

# **Biologia dell'organismo, fra salute umana ed OGM: la sorpresa di scoprire un campo di battaglia**

*Giuseppe Longo*

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[www.di.ens.fr/users/longo](http://www.di.ens.fr/users/longo)

European Network Scientists Social Environmental Responsibility

G. Longo, M. Montévil, *Perspectives on Organisms: Biological Time, Symmetries and Singularities*, Springer, Berlin, 2014.

G. Longo, *Le cauchemar de Prométhée. Les sciences et leurs limites*. PUF, Paris, 2023.

# **The “internal” ethics of knowledge, in science**

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To propose explicit and clear **principles**

These allow to “make a **step aside**” and explicit **critiques**

**Critical thinking: Science & Democracy:**

“sustained, collective, critical enquire” and a proposing minority

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**Critical thinking: Science & Democracy:**

“sustained, collective, critical enquire” and a proposing minority

*Biography:* my experience from Mathematics of Logic and  
Computing (Pisa + Buiatti, Maffei) to 10 years of  
collaboration with **theoretical physicists** (Paris: FB, TP, MMS)

In **Biology**, with C. Sonnenschein, A. Soto (endocrine disruptors,  
Boston) and others, since 2008, e.g. 8 authors:

*"From the century of the genome to the century of the organism:*

*New theoretical approaches", a Special issue of **Progress in***

**Biophysics and Molecular Biology**, 122, 1, Elsevier,

2016.

# Scientism vs Science

**Scientism**, *some properties*:

- 1- **occupy** reality with existing tools (possibly one: e.g. “Information”)
- 2 - projecting the **latest machine** on the world (brain, DNA ...)
- 3 - **science for control**: flatten on one dimension, “*follow the rule*”

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**J. Monod**, *Chance and necessity*, 1970 :

« The cell and ... the molecular processes are a *Cartesian Mechanism*, autonomous, exact, independent from external influences ...

*Necessarily stereospecific* molecular interactions explain the structure of the code ... a *boolean algebra*, like in computers.

*Genes define completely* the tridimensional folding of proteins ».

**A. Grothendieck**, 1971: Darwin’s science, Monod’s “**scientism**”...

Elowitz, M. et al.. (2002). Stochastic Gene Expression in a Single Cell. *Science*, 297(5584)

Chahinian, H. et al. The Epigenetic Dimension of Protein Structure.

*Biomolecules* 2022, 12, 1527

# The “programming” metaphor and dogmas

**1 - the Central Dogma of Molecular Biology** (summarized: the “information” contained in DNA is “**complete**” as to the development and evolution of organisms (Crick, 1958), a computer program (recall *Hilbert’s program*, 1900: finite strings of signs))

**2 – the dogma that macromolecular interactions are “exact”,** (stereo-)specific, like the “key-lock” or “hand-glove” correspondence ... this is “*necessary* to transmit the genetic information” (Monod, 1970); against physical-chemistry (Paldi, ‘22)

Thus, J. Doudna (Nobel Award, 2020):

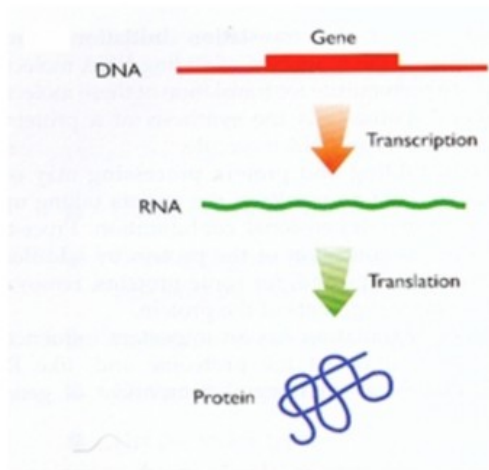
“we have the power to control Evolution”

(2017 book: **1** is explicit, **2** is implicit: *NGT for GMO’s in EC*)

# Central Dogma of Molecular Biology, Crick, Watson, 1958-62:

“*Information*”

