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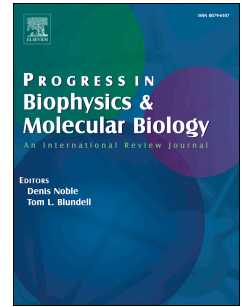
A timeless biology

Arturo Tozzi, James F. Peters, Clifford Chafin, Domenico De Falco, John S. Torday

A TIMELESS BIOLOGY

Arturo Tozzi (Corresponding Author)

Center for Nonlinear Science, University of North Texas, Denton, Texas 76203, USA
tozziarturo@libero.it

James F. Peters
Department of Electrical and Computer Engineering, University of Manitoba
75A Chancellor's Circle
Winnipeg, MB R3T 5V6 CANADA
James.Peters3@umanitoba.ca

Clifford Chafin
Roto9 Energy, Chapel Hill, NC, USA
cliff.chafin@gmail.com

Domenico De Falco
Second University of Naples, Dipartimento di Ingegneria Industriale e dell'Informazione, Aversa, Caserta, Italy
domenico.defalco@gmail.com

John S. Torday
Department of Pediatrics
Harbor-UCLA Medical Center, 1124 W.Carson Street
Torrance CA 90502
jtorday@labiomed.org

Contrary to claims that physics is timeless while biology is time-dependent, we take the opposite standpoint: physical systems' dynamics are constrained by the arrow of time, while living assemblies are time-independent. Indeed, the concepts of "constraints" and "displacements" shed new light on the role of continuous time flow in life evolution, allowing us to sketch a physical gauge theory for biological systems in long timescales. In the very short timescales of biological systems' individual lives, time looks like "frozen" and "fixed", so that the second law of thermodynamics is momentarily wrecked. The global symmetries (standing for biological constrained trajectories, i.e. the energetic gradient flows dictated by the second law of thermodynamics in long timescales) are broken by local "displacements" where time is held constant, i.e., modifications occurring in living systems. Such displacements stand for brief local forces, able to temporarily "break" the cosmic increase in entropy. The force able to restore the symmetries (called "gauge field") stands for the very long timescales of biological evolution. Therefore, at the very low speeds of life evolution, time is no longer one of the four phase space coordinates of a spacetime Universe: but it becomes just a gauge field superimposed to three-dimensional biological systems. We discuss the implications in biology: when assessing living beings, the underrated role of isolated "spatial" modifications needs to be emphasized, living apart the evolutionary role of time.

KEY WORDS: time; gauge theory; symmetries; constraints; informational entropy; evolution

INTRODUCTION

In order to emphasize the intrinsic failure of the physical laws in the assessment of the overwhelming biological complexity, it has been proposed that physics is essentially based on timeless dynamics, while irreversible time is a prominent feature of biota (Ulanowicz, 2017). Here we go through the opposite hypothesis, i.e., that macroscopic physics is time-constrained, while living beings tend towards an effort to "freeze" and "slow" the arrow of time. Perhaps, time does not exist at the micro-level of quantum vacuum and Planck scales (Rovelli, 1991). Yet, time modifies according to the Einstein special and general relativity (Einstein, 1905) at the relativistic macro-scales and at

very high energies. However, at the meso-scales of the environmental niches that allow life, time is relatively stable. Here we show how such stability is very important for life evolution as we know it, and what it is like to be a living being closely depends on the stable, rather continuos time passing. Many current theories emphasize the foremost role of the "time" and "timescales" in different biological fields, from cellular function to neural activity (Linkenkaer-Hansen et al, 2001; Kravchick and Jordan, 2015; Papo, 2015). Is such a tenet true? Although stochastic variables and random fluctuations regulated by the Langevin and the Fokker-Planck equations frequently occur (Ribrault et al, 2011), biological activities are only partially Brownian, since they are "constrained". For example, the protein-folding final conformation is dictated by the minimum frustration principle on long evolutionaly timescales. Such principle states that proteins' energy decreases more than expected, as they assume conformations progressively more like the native state (Bryngelson and Wolynes, 1987; Ferreiro et al, 2011). A strong bias in the protein's surface energy landscape towards the lowest energetic basin occurs, overcoming the asperities of the rugged landscape (Onuchic et al., 1997; Sutto et al, 2007; Tozzi et al., 2016). In other words, proteins were enriched by evolution for sequences with the propensity to fold into the lowest energetic structures. Constraints also occur in countless other systems, from the nonlinear chaotic paths governed by strange attractors, to the structure of biological entities, ruled by their specific genetic pools. Despite the large number of different scenarios, the processes governing constraints on physical and biological systems may be generalized, taking into account the universal principle of the second law of thermodynamics, which states, in Planck's formulation, that "*every process occurring in nature proceeds in the sense in which the sum of the entropies of all bodies taking part in the process is increased*". In this framework, the concepts of "virtual displacement" - from the far-flung branch of analytical mechanics - come into play (Sommerfeld 1952; Landau and Lifshitz, 1976; Goldstein, 1980; Torby1984).

