

THE HIDDEN DIMENSIONS OF THE CENTRAL NERVOUS SYSTEM

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Several papers, taking into account the big data outburst and novel, powerful computational tools, are starting to unveil an intricate state of affairs concerning brain dimensions. Indeed, various brain activities and their correlated mental functions can be assessed in terms of trajectories embedded in phase spaces of dimensions higher than the canonical ones. We show how, surprisingly, brain further dimensions may stand not just for methodological devices that allow a better mathematical treatment of otherwise elusive cortical activities, but also for functional or anatomical relationships among real nervous functions. Further, we describe how it is feasible to extract hidden multidimensional information from real or artificial neurodata series, and demonstrate how our mind dilutes, rather than concentrate as currently believed, the inputs coming from its surrounding environment. The principle “the higher the dimensions, the higher the information” might explain the occurrence of our mental activities and elucidate the mechanisms of the human diseases in which dimensionality reduction occurs.

INTRODUCTION

A physical or biological sequence of facts, operations and activities has been conventionally depicted in terms of moving particles embedded in a three-dimensional graph. In this simple, rather intuitive abstraction, the axes x, y and z stand for the canonical three spatial dimensions, while time passing is portrayed in terms of particles' trajectories (Xing et al., 2016) (**Figure A**). To make an example, the trajectories displayed by the BOLD activation of cortical areas after a visual stimulus can be drawn as interactive static plots, or visualized as animations. However, the current availability of big data and fully-novel computational tools starts to unveil much more complicated matters. Indeed, such innovations have led to a growing interest for multidimensional approaches (Dekker et al., 2017). What does it mean “multidimensional approaches”? In order to provide the answer, we need to think in more abstract terms than usual: while the visualization of low-dimensional data is relatively straightforward in a three-dimensional plot, it is not always obvious how to visualize high-dimensional datasets in a similarly intuitive way (Heusser et al., 2017). It is feasible to add novel dimensions to the canonical ones, or in other terms, other axes apart from x, y and z . For example, if we introduce a further axis, the particles are allowed to move in four, instead of three, dimensions (plus time) (**Figure B**). This methodological step is highly profitable, because it makes easier to study systems dynamics in higher dimensions, where more information about the particles' trajectories can be achieved.

The trend towards multidimensional tactics is taking place in far-flung disciplines. Inspired by the periodic table, Reymond (2015) grouped chemical compounds in a multidimensional space, in which neighbors have related properties; further, Cardesa et al. (2017) uncovered energy cascades in five dimensions (three-dimensional space, time and scale) endowed in the turbulent flows of simple water-like fluids. This paves the way for similar analyses in geophysical and industrial flows, conducting and quantum fluids, plasmas. As a matter of course, the assessment of the most complex object at all, e.g., the human brain, could not fail to fulfil these multidimensional efforts. When brain activities are portrayed as locations at different points in time, therefore linear and nonlinear nervous dynamics, neural functions and mental observables could be described as scalars or vectors measured at different locations of multidimensional phase spaces (Lech et al., 2016). The key question here is: which kind of further dimensions could be deployed, in the experimental assessment of the brain activity? Neuro-researchers have a large freedom of choice: they are allowed to insert all the axes they require (**Figure C**), and to locate on the further axes whatever parameter they want, from spike frequencies to synchronized oscillations, from nonlinear fields to attractors, from color perceptual spaces to tactile qualities, from other spatial dimensions to the neural clusters' number. For a few examples, see **Figure B-F**. Of course, the arbitrarily chosen dimensions must provide testable hypotheses and experimental validation, in order to leave the realm of the pure abstraction and acquire scientific relevance. In the following, we will describe recently-developed techniques that allow the use of extradimensions in neuroscience. We will then expound the multidimensional approaches to a wide range of brain activities and mental functions. We will discuss how recent data point towards the real presence of hidden, further dimensions where nervous activity might take place, so it is quite true to state that the brain operates in dimensions higher than its surrounding environment.