**En 1960**

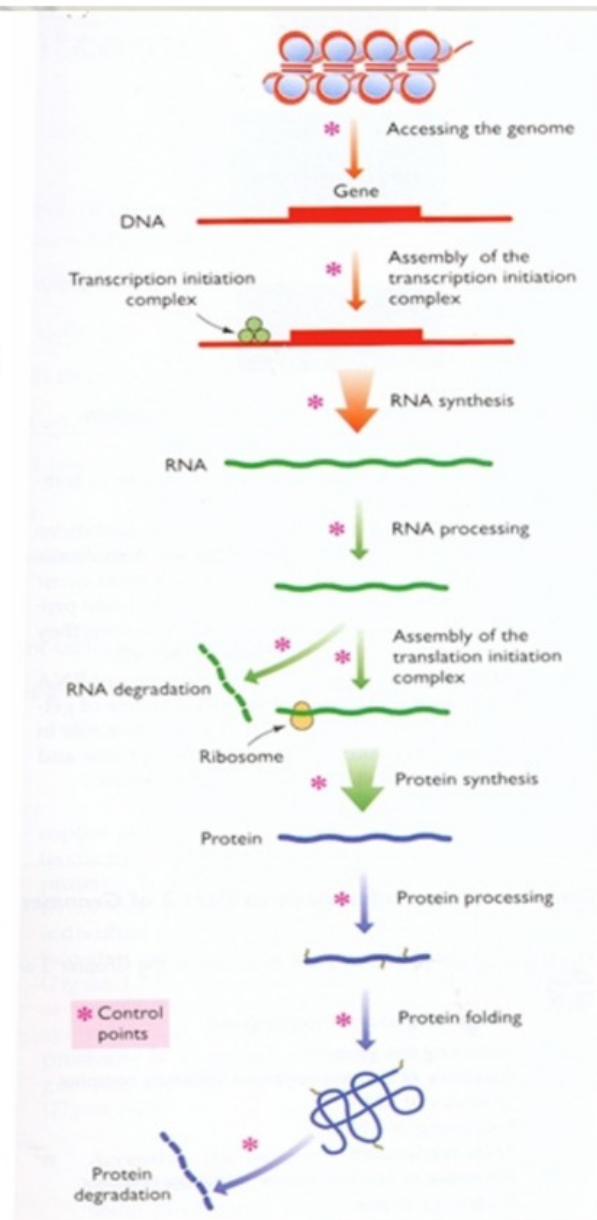


(d'après Brown, 2002, in *genomes*)

**En 2000**

Transcription

Traduction



In University and High Schools textbooks, today



# **The double language: an Ethical Issue**

## **Strong consequences from vague assumptions (information, program...)**

P. Ball (former editor of Nature) *on the Dogma(s)*:

... these « **misleading narratives** are routinely perpetuated in the teaching of Molecular Biology, indeed in so much of the technical, the lay, and the philosophical literature »

Similarly, **in private**, many acknowledge the “informal” or “just metaphorical” use of these “narratives”... **yet, basically wrong**

E. Fox-Keller, *Making Sense of Metaphor*, 2020

P. Ball *How Life Works: A User's Guide to the New Biology*, 2023

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The **double ethical standard**: *private remarks, public science*

(“better to “sell” ”)

# **Some consequences of a failed Internal Ethics of Science**

Collaboration with C. Sonnenschein, A. Soto, Biology, Tufts U.,  
Boston: endocrine disruptors and cancer

and in

European Network of Scientists for Social and Environmental  
Responsibility  
<https://ensser.org/>

# “Doses” of Chemicals in the Ecosystem

## ***Unnoticed* Endocrine disruptors:**

82,000 artificial molecules produced in the XX century

**(FDA Report to Congress, 2008)**

- *Do not worry: not stereo-specific and small doses*

In order to carry information from the genetic program, molecular interactions are ***necessarely stereospecific*** (key-lock) ...

[Monod, 1970], [Collins, 1999], [Doudna, 2017]

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*No:*

- **non-linear** effects, **low** chemical affinities
- **varying** association/dissociation constants (**contextual**)
- to be given in **probabilities**, depending on the **context** [Elowitz, 2002]

# Endocrine Disruptors and Carcinogenes

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- **Endocrine target organs**, cancer general increase (1994 – 2012) :  
*breast* 26% ; *testis* 56% ; *prostate* 94%  
**thyroid cancer** ( +285% in 30 years, till 2012)

S. De Coster, N. van Larebeke, Endocrine-disrupting chemicals, **J. Environ. Public Health** 2012

N. Howlander, et al, SEER Cancer Statistics Review, 1975–2012  
**National Cancer Institute.**

E. Diamanti-Kandarakis, A. Soto et al. *Endocrine-disrupting chemicals: an Endocrine Society scientific statement. Endocr Rev* 30:293-342, 2009

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- **The case of asbestos** (Maltoni '70s; Huang, 2011: not mutagenic)
- **Lowering by 50% (!) of human spermatozoa density** since 1950's

N. Skakkebaek, *Sperm counts, testicular cancer, environment*, **BMJ**, 2017

M. Montévil, *Disruption du vivant dans l'Anthropocène*, 2024



## **DNA *sequencing*, 2001:**

- Fantastic technological achievement
- Little science, no ethics (selling “*decoding*” to the general public)

# **DNA sequencing, 2000-01** (major technological achievement)

*F. Collins, 2001*: « we have grasped the **code written by God** »