In this paper we will try to elucidate that, in the evolution of living beings, close relationships occur among displacements, information and time. Such findings make it possible to let us hypothesize a theory of time as a gauge field. The manuscript encompasses four sections. The first section describes the virtual and real constraints in the framework of a "frozen" time. The second section, taking into account probabilistic arguments, shows how is possible to insert virtual constraints on the Shannon entropy's plot, in order to correlate informational entropy with the arrow of time. The third section illustrates the procedure to sketch gauge theory based on the three above mentioned ingredients: constraints, probabilities and time. The fourth section describes an evolutionistic cosmic account based on the laws of symmetries.

1) **VIRTUAL CONSTRAINTS**

This section describes "virtual" and "real" constraints in the framework of a "frozen" time. Here we show how the natural paths of particle trajectories dictated by long timescales (standing in our case for the increase of thermodynamical entropy occurring in our Universe as time slowly passes) can be broken by the "virtual constraints", i.e., the very short timescales of the living beings, in which time is temporarily "frozen".

In technical terms, the key concept of virtual constraints is a dynamically imposed outer feedback control, so that the trajectory of a particle or an agent in the system's phase space can be "forced" towards the desired orbits and outputs (Canudas-de-Wit, 2004). Virtual constraints reduce the degrees of freedom, coordinating the evolution of the various links throughout a single variable. A closed-loop mechanism is achieved, wherein dynamic behaviour is fully determined by the evolution of simplest lower-dimension system (Stepp et al., 2010). The resulting system is called a "virtual limit system".

In mathematical terms, we define a set of $n - 1$ outputs (or constraints):

$$y = \varphi(p, q) = \vec{q} - h(\theta, p) = \vec{q} - h(\theta, p(t)),$$

where y and $\varphi(p, q)$ are the outputs or constraints, $\vec{q} \in R^{n-1}$ is an $n - 1$ dimensional real-valued vector that gives the actuated coordinates and velocities, p is the set of the design parameters, $\theta \in R$ is the unactuated variable, $\theta(q)$ is a function of the generalized coordinates of q. The latter equation describes the most general condition. In other words, constraints can be mathematically assessed through a well-established procedure that takes into account a wide range of systems' parameters.

An inner-feedback loop is used to perform output feedback linearization in a local domain, where the matrix is invertible:

$$\psi(q)u = k(q; \dot{q}) + v,$$

where v is the outer feedback loop. Note that the equation includes a term $\dot{q}$ which depends on time, where the upper

dot stands for the partial time derivative, i.e., $\dot{q} = \dfrac{\partial q}{\partial t}$ (Canudas-de-Wit, 2004).

If an outer feedback loop v is designed to zeroing the output y, we get a partially linearized system in the form:

$\ddot{y} = v.$

Then the full system dynamic is captured by the solutions of:

$$\alpha(\theta)\ddot{\theta} + \beta(\theta)\dot{\theta}^2 + \gamma(\theta) = 0,$$

together with the imposed constraint for mean q-value:

$$\overline{q} = h(\theta, p),$$

where $\theta(q)$, $\alpha(\theta)$, $\beta(\theta)$ and $\gamma(\theta)$ are scalar functions depending on the inner feedback loop.