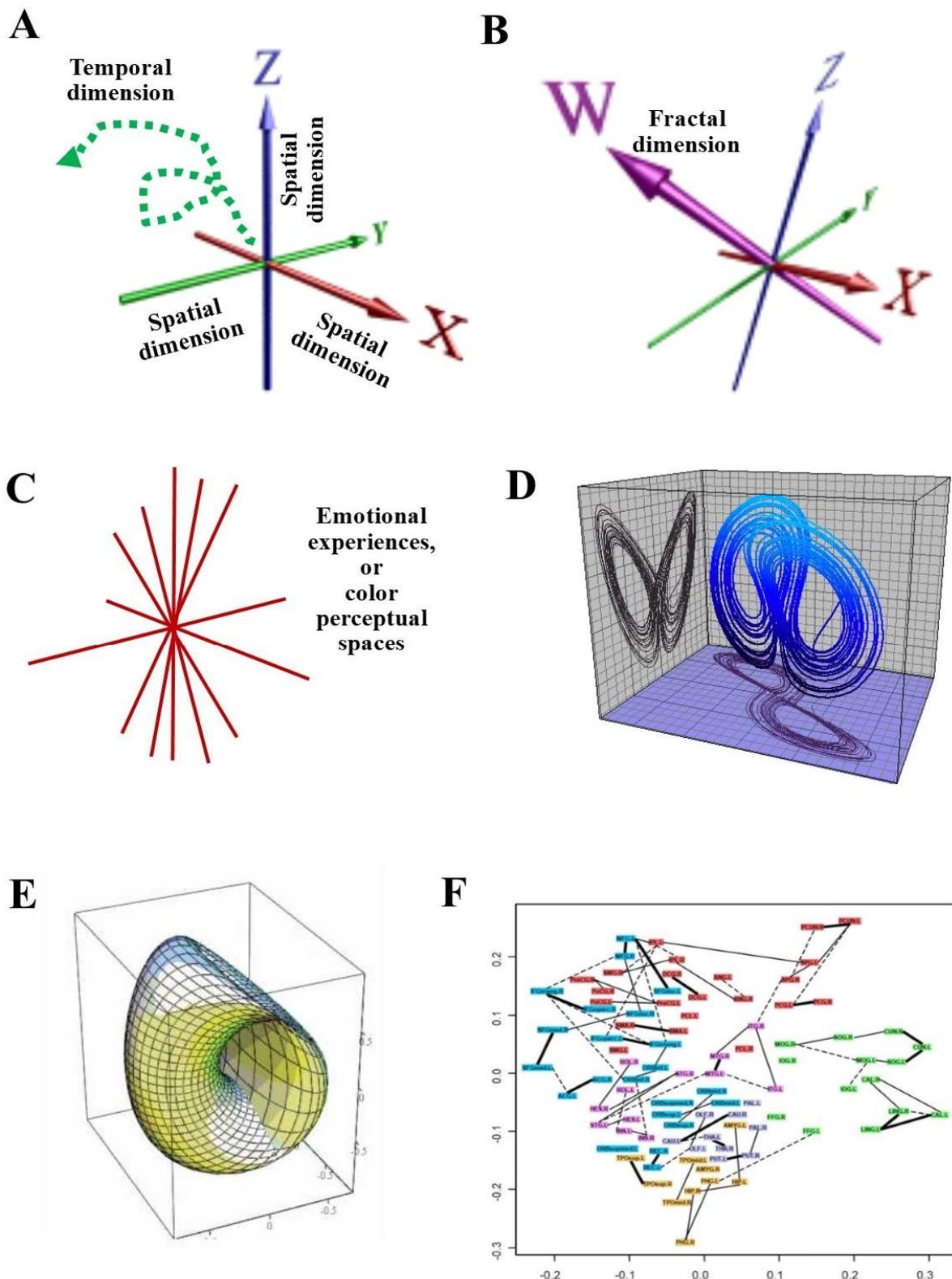


Figure. Different ways to cope with further nervous dimensions. **Figure A** illustrates the canonical picture of three spatial dimension plus time. The latter is depicted as a particle trajectory. **Figure B** illustrates the arbitrary insertion of a further dimension, in this case a fractal one. **Figure C:** a sheaf of functional multidimensions, that might stand for different mental or biological parameters (in this case, either emotions, or perceptions). **Figure D:** Multidimensional attractors produced by the complex, nonlinear dynamics of the

brain at the edge of chaos. **Figure E.** A Clifford torus, displaying four-dimensional, donut-like nervous spatial trajectories. **Figure F.** Multidimensional scaling: regions are color-coded by membership of main systems, identified by cluster hierarchical analysis. The x axis stands for anterior-posterior locations, while the y axis for inferomedial-superolateral ones; lines indicate statistically significant inter-regional correlations. It is easy to see that the dimensions to assess might be almost countless
Credits: **Figures A and B** are modified from <http://eusebeia.dyndns.org/4d/vis/01-intro>; **Figure D** is modified from <https://www.mat.ucsb.edu/g.legrady/academic/courses/03w200a/multidimensional/index.html>; **figure E:** from <https://www.youtube.com/watch?v=TW1PisramO4>; **Figure F:** from “Modelling, Analysis and Visualization of Brain Connectivity. Jos Roerdink”,<http://slideplayer.com/slide/8566493/>.

1) THE UNREASONABLE MULTIDIMENSIONAL POWER OF NOVEL ANALYTICAL TOOLS

Electroencephalography (EEG), functional MRI (fMRI) and magnetoencephalography (MEG) have been proven to be very useful in order to unveil neural network dynamics in the classical three dimensions-plus time. The data extracted from these standard neurotechniques can be now successfully assessed in the language of innovative, sophisticated scientific tools (Morone et al., 2017). Here we describe new mathematical weapons, previously unknown to neuroscientists, that will soon allow to analyze in multidimensional contexts the huge mess of data sets provided by the big data outburst (Curto 2016). Some of them make it possible to scale efficiently to high dimensions: Shah and Koltun (2017) introduced a clustering algorithm that untangles heavily mixed clusters and achieves high accuracy across multiple domains. It was successfully tested on large datasets of faces, hand-written digits, objects, newswire articles, protein expression levels and sensor readings from the Space Shuttle (Shah and Koltun, 2017). Other novel tools assess the space embedding linear combinations of neuronal patterns in response to specific task conditions: Rigotti and Fusi (2016) proposed a novel method that exploits fMRI Repetition Suppression, in order to measure the hidden dimensionality of the set response vectors. This technique, measuring the microscopic overlap between response vectors even in brain areas that do not display discernible average differential BOLD signal, identifies cortical circuits that integrate multiple independent information pathways. The importance of dimensionality lies in its relationships with neural circuit’s functionality. Indeed, the response vectors’ dimensionality is higher in areas involved in multi-stream integration and lower in regions where inputs from independent sources do not interact (Rigotti and Fusi, 2016).

A noteworthy, recently developed technique takes into account a feature hidden in neurodata: the fractal dimension. It is used for the assessment of biomedical analysis waveforms, in particular of the complexity of EEG time series (Pritchard, 1992; Heet et al., 2010; Fetterhoff et al., 2014; Tozzi, 2015a). Indeed, it has been demonstrated that neurodata series encompass self-similarity at different temporal and spatial scales. In our framework, this fractal finding stands for a further (non-integer or fractional) dimension that allows the extraction of larger amounts of information from canonical techniques, such as EEG and functional fMRI. Another important, novel tool is the energy landscape analysis, a data-driven approach to neuroimaging data (Watanabe et al., 2014), that has been used, in particular, for the assessment of MRI imaging series recorded from healthy individuals (Ezaki et al., 2017). Kang et al. (2017) built an energy landscape for the fMRI state dynamics of the subcortical brain network during resting state. They evaluated alterations in energy landscapes following perturbation in subcortical brain system’s network multidimensional parameters (such as maximal number of attractors, unequal temporal occupations and readiness for system’s reconfiguration). Even small perturbations in the network parameters caused a significant shift in the energy landscape, allowing the assessment of diverse nervous functions that may emerge due to the reconfiguration of the default brain network at rest.

The connectome turns multidimensional. Network science, an interdisciplinary spin-off of graph theory, envisages the brain in terms of the connectome, i.e., a system of nodes and edges that describes the nervous system as a series of various interacting regions. Recent improvements are starting to take into account not just the static links, but also the temporal, non-permanent ones (Li et al., 2017). Complex network (graph-theory) analyses applied to MEG/EEG signals allow the assessment of both canonical and non-canonical dimensions, such as spike frequencies, connectivity, activity magnitude, complex network properties (Kida et al., 2016). Developments in source reconstruction algorithms are leading to novel neuronal metrics (standing for further dimensions) good enough to provide insights into the multidimensional dynamics of various neural representations (Kida et al., 2016). The organization of complex networks can be assessed through higher-order connectivity patterns: such approaches allowed Benson et al. (2016) to reveal unexpected hubs and geographical elements endowed in the very structure of the nervous connectome. On the other hand, Caiafa and Pestilli (2017) described multidimensional arrays able to assess diffusion-weighted magnetic resonance data. By evaluating 1,490 connectomes, thirteen tractography methods and three data sets, they elucidated the relationships among connectome nodes, edges, white matter fascicles and diffusion data. These methods provide anatomical manipulation in multidimensions on white matter

tracts, allowing either statistical inference, or the study of the white matter geometrical organization. Novel statistical machine-learning methods, such as multivariate pattern analysis, generate stimulus response models in a data-driven fashion that allows the study of human cognition through fMRI (Mandelkow et al., 2016). Indeed, dynamic functional network connectivity analyzes time evolution of coherent dynamic's changes in the whole brain. Vergara et al. (2017) developed an information theory framework that estimates the bits of information flowing among subsets of neural networks' functional domains. Clusters of cross domain mutual information point towards scarce information sharing between cognitive and sensitive areas. These findings show that, when information theory is applied to states estimated from pairs of multi-network functional domains, it is able to unveil additional, multidimensional features of functional connectivity (Vergara et al., 2017).