*C. Venter, 2001*: the "decoder" of the human genome

*R. Weinberg, 2002*: “Cancer biology, now an exact science:  
genetherapies in a few years” (20.000 quotes in a few months)

*A. Von Eschenbach, 2003*, director Nat. Cancer Inst. 2003: "To eliminate the suffering and death from **cancer**, and to do so by 2015"

**Diagnosis and prognosis** within two or three years ...

*NO WAY !* Light-microscope histology (till today)

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*C. Venter, interview for the Spiegel, July 29, 2010:*

*Title: « **We have learned nothing from the genome** »*

*« ... **phonies** ... the ill-founded belief that those who know the  
DNA sequence also know every aspect of life, a nonsense ... »*

*R. Weinberg, 2014 : « all wrong: messy DNA » (very few quotes)*

**The ethical issue:**

**An a-critical science,  
Business promoting a failed “theory”  
(complete “control” by the DNA,  
Exact macro-molecular interactions)**

**Today's consequences on plants:**

**GMOs based on NGT**

# **Today's consequences on plants: GMOs based on NGT**

(New Genetic Technologies: Crispr)

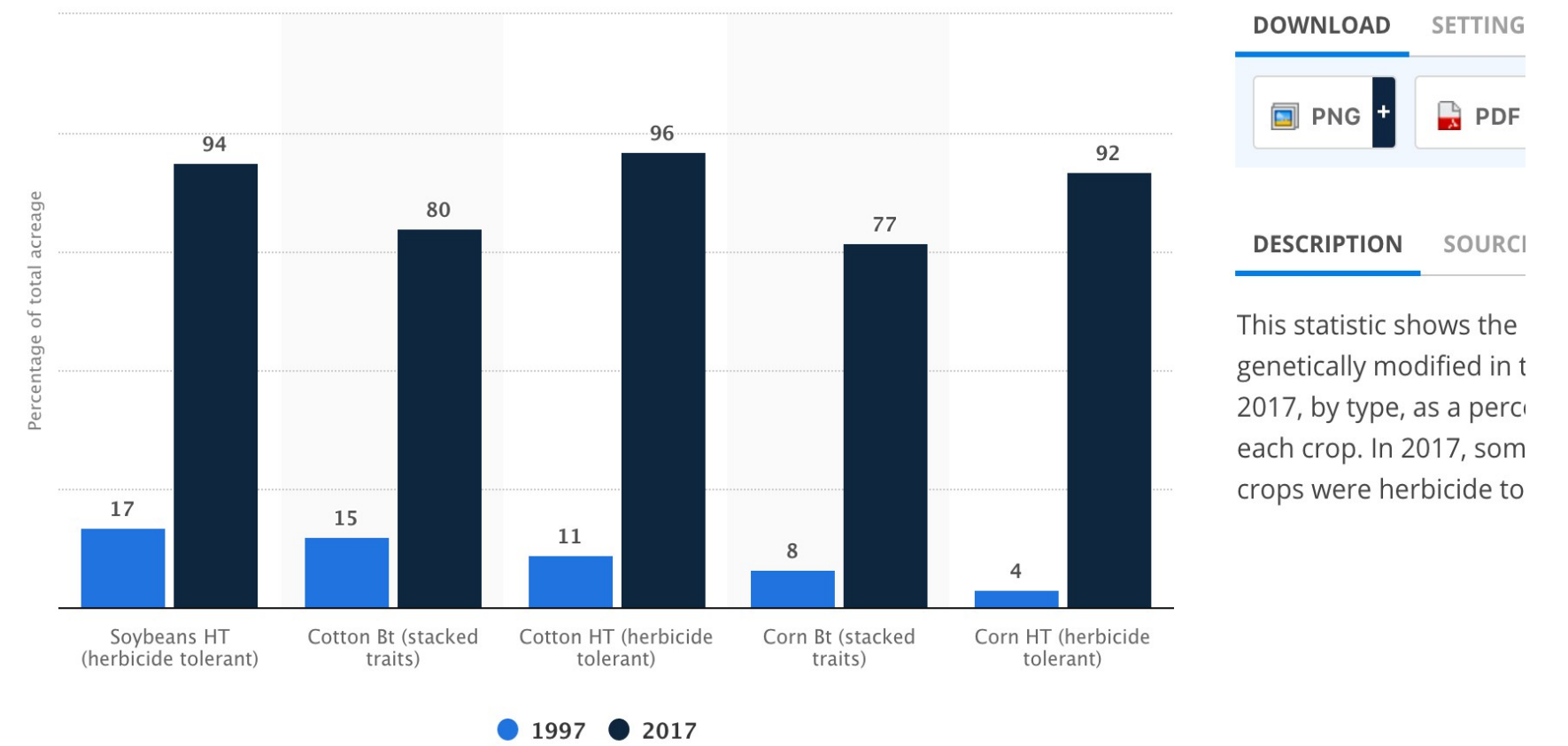
Nobel Award: J. Doudna, E. Charpentier, 2020.