In conclusion, the virtual constraints are forces external to the system's phase space (in our case, the increase of cosmic entropy achieved in very long timescales), able to modify an internal trajectory towards the required one (in our case, the temporary, short, local decreases of cosmic entropy occurring in living systems).

This process allows one to deal with high-dimensional systems with underactuated degree one, by only analyzing this second-order nonlinear equation.

In analytical mechanics the researchers cope with under-actuated Lagrangian systems of the form:

$$\frac{d}{dt}\left(\frac{\partial L}{\partial \dot{q}}\right) - \frac{\partial L}{\partial q} = B(q)u,$$

where q and $\dot{q}$ are vectors of generalized coordinates and velocities, $L(q; \dot{q})$ is a Lagrangian of the system, $B(q)$ is a matrix function of an appropriate dimension (with rank equal to the number of inputs) and u is a vector of independent control inputs. The under-actuation means that dim $u <$ dim q, i.e., the number of actuators is less than the number of its degrees of freedom.

A virtual displacement is an assumed change of system coordinates occurring while time is held constant. It is called "virtual" rather than "real", since no actual displacement (in our case, the increase of entropy in a single place of the Universe where life occurs) takes place without the passage of time. Computerized simulations may be performed to see what happens to physical and biological paths when time is kept fixed, *e.g*, during the movements of animals in an environment, or during cytoplasmatic enzymatic reactions. For further details about the methodology, see **Figure 1**.
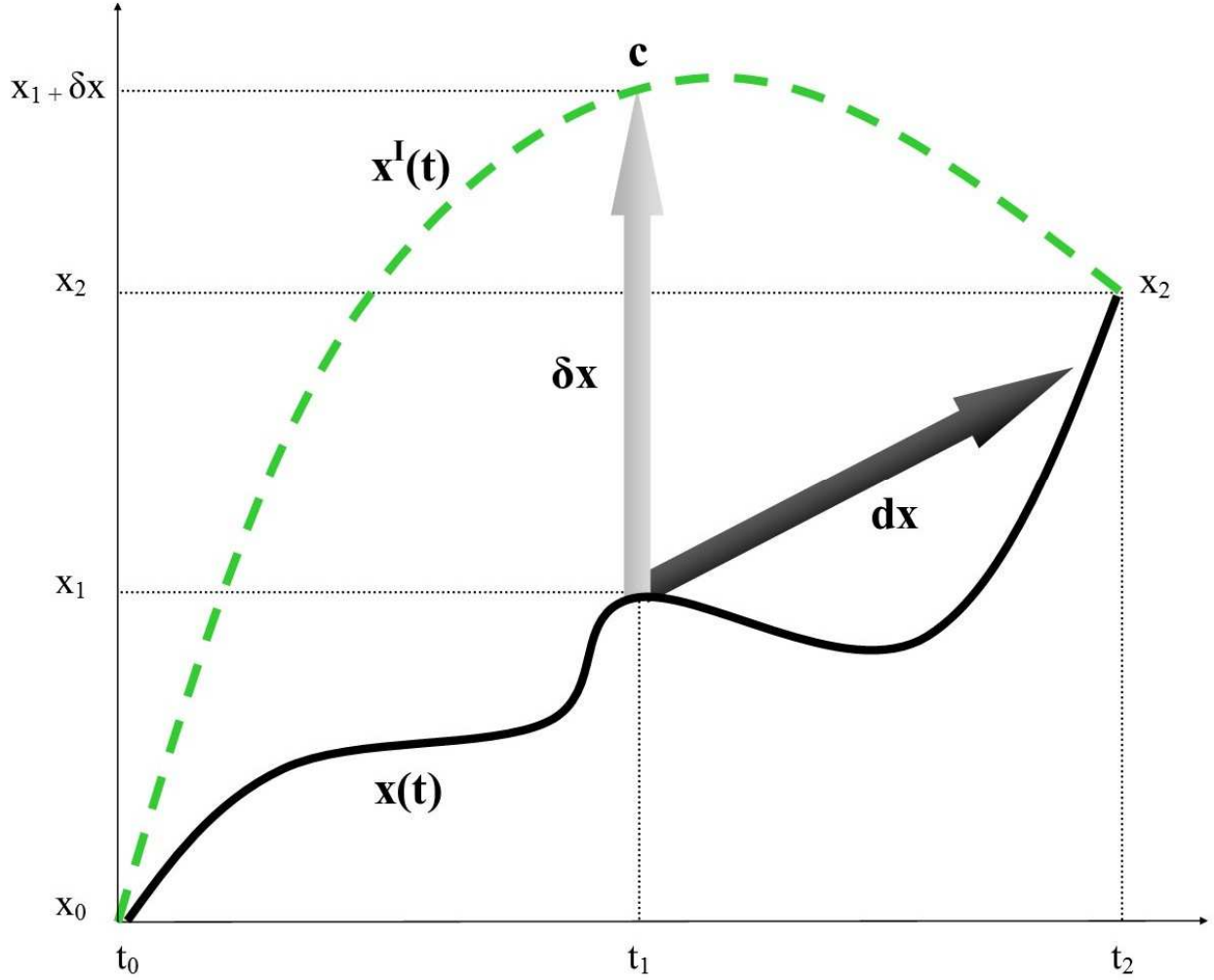
Figure 1. Real and virtual trajectories in a graph plotting time t on the X-axis and the space x on the Y-axis. The Figure evaluates two trajectories which both display a starting position at x_0 and an ending position at x_2. The black solid curve x(t) stands for the particle trajectory, while the dotted green curve x^I(t) for a possible virtual trajectory. At position x_1 and time t_1, the virtual displacement δx (from x_1 to the point c) is illustrated (grey arrow). The regular displacement dx is a vector pointing in the direction of the motion (black arrow), which arises from differentiating with respect to time parameter along the path of the motion. In contrast, the virtual displacement δx is a tangent vector to the constraining manifold at a fixed time. It arises from the differentiation with respect to the enumerating paths of the motion, varied in a manner consistent with the constraints.