Also, novel multidimensional tools help researchers to further improve already existing neurotechniques. To make an example, the utility of the otherwise successful independent vector analysis is circumscribed, because of the extremely noisy nature and large variability of the source component vector distribution. In order to overtake these limitations, Kuang et al. (2017) proposed an adaptive fixed-point algorithm that analyzes multiple-subject complex-valued data, allowing an easier detection of information encompassed in fMRI series. Their model, tested both on simulated and experimental fMRI data, is suitable for decomposing multi-subject complex-valued information, and, in particular, for solving a harassing problem in neuroscience: the subjective variability of the brain function (Kuang et al., 2017). The brain connectome can be currently assessed not just in terms of neural nodes, but also of molecular, cellular and neurochemical networks. Sousa et al. (2017) performed transcriptome sequencing of 16 regions of adult human, chimpanzee, and macaque brains. Integration with human single-cell transcriptomic data revealed global, regional and cell-type-specific species-expression differences in genes representing distinct functional categories. For their part, Noori et al. (2017), through advanced data mining and supervised machine learning, developed a multiscale, multilayer neurochemical connectome of the rat brain. Their tool is a freely available resource for systems analysis of motor, sensory, emotional and cognitive information processing. The last statement emphasizes the growing role of open sources in neuroscience. Advances in neuroimaging of healthy adults, including the ones driven by the Human Connectome Project, allow big data to be investigated through the recently-developed computational tools (Eickhoff et al., 2016) and offer exciting prospects for accelerated progress in characterizing brain networks and their anomalies (Van Essen and Barch, 2015).

The reverse is feasible too: back from higher to lower connectome dimensions. Despite their huge potentialities, brain's high-dimensional reconstructions are currently flawed by a severe technical limitation: they are computationally expensive and, therefore, very difficult to cope with. These restrictions can be tackled through a recently-introduced approach, i.e, dimensionality reduction. Several dimension reduction techniques are available, from the popular principal component analysis, to the more advanced factor analysis, ICA, MAVE (Nylen and Wallisch, 2017). Ye et al. (2015), using coupling patterns encoded in the brain connectivity graphs, explained how high-dimensional, complex geometries can be mathematically embedded into lower dimensions. Via techniques of tractography-derived structural connectome on data acquired from healthy subjects, they tested both linear and nonlinear dimensionality reduction techniques and demonstrated that the most influential regions, such as rich-club members, are more centrally mapped (Ye et al., 2015). In turn, Heusser et al. (2017) introduced HypeTools, a Python toolbox for visualizing and manipulating large, high-dimensional datasets. In their case, dimensionality reduction is used in order to embed high-dimensional datasets in a lower-dimensional space, therefore plotting the data through a simple (yet powerful) device with many options for data manipulation. Just as the location of an object moving through a canonical space can be visualized in terms of a three-dimensional trajectory, HyperTools uses dimensionality reduction algorithms to create similar two- and three-dimensional trajectories for time series of high-dimensional observations (Heusser et al., 2017). Besides, Shah and Koltun (2017) developed a joint clustering, dimensionality reduction algorithm good enough to scale up to high dimensions large datasets, such as faces, hand-written digits, objects, protein expression levels, sensor readings from the Space Shuttle. Summarizing, multidimensional reconstructions extracted from real neurodata provide a huge amount of information; their main defect, i.e., computationally untreatable complexity, will be soon tackled by powerful, next-to-come advances.

2) TOPOLOGY AND SYMMETRIES COME INTO PLAY

Recognizing the limitations of element-wise set-theoretic constructions in accommodating brain activity, neuroscientists are trying to move beyond the classical approaches (Posina, 2015). One of the most promising is topology, a branch of mathematics able to describe systems with any number of dimensions. When topology meets the physics of the brain, we are in front of a general model of neuronal activity, in terms of multidimensional manifolds and computational geometry, that has the potential to be operationalized. Indeed, topology works like a telescope and

microscope at the same time: zooms into networks to find hidden neuronal structures and sees the larger cortical areas at the same time. In touch with old scholars (Whitehead, 1919; Lewin, 1935) current scientists suggest that the world and its dynamics can be described in terms of mappings and projections taking place on topological structures (Milton et al., 2015). Systems' properties of physical and biological spaces can be translated to abstract mathematical spaces, and *vice-versa*, leading to the development of higher dimensional tools. Consistent with this trend, the last decade has seen an uptick in the use of topological ideas in neuroscience, especially for understanding neural codes (Curto 2016) and extract from experimental data higher dimensional models of percept, concept, emotion, memory and neural information (Posina, 2015). Baas (2017) projected sets of spike trains to a topological manifold, achieving a novel space with a richer structure wide enough to encompass not just simple spatial stimuli. Indeed, recovering the shape of the space in which rats are moving, the Author detected and separated the influence of the various stimuli forming the neural (cognitive) space of spike trains. To sum up, topology allows to build phase spaces with more dimensions, therefore with more information to analyze.

The geometry inside: nested multilevel correlations. It has been recently demonstrated that real networks are not just random combinations of single ones, but are organized according to hidden geometric correlations between layers (Kleinberg et al., 2016). These correlations allow the detection of multidimensional communities, e.g., sets of nodes that are simultaneously similar in multiple layers. This type of multidimensionality enables accurate trans-layer link estimates, so that connections in one layer can be predicted by observing the hidden geometric space of another (Kleinberg et al., 2016). The recent availability of complex datasets led to the necessity to develop methods able to extract as many hidden patterns as possible from experimentally detected traces. The challenge lies in transforming the detected patterns into experimental knowledge, through topological tools strictly intertwined with the complex network analysis and the language of graph theory. For example, Fukushima et al. (2017) suggested that, when connectivity exhibits an integrated network topology, structural and functional features become more closely linked to each other, because direct structural connections mediate a larger proportion of neural communication within functional modules. Maletić and Zhao (2017) proposed new information entropy measures for the characterization of multidimensional structures extracted from complex datasets, complementing the conventionally-applied algebraic topology methods. Assessing topological relationships, multilevel entropy measures and simplicial complexes endowed in taxi driver's cognitive maps, the Authors were able to track transitions to high-dimensional structures (Maletić and Zhao, 2017). In turn, Merelli et al. (2015) proposed a methodology, based on topological data analysis, that captures the internal organization's changes in complex systems: this means that the topological invariants endowed in a multivariate time series can be used for the computation of a novel entropy measure, the so-called weighted persistent entropy. The latter allows to track the nonlinear changes correlated with phase transitions and network reorganizations.