**At the core of the NGT's debate in Europe, 2024**

ENSSER (European Network of Scientists for Social and Environmental Responsibility): <https://ensser.org/>

*No reflections on previous GMOs experiences....:*

# Percentage of genetically modified crops in the U.S. in 1997 and 2017, percent of total acreage)



Soybean, Cotton, Corn (*HT*, *BT* (Bacil. Thuring., against bollworm)).  
Similar data in the Americas

Giraud T. *L'attention au Vivant*, 2024

# GMO's in the Americas

100% of the GM crops grown in Canada are now **herbicide-tolerant (HT)**. Globally, this number is 88% (vs BT).

- **No increase in yields** w.r. to Europe: Eu allowed only 20 % GMOs in Portugal, Romania, Spain: *Teosinte*, inedible maize: uncontrolled diffusion in GMOs' fields, an “adaptive crop-to-wild introgression of transgenic maize”—the “noxious weed”

(Giraud, 2024), (Le Corre et al. 2020)

- **Herbicide sales in**

*Canada*: + 244% since GM crops introduction, from 1994 and 2021.

*Argentina*: + 400 % per surface, from 2000 to 2021 (Roundup)

Genetically Modified Crops and Herbicides. March 2023

<https://cban.ca/gmos/issues/pesticides/>



# GMO's in India

**BT cotton** (*seeds* patented: produces of the toxin, no insecticides) initially solved **bollworm** problems, with no pesticides.

Epidemics of **secondary pests** (white fly, jassids, mealybug) not controlled by BT toxins began to occur,

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*Then increasing* the use of insecticides in BT cotton, as well as increasing levels of insecticide resistance.

In 2013, pre-2002 **levels were exceeded** (bollworm)

<https://www.resilience.org/stories/2020-09-09/the-failure-of-gmo-cotton-in-india/>

BT GMOs: uncontrolled massacre of **symbionts** in the humus and more (e.g. the monarch butterfly)

Other GMOs crops: **antibiotic** resistance, **buy** seeds....

(Then C, Bauer-Panskus, *Environ Sci Eur.* 2017; 29<sup>(1)</sup>: 1).

# Pesticides (HT) and/or BT GMO's

Major decrease of **microbial flora and fauna** (fungi, roots, soil):

Solution: buy fertilizers from Bayer-Monsanto (Areva)

- M. Castaldini, et al, 2005, Impact of Bt Corn on Rhizospheric and Soil Eubacterial Communities and on Beneficial Mycorrhizal Symbiosis in Experimental Microcosms, *Applied environment. Microbiology*, 71: 6719-29
- M. A. Badri et al., 2009, Unintended molecular interactions in transgenic plants expressing clinically useful proteins..., *Proteomics*, 9: 746–756.

Decrease of **insects biomass** by 70% (Giraud, 2024)

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Le Monde & The Gardian: *Le fichage à grande échelle de personnalités gênantes pour l'industrie agrochimique*, 28/9/24 (500 researchers)

[https://www.lemonde.fr/planete/article/2024/09/27/revelations-sur-le-fichage-a-grande-echelle-de-personnalites-genantes-pour-l-industrie-agrochimique\\_6336026\\_3244.html](https://www.lemonde.fr/planete/article/2024/09/27/revelations-sur-le-fichage-a-grande-echelle-de-personnalites-genantes-pour-l-industrie-agrochimique_6336026_3244.html)

# New GMOs in Europe

EC website of the NGT proposal (Crispr), 2024:

"A NGT plant is considered equivalent to conventional plants when it differs from the recipient/parental plant by **no more than 20 genetic modifications** of the types referred to in points 1 to 5, in any DNA sequence sharing sequence similarity with the targeted site that can be **predicted by bioinformatic tools**"

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1 - No way to exclude more than the “computer simulated” mutations

2 - In SARS-CoV-2, one mutation, N439K: changing affinity to a cell receptor.

Harvey, WT, et al. 2021 “SARS-CoV-2 variants, spike mutations and immune escape”, *Nature Reviews Microbiology*, vol.19

# More Theory and Epistemology

**The GMO's abuse: a direct consequence of**

- **the *Central Dogma***

- **the “*exact stereospecific macro-molecular interactions*”**

(“necessary to transmit **information**”, Monod, 1970)

(un omaggio a *Marcello Buiatti*:

“Nulla di più pratico in scienza di una buona teoria”, Boltzman)



# Digital Information? Shannon vs. Turing-Kolmogorof

An opposition, as for *complexity* = (amount of) digital information:

Maynard-Smith J. *The idea of Information in Biology*. **The Quart. Rev. Biology**.  
74 : 495, 1999. (See Longo 2019 *Information at the Threshold of*  
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## 1. Information Transmission and Physics (Shannon-Brillouin):

**highly improbable = higher information = higher “order”**

(thus, **higher entropy = higher probability**, as in Physics).

