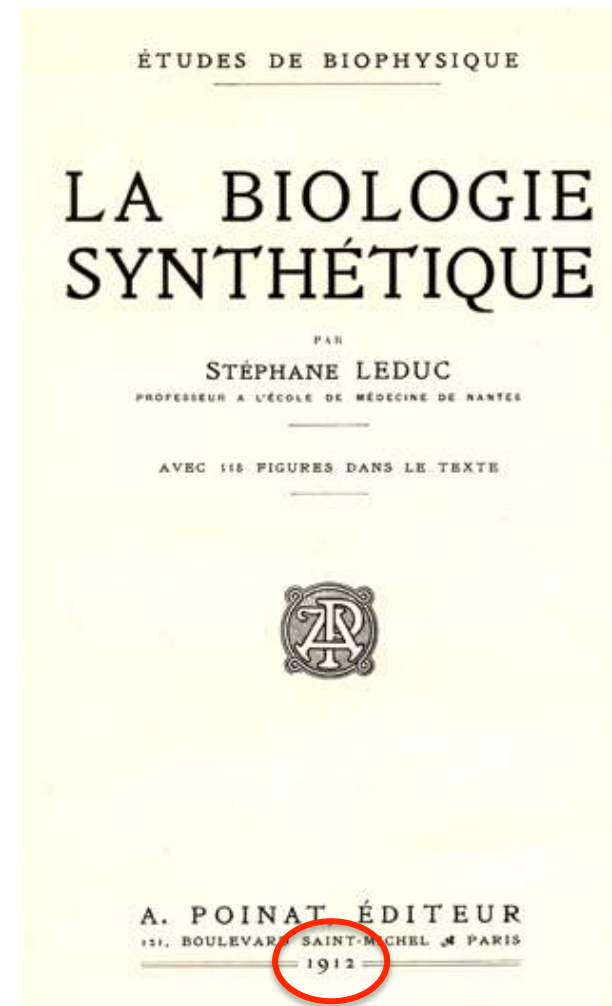
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## Synthetic biology: Are we reinventing the wheel?

Schleiden and Schwann (1832) establish a **cell theory** based on the idea of physical processes derived from crystallisation. They later gave up this idea.

### James Danielli (1970)

The age of synthesis is in its infancy, but is clearly discernable. In the last decade (1960-70), we have seen the first syntheses of a protein, a gene, a virus, a cell, and of allophenic mice. Nothing with such dramatic implications has ever been seen in biology before. Previously, plant and animal breeders have been able to create what are virtually new species, and have been able to do so at a rate which is of the order of  $10^4$  times that of average evolutionary processes. A further increase in rate is now on the horizon. We need a few additional "firsts" before this will occur: (1) to be able to synthesize a chromosome from genes and other appropriate macromolecules; (2) to be able to insert a chromosome into a cell; or, alternatively to (1) and (2), to be able (3) to insert genes into a cell in some other way; (4) we must also learn how to bring the set of genes, which is introduced into a cell, within the domain of cellular control mechanisms, so that they do not run wild in the cell. None of these problems appear to be of exceptional difficulty.



<http://www.peiresc.org/bstitre.htm>





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## Syn3.0 : a streamlined synthetic genome

*Mycoplasma mycoides* JCVI-syn3.0: 531 kilobase pairs, 473 genes, 149 « unknown » genes: **NO!** just over 70 (mostly transporters) remain unknown when proper knowledge is used

Example: a target-specific endoprotease, RppA/YsxB, cleaves off the nine N-terminal residues of ribosomal protein L27 (involved in ribosome assembly and peptidyl transferase catalysis) to make it functional.

This kludge has been observed in Firmicutes (and in the derived Tenericutes, to which *M. mycoides* belongs). This protease (MMSYN1\_0500) is essential in *Staphylococcus aureus*, and persistent in *Bacillus subtilis*

It is expected that this gene/protein, absent from *E. coli* where L27 is not truncated, will be absent from non Firmicutes



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- State of the art: from genetic engineering to synthetic biology
- **A key to life: information is physical**
- The power of Nature: recruiting contextual information
- The power of human craft: *Homo sapiens* is an invasive species
- A way for the future: keep natural information available



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# What life is

**Program** (an “orchestra score”)

**Machine** (“chassis”) allowing the program to be expressed via a coding process

**Metabolism:** dynamic coupling processes involving chemical changes with **coding** from the program to a second level (introducing an essential asymmetry that differs conceptually from feedback)



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## Cells as computers making computers