Giusti et al. (2016) explored the use of simplicial complexes, i.e., tools from algebraic topology that assess higher-order networks. The technique is promising for the assessment of neurodata extracted both from electrophysiological recordings in animal models, and from hemodynamic fluctuations in humans. The Authors posit that simplicial complexes have the potential to eclipse graph theory in unraveling the fundamental mysteries of cognition (Giusti et al., 2016). These types of network geometry attract increasing attention, because their wide range of applications from data mining, to routing protocols in the Internet (Bianconi and Rahmede, 2016). Higher order networks display a natural geometric interpretation that describes the interactions between two or more nodes. Such networks might encompass simplicial complexes formed not only by classic nodes and links, but also by triangles and tetrahedra glued along their faces. This extension captures the emergent community structure and the dependence of the degree distribution on the dimension (Bianconi and Rahmede, 2016).

Two is better than one. The last, but not the least, another strong concept recently came into play from topology: the Borsuk-Ulam theorem (BUT), which states that a single point on a circumference maps to two points on a sphere (Borsuk, 1933; Matoušek, 2003). In neuroscientific terms, this means that a cortical region embedded in lower dimensions gives rise to two regions with matching description in higher dimensions (Tozzi et al., 2017a). The dimensions described by BUT do not stand just for spatial ones (as in the case of a circle and a sphere), but also for abstract dimensions (such as biological complexity, fractional quantities, fractal measurements) (Peters, 2016; Tozzi and Peters, 2016b). The BUT perspective allows a feature (e.g., a shape, a trajectory, a vector, or an energy) located in the environment to be translated to an abstract space, and vice versa. Achieving maps from one system to another, researchers are enabled to enrich and elucidate brain activity extracted from real neurodata (Tozzi and Peters, 2016a).

Some of the BUT predictions have been recently confirmed, suggesting that its topological framework can be fruitfully used in neuroscience. The BUT forecasts the presence of at least two brain regions equipped with the same features. Recent papers support this claim: for example, Karaman et al. (2016) identified the existence of antipodal behavioral patterns of neural activities. Also, Hoffmann and Triesch (2017) demonstrated that brain connectivity comes into pair. They described, in a network in which connection probabilities are symmetric in pairs, the occurrence of abundant

bidirectionally connected neuron pairs, which far exceeds what would be expected in a random network. Still, the BUT framework expects that the brain displays matching areas encompassing the same mental faculty, and that such activity halves during other mental functions. In touch with this claim, Waskom and Wagner (2017) state that: “Examining targeted prefrontal regions, we found that pairs of voxels with similar context preferences exhibited spontaneous correlations that were approximately twice as large as those between pairs with opposite context preferences.”

The hidden relationships between symmetry breaks and multidimensions. A key feature of complex dynamical approaches to brain function (de Arcangelis and Herrmann, 2010; Beggs and Timme, 2012; Zare and Grigolini, 2013; Tozzi, 2014; Dehghani-Habibabadi et al., 2017) lies in the observation that nonequilibrium phase transitions may lead to symmetry breaks (Scholz et al., 1987). Jirsa et al. (1998) focused on the left-right cortical symmetry and provided a bimodal description of the brain activity connected to behavioral dynamics. Further, it has been demonstrated that, when an acoustic stimulus frequency is systematically changed, a spontaneous transition in coordination occurs at a critical frequency, in both motor behavior and brain signals (Jirsa et al., 1994). The study of the temporal organization of large-scale brain networks in whole-brain resting fMRI data demonstrated that the spontaneous transitions between networks of interacting brain areas are predictable (Vidaurrea et al., 2017). More specifically, network activity is organized into a hierarchy of two distinct metastates (higher-order cognition and sensorimotor systems), such that transitions are more probable within, than between, metastates (Vidaurrea et al., 2017).

Dimensional reduction and symmetry break display close relationships. It has been proposed that symmetry stands for features with matching description lying in higher dimensions, while the corresponding symmetry break for a single point lying one dimension lower (Tozzi and Peters, 2016b). Recent approaches to brain phase spaces reinforce the concomitant role of symmetries and energy requirements in nervous function, because symmetries are strictly correlated with neural thermodynamic activity (Roldán et al., 2014). Introducing novel topological tools that analyze enthalpy, free-energy and entropy in fMRI studies of the brain, Tozzi and Peters (2017) provided a testable approach able to proceed from abstract topology to real thermodynamic nervous activity and symmetry breaks. Hence, changes in thermodynamic parameters and dimensions occur in the brain during symmetry breaks and transitions from one functional state to another. This means that abstract topological approaches may display real, energetic physical counterparts accessible to current neurotechniques.

Recent papers describe physical gauge theories applied to the brain activity (Sengupta et al., 2016; Tozzi et al., 2017c). The Authors assess nervous activity via the physical and mathematical procedures of gauge theory, examining the possibility that brain function is driven by one or more continuous forces, called gauge fields, that originate inside or outside the CNS. In particular, the above-mentioned framework analyzes the idea of symmetries, that stands for the cornerstone of gauge theories. These approaches, based on symmetries and symmetry breaks, allow a methodological assessment of brain dynamics, defined in terms of energetic gradient-descent trajectories taking place on curved paths of the brain phase space. In touch with these symmetry issues, Robinson et al. (2016) analyzed the activity eigenmodes of the bi-hemispheric brain and its spatial structure. Interhemispheric connections between homologous regions via the corpus callosum lead to splits, that depend on symmetric or anti-symmetric activity between opposite areas (Robinson et al. 2016). The symmetric properties of the lowest eigenmodes constrain the interhemispheric connectivity strengths and mono-hemispheric mode spectra, so that, consistent with observations, spontaneous brain activity turns symmetric between hemispheres. In order to keep the proper brain function, neural activity needs to be tightly coordinated within the brain network and manifolds. Pillai and Jirsa (2017) described structured flows on manifolds, providing a formal description of behavior in terms of low-dimensional processes that emerge from the symmetric and invariant properties of the network’s dynamics (Pillai and Jirsa, 2017). They demonstrated that symmetry breaks in network connectivity give rise to timescales hierarchies, resulting in the emergence of attractive functional subspaces. Therefore, the Authors stated, behavior emerges when appropriate conditions imposed by energetic constraints upon the couplings are satisfied, justifying the conductance-based nature of synaptic couplings. In short, a topological, abstract framework, consisting of brain symmetric functions mapped on abstract multidimensional manifolds, describes general principles that predict how behavior and task rules are represented in the real brain.

3) A JOURNEY INTO MENTAL HIDDEN DIMENSIONS

In the previous Section, we described how further nervous dimensions, extrapolated from simulations or real neuro-data analyses, stood for methodological devices that allow mathematical treatment of the brain activity. Here we will focus on multidimensional structures that might display a real (anatomical or functional) counterpart in the central nervous system. Indeed, recent papers point towards the human brain as equipped with multidimensionality. This claim is

doomed to be highly controversial, because the mind of a human observer, perhaps due to evolutionary constraints, is not capable to perceive, and even to imagine, bodily spaces and structures made up of four or more dimensions.

