La singularité physique du vivant, où en sommes nous ?

Les enjeux de l'aléatoire et du temps

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and Biology Department, Tufts Univ., Boston
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My motivations: **interfaces Maths-Phys-Bio**

From the foundation (and the philosophy) of Mathematics as **an annex of a Philosophy of Language,**

Towards an essential component of **a Philosophy of Knowledge,** actually, of **a Philosophy of Nature**

Aim:

- a constructive **epistemology of Mathematical Structures** (objects, categories, invariants, transformations …)
- a search for **unity** in science, also by **dualities, bridges** ...

Opening to theoretical foundations in Physics and Biology ...

Mathématiques et philo de la nature

Philosophy
of Mathematics
and
Natural Science

BY

HERMANN WEYL

REVISED AND AUGMENTED
ENGLISH EDITION
BASED ON A TRANSLATION BY
OLAF HELMER

PRINCETON
PRINCETON UNIVERSITY PRESS
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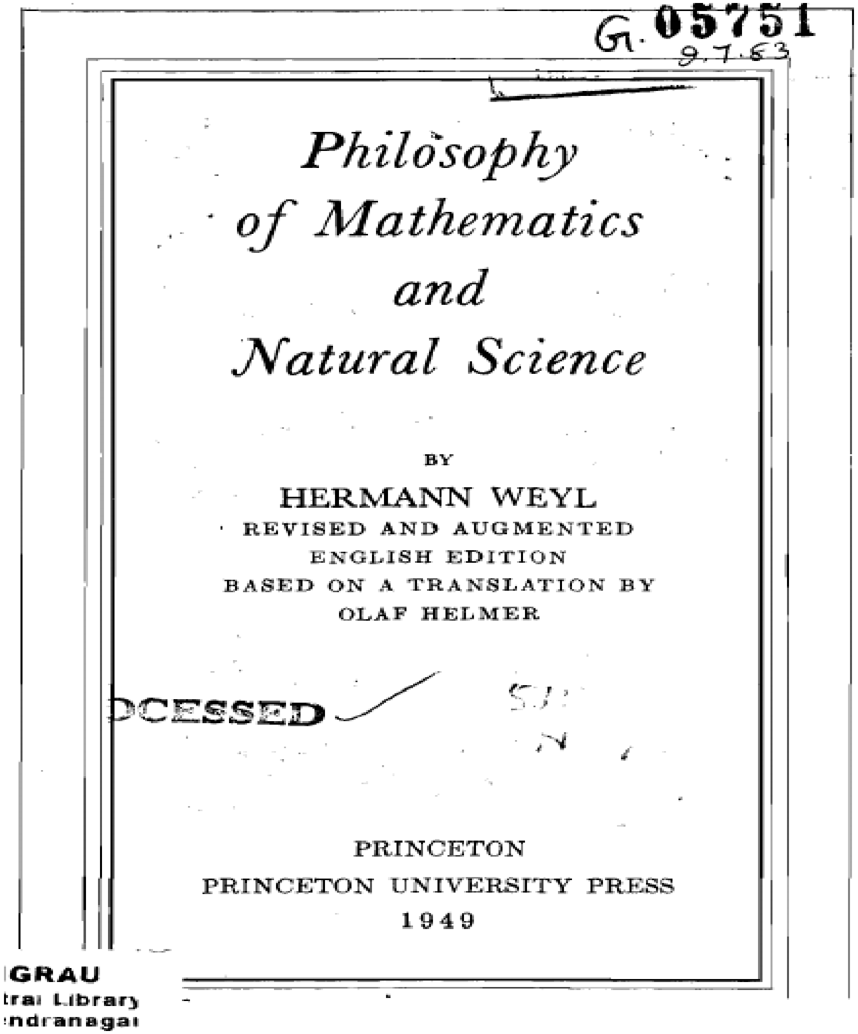
Mathématiques et philo de la nature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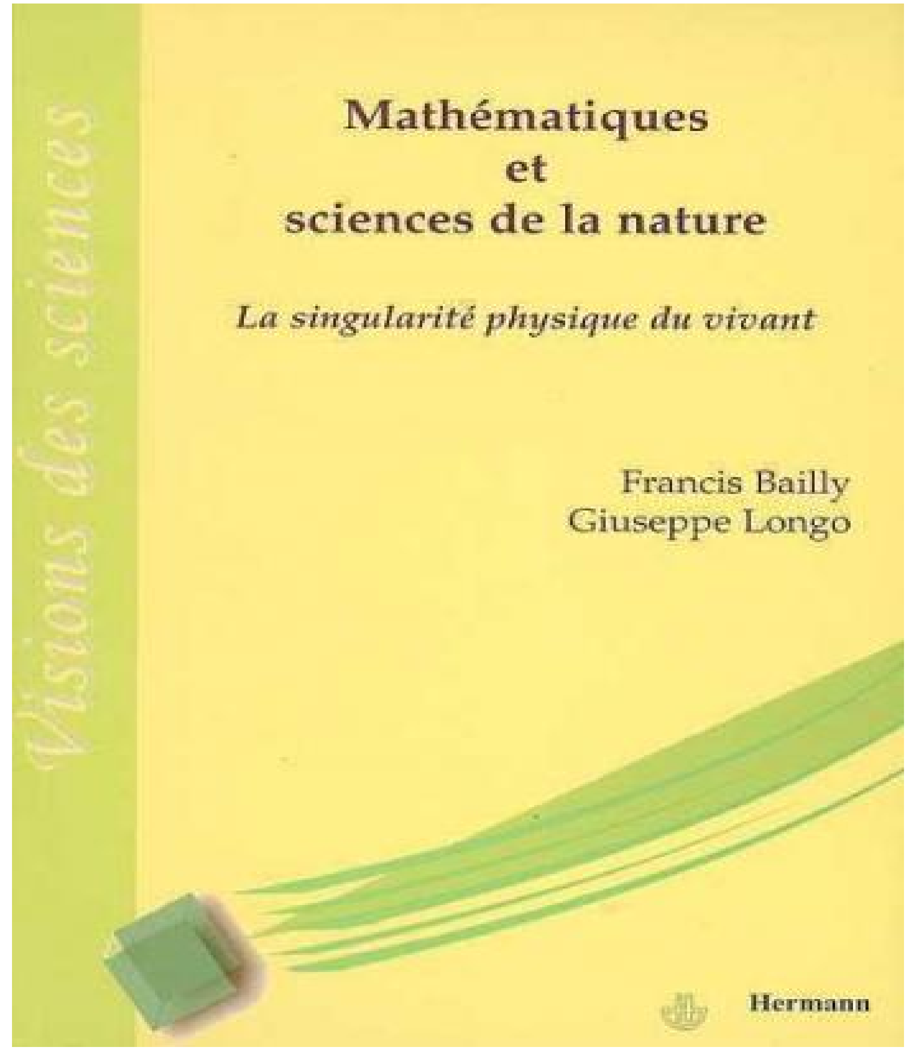