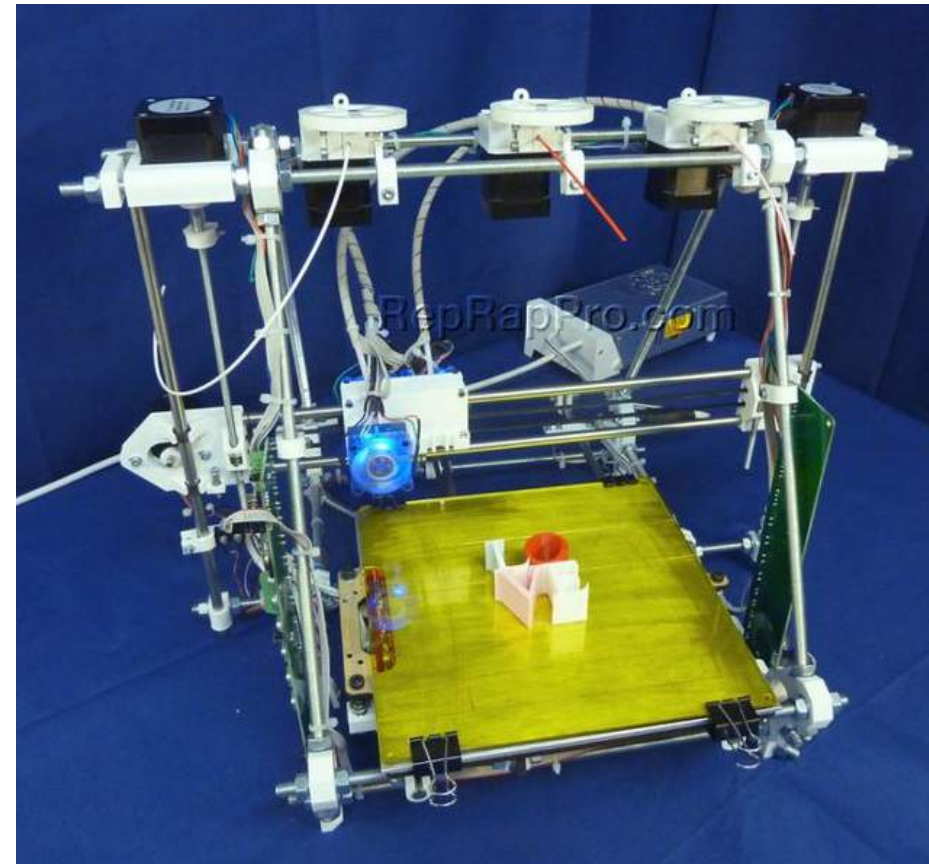
REPRAP (replicating rapid prototyper, 2004) aims at making a self-reproducing 3D printer:

The machine produces most of its components (= “biobricks”)

What is missing:

- The program
- The assembly line (time and space management, and specific functions such as lubrication)

<http://reprap.org/>

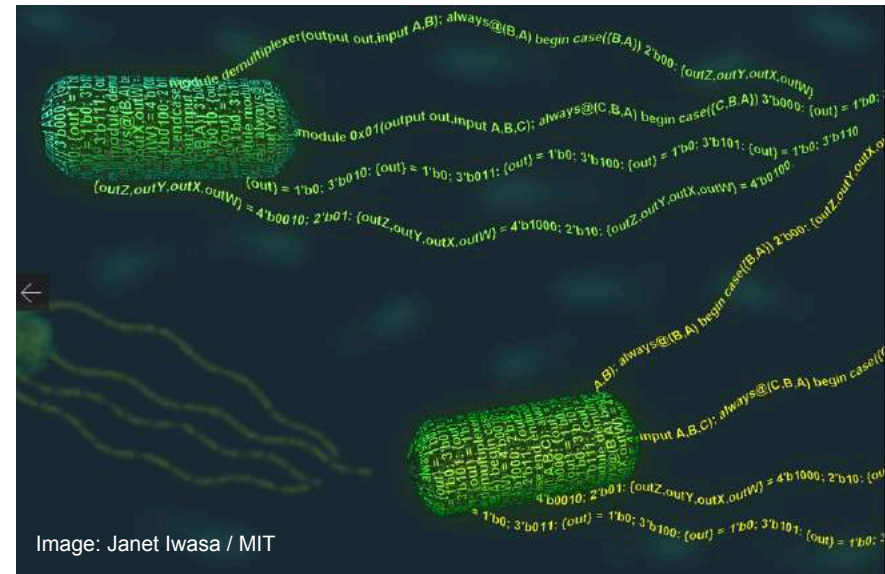




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Voigt and his colleagues at MIT and Boston University have created with the National Bureau of Standards a programming language for living cells

## More than a linguistic metaphor



*“It is literally a programming language for bacteria. You use a text-based language, just like you’re programming a computer. Then you take that text and you compile it and it turns it into a DNA sequence that you put into the cell, and the circuit runs inside the cell.”*

Yet, **what about the cell “chassis”?**

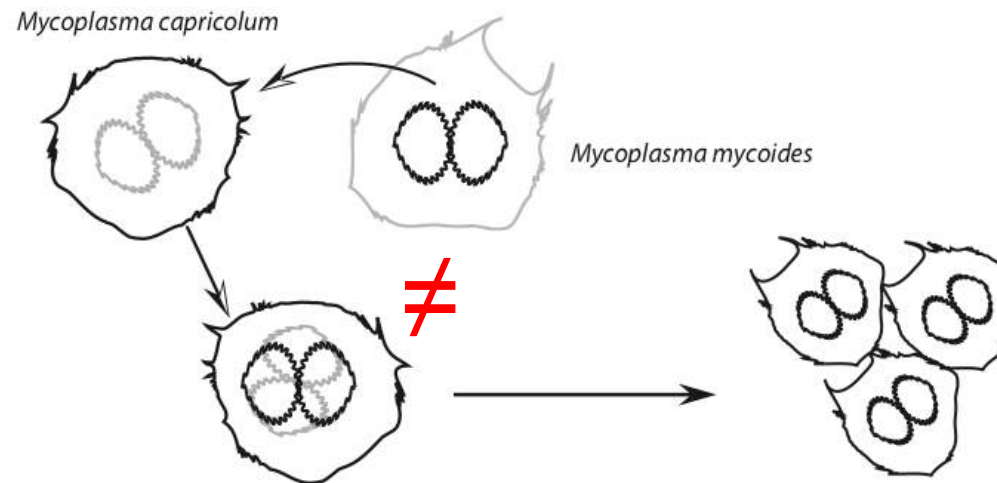


## Where forms matters

The program  
**replicates** (makes  
an identical copy)

