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Nature and Artifice
An avatar of domestication: GMOs

BioCampus, Copenhagen
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Genetics of Bacterial Genomes
http://www.pasteur.fr/recherche/unites/REG/

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Take home message

- At first, humans protect Nature against humans; Artifice is perceived as dangerous
- Then, because Nature in by essence unpredictable, it is understood as not friendly, but needing to be tamed
- Hence, domestication of plants and animals marks humanisation, starting the Neolithic Age with control over Nature
  - Because it is the oldest extant civilisation, the Chinese civilisation is better prepared to understand the value of Artifice
- GMOs are the latest avatar of domestication
  - The fear of Artifice leads to the dangerous thought that plant GMOs are dangerous while animal GMOs are safe
- A way to gain control on living organisms is to **reduce** their ability to evolve

A deep challenge: demographic explosion

- 200,000-100,000 BP Birth of *Homo sapiens* ssp. Sapiens
- 17,000-12,000 BP Domestication of dog (*Canis canis*)
- 12,000 BP Domestication of fermentation microbes (lactobacilli and fungi)
- 10,000-9,000 BP Domestication of rice (*Oryza sativa*) and wheat (*Triticum aestivum*)
- 10,000 BP Domestication of cattle (*Bos taurus*)
- 9,500 BP Domestigation of pig (*Sus scrofa*)
- 9,000 BP Domestication of maize (*Zea mays* ssp. Parviglumis)
- 6,000 BP Domestication of horse (*Equus caballus*)
- 5,000 BP Domestication of silkworm (*Bombyx mori*)

- 1764 Kolreuter fertilizes plants artificially
- 1866 Mendel establishes the first laws of genetics
- 1940-1960 The Green Revolution (maize and wheat breeding, er, and seed development based on irradiation and chemical mutag
- 1973 The first bacterial GMO
- 1984 The first transgenic mice
- 1987 Quantitative Trait Loci are used to speed up selection of
- 1994 The first GMO food reaches the food market

1800 1 billion
1928 2 billion
1961 3 billion
1974 4 billion
1987 5 billion
1999 6 billion

What life is

Three processes make life:

- A programme (a “book of recipes”)
  - Information transfer => genomics decyphers the programme associated to the cell

Forces coupling the genome structure to the structure of the cell (the cell factory):

- A machine putting the programme into action
  - Metabolism
  - Compartmentalisation

The cell is the atom of life

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Information transfer

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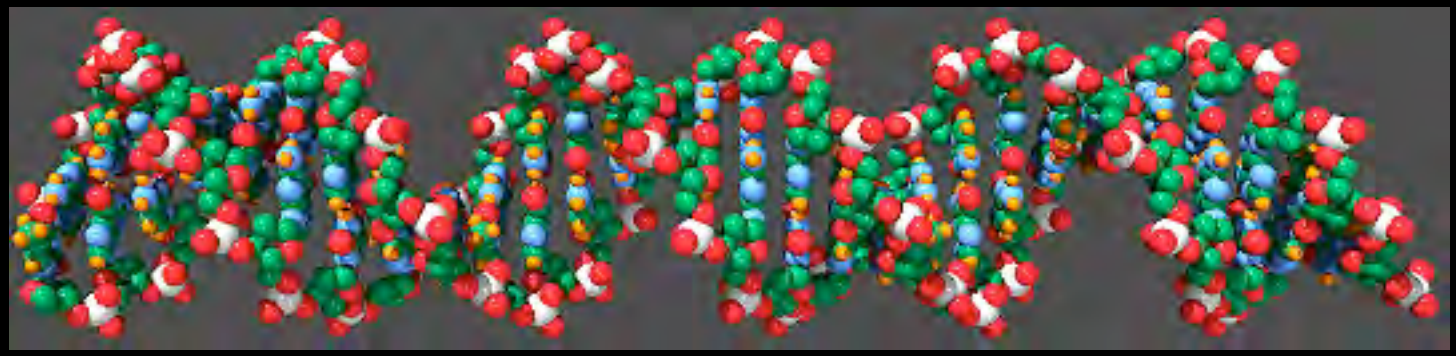
Deoxyribonucleic acid (DNA) stores the memory of the genetic programme. It chains four types of basic building blocks. Two strands are intertwined, making a double helix.