Or, *information is negentropy* (Brillouin, 1956), thus it is  
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## 2. Algorithms (Turing - Kolmogorof): A finite incompressible (highly disordered) sequence has the *highest complexity*:

**higher entropy = higher complexity = higher information**

Or, an organized message (highly improbable) is compressible, thus ***less information***: *information is co-variant* with entropy<sub>5</sub>

# Digital Information?

Turing and Shannon's Information:

**Dualism:** Hardware *vs* Software (from smoke signs to Computers),  
a fantastic and powerful invention, *for machines*

The “**radical materiality** of life”:

- These macromolecules (DNA....)
- These membranes...
- This “flesh” as such...
- e.g. Water; Role of torsions and pressures on chromatine

(Lesne, A., Victor, J.M., 2006)

**Confusing:**

- *Flows* or ***gradients of flows*** (depending on matter) with information
- Information's dualism with “**non-specificity**”  
(e.g. endocrine disruptors: they act with different probabilities)

# **From Geodetics to “Imperative Pythagorism”**

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Weyl: “any fundamental principle in physics is a symmetry principle”  
**Conservation laws** as *continuous* symmetries (Noether, 1918)

Continuous vs Discrete phase spaces: Riemann, Noether, Weyl...:  
Einstein-Bohr debate, 1930s:  
*when the “discrete” steps in, causality goes out*

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Continuous vs Discrete phase spaces: Riemann, Noether, Weyl...:  
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*when the “discrete” steps in, causality goes out*

**Programming** is always *imperative*: programs give orders even in  
*Functional and Object Oriented Languages* (Church-Rosser and  
Normalization theorems) + *Compilers & Operating Systems*

**Control and promise** (everything):

J. Doudna (Nobel Award 2020), S. H. Sternberg "*A Crack in Creation:  
Gene Editing and the Unthinkable Power to Control Evolution*", 2017.  
M. Audétat, ed. "*Pourquoi tant de promesses?*", 2015.

# The indirect fall-out of “bad” metaphors

E. Fox-Keller (2020) on the information & programming metaphors:

- it “illustrates and explicates the **aggressive, competitive** aspects of ecology, the **passivity** of Nature, the **causal powers** of DNA”

Yes: Programming is always *imperative*: programs **give orders**

- Yet ... “it has been evocative and creative, and indeed provided *crucial incentive*”

Incentive? Applications? ....

*Longo-Mossio* comparison, 2020:



# The geo-centric (Ptolemaic) astronomy

Remarkable **observations** (Ptolemaic Astronomy):

- when Jupiter and Saturn are in conjunction then Mars necessarily appears in this or that constellation.
- differences in the Jupiter–Mars proximity induce differences in the relative position of Mars, with great regularity (*Just looking at the sky*).

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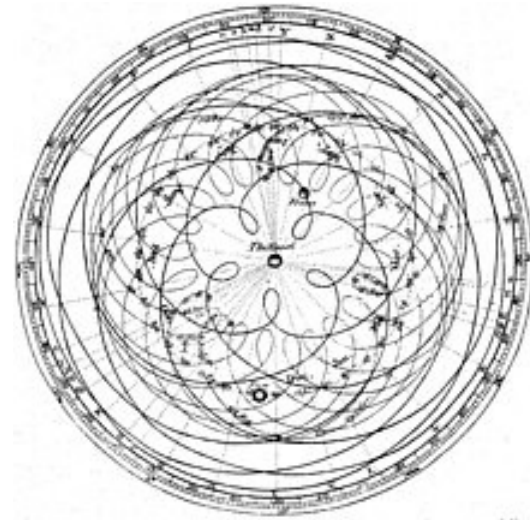
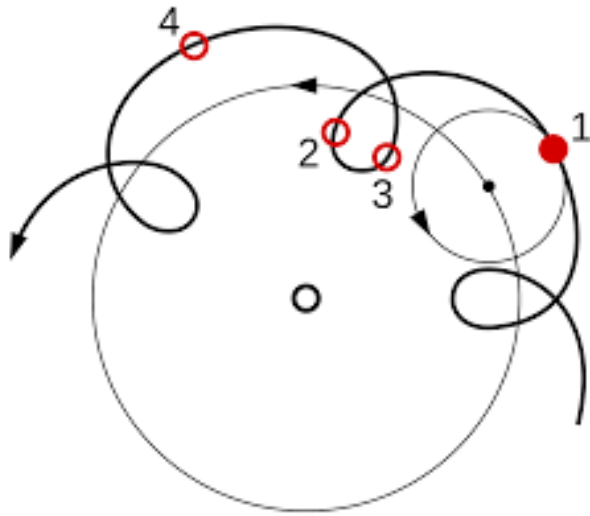
**Ibn Yunus** (Egypt, ca. 1000 AD):

- spherical trigonometry and computed practically all visible relative positions of planets and celestial bodies
- immense astronomical tables, the Alfonsine Tables (Catholic Spain, 1483), widely used in navigation (*He deserved a Nobel Award in Astronomy*).

