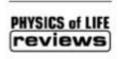




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# Reply to comment

# Brain projective reality: Novel clothes for the emperor Reply to comments on "Topodynamics of metastable brains" by Arturo Tozzi et al.

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First of all, we would like to gratefully thank all commentators for the attention and effort they have put into reading and responding to our review paper [this issue, Tozzi et al. [44]] and for useful observations that suggest novel applications for our framework. We understand and accept that some of our claims might appear controversial and raise skepticism, because the overall neural framework we have proposed is difficult to frame in established categories, given its strong multidisciplinary character. To make an example, Elsevier is publishing the British Neuroscience Association (BNA) 2017 Special Issue Collection. However, our paper could not fully fit in any of their Special Issues-attention, motivation, behavior, sensory and motor systems; novel treatments and translational neuroscience; genetics and epigenetics; learning and memory; neurodegenerative disorders and ageing; developmental neuroscience; neuronal, glial and cellular mechanisms; neuroendocrine and autonomic nervous systems; psychiatry and mental health; methods and techniques. Perhaps because our paper was mathematically, physically, biologically (neuroscientifically), and phenomenologically motivated from the start? Nevertheless, venturing in novel, fresh, testable proposals is badly needed in contemporary neuroscience, so to break into "the utter darkness of the inner mechanism of psychic acts... during the production of the concomitant phenomena of perception and thought, namely, feelings, consciousness and volition"-as Cajal had already observed in his opus magnus 'Textura'. But as he soberly confessed: "This ideal is still very distant" [38, p. 1,141]. In the pursuit of that very ideal, neuroscience and psychology have had, and continue to have, a plethora of movements and schools of thought: behaviorism, cognitivism, neural Darwinism, social

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constructivism, Bayesian optimization...In our paper, we propose to go a step further, via the notion of topodynamics, towards "projectionism." In what follows, trying to elucidate the main features of this Emperor's new clothing, we proceed with the responses to the comments received.

# 1. Where are the proofs?

Among all the commentators, one (Lerner, [this issue]) has argued that the target paper is lacking the evidence of topological dynamics in the brain. It is somehow unexpected that Lerner fails to see the provided justifications and evidences that are discussed in much detail in the target paper itself. Even though this is a single case, we prefer to address it form the start, since it concerns the validity of our approach. At the same time, constricted by the space limitations of this reply, we can only provide very brief additional comments about that. As suggested by Erdi [this issue], looking at very recently published papers as well as at older ones through a topological lens, we find several methodological clues in favour of our framework.

#### A torus-like functional structure

An important theoretical prediction of our review paper has been already experimentally confirmed. A torus-like functional structure has been recently reported in functional landscapes' trajectories traced through dynamic EEG brain connectivity data (Xing et al., 2017). Additionally, in their comments Papo [this issue] and Friston [this issue] have pointed out that Finkelstein et al. (2015) demonstrated a 3D head-direction mechanism represented in azimuth × pitch toroidal coordinates in bats, which could support navigation in 3D space. Indeed, consistent with their toroidal model, head-direction pitch-cell tuning was unimodal, circular, and continuous within the available 360° of pitch. Furthermore, our model had predicted diffuse, long-range cortical interactions, in order to allow the brain to "build" the required multidimensional torus-like functional structure. In a recent work, Moore et al. (2017) measured neocortical sub- and supra-threshold dendritic membrane potential from distal-most dendrites in freely behaving rats, and demonstrated that dendritic action potentials firing rates were several-fold larger than somatic ones. Their data also point towards the occurrence of a hybrid, analog-digital coding in the dendrites, equipped with egocentric spatial maps comparable to pyramidal neurons (Moore et al., 2017). This confirms our own prediction that neural activity must not be limited to the "classical" extracellular somatic spikes, but must be extended to other neural structures, such as the dendrites.

## Default mode network's symmetries

Tozzi and Peters (2016) described a functional torus occurring during the brain default mode network's activity. This torus must be equipped with antipodal points, i.e., a symmetry in which two brain areas are activated together with the same EEG frequency (or with the same fMRI entropy values). In turn, when the functional torus is "broken", e.g., during the deactivation of the default mode network, this kind of symmetry must be broken. A few years ago Fingelkurts and Fingelkurts (2010) published data that support the idea that in resting state two homologous (symmetrical) EEG channels exhibit the same frequency pattern. Indeed, they showed that analysis of EEG short-term spectral pattern (SP) types in different EEG channels within the same observation revealed that the same type of SP can be observed simultaneously in two EEG channels in 70% of observations during one minute EEG (notice that in the majority of cases these were homologous EEG channels – for example O1-O2 – and therefore have homologous functions).

## Complex perceptual stimuli

In full agreement with our proposal that cortical neurons are significantly driven by interactions occurring across stimulus dimensions at all temporal levels and spatial scales, Sloas et al. (2016) were able to quantitatively describe the dependence between neural response and stimulus dimensions. More specifically, they demonstrated that auditory cortical neurons in mice are sensitive to interactions across dimensions, indicating significant integration across stimulus dimensions (such as center frequency, intensity, and bandwidth). This suggests that cortical representations of complex perceptual stimuli are not captured by low-dimensional characterizations.

