IN SEARCH OF GAUGE THEORIES FOR LIVING CELLS: A TOPOLOGICAL EXPLORATION ON THE DEEP STRUCTURE OF BIOLOGICAL COMPLEXITY

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ABSTRACT

Gauge theories had a tremendous impact in particle physics and have been recently proposed in order to assess nervous activity too. Here, taking into account novel claims from topology, the mathematical branch which allows the investigation of the most general systems activity, we aim to sketch a gauge theory addressed to the fundamentals of cellular organization. In our framework, the reference system is the living cell, equipped with general symmetries and energetic constraints standing for the intertwined biochemical, biomolecular, and metabolic pathways that allow the homeostasis. Abstractly, these functional movements follow donut-like trajectories. Environmental stimuli stand for forces able to locally break the symmetry of metabolic pathways, while the species-specific DNA is the gauge field that restores the general homeostasis after external perturbations. We show how the Borsuk-Ulam Theorem (BUT), which states that a single point on a circumference maps two points on a sphere, allows an inquiry of the evolution from inorganic to organic structures and the comparison between prokaryotic and eukaryotic metabolisms and whole functionalities. Furthermore, using recently developed BUT variants, we operationalize a methodology for the description of cellular activity in terms of topology/gauge fields and discuss about the experimental implications and feasible applications. A new avenue for a deeper exploration of biological complexity looms.

Introduction

A gauge theory states that, in systems equipped with an internal symmetry and a preserved physical quantity, the local symmetry breaks due to external forces are counteracted by another force, called gauge field (Zeidler, 2011). Gauge theories, successfully developed in physics (Higgs, 1964), have been recently proposed for the evaluation of neuronal activities (Sengupta et al., 2016). Here we make an effort to operationalize a gauge theory also for cellular function. It is a very difficult task, because managing the overwhelming numbers of molecular states and interactions continues to be a fundamental obstacle in building predictive models of biological systems (Sneddon et al. 2011); it is so despite pioneering works in bioenergetics and systems science which already obtained staggering figures for the minimal information describing the simplest cells (Morowitz, 1968, Riedl, 1978).

We will try to overtake the overwhelming complexity of cellular activity with the invaluable help of recently developed topological tools. The Borsuk-Ulam theorem (BUT) states that, when a pair of opposite (antipodal) points on a 3D sphere are mapped onto a 2D a circumference, their projections have matching description (Tozzi and Peters, 2016a) Recently developed BUT variants can be summarized as follows: a single feature embedded in a n dimensions M^n manifold maps to two features with matching description on a M^{n+1} manifold (Tozzi and Peters 2016b; Peters and Tozzi, 2016a; Peters, 2016). Single features may stand for physical or biological characteristics, such as points, lines, surfaces, functions, vectors, spatial or temporal patterns, movements, particle trajectories, thermodynamic features, signals and, above all, symmetries. The manifold M may be equipped with every kind of curvature: concave, flat or convex (Tozzi, 2016; Peters et al., 2016). The number n may stand for different kinds of dimensions, e.g., spatial, temporal, complexity, and for different numbers, e.g., natural, rational, irrational, imaginary. Matching features can be described as paths or trajectories on *abstract* structures and allow system features commensurability. It looks like a transparent glass sphere between a light source and your eyes. You watch two lights on the sphere surface instead of one. But the two lights are not just images, they are also real. Matching features can be thus assessed at one level of observation, while single features at a lower one. Symmetries are widespread invariances underlying the function and activity of physical and biological systems at every level of organization. Standing for the most general features of systems, even more general than the entropy constraints, symmetries provide a general approach to every kind of biological function (Tozzi and Peters 2016b). Symmetry breaks are detectable at a lower level of observation—in other words, a single feature stands for broken symmetry, which can be restored at one level higher. Therefore, matching descriptions are restored symmetries. If we evaluate systems just one dimension higher, we are able to find the otherwise apparently hidden symmetries.

In this paper, our aim is addressed to build a gauge theory for *topological* cells, with potential to be used as a general methodology able to describe in depth the structural and functional complexity of living beings.

TOPOLOGICAL CELLS

Complexity Index. This section aims to apply the above mentioned topological concepts to biological cellularity (i.e., *topological* cells). In a topological framework, biologically significant environmental components become matching points into the cell. Every type of living cell displays maps with different function and description and lies in a dimension higher than the environment. In order to evaluate living cells in terms of features embedded in M^n manifolds, we need at first to search and define the parameter which stands for our n value, i.e., the complexity index.