# The geo-centric (Ptolemaic) astronomy

**Major “waste of time”** (and knowledge distortion):

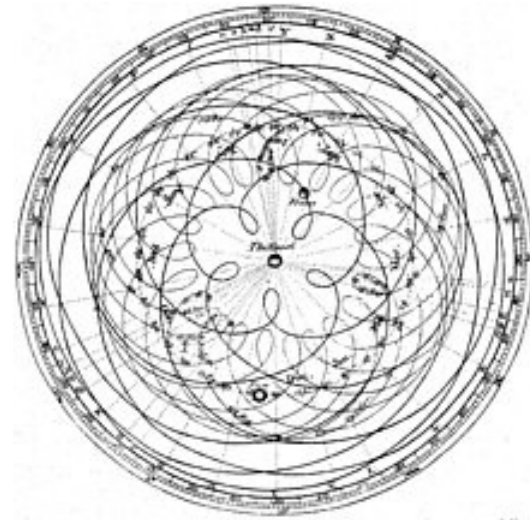
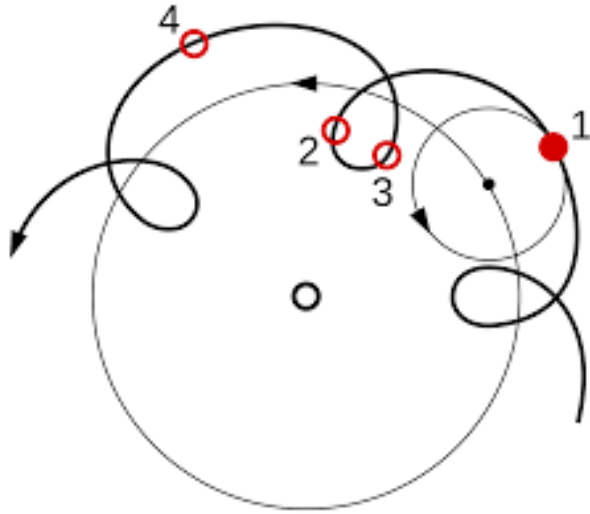
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- but *incompatible with* Galileo’s **inertia**



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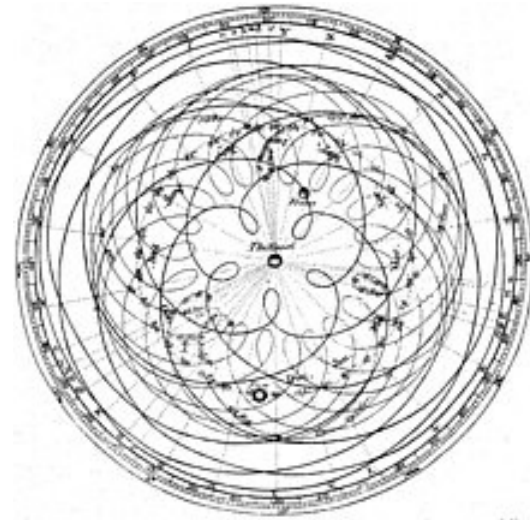
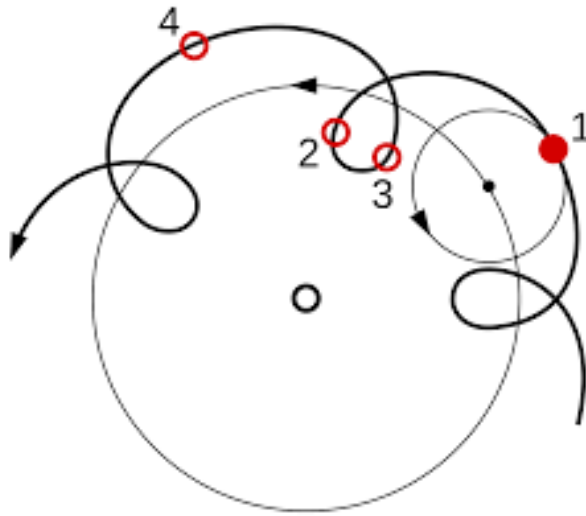
**Astrology**

Islami, Longo, 2017; Longo, Mossio, 2020

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## Astrology

Islami, Longo, 2017; Longo, Mossio, 2020

“Genetic astrology” (Jablonka E., 2013):