The cell chassis  
**reproduces** (makes  
a similar copy)

This split is the  
basis of evolution



It calls for conceptualising what makes **form**  
**We need a theory of information in biology**



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## Theseus' ship

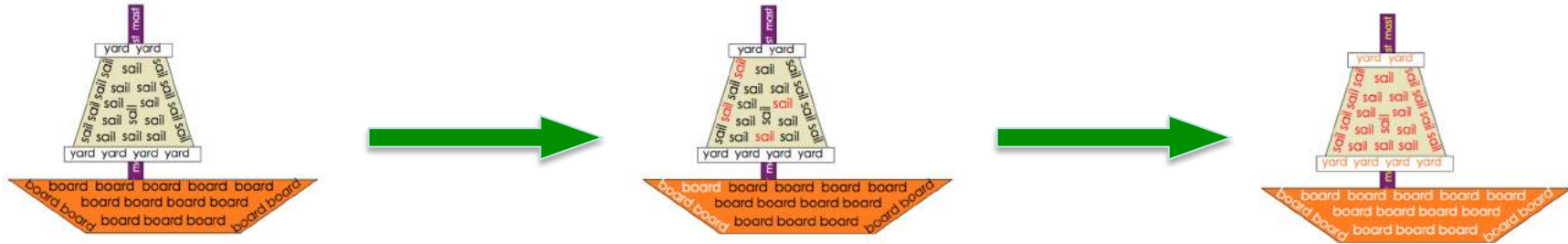
*The ship wherein Theseus and the youth of Athens returned had thirty oars, and was preserved by the Athenians down even to the time of Demetrius Phalereus, for they took away the old planks as they decayed, **putting in new and stronger timber in their place**, insomuch that this ship became a standing example among the philosophers, for the logical question of things that grow; **one side holding that the ship remained the same, and the other contending that it was not the same***

Plutarch 75 ACE (translated by John Dryden, 1994)



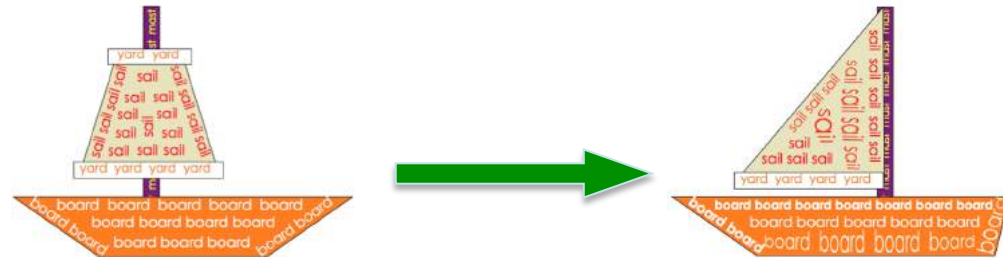
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# Form: Permanence and change

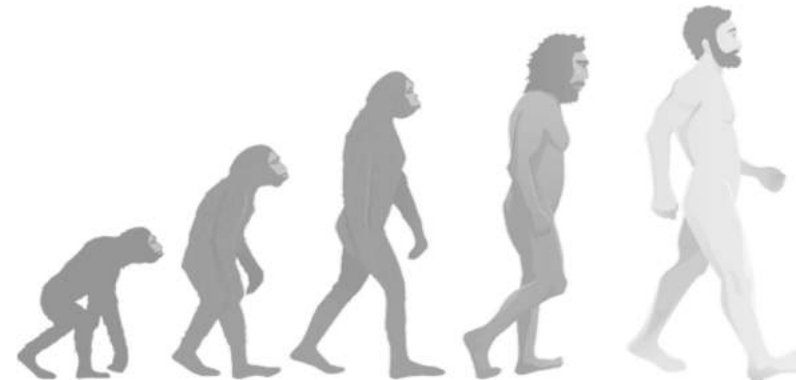


• short time scale

• • • • •



• long time scale  
(theory of evolution)







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**Information is  
physical**

**Matter / Energy / Space / Time**

- Classic Physics
- Quantum Physics
- Chemistry
- Biology
  - Development
  - Neurobiology
  - Linguistics
- Mathematics