2) INFORMATION ENTROPY AND TIME

This section, taking into account probabilistic arguments, shows how is possible to locate virtual constraints on the Shannon entropy's plot, in order to correlate informational entropy with the arrow of time. Real displacements are governed by the second law of thermodynamics: in every system, either physical or biological, the thermodynamical entropy relentlessy increases from time T_0 to $T_2 = \infty$, until its maximum value. In our case, it is however preferable to use the informational entropy, instead of the thermodynamical one. Indeed, the two entropies are linked through the formula:

$S = k\,H$

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in which S is the thermodynamical entropy, k is the Bolztmann constant and H is the Shannon informational entropy. The informational entropy, apart from the invaluable advantage of quantifying the macroscopic states without a perfect knowledge of the microscopic ones, is not directly linked with time, allowing us to remove such parameter from our system. Indeed, the Shannon's plot of informational entropy does not encompass the parameter time. If we want to introduce the arrow of time on the Shannon's curve, we may superimpose another, third dimension to its classical 2-D plot (**Figure 2**). The vector of time ζ lies in a plane forming an angle A with the 2-D plane of Shannon entropy. Note that the timescales expressed by the vector ζ in the graphic may vary, depending on which system we are evaluating. As an example, if we take into account the system Universe, T_0 stands for the state of minimum entropy – the initial Big Bang -, while $T_2 = \infty$ stands for the state of maximum entropy, *i.e.*, the hypothetical final state of the Universe. Starting from the probability of a virtual constraint c, we may calculate the corresponding point T_1 on the arrow of time, in order to assess and quantify how much time is still required to reach $T_2 = \infty$ (which stands for the system's "real" final state at the energetic equilibrium). There is still an unknown, crucial parameter to measure: the value of the angle A, which is not implied to be constant, but could change in different examined systems.

If we know the value of of the angle A, we are allowed to recognize how long the biological system will take, in order to complete its biological path in cosmic times.