More work with T. Paul and M. Mugur-Schachther

Theory before or with Mathematics (like in Physics)

Main Themes:
Mathematics and Physics share the

Principles of Conceptual Constructions

e.g. the role of *invariants* and *transformations* in constructing Mathematical and Physical Theories:

- **Symmetries** = conservation laws, *steady flows* ...
- **Genericity** of objects and **specificity** of trajectories

Both fully specified by symmetries *and* at the infinite limit ...

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Beyond **causality**, in Physics: the lesson of Relativity:
« Causes become interactions and these interactions themselves constitute the fabric of the universe of their manifestations, its geometry: modifying this fabric appears to cause the interactions to change; changing the interactions modifies the fabric » [Bailly, Longo, 2006, cap 1.3.5]

… and in Biology ?

Theory before or with Mathematics (like in Physics)

I. M. **Gelfand** in his **Kyoto Prize Lecture**, 1989 : The use of physico-mathematical tools in biology « is rather dangerous, because *it usually implies the priority of mathematical and computer modes over real biological systems*. In many cases, *models are considered as full substitutes for natural phenomena*, and become subjects of self-perpetuating studies »

Biological theorizing do not need be based on the same conceptual constructions as physics!

First Theretical Frames, *then*, if possible, mathematics ...

Yet, Mathematics is an open, ever ending construction.

Hints to the theoretical principles for "**specificity**", **time** and **randomness** ...

Specifying biological specificity

The molecular way :

« Necessarely **stereospecific** molecular interactions explain the structure of the code … a boolean algebra, like in computers » [Monod, 1970]

« Biological **specificity** must be entirely found in complementary combining regions on the interacting molecules » [Pauling, 1987]

Longo, G. 2018 The Biological Consequences of the Computational World: Mathematical Reflections on Cancer Biology. *Organisms. A journal in Biological Biology, 2018.*

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A (very) different perspective:

“macromolecular interactions are stochastic, they are given in probabilites and these probabilities depend on the context”
[Longo, Montévil, 2015] *from* Kupiec JJ (1983) ; Elowitz M. et al. (2002) ; Raj A.et al. (2008)

“**Biological specificity** is situated at the level of organisms (and *observable* phenotypes), beginning with *individual* cell and it is based on the historicity and contigency of each organism”. *(more later)*

Randomness: From Noise to Functional Randomness

The prevailing molecular/discrete-informational paradigms:

« l’évolution est due à du bruit » (Monod, 1971);
« …mauvais fonctionnement du programme génétique » (Jacob,'72)

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Noise Biology: *Statistical Physics* (critique: Bravi, Longo, 2015):
Fluctuations "average out", Central Limit Theorem, Law of Large Numbers

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Fluctuations "average out", Central Limit Theorem, Law of Large Numbers

Instead: **Randomness is not noise:**

It contributes to **variability** *which implies* **diversity** *and* **adaptability**
a component of **structural stability**
(e.g., a few individuals in a population, small numbers in species **…)**

where **adaptivity**, is possibly given by Darwin's "correlated variations"

The role of randomness in *Ontogenesis*

Diversity of Biological Stochasticity, by “small numbers”*:*

1. Drosophila's eyes: random distribution of photoreceptor, 800 ommatidia
2. Vertebrates' liver: (only?) average functionality of hepathocytes matters:

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2. Vertebrates' liver: (only?) average functionality of hepathocytes matters:
false! 50% (ana-)poly-plody, functional to diversity of toxic shocks (**500ml**)

3. (Large) Mammals' Lungs: *average* functionality of lung's cell, but also *diversity* of fractal and alveoli's structure is functional (adaptive) (Pocock,'06)
4. Immune System: its functionality is *in* **diversity** (Thomas et al. 2008).

Diversity by Plasticity:

from

eukaryotes' cytoskeleton (shaped + selected by gravitation, (Bizzarri et al.,'14))

to

(large) brains (shaped + selected by the ecosystemic interactions)

(Bravi, Longo, 2015)

The role of randomness in *Phylogenesis*

Integrate randomness in the **Theory** (analogy: Quantum Mechanics):

- An phylogenetic (and ontogenetic) trajectory is
  a cascade of changes of phenotypes and of biological organization**,**
  its result depends on this history (**specificity** of each organisms) (Villloutreix)

- A phylogenetic trajectory is scanned by **rare** events (which also change the Phase Space)

Randomness is **Unpredictability** w.r.t. to the **Intended Theory**

No absolute notions of Randomness:

Calude, C & Longo, G. "Classical, Quantum and Biological Randomness as Relative Unpredictability" *Natural Computing*, vol. 15, 2, 263–278, Springer, 2016

- Radomness in Evolution: the **unpredictable changes of Phase Space**... %

Back to *Physics*: What is a Phase Space ?