**Information**



We need a **theory of information in biology**



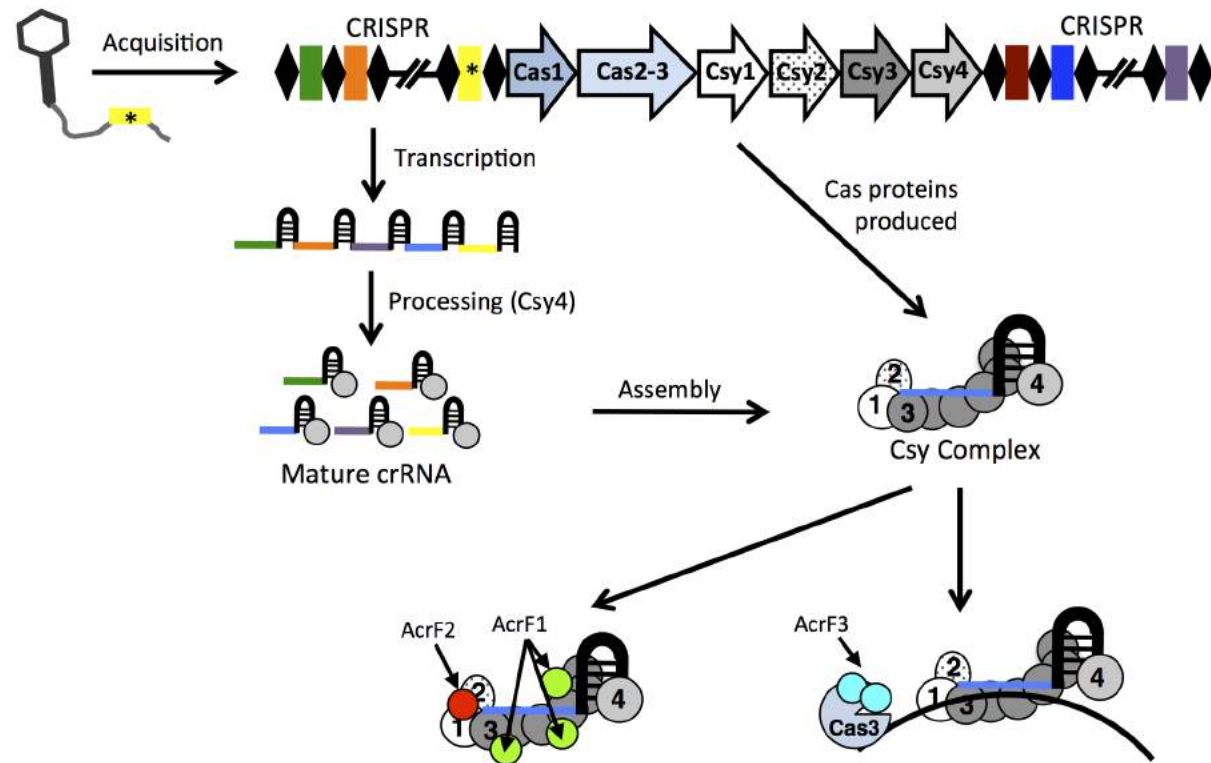
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## Power of Nature: CRISPR again

Cells memorise that they were infected by viruses (bacteriophages) and transmit this information to their progeny by recruiting cognate information and placing it within their genome



Phage fight back, via inactivating Cas and modifying it into a repressor

KL Maxwell PLoS Pathogens (2016) <http://dx.doi.org/10.1371/journal.ppat.1005282>



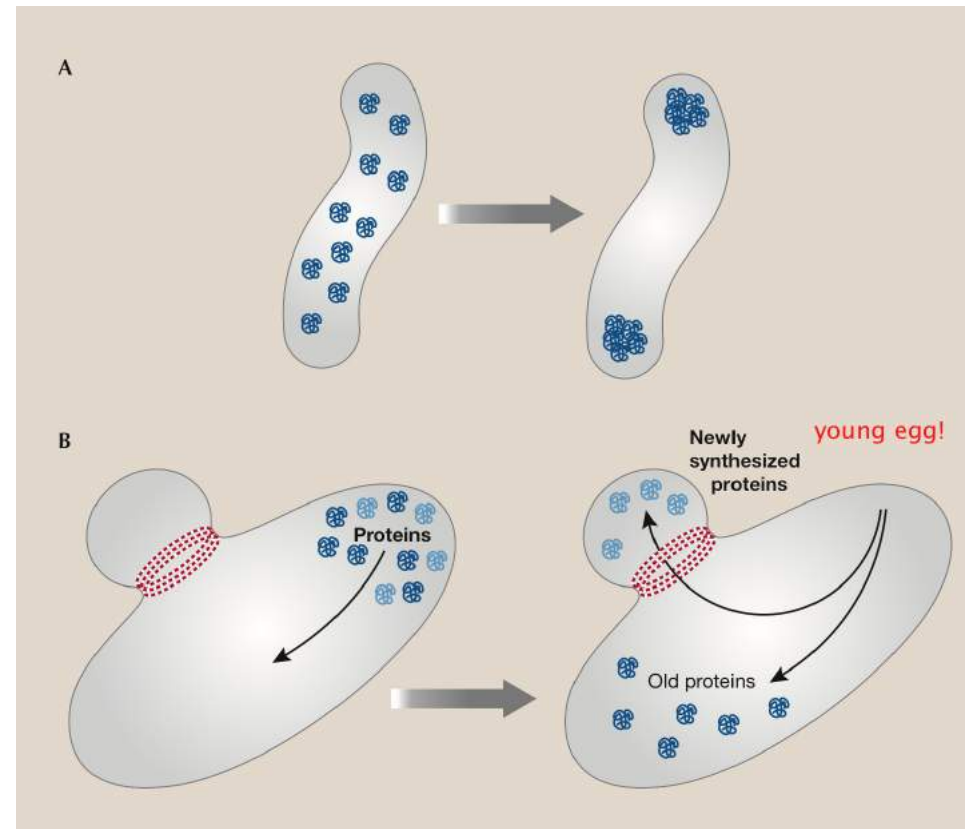
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# Babies are born very young!