The next section answers the question: how can we find the value of the angle A? Here, the formalism of a gauge theory will come into play.
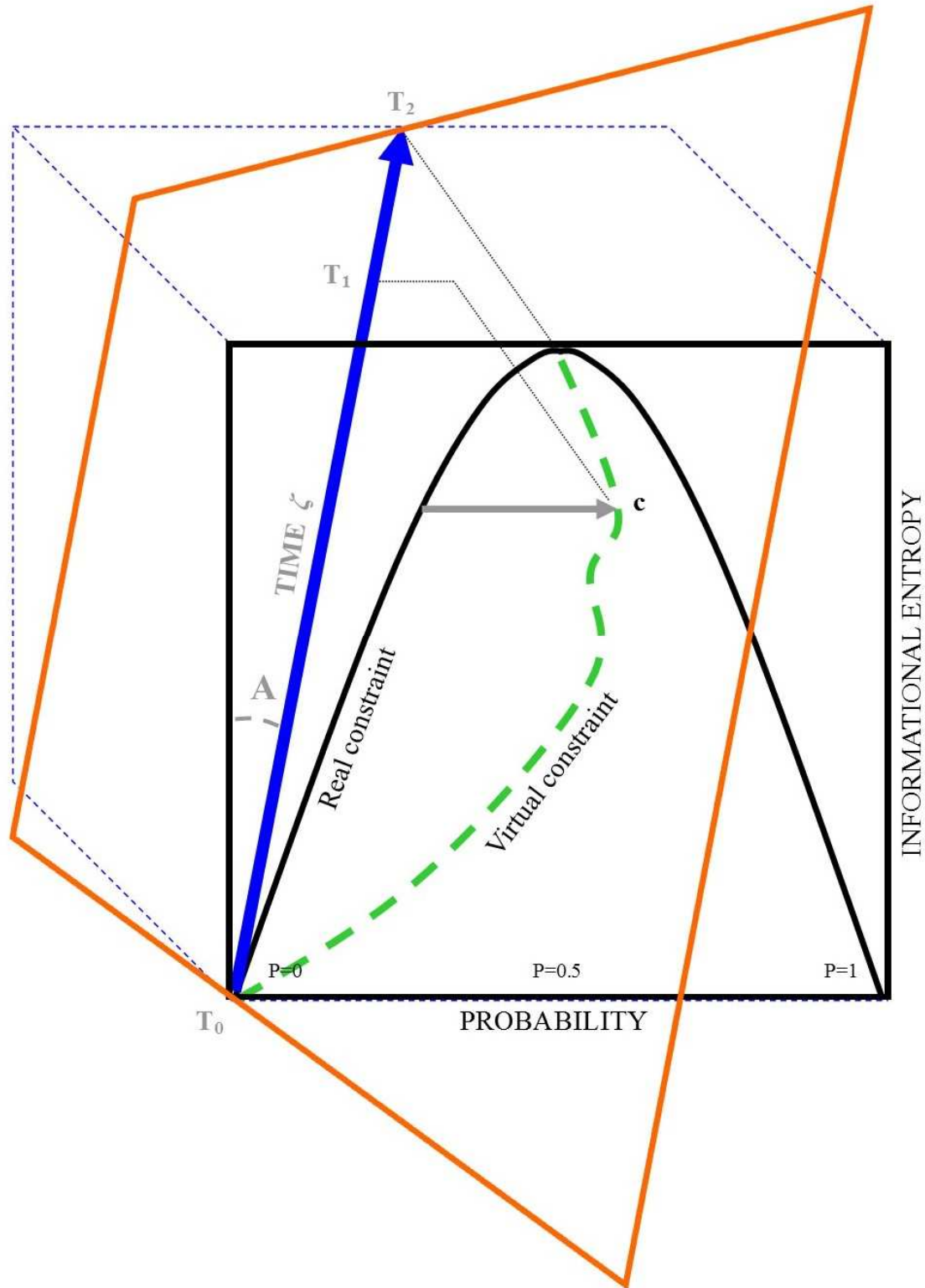
Figure 2. The informational entropy is plotted as a function of the random variable p, in the case of two possibilities with probabilities p and (1-p). The solid line black stands for the Shannon entropy (under ergodic conditions). The values p=0 and p=1 stand for the minimum entropy, p= 0.5 for the maximum entropy. The arrow of time ζ lies on a third coordinate of the phase space and is equipped with the angle A. Due to the energetic gradient flows dictated by the second law of thermodynamics, time, in its route from T_0 to $T_2 = \infty$, is correlated with an increase in informational

entropy. Given a virtual displacement c on the virtual trajectory (dotted black line), the corresponding value of T_1 on the arrow of time can be calculated, provided the value of A is known.