## Emotion and cognition

According to our framework, brain-mind operations (for instance, emotion and cognition) are dual in nature, i.e., they stand for the same activity with different descriptions, despite the fact that emotional states (the so-called emotional feelings) are often treated as different from cognitive states, such as those related to the perception of external stimuli. A recently published paper (LeDoux and Brown, 2017) supports this understanding. It challenges the conventional view which argues that emotions are programmed in subcortical circuits, and proposes instead that emotions are higher-order states instantiated in cortical circuits. They argue that conscious experiences, regardless of their content, arise from one and the same brain neurodynamic architectonics and propose a higher-order theory that accounts for

self-awareness of both conscious and emotional experiences (for a similar conceptualization, see also Fingelkurts et al., 2010a, 2013).

#### Topological findings

Two novel, recent findings throw a bridge between the Borsuk-Ulam theorem's antipodal points and the symmetric bidirectional connections in local cortical networks. In the first paper, a probabilistic mathematical analysis shows that the occurrences of bidirectional paths and non-random structures are closely linked in a network equipped with pairs of symmetric connections (Hoffmann and Triesch, 2017). This means that an overabundance of reciprocally connected pairs occurs, at least when pairs of neurons or neuronal assemblies are more likely to be connected than others. The second paper (Waskom and Wagner, 2017) is in touch with our prediction that the brain displays matching points (regions) encompassing higher mental functions. Indeed, these authors, examining fine-scaled subnetworks in targeted prefrontal regions, found that pairs of voxels with similar context preferences exhibit spontaneous correlations, approximately twice as large as those between pairs with opposite context preferences. As we have predicted, the regions' features must double, compared with regions encompassing lower mental functions. This means that the abstract representations that support goal-directed cognition are constrained by an intrinsic functional architecture, prompting new models of information representation in the association cortex.

Another recent study points towards a topological organization as an universal mechanism for local density control in cultured neural progenitor cells (NPCs). Kawaguchi et al. (2017) discovered that the NPCs' morphology and macroscopic patterns resulting from cell-to-cell interactions depend on interspersed topological defects with winding numbers of +1/2 and -1/2. Single-cell-level imaging around the defects clarified that cells not only concentrate at +1/2 defects, but also escape from -1/2 defects. A very similar mechanism of instability around (this time reversible) microcolumnar topological defects has been also recently proposed by Tozzi et al. (2017b), in order to explain the possible mechanisms underlying the neural code. Therefore, topological defects might be seen as a general mechanism in biology and neuroscience.

#### Intraneuronal mechanisms

In touch with Garreffa's comment [this issue], our framework supports the hypothesis that a preparatory, predictive coding is "a priori" located in the brain. Apart from the "classical" meso- and macro-level "predictive coding" accounts by Allen and Friston (2016), it has been recently demonstrated that the micro-level of neuronal intracellular activity is also involved (Mauger et al., 2016): neurons are equipped with a nuclear pool of polyadenylated transcripts that retain selected introns. Regulated intron retention in fully transcribed RNAs represents a mechanism to rapidly mobilize a pool of mRNAs in response to neuronal activity. This means that neurons encompass a stable reservoir of precursors that are then modified, according to the cellular requirements dictated by the different stimuli. In touch with this claim, recent observations underscore the instructive role of intrinsic mechanisms in synapse formation. Indeed, Sando et al. (2017) demonstrated that hippocampal circuits can develop independently of excitatory neurotransmission. This means that synapses assembled in the absence of activity are structurally mature. Loss of release did not disrupt the morphogenesis of presynaptic terminals and dendritic spines, suggesting that synaptic vesicular release of glutamate is unnecessary for synapse, assembly, morphogenesis and maintenance (Sando et al., 2017). See also Navarro et al. (2017) for a general description of the intraneuronal information processing mechanisms, which include tagging molecules for guidance of protein synthesis in postsynaptic spines, in concordance of presynaptic and postsynaptic neuronal activities. Summarizing, we could state that the above described intracellular mechanisms stand for a Kant's a priori, for a Friston's prior, and (in our terms) for a pool of symmetries, available into the neuron before its "interaction" with the environment. This means that the influential Locke's account of the mind as a "tabula rasa" filled with environmental sensations needs to be fully rejected.

# Last news

A very recent paper, although not quoting us, provides additional support to our multidimensional account of the brain operational architectonics. Reimann et al. (2017) found, in the artificial micro-columnar network developed by the Blue Brain Project, several geometrical structures, termed cliques. The latter are multidimensional, and, in touch with our BUT, display pairwise correlations that increase with dimensions. The results of the study by Riemann et al. (2017) also confirm our theoretical conclusion that brain functions/operations are dual: the same features with matching description can be found both at the micro-levels (shown by Reimann et al. using a computational model of the neuronal network), and at the macro-levels of our multi-dimensional torus surrounding the whole, real, human brain.