Life keeps creating and recruiting information

A further power of Nature:

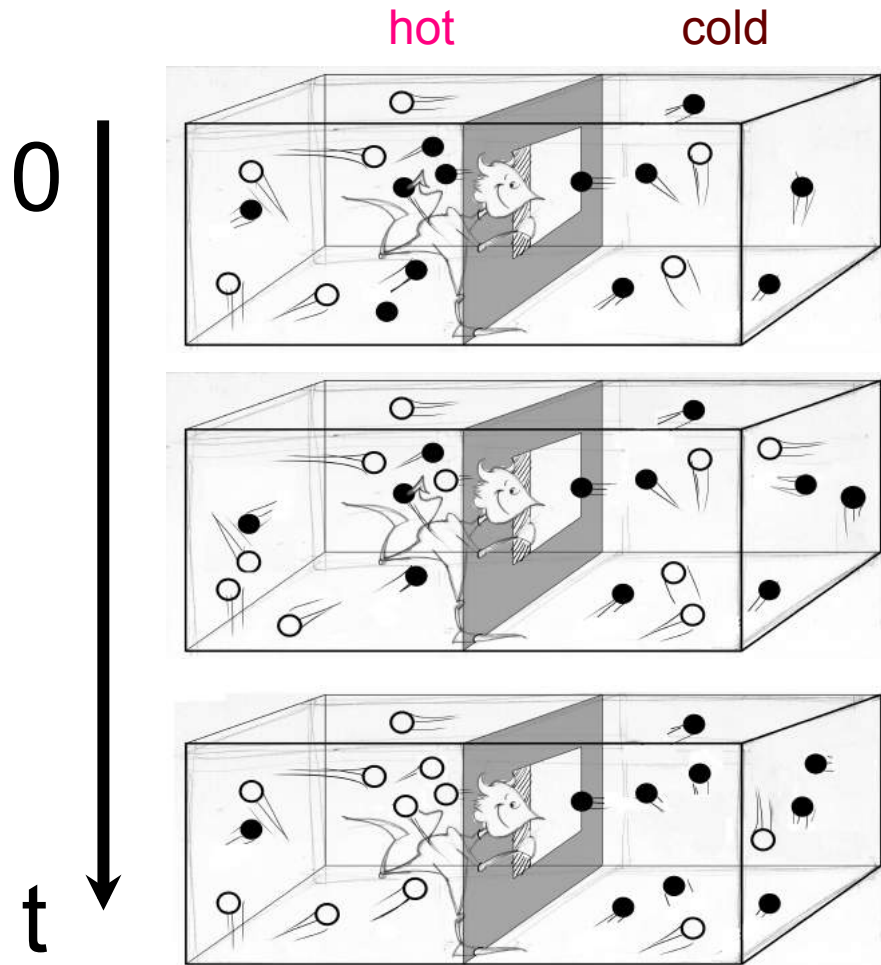
Separating between old and young. This is the mark of the ability to manage information



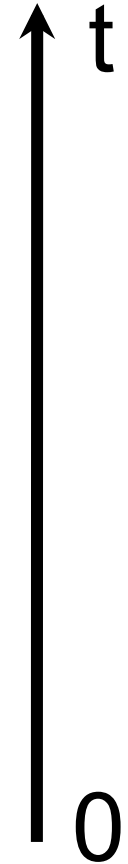


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# Maxwell's demon



The demon accumulates information reversing the course of time if he **measures** the speed and the position of the gaz atoms, memorising an **information** to calculate when he must close the trapdoor; resetting (**erasing**) the memory after each measurement **costs energy**





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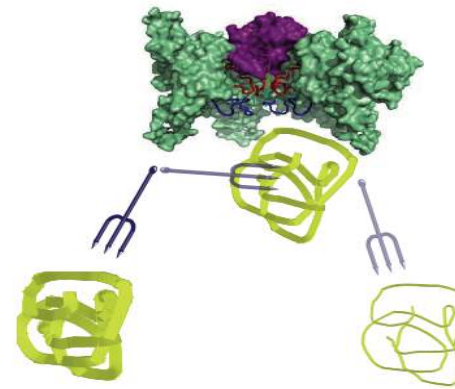
## Erasing memory costs energy

A synthetic biological chassis  
should refrain from inventing

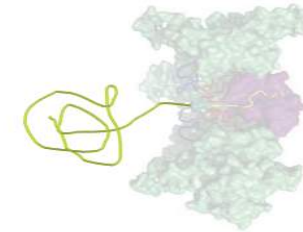
**Creating information does not  
need to consume energy (Rolf  
Landauer, 1961)**

Resetting memory for further  
creation requires energy

Biological processes coping with  
aged structure use an energy-  
costly process to discard the old  
entities



non functional entities  
are recognised and  
degraded



The degradation machinery **uses  
energy to refrain from degrading**  
a functional entity



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## Natural selection builds on Maxwell's demons



The dinosaur ancestors of today's birds lost their teeth about 80 million years ago, **but not the ability to grow them**

Natural selection:

Memorising what is functional (locally) to prevent its destruction, i.e. use energy not to destroy but **to prevent destruction of what works**, without design or purpose

**A « useless » contraption that is running properly will be kept for many generations**

**This allows organisms to anticipate an unpredictable future**

<http://waitbutwhy.com/2014/10/dark-secrets-bird-world.html>



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## Nature's craft: Invasive species

Competition, rivalry evolved together for billions of years

Co-evolution is the rule: Predators and preys control each other

Moving place for an organism in isolation leads it either to disappear or to become invasive



*Mikania micrantha* killing a banana tree (Lamma Island, Hong Kong)





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## Human life constructs are crippled

Domestic plants or animals seldom survive in the wild in the absence of man; the nearer to their wild origin, the better chances of survival they have

Nature rapidly reverts to its anterior state



Rice field near Fukushima

© Greenpeace



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Yet...

150<sup>th</sup> anniversary of Mendel's discovery



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## Human artefacts are destructive

Physico-chemical artefacts are meant to destruct life (ploughing, pesticides, herbicides...)