3) GAUGE PROCEDURES

Here we illustrate the procedure in order to calculate the angle A, by sketching a gauge theory based on the three above mentioned ingredients: constraints, probabilities and time. In other words, we examine the possibility to build a differential geometry-based theory of the real (cosmic, long timescales) and virtual (biological, short timescales) trajectories' phase space. At first, we need a system equipped with real displacements - the real trajectories of particles or events in cosmic timescales - that stand for the continuous, global symmetries. Such symmetries are the energetic constraints that the second law of thermodynamics enforces on the system. While energetic gradient flows occur just in long timescales, in the very instant in which T is "frozen", fixed and equals to zero, virtual displacements occur. The latter stand for a continuous group of local transformations able to "break" the symmetry. The local loss of symmetry caused by living beings (a disturbance of the gradient flow) needs however to be ripristinated. In order to achieve this symmetry repair, we need to introduce a so-called gauge field, i.e., in our case, time, able to restore the gradient flow. Note that a gauge theory requires gauge fields to be continuous. Indeed, time, which is not continuous when approaching the light speed as dictated by Einstein's special relativity, nevertheless are almost continuous at the nonrelativistic timescales of the life.

There are many possible ways to deal with a theory of the virtual displacements in a differential geometric sense, for example by analyzing them in terms of sections of fibre bundles, jet manifolds and Ehresmann connections (Abraham and Marsden, 1978; Kolar and Michor, 1993; Lang, 1995). In order to quantify the required forces and in particular the angle A described in the previous paragraph, we proceeded as shown in **Figure 3**. The whole procedure is modified from Tozzi et al. (2017b). In the example described in **Figure 3A**, we depicted four areas (standing for the biological activity of four living beings in short timescales) as rotating circles, where rotations along the circumference stand for their probability densities. The geometric "link" between the real 3D manifold (depicted in **Figure 3A**) and an abstract manifold (depicted in **Figure 3B**) can be defined in terms of "connections" (Ehresmann 1950; Sengupta et al., 2016). According to the covariant version of a gauge theory, the correction terms are reinterpreted as couplings to an additional divergent counter term, the gauge field, by allowing the symmetry parameter to vary from place to place in the local coordinate system. **Figure 3E** illustrates the procedure. In other words, we need to introduce the vector ψ, equipped with the angle A, which stands fo the global value of the required gauge field. This procedure allows us to extrapolate from A the values of the gauge field required to keep the trajectories invariant under different virtual displacements.

Our framework resembles a gauge theory, but with some distinctions. The physical gauge theories are based on three tenets (Zeidler 2011):

a) The system is equipped with a continuous, preserved "global" symmetry (and a corresponding Lagrangian).
b) The system displays a continuous group of "local" transformations, equipped with a Lie group.
c) The Lagrangian is kept invariant under such local transformations by a "gauge field", i.e. a continuous force acting on the system.