# 2. Is our approach an oversimplification?

Starting from rather simple "abstract" claims, we have built a plausible general framework, able to elucidate disparate "real" phenomena of brain activity. Summarizing our novel topological approach, we observe that, just by taking into account projections among functional or real dimensions in a metastable brain (Fingelkurts and Fingelkurts, 2004, 2017), we achieve a system of mappings that fits very well with experimental results, as argued in the previous paragraphs. However, some commentators (Lerner directly, and, in a more nuanced way, Jausovec [this issue]) have expressed the concern that a mathematical/topological approach to systems features "talks" in rather general and abstract terms, leaving apart the overwhelming complexity of the human brain and the peculiar features of individuals and of single neural processes.

# "The unreasonable power of topology in neuroscience"

We, however, in touch with recent claims, ask whether physics of the mind is possible, and whether it is possible to describe the mind based on the few first principles as physics does (Perlovsky, 2016). In our paper, we have tried to go a bit further—paraphrasing a seminal paper of Wigner (1960), we would like to highlight the "unreasonable power of topology in neuroscience". Indeed, elementary topological structures reveal entirely unforeseen connections in the study of brain function: they allow an unexpectedly close and accurate description of neural phenomena in these connections. Using Wigner's words, we may state that topology's enormous usefulness is something bordering on the mysterious, because, although we do not know why topology works so well, however its accuracy seems to override the concerns about its truth and consistency. Indeed, in spite the baffling complexity of the brain (Fingelkurts et al., 2010a), topology leads to the discovery, description, and assessment of certain neurophysiological regularities and invariant properties that can be formulated in terms of accurate mathematical concepts. In our paper, we tried to show how topology plays a sovereign role in the metastable brain affairs, so that the laws of the nervous activity can be formulated in the language of mathematics and the language of mathematics offers a precise language of nature. Starting from a top-down approach (the neural topology), we tried to assess the apparently irreconcilable physical and psychological "coins" of the brain. In touch with a neutral monistic account of the brain, that emphasizes a common neutral element able to connect the brain and the mind (Fingelkurts et al., 2010b), we believe that the true bridge among them is the mathematics. Of course, this sort of "rationalism" is condemned to metaphysics, unless we do not provide (as we did) testable, empirical previsions, in touch with Quine's naturalized epistemology.

#### Dynamics of the metastable brain

In his comment, Jausovec [this issue] asked about the proofs of a metastable activity of the brain. We do not think that this is an objection, as he asked this rhetorical question and then answered by himself bringing several examples that show how the brain is indeed functioning in the metastable regime. In fact, a clean definition of metastability is provided in our paper, and it is sufficiently well explained why the neuronal assemblies as well as their larger spatiotemporal conglomerates are metastable. But we are aware that the concept of a metastable, multidimensional brain is not widely recognized and accepted yet, despite active work within this domain in neuroscience (for review see Fingelkurts and Fingelkurts, 2017). A lot of research is still left to be doneand topological concepts that take into account metastable principle might come into play. In this context, the Erdi's comment [this issue] is important. He suggested that a mathematical tool - neuropercolation - could be used to model the metastable regime of brain functioning. Indeed, neuropercolation allows modelling of the collective properties of interacting neural populations in brain networks that are near critical states, when the behavior of the system changes abruptly (Kozma et al., 2005). It provides a useful framework to describe abrupt transitions and critical phenomena in spatially distributed largescale networks, in particular, in brain metastable networks with transient dynamics, as operational architectonics suggests(Fingelkurts et al., 2010a,b, 2013). Indeed, neuropercolation and topodynamics could be plausibly integrated due to the fact that they both use a topological approach to explore the relation between dynamical sub-systems (neuronal assemblies and their larger spatio-temporal conglomerates), where more abstract representations correspond to higherdimensional spaces (complex OMs).

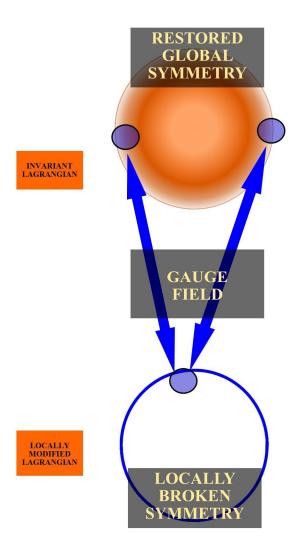
In this respect, Lerner's critique [this issue] is difficult to tackle, because it relates to mathematical and formal details that have been largely referred to the cited literature. Unexpectedly,he did not go through our references at all. The answers to his questions, in particular concerning all the mathematical proofs, are clearly stated in our previous published and quoted papers, that plainly explain why a decrease in dimensions gives rise to a decrease in energy; why the energetic requirements depend on affine connections and continuous functions; why descriptively similar points and regions do not need necessarily to be antipodal; why two cortical regions with the same entropy values can be assessed together; why many brain functions are believed to occur on functional negative-curvature manifolds; why the term "dimension" does not stand for a spatial one, but for "functional" ones; why more dimensions mean more complexity and information; why the functional cortical paths can be compared to moving particles in a phase space; and finally why neuronal assemblies allow synchronization.

One of the standpoints of our building is the correlation among topological landmarks, information and thermodynamic entropies. This follows the route pursued by Ingarden and Górniewicz (1990), who gave a hierarchical classification of different concepts of shape of compact connected sets, the most general among them being the homological shape. Giving a probability distribution of shapes, we can define a shape entropy, a mean shape

and shape fluctuations. This enables a formulation of information thermodynamics of shape and its applications to different fields, including the physics of the brain.