Back to *Physics*: What is a Phase Space ?

- *First*: Descartes, Newton invention of space (with Galileo's Relativity: invariance at constant speed)

  Kant's analysis: **space** (and time) are the a priori, the *condition of possibility* to do (mathematical) physics:

  e.g. write Newton's equations in space and time

- *Then*:

  XIX century (**Hamilton**, Gibbs, Poincaré …):

  A complete determination of physical processes requires

  space or time **parameters** *plus* a pertinent **observable**:

  (position, momentum) *or* (time, energy)

  two possible (classical) **Phase Spaces**

Main Theoretical Construction in Physics

The theoretical physicist's main job: **invent the right Phase Space**!

(i.e. propose the pertinent parameters and observables)

That is:

- Consider the invariant properties (conservation) and define the

Phase Space

as locus for the full determination of “trajectories”

(it may be very abstract, e.g. *infinite dimensional Hilbert* space in Quantum Mechanics, cf Statistical Mechanics)

Within these spaces, then mathematically define **specific** trajectories of **generic** objects

Diversity and Unity in Physical Theories

- **Physics:** *Different theories and Phase Space*s:
  Classical Mechanics (position and momentum)
  Thermodynamics (time; energy; entropy (not conserved))
  Relativity (Space***x***Time *add* Energy***x***Momentum Tensor)
  Quantum Mechanics (Hilbert Spaces, bounded operators)

- Each of these theory uses a
  pre-defined **Phase Space.** Unity: **conservation laws … :**

- ***An issue of symmetries*** (Noether's Theorems, 1920)
  Noether → Hamilton → Newton → Kepler ...
  Noether → Hamilton → Schrödinger …

Weyl's work on symmetries (Gauge Theory) and *foundations*.

Darwinian Evolution, a history: some principles

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« It is the theory which decides what can be observed.» A. Einstein

- Darwin's pertinent observables:
  phylogenetic trajectories of ***organisms*** and ***species*****,**

  In general: **organisms** and **phenotypes** (for us, this begins with the **cell**):
  history *dependent:* no pregiven list of observable phenotypes

Darwin's principles on *heredity*:

1. **Descent** *with* **modification** (cf. Buffon, Lamarck)
2. **Selection** (of the incompatible; i.e. death)

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Note: **1.** is a ***non-conservation*** *principle* (cf. Hamilton): thus, no way to propose an invariant **Phase Space** for the Theory

Longo, Montévil, Sonnenschein, Soto *In Search of Principles for a Theory of Organisms*, 2015

Partial Summary

Physics

*(by existing and **new** maths)*

Biology

(concepts? mathematics?)

Specific trajectories

Generic objets (= maths)

Fixed Phase Space (in each Th)

Partial Summary

Physics	**Biology**
*(by existing and **new** maths)*	*(concepts? mathematics?)*
Specific trajectories	Generic (possible) trajectories
Generic objets (= maths)	Specific (historical) objets
Fixed Phase Space (in each Th)	Changing Phase Space (Evolution)

The Theoretical Challenge: Invariance in Science

Mathematics: since Euclid’s symmetries to … Category Theory
a science of invariants and invariance preserving transformations

Physics: *conservation* properties, as *symmetries* (invariance):
– momentum, Galileo's **inertia**, (a **default state),**
– Energy ...

Information Theories: since *Morse*: independence of dimension,
independence of hardware and coding (*Turing* and *Shannon*)

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– Energy ...

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Contra, *in* **Biology**:
- **Trajectories** and organismal **structural stability** based also on *variability* and *diversity* (symmetry changes), which is **not noise**
- Radical **dependence of biological processes** on their ***material*** (physico-chemical) structure: DNA, RNA … membranes: the living state of matter

Our tentative "a priori": Theory first (like in Physics)

- **Default state**:
  « ***reproduction with variation*** and motility »

- **Principle**:
  « biological dynamics are the ***never identical iteration*** of a morphogenetic process »

  Longo, Montévil, Sonnenschein, Soto *In Search of Principles for a Theory of Organisms*, **Journal of Biosciences**, 2015

- **Biological organisation**:
  « ***organization with variation*** as closure of constraints»

  Montévil, Mossio, **Theor. Bio.,** 2015

These are **conditions of possibility** for constructing biological knowledge (the Kantian terminology of Phase Space, "a priori", *reversed*)

The "Phase Space" follows … more ongoing work … (Paul Villoutreix)

Summary

Physics

*(by existing and **new** maths)*

Biology

(concepts? mathematics?)

Stable theoretical symmetries

Specific trajectories

Generic objets

Fixed Phase Space

Anhistorical objects

Conservation principles

Randomness (in the Ph. Space)

Summary

Physics	**Biology**
*(by existing and **new** maths)*	*(concepts? mathematics?)*
Stable theoretical symmetries	Unstable theoretical symmetries
Specific trajectories	Generic (possible) trajectories
Generic objets	Specific (historical) objets
Fixed Phase Space	Changing Phase Space
Anhistorical objects	Historicity of objects
Conservation principles	Darwin's non conservation principle
Randomness (in the Ph. Space)	Randomness = unpred. of the Ph. Space

Question de temps

Question de temps

- Stress the correlations, in Physics**:**

  Random event

  Symmetry breaking

  Irreversibility of processes (time)

- From Aristotle to Newton, to Einstein:

  time is an "epiphenomenon of movement", used as a parameter (in equations)