The Lagrangian, through its connections with Noether's theorem, throws a bridge between symmetries and energetic requirements. However, the concept of the Lagrangian is slightly different in our model: instead of referring to the principle of least action and the "preservation" of a physical quantity as usual in gauge theories, it refers to the "dissipation" of a physical quantity through gradient flows.
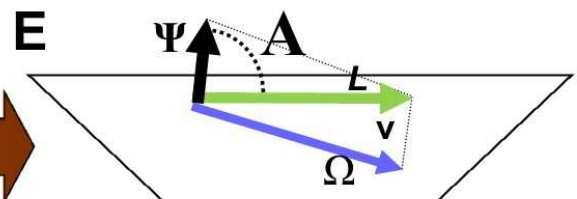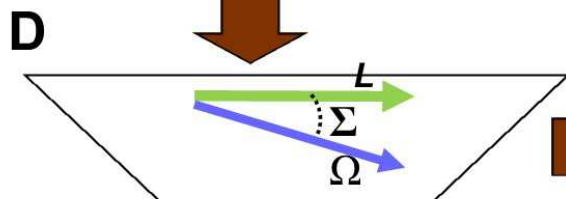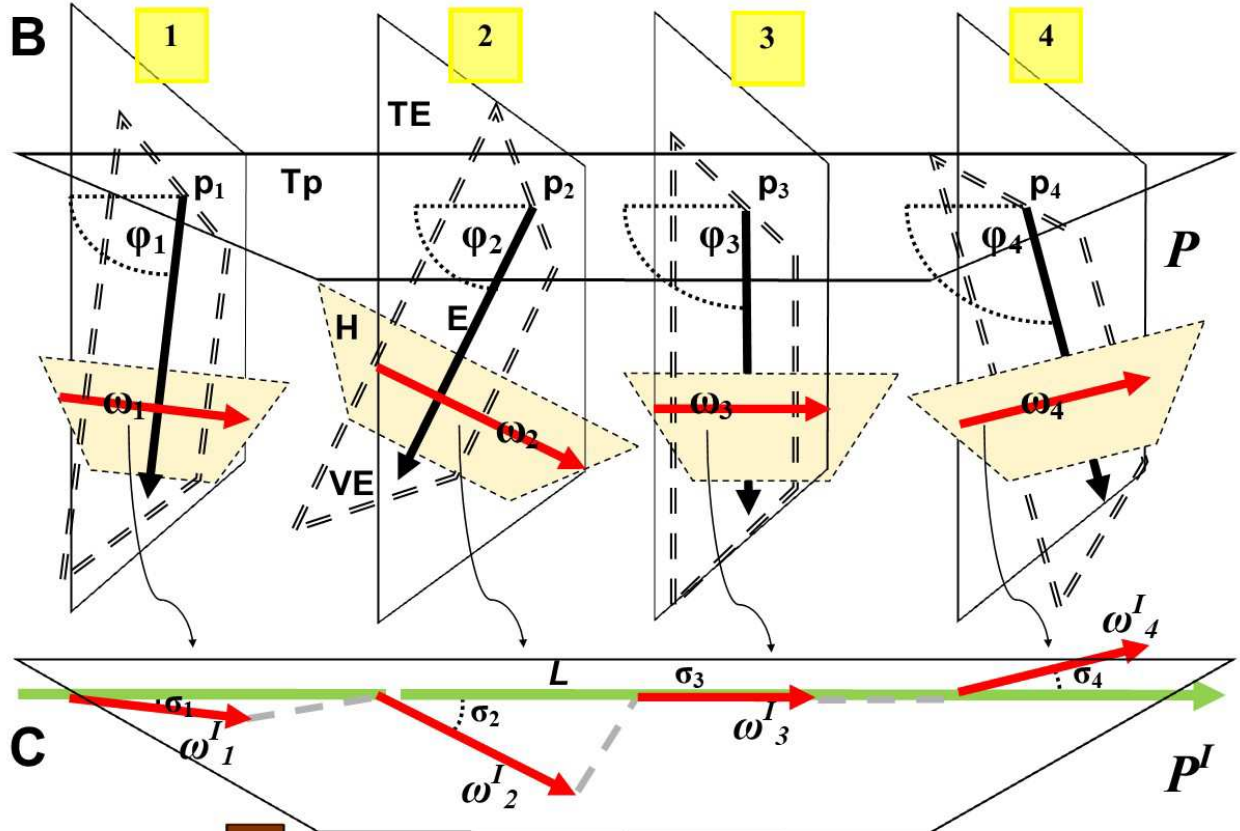
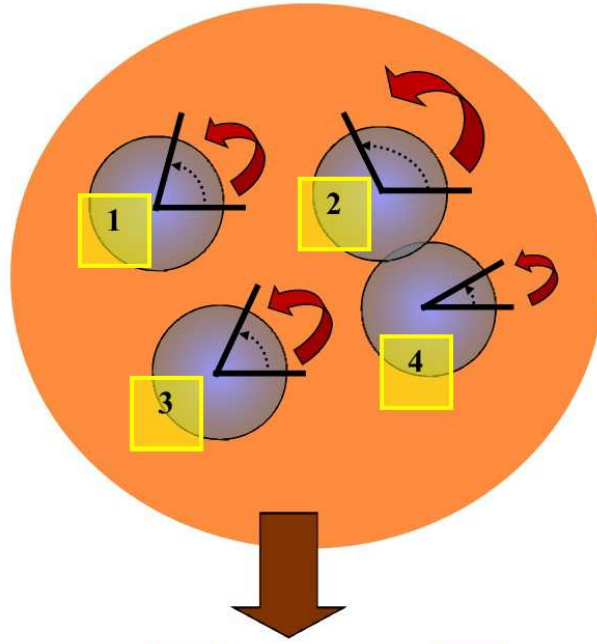**Figure 3**. Displacements in a system equipped with a global, invariant symmetry. The global symmetry stands for the constrained energetic paths towards a cosmic increase in entropy, dictated in long timescales by the second law of thermodynamics. Four virtual displacements, e.g., the anti-entropic activity of four living beings, are expressed as measures of probability states in four areas of a 3D system, at time kept fixed at zero. The four displacements' activity is expressed in terms of the circular movements taking place on a disk (**Figure 3A**) and mapped on a an abstract mathematical structure (**Figure 3B**). After a procedure of connection (**Figure 3C**) the gauge field (the vector ψ, equipped with our required angle A) can be calculated (**Figures 4D-E**). The gauge field stands here for time, continuous at the nonrelativistic timescales of the living beings. For further technical details about the mathematical apparatus, see Tozzi et al. (2017b).