The hidden dimensions of perceptual spaces. A “perceptual space” of a sensory domain is a mental workspace of points (or vectors, or tensors) that capture similarities and differences in judgments, enabling further processing such as classification and naming (Zaidi et al., 2013; Victor et al., 2017). Perceptual spaces are not traceable to single-neuron properties and span across all the sensory cues: from colors to environmental sounds, from faces recognition to auditory textures, from tactile quality to odor. The best studied, i.e., the color’s perceptual space, is correlated with the three cone absorption spectra and is believed to lie in more than three dimensions-plus time (Victor et al., 2017). Combinatorial strategies are needed in order to represent each separate neuronal population in high-dimensional spaces. The Authors focused on a ten-dimensional domain of visual textures, assessed through psychophysical measurements in human observers. This multidimensional approach to color vision suggests two combinatorial strategies of perceptual space’s representation: the first is based on projections onto coordinate-like axes equipped with Euclidean geometry, the second on activity patterns, scattered throughout the whole multidimensional space equipped with peculiar global curvatures (Victor et al., 2017). Multiple types of local image statistics capture luminance distributions, spatial contrast, oriented segments and corners, allowing the analysis of textures, surfaces and forms (Victor et al., 2017b). Such multifaceted visual processing is difficult to assess, because of the very high dimensionality and the interaction of the different kinds of statistics. In order to tackle the problem, Victor et al. (2017b) focused on binary images on a square lattice, using a reduced set of stimuli which nevertheless taps many kinds of local statistics. Assessing 16 observers in a ten-parameter space, the Authors found that local image statistics shapes a perceptual space that is highly stereotyped across observers. This means that accurate predictions can be drawn for sensitivities to complex combinations of local image statistics in a 10-dimensional space. The same might stand for other cues. For example, it is possible that, during complex sounds processing, the neurons of auditory cortex integrate across multiple dimensions of sound (such as center frequency, intensity and bandwidth), and not just across the few ones detected by traditional studies (Sloas et al., 2016). The latter Authors built an evolutionary algorithm and a statistical method for nonlinear regression that is able to quantitatively explore cortical responses to five-dimensional auditory stimuli in mice. Summarizing, sensory cortical neurons seem to be driven by interactions across different inputs dimensions, in ways that are not caught by low-dimensional characterizations (Sloas et al., 2016).

Stimuli reduce the dimensionality of cortical activity. A few papers that assess connectome arrangements provide indirect proofs of human brain multidimensionality. Mazzucato et al. (2016) assessed the activity of ensembles of simultaneously recorded neurons and demonstrated that stimuli reduce the dimensionality of cortical activity: the more the network’s ensemble size grows, the more neurons are recruited, the more the dimensions. In particular, they showed that the default mode network displays higher dimensionality, compared with other brain functional networks. In touch with these claims, Zamora-López et al. (2016) compared the connectomes of *C. elegans*, cats, macaques and humans to surrogate networks in which either modules or hubs are destroyed. They demonstrated that functional complexity always decreases in the perturbed networks. A comparison between simulated and empirically obtained resting-state functional connectivity points towards the human brain at rest lying in the largest complexity that can be hosted by its anatomical connectome (Zamora-López et al., 2016). Roland et al. (2017) examined the space-time dynamics of excitation/inhibition in dendrites and axons, over four visual areas of ferrets exposed to scenes with stationary and moving objects. The visual stimuli broke the tight balance, such that networks exhibited longer episodes of net excitation, followed by a compensatory mechanism of net inhibition. Within 80 ms, the excitation-inhibition’s space-time dynamics produced a flow on a low three-dimensional manifold that reduced the complexity of neuron interactions over the whole network. This means that, in contrast to pure temporal dynamics, low dimensional flows evolved to distinguish the simple visual scenes (Roland et al., 2017).

The discovery of stimulus-induced synchronization in the visual cortex suggests that the correlations among low-level stimulus features are encoded by the temporal relationship between neuronal discharges. Therefore, temporal coherence might stand for a signature of perceptual grouping, providing a link between temporal coordination and cognitive functions (Singer and Lazar, 2016). The Authors assigned different coding functions to low-dimensional dynamics features (such as synchronized oscillations and phase shifts) and high-dimensional non-linear ones. Performing chronic multisite recordings from the visual cortex of anesthetized cats and monkeys trained to solve cognitive tasks, they proved that the low-dimensional dynamics, characterized by synchronized oscillations and large-scale correlations, are nothing more than the results of computations performed in the high-dimensional state-space of recurrently coupled networks (Singer and Lazar, 2016). In brief, according to these Authors, the multiplicity of the neural architecture in different sensory systems provides the opportunity to compare their dissimilar solutions to two common requirements: the need for dimensionality reduction and the effectiveness of the higher-order statistical structure inherent in natural sensory inputs (Zaidi et al., 2013). In the sequel, we will see that there exists another

possible solution, in order to elucidate the relationships between the different dimensionalities of the brain and the environment.

Emotions and goals in extra dimensions. Here we provide a few experimental examples that illustrate how multidimensional approaches can be used in order to assess disparate mental activities. Emotional states of consciousness (also termed emotional feelings) are traditionally viewed as innately programmed in subcortical areas (LeDoux and Brown 2017). Are such emotional experiences embedded in a complex, high-dimensional categorical mental space? Claims about the geometric organization of the semantic space of emotion have sparked intense debate, in particular among Authors who support modified versions of the “higher-order theory of consciousness” (Lau and Rosenthal, 2011). The theory assesses the relationships between conscious states and higher-order representations, predicting that the latter portray oneself as being in particular mental states (Lau and Rosenthal, 2011). It is tempting to compare the described higher-order mental activities with the occurrence of higher mental dimensions. In order to quantify the distribution of reported emotional states and the boundaries between emotion categories, Cowen et al. (2017) analyzed a series of self-reported emotional states elicited by short videos. The array of reported emotional experiences was assessed in terms of discrete and dimensional geometries. The Authors found that the videos elicit 27 distinct varieties of reported emotional experience that uncover gradients of emotions (for example, from anxiety to fear to horror to disgust) that correspond to smooth variation in affective dimensions, such as valence and dominance. As stated above, the temporal sequence of a brain individual’s trace can be represented as a trajectory (termed in this case a “thought chart”) in a phase space. Assuming that the topological space containing all the possible brain states might be a very high dimensional manifold, Xing et al. (2017) proposed an unsupervised manifold learning framework, able to reconstruct and visualize such huge structure and to provide a novel data-driven framework for brain states’ classifications. They examined the temporal EEG connectomes of 20 healthy volunteers, both at rest and during an emotion regulation task. A computerized procedure of nonlinear dimensionality reduction was then performed, in order to reconstruct and embed the learned manifold in a lower-dimensional Euclidean space. They demonstrated that the thought charts of resting and emotion regulation task describe two distinct trajectories on the high-dimensional topological space. Such approach has potential applications in neurofeedback, via real-time thought chart visualization, because it allows new trajectories to be inserted on-line via out-of-sample embedding (Xing et al., 2017).