Despite its power, Nature surrenders quickly when facing the human demographic explosion

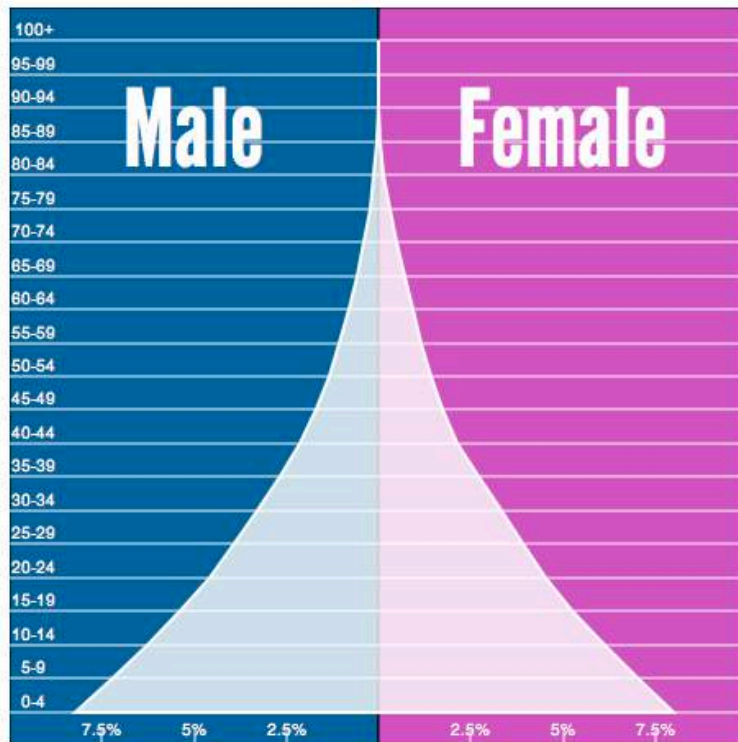




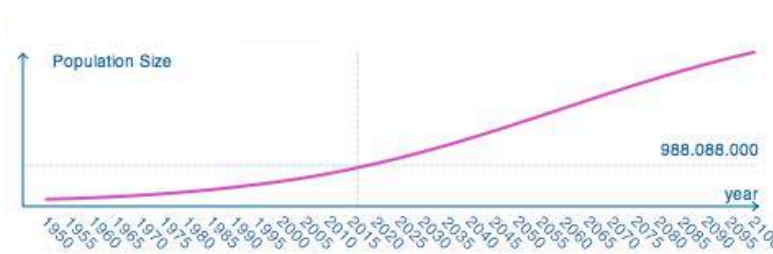
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# Sub-Saharan Africa 2016

Population: **988.088.000**



## *Homo sapiens* is an invasive species

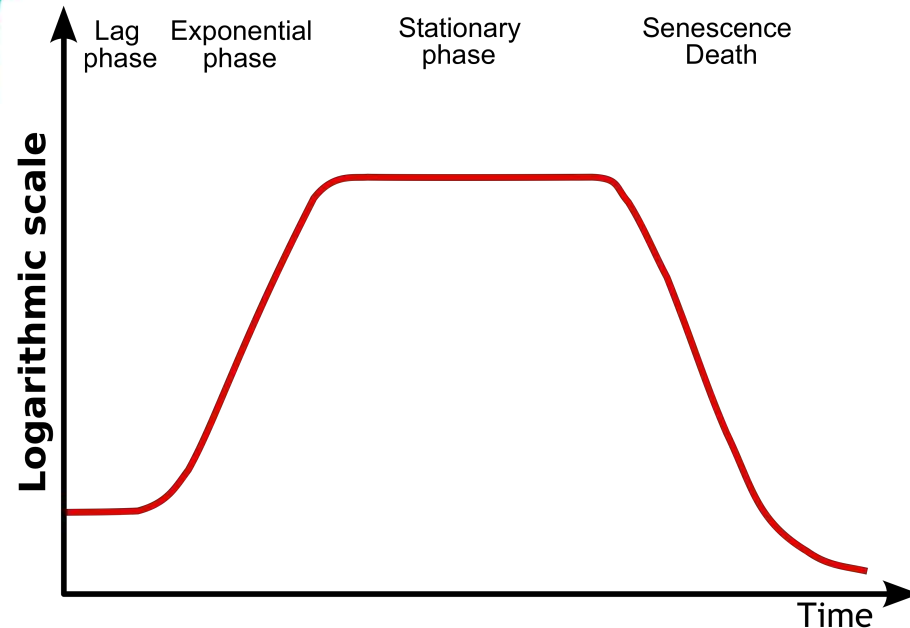


150<sup>th</sup> anniversary of Mendel's discovery



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## A universal life curve



This is the normal course of lifespan  
of a species

Asking for everlasting growth is an  
illusion (including in economy)

The descent is inevitable

We should try and make it differ from  
collapse

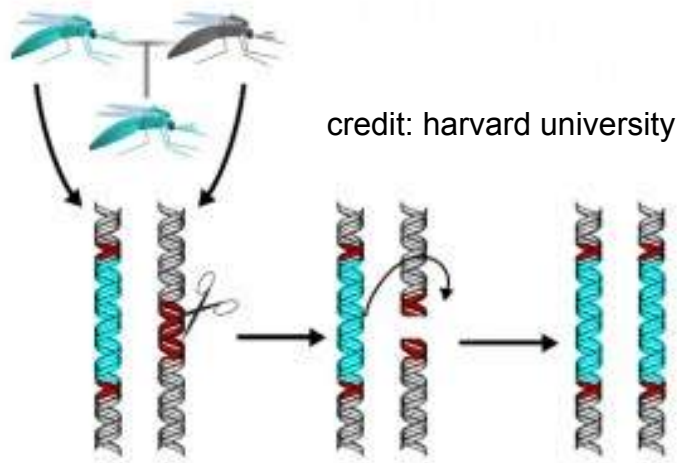
With living organisms, using non-  
mendelian genetics allows us to  
skew this general birth and death  
curve