### A topological gauge theory for brain activity

In his comment, Friston[this issue] emphasizes the possible importance of a gauge theory for the assessment of brain function. Here we would like to stress that gauge theories can also be evaluated through the Borsuk-Ulam theorem. Indeed, the three main ingredients required to sketch a gauge theory are: 1) a system equipped with a symmetry and a correlated, measurable Lagrangian; 2) a continuous Lie group of local forces which break the symmetry locally; 3) one or more gauge fields, (possibly) external to the system, able to restore the broken symmetry and to keep the Lagrangian invariant, despite the local forces. The importance of such an approach rests upon the implicit ability to measure unknown quantities: if we know two of the ingredients (for example, the values of the Lagrangian and the total forces applied to the system), we can extrapolate and calculate the value of the third (for example, the gauge field), via procedures from differential geometry such as vectors' and tensors' projections. In a Borsuk-Ulam theorem context, the gauge field stands for the continuous function required to go from one level to another (see Figure 1 for a simplified sketch).



**Figure 1**. The Borsuk-Ulam theorem in the context of a gauge theory. As Borsuk-Ulam theorem and its variants require a function which needs to be continuous, a gauge theory requires a continuous gauge field. Modified from Tozzi et al., 2017c (forthcoming).

# Possible biochemical correlates of brain fourth dimension

Concerning the possible neurophysiological mechanisms involved in our framework of brain multidimensional symmetries, we could achieve further insights by assessing the action mechanism of some active chemical substances. For instance, it is well known that high doses of lysergic acid diethylamide (LSD) may give to a subject the experience of additional spatial or temporal dimensions. Subjects under LSD report that static objects in three dimensions seem to move relative to one or more additional spatial dimensions (Katz et al, 1968). Under LSD, as compared to placebo, a huge increase in correlation among disparate regions in the brain occurs (Carhart-Harris et al., 2017). In particular, the visual cortex increases its connectivity with other brain areas: this helps to explain, in our framework, the increase of spatial and temporal dimensions reported by users. From a pharmacological point of view, LSD leads to cross-activation of 5-HT2A receptor heteromers for a very long time, and increases glutamate release in the cortical layers IV and V, leading to their excitation (Moreno et al., 2011). Therefore, because brain modules' increased synchronization/connectivity is both predicted by our model and artificially achieved via LSD intake, it is tempting to speculate that the features of a physiological four dimension of the brain activity could be correlated with the same biomolecular mechanisms as those that underlie the LSD abnormal subjective effects.

#### 3. Possible further topodynamic developments of the metastable brain

Many commentators, seemingly aware (even more than us) of the hidden potentialities of topological approaches to brain function, propose to use topodynamic accounts also in neural contexts different from the ones we tackled, and in designing mathematical and computational models of fundamental brain-mind processes.

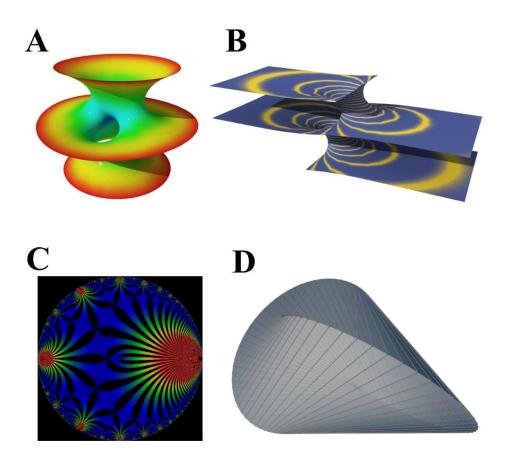
## Novel approaches for brain topological dynamics