Physical time *vs.* Randomness
Synthetic Remarks

1. Quantum Physics: Randomness

1.1 Measurement: non-commutative (a symmetry breaking)

1.2 Projection of the wave vector (***irreversible*** sym. breaking)

2. Classically*,* ***irreversible time*** appears in

2.1 **Deterministic** chaos, where *randomness is* unpredictability (a *symmetry breaking at finite time*; **knowledge decreases**)

2.2 **Thermodynamics**: increasing entropy (dispersion of trajectories, *diffusion* of a gas, of heath… along *random* paths)

Notes: underlying a diffusion (e.g. **energy dispersal**) there is always a *random path;*

2.1 and 2.2: dispersion of trajectories (**entropy** increases in both)

Symmetries and their breaking

A triangular relation (in existing physical theories):

Random event ⟷ **irreversibility** of processes (time)

Symmetry breaking

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

Longo G., Montévil M., Models vs. Simulations: a comparison by their Theoretical Symmetries. *Invited Paper*, **Springer Handbook of Model-Based Science**, 2015.

The forms of time : from physics to the double irreversibility of biological time

Geometrization of time in Physics

- **Simple geometries:**

1. **Linear** (absolute) **time**: the Cantor real line:
2. **Oriented** Line (thermodynamics): an arrow along Cantor's reals:

H. Weyl's phenomenological critique of "Cantorian" time [Das Kont., 1918]:
"the ***pointwise*** present makes no sense: it is already gone...
Present is an interval of cohexisting past (retension) and future (protension)"

cf. **St Augustin's** extended present

Weyl: "yet, so far, we have no better treatment of physical time"

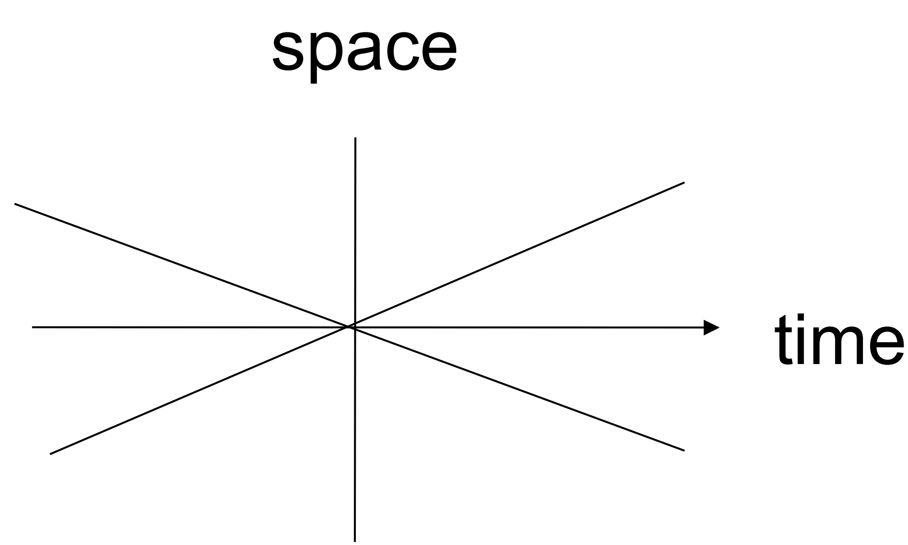
Geometrization of time in Physics

More geometries of time:

Recall**:**

1. Linear (absolute) time: the Cantor real line:
2. Oriented Line (thermodynamics): an arrow along Cantor's reals:

3. **Relativistic time** in Minkoski's space-time:



4 - Feynmann: preserve the *fundamental* **TCP** symmetry (Time-Charge-Parity):

C is *negative* in an anti-particle, thus :

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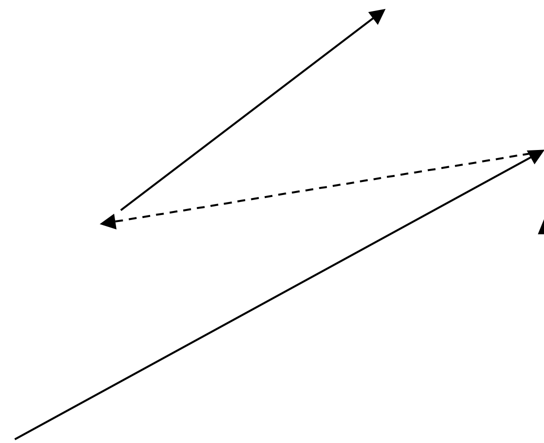
time goes “zig-zag”



Anti-particle creation

More in this direction:

C. Rovelli, L'ordine del tempo, 2017

Rhythms of Life
or
a two dimensional time in Ontogenesis

Key Physical Observables, the *parameter* time

Physics: central role of

- ***Energy*** (from Galileo's inertia to QP energy spectrum)
- ***Invariants*** (geodesics and conservation, as *invariants* of physical determination, w.r. to ***transformations***, e.g. symmetries, **Noether**)

More:

- ***Major physical constants***: G, c, h…. (dimensional), α ...
- ***Time:*** one dimension, a **parameter** in equations or *an "epiphenomenon"* of movement (Aristotle, Newton, Einstein…)

Biological Time and Rhythms, in Ontogenesis
(an introduction)

Biology: Conceptual priority of

- ***Organization:*** *thus, its irreversible setting up and maintenance, a new observable* in the same (?) dimension as thermodynamical *t* ; its proper irreversibility (e.g. embryogenesis)
- ***Time*** for **organisms**, **two** dimensions:

  1 - ***External-physical*** rhythms, same dimension as thermodynamical *t*

  2 - *Internal rhythms* (derived from **non-dimensional** values: major ***constant***; an orthogonal dimension w.r.to physical time)

Bailly F., Longo G., Montévil M. *A 2-dimensional Geometry for Biological Time*. In Progress in Biophys., Molecular Biology: vol. 106, n. 3, 474 – 484, 2011

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Time as an **operator**, in **evolution**:

Bailly F., Longo G. *Biological Organization and Anti-Entropy*, in J. of Biological Systems, Vol. 17, n. 1, 2009. (Also in Longo, Montévil, 2014)

Biological Rhythms, in *Ontogenesis*

1. ***External-physical*** rhythms (**Ext**: periods or physical frequencies):

    dimensional: s, Hz… exp($i\omega t$): daylight, seasons…)

2. ***Internal rhythms*** (**Int**: physiological functions):

non-dimensional: metabolic rhythms; ***heart beats,***

respiration … **b** $\approx 1.2 \times 10^9$, **r** $\approx 0.8 \times 10^9$ in mammals;

- *pure numbers*: they *produce* time scales as a function of the mass, e.g. LifeTime $\approx W^{1/4}$

Geometric scheme for *two* dimensional Biological Time

1. **Thermodynamical oriented time t:** the horizontal axis --------> t

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2. **Compactified dimension R:** the circle

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   Internal rhythms (Int): physiological functions

Their product:

Taking into account also **External** Rhythms (Bailly, Longo, Montevil, 2010)

1. **Ext**: Day/Night…
2. **Int**: heart beats, respiratory … (+ the internal “trace” of Day/Night)

Geometric **Theoretical** Schemata for biological time

Taking into account also **External** Rhythms (Bailly, Longo, Montevil, 2010)

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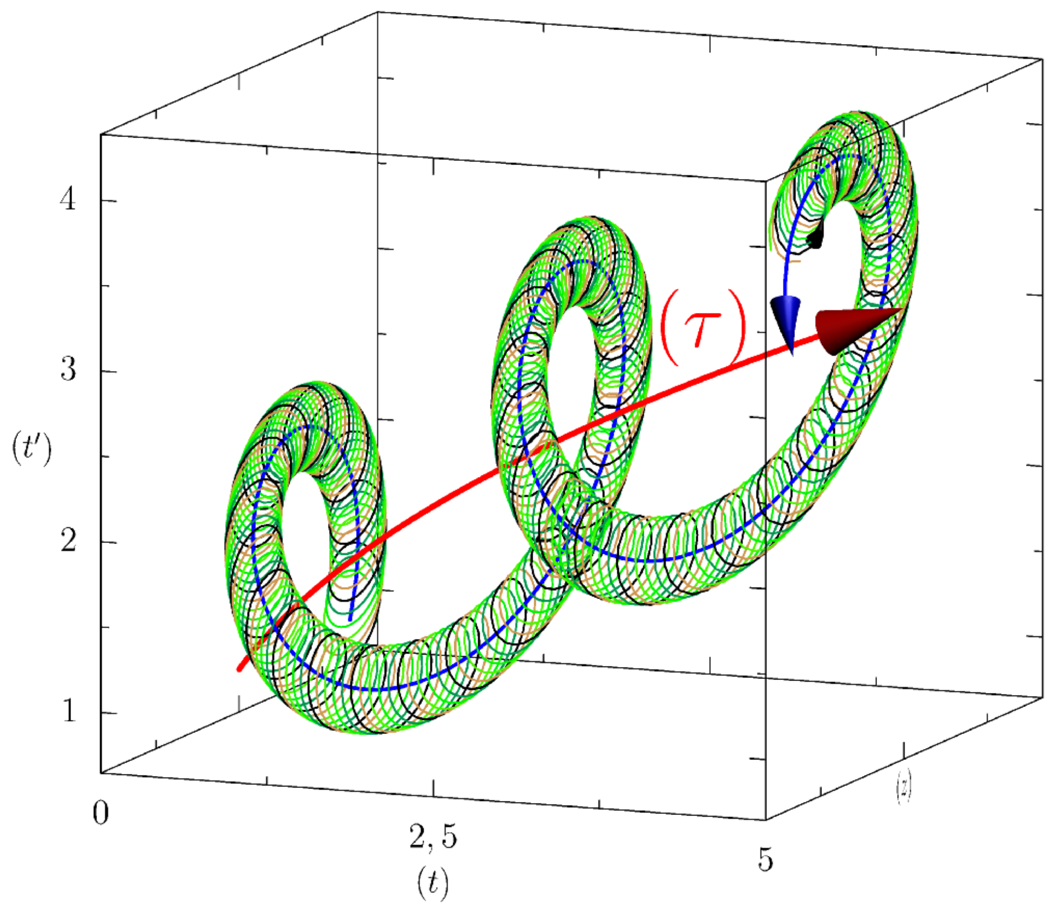
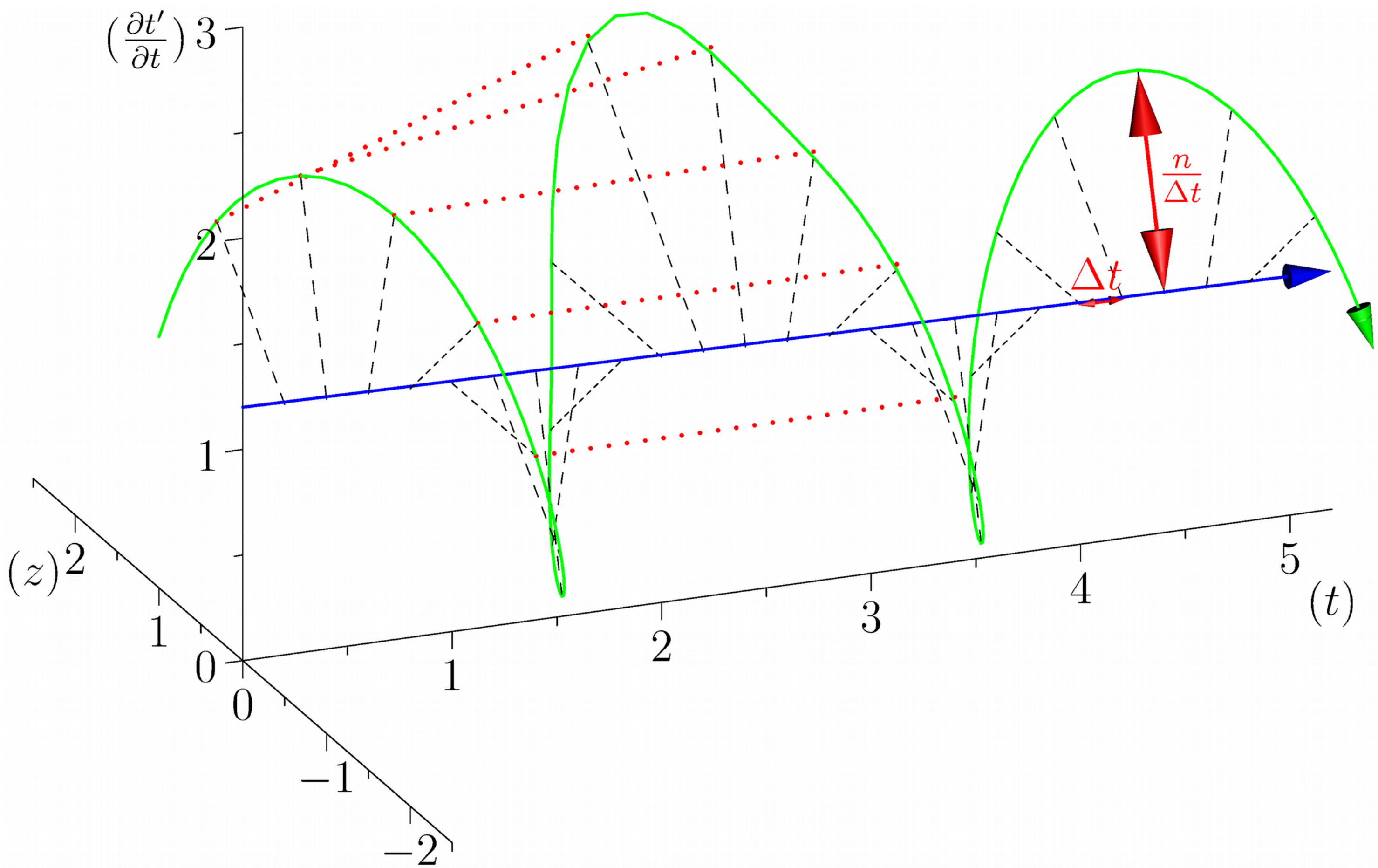
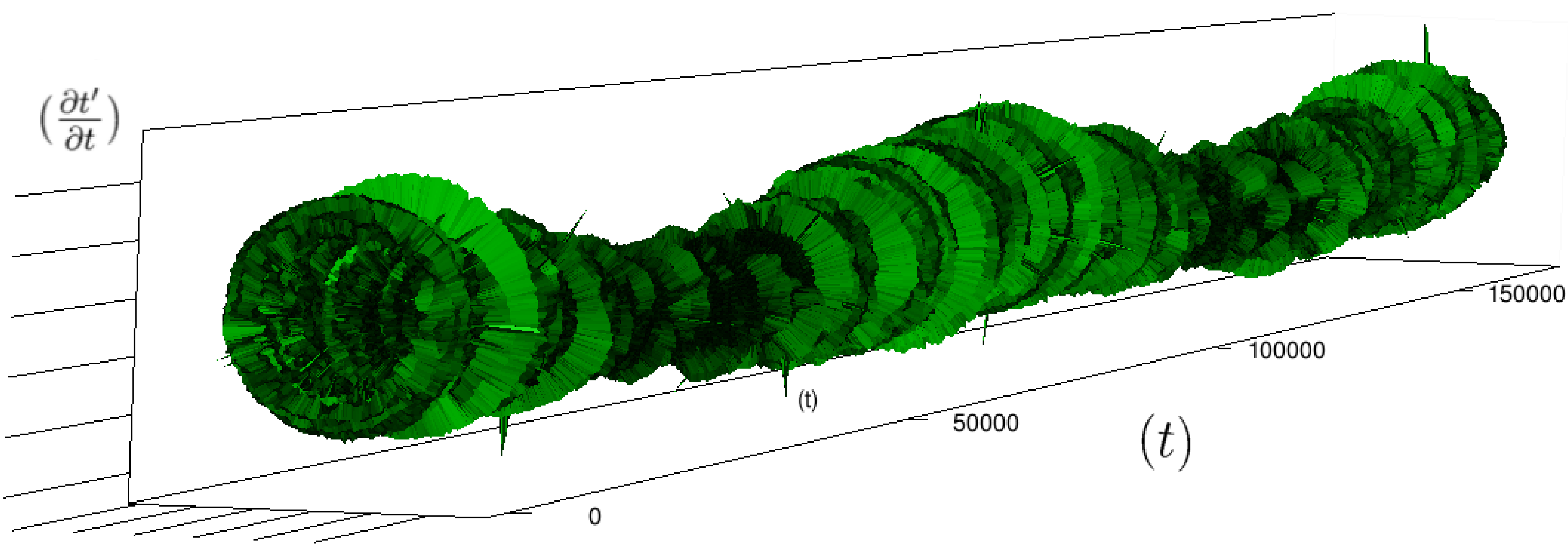


Enlarge at constant speed (**acceleration = more space in equal time**): 200 beats per circle; and **renormalize**

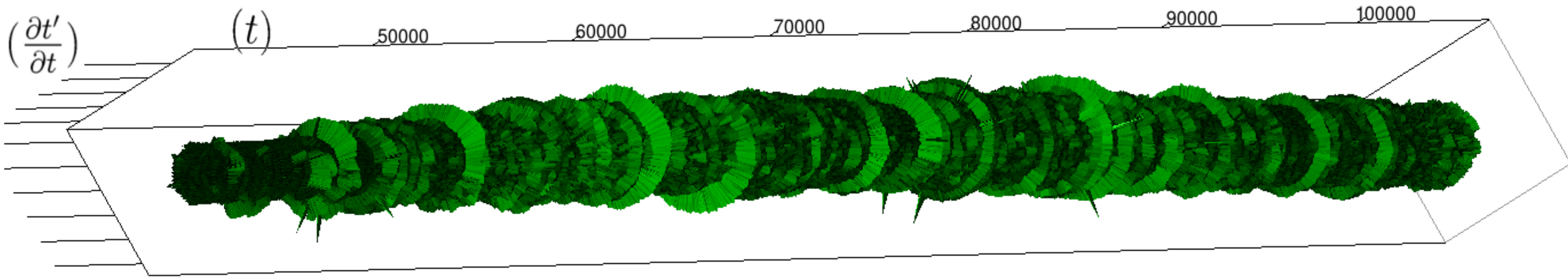


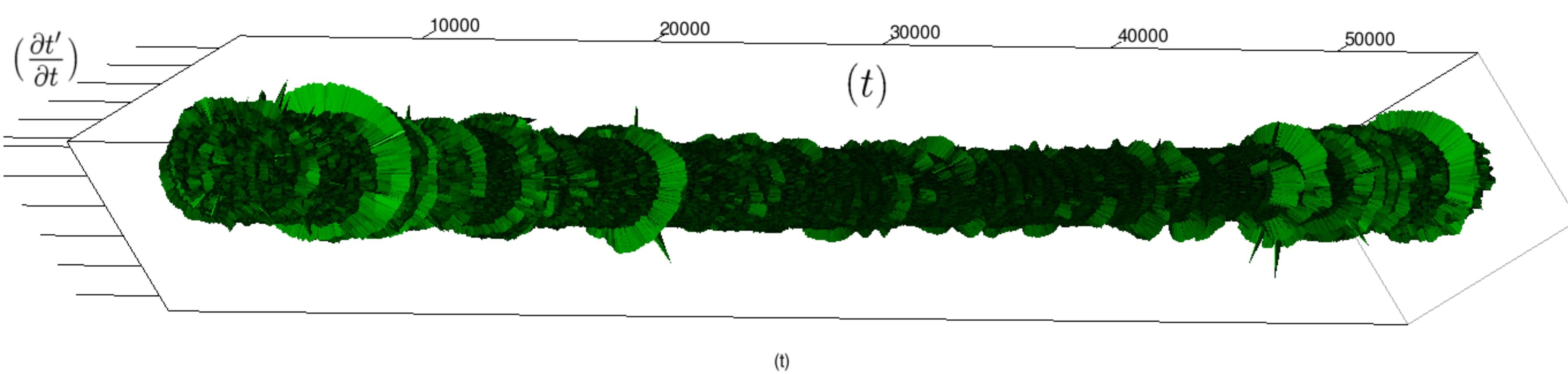
Cardiac Rhythm: **two days**

Sample s20011 from The Long-Term ST Database, [13]



Cardiac Rhythm: ***day*** vs. ***night*** (200 beats per circle)





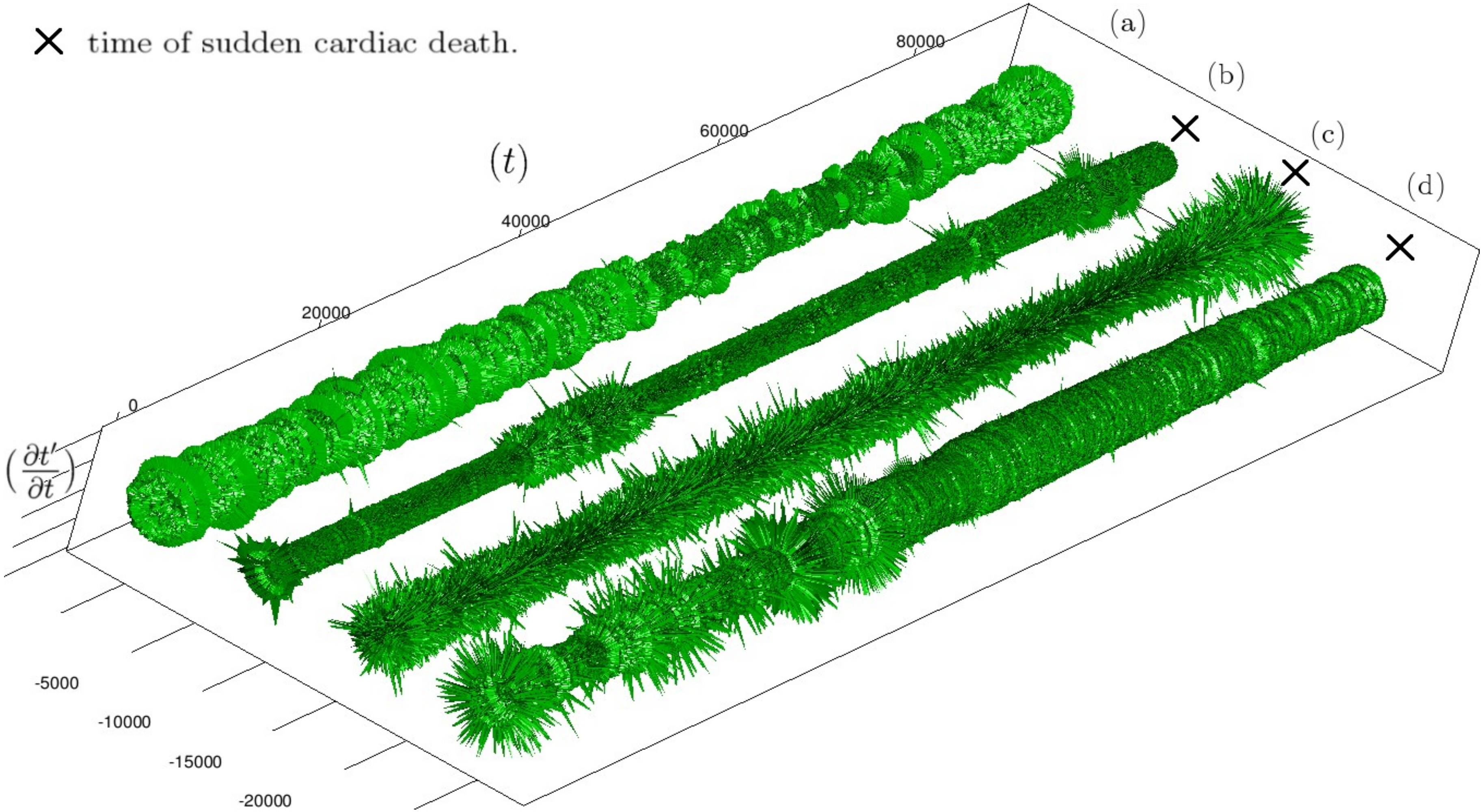
Comparison (sudden cardiac death): (a) Healthy case,

(b) Female aged 67 with sinus rhythm and intermittent pacing.

(c) Female, 72, with atrial fibrillation.

(d) Male, 43, with sinus rhythm.

Data from samples 51, 35 and 30, The Sudden Cardiac Death Holter Database, 2009 (200 beats).



A critique, for future work

The “**geometrization**” of phenomenal time, we owe to physics, is a major limitation to understanding (see H. Weyl, Das Kontinuum,1918, on this specific issue, continuity)

Spatialising time misses **randomness** as relative unpredictability is a “time issue”: “predicere”

Ongoing work :
on randomness *as differing* from incompressibility, a recent form of the spatialization of time

The Time of History: Phylogenesis, *in short*

G. Longo. *How Future Depends on Past Histories and Rare events in Systems of Life*, in **Foundations of Science**, 2017

The Time of History: Phylogenesis, *in one slide*

Time in Biological Evolution:

1 – *if phenotypes are the relevant* **observables**, *then* **time evolution** *include the changes of the phase space*

2 - **rare** *events crucially contribute to history: e.g.* **speciation** *by a hopeful monster (no averaging-out [Bravi, Longo, 2015])*.

3 - A *distinction between*: **time of processes** *vs.* **time of history,** as different observable times in the same (? *new*?) physical dimension:

e.g. flames, hurricanes, micelles … **processual time**, *no historical* changes

4 - **synchronic measurements** *vs.* **diachronic measurements** (as access to past histories or **how the past "determine the future"**)

G. Longo. *How Future Depends on Past Histories and Rare events in Systems of Life,* in **Foundations of Science**, 2017

PHYSICS	BIOLOGY
specific trajectories (geodetics) and **generic objects**	**generic trajectories** (possible/compatible with ecosystem) and **specific objects**
point-wise criticality	**extended criticality**
(Schrödinger) **energy** is an **operator** (Hf), **time is a parameter** $f(t,x)$	**energy** is a **parameter** (allometry), **time** is an **operator** (measured by entropy and anti-entropy production)
reversible time (or irreversible for degradation-simplified thermodynamics)	**double irreversibility of time** (thermodynamics and phenotypic complexity constitution)
randomness is **non deterministic** or deterministic non predictability **within a pre-given space phase**	**randomness** is **intrinsic indetermination** made by changing phase space (ontogenesis and phylogenesis)

Table 1. A possible theoretical differentiation between inert and living matter is described through conceptual dualities.

Some applications in Economy…

A radical critique of equations in Economy (economy of equilibria):

Ҫhanging Phase Spaces *and* **enablement**

- T. Felin, S. Kauffman, R. Koppl, G. Longo. *Economic Opportunity and Evolution: Beyond Bounded Rationality and Phase Space*. In "Strategic Entrepreneurship Journal", 8, 4: 269–282 (2014)

- R. Koppl, S. Kauffman, T. Felin. G. Longo, *Economy for a Creative World.* Preliminary version of this target article in "Journal of Institutional Economics", 11, 01, pp 1 - 31, March 2015.

  (In September 2016, in Boston, this paper was awarded the prize for best paper appearing in JOIE in the previous calendar year - this prize is entitled to Elinor Ostrom, 2009 Nobel Award winner in Economy)

Awareness of the limits of reductions and flat transfers

I.M. **Gelfand** in his **Kyoto Prize Lecture**, 1989 : « [The use of physico-mathematical tools in biology] is rather dangerous, because *it usually implies the priority of mathematical and computer modes over real biological systems*. In many cases, *models are considered as full substitutes for natural phenomena*, and become subjects of self-perpetuating studies »

Montévil, M., Speroni, L., Sonnenschein, C., Soto A.M., *Modeling mammary organogenesis from biological first principles: cells and their physical constraints*. **Prog. Biophys. Mol. Biol.**, 122, 58-69, Soto, Longo, Noble eds., 2016.

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M. **Gromov**, M., 2012, European Congress of Mathematics, Krakow, July 2012.

« ...there must be a *new world of mathematical structure*s shadowing what we see in Life, a new language we do not know yet, something in the spirit of the language of calculus we use when describing physical systems »

Sarti, A, Citti, G, Piotrowski, D *Differential heterogenesis and the emergence of semiotic function*. **Semiotica**, 2018.

Some references (papers *downloadable:* Google: Giuseppe Longo)

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