Distributed patterns in sensory cortex are organized across circuits equipped with an intrinsic functional architecture arranged along relevant stimulus dimensions (Waskom and Wagner, 2017). The latter Authors asked whether similar organizational principles might underlie also distributed representations of more abstract information, such as rules or goals. Because the human prefrontal cortex supports goal-directed behavior by representing task context information through higher-order processes, the Authors used multivariate decoding and analyses of spontaneous correlations to show that context representations are distributed across subnetworks within the prefrontal cortex (Waskom and Wagner 2017). They found that pairs of voxels with similar context preferences exhibited spontaneous correlations, twice as large as those between pairs with opposite context preferences. Such subnetwork organization was stable across task-engaged and resting states. Therefore, the abstract multidimensional representations supporting goal-directed cognition are constrained by an intrinsic functional architecture. In turn, Agus et al. (2015) investigated the possible existence of a graphical facilitation effect on probabilistic reasoning. Measures of psychology undergraduates’ performances on problems presented in both verbal-numerical and graphical-pictorial formats were assessed. The Authors noticed that the best predictor of good performance is the confidence in solution correctness under the condition of time pressure administration. This finding suggests that the occurrence of a graphical facilitation could be the result of a multifactorial interaction among multiple contextual and individual dimensions (visuo-spatial and numerical prerequisites, statistical anxiety, attitudes towards statistics and the confidence in response correctness), rather than being strictly related to the problem presentation format (Agus et al. 2015). This latter example demonstrates that brain function’s multidimensionality might also refer to subjective features of the studied population.

Consciousness: the multidimensional device of the brain? Recent claims suggest that the brain modifications correlated with consciousness might reflect the action of projective transformations. In particular, Rudrauf et al. (2017) introduced a mathematical model of embodied consciousness, in which the spatial field of consciousness is described in terms of projective geometry and is under the control of a process of active inference. This spatial field of consciousness, according to the Authors, is able to combine multisensory evidence with prior beliefs in memory. The single individuals’ points of view and perspectives are selected according to preferences, so that the choice of projective frames governs how expectations are transformed by consciousness (Rudrauf et al. 2017). An increasing interest has been raised by the integrated information theory of consciousness (Tononi 2008; Koch et al., 2016), despite it is flawed by practical and theoretical problems. Indeed, measuring integrated information from neuronal signals requires the difficult assessment of all the elements at the same time; furthermore, the interpretation of the required spatial partition becomes rather vague in continuous time-series variables extracted from nonlinear dynamics. In order to tackle these issues, Tajima and Kanai (2017) ranked the topological dimensionality of shared continuous attractor dynamics with integrated information. The effects of unobserved nodes on the attractor dynamics can be assessed using a novel

technique, termed delay-embedding, able to quantify the dimensionality of an embedded attractor, starting just from partial observations (Tajima and Kanai, 2017). In touch with the above-mentioned gauge theories of the brain, topological dimensionality points towards a critical property of integrated information, i.e., its invariance to general coordinate transformations. This means that topological approaches allow the extension of the current notions of integrated information theory of consciousness to continuous dynamical systems too (Tajima and Kanai, 2017).

Whereas a pairwise causal influence between two neural elements can be assessed with existing methods, quantifying multiple influences poses two major mathematical difficulties: overestimation and non-causal confounding influences. To solve the problem, Oizumi et al. (2017) derived a measure of integrated information where causal influences among elements are statistically disconnected. Integrated information is here geometrically interpreted as the divergence between the actual probability distribution of a system and an approximated one. This framework allows a methodological unification of a wide range of information theoretic measures, such as mutual information, transfer entropy, stochastic interaction and integrated information. This novel concept of “geometrical integrated information” is very promising, because it quantifies the strength of multiple causal influences among elements, by simply projecting the probability distribution of complex systems onto constrained multidimensional manifolds.

4) MULTIDIMENSIONAL LESSONS FROM VIRTUAL AND REAL NEURODATA

Multidimensional lessons from artificial neuronal networks. Within the brain networks, tens of millions of multidimensional geometrical structures have been recently uncovered. Reimann et al. (2017) assessed a virtual network of artificial cortical neurons, using a simplicial complexes’ technique that assesses the direction of network information flows. In response to virtual stimuli, synaptically connected neurons are bounded into multidimensional geometrical structures, termed functional cliques. The latter evolve in a stereotypical sequence towards the transitory appearance of increasingly complex structures, up to eleven dimensions. The more neurons in a clique, the higher the dimension of the resulting geometric object. Cliques of progressively higher dimensions assembled momentarily to enclose high-dimensional holes (referred by the Authors as cavities). Therefore, according to these Authors, the brain reacts to stimuli by building a tower of temporary multidimensional blocks, starting with mono-dimensional rods, then bi-dimensional planks, three-dimensional cubes and more complex multidimensional geometries. Experiments were then performed on real brain tissue, suggesting that, during development, the brain constantly rewires in order to build as many high-dimensional structures as possible (Reimann et al., 2017).

Multidimensional lessons from human neurodata. Brain symmetric states display dimensions higher than the asymmetric ones, so that the space of interest might not refer just to dynamical neural spaces, but also to detectable physical cortical locations. In such a vein, Stemmler et al. (2015) demonstrated that animals can navigate by reading out a simple population of grid cell activity across multiple spatial scales. Combining population vectors at different microscopic dimensions allows to predict neural and behavioral correlates of multiscale grid cell readout, encompassing both entorhinal grid cells and hippocampal place cells. While the spatial activity of a single grid cell does not constitute a metric, a hierarchically organized ensemble is able to provide a distance measure (Stemmler et al., 2015). The human brain exhibits the ability, peculiar among the living beings, to connect past, present and future events in a coherent picture, as if *Homo sapiens* was allowed to watch past-present-future glued together in a mental kaleidoscope (Tozzi and Peters, 2016a; Fingelkurts and Fingelkurts, 2014). This observation led to the hypothesis that the brain activity might take place on a multidimensional torus. Indeed, recent findings suggest that the trajectories followed by human thoughts, such as mind-wandering and memory retrieval, might take place in the functional space of a donut-like, four-dimensional hypersphere, undetectable in the usual three dimensions (Tozzi and Peters, 2016a) (**Figure E**). These Authors retrospectively evaluated fMRI series, looking for the topological hallmarks of a fourth dimension. The existence of a functional hypersphere can be identified through its brain surface’s “hallmarks”, i.e., the simultaneous activation of areas opposite each other. In other words, the Authors looked for the three-dimensional “shadows” of a four-dimensional torus, because the BUT predicts that “antipodal points” will be simultaneously activated on a multidimensional brain. And they found them.