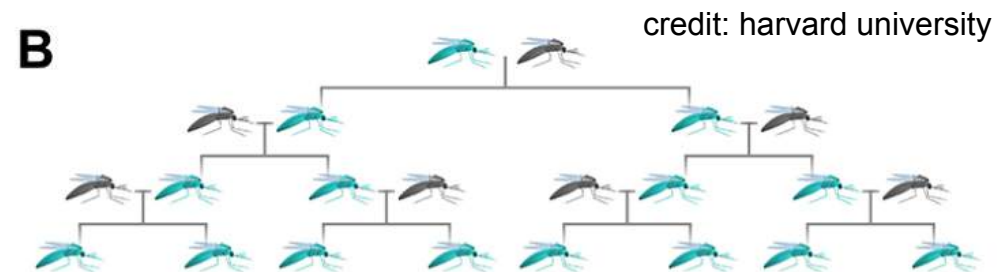
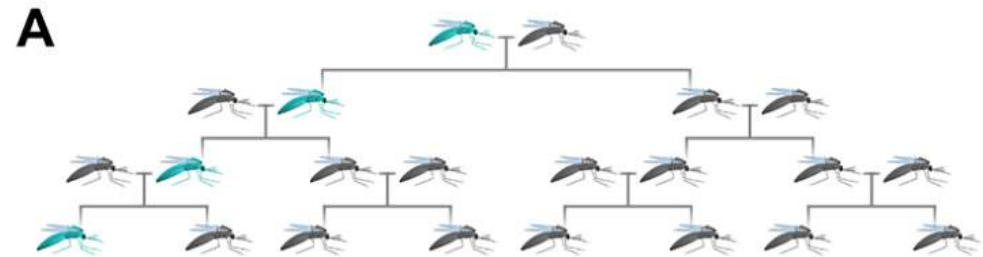
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Gene drive is a natural process recruited as a strategy to artificially increase a gene's inheritance rate

CRISPR/Cas can be used to drive inactivation of a particular gene



## Gene drive



A. Mendelian inheritance

B. « Selfish » gene-driven inheritance



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# Archaea: harmless SynBio chassis

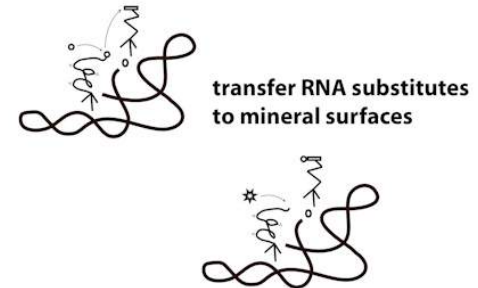
Combining the RNA-metabolism (protocyttoplasm) and the RNA-genome (protonucleus) worlds gave rise to the ancestor of **Eukarya** (Protokarya)

Opening up an escape route (resistance to phagocytosis)

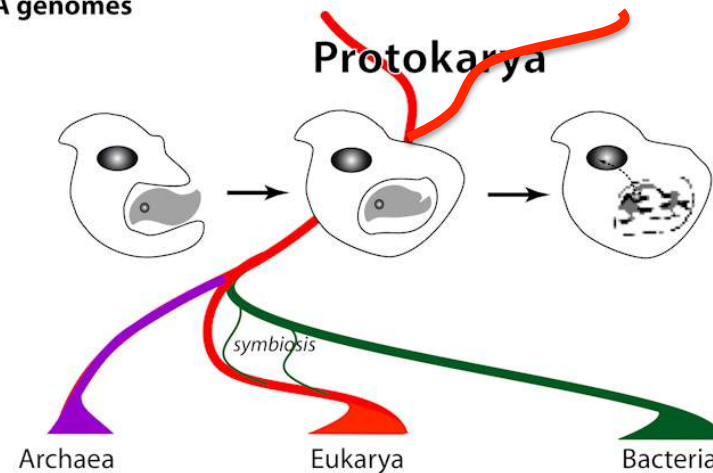
**Archaea** (no fusion, never authentic pathogens)  
**Bacteria** (resistant envelope)

Surface metabolism

RNA metabolism



RNA genomes  
DNA genomes





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# A worrying context for nature