Garreffa [this issue] suggested to extend the "picture" described by the BUT also to the assessment of non-electric oscillatory activity. In this context, he introduced a mechanical hypothesis (hyper-oscillating system) as an additional operating entity that takes into account, aside of the well-known BOLD-related nervous functions, also the active role of cerebral vascular dynamics in brain function. He wonders whether it is possible to introduce a new "wired" signaling scenario, including cardiac activity and breathing, in Borsuk-Ulam theorem terms. This is in touch with very recent findings, suggesting that cerebrospinal fluid and intracranial venous volume react inversely to changes in intracranial arterial volume (Laganà et al., 2017). Garreffa also wondered whether electromagnetic brain field (EMBF) in IPST level of the brain operational architectonics is the only emergent level that can constitute the OST level, and whether other non-electrical phenomena could be eligible. Yes, indeed, the EMBF is related with other nonelectrical fields in the brain and they are interrelated. In this respect, other oscillatory non-electrical phenomena could participate (to some extent, these interrelations are discussed in Fingelkurts et al., 2010a). Furthermore, Cankaya and Deli [this issue] suggested to complement the BUT calculations with the use of the matrix formulations borrowed from quantum mechanics, in order to assess brain activity states. Jausovek [this issue], in his turn, emphasized the possibility of applying our framework to study the individual differences in psychometric intelligence. Specifically, he believes that rate rapid transitional processes (RTPs) in brain activity and their synchronization among different brain locations could be strongly related to intelligence and its type. The preliminary data with RTP's synchrony (a.k.a. "operational synchrony") pointed that this might be a case (Fingelkurts and Fingelkurts, 2002), but further studies with a large sample of subjects are needed. Erdi [this issue] proposed to integrate topodynamics approach discussed in our target paper [Tozzi et al., 2017a, this issue] with neuropercolation model of neural populations with mixed local and non-local interactions. Henry [this issue] suggested the possibility to extend BUT in order to implement the current heterogeneous computing environments and hardware. He proposes very intriguing future scenarios that allow our model to be realized in practical computing applications. For example, he suggests extending topology and proximity in the current state-of-the-art of artificial deep learning neural networks, which are already able to generate a large number of feature vectors (i.e. signals) during training and classification. In order to pursue these useful suggestions, more advanced topological tools, as well as novel, more sophisticated forms of Borsuk-Ulam theorem are required. To make an example, instead of antipodal points or regions on the surface of a hypersphere (in our case, the brain), we could assess antipodal "Cech complexes", i.e., collections of intersecting neighborhoods (called balls) on the cortical surface. Such complexes could give us further reach in projections to higher-dimensional spaces. The trick is to consider the description of a Cech complex on the surface of a sphere: while in 3D the intersecting balls would be glued to the surface of a 3D hypersphere, in 2D the balls are intersection circles (all having elements in common).

## Assessing complex phase spaces

As proposed by Friston [this issue] and Papo [this issue], the brain activity, instead of occurring in the "classical" Euclidean space of the central nervous system anatomy, might take place in metric and statistical functional spaces with particular geometries. To make an example, the sophisticated functional spaces of brain nonlinear dynamics suggested by Papo require manifolds much more complex than the "classical" 3D timespace. Topodynamics, with its

emphasis on symmetries on abstract manifolds, allows to embed brain trajectories, detected both by EEG and functional neurotechniques, on countless abstract manifolds, in order to improve the knowledge of their dynamics. Apart from the toroidal surfaces described in the main article (Tozzi et al., 2017a, this issue) other possible examples of abstract metric spaces where to cast nervous representation and inference problems are provided in Figure 2. Furthermore, other mathematical/topological approaches are worth to be pursued: in such a vein, the brain antipodal points might stand for Riemannian toroidal surfaces. They can be (relatively) easily studied, because the mathematics able to explain trajectories on torus-like structures is already available. Further, in our target paper we did not talk about yet another peculiar feature of the Borsuk-Ulam theorem: the projections. We stated that matching descriptions in  $R^n$  map to a single description in  $R^{n-1}$ . But we did not take into account that both  $R^n$  and  $R^{n-1}$  could be embedded in a manifold of higher dimensions, say  $R^{n+1}$ . Considering this possibility means that the projections (imagine them as double-arrowed lines) from  $R^n$ to  $R^{n-1}$  might belong to a widerdimensional spectrum that includes also  $R^{n+1}$ . The above-mentioned double-arrowed lines could be of different length, depending on the distance between  $R^n$  and  $R^{n-1}$ . A different arrow length might stand for the intensity of the force required to make the mappings. The closer  $\mathbb{R}^n$  is to  $\mathbb{R}^{n-1}$ , the shorter the line, and the lesser the required energy to perform the projection. In sum, we achieve a single system, that we might call the "multi-BUT", equipped with three levels of dimensions, instead of the canonical two of the classical BUT. Considering projections takes us into a completely novel mathematical territory to explore: the fibre bundle territory.



**Figure 2.** Possible abstract manifolds where to embed real brain activities. Changes in curvatures on such manifolds, in touch with information geometry, might stand for differences in mental or brain activities. **2A**: Costa's three ended, complete embedded, minimal surface. **2B**: Riemann's minimal surface; three levels are rendered, with a texture showing that the intersection with horizontal planes is circular. **2C**: Real part of the complex j-invariant as a function of the nome q on the unit disk. This type of repetitive modular oscillation has been recently found in the electric rhythms of the human EEG (Tozzi et al., 2017d). **2D**: Oloid surface, where patches can be flattened into a

plane; while rolling on a flat surface, its center of mass performs a motion different from a linear one. (Credits. **A** and **B**: Anders Sandberg, CC BY-SA 3.0; **C**: Linas Vepstas, CC BY-SA 3.0; **D**: KoenB, Share Alike 3.0 Unported).