4) CONCLUSION: SYMMETRIES AND EVOLUTION

We showed how the vector of time might stand for the energetic gradient of the system, locally "broken" by timeless perturbations. In analytical mechanics, the concept of virtual displacement - related to virtual work - is meaningful only when discussing a system subject to constraints on its motion. As stated above, this is the case of physical and biological activity. Because virtual displacements occur exclusively in space, the underrated role of the sole "spatial" modifications needs to be emphasized when assessing physical and biological activities. While virtual displacements take place, time is fixed and $\delta t = 0$, so that changes in physical/biological functions are independent of time passing. When time equals = 0, the real trajectory does not exist, because it is just the passing of time that gives rise to real displacements.

In this framework, the concepts of constraints and virtual displacement (Torby 1984) are going to be game changing. A virtual displacement is an assumed change of system coordinates occurring while time is held constant. It is called "virtual" rather than "real", since no actual displacement takes place with absence of time passing.

Therefore, we may draw a few conclusions:

1) In analytical mechanics, the concept of virtual displacement - related to virtual work - is meaningful only when discussing a system subject to constraints on its motion. As stated above, this is the case of biological activity.

2) Virtual displacements occur exclusively in space. The underrated role of the sole "spatial" modifications needs to be thus emphasized, when bearing in mind biological activities. Changes in spatial conformations may underline functional divisions in different zones of the biological melieu: for example, in touch with recent "neo-phrenonogical" claims (Tozzi, 2015), variations in psychological states could be correlated with different brain areas; further, various protein functions could depend just on spatial conformation's changes.

3) While virtual displacements take place, the time is fixed and $\delta t = 0$. The finding that changes in biological functions can be independent on the passage of time leads to several corollaries. To make an example, the role of pairwise entropy in neurofunctional studies needs to be re-evaluated: it takes into account the temporal overlapping of on\off states in brain subareas; however, if activity takes place in absence of time changes, such correlations become overestimated in the study of brain functions.

4) Virtual displacement mapping is an alternate name for parallax mapping, a system of three- dimensional displacement of surfaces, by which textures on flat surfaces give the illusion of depth. Virtual displacementmay therefore be the clue for a better comprehension of the three-dimensional perception (either visual, or acustic, tactile, chemical and so on) in living beings's nervous systems.

We would like to bring to the end with a remark concerning gauge theories. In touch with recent claims regarding the human brain activity (Sengupta et. al., 2016; Tozzi et al., 2017b) and cellular metabolism (Tozzi et al., 2017a), our work provides a further theoretical confirmation that gauge theories could be suitable not just for the canonical, well-estabilished assessment of physical particles and fields, but also for quantitative approaches to biological issues.

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