- R. Plomin (2019) *Blueprint: How DNA Makes Us Who We Are*. MIT Press
- J. Doudna and S. Sternberg (2017) *A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution*. London
- J. Doudna on Youtube: “defeat (almost) all diseases and... death”

# Today's consequences: the New GMO's

J. Doudna's 2017 book, **CRISPR-Cas9**: *fantastic tool*, but...

“**control** evolution", by re-reprogramming DNA

by "editing it, **exactly**", "like with **scissors**"... (*metaphors...*)

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In laboratories:

1 - they **act on large numbers of cells**, by "choosing" the cells where the process has worked (cherry-picking)

2 - even **gene knockout**, which has been known to do for decades, may not work (it may not succeed and the damaged genes continue to produce proteins, many of which are still functional),

3 – unpredictable **collateral damages**; editing-**resistance**

4 – **genomic instability**, when CRISPR-Cas9 is applied to animals

Bock, C, et al., *Nature Reviews*, vol. 2, pp. 1–2, 2022

Smits, AH, et al., *Nature Methods*, vol. 16, 2019

Burgio G., et al. *Trends in Genetics*, vol. 36, 2020

Mehta et al. *Genome Biology*, vol. 20, art. 8, 2019

# Today's consequences: the New GMO's

More Critiques:

- often **unreachable** genetic targets;
- **off-target** effects;
- the intrinsic **unpredictability** of many *phenotypic* consequences of such a powerful technique.

Chaudhari et al., *The CRISPR Journal*, vol. 3, 2020;

Höijer I. et al., *Genome Biol*, vol. 21 2020,

Modrzejewski D. et al. *Front Plant Sci*, vol. 11 2020

Longo G. Les nouveaux organismes génétiquement modifiés (NOGM) : pour un “principe de précaution scientifique”, *Philosophy World Democracy*, 9, 2023



# GMOs in Europe, summary

The EC website of the NGT proposal, summary and background:

[https://food.ec.europa.eu/plants/genetically-modified-organisms/new-techniques-biotechnology\\_en](https://food.ec.europa.eu/plants/genetically-modified-organisms/new-techniques-biotechnology_en)

A page with FAQs about it, also from the EC:

[https://ec.europa.eu/commission/presscorner/detail/en/qanda\\_23\\_3568](https://ec.europa.eu/commission/presscorner/detail/en/qanda_23_3568)

And the main NGO reactions:

<https://friendsoftheearth.eu/press-release/eu-commissions-new-gmos-proposal-sacrifices-consumers-rights-and-puts-nature-at-risk/>

<https://www.greenpeace.org/eu-unit/issues/nature-food/46731/gmo-deregulation-disregards-safety-and-consumer-rights-greenpeace/>

The discussion is still open (Commission/Parliament), October 2024

**Huge amounts of money joins an incomplete, vague... aggressive  
“theoretical” frame**

# Epistemic Corruption

*From GMOs:*

“Investigation reveals mass profiling of 'opponents' of the agrochemical industry” (500 researchers, several from ENSSER)

By S. Foucart, M. Gibbs (**Le Monde**) and  
E. DeBre (**Gardian**), September 28, 2024

[https://www.lemonde.fr/en/environment/article/2024/09/27/investigation-reveals-mass-profiling-of-opponents-of-the-agrochemical-industry\\_6727428\\_114.html](https://www.lemonde.fr/en/environment/article/2024/09/27/investigation-reveals-mass-profiling-of-opponents-of-the-agrochemical-industry_6727428_114.html)

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*To Human Health:*

“Epistemic Corruption, the Pharmaceutical Industry, and the Body of Medical Science” (ghost managed medicine)

“When a knowledge system importantly loses integrity, ceasing to provide trusted knowledge, we can label this epistemic corruption. ... abundant evidence that the involvement of pharmaceutical companies corrupts medical science...”

S. Sismondo, **Frontiers Res. Metr. Anal.**, 6, 2021;....

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*To Human Health:*      **Junction:** *abuse of antibiotics* (USA: 70% ...)

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*Alternative paths*  
the theoretical contribution

# Towards a Theory of Organisms

*Darwin's principles at the organismal level:*

1 - **Reproduction** with variation and motility (*cell's default state*)

*under massive (and divers) constraints:*

cell-to-cell, tissue (tensegrity...), hormonal system  
e.g.: from hearth to... intestine epithelia

2 – **Selection** (*as exclusion of the incompatible*)

(predecessor: Edelman's Neural Darwinism; the Immune System)