#### Pairwise tool and the brain

As noted by Kakiashvili et al.'s [this issue], pairwise comparisons (PCs) could be "paired" with our topodynamical approach. This is in touch with their recent geometric interpretation of PCs in terms of the differential-geometric notion of holonomy, that might allow brain research to be directly related to intuitive, invariant geometric explanations in terms of abstract manifolds. For example, Oizumi et al. (2017) proposed a holistic framework, based on the same information geometry suggested by Friston [this issue]. Their measure of integration quantifies the strength of multiple causal influences among elements, by projecting the probability distribution of a system onto constrained manifolds. The amount of integrated information is geometrically interpreted as the divergence between the actual probability distribution of a system and an approximated probability distribution, where causal influences among elements are statistically disconnected. Further, Mailly et al. (2017) recently described a computerized method to build a multi-modal and multi-dimensional model of brain structures based on series of Acetylcholinesterase and Nissl stained sections, providing powerful tools for integration of observations derived from various technical approaches. In this context, another tool might come into play: the de Rham cohomology (Hazewinkel, 2001). It is a tool belonging both to algebraic and differential topology, capable of expressing basic topological information about smooth manifolds in a form particularly adapted to the concrete representation of computations and differential equations. Summarizing, such novel developments open the road to recognition of classical topological-geometric invariants, where the latter provide characteristic classes of simple geometric structures, such as closed compact manifolds, which are part of the Borsuk-Ulam theory.

## Computational scenarios of neural Darwinism

If finally the king is naked, as suggested by Friston [this issue], and our projectionism holds true, what happens to a 3D (plus time) input (say the visual scene of a cat), when it is projected onto the higher-dimensional functional manifolds endowed in our brain? Does our central nervous system encompass two (or more) antipodal representations of the cat? Could the two (or more) mental images with matching description encompass, for example, both the emotional and rational aspects of the cat (such as tenderness and genus)? What if one of the antipodal images is located, say, in the insula (where emotions are produced), and the other in the frontal lobe (where rationality lies); or one image is located in the "what" ventral pathway (that describes the stored memory of the cat), and the other in the "where" dorsal pathway (that describes the bodily motor response of our organism to the cat's view)? Such theoretical 4D cat locations might explain why the brain code is believed to be sparse, and why a brain site for the consciousness has never been found. The several mental features of the cat (rational, emotional, motor responses to its view) might be scattered in different nervous areas with matching description, lying on different trajectories of the functional multidimensional torus. A computational model describing this scenario has been recently tackled by Tozzi and Peters (2017). They introduced a variant of Selfridge's Pandemonium (i.e., a winner-takes-all, hierarchic, Darwinian, parallel, neural architecture) that takes into account two novel architectural features, namely: a) "demons" able to recognize topological features of visual scene shapes, and b) low-level representations of objects in our environment mapped to higher-dimensional neural networks.

To conclude our reply, we would like to develop the "evolutionary" comment by Jausovec [this issue], with which we agree, when he mentions Jerison's views (1991) about the brain as a "mapping machine", in which maps are different representations of the external world, so that the number of these maps is related to the complexity of viewing and representing the environment. This is in complete agreement with our tenet that the brain function lies in dimensions higher that the external world. Recent descriptions of the projective architecture in the nervous systems of invertebrates (Hartenstein, 2017) and in the central nervous system of vertebrates (Wullimann, 2017) corroborate the amazing extension and complexity of their mapping systems. Indeed, "the topological inventions of life" (Marijuán, 1997) have represented the most fundamental evolutionary processing tool for the organism (and its central nervous system) being in the world. Our framework explains why hominids have larger brain, compared with other animals: the surplus of neurons, connections and nodes allow to assemble a larger (multidimensional) functional phase space, different from the environmental 3D plus time, where the more advanced human mental computations might take place. Therefore, the true reductionist level that explains the human mind is located in this large phase space, whatever its still unknown shape could be. It is also the gist of Friston's [this issue] elegant closing comment: the elusive phenomenon of consciousness has escaped "topodynamically" to higher dimensions.

