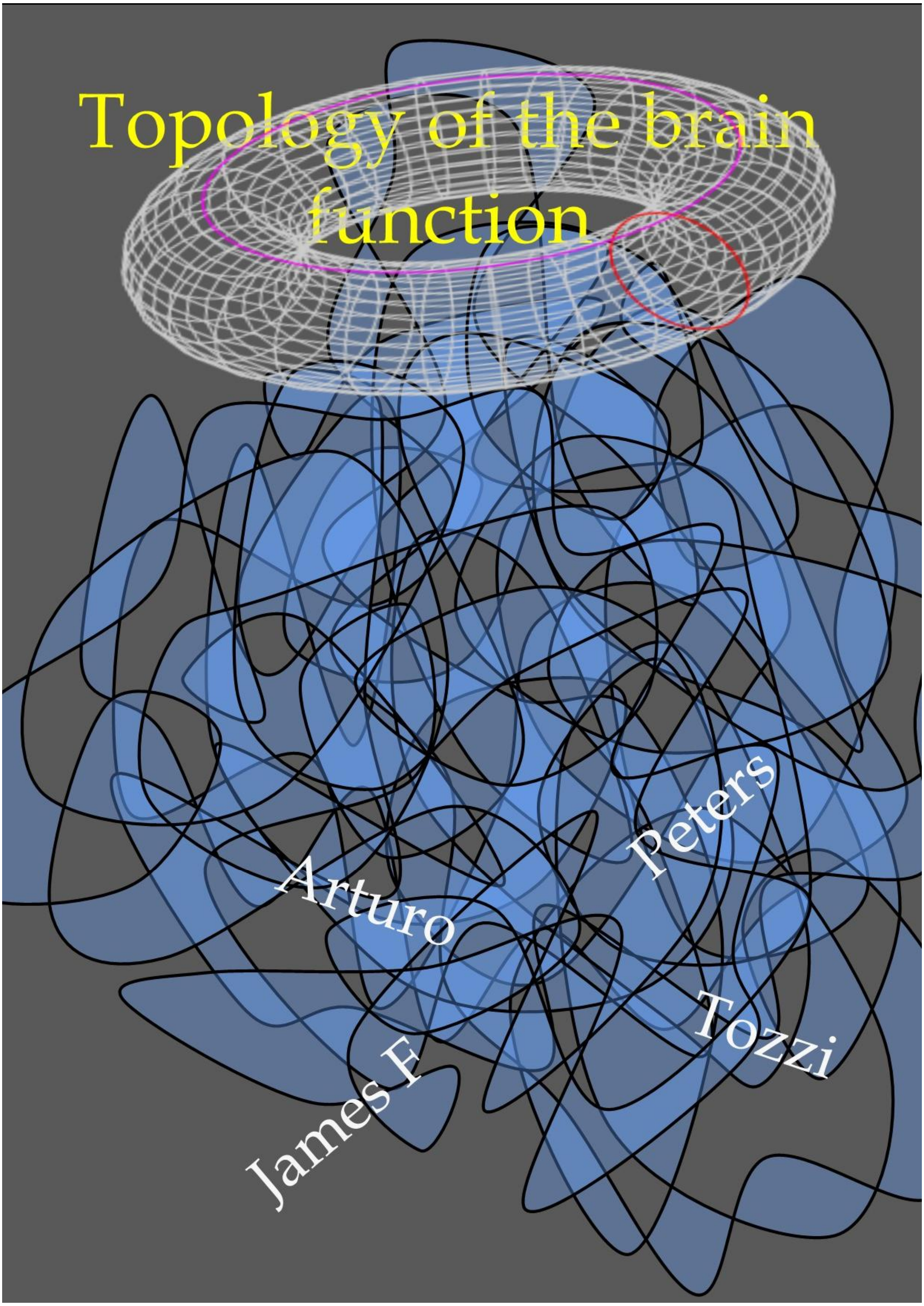

Topology of the brain function

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TOPOLOGY OF THE BRAIN FUNCTION

A summary of our published and unpublished papers

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This manuscript encompasses our published and unpublished topological results in neuroscience. Topology, the mathematical branch that assesses objects and their properties preserved through deformations, stretching and twisting, allows the investigation of the most general brain features. In particular, the Borsuk-Ulam Theorem (BUT) states that, if a single point projects to a higher spatial dimension, it gives rise to two antipodal points with matching description. Physical and biological counterparts of BUT and its variants allow an inquiry of the brain activity. The opportunity to treat the nervous system as a topological structure makes BUT a universal principle underlying neural phenomena and brain function.

CONTENT

The fourth dimension of brain activity and novel correlated neurotechniques

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Note concerning the published papers:
the versions reported here are just sketches of the finally published manuscripts

TOWARDS A FOURTH SPATIAL DIMENSION OF BRAIN ACTIVITY

Current advances in neurosciences deal with the functional architecture of the central nervous system, paving the way for “holistic” theories that improve our understanding of brain activity. From the far-flung branch of topology, a strong concept comes into play in the understanding of brain signals, namely, continous mapping of the signals onto a “hypersphere”: a 4D space equipped with a donut-like shape undectectable by observers living in a 3D world. Here we show that the brain connectome may be regarded as a functional hypersphere. We evaluated the features of the imperceptible fourth dimension based on resting-state fMRI series. In particular, we looked for simultaneous activation of antipodal signals on the 3D cortical surface, which is the topological hallmark of the presence of a hypersphere. Here we demonstrate that spontaneous brain activity displays the typical features which reveal the existence of a functional hypersphere. We anticipate that this introduction to the brain hypersphere is a starting point for further evaluation of a nervous’ fourth spatial dimension, where mental operations take place both in physiological and pathological conditions. The suggestion here is that the brain is embedded in a hypersphere, which helps solve long-standing mysteries concerning our psychological activities such as mind-wandering and memory retrieval or the ability to connect past, present and future events.

An *n*-sphere is a n-dimensional structure that is a generalization of a circle. Specifically, an n-sphere with radius R is set of n-tuples of points. For example, a 2-sphere is a set points on the perimeter of a circle in a 2D space, a 3-sphere is a sets of surface points in a 3D space (a beach ball is a good example) and a 4-sphere is set of points on the surface of what is known as a hypersphere. The prefix “hyper” refers to 4- (and higher-) dimensional analogues of 3D spheres. In mathematical terms, a 4-sphere, also called *glome* or generically *hypersphere*, is a simply connected manifold of constant, positive curvature, enclosed in an Euclidean 4-dimensional space called a *4-ball*. The term glome comes from the Latin “glomus”, meaning ball of string. A 4-sphere is thus the surface or boundary of a 4-dimensional ball, while a 4-dimensional ball is the interior of a 4-sphere. A glome can be built by superimposing two 3-spheres whose opposite edges are abstractly glued together: we obtain a topological structure, the *Clifford torus*. A Clifford torus is a special kind of torus (donut shape) that is a minimal surface which sits inside a glome and is equipped with intricate rotations, called *quaternionic movements* (**Figure 1**). Such a torus has the same local geometry as an “ordinary” three-dimensional space, but its global topology is different. The hypersphere, requiring four dimensions for its definition just as an ordinary sphere requires three, is not detectable in the usual spatial 3-dimensions and is thus challenging to assess. **Figure 1** shows the possible ways to cope with a 3D visualization of a glome. In this paper, we hypothesize that brain activity is shaped in guise of an hypersphere which performs 4D movements on the cortical layers, giving rise to a functional Clifford torus where mental operations take place.

Experimental and theoretical clues allow us to conjecture that the brain activities (at least some of them) are embedded in a torus lying on the surface of a hypersphere. The theoretical claims of brain multidimensionality are widespread *(1-3)* and models charachterized by dimensionality reduction have been used in the study of human central nervous system *(4)*. It has been demonstrated that spontaneous activity structures of high dimensionality – termed “lag threads” - can be found in the brain, consisting of multiple highly reproducible temporal sequences *(5)*. Recent findings suggest that nervous structures process information through topological as well as spatial mechanisms. For example, it is has been hypothesized that hippocampal place cells create topological templates to represent spatial information *(6)*. The glome displays a double-torus shape, *i.e.*, the trajectory followed by a particle inside the torus is closed and similar to a video game with biplanes in aerial combat. When a biplane flies off one edge of gaming display, it does not crash but rather

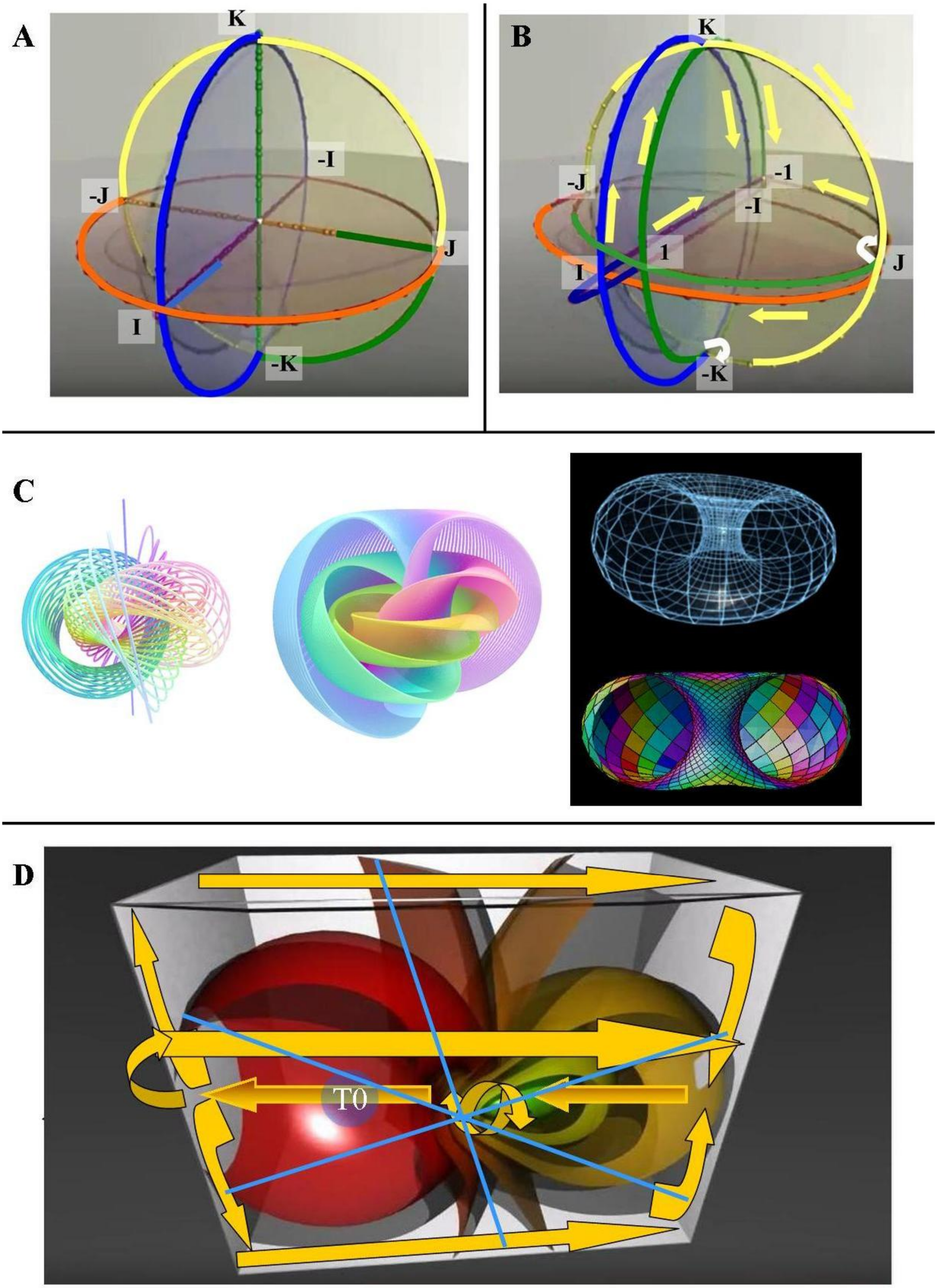

Figure 1. Different ways to depict a hypersphere. To better understand the concept of a 4-sphere, the images should be watched during their complicated movements, *i.e.*, it is helpful to watch the videos mentioned below.