Remarkably, the genome programme reads like a text:

```
....GCGGTATTTTGATGGAGTTATACGGAAGGGATGTTC....
....CGCCATAAAACTACCTCAATATGCCTTCCCTACAAG....
```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DNA replication

DNA

The text of one half of the helix entirely specifies the text of the other half, as the positive and negative views of a photograph specify each other

A => T

C => G

T => A

G => C

=>

<=

Errors result in evolution

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From the genetic programme to the cell

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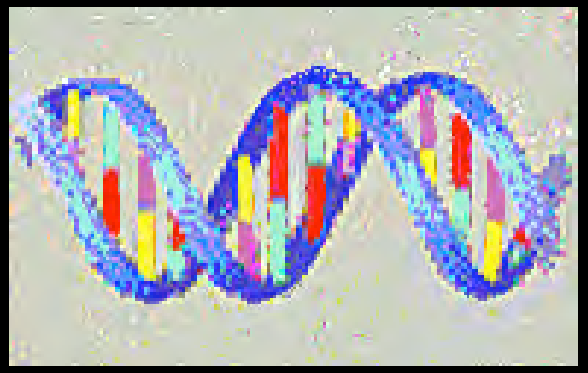
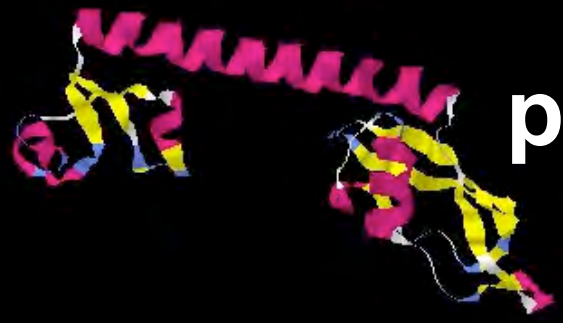
When the machine reads the programme, it performs actions. A special machinery reads the DNA and copies it into active objets, the proteins (enzymes are proteins).



DNA



protein

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The cell factory

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A cell looks like a computer which would programme the construction of similar computers

It has a magnetic tape, or hard disk (the « genetic programme ») and reading devices which allow it to read the programme and put it into action

The « cloning » of the ewe Dolly performed that action: moving the programme from a machine (a cell) to another one (an egg without a nucleus)

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A core law: the genetic code

Meaningful parts of the four-letter DNA text (genes) are translated into a twenty letters text, the text of a protein. The cypher driving the correspondence is named the genetic code

For example “ TCA ” in DNA means “ S ” (a chemical residue, “Serine”, among the twenty amino acid types) in the protein

In turn, proteins manipulate DNA, making the process recursive

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Recursivity

The programme is like a book of recipes: depending on the environment some recipes are used, some are not; so, the same programme can have different outcomes.

The major action of the programme is to direct synthesis of agents that control the programme in such a way as to express relevant parts, and also to construct the agents themselve. This latter process (recursivity) has extraordinary consequences, as illustrated in Escher's paintings

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The end of mechanicism

The ultimate lesson of the metaphor of the genetic programme is that living organisms are those material systems that are poised to be ultimately unpredictable to be able to cope with an unpredictable future…

This allows them to create some progeny that can survive in an unpredictable future.

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A general constraint hindering engineering: evolution

Variation / Selection / Amplification

Stabilisation

Evolution

creates

Function

capture (recruits)

Structure

codes

Sequence

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From domestication to GMOs

- The aim of domestication is to provide stability in time, to **reduce** the lack of predictability
- This results in a first step of blind genetic manipulation: crosses between breeds and individual with apparent « interesting » characters
- Presence of uncontrolled variation led to target specific genes: this led to GMOs
- In a second step, improving the GM techniques allowed using living organisms as factories for producing specific products in a stable way

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Plant GMOs: improving crop yields and product quality