Using novel topological techniques of computational proximity, Peters et al. (2017a) furnished evidence that a four-dimensional nervous activity does exist: in other words, a ceaseless, functional four-dimensional cap surrounds the brain. The Authors introduced a method for the measurement of information level in fMRI neural data sets, based on image subdivision in small polygons that encompass dissimilar entropic content. This method allows the detection of hidden temporal patterns of entropy/information in fMRI images. The Authors, looking for the presence of a fourth dimension’s distinctive hallmarks in a temporal sequence of two-dimensional images taken during spontaneous brain activity, found entropic patterns that closely resemble the trajectories foreseen by the presence of a brain hypersphere.

Does the brain activity lie in dimensions higher than the environment? Topological models predict that: (a) increases in anatomical/functional dimensions and symmetries might occur in the path from the lower to the higher activities of the brain, therefore (b) information entropy in the primary sensory areas is lower than in the higher associative ones. Contrary to common belief, this points towards a brain that increases the complexity from the perceived object to the idea of it: an imagined (or perceived) dog encompasses more information than the real dog, because the former is filled with novel emotional and cognitive meanings (for example when looking at a dog, one might think: “how nice is it!” “it is a canid”, and so on). In order to demonstrate the counter-intuitive hypothesis that the brain activity might occur in dimensions higher than the three-dimensional (plus time) environment, Peters et al. (2017b) retrospectively assessed fMRI series and found that, during visual stimulation, the Rényi entropy (i.e., the information) is higher in associative cortices than in the visual primary ones. Therefore, rather than distillate the message from the external world, our brain scatters the incoming input in higher functional dimensions. A recent paper by Dasgupta et al. (2017) substantiates the idea that also in insects the nervous system displays increases in dimensions, when compared with the environment. The Authors assessed fruit flies during the task of similarity search-for example. The fly’s olfactory circuit is able to assign similar neural activity patterns to similar odors, so that behaviors learned from one odor can be applied when a similar one is experienced. Surprisingly, flies solve this problem with a variant of a computer science algorithm termed locality-sensitive hashing, that dilutes the incoming message on many group of neurons, instead of concentrating it on a few ones (Dasgupta et al., 2017).

In touch with these claims, Axelrod et al. (2017) demonstrated that we generate internal experience through the simultaneous activation of different cognitive systems, as if they were interrelated in higher dimensions. In order to test the hypothesis that our mental experience is mediated by a combination of activities of multiple cognitive processes, the Authors evaluated four functional magnetic resonance imaging experiments with the same participants. They demonstrated that, during a self-generated mental activity such as recalling personal memories, three cognitive processes (retrieving memory of events, building a vivid scene in our mind, moving back in time) are pooled over in order to operate simultaneously. Therefore, the subjective impression that each of our internal experiences is a unitary, indivisible entity is accomplished by the brain through a combination of different components, that might lie in higher dimensions. This also means that the concept of the “grandmother neuron” is likely condemned to disappear.

5) IT’S NOT TRUE, BUT I STILL BELIEVE IT: ARE NERVOUS MULTIDIMENSIONS A TECHNICAL DEVICE, OR REAL BRAIN FEATURES?

When assessing nervous activity, two different ways are viable in order to cope with multidimensions. In many of the papers quoted in our review, extra-dimensions stand for a technical device pursued just for methodological purposes, that makes it possible to deal with the overwhelming complexity of the nervous activity. There is, however, another conceivable use of brain further dimensions. Some Authors provide further dimensional axes in order to describe true brain extra-dimensions, and not just abstractions. Yet, the borders between the two approaches are not so neat at all, because the mathematics usually applied to study networks and brain function cannot detect the required high-dimensional structures and spaces. This may also explain why it is so hard to understand the brain. We cannot be sure whether the above-mentioned Authors literally mean that the brain is a multidimensional object. It is difficult to understand whether to read these papers as meaning that neural activity is in some way analogous to a multidimensional structure, or as we’re being asked to believe that the brain actually is, or contains, one. But then, does it really matter? As suggested by Petlevski (2017), these topological models offer a very large “perceptual module” that includes internal nervous processing too. Because of our limited three-dimensional perception, this type of multidimensional realism of the brain may not be readily accepted, despite the Authors were able to provide a series of methods and proofs for the empirical assessment of imperceptible hidden dimensions.

To sum up, are we in front of a multidimensional brain, or a three-dimensional brain that operates in multidimensions? The answer might be just one: it does not count, as long as the models of topological connectome are able to elucidate nervous processing and provide testable hypothesis. What counts, apart from epistemological matters about the realism of entities and theories, is that the study of changes in brain dimensions is a promising novel tool. Approaching brain multidimensions, a large amount of top-down, deductive rationalism is required, because they talk about mappings and projections among different activity levels. We must remember that, despite neural networks are known to exhibit rich, lower-order connectivity patterns at the level of individual nodes and edges, nevertheless, higher-order organization is

still largely unknown. We believe that a complete description of nervous phenomena can be achieved just by looking at its higher levels, where the differences are more easily detectable and assessable.

6) BRAINS IN HIGHER DIMENSIONS: WHAT NEXT?

Despite the limitations correlated with the still insufficient computational power of our current technology and algorithms, the study of the hidden dimensions of the brain is a promising approach. Therefore, we are allowed to ask about the possible future developments of such powerful tools. In this review we limited our description to the hidden dimensions of the brain; however, recent studies start to unveil that other underestimated actors display the computational powers previously believed to be exclusive of the brain. Here we provide a few examples. Despite the integration of somatosensory information is generally assumed to be a function of the central nervous system, Du et al. (2017) described fully functional GABAergic communication within rodent peripheral sensory ganglia. Sensory neurons express major proteins necessary for GABA synthesis and release GABA in response to depolarization: this means that sensory ganglia can modulate transmission of pain-related signals from the peripheral sensory nerves to the CNS (Du et al., 2017). Also, it has been demonstrated that peripheral receptors not just play a role in information processing and perceptual synthesis, but might have cognitive effects by themselves (for a survey, see Tozzi, 2015b). For example, Pruszynski and Johansson (2014) discovered that first-order neurons in the tactile system provide signal edge orientation, via both the intensity and the temporal structure of their responses. They perform feature extraction computations that are typically attributed to the cortical neurons. These findings point towards nervous peripheral structures, such as somatosensory ganglia and receptors, representing a hitherto underappreciated site of sensory integration. This enlarged framework of nervous activity offers a potential target for larger multidimensional approaches to neural function, not limited just to the brain (Du et al., 2017).