Biological complexity has been widely discussed during recent decades from multiple points of view: evolutionary (Bonner, 1988); Boolean networks (Kauffman, 1993); cellular automata (Wolfram, 2002); Turing machine (Danchin, 2009); operating systems (Yan et al., 2010); and different kinds of scalable computer models have also been developed (Ayyadurai et al., 2011; Helikar et al., 2012). Inspired by (Mariotti, 2008), we may say that an appropriate complexity index across biological scales should be

evaluated in terms of a product of several factors, such as number of genes, average splicing events, number of differentiated cell types, and energy rate; and quite probably that product should be divided by the life span and the total mass expressed in adequate units. Notwithstanding that, herein we decided to use the sole energy rate that, although not fully representative of the whole biological complexity, nevertheless is an important and very manageable general parameter. Indeed, the *energy rate density* is the amount of energy across the system per unit time per unit mass (in CGS metric units erg/s/g; in MKS units joule/s/kg). Regardless of the units used, energy rate density describes the flow of energy that circulates through any living system of a given mass, and has been proposed as a proxy of systemic complexity along the evolutionary process (Chaisson 2010, 2014). Energy rate density, equivalent to the specific metabolic rate in biology, has gained traction in recent years, with many diverse applications in various disciplines, including ecology, ethology, and behavioral science (Neubauer 2012). The estimates of complexity metrics for plants and animals are provided in **Figure 1**. Indeed when we proceed towards more *advanced* cells, such as from archaea and prokaryotes to eukaryotes, we achieve biological systems with increasing complexity. For instance, prokaryotes stand for a S^n sphere and eukaryotes for a S^{n+1} sphere. Cellular pathways stand for single points on S^n and for matching points on S^{n+1}. The more the cell is complex, the more the corresponding metabolic patterns become *transmolecular,* being massively involved with the whole signaling, transcriptional, translational, transportation, and degradative apparatuses of the rest of the cell. Additionally, in more evolved cells, protein domain recombination equipped with higher levels of modularity gives rise to increased complexity of the system's molecular components themselves (Koonin, 2010). Just in signaling terms, eukaryotes are counting with around two dozen of major classes of signaling pathways, versus the three main classes of prokaryotes (Marijuán, et al., 2010). These supernumerary pathways subsequently organize the developmental process of the multicellular by following the equivalent of a *signaling master plan* (Gerhardt 1999; Marijuán et al., 2013). Most of the developmental, morphological, and physiological correlated processes are based on a series of balances and symmetry breaks between opposed pathways, organized in circuits of astonishing complexity, but finally describable in symmetry terms. In sum, going from lower to higher complexity dimensions spheres, we achieve not just an increase in matching, superimposed biomolecular and metabolic patterns, but also an exponential increase in the number of symmetries.

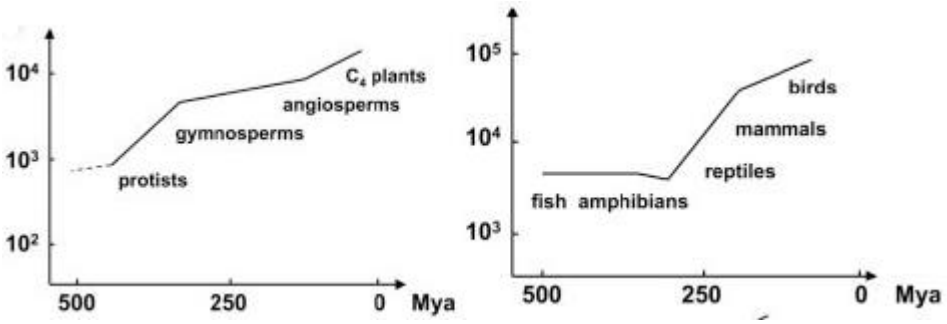

Figure 1. Chausson's complexity estimates for different biological structures. Modified from: http://www.informationphilosopher.com/solutions/scientists/chaisson/

Energy. Going from a higher to a lower dimension, a decrease of half of information and energy occurs, and vice versa (**energy-BUT**). There exists a physical link between the abstract concept of BUT and the real energetic features of systems formed by two spheres S^n and S^{n-1}. When two antipodal points on an *n*-sphere S^n map to a *n*-Euclidean manifold where S^{n-1} lies, a symmetry break/dimensionality reduction occurs, and a single point is achieved (Peters and Tozzi, 2016b). It is widely recognized that a decrease in symmetry goes together with a reduction in entropy and free-energy (in a closed system) (Roldán et al., 2014) It means that the single mapping function on S^{n-1}displays energy parameters lower than the sum of the two corresponding

antipodal functions on S^n. Therefore, a decrease in dimensions gives rise to a decrease of energy and energy requirements. BUT and its variants become physical quantities, because we achieve a system in which energetic changes do not depend anymore on thermodynamic parameters, rather they depend on topological features such as affine connections and homotopies. The energy-BUT concerns not just energy, but also information. Indeed, two antipodal points contain more information than their single projection in a lower dimension. Dropping down a dimension means that each point in the lower dimensional space is simpler, because each point has one less coordinate. In sum, energy-BUT provides a way to evaluate the decrease of energy in topological, other than thermodynamic, terms. Matching features display a doubled energy, compared with their corresponding single feature, in order that a *force* is required to go from the lesser dimension to the higher. It is in touch with biological claims. Indeed, with increase in evolutionary cellular complexity, the energy requirements become larger. To make an example, an average protozoan has nearly 5000 times more metabolic power than a single bacterium and can support a genome several thousand times larger (Lane and Martin, 2011). Successive levels of potency are organized along the evolutionary and developmental processes. In prokaryotic species, there exists an approximately quadratic relationship between the total number of genes and signaling components (Galperin, 2005), while the increase is exponential in eukaryotes (Marijuán et al., 2013). In the same vein, the information contained in a single feature embedded in a lower level is half the information contained in matching features embedded in the higher level. Because single features comprehend less information and less entropy than matching features, it also means that the environment contains less information and complexity than living beings.