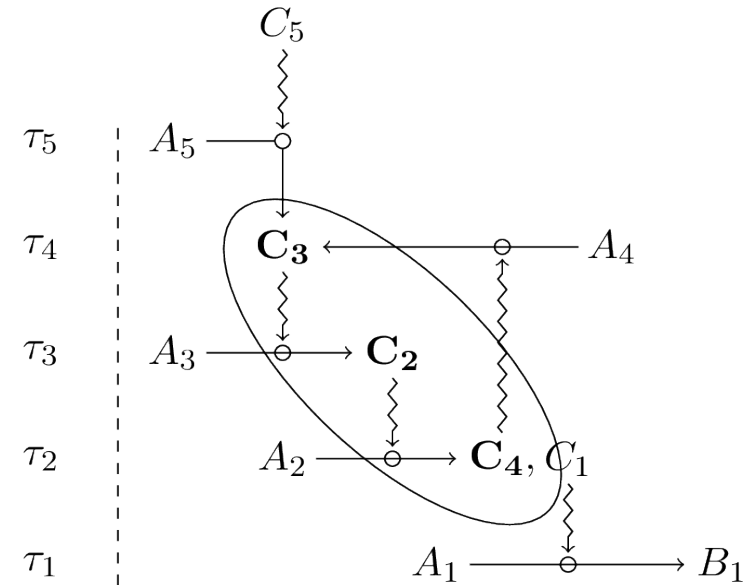
Soto A., Longo G. (guest eds), **From the century of the genome to the century of the organism: New theoretical approaches** Special issue of *Progress in Biophysics and Molecular Biology*, 122, 1, 2016.

## *Alternative paths: Closure of Constraints*

Noble's Biological Relativity:  
*no privileged causal level in*  
*Biology* (2012: molecular, cell,...  
ecosystemic). **No Driving Level**

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Activity (flows) canalized by  
*constraints* produced by flows (Darwin)

- Montévil, Mossio, *Theor. Bio.*, 2015
- Soto, Longo, Noble (eds), *PBMB*, 2016
- Bich L., Mossio M., Soto A. **Glycemia Regulation** *Frontiers Physiology* 2020



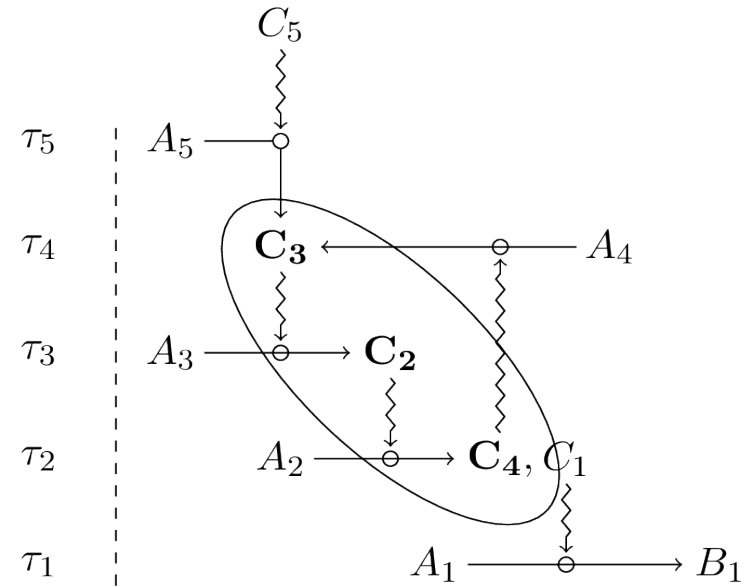
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The DNA and the subsequent  
molecular cascades do not  
completely determine the  
organismal dynamics,

*since the organismal dynamics  
contribute to determine the DNA  
and the subsequent molecular  
cascades*

(Sharma A. et al., (2023) *Nature*,  
622, October 12, 321)



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- Bich L., Mossio M., Soto A. **Glycemia Regulation**, *Frontiers Physiology*, 2020

## Some readings

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Fox Keller, E. **The century of the gene,** Harvard U. P., 2000.

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- Longo G., Montévil M., **Perspectives on Organisms: Biological Time, Symmetries and Singularities**, *Springer*, Berlin, 2014.
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- Longo G., **Le cauchemar de Prométhée. Les sciences et leurs limites**, Paris, *PUF*, 2023.

## Non-specificity (and internalization of past contexts)

**Precursor erythroid cells** differentiate into red blood cells when their erythropoietin receptors bind with *erythropoietin*

*However*, precursor erythroid cells which have been engineered to lack erythropoietin receptors and instead have receptors for prolactin do **differentiate into red blood cells when they are exposed to prolactin**, a hormone associated with **lactation** (Socolovsky et al., 1997)

*Conversely*, **mammary epithelial cells** engineered to have a **hybrid receptor** with an extracellular part of a prolactin receptor and an intracellular part of an **erythropoietin receptor**. These engineered cells respond like normal mammary epithelial cells to prolactin

(Briskin et al., 2002).