Information in Biology: metaphor or model?
Biological Organization as “Anti-entropy”

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Francis Bailly, Giuseppe Longo. Mathématiques et sciences de la nature. La singularité physique du vivant. Hermann, Paris, 2006. (Soon in English)
Since the ‘40s: **Information, the new observable**

Main observable in Physics: **energy**

- From *Galileo inertia* (**energy** conservation) to
- *Hamilton least action principle* (geodetics) and
- *Quantum Spectral Analysis of energy*

What about Biological Evolution and Ontogenesis?

**Information!**
That is, *biological organization = information*

Recent alternatives, *from Physics*:
organization as **coherence structures** in Critical Transitions
Schrödinger, What is life? (1944), part I

- Schrödinger’s remark on drosophila eye colour «We call … “locus”, or, if we think to the hypothetical material structure which serves as support of it, a “gene”. In my opinion, the fundamental concept is more the difference of properties than the property itself »

The (great) physicist attitude: propose general principles (Galileo’s gravitation and inertia… geodetics principles).
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• Schrödinger’s remark on drosophila eye colour «We call … “locus”, or, if we think to the hypothetical material structure which serves as support of it, a “gene”. In my opinion, the fundamental concept is more the difference of properties than the property itself »

The (great) physicist attitude: propose general principles (Galileo’s gravitation and inertia… geodetics principles).

• Chromosomes: a code-script (encoded information?) « In calling the structure of the chromosomes a code-script, we mean that the all-penetrating mind, once conceived by Laplace… could tell from their structure how the egg would develop… . »

Schrödinger’s right consequences of his principles! Today, the code-script has been fully decoded…
Physical Determination (Classical)

Laplace’s view:

A) determination $\Rightarrow$ predictibility

and

B) determination $\neq$ randomness

[Laplace, Philosophie des Probabilités, 1786]
Physical Determination (Classical)

Laplace’s view:

A) determination ⇒ predictibility

and

B) determination ≠ randomness

[Laplace, Philosophie des Probabilités, 1786]

[J. Monod, Le hasard et la nécessité, 1970]

Aspects of the Laplacian view:

1. Central dogma, ‘58: linear unidirectional “information” from DNA to proteins (predictable since/thus “programmable”).

2. The “one gene - one protein” theory since the ‘30s (Baedle and Tatum), till Perutz[1987]
Consequences of informational paradigms on Embryogenesis and Physiology:

Bottom up

organisms

 tissues and organs

 cells

 organelles

Subcellular and molecular data and mechanisms
Consequences of informational paradigms on Embryogenesis and Physiology:

Both the
• the one gene - one protein hypothesis and
• the Central Dogma
Provide, by their linearity, a conceptual reversibility (if not a “time” reversibility) of processes.

Thus from a character one should be able to “revert” to the gene (or segment of DNA)
Thus: the gene of…
The DNA, the locus of Digital Information + Central Dogma + its Conceptually reversible extension

*The gene of:*

- The *gene of marital fidelity* (Young et al., *Nature*, 400, 766-788, 1999)
- **Obesity** (N.Y. Rockefeller Center, 2000: 20 million dollars?)
The DNA, the locus of Digital Information + Central Dogma + its Conceptually reversible extension

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- **Obesity** (N.Y. Rockefeller Center, 2000: 20 million dollars?)

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- Sociability
- Longevity
- Seduction
- Mathematics
- **Academic freedom** (??)

[Charles Auffray, *Qu’est-ce qu’un gène?*, 2004]
Information? Just a metaphor...
Information? Just a metaphor...

• If a mathematical notion is used with rigor, one sees the “shortfalls”, the conceptual and physico-mathematical consequences… (like Schrödinger and … Turing’s imitation, 1950, vs. modelling, 1952).

• While the mathematical model simplifies, the metaphor complicates. It adds a track for mind, it (implicitly) refers to a another conceptual framework, a universe of methods and of knowledge that one transfers onto the intended one.

• Example: information (Shannon//Kolmogorof) is “not sensitive to coding”, while “morphological (geometric) organization” is “sensitive to coding” (e.g. Cartesian dimension, folding …)
The myth (also a consequence of “digital information”)

- the *stability* and the *organisation* of the DNA and the subsequent molecular cascades *completely determines* the *stability* and the *organisation* of the cell and the organism, by its complete informational content.
The myth (also a consequence of “digital information”)

• the stability and the organisation of the DNA and the subsequent molecular cascades completely determines the stability and the organisation of the cell and the organism, by its complete informational content.

False! Since:

• the stability and the organisation of the cell and the organism causally contribute to the stability and the organisation of the DNA and the subsequent molecular cascades

(see, say, [Fox Keller The century of the gene, 2000]; [Brett et al. 2001; Bartel, 2004; Longo, Tendero, 2007])

Yet, incompleteness of molecular analyses, does not mean “useless”!
From Physics to Biology by “Conceptual Dualities”
Dualities in Physics vs Biology
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1. **Physics**: variation (gaussian…)
   Biology: **variability** (individuation; the main invariant ?)
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   Biology: *generic trajectories* (compatible) and *specific objects*
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3. **Physical randomness**: *deterministic impredictibility* or *intrinsic indetermination* within a given phase space
   
   Biological randomness: *intrinsic indetermination* due to change of the phase space - phylogensis (ontogenesis?)
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4. **Physics**: *energy* as operator $Hf$, *time* as parameter $f(t,x)$
   - **Biology**: *energy as parameter, time as operator* “anti-entropy” (dual to entropy) [Bailly, Longo, 2009]
Schrödinger, the hinted proposal:

- « … let’s try to hint to the possible meaning of the principle of entropy at the global scale of a living organism, while forgetting for the time being all what we know on chromosomes »

Our two assumptions:

1. Time identified with “entropy production”
2. A new observable:
   - **anti-entropy** as a quantification of **organization** (complexity), a proper **biological observable**
Schrödinger, part II: the global view

Schrödinger’s suggestions, 1944:
A footnote: “… negative entropy as part of Gibbs Free Energy”
   \( G = H - TS \), where \( H = U + PV \)
“(negative) entropy as (part of)
   Gibbs Free Energy” ≠ Shannon’s information !”
(it is defined by different principles)

Our approach:
A quantifiable notion of organization or complexity as anti-entropy,
inspired by thermodynamics, but adding one more principle to the
three existing ones … %%
Beyond Schroedinger’s « negative entropy »: 
Anti-entropy

Anti-entropy not negative entropy (a lowering of entropy) but a new observable:

biological organization vs. energy in physics.

W.r. to physics as a further reason for the irreversibility of time

A (wild analogy): anti-matter … %

In J. of Biological Systems, 17, 1, 2009. (downloadable)
Anti-matter (and anti-entropy) as different “objects”

Energy in anti-matter has the same dimension and the opposite sign (the negative solution of Dirac’s equation)

- the opposite sign of charge of matter.

It is not a lowering of energy, but a different observable:

- positron (anti-electron) yields negative energy (positive charge),
- anti-proton yields negative energy (negative charge)

Thus, not just a different state of the electron or the proton, but different quanta

related to destruction of matter and production of energy, the double!
Organization or Complexity $K$ as anti-entropy, a new *biological* observable

- Complexity $K$ as *anti-entropy* $S^-$, that is $-K = S^-$, to be defined by the *existence and interaction of the different levels of organization* and specified as

$$K = \alpha K_c + \beta K_m + \gamma K_f$$

- $K_c$ (combinatorial complexity)
- $K_m$ (phenotipic complexity)
- $K_f$ (network complexity)

$K$: a new observable, yet *same dimension* as $S$, *handled by*

1. Extra *principles* for $K$, *(in-*)equalities
2. A “balance equation”…. 

*Extensions* of physical theories in the sense of Logic…
Use $K$ (and $S^+$) in (in-)equalities
(add an observable and a principle)

1. A **principle** of “existence and maintenance of anti-entropy” $K$:
   
   $K \geq 0 \quad \text{and} \quad \frac{dK}{dt} \geq 0$  
   (1)
Use $K$ (and $S^+$) in (in-)equalities
(add an observable, a principle and an equation)

1. A **principle** of “existence and maintenance of anti-entropy” $K$:
   $$K \geq 0 \quad \text{and} \quad \frac{dK}{dt} \geq 0 \quad (1)$$

2. A **balance equation** relating metabolism, $R$, to entropies $K+S^+$,
   $$R = \text{ad}M/dt + T(dK/dt - dS^+/dt) + T\sigma \quad (2)$$
Use \( K \) (and \( S^+ \)) in (in-)equalities
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2. A **balance equation** relating metabolism, \( R \), to entropies \( K+S^+ \),
   \[
   R = a dM/dt + T (dK/dt - dS^+ /dt) + T \sigma \quad (2)
   \]
   *to be derived from:*
   metabolism \( [R] \) = the difference between the fluxes \( J_G \) of free energy \( G \) entering and exiting though the surface \( \Sigma \),
   \[
   R = \Sigma (J_G(x) - J_G(x+dx)) = - \Sigma dx (\text{div} J_G)
   \]
   *and from a conservation equation:*
   \[
   - \text{div} J_G = dG/dt + T \sigma \quad (\sigma \text{ is the speed of entropy prod.})
   \]
More from: F. Bailly, G. Longo. *Biological Organization and Anti-Entropy* ...

(add an observable and a principle)

\[
R = - \text{div} J_G; \quad - \text{div} J_G = dG/dt + T\sigma
\]

where: \( G \) is Gibbs free energy; \( \sigma \) speed of entropy production

Thus, usually:
\[
G = H - TS
\]

But, now \( S \) is total “entropy” (now \( S = K + S^+ \)), \( T \) is temperature, \( H = U + PV \) system’s enthalpy

(\( U \) is the internal energy, \( P \) and \( V \) are pressure and volume)

and we may consider \( H \) to be the mass, \( M \), modulo a dimensional constant \( a \) (\( H = aM \)).

Thus:
\[
R = adM/dt + T(dK/dt - dS^+/dt) + T\sigma \quad (2, \text{above})
\]
Summary:
(add an observable, a principle, extend an equation)

1. A principle of “existence and maintenance of anti-entropy” \( K \):
   \[ K \geq 0 \quad and \quad dK/dt \geq 0 \quad (1) \]

2. A balance equation relating metabolism, \( R \), to entropies \( K+S^+ \),
   \[ R = adM/dt + T(dK/dt - dS^+/dt) + T\sigma \quad (2) \]

A “classical” derivation (energy conservation principles)

from:
\[ R = - \sum dx(divJ_G); \quad -divJ_G = dG/dt + T\sigma \]

where: \( G \) is Gibbs free energy; \( \sigma \) speed of entropy production

But:

with the extra observable \( K \) (anti-entropy)
Focus on $T\sigma$ in (2)

1. A principle of “existence and maintenance of anti-entropy” $K$:
   \[ K \geq 0 \quad \text{and} \quad \frac{dK}{dt} \geq 0 \quad (1) \]

2. A balance equation relating metabolism, $R$, to entropies $K^+ + S^+$,
   \[ R = a\frac{dM}{dt} + T(\frac{dK}{dt} - \frac{dS^+}{dt}) + T\sigma \quad (2) \]
Focus on $T\sigma$ in (2)

1. A **principle** of “existence and maintenance of anti-entropy” $K$:
   
   $K \geq 0 \text{ and } dK/dt \geq 0$ \hspace{1cm} (1)

2. A **balance equation** relating metabolism, $R$, to entropies $K+S^+$,
   
   $R = adM/dt + T(dK/dt - dS^+/dt) + T\sigma$ \hspace{1cm} (2)

$T\sigma$ is the **rate of entropy production** ($\times T$, temperature), a fundamental dimension in **dissipative systems**

(i.e. far from equilibrium, permanent exchange of energy and mater; Prigogine, since 1940’s, [Nicolis, Prigogine, 1977])

Where $\sigma$ is **global** observable, which depends on all irreversible processes

Towards an application... (out of two): Gould
Gould’s growth of biological complexity
[Wonderful Life, 1989]
How to understand increasing complexity?

No way to explain this in terms of random mutations (only):

1. DNA’s (genotype) **random mutations** statistically have probability 0 to cause globally increasing complexity of phenotype (examples: mayfly (ephemeral); equus…[Longo, Tendero, 2007])

2. Darwin’s evolution is **selection of the incompatible** (“the best” makes no general sense)

3. Greater probabilities of **survival** and reproduction **do not imply** greater **complexity** (bacteria, … lizard…) [Maynard-Smith, 1969]

   *Gould's idea: symmetry breaking in a diffusion*...
Morphological Complexity along phylogenesis and embryogenesis

Specify (quantify) Gould’s informal “complexity” as morphological complexity $K = - K$

\[ K = \alpha K_c + \beta K_m + \gamma K_f \]

- $K_c$ (combinatorial complexity) = cellular combinatorics as differentiations between cellular lineages (tissues)
- $K_m$ (phenotypic complexity) = topological forms and structures (e.g., connexity and fractal structures)
- $K_f$ (functional complexity) = metabolic relations, neuronal and cellular (interaction) networks

(Caenorhabditis elegans, see [Bailly, Longo, 2009])
Some technicalities: how to derive the diffusion equation

\textit{Schrödinger’s operatorial approach:}

from total energy \( E = \frac{p^2}{2m} + V(x) \) \hspace{1cm} (1)

with \( V(x) \) potential

\( (e.g. \ E = \frac{p^2}{2m} + \frac{kx^2}{2}, \text{ the harmonic oscillator}) \)

associate \( E \Rightarrow i\hbar \partial / \partial t \) \text{ and } \( p \Rightarrow i\hbar \partial / \partial x \)

and obtain:

\[
i\hbar \frac{\partial \psi}{\partial t} = \hbar^2 \frac{\partial^2 \psi}{\partial x^2} + v \psi \quad \text{(Schrödinger Eq.)}
\]
Some technicalities: how to derive the *diffusion* equation

**Schrödinger’s operatorial approach:**

From total energy \( E = \frac{p^2}{2m} + V(x) \) (1)

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and obtain:

\[
\text{i}\hbar \frac{\partial \psi}{\partial t} = \hbar^2 \frac{\partial^2 \psi}{\partial x^2} + v \psi \quad \text{(Schrödinger Eq.)}
\]

*Our operatorial approach applies to \( T\sigma \), a power :

thus \( T\sigma \) *is a product of forces by fluxes* ( \( \sim \) the square of a mass)

\[
T\sigma = \zeta_b M^2 + T\sigma_{0b} \quad (2) \text{ the analog of (1)}
\]
Some technicalities: how to derive the diffusion equation

Our operatorial approach:

from total entropy production \[ T\sigma = \xi_b M^2 + T\sigma_{0b} , \]
where \[ T\sigma \] has the role of \( E \) and \[ M \] the role of \( p \),
associate \( T\sigma \Rightarrow \partial/\partial t \) and \( M \Rightarrow \partial/\partial K \) \((*)\)

(cf. Schrödinger’s operatorial transformations:
associate \( E \Rightarrow \text{ih}\partial/\partial t \) and \( p \Rightarrow \text{ih}\partial/\partial x \) \((**))\)

Thus we obtain:

\[ \partial m/\partial t = D_b \partial^2 m/\partial K^2 + \alpha_b m \quad (3) \]

where \( m \) is bio-mass density

(cf. \( \text{ih}\partial\psi/\partial t = \hbar^2 \partial^2 \psi/\partial x^2 + v \psi \) (Schrödinger Eq.)
in the complex field)
A diffusion equation:
\[ \frac{\partial m}{\partial t} = D_b \frac{\partial^2 m}{\partial K^2} + a_b m(t,K) \]  \hspace{1cm} (3)

A solution
\[ m(t,K) = \left(\frac{A}{\sqrt{t}}\right) \exp(at) \exp(-K^2/4Dt) \]

models Gould’s asymmetric diagram for Complexity in Evolution (diffusion \(\Rightarrow\) random paths...), also along \(t\):
(biomass and the left wall for complexity, archeobacteria original formation)

F. Bailly, G. Longo. Biological Organization and Anti-Entropy…

Next picture by Maël Montevil:
Theoretical changes w.r. to Physics in
\[
\frac{\partial m}{\partial t} = D_b \frac{\partial^2 m}{\partial K^2} + \alpha_b m
\]

With regard to the “analog” of the physical Hamiltonian:

\[ T_\sigma = \zeta_b M^2 + T_\sigma_{0b} \]

a) \( T_\sigma \) plays role of *physical energy* (it is actually a power)
b) \( M \) (bio-mass) plays the role of *momentum* \( p \) (\( M \) squared intervenes in \( T_\sigma \), just as \( p \) does in \( E \)).

As for the operatorial approach:

1. **Entropy variation**, multiplied by temperature, instead of *physical energy* (becomes \( \frac{\partial}{\partial t} \))
2. **(Bio-)Mass** instead of *momentum* (which is proportional to a mass) and (becomes \( \frac{\partial^2}{\partial K^2} \)),
3. **Anti-entropy** or complexity instead of *space* (\( K \) instead of \( x \) in \( \frac{\partial^2}{\partial K^2} \)) *(real coefficients instead of complex ones)*
**K_c for *Caenorhabditis elegans***

\[ N(t) \text{ total number of cells (at time } t) \]

\[ n_j(t) \text{ cells of lineage } j \text{ (at time } t) \]

\[ K_c \text{ as the log of } \frac{N!}{\prod n_j!} \]

\[ K_c = k_B [\text{Log}(N!) - \sum_j \text{Log}(n_j!)] \]
$K_c$ for *Caenorhabditis elegans*

$K_c = k_B \left[ \log(N!) - \sum_j \log(n_j!) \right]$
More (wild) dualities from Physics towards Biology

.... by conceptual dualities:

In Physics, crucial:

absence of origin of time (and space)

constitution of invariants, i.e. conservation of observable quantities (Noether’s theorems, ‘20), e.g. Energy.

In Biology, crucial:

existence of an origin of time (and space)
From Physics towards Biology ? …

Pauli's Theorem (1933):
“The lower bound for the energy operator implies that time is not an operator, but a parameter”

In Physics: no origin of time (energy conservation)

In Biology: existence of an origin of time (or “time has a lower bound”)

Question: if time an operator (= the setting up of organization) does this implies that energy cannot be an operator, but a parameter? (a theoretical justification of scaling laws ...
Summary and some Philosophy
(Physical vs. Biological observables)
*in our three (correlated) approaches:*

1 - *organization* or complexity as *anti-entropy* (This lecture)

2 - a *two dimensional time* (*not linear time*)

3 - *extended criticality* (*a physical oxymore*), *JBS*, 16, 2, 2008.

Common point to the approaches in 1, 2 and 3:

“Consistent” *extensions*, in the sense of Logic, *not* incompatible with current physical theories, *but not realized*:

1: “=“ instead of “≤” (*anti-entropy goes to 0*)
2: collapse the extra dimension (*a time bifurcation*);
3: contract the extension of criticality (*from interval to point*).
“Methodological” conclusion

... back to:

The dogma: « life can be explained on the basis of the existing laws of Physics » [Perutz, 1987].

(Galileo, Einstein, Bohr ?…)

Confusing the ontological stand and the theoretical issue: a Theoretical issue, not an Ontological one…

Do we want to replace it by the opposite dogma?

No, but this dogma is not “unification” (nor “reduction”…), but a prejudice concerning existing principles.

(e.g. of “unifications/reductions”: Relativistic/Quantum fields; Thermodynamic/statistical physics; Sub-lunar/supra-lunar…)
Fundamental = Elementary ?

The principles:

The *world* is made out of “solid bricks”, one on top of the other…

The *organism* is made out of molecules… (like Galileo and Einstein’s falling bodies?)

   (in Logic: a *predicativist* fashion, solid bricks one on top of the other)

Moreover:

   The elementary *and* simple

   vs.

   The elementary *and* complex (Bio + Q. Phys)
More lessons from Physics

• **H. Weyl** on the **epistemological** lesson of Relativity Theory:
  “Objective knowledge begins when the subject explicitly lays the
  *reference system* and the *measure*”
  (and their relations by *Gauge Theory*)

**Quantum Physics** relativizes even further the subject-object relation
(a polarity or entanglement): base or reference system *constituted in measure*

In **Biology**:
• is it a matter of the choice even of the observables and parameters? (complexity, time as a 2-dimensional operator…)
• within changing phase spaces? Randomness?
• Pauli’s theorem and the lower bound of time …
Some references

http://www.di.ens.fr/users/longo or Google: Giuseppe Longo