Biomolecular pathways are topological strings. A recently developed BUT variant is particularly useful in our context, describing the topological existence of strings, e.g., paths defined by moving particles. The Str-BUT variant may use particles with closed trajectories instead of points. The usual continuous function required by BUT (Peters and Tozzi, 2016a) is replaced by a proximally continuous function, which guarantees that, whenever a pair of strings (regions that are world lines) are close (near enough to have common elements), then we always know that their mappings will be also be close. A string is a region of space with either bounded or unbounded length. A region of space X is a worldsheet, provided X is covered with strings. By covered, we mean that if x is a point in X, then x belongs to at least one string. As a particle moves through space following a world line (Olive and Landsberg, 1989), interactions occur at the junctions of world lines. For a mathematical treatment, see **Supporting information**. As time evolves, a particle leaves a trace of its movements along a surface that is *remembered*. One of the noteworthy features of strBUT is that strings can be described as movements on a donut-like torus. A string is then a remembered part of a hypersphere surface over which a particle travel. In order to map S^{n-1} to S^n, we need to work with higher dimensional spaces containing regions where each point in S^n has one more coordinate that a point in S^{n-1} (**Figure 2**).

In our framework, the closed paths described by strBUT stand for biochemical pathways occurring in both prokaryotic and eukaryotic cells. Indeed, in all the living cells, molecular components and signal pathways are densely connected with the rest of systems. The tight coupling among different systemic activities, such as transcription, differential splicing, domain recombination, and cell differentiation gives rise to an omnipresent signaling system that is in charge of receiving and interpreting all kind of inner/outer environmental inputs. Transmembrane molecular mechanisms continuously sense the external and internal milieu, leading to amplification cascades and mobilization of many different actuators (Gerhardt, 1999; Marijuán et al., 2013). As an illustration, how a real genome (pertaining to *E. coli K-12*) may react to very different kinds of environmental and inner stimuli can be evalauted in genomic and proteomic terms too (Marijuán et al., 2015). An intertwined, ever changing play occurs between incoming signals and inner controlling mechanisms. Because the string paths are closed and display a hole in their structure, it means that the massive networking of the whole biomolecular and metabolic patterns has to be amenable to description in abstract terms by means of trajectories traveling on donut-like structures. Indeed, every single biomolecular pathway distinguishable in the cell may be taken as a closed string, either longer or shorter, and due to functional and topological proximity (Peters, 2016), it becomes intertwined with other strings in order to preserve the general homeostasis. Thereafter, the strBUT could be encompassed in the general context of cellular pathways, metabolic and otherwise. Metabolic responses encompass most of the genomic repertoire in prokaryotic cells, while they do not represent more than about 10 % in eukaryotes. Furthermore, because

metabolic paths (the centrality of glucose degradation, and finally ATP production) are often the same in prokaryotes and eukaryotes, we may instead think in terms of difference in complexity when we also take into account signaling and controlling paths. Indeed, in eukaryotes, thanks to the enslaved mitochondria and their endless ATP supply, the bulk of complexity lies in the accompanying retinue of signaling, transcription, splicing, translation, transportation, and degradation processes. All these processes are functionally different, but all of them are crisscrossed and topologically interrelated. For instance, the qualitative difference between signaling and metabolic pathways was admirably described by Gerhardt (1999, p. 228):

"As information transfer pathways, these signaling pathways are basically different from metabolic pathways, even though both are called 'pathways'. In a biosynthetic metabolic pathway, a carbon compound passes through a series of enzymatic steps, with appropriate energy inputs, undergoing modifications until it emerges as an end product ready for incorporation into a macromolecule or complex lipid. But in a signal transduction pathway, carbon atoms and energy are not passed along. Only an impulse is relayed by way of successive reversible changes of state of switch-like intermediates. At the end of the pathway, the transduced signal activates or inhibits some target protein […] the most frequent target of signaling is transcription, and some pathways affect only transcription."

Under our strBUT perspective, ALL biochemical, biomolecular, signaling, and metabolic pathways may be treated similarly. And that's a great analytical advantage.