### REFERENCES

- 1) Allen M, Friston KJ. 2016. From cognitivism to autopoiesis: towards a computational framework for the embodied mind. Synthese, DOI 10.1007/s11229-016-1288-5
- 2) Carhart-Harris RL, Muthukumaraswamy S, Roseman L, Kaelen M, Droog W, et al. 2017. Neural correlates of the LSD experience revealed by multimodal neuroimaging. PNAS, 113 no. 17, 4853–4858, doi: 10.1073/pnas.1518377113
- 3) Chankaya MN, Deli E. 2017. Changes in brain entropy are related to abstract temporal topology. Comment on "Topodynamics of metastable brains" by Tozzi et al. Physics of Life Reviews, "this issue".
- 4) Erdi P. From phase transitions to the topological renaissance. Comment on "Topdynamics of Metastable Brains" by Arturo Tozzi et al. Physics of Life Reviews, "this issue".
- 5) Fingelkurts A.A., Fingelkurts A.A. Short-term EEG spectral pattern as a single event in EEG phenomenology. The Open Neuroimaging Journal, 2010, 4, 130-156.)
- 6) Fingelkurts AA, Fingelkurts AA, Neves CFH. Consciousness as a phenomenon in the operational architectonics of brain organization: Criticality and self-organization considerations. Chaos, Solitons & Fractals 2013; 55:13–31.
- 7) Fingelkurts AA, Fingelkurts AA, Neves CFH. Emergentist monism, biological realism, operations and brainmind problem: Reply to comments on "Natural world physical, brain operational, and mind phenomenal space-time" by An.A. Fingelkurts, Al.A. Fingelkurts, C.F.H. Neves. Physics of Life Reviews 2010b;7(2): 264–268.
- 8) Fingelkurts AA, Fingelkurts AA, Neves CFH. Natural world physical, brain operational, and mind phenomenal space–time. Physics of Life Reviews 2010a; 7(2):195–249.
- 9) Fingelkurts AA, Fingelkurts AA. Exploring giftedness. In: Advances in Psychology Research, Vol. 9, Nova Science Publishers, 2002, pp. 137-155.
- 10) Fingelkurts AA, Fingelkurts AA. Information flow in the brain: Ordered sequences of metastable states. Information 2017, 8, 22; doi:10.3390/info8010022.
- 11) Fingelkurts AA, Fingelkurts AA. Making complexity simpler: multivariability and metastability in the brain. Intern. J. Neuroscience, 2004; 114:843–862.
- 12) Finkelstein A, Derdikman D, Rubin A, Foerster JN, Las L, Ulanovsky N. 2015. Three-dimensional head-direction coding in the bat brain. Nature 517, 159–164 (08 January 2015) doi:10.1038/nature14031
- 13) Friston. 2017. The Emperor's new topology. Comment on "Topodynamics of Metastable Brains" by Arturo Tozzi et al. Physics of Life Reviews, "this issue".
- 14) Garreffa G. 2017. The Physics Inside our Brain. Comment on "Topodynamics of Metastable Brains" by Arturo Tozzi et al. Physics of Life Reviews, "this issue".
- 15) Hartenstein V. The Central Nervous System of Invertebrates. In: The Wiley Handbook of Evolutionary Neuroscience. Stephen V. Shepherd (ed.). John Wiley & Sons, Ltd. Chichester, UK, pp: 173-235.
- 16) Hazewinkel M. 2001. De Rham cohomology. Encyclopedia of Mathematics, Springer, ISBN 978-1-55608-010-4
- 17) Henry CJ. 2017. A Computational Discussion on Brain Topodynamics Comment on "Topodynamics of Metastable Brains" by Arturo Tozzi et al. Physics of Life Reviews, "this issue".
- 18) Hoffmann FZ, Triesch J. 2017. Nonrandom network connectivity comes in pairs. Network Neurosci. Winter 2017, Vol. 1, No. 1, Pages: 31-41
- 19) Ingarden RS, Górniewicz L. 1990. Shape as an Information-Thermodynamical Concept and the Pattern Recognition Problem. Mathematische Nachrichten. 145, 1, 97–109. DOI: 10.1002/mana.19901450108
- 20) Jaušovec N. 2017. The neural code of thoughts and feelings: Comment on "Topodynamics of metastable brains" by Tozzi et al. Physics of Life Reviews, "this issue".
- 21) Jerison, H., 1991. Brain Size and the Evolution of Mind. American Museum of Natural History, New York.
- 22) Kakiashvili T, Koczkodaj WW, Magnot J-P. 2017. Approximate reasoning by pairwise comparisons as a possible: Supplement to "Topodynamics of metastable brains" by Arturo Tozzi, et al. Physics of Life Reviews, "this issue".
- 23) Katz MM, Waskow IE, Olsson J. 1968. Characterizing the psychological state produced by LSD". J Abnorm Psychol. 73 (1): 1-14. doi:10.1037/h0020114. PMID 5639999.
- 24) Kawaguchi K, Kageyama R, Sano M. 2017. Topological defects control collective dynamics in neural progenitor cell cultures. Nature (2017) doi:10.1038/nature22321
- 25) Kozma R, Puljic M, Balister P, Bollobas B, Freeman WJ. (2005) Phase transitions in the neuropercolation model of neural populations with mixed local and non-local interactions. Biol Cybern 92(6):367–379.
- 26) Laganà MM , Shepherd SJ, Cecconi P, Beggs CB. 2017. Intracranial volumetric changes govern cerebrospinal fluid flow in the Aqueduct of Sylvius in healthy adults. Biomedical Signal Processing and Control, 36, 84–92
- 27) LeDoux JE, Brown R. 2017. A higher-order theory of emotional consciousness. PNAS, Vol. 114 no. 10, E2016–E2025, doi: 10.1073/pnas.1619316114