The last frontier: looking for the biochemical nervous correlates of further dimensions. Once assumed that multidimensional brain dynamics might occur, could their neurophysiological mechanisms be hypothesized? By incorporating cellular and transcriptional data on individual nodes with network models of the connectome, studies have begun to elucidate the microscopic mechanisms underpinning the macroscopic organization of the whole-brain networks (Crossley et al., 2016). Further insights could be provided through the assessment of the pharmacodynamics of active chemical substances (Tozzi et al., 2017b). To make just an example, high doses of lysergic acid diethylamide (LSD) cause the subjective report of additional spatial or temporal dimensions' perception. Individuals under the effect of LSD describe static objects in three dimensions that seem to move relative to additional spatial dimensions (Katz et al., 1968). Carhart-Harris et al. (2017) demonstrated that LSD provokes increases in correlation among different brain regions, compared with placebo. The described increases in connectivity between visual cortex and other brain areas might help to explain the subjective account of spatial and temporal dimensions' increase. Because the pharmacological effects of LSD lead to a prolonged cross-activation of 5-HT_{2A} receptor heteromers and to increase in glutamate release in specific cortical layers (Moreno et al., 2011), it might be speculated that the functional occurrence of brain further dimensions could be correlated with the biomolecular mechanisms that underlie active mental substances' mental effects.

I want to live forever. It is currently believed that, while physics is based on timeless laws, biology is time-dependent and characterized by irreversible dynamics (Ulanowicz, 2017). However, recent claims suggest a rather different hypothesis, i.e., that homeostatic living beings provide an effort to slow the arrow of time (Tozzi et al., 2018). The same occurs during our higher mental activities, such as memory retrieval, imagination and mind wandering, when the same thoughts are continuously represented, as if the second law of thermodynamics was momentarily wrecked. How can our mind "freeze" the time beyond singular instants? A possible, theoretical explanation is that, as stated before, mental dynamics take place on a donut-like structure, where monotonous, closed trajectories allow the thoughts to relapse. There is, however, another, more speculative possibility that might elucidate why our mind fixes time in an apparently continuous present. Preliminary, unpublished works are assessing the possibility that, when mapping from lower to higher dimensions, systems' dynamics might become undetectable. This would mean that time flows in lower dimensions, while is static in higher ones. Projecting to higher dimensions, a dynamical system might lose its trajectories, so that time is erased and temporal evolutions disappear. A feasible possibility is that static symmetries detectable in higher dimensions are broken in lower ones, giving rise to lower-order detectable dynamics.

Dimensional changes in human diseases. To better understand, diagnose, and treat psychiatric primary and secondary disorders, it is crucial to achieve deeper insights into brain circuits in health and disease, both in humans and animal models (Van Essen and Barch, 2015). Abnormal brain connectivity and network dysfunction have been suggested as the paradigm that will allow us to really understand psychiatric disorders (Fornito et al., 2015; Crossley et al., 2016). For example, Odish et al. (2015) demonstrated the presence of longitudinal modifications of the structural connectome in (pre) Huntington's disease, compared with healthy controls: these dynamics correlated with changes in clinical and cognitive measures. Other brain disorders, including schizophrenia and Alzheimer's disease, display specific lesions, more likely to be located in the connectomic hubs (Crossley et al., 2014). Diffusion tensor imaging-based studies, together with multi-shell tractography and probabilistic fiber tracking, have identified global and local connectome disruptions (reduced global clustering and efficiency, as well as increased global path length) and extensive patterns of reduced connectivity also in Parkinson's disease (Kamagata et al., 2018; Shah et al., 2017). Gleichgerrcht et al. (2015) provided evidence that epilepsy too is likely to be related to abnormal function within specific brain networks. The last, but not the least, the Human Connectome Project, gathering data from healthy young adults aged 21-35, is achieving a high-quality dataset for comparability with other populations. Ongoing studies include: Amish Connectome Mental Illness, Anxiety and Depression in Teenagers, Human Connectomes for Low Vision, Blindness, Sight Restoration (<https://www.humanconnectome.org/disease-studies>).

One could readily anticipate that multidimensional approaches to network theory will allow a novel level of assessment of human diseases, currently undetectable by the standard techniques. The problems to tackle are huge: we have to take into account that the large number of different network organizations and fiber tracts' connections make the changes that can distinguish groups not sufficient to diagnose the disease of an individual patient (Kaiser, 2013). Nevertheless, just to make an example of the huge potentialities of the novel approaches, these challenges could be overturned by a multidimensional description of structural, functional, effective and dynamic connectomes. Using simulated lesion studies of both targeted and random removal, the generated abnormalities in brain connectivity could be visually assessed, by inspecting the topological alterations of neural connections (Ye et al. 2015; Crossley et al., 2014). Kang et al. (2017) demonstrated that energy landscape analysis could be an important tool in order to investigate the alterations in brain networks that might underlie brain diseases. Neurodevelopmental brain disorders might arise from imbalances in excitatory and inhibitory (E/I) brain circuitry that cannot be captured by the classical one-dimensional model (O'Donnell et al., 2017). The latter Authors combined computational simulations with analysis of in vivo two-photon Ca²⁺ imaging data, recorded from the somatosensory cortex of a mice model of Fragile-X Syndrome (O'Donnell et al., 2017). Their results suggest that the basic E/I imbalance model should be updated to higher dimensional approaches, that can better capture the multifaceted computational functions of neural circuits.

Recent approaches demonstrate the feasibility of precision medicine paradigms in order to assess many complex, multifactorial diseases (Li et al., 2015). For example, patients affected by the Type 2 diabetes (T2D) display a wide range of phenotypes and susceptibilities to diabetes-related complications, including neurologic impairment. Li et al. (2015) developed a precision medicine approach that characterizes the complexity of such patient populations. Starting from high-dimensional electronic medical records, genotype data from more than 11,000 individuals and topology-based patient-patient networks, they identified three distinct subgroups of T2D, characterized by different complications and outcomes. Also, they performed a genetic association analysis of the emergent T2D subtypes, in order to identify subtype-specific genetic markers. This technique discovered thousands of single-nucleotide polymorphisms mapping to unique genes specific to the three T2D subtypes (Li et al., 2015). The use of novel meta-analytic approaches in neuroscience has been described by Crossley et al. (2016), who applied network analysis methods to previously published studies and/or publicly accessible databases. They termed this strategy of combining connectivity with other brain features: "meta-connectomics". They showed how network analysis of task-based neuroimaging studies can be used in order to infer functional co-activation from primary data of regional activations. This approach, relating cognition to functional network topology, shows how the brain is composed of cognitively specialized functional subnetworks or modules, linked by a rich club of less specialized regions. Also, meta-connectomics makes it possible to link meta-analytic maps of disorder-related MRI abnormalities to the complex topology of the normative connectome.

In sum, the issue of the multidimensional brain is an exciting field of research, potentially able to provide integrative insights into nervous organization. It is easy to foresee that the hidden dimensions of the brain, either abstract or real, will play a foremost role in the future assessment of both neural function and psychiatric disorders.

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