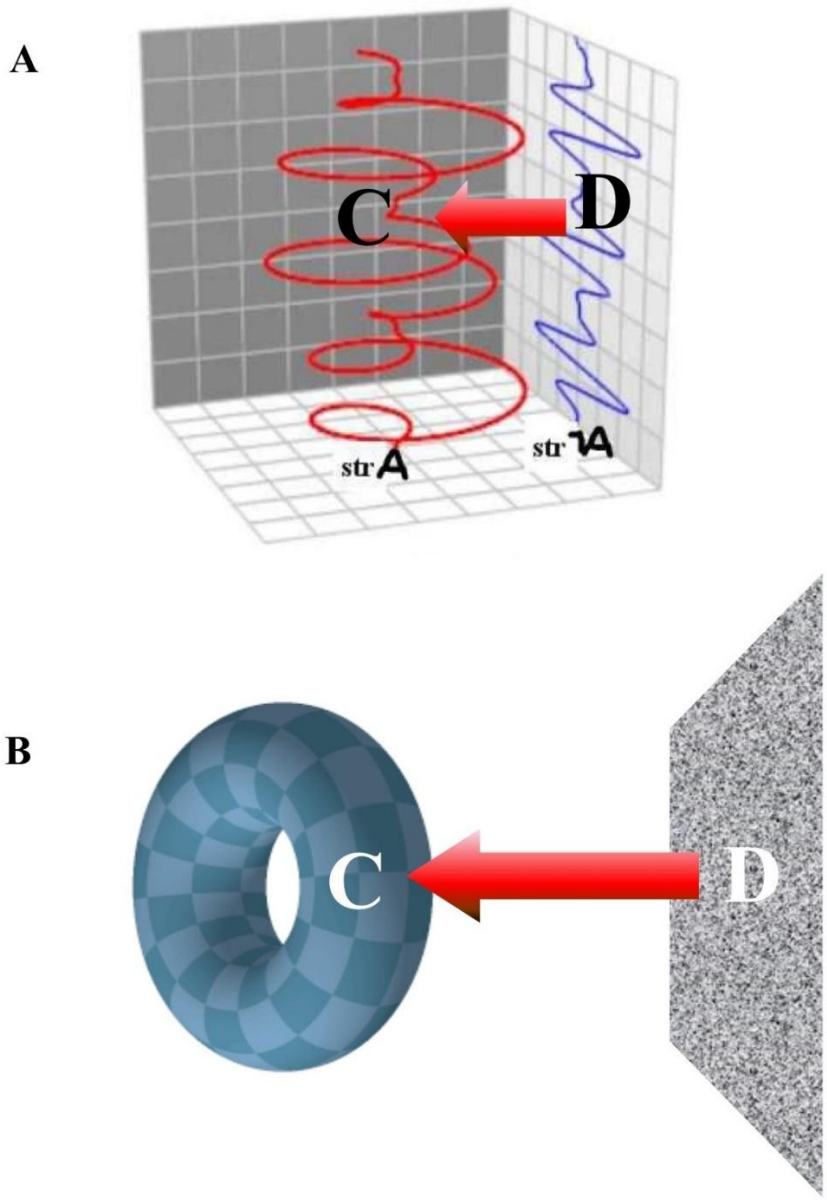

Figure 2. StrBUT allows to proceed from linear to multidimensional paths. **Figure 3A** illustrates two regions strA and [strA, where strA is embedded in a higher dimension C (a worldsheet) and [strA in a lower dimension D. strA and [strA stand for antipodal points with matching description. The path D stands for an environmental input reaching cell receptors. According to the dictates of strBUT, when we start from the evaluation of the linear pattern D, we could be able assess its movements in C, e.g., one dimension higher. C stands for cellular metabolic pathways. Because the more the dimensions, the more the information, we achieve, from the knowledge of the simpler pathway D, the more complex C. As stated by strBUT, C may be described as a torus. Therefore, the movements of D become linear movements on a torus, equipped with more information content than C (**Figure 3B**).

How to build a topological cell? At first, we embedded the whole cells, their metabolic machinery and their DNA in different n-spheres, depending on their known degree of complexity, quantified through their energy rate density. An example is provided in **Figure 3**. Few DNA segments (genes) and string-like metabolic pathways on a n-sphere give rise to many DNA segments and metabolic pathways on a n+1 sphere, in which n+1 = higher complexity. It also means that living cells display a higher number of symmetries, compared with the surrounding environment. The increase is transitory, because, in biological entities, a local decrease of entropy occurs, apparently against the second law of thermodynamics. When a biological structure increases its complexity dimensions in evolutionary timescales, then it displays antipodal points. Thus, biological structures increase symmetries and matching functions when their complexity increases. It also means that BUT is a general feature of biological systems. **Figure 3** shows how, with increases in complexity, the original single points (or strings) embedded in less complex S^n spheres become matching points on spheres of higher dimensions. Going towards higher dimensions, we achieve an exponential increase of matching points. This is in touch with the exponential growth of pathways and subsystems described in eukaryotic cells, compared with prokaryotic ones (Marijuan et al., 2010, 2013). According to the dictates of a BUT variant, the single points stand for broken symmetries, while the two matching points for restored symmetries. The energy-BUT comes into play when the cells, equipped with high energetic levels due to their enlarged energetic machinery (via mitochondrial endocytosis), might give rise to the passage towards higher dimensions. It also means that, starting from the lower complexity of an inanimate environment, we achieve an enormous increase of complexity in living cells. The further evolution of biological systems, in touch with the concept of *bricolage* which describes novel eukaryotic rearrangements of prokaryotic signaling systems, plus the incorporation of mitochondria, nuclear membrane, cytoskeleton, endocytic matrix, flagellum, etc. makes possible the display of a finite, although enormously high, number of intrinsic symmetries, which are the toolbox from where modular molecular assemblies are organized.