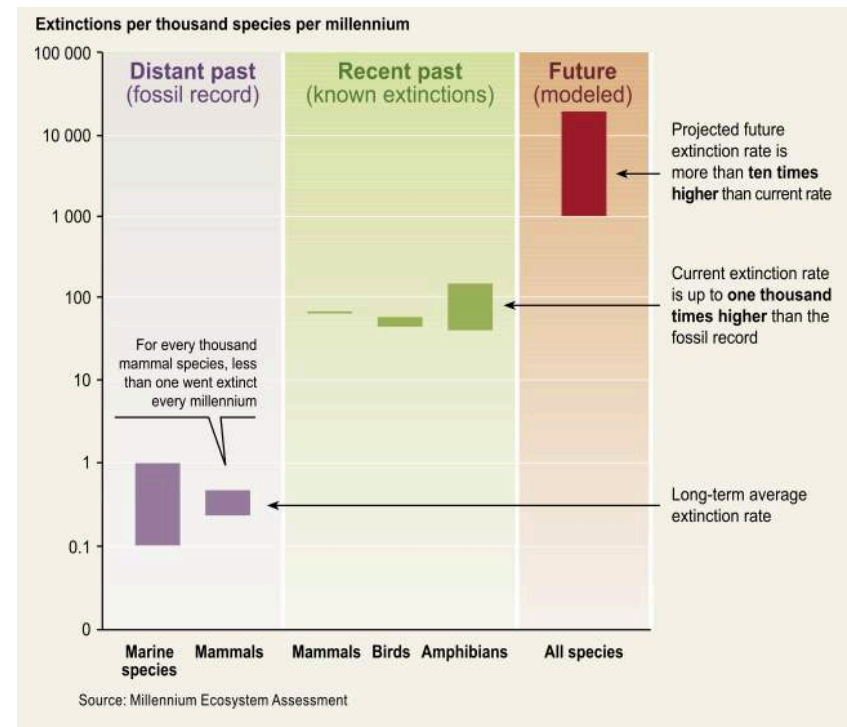
## Insects and plants disappear from Europe



*Aporia crataegi* Black-veined White



*Centaurea cyanus* Cornflower





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## Man away... ... back to Nature

Despite the very negative consequences of radioactivity, the local absence of *Homo sapiens* has a positive outcome



Tchernobyl  
© mmatting



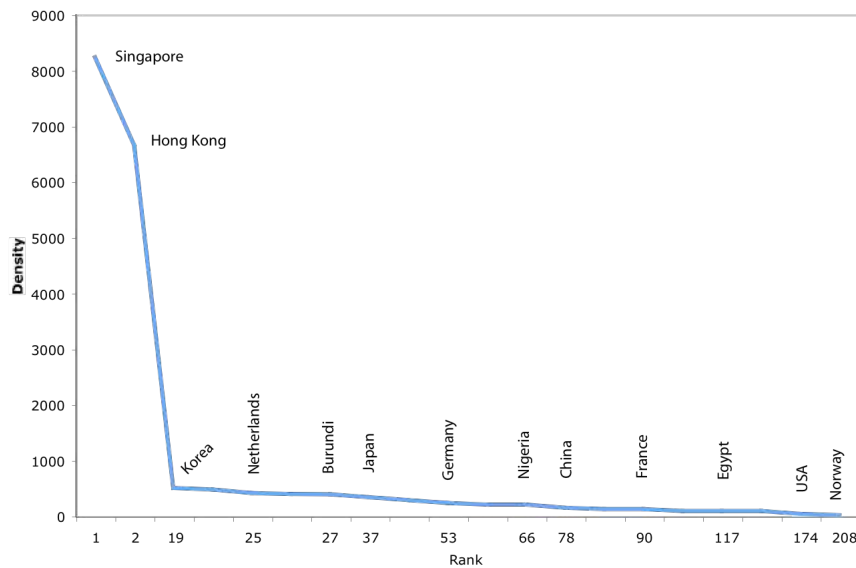
Fukushima  
© Arkadiusz Podniesinski



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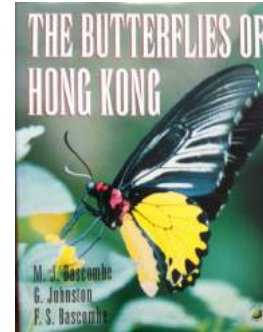
# Hope? Nature in Hong Kong

## Human density in Hong Kong

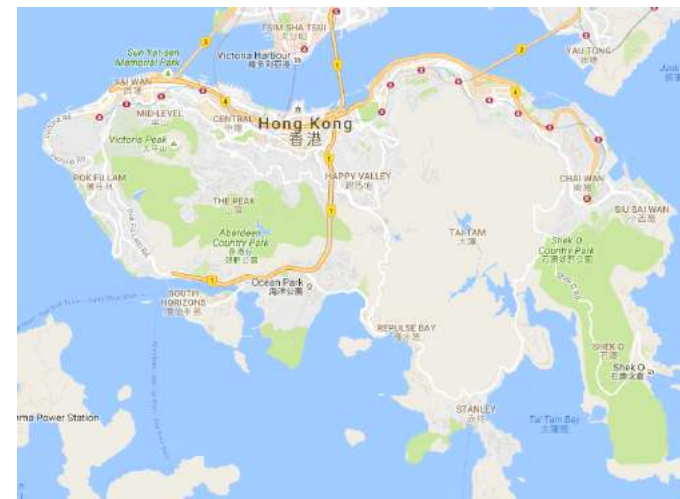


Despite an enormous human density the Hong Kong government succeeded in preserving wild life (for the time being...)

150<sup>th</sup> anniversary of Mendel's discovery



*Heliophorus epicles*, subspecies *phoenicoparyphus*, lives from the North of India to Thailand, and the southern provinces of China. It can be seen on the Victoria peak in Hong Kong. Its caterpillar feeds on *Polygonum chinense*





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[www.normalesup.org/~adanchin/causeries\\_en.html](http://www.normalesup.org/~adanchin/causeries_en.html)

*Οὐδὲν χρῆμα μάτην γίνεται ἄλλα πάντα ἐκ λόγου τε καὶ ὑπ' ἀνάγκης*

**ΛΕΥΚΙΠΠΟΣ**