- C**rosses between plant variants permitted screening for new breeds: producing variants became essential**
- **Plants are mutagenized** (often by irradiation) to produce more variants
- **Variants are unpredictable**. Together with « useful » mutations they carry **many** other mutations, often deleterious, requiring a long selection process to obtain the required plants. Also, their behaviour is difficult to control
- **Genetic engineering modifies only one, or a small number** of targeted genes, directly going to the desired properties. **GMOs are more predictable than mutants obtained by the more traditional (also artificial) approaches**
- **Genetic engineering aims at stabilizing the outcome (phenotype)**: note that this goes against the ability of plants to evolve. Hence, **GMOs are less fit to the non- humanized (wild) environment**

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Animal GMOs: humanisation of organs

- The initial goal of animal GMOs was similar to that of plant GMOs, improving quality of animal products, or using the animal as a factory
- Interest for health care created a new **Unmet Need**, associated to phylogenetic proximity between animals and humans: using GMOs as providing tissue substitutes.
- Humanizing organs is widely accepted by the public, despite its obvious danger:
  - **Animal tissues contain retroviruses**
  - **Emerging diseases are often caused by transfer from animals to humans (eg HIV, SARS, Hantah etc)**

Nature is pre-adapted through evolution, it can therefore be more dangerous than Artifice

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- Biological adaptation is the easier, the closer the organism from Humans
- e.g., coming from Humans, human blood is dangerous
- Natural processes are more difficult to control than artificial processes
- Progress in applications of biological knowledge is linked to **increasing our control** over the processes, i.e. getting ever more artificial, e.g. inventing efficient artificial blood would be an immense progress (cf HIV, BSE, Hepatitis, etc)

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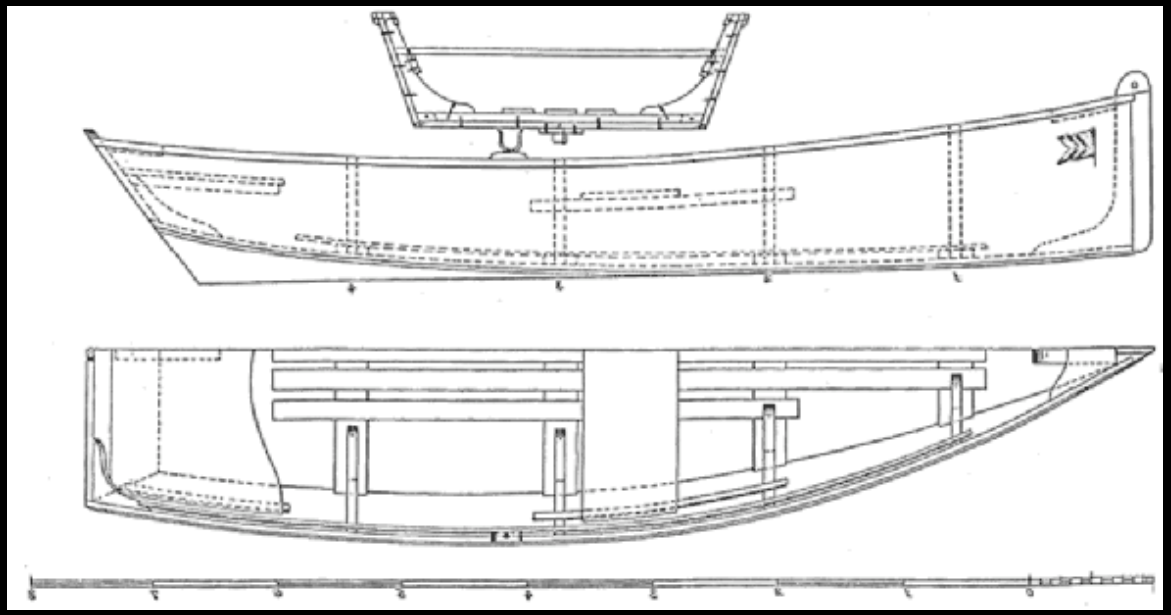
A caveat: The Delphic Boat

- Genes do not operate in isolation
- Proteins are part of complexes, as are parts in an engine
- It is important to understand their relationships, as those in the planks which make a boat



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Thank you

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