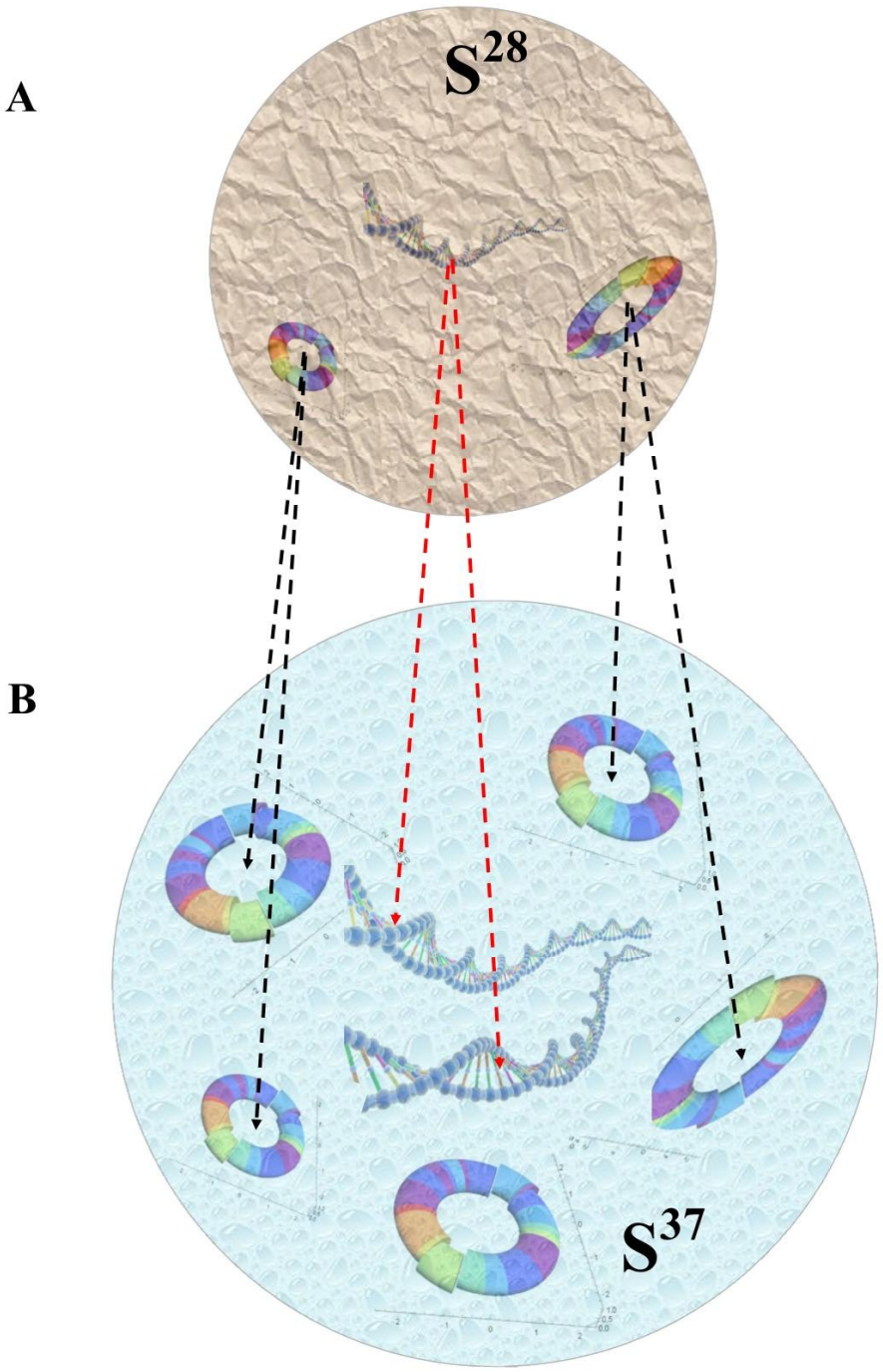

Figure 3. Protists (**Figure 3A**) and angiosperms (**Figure 3B**) in the framework of BUT and its variants. The two cells are embedded in n-spheres in which n stands for their energy rate density. Metabolic pathways are depicted as strictly interconnected string-like toruses that give rise to the intertwined multi-levels of activity typical of biological entities. The projection from the lower-dimensional sphere to the higher-dimensional one leads to an increase in number of metabolic pathways (black arrowhead lines) and DNA strands (red arrowhead lines).