Figure 1A shows the three circumferences embedding a “normal” 3-sphere in a 3D space equipped with the “classical” 3D coordinates.

Figure 1B shows how the superimposition of another 3-sphere (which circumference is glued together with the one of the sphere of **Figure 1A**) gives rise to a 3-sphere (from video https://www.youtube.com/watch?v=XFW769hqa1U). Each apparent line segment is really two line segments, one arching upward into the third dimension and the other arching downward. Observe how opposite sections of the rim fit together, rather than trying to visualize the whole thing at once the way you would visualize a sphere. The four pairs of antipodal points (called *1*,*-1*, *k*, *-k*, *j*,*-j* and *i*, *-i*) give rise to the so-called "quaternion group", equipped with two possible types of reciprocal 4D rotations. Some of the quaternion rotations are depicted, as an example, by the yellow and white arrows.

Figure 1C shows how a glome can be formed by different circles arranged in 4D (right panel). The shape of the glome is everchanging, depending on the number of circles taken into account and their trajectories (see the video at http://nilesjohnson.net/hopf.html). The central and left panels show another way to depict a hypersphere: two spheres glued together along their spherical boundary give rise to a Clifford torus (https://en.wikipedia.org/wiki/Clifford_torus#/media/File:Clifford-torus.gif shows a stereographic projection of a Clifford torus performing a simple rotation through the *xz* plane).

Figure 1D shows the 3D Stereographic projection of the "toroidal parallels" of a glome (from https://www.youtube.com/watch?v=QlcSlTmc0Ts ; see also http://www.matematita.it/materiale/index.php?lang=en&p=cat&sc=2,745). The orange arrows illustrate the trajectories followed by the 4D quaternionic movements of a Clifford torus when projected onto the surface of the 3D space in which it is embedded. Note that the arrows follow the external and medial surfaces of the 3D space in a way that is predictable. Just one of the possible directions of the quaternion movements is displayed: the flow on a Clifford torus may occur in each of the four planes. In this case, the spheres on the left increase in diameter, forming a circle of increasing circumference on the left surface of the 3D space. Conversely, on the opposite right side, the spheres shrink and give rise to a circle of decreasing circumference on the right surface of the 3D space. The blue lines depict some of the possible antipodal points predicted by the Borsuk Ulam Theorem. To give another example, *J* and *-J* are antipodal points in **Figure 1B**.

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it comes back from the opposite edge of the screen *(7)*. Mathematically speaking, the display edges have been "glued" together. The human brain exhibits similar behavior, *i.e.*, the unique ability to connect past, present and future events in a single, coherent picture *(8,9)*, as if we were allowed to watch the three screens of past-present-future glued together in a mental kaleidoscope. The same occurs during other brain functions, *e.g.*, memory retrieval, recursivity of imagination and mind wandering *(10)*, in which concepts appear to be "glued" together, flowing from a state to another. The torus is naturally visualized intrinsically, by ignoring any extrinsic properties a surface may have (it is thought that all the movements onto a torus surface are performed just by trajectories internal to its structure). For example, take a sheet of paper and bend it into a half-cylinder. The extrinsic geometry of the paper has obviously changed, but the paper itself has not been deformed and its intrinsic geometry has not varied. What would you see if you lived in a closed three-manifold? You should be able to see yourself, via the intrinsic structure provided by the glued surfaces of a hypersphere, in an otherwise unperceivable 4D space[7]. In the same way, we humans perceive our thoughts intrinsically and naturally adopt "private", subjective standpoints.

MATERIALS AND METHODS

The movements of particles on a glome.

At first, we need to mathematically define a hypersphere *(11,12)*. It is an n-sphere formed by points which are constant distance from the origin in (n+1)-dimensions. A 4-sphere (also called glome) of radius r (where r may be any positive real number) is defined as the set of points in 4D Euclidean space at distance r from some fixed center point **c** (which may be any point in the 4D space).

In technical terms, in our study we projected onto a 3-D surface a map of a glome equipped with Sp(1) or SU(2) Lie groups. The 4-sphere is parallelizable as a differentiable manifold, with a principal U(1) bundle over the 3-sphere. The only other spheres that admit the structure of a Lie group are the 0-sphere $\mathbf{S}^0$ (real numbers with absolute value 1), the circle $\mathbf{S}^1$ (complex numbers with absolute value 1), $\mathbf{S}^3$, and $\mathbf{S}^7$.

The 4-sphere's Lie group structure is Sp(1), which is a compact, simply connected symplectic group, equipped with with $\frac{\dim}{R} = 1(2\times 1+1) = 3$ and quaternionic 1×1 unitary matrices. Indeed, the glome $\mathbf{S}^4$ forms a Lie group by identification with the set of quaternions of unit norm, called versors *(13)*. The quaternionic manifold is a cube with each face glued to the opposite face with a one quarter clockwise turn. The name arises from the fact that its symmetries can be modelled in the quaternions, a number system like the complex numbers but with three imaginary quantities, instead of just one *(14)*. For an affordable, less technical treatment of quaternions, see *(15)* and the correlated, very useful video: http://blogs.scientificamerican.com/roots-of-unity/nothing-is-more-fun-than-a-hypercube-of-monkeys/ .

In addition: Sp(1) ≈ SO(4)/SO(3)≈Spin(3)≈SU(2).
Thus, Sp(1) is equivalent to - and can be identified with - the special unitary group SU(2).

The Borsuk-Ulam Theorem.

Brains equipped with a hypersphere is a counter-intuitive hypothesis, since we live in a 3D world with no immediate perception that 4D space exists at all, *e.g.*, if you walk along one of the curves of a 4-ball, you think are crossing a straight trajectory, and do not recognize that your environment is embedded in higher dimensions. We need to evaluate indirect clues of the undetectable fourth dimension, such as signs of the glome rotations on a familiar 3D surface. In other words, rotations of a torus embedded in a 4-ball can be identified through their "cross section" movements on a more accessible 3D surface (**Figure 1D**), as if you recognized an object from its shadow projected on a screen. The presence of a glome can be detected invoking the Borsuk-Ulam Theorem (BUT), which states that every continuous map from a hypersphere to a 3D Euclidean space must identify a pair of antipodal points (i.e., points directly opposite each other) (**Figure 1D).** This leads naturally to the possibility of a region-based, instead of a point-based, geometry in which we view collections of signals as surface shapes, where one shape maps to another antipodal one.
Continuous mappings from object spaces to feature spaces lead to various *incarnations* of the Borsuk-Ulam Theorem, a remarkable finding about Euclidean n-spheres and antipodal points by K. Borsuk *(16)*. Briefly, antipodal points are points opposite each other on a circle or on what is known as an n-sphere (called *hypersphere*). There are natural ties between Borsuk's result for antipodes and mappings called homotopies. The early work on n-spheres and antipodal points eventually led Borsuk to the study of retraction mappings and homotopic mappings *(17-19).*
The Borsuk-Ulam Theorem states that:
Every continuous map $f: S^n \to R^n$ *must identify a pair of antipodal points.*

The notation S^n denotes an n-sphere, which is a generalization of the circle. That is, an *n-sphere* with radius R is a set of n-tuples of points $(x_1 ... x_n)$ in *n+1* dimensional Euclidean space that are at distance R from a central point, with:

2-sphere $S^1 : x_1^2 \to R^2$ (circle perimeter),
3-sphere $S^2 : x_1^2 + x_2^2 \to R^2$ (surface),
n-sphere $S^n : x_1^2 + x_2^2 + x_3^2 + ... + x_n^2 \to R^2$. (smallest hypersphere surface)

Points are *antipodal*, provided the points are diametrically opposite *(20).* Examples are the endpoints of a line segment or opposite points along the circumference of a circle, or poles of a sphere. An *n*-dimensional Euclidean vector space is denoted by R^n. In terms of brain activity, a feature vector $x \in R^n$ models the description of a brain signal.

To complete the picture in the application of the Borsuk-Ulam Theorem in brain signal analysis, we view the surface of the brain as a sphere and the feature space for brain signals as finite Euclidean topological spaces. The Borsuk-Ulam Theorem tells us that for description $f(x)$ for a brain signal x, we can expect to find an antipodal feature vector $f(-x)$ that describes a brain signal on the opposite (antipodal) side of the brain. Moreover, the pair of antipodal brain signals have matching descriptions.

Let X denote a nonempty set of points on the surface of the brain. A topological structure on X (called a brain topological space) is a structure given by a set of subsets τ of X, having the following properties:

(Str.1) Every union of sets in τ is a set in τ
(Str.2) Every finite intersection of sets in τ is a set in τ

The pair (X, τ) is called a topological space. Usually, X by itself is called a topological space, provided X has a topology τ on it. Let X, Y be topological spaces. Recall that a function or map $f: X \to Y$ on a set X to a set Y is a subset $X \times Y$ so that for each $x \in X$ there is a unique $y \in Y$ such that $(x, y) \in f$ (usually written $y = f(x)$). The mapping f is defined by a rule that tells us how to find $f(x)$. For a good introduction to mappings, see *(21).*
A mapping $f: X \to Y$ is continuous, provided, when $A \subset Y$ is open, then the inverse $f^{-1}(A) \subset X$ is also open. For more about this, see *(22).* In this view of continuous mappings from the brain signal topological space X on the surface of the brain to the brain signal feature space R^n, we can consider not just one brain signal feature vector

$x \in R^n$, but also mappings from X to a set of brain signal feature vectors $f(X)$. This expanded view of brain signals has interest, since every connected set of feature vectors $f(X)$ has a shape. The significance of this is that brain signal shapes can be compared.

A consideration of $f(X)$ (set of brain signal descriptions for a region *X*) instead of $f(x)$ (description of a single brain signal x) leads to a region-based view of brain signals. This region-based view of the brain arises naturally in terms of a comparison of shapes produced by different mappings from X (brain object space) to the brain feature space R^n. An interest in continuous mappings from object spaces to feature spaces leads into homotopy theory and the study of shapes.

Let $f, g : X \to Y$ be continuous mappings from X to Y. The continuous map $H : X \times [0,1] \to Y$ is defined by $H(x,0) = f(x), \quad H(x,1) = g(x),$ for every $x \in X$.

The mapping *H* is a *homotopy*, provided there is a continuous transformation (called a deformation) from *f* to *g*. The continuous maps *f, g* are called homotopic maps, provided $f(X)$ continuously deforms into $g(X)$ (denoted by $f(X) \to g(X)$). The sets of points $f(X)$, $g(X)$ are called shapes. For more about this, see *(23,24)*.

For the mapping $H : X \times [0,1] \to R^n$, where $H(X,0)$ and $H(X,1)$ are *homotopic*, provided $f(X)$ and $g(X)$ have the same shape. That is, $f(X)$ and $g(X)$ are homotopic, provided

$\|f(X) - g(X)\| < \|f(X)\|$, for all $x \in X$.