- 28) Lerner VS. Letter to Editor: Comment on "Topodynamics of metastable brains" by Tozzi et al. Physics of Life Reviews, "this issue"
- 29) Mailly P, Haber SN, Groenewegen HJ, Deniaud J-M. 2017. A 3D multi-modal and multi-dimensional digital brain model as a framework for data sharing. Journal of Neuroscience Methods. Volume 194, Issue 1, 15 December 2010, Pages 56–63. http://doi.org/10.1016/j.jneumeth.2009.12.014
- 30) Marijuan PC. 1997. The topological inventions of life: From the specialization of multicellular colonies to the functioning of the vertebrate brain. World Futures 50 (1): 617-631.
- 31) Mauger O, Lemoine F, Scheiffele P. 2016. Targeted Intron Retention and Excision for Rapid Gene Regulation in Response to Neuronal Activity. Neuron. 2016 Dec 21;92(6):1266-1278. doi: 10.1016/j.neuron.2016.11.032.
- 32) Moore JJ, Ravassard PM, Ho D, Acharya L, Kees AL, Vuong C, Mehta MR. 2017. Dynamics of cortical dendritic membrane potential and spikes in freely behaving rats. Science. 2017 Mar 24;355(6331). pii: eaaj1497. doi: 10.1126/science.aaj1497. Epub 2017 Mar 9.
- 33) Moreno JL, Holloway T, Albizu L, Sealfon SC, González-Maeso J. 2011. Metabotropic glutamate mGlu2 receptor is necessary for the pharmacological and behavioral effects induced by hallucinogenic 5-HT2A receptor agonists. Neurosci Lett. 2011 Apr 15;493(3):76-9. doi: 10.1016/j.neulet.2011.01.046. Epub 2011 Jan 27.
- 34) Navarro J, del Moral R, Marijuán PC. Intraneuronal Computation. Charting the Signaling Pathways of the Neuron. In: The Wiley Handbook of Evolutionary Neuroscience. Stephen V. Shepherd (ed.). John Wiley & Sons, Ltd. Chichester, UK, pp: 49-87.
- 35) Oizumi M, Tsuchiya N, and Amari S-i. 2017. Unified framework for information integration based on information geometry. PNAS, vol. 113 no. 51, 14817–14822, doi: 10.1073/pnas.1603583113
- 36) Papo D. 2017. Beyond the anatomy-based representation of brain function: Comment on "Topodynamics of metastable brains" by Arturo Tozzi et al. Physics of Life Reviews, "this issue".
- 37) Perlovsky LI. Physics of the Mind. Front SystNeurosci. 2016 Nov 15;10:84. eCollection 2016.
- 38) Ramon y Cajal S. 1899-1904. Textura del sistema nervioso del hombre y de los vertebrados. N. Moya. Madrid. pp:1141. English edition 1995, Oxford University Press, New York.
- 39) Reimann MW, Nolte M, Scolamiero M, Turner K, Perin R, et al. 2017. Cliques of Neurons Bound into Cavities Provide a Missing Link between Structure and Function. Front. Comput. Neurosci., 12 June 2017 | https://doi.org/10.3389/fncom.2017.00048
- 40) Sando R, Bushong E, Zhu Y, Huang M, Considine C, et al. 2017. Assembly of Excitatory Synapses in the Absence of Glutamatergic Neurotransmission. Neuron, 94, 2, 312–321.e3.
- 41) Sloas DC, Zhuo R, Xue H, Chambers AR, Kolaczyk E, Polley DB Sen K. 2016. Interactions across Multiple Stimulus Dimensions in Primary Auditory Cortex. eNeuro 11 August 2016, ENEURO.0124-16.2016; DOI: https://doi.org/10.1523/ENEURO.0124-16.2016
- 42) Tozzi A, Peters JF. 2016. Towards a Fourth Spatial Dimension of Brain Activity. Cognitive Neurodynamics 10 (3): 189–199. doi:10.1007/s11571-016-9379-z.
- 43) Tozzi A, Peters JF. 2017. A Novel Pandemonium Architecture Based on Visual Topological Invariants and Mental Matching Descriptions. viXra:1705.0223.
- 44) Tozzi A, Peters J, Fingelkurts AA, Fingelkurts AA, Marijuan P. 2017a. Topodynamics of metastable brains. Physics of Life Reviews, "this issue".
- 45) Tozzi A, Peters JF, Ori O. 2017b. Cracking the barcode of fullerene-like cortical microcolumns. Neurosci Letters. 644, 100–106. http://dx.doi.org/10.1016/j.neulet.2017.02.064.
- 46) Tozzi A, Sengupta B, Peters JF, Friston KJ. 2017c. Gauge Fields in the Central Nervous System. In: The Physics of the Mind and Brain Disorders: Integrated Neural Circuits Supporting the Emergence of Mind, edited by Opris J and Casanova MF. New York, Springer; Series in Cognitive and Neural Systems. ISBN: 978-3-319-29674-6. Forthcoming.
- 47) Tozzi A, Peters JF, Jausovec N. 2017d. A repetitive modular oscillation underlies human brain electric activity. Neurosci Lett. 10.1016/j.neulet.2017.05.051 (in press).
- 48) Waskom ML, Wagner AD. 2017. Distributed representation of context by intrinsic subnetworks in prefrontal cortex. PNAS, vol. 114 no. 8 > Michael L. Waskom, 2030–2035
- 49) Wigner E. 1960. The Unreasonable Effectiveness of Mathematics in the Natural Sciences. In: Communications in Pure and Applied Mathematics, vol. 13, No. I. New York: John Wiley & Sons, Inc.
- 50) Wullimann MF. Nervous System Architecture in Vertebrates.In: The Wiley Handbook of Evolutionary Neuroscience. Stephen V. Shepherd (ed.). John Wiley & Sons, Ltd. Chichester, UK, pp: 236-278.
- 51) Xing M, Ajilore O, Wolfson OE, Abbott C, MacNamara A, et al. Thought Chart: Tracking Dynamic EEG Brain Connectivity with Unsupervised Manifold Learning. Brain Informatics and Health. Series: Lecture Notes in Computer Science, Year: 2016, Volume 9919, Page 149 DOI: 10.1007/978-3-319-47103-7\_15