A GAUGE THEORY FOR TOPOLOGICAL CELLS

Gauge theory in physics is a field theory, in which the Lagrangian, e.g., a function that summarizes the dynamics of the system, is invariant under a continuous group of local transformations (Zeidler, 2011). What does it mean? We will try to explain what a gauge theory is, trying to convey the geometric intuition rather than the rigorous formalism. Gauge theory originates from physics; however, they could hypothetically be applied to countless fields of biology, including cell function. Here we hypothesize that cellular activity is due, at least partially, to a gauge theory. The most important question is the following: is it possible to transfer the powerful gauge symmetries from their natural environment of physics particles to the soft and much more complex living structures? In other words, are we allowed to sketch a gauge theory of cellular function? The answer rests on the possibility to recognize in biological structures the tenets of a gauge theory:

1. The chance to apply differential geometry to living structures.
2. The presence of a living system equipped with a continuous symmetry and a physical quantity to preserve, e.g., the Lagrangian, according to the Noether theorem;
3. The presence of local forces acting on the system, e,g. in technical terms, a continuous group of local transformations.
4. The presence of counterbalancing force, called gauge field, which is able to restore the general symmetry broken by the above mentioned local transformations.
5. In order to allow a comparison among the required forces, they all need to perform the some kind of movements. In technical word, the forces need to be equipped with a Lie group. To make an example, all the forces that travel along a circumference belong to the same Lie group, called U(1).

The underlying concept of gauge theories is quite simple: *gauge* means *choice*. A gauge is a *coordinate system* that varies depending on one's *location* with respect to some *base space*. When sketching a gauge theory, one can freely choose a symmetry a priori. By fixing a gauge, the model becomes easier to analyze mathematically. However, the tractability of the resulting problem can be heavily dependent on the choice of gauge that one fixed. A gauge theory is an abstract conjecture that needs to be tested by severe investigations (Tozzi et al, 2017, to appear).

Therefore, we need to find at first biological counterparts of the above mentioned tenets. The cellular biomolecular pathways, e.g., the topological strings moving in guise of torus trajectories, might stand for the required global symmetry. We can definitely bring strBUT into the picture. The trick here is to have a proximately continuous mapping f from a torus X to R^n, so that f(strA) = feature vector of string strA in X. Let sheetA be a region of X that is a worldsheet. We introduce a second proximately continuous mapping g: from 2^X (family of strings on X) to R^n, so that f(sheetA) = feature vector of worldsheet sheetA on X.
All the intertwined contiguous strings stand for the Lagrangian, which value is known, because it corresponds to Chaisson's energy rate density, expressed in erg s^{-1} g^{-1}. The global symmetry stands, in biological terms, for cellular homeostasis. The environmental stimuli acting on the cells receptors stand for the local transformations and give rise to local losses of symmetries into the cell. *The species-specific DNA stands for the required gauge field: the genome originates the "force" that counteracts the local environmental transformations acting on the cell.* Such a gauge field restores the locally-broken global cellular symmetry.
In order to operationalize the whole procedure, we need that the three ingredients, e.g., global symmetry, local transformations, and gauge field, are all of them equipped with the same kind of movements, so that they can be compared. Indeed, the particle movements on C (in **Figure 2B**) may be described in terms of the proper Lie group. We may take into a Lie group which movements take place on torus, donut-like structures. A torus can have a topology defined on it. The trick is to define a basis, so that the union and intersection of all sets in the basis gives us the members of the topology. In other words, we need to evaluate real external forces, metabolic cellular pathways, and DNA function in terms of abstract trajectories on a torus-like structure. In such a way, we are allowed to calculate the energetic values of the three ingredients. **Figure 4** illustrates how to build a gauge theory for cells. The differential geometry techniques in order to build a gauge theory are formally described in Sengupta et al. (2016) and in Tozzi et al. (2017, to appear).