It was Borsuk who first associated the geometric notion of shape and homotopies. This leads into the geometry of shapes and shapes of space *(25)*. A pair of connected planar subsets in Euclidean space R^2 have equivalent shapes, provided the planer sets have the same number of holes *(22)*. For example, the letters e, O, P and numerals 6, 9 belong to the same equivalence class of single-hole shapes. In terms of brain signals, this means that the connected graph for $f(X)$ with, for example, an *e* shape, can be deformed into the 9 shape.

This suggests yet another useful application of Borsuk's view of the transformation of shapes, one into the other, in terms of brain signal analysis. Sets of brain signals not only will have similar descriptions, but also dynamic character. Moveover, the deformation of one brain signal shape into another occurs when they are descriptively near *(26)*.

Brain activity and hyperspheres.

In the last paragraphs we have developed a mathematical model of antipodal points and regions casted in a biologically informed fashion, resulting in a framework that has the potential to be operationalized and assessed empirically. To evaluate a hypersphere in terms of a framework for brain activity, we first need to identify potential brain signal loci where quaternion rotations might take place. The natural candidate is the spatially embedded network of the human connectome *(27)*, a non-stationary, highly dynamical structure *(28,29)* characterized by complex topological features and an ever-changing geometry *(30)* (**Fig. 2A**). We embedded the brain in the 3D space of a Clifford torus and looked on cortical surfaces for antipodal points or shapes (**Fig. 2B**). The antipodal points evoked by BUT were viewed as brain signals opposite each other on a glome, *i.e.*, when a brain surface is activated, we identified the simultaneous activation of antipodal surface signals as a proof of a perceivable "passing through" of the fourth dimension onto the brain 3D surface. The main benefit here is that, according to the BUT dictates, for each given brain signal we can find a counterpart in the antipodal positions on the cortical surface.

We have corroborated our brain hypersphere hypothesis with published resting-state fMRI data. We evaluated movies or Figures from 14 available experimental studies and/or metaanalyses describing the brain spontaneous activity, looking for the hallmarks of the hypothesized BUT.

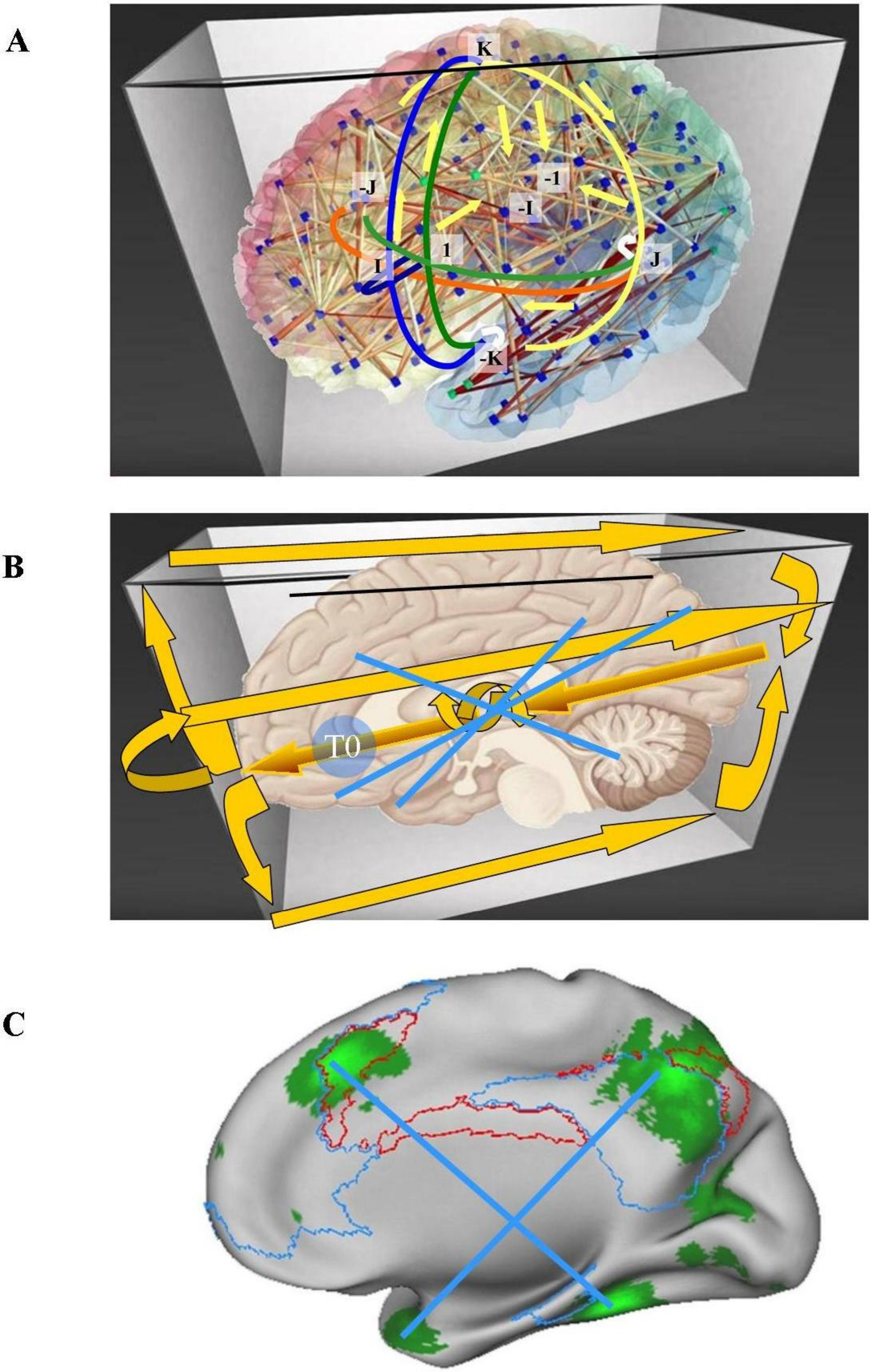

Figure 2. The concept of hypersphere in the framework of brain functional activity.
Figure 2A shows the brain connectome (both the emispheres are depicted) embedded in the 3D space shown in **Figure 1D**. The position of the hypersphere displayed in Figure is just one of the countless possible: being the glome a functional structure equipped with many rotations and trajectories, it can be placed in different points of the brain surface.

Figure 2B. The right brain emisphere is embedded in the 3D space described in **Figures 1D and 2A**. The orange arrows show the 3D projections, in case the brain was located in a 4-ball. The red-orange arrow shows the trajectory of the main stream of the Clifford torus in this case. We displayed just the trajectory from right to left; however, also the opposite trajectory, from left to right, and countless others, can be exploited by the torus during its movements in 4D. The small circle labelled T0 depicts one of the possible starting points, the first activated cortical zone. The nomenclature is borrowed from **Figure 1D**. The blue lines predict the simultaneously activated antipodal points, according to the dictates of the Borsuk Ulam Theorem.

Figure 2C depicts a real pattern of fMRI temporal activation. Significant meta-analytic clusters associated with mind-wandering and related spontaneous thought processes (green clusters) juxtaposed with outlines of the default mode network (blue) and the frontoparietal control network (modified from *29*). We can correctly identify the predicted antipodal points (blue lines). Given one point (a brain signal), there is a second point (another brain signal) at the opposite end of a straight line segment connecting them. Other patterns ascribable to the Borsuk Ulam Theorem are available in **Supplementary materials**.

Which studies did we evaluate, and why?

Spontaneous oscillations are intrinsic, low-frequency fluctuations of cerebral activity which cannot be attributed to the experimental design or other explicit input or output *(31)*. Among the networks exhibiting coherent fluctuations in spontaneous activity, the “default-mode network” (DMN) is worth of mentioning, because it includes functionally and structurally connected regions that show high metabolic activity at rest, but deactivate when specific goal-directed behavior is needed *(32)*. Spontaneous oscillations recapitulate the topographies of fMRI responses to a wide variety of sensory, motor and cognitive task paradigms, providing a powerful means of delineating brain functional organization without the need for subjects to perform tasks *(33)*.

We favoured studies focused on intrinsic, instead of task-evoked activity, because the former is associated with mental operations that could be attributed to the activity of a glome - “screens” are glued together and the trajectories of particles (or thoughts!) follow the internal surface of a Clifford torus -. For example, spontaneous brain activity has been associated with mind-wandering or day dreaming propensities *(34)*, construction of coherent mental scenes, autobiographical memories *(35)*, experiences focused on the future (for a description of the terminology, see *10*) and dreaming state *(36)*. Recent evidence also suggests overlap between the DMN and regions involved in self- and other-related mental operations – such as affective and introspective processes *(37-39)*. It has been hypothesized that spontaneous functional connectivity patterns at rest might constitute a “signature of consciousness”, reflecting a stream of ongoing cognitive processes *(40)*. It has also been proposed that spontaneous activity is highly variable among individuals, depending on local brain differences, somatosensory awareness, age span, race, culture and so on *(41,42)*. We speculate that such variabily might be correlated with those differences in Clifford torus’ structure and movements illustrated in the main text. A brain glome has the potential to constitute a conceptual bridge, because it exhibits both anatomical/functional (spontaneous brain activity and DMN) and psychological correlates (spontaneous, deliberate, self-generated thoughts).

The images and movies we examined were extrapolated from the following papers:

- *a) Ajilore, O. et al. Constructing the resting state structural connectome. Front. Neuroinform. 7:30 (2013).*
- *b) Andrews-Hanna, J.R. et al. The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann. N. Y. Acad. Sci.* ***1316,*** *29-52 (2014).*
- *c) Barttfeld, P. et al. Signature of consciousness in the dynamics of resting-state brain activity. Proc. Natl. Acad. Sci. U. S. A.* ***112,*** *887-892 (2015).*
- *d) Fox, M.D., Raichle, M.E. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat. Rev. Neurosci.* ***8,*** *700-711 (2007).*
- *e) Fox, K.C. et al. The wandering brain: meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. Neuroimage* ***111,*** *611-621 (2015).*
- *f) Gravel, N. et al. Cortical connective field estimates from resting state fMRI activity. Front. Neurosci. 8: 339 (2014).*
- *g) Gusnard, D.A. et al. Medial prefrontal cortex and self-referential mental activity: relation to a default mode of brain function. Proc. Natl. Acad. Sci. U. S. A.* ***98,*** *4259-4264 (2001).*
- *h) Harrison, S.J. et al.. Large-scale probabilistic functional modes from resting state fMRI. Neuroimage* ***109,*** *217-231 (2015).*
- *i) Karahanoglu, F.I., Van De Ville, D. Transient brain activity disentangles fMRI resting-state dynamics in terms of spatially and temporally overlapping networks. Nat. Commun. 6:7751 (2015).*
- *j) Liu, X. et al. Decomposition of spontaneous brain activity into distinct fMRI co-activation patterns. Front. Syst. Neurosci. 7:101 (2013).*
- *k) Mao, D, et al. Low-Frequency Fluctuations of the Resting Brain: High Magnitude Does Not Equal High Reliability. PLoS One 10(6):e0128117 (2015).*
- *l) Mitra, A. et al. Lag threads organize the brain's intrinsic activity. Proc. Natl. Acad. Sci. U. S. A.* ***112,*** *E2235-2244. (2015).*

m) *Power, J.D. et al. Studying brain organization via spontaneous fMRI signal. Neuron.* ***84,*** *681-696 (2014).*
n) *Raichle, M.E. A paradigm shift in functional brain imaging. J. Neurosci.* ***29,*** *12729-12734 (2009).*

RESULTS

We found that all the analyzed temporal series displayed the predicted signs. The whole fMRI sequences of brain region activations, apart from differences depending on slight methodological distinctions among studies, exhibited a stereotyped topographical pattern of activity, such that brain loci are activated together with their antipodal points (**Figure 2C and 3**). We found highly reproducible topography and propagation through subsets of regions that are shared across multiple trajectories: it corroborates the predictions of BUT and brain hypersphere. Brain activity is temporally driven by a functional glome, intrinsic to the brain and (probably) embedded in the very anatomical structure of the connectome. A 4D cap surrounds the brain, equipped with trajectories following quaternion rotations along the nodes of the connectome.

CONCLUSIONS

Our study uncovered ample evidence of hypersphere in experimental fMRI series obtained during spontaneous activity, raising the possibility that brain activity lies on a glome, embedded in 4D space. The reproducibility of the BUT hallmarks suggests that this organizational feature is essential to normal brain physiology and function. Further studies are needed to evaluate what happens when other other techniques are used, *e.g*., EEG and diffusion tensor imaging. Does evoked, task-related activity exhibit the same features? Further investigations will elucidate whether, following the stimulus onset, the multidimensional space outlined by cortical activity is invariant or reduced *(2,3)*. Because neighboring images of the same object are related by glide reflections translations *(7)*, it remains to be seen what the implications of the hypersphere would have for consciousness, perception of time and the nature of reality. Our "deterministic" account of linear transformations needs to be contextualized, taking into account the suggestions of the brain as an energetic, complex, nonlinear system equipped with attractors and random walks *(43-45)*. The role of electromagnetic currents needs to be re-evaluated, *i.e*., do such currents contain the message, or, as recently suggested *(46)* do they serve other kinds of functions? For example, it has been proposed that features of a brain signal with spectral peaks in preferred bands (gamma, beta and so on) provide a basis for feature vectors in a 4D euclidean space *(47)*. Further, the hypersphere, due to different transformations of the quaternionic group, continuously changes its intrinsic structure. In this context, it is reasonable to speculate that each mental state corresponds to a different glome topological space.

ACKNOWLEDGEMENTS

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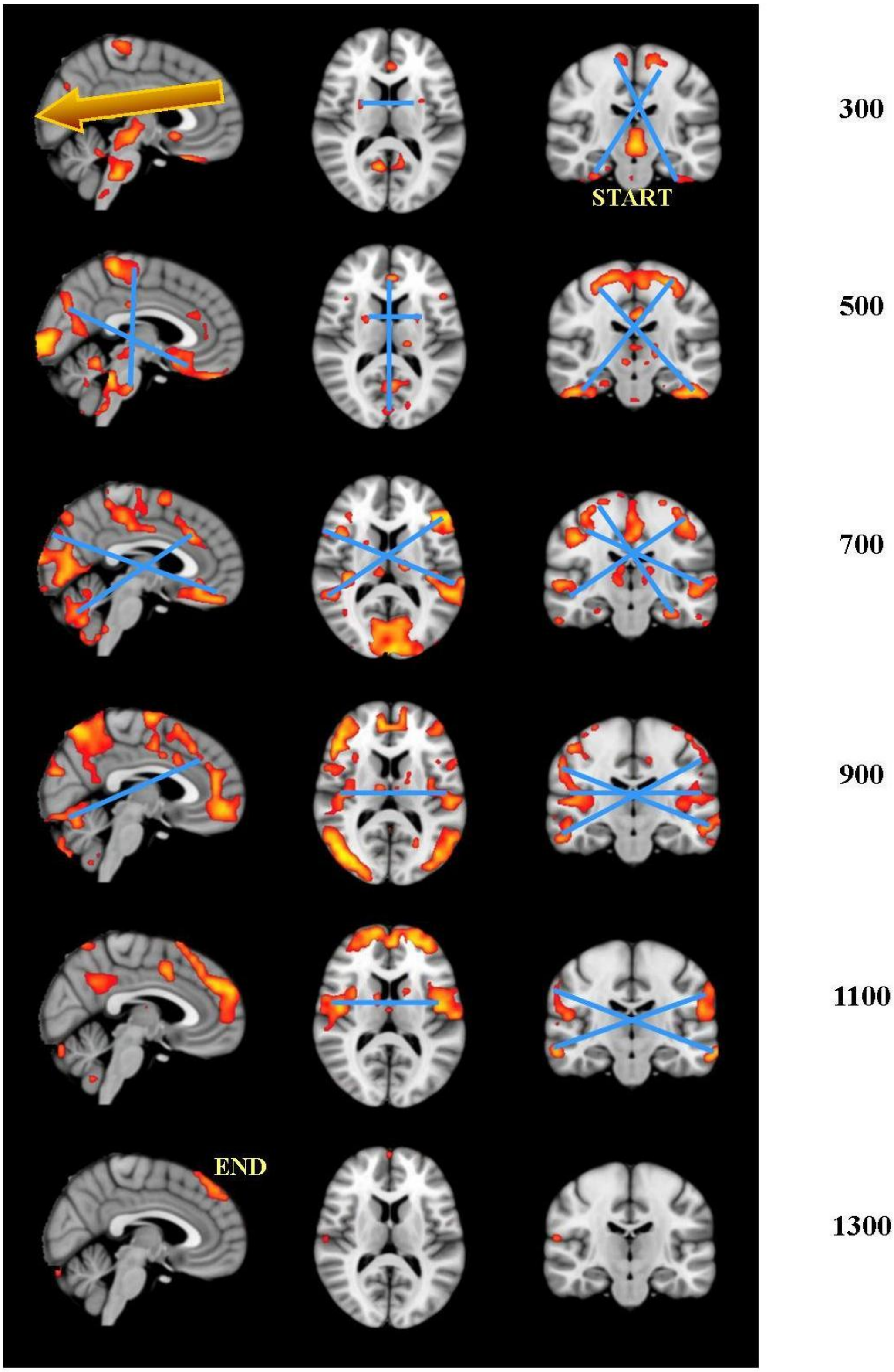

Figure 3. Video frames showing "lag threads" computed from real BOLD resting state rs-fMRI data in a group of 688 subjects, obtained from the Harvard-MGH Brain Genomics Superstruct Project (modified from *5*). Note the widely diffused presence of BUT hallmarks (blue lines) at different times. The times are expressed in milliseconds.

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BRAIN TISSUE TESSELLATION SHOWS ABSENCE OF CANONICAL MICROCIRCUITS

We provide a novel, fast and cheap method for the morphological evaluation of simple 2-D images taken fromhistological samples. This method, based on computational geometry, leads to anovel kind of “tessellation” of every type of biological picture, in order to locate the zones equipped with very fine-grained differences in the tissue texture, compared with the surrounding ones. As an example, we apply the technique to the evaluation of histological images from brain sections and demonstrate that the cortical layers, rather than being a canonical assembly of homogeneous cells asusually believed, display scattered neuronal micro-clusters equipped with higher activity than the surrounding ones.

The current paradigms in neuroscience regard the cortex as homogenous,*i.e.*, all areas are composed of a basic, repeated assembly of the same canonical microcircuit (1, 2, 3, 4). However, novel data point towards an alternative hypothesis. Some authors claim that each neocortical region represents an independent organ, dedicated to a complete and distinct function (5, 6). This idea, first put forward by Gall and Spurzheim, is still tangible in many current mapping studies aimed at localizing functions, commonly referred to as functional segregation specialisation. Such functional cartography with the aid of neuroimaging techniques has been characterized as “phrenology” (7). Contrary to the standard model, the cerebral cortex is composed not only of discrete organs or regions, but also of distinct and unique neuronal assemblies spanning from the macromolecular to microcircuit scale. The cortex comprises extremely heterogeneous cells, with distinct regional variations, receptor repertoire and intrinsic microcircuitry (8): this suggests that every neuron (or group of neurons, of assemblies of neuronal/glial cells, or intra- extra-cellular ensembles) embodies different molecular information that has an operational effect on neuronal computation (9, 10).

A morphological analysis of simple 2D images taken from stained histological samples gives insights into the micro-anatomical structure of tissues and enables high-resolution mapping of neural circuitry. However, such procedures lack the possibility to evaluate the neural functional states and do not allow systematic profiling of neurons based on their connectivity. Further, the conditions of regularity and isotropy, required by standard morphometric procedures, are not fulfilled in the central nervous system, where cells are distributed in a highly complex manner. The more we investigate, the more we discover different roles and abilities in apparently homogenous populations of neurons (11): the complexity and cellular heterogeneity of neuronal circuitry presents a major challenge to understanding the role of discrete neural populations in controlling behaviour. Here we propose a modified Voronoï tessellation (Keypoint-based Voronoï Tessellation, KVT) able to give insights into the physiological and pathological functional state of neural tissues too.

MATERIALS AND METHODS

1 Voronoï Tessellation Method Using Gradient Orientation-Based Generating Points

To establish a framework for the proposed approach to analysing images extracted from histological sample, we briefly introduce a Voronoï tessellation (tiling) of images (**Figure 1A**) (12, 13, 14). The story starts with the selection of a set *S* (a part of a histological picture) containing generating points (sites) (*p* in **Figure 1A**), so that the characteristics (e.g., being part of an edge or a corner, having a distinctive gradient orientation or colour brightness) of each site is different from the characteristics of any other. In other words, the study of histological images is aided by identifying points (pixels) in each image where the angle of the tangent (gradient orientation) to a point is different from the gradient orientation of other pixels in the same image. Different gradient orientations reflect differences in the texture of a histological image. By detecting differences in the gradient orientations of the pixels in a histological image, we are able to identify very fine-grained differences in the tissue texture. We know that every pixel in an image has a gradient orientation (angle of a tangent to a pixel) (15). And the latter is a good choice for a generating point, since pixel gradient orientations tend to fluctuate sufficiently to make it possible to find pixels that are not close together, and which reflect the characteristics of widely separated histological zones. Sites chosen based on their gradient orientation angle are a form of what are known as “keypoints”. In this study, site pixels have been chosen so that each site has gradient orientation that is different from that of any other site.

After choosing a set of generating points *p* (*i.e.*, keypoints) as sites, the next task is to cover an image with non-overlappingconvex polygons, called “Voronoï regions”. A Voronoï region (V in **Figure 1A**) is a set of points in an image that are closer to *p*than to any other site in *S*. The collection of polygons in a Voronoï tessellation is also called a “Voronoï mesh”. A gradient orientation-based Voronoï tessellation provides insights concerning the physiological and pathological functional state of neural tissues. The Voronoï tessellation method has a 90-year history cogently explained in (16) with many variations (17). Our study introduces an application of what is known as “maximal nucleus clustering” in Voronoi mesh (18). A “nucleus cluster” is a collection of mesh polygons adjacent to a central polygon, called the “nucleus”(N in **Figure 1B**). When the number of polygons adjacent to the nucleus is maximal, then the resulting “maximal nucleus cluster”(M in **Figure 1B**) resides on those parts of an image having the greatest change and greatest accumulation of neighbouring Voronoï regions in close proximity to each other, in order that each site has a different gradient orientation.

Such tessellations of histological images provide information concerning spatial distribution, because the polygonal areas do not vary much when the cells are regularly distributed. On the contrary, smaller and larger polygons occur when cellular clusters (characterized by generating points with gradient orientations close to the gradient orientation angle of a nucleus) are displayed and may be identified by simple algorithms. Voronoï tessellation has been used to evaluate the numerical density and spatial distribution of neuronal and glial cells, because it takes into account the topographical features typical of the CNS (19). It has been also used to investigate spatial relations between neural mosaics in retina, in order to evaluate possible constraints or connectivity between different co-localized cellular populations (20).

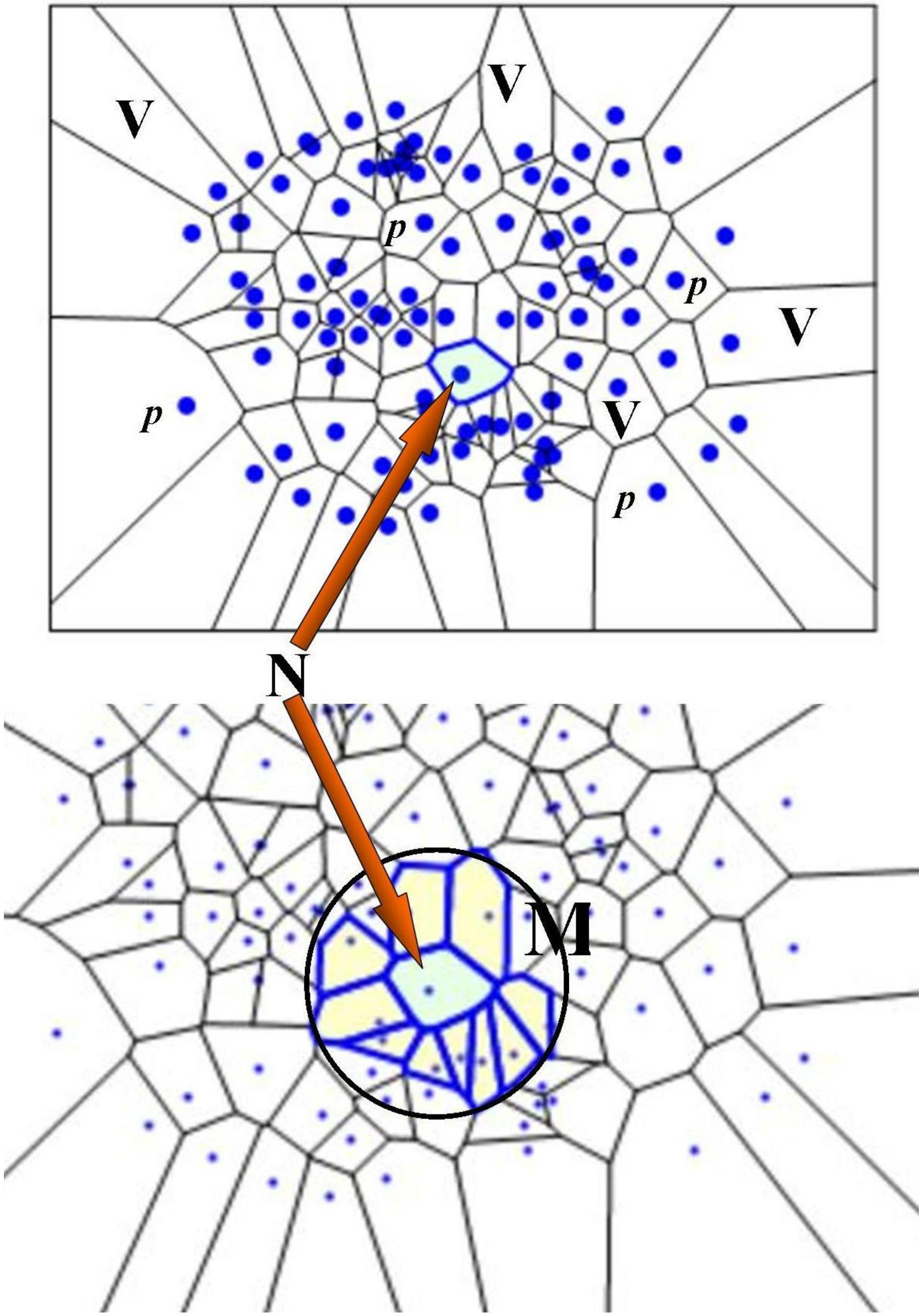
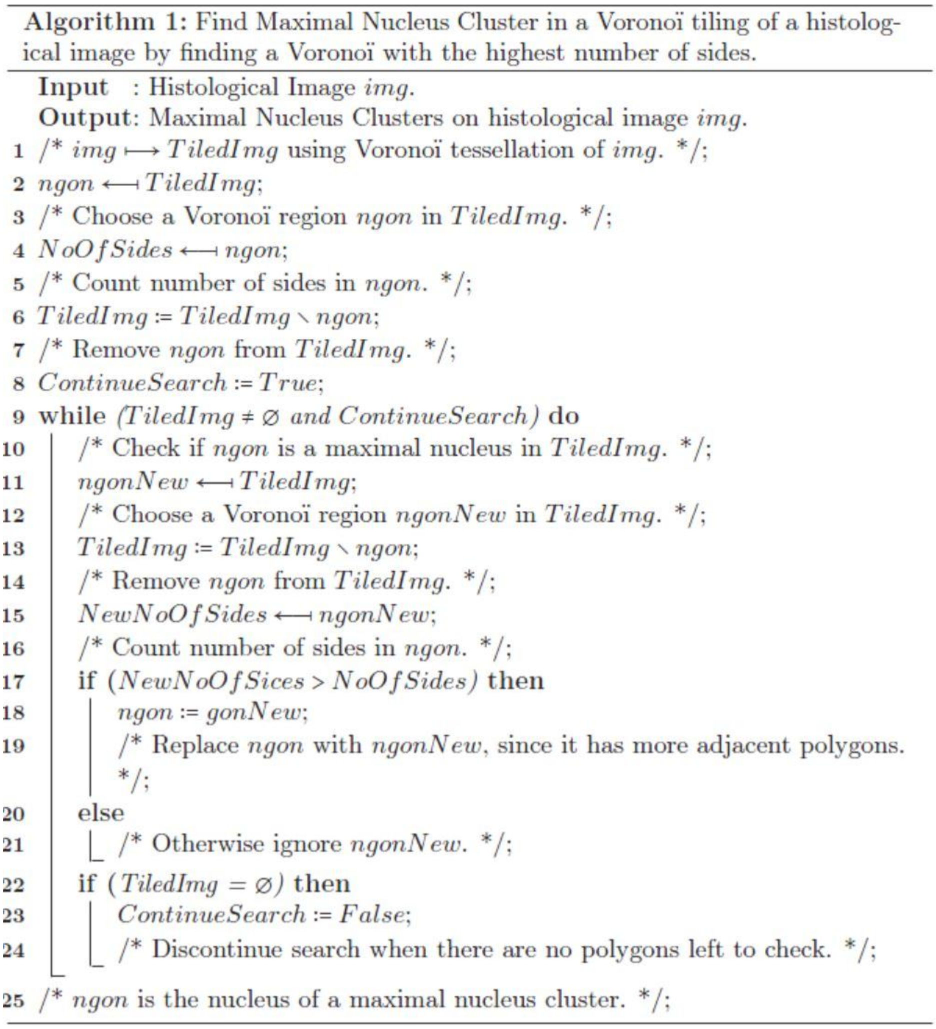


Figure 1.A collection of Voronoï regions, called Voronoï mesh, at low and high magnification (at the top and the bottom, respectively). The Figure illustrates, as an example, some generating keypoints (p), some Voronoï regions (V), a nucleus (N) and its corresponding maximal nucleus cluster (displayed into the circle M).

For technical readers, **Algorithm 1** gives the steps to find a maximal nucleus in a tessellated (tiled) histological image. Briefly, after a gradient orientation-based tiling of an image, those Voronoï polygons with the highest number of sides are maximal nuclei of clusters formed by each maximal nucleus and its adjacent polygons (one adjacent polygon for each edge of the nucleus).



Algorithm 1: Find Maximal Nucleus Cluster in a Voronoï tiling of a histological image by finding a Voronoï with the highest number of sides.

```
Input  : Histological Image $img$.
Output: Maximal Nucleus Clusters on histological image $img$.
/* $img \longmapsto TiledImg$ using Voronoï tessellation of $img$. */;
$ngon \longleftarrow TiledImg$;
/* Choose a Voronoï region $ngon$ in $TiledImg$. */;
$NoOfSides \longleftarrow ngon$;
/* Count number of sides in $ngon$. */;
$TiledImg \coloneqq TiledImg \setminus ngon$;
/* Remove $ngon$ from $TiledImg$. */;
$ContinueSearch \coloneqq True$;
while $(TiledImg \neq \emptyset$ and $ContinueSearch)$ do
    /* Check if $ngon$ is a maximal nucleus in $TiledImg$. */;
    $ngonNew \longleftarrow TiledImg$;
    /* Choose a Voronoï region $ngonNew$ in $TiledImg$. */;
    $TiledImg \coloneqq TiledImg \setminus ngon$;
    /* Remove $ngon$ from $TiledImg$. */;
    $NewNoOfSides \longleftarrow ngonNew$;
    /* Count number of sides in $ngon$. */;
    if $(NewNoOfSices > NoOfSides)$ then
        $ngon \coloneqq gonNew$;
        /* Replace $ngon$ with $ngonNew$, since it has more adjacent polygons. */;
    else
        /* Otherwise ignore $ngonNew$. */;
    if $(TiledImg = \emptyset)$ then
        $ContinueSearch \coloneqq False$;
        /* Discontinue search when there are no polygons left to check. */;
/* $ngon$ is the nucleus of a maximal nucleus cluster. */;
```

2 Are there relationships between morphology and function?

It is intuitively difficult to see any way to infer the degree of "functional activity" of neurons from the inhomogeneity of their distribution on histoslides. In this more theoretical paragraph, we evaluate the functional implications of our framework, introducing the concept of Borsuk-UlamTheorem (BUT) and matching signals. The basic form of BUT tells us that there exist a pair of antipodal (opposite) points on the circumference that map to a single pointin a line (21, 22, 23). The two antipodal points are indeed assessed at one level of observation, while the single point is assessed at a lower level (24, 25). This means that, if we embed a maximal nucleus cluster in a circumference, there exist two antipodal points with matching description (**Figure 2A**). Furthermore, the two opposite points can be used not just for the description of simple topological points (26, 27), but also of more complicated features, such as functions or signals (15, 18, 26). If we evaluate central nervous system (CNS) "activity" instead of "points", this BUT variant (called ReBUT) leads naturally to the possibility of a region-based, not simply point-based, brain geometry. Therefore, reBUT provides a handy vehicle in expressing the relationship between Voronoï polygons that serve as cluster nuclei.

In the tiling of histological images, it may occur that more than onemaximal nucleus cluster can be found, all of them equipped with the same number of sides (i.e., such maximal nucleus clusters have matching description). Thus, from reBUT, different maximal nucleus clusters may be embedded in the same circumference and might have matching functional description (**Figure 2B**). This means that systemsphenomena (e.g., functions, or different types of activity) could be characterized as antipodal points with matching description, in order that the functions of signal shapes can be compared (18, 27). It might be objected that maximal nuclei polygons are not properly circular, because they display a polygonal shape and sometimes also a concave structure, different from the circumference's convexity required by the basic form of BUT. However, the BUT can be generalized also to symmetries occurring on flat or concave manifolds (18, 28). In other words, whether the system displays a concave, convex or flat shape, it does not count: we may always find the points with matching description predicted by BUT.

In conclusion, it might be speculated that changes in morphological features could be correlated with variations in physical functions. Thus, gradient differences in the various zones of the picture might be linked with different functional counterparts.

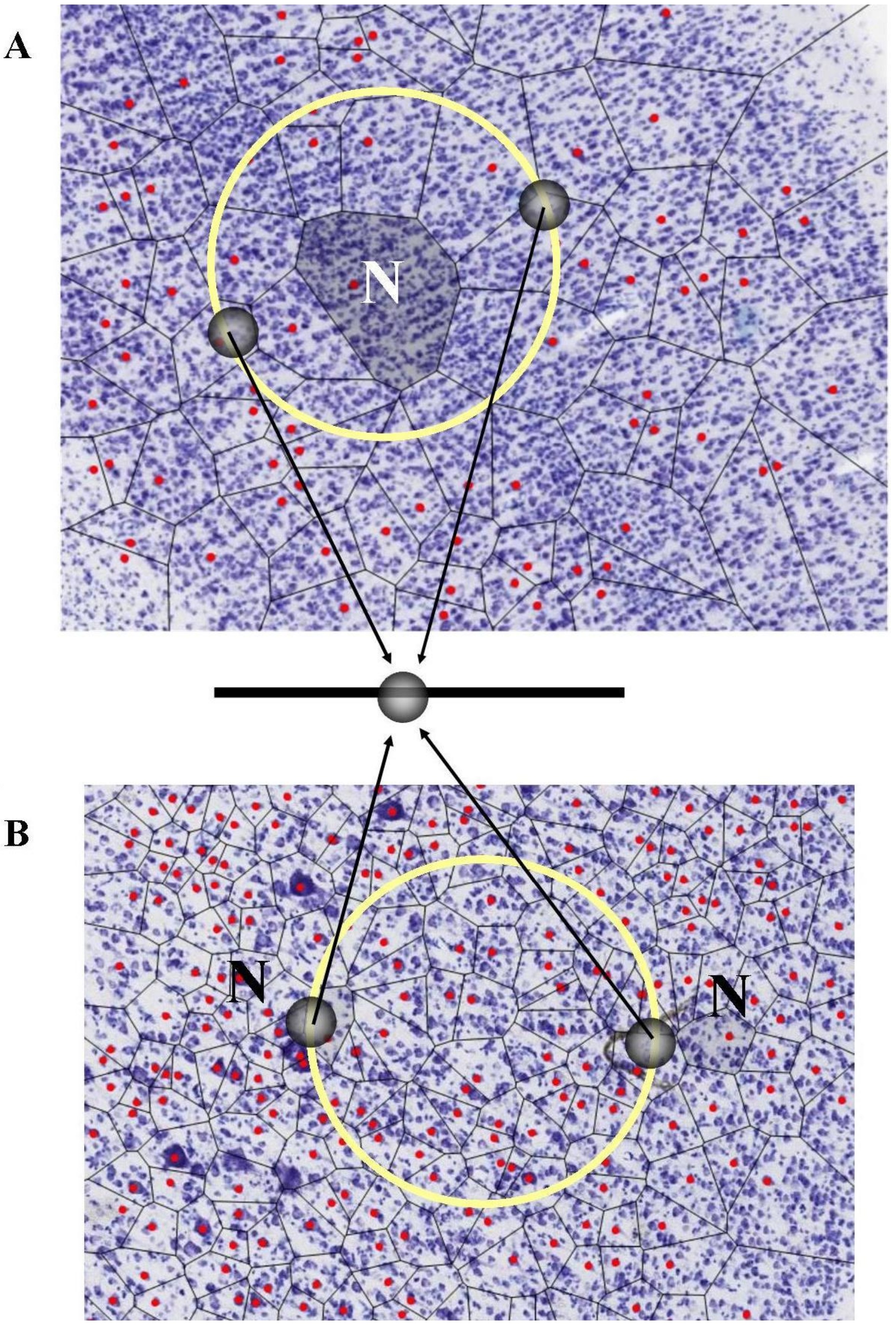


Figure 2A. The Borsuk-Ulam theorem applied to histological brain tessellation. Note that a single maximal nucleus (N) displays two antipodal points with matching description. **Figure 2B**. The use of reBUT. Note that, this time, two different maximal nuclei display matching description.

3 Materials

We achievedKVT tessellations on histological, whole-brain coronal slices from adult Chlorocebus aethiops. We took the brain images from the website Brain Maps.org (http://brainmaps.org/index.php). We assessed the Dataset ID 42, species Chlorocebusaethiops, adult, Nissl stain, embedded in gelatin, coronal plane, resolution 0.46 microns/pixel, section thickness 40 microns (http://brainmaps.org/ajax-viewer.php?datid=42&sname=385). We performed KVT on images at different magnifications, from 10x to 40x, and on separate or consecutive slices. Different cortical areas were examined.

RESULTS

We found that, everywhere in the cortex, isolated small clusters of higher activity can be noticed in different layers (**Figures 3 and 4**). The clusters are scattered, *i.e.*, some micro-areas of a specific layer are more active than the adjacent others embedded in the same layer. In most of the tessellations, more than one clusteris detectable.

We evaluated pictures taken from the following cortical areas: cingulate gyrus, area 4, area 3b, intraparietal sulcus, lateral sulcus, superior temporal gyrus, superior temporal sulcus and inferior temporal sulcus.

We performed KVT tessellations on 25 samples at four different magnifications (4x, 10x, 20x, 40x) and we found:

Absent clusters: (1/25 samples). Note that the absence of a cluster was localized in area 3b.

One maximal cluster: (10/25 samples). This feature was more frequent in higher magnification images (20 and 40x)

Two maximal clusters: (9/25 samples). This feature was scattered all over the magnifications.

More than two maximal clusters: (5/25 samples). This feature was more frequent in smaller magnification images (4 and 10x).

The clusters were localized in all the layers from I to VI, but were more frequent in layers II-III (18/25 samples).

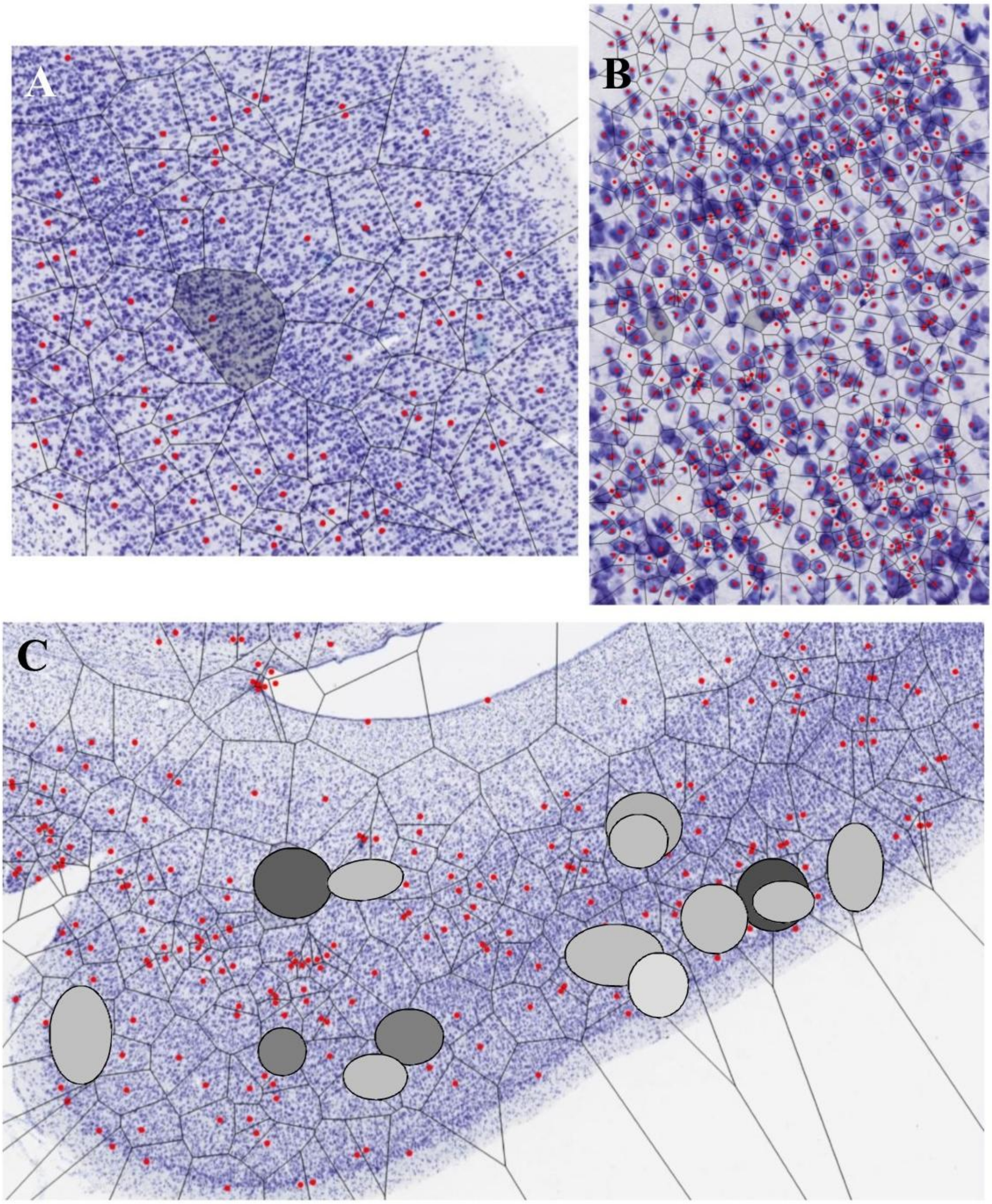


Figure 3. Examples of Keypoint-Based Voronoïdiagrams on images taken from cortical slices of Chlorocebus aethiops at different magnifications.

Figure A. an isolated clusterof activity (shaded in grey) is visible in layer IV of the inferior temporal sulcus at low magnification. This Voronoï diagram is characterized by one distinct nucleus and its surrounding mesh cluster.

Figure B. Two isolated clusters of activity are visible in layer II of the intraparietal sulcus at high magnification.

Figure C. Mesh clusters of activity on 10 superimposed, consecutive brain images from the inferior temporal sulcus at low magnification. The black circles refer to the presence of mesh clusters at high activity in the deepest slices, the grey circles in the intermediate slices and the white circles in the most superficial ones. Note the presence of many small, isolated clusters in all the brain layers.

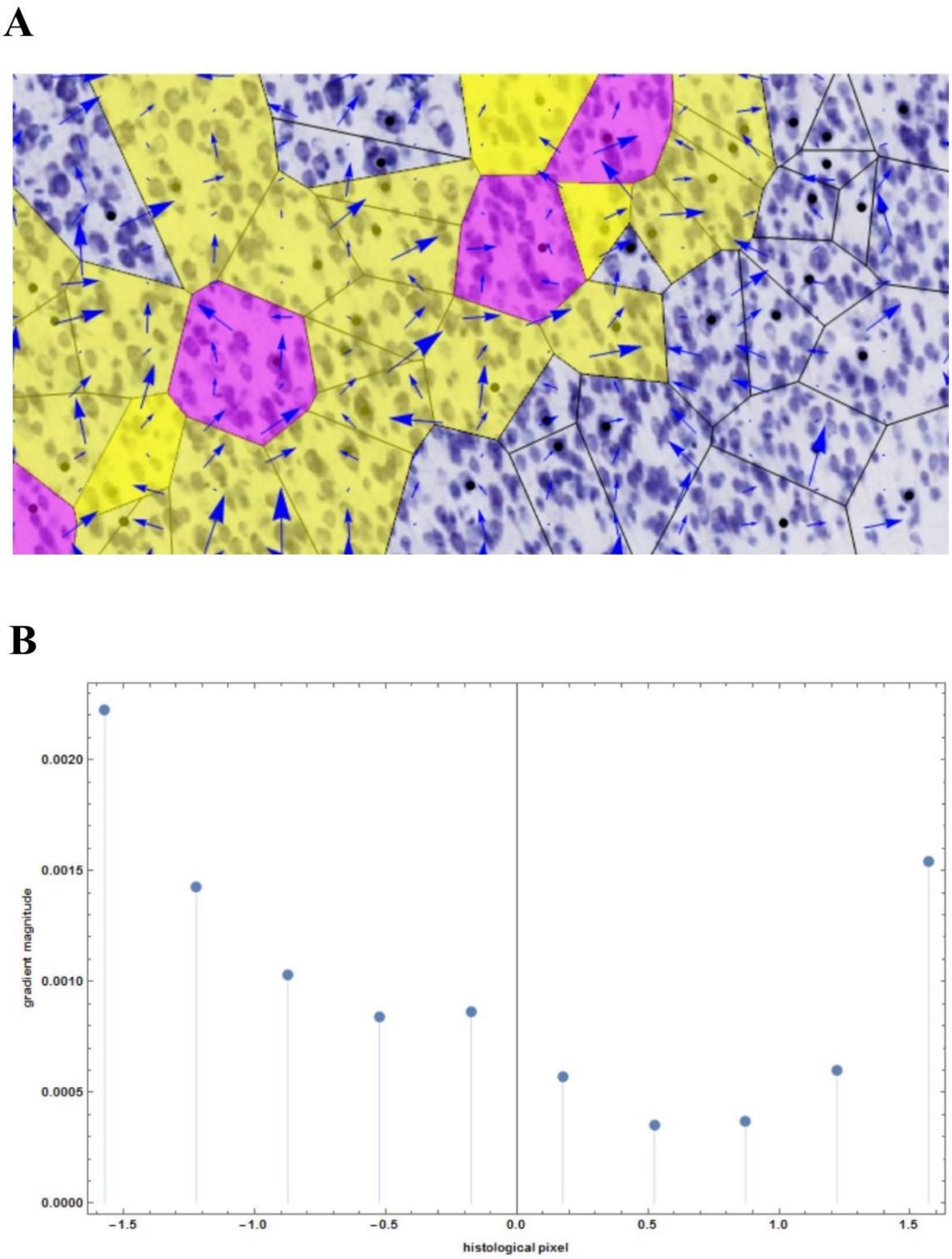


Figure 4A. The tessellated image contains arrows of varying size that represent the gradient orientation of the tangent vectors for each of the different gradient orientations found. The thicker arrows indicate higher gradient magnitudes. A maximal nucleus cluster collects together those regions containing the highest number of pixels, each with a different gradient orientation. So it is entirely possible that some pixels outside the maximal nucleus cluster will have different gradient magnitudes: it tells that, although such pixels are not highly concentrated, they do reflect high gradient magnitudes. **Figure 4B** presents histograms showing the number of pixels with different gradient orientations. Each histogram spike indicates those pixels with a particular gradient magnitude, such as 0.0035 for those pixels with gradient magnitudes slightly greater than 0.

CONCLUSIONS

We showed that it isfeasible to detect clusters of activity in tessellated 2D images. Given any image, it is possible to assess maximal nucleus clustersin a Voronoï tiling of histological images. The gradient orientation-based Voronoï regions outside the greatest clustering (mesh cluster around a maximal nucleus) are descriptively different, since each generating point has a different gradient orientation angle. In the language of proximity spaces, polygons outside the mesh cluster are *spatially far* from the nucleus, since no polygon outside the mesh cluster has any points in common with the nucleus, and *descriptively far* from the nucleus, since the description of the generating point for the Voronoï region is not the same as the description of the generating points of the polygons outside the mesh cluster.

Therefore, aVoronoï region that has the highest number of adjacent polygons indicates both a part of a histological image where there is the greatest clustering around a particular region, and the greatest "activity". These observations suggest that activity of the part of brain occupied by clusters is greater than the surrounding regions. Evidence comes from the fact that in all cases there are few nucleus clusters. The highest number of adjacency polygons surrounding a cluster nucleus indicates where there is the greatest concentration of symmetry among the regions of the brain images. As expected, at higher magnifications, fewer clusters are found. Smaller convex polygons are more interesting, because they belong to clusters of polygons surrounding small cluster nuclei: these clusters are important and serve as means of identifying those parts of a cortical image with more activity.

Our results show that the cortex is not a stereotyped sequence of homogeneous neurons as previously believed, but contains instead islands where the activity is higher than the surrounding ones. It is in touch with "phrenological" claims, against the standard version of canonical microcircuits view of the brain. The anatomical micro-structure of the brain is constrained towards peculiar points in each layer. Further, it is noteworthy that the activity clusters do not involve just the Nissl-stained neurons, but also their surrounding melieu. This means that other structures apart neurons contribute to the increase of activity found in specific brain micro-areas. The gradient differences are associated with variations in the conformation of the otherwise apparently homogeneous neural assemblies: we hypothesize that they could stand, due to reBUT, for still unknown functional differences among cortical microareas. In such a vein, the recognition of the most active cortical micro-areas through a simple morphological processing technique also allows a preliminary choice of the micro-zones to evaluate through more sophisticated techniques, such as immunohistochemistry.

In conclusion, we provide a method of physical/biological images evaluation which is easy to perform, fast (it takes 3-8 secondsfor each KVT analysis), cheap, and able to give us information about the most "active "histological areas. We are thus allowed to detect information from a morphological picture. In the case of histological brain tissue, our results could be summarized with a definition: "phrenology", a term which emphasizes the delicate and heterogeneous nature of cortical hierarchies with deep structures and the distribution of information coding over multiple levels and timescales (6, 29). Our study shows that 2D tessellations using algorithms that have been published (18) can be adapted to histological pictures, in the evaluation of medical and biological images.

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PRIMARY EVIDENCE OF A DONUT-LIKE, FOURTH SPATIAL DIMENSION IN THE BRAIN

(BOLD-independent computational entropy assesses functional tori in brain fmri images)

We introduce a novel method for the measurement of information in fMRI neuroimages, *i.e.*, nucleus clustering's Rényi entropy derived from strong proximities in feature-based Voronoï tessellations, *e.g.*, maximal nucleus clustering (MNC). We show how MNC is a novel, fast and inexpensive image-analysis technique, independent from the standard blood-oxygen-level dependent signals, which facilitates the objective detection of hidden temporal patterns of entropy/information in zones of fMRI images generally not taken into account by the subjective standpoint of the observer. In order to evaluate the potential applications of MNC, we looked for the presence of a fourth dimension's distinctive hallmarks in a temporal sequence of 2D images taken during spontaneous brain activity. Indeed, recent findings suggest that several brain activities, such as mind-wandering and memory retrieval, might take place in the functional space of a four dimensional hypersphere, which is a double donut-like structure undetectable in the usual three dimensions. We found that the Rényi entropy is higher in MNC areas than in the surrounding ones, and that these temporal patterns closely resemble the trajectories predicted by the possible presence of a hypersphere in the brain.

In this paper we introduce a novel technique of fMRI images analysis, called computational proximity method, *i.e.*, nucleus clustering in Voronoï tessellations (Peters and Inan, 2016a). The images are subdivided in contiguous (without interstice or overlap) polygons, called the "Voronoï polygons". They yield a density map, called "tessellation", that makes it possible to make an objective measurement of the polygon areas' spatial distribution and helps to define "random", "regular" and "clustered" distributions (Duyckaerts and Godefroy, 2000; Franck and Hart, 2010; Edelsbrunner, 2014). Tessellations have been already used in neuroscience, *i.e.*, to investigate spatial relations and connectivity between neural mosaics in the retina (Mozos et al., 2011) or to evaluate histological cortical sections (Peters at al., 2016). In a Voronoï tessellation of an fMRI image, of particular interest is the presence of maximal nucleus clusters (MNC), *i.e.*, zones with the highest number of adjacent polygons (Peters et al., 2016). The MNC clustering approach includes a main feature of level set methods, namely, a nucleus boundary that is embedded in a family of nearby level sets (Saye and Sethian, 2011). MNC reveals regions of the brain, independent from blood-oxygen-level dependent (BOLD) signals, characterized by different gradient orientation and diverse functional dimensions.

To evaluate the power and potentialities of this novel approach, we used it in order to test the brain-hypersphere hypothesis. Indeed, it has been recently hypothesized that brain activity is shaped in the guise of a functional hypersphere, which performs complicated 4D movements called "quaternionic" rotations (Tozzi and Peters, 2016a). They give rise to the so called "Clifford torus", a closed donut-like structure where mental functions might take place. The torus displays glued trajectories similar to a video game with spaceships in combat: when a spaceship flies off the right edge of the screen, it does not disappear but rather comes back from the left (Weeks, 2002). The human brain exhibits similar behaviour, *i.e.*, the unique ability to connect far-flung events in a single, coherent picture (Atasoy et al., 2016). During brain functions such as memory retrieval and mind-wandering, concepts flow from one state to another and appear to be "glued" together. It has also been recently proposed that the brain, when evaluated in the proper dimension (Kida et al., 2016), is equipped with symmetries in one dimension that disappear (said to be "hidden" or "broken") in just one dimension lower (Tozzi and Peters, 2016b). A symmetry break occurs when the symmetry is present at one level of observation, but "hidden" at another level: it suggests that a 4D hypersphere could be equipped with symmetries, of great importance in order to explain central nervous system (CNS) activities, undetectable at the usual 3D cortical level.

Although we live in a 3D world with no immediate perception that 4D space exists at all, the brain hypersphere rotations can be identified through their "cross section" movements on a more accessible 3D surface, as if you recognized some object from its shadow projected on a screen. We may thus evaluate indirect clues of the undetectable fourth dimension, such hypersphere rotations' hallmarks or signs on a familiar 3D surface. Here we show that, in temporal fMRI series from spontaneous brain activity, MNC discloses the typical patterns of quaternionic rotations and hidden symmetries.

MATERIALS AND METHODS

1 Samples. Spontaneous activity structures of high dimensionality (termed “lag threads”) can be found in the brain, consisting of multiple highly reproducible temporal sequences (Mitra et al., 2015). We retrospectively evaluated video frames showing “lag threads” computed from real BOLD resting state rs-fMRI data in a group of 688 subjects, obtained from the Harvard-MGH Brain Genomics Superstruct Project. We assessed 4 sets of coronal sections (including a total of 54 Images) from the published videos (Threads 1, 2, 3 and 4):
http://www.pnas.org/content/suppl/2015/03/24/1503960112.DCSupplemental
We favoured studies focused on intrinsic, instead of task-evoked activity, because the former is associated with mental operations that could be attributed to the activity of a torus: “screens” are glued together and the trajectories of thoughts follow the internal surface of a hypersphere. For example, spontaneous brain activity has been associated with day dreaming propensities, construction of coherent mental scenes, autobiographical memories, experiences focused on the future, dreaming state (for a description of the terminology, see (Andrews-Hanna et al., 2014). Each tessellated image leads to the MNC mesh clustering described in the next paragraph.

2 Generating Points in Voronoï Tilings of Plane Surfaces. This section introduces nucleus clustering in Voronoï tessellations of plane surfaces (Peters 2016; Edelsbrunner, 2006). A Voronoï tessellation is a tiling of a surface with various shaped convex polygons. Let *E* be a plane surface such as the surface of an fMRI image and let *S* be a set of generating points in *E*. Each such polygon is called a Voronoï region $V(s)$ of a

$$V(s) = \left\{ x \in E : \|x - s\| \le \|x - q\| \text{ for all } q \text{ in } S \right\}.$$

In other words, a Voronoï region $V(s)$ is the set of all points *x* on the plane surface E that are nearer to the generating point *s* than to any other generating point on the surface (**Figures 1A-B**). In this investigation of fMRI images, each of the generating points in a particular Voronoï tessellation has a different description. Each description of generating point *s* is defined by the gradient orientation angle of *s*, *i.e.*, the angle of the tangent to the point *s*.

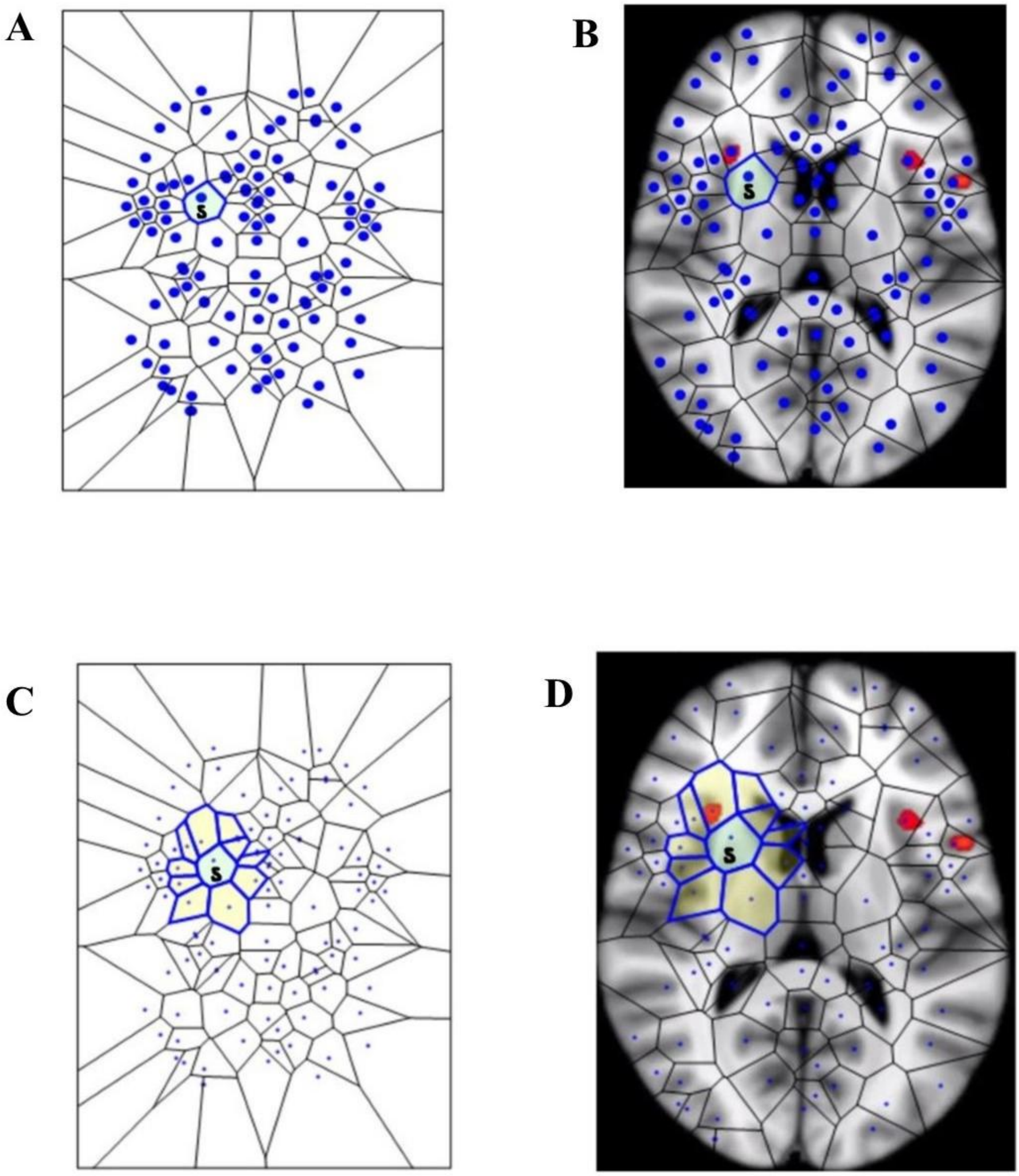


Figure 1. **1A:** surface tiling of a sample Voronoï region $V(s) =$ . Each •in the tiling represents a generating point with particular features, such gradient orientation and brightness. There are no two • that have the same description. For this reason, every Voronoï region has a slightly different shape. This tiling is derived from the fMRI image in **Figure 1B,** which displays Voronoï region $V(s)$ on a fMRI image taken from Mitra (11). **Figure 1C** displays a sample maximal nucleus cluster *N* for a particular generating point represented by the dot • in N. In this Voronoï tiling, the nucleus N has 10 adjacent (strongly near) polygons. Since N has the highest number of adjacent polygons, it is maximal. This *N* is of particular interest, since the generating point • in N has *a gradient orientation that is different from the gradient orientation of any other generating point in this particular tiling.* In **Figure 1D**, the maximal nucleus cluster *N* is shown *in situ* in the tiling of an fMRI image.

3 Nucleus Clustering in Voronoï Tilings. A *nucleus cluster* in a Voronoï tiling is a collection of polygons that are adjacent to (share an edge with) a central Voronoï region, called the cluster nucleus. In this work, the focus is on maximal nucleus clusters, which highlight singular regions of fMRI images. A pair of Voronoï regions are considered *strongly near*, provided the regions have an edge in common (Peters and Inan, 2016; Peters, 2016). A *maximal nucleus cluster N* contains a nucleus polygon with the highest number of strongly near (adjacent) Voronoï regions (**Figures 1C-D**).

The gradient orientation angle θ of a point (picture element) in an fMRI image is found in the following way. Let *img*(x,y) be a 2D fMRI image. Then

$$G_x = \frac{\partial img}{\partial x},$$

$$G_y = \frac{\partial img}{\partial y},$$

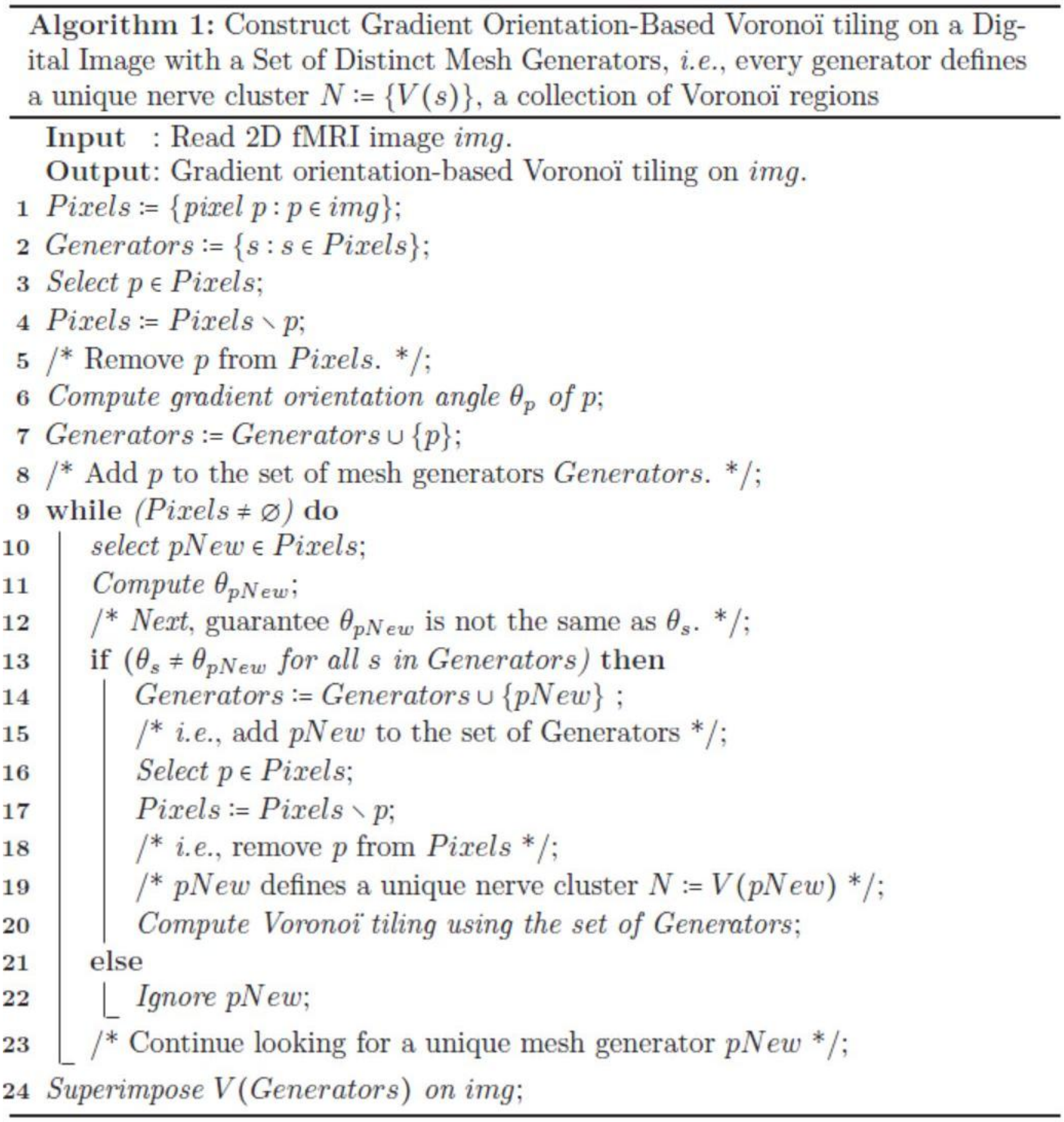
$$\theta = \tan^{-1}\left[\frac{G_x}{G_y}\right]\tan^{-1}\left[\frac{\frac{\partial img}{\partial y}}{\frac{\partial img}{\partial x}}\right] = \arctan\left[\frac{\frac{\partial img}{\partial y}}{\frac{\partial img}{\partial x}}\right].$$

In other words, the angle θ of the generating point of mesh nucleus is the arc tangent of the ratio of the partial derivatives of the image function at a particular point (x,y) in an fMRI image.

In sum, for each fMRI temporal frame from Mitra et al. (2015), we produced tessellated images with one or more maximal mesh regions (i.e., a maximal region which contains the maximal number of adjacent regions). Furthermore, we produced tessellated images showing one or more MNC. Each maximal nucleus cluster *N* contains a central Voronoï region - the nucleus - surrounded by adjacent regions, *i.e.*, Voronoï region polygons.

4 Steps to Construct a Gradient-Orientation Mesh. Here we give the steps to build Voronoï tiling, so that every generating point has gradient orientation (GO) angle θ that is different from the GO angles of each of the other points used in constructing the tiling on an fMRI image (see **Figure 2**). The focus in this form of Voronoï tiling is on guaranteeing that each nucleus of mesh cluster is derived from a unique generating point. This is accomplished by weeding out all image pixels with non-unique GO angles. The end result is a collection of Voronoï regions that highlight different structures in a tessellated fMRI image. Each Voronoï region *V*(*s*) in a GO mesh is described by feature vector that includes the GO of the generating point *s*.

Since each s is unique (not repeated in the Generators set in **Figure 2**), each nucleus mesh cluster *N* has a unique description. Taking this a step further, we identify maximal nucleus clusters on a tessellated fMRI image. In effect, each maximal *N* tells us something different about each region of a tiled fMRI image, since we include, in the description of a maximal nucleus, the number adjacent regions as well as the GO of the nucleus generating point.



```
Algorithm 1: Construct Gradient Orientation-Based Voronoï tiling on a Digital Image with a Set of Distinct Mesh Generators, i.