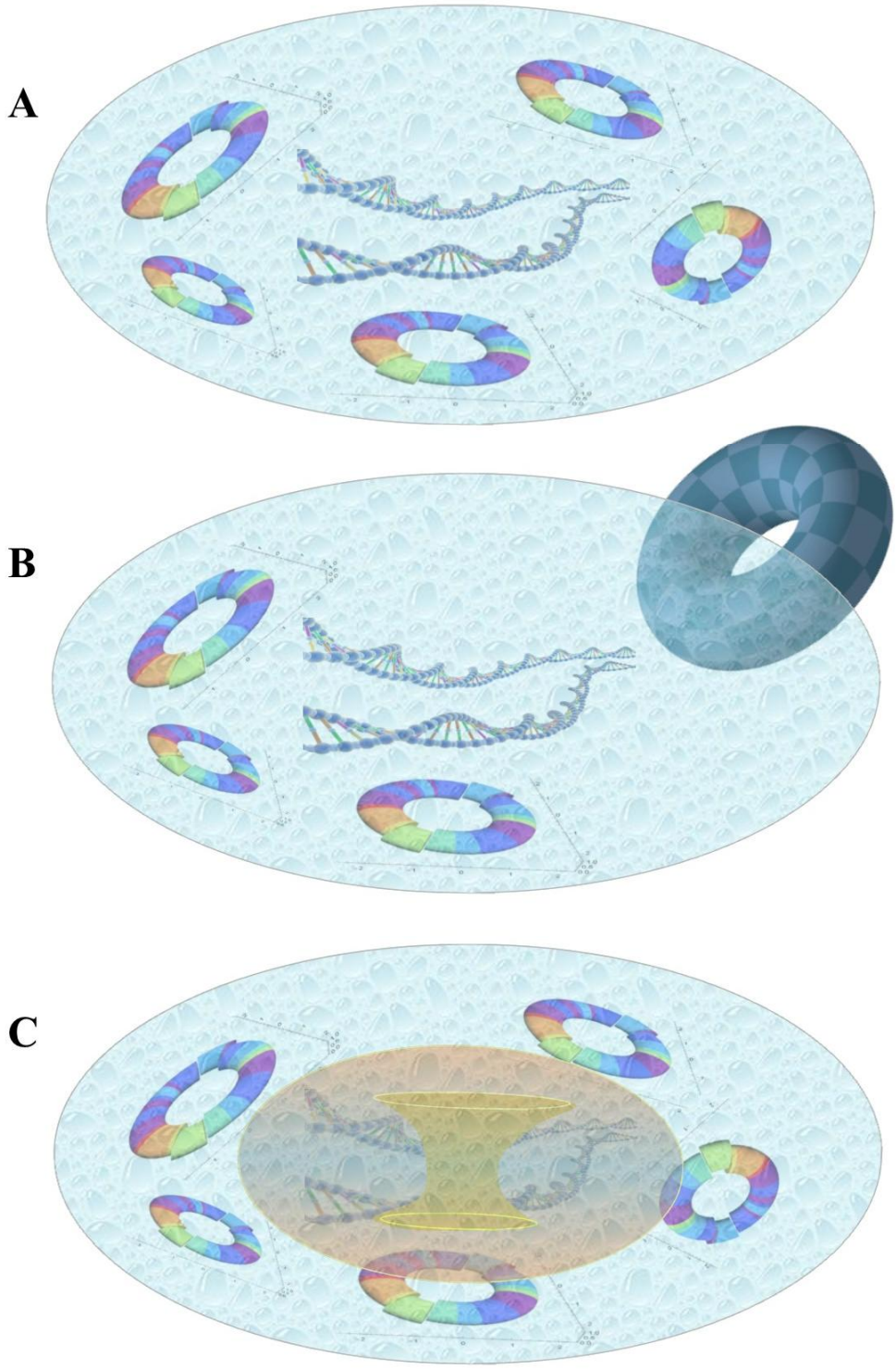

Figure 4. A simplified sketch of a gauge theory for cellular function. **Figure 4A** illustrates a cell with its intertwined metabolic pathways, displayed in guise of strings words. Every string stands for one of the different biochemical pathways that contribute to cellular homeostasis. In gauge terms, all the strings together stand for the general symmetry of the cellular system. When an external perturbation occurs (**Figure 4B**), it gives rise to local losses of symmetries into the cell, illustrated as the disappearance of some few strings. In order to restore the general symmetry, a continuous gauge field is requiered, which exerts a

force opposite to the external perturbation (**Figure 4C**). Such a gauge field originates from the DNA. Note that all the forces are depicted in guise of torus-like abstract movements, and are thus comparable one each other.

DISCUSSION

Topology, the mathematical branch which assesses the objects' properties preserved through deformations, stretching and twisting, allows the investigation of the most general activity features of biological systems. In particular, the biological incarnations of BUT and its variants allow an inquiry of the evolution from inorganic to organic structures and the comparison between prokaryotes and eukaryotes metabolisms. In order to elucidate the general mechanisms and the evolution of cellular functions, we introduced a topological framework with keeps into account two variants of the BUT: a string-variant (strBUT) and an energy-variant (energy-BUT). We showed how topological tools allow us to assess the big divide of biological complexity in the framework of BUT variants. The invaluable opportunity to treat *real* systems as *abstract* topological structures makes BUT a universal principle underlying natural phenomena.

The general BUT scheme allow systems' properties in the real space to be translated to abstract spaces, in guise of particles travelling on dimensions of donut-like structures. This model talks about a topological world, made of natural projections, where the connections among signals occur via proximity and mappings equipped with a structural order. There exist intertwined levels, correlated by maps, where different energy levels allow dimension increases or decreases. The world is a map from a level to another, and the cell is a rather constrained structure determined by factors external to itself. In such a vein, life is mapping, change of dimensions towards an increasing complexity, which leads, in living beings, to local increases of thermodynamic parameters and information.

In touch with the concept of complex systems, defined as any system that cannot be fully understood by reducing it to its parts, we took into account the relational impacts of organization in natural systems, based on *organized* rather than on the sole *particulate* matter (Rosen, 1991). In a posthumous essay (Rosen, 2000): "The Schrodinger Question: What Is Life? Fifty Years Later", this author described the genome as a *force generator* acting upon the *inertial* enzyme and protein components of the cytoplasm (the whole scheme being developed via category theory and metabolic/repair systems), quite in line with the main idea herein developed. Indeed, as our paper sketches, a general gauge theory of cell function and biological complexity looks feasible, to be cast in a testable fashion, in which symmetries and energetic constraints play a foremost role in order to operationally describe living beings' functionalities. We hypothesize that the general symmetries, equipped with a Langrangian given by the internal homeostasis, stand for the whole cellular biomolecular network. Note that in this framework the general symmetries are more than ones. The local transformations stand for the environmental inputs, which locally break the general cellular symmetries. In order to restore the broken symmetries, a gauge field is required. In this case, the gauge field might stand for the action of the cellular genome. Every species displays a different genetic repertoire, each one corresponding to a unique gauge field. The importance of a gauge theory for living beings lies on the chance to predict and calculate unknown parameters. If we know the values of two of the three ingredients, we may achieve the value of the third, via differential geometry. In our model, the general symmetry values are known, because they correspond to the energy rate density typical of every cellular species. Vice versa, given a vector value (say, an energetic value) for DNA and environmental stimuli, we could calculate the energy vector of the cellular symmetries. For example, we may assess which is the maximum external force which can be applied without destroying a given cell type. Through simulations that progressively increase the force of the external stimuli, it is also possible to know what is the minimum energy required for archaea, prokaryotes or eukaryotes.

Hutchinson et al (Hutchinson et al., 2016) recently described the minimal bacterial genome, e.g., the simplest artificial cell capable of autonomous growth. However, their cell is unrealistic, because they used a growth medium provided with an exceeding amount of metabolites and micronutrients. A gauge theory might help

to calculate the amount of DNA energy (and genes) required in order to build a more realistic and self-sustained minimal bacterial genome within a natural environment, without the help of any sophisticate artificial feeding. But, by far, the biggest challenge of the gauge approach would correspond to the framing of a new interpretation, symmetry based, of developmental processes.

We would like to bring to an end with some caveats and warnings (and further speculations!). Too many questions are still open. For instance, could we reconcile the gauge approach not only with the homeostasis, but also with the advancement of a life cycle, e.g., its *closure* with either reproduction or death? It would be very useful, both for the prokaryotic *simple* life cycle organization and for the eukaryotic *topology-laden* stages of cellular life, to encompass differentiation as well as apoptosis/necrosis (Joo et al, 2016). Using the cycle as general symmetry reference would be a very fruitful step to take. The abstract *strings* constituting cell cycles might have also other features apart from the ones suggested in our paper. For example, the cycle advancement can be cast with different paths, depending either on environmental inputs, or disturbances, internal randomness, and so on. Maybe we could take into account multidimensional *attractors* equipped with basins of many possible states: see for instance the giant component that emerges for linked metabolic reactions in *E.coli*, with star-like topology (Almaas et al., 2004). Then the force arising from the genome, after receiving the appropriate *signals*, could modify some of the trajectory dimensions, so that the whole system is able to come back to the attractor/s. This can be seen in the way a real genome responds to external and internal disturbances (Marijuan et al., 2015). A few critical points, or multimensional junctures, could be topologically important, as they become singularities leading to novel attractors or sub-basins. In the biomolecular literature they are known as *checkpoints* (Marijuan et al., 2013). These cellular checkpoints become extreme *bottlenecks* that connect different regions of the same torus, or alternatively they could pertain to different toruses (e.g., in the case of cellular division leading to differentiation). Furthermore, if we take into account the whole *multicellular space*, would a global torus emerge from the fusion/mosaicism of the little cellular ones, via the massive information flow of shared signaling events? If we instead take into account a *multicellular time*, e.g., the structure of rhythms within rhythms (with a circadian central adaptive pattern), could we think on something like the *"torus of today"* applied to the customary behavioral repertoires displayed by all animals into their natural environments?

In such a multifaceted context, the powerful strBUT approach displays the big advantage to treat all the trajectories as if they were embedded in a torus-like structure. It allows the comparison of completely different kinds of flows in a single, coherent scheme. In sum, the torus is the abstract space of the whole cell survival trajectories, carefully guarded by another torus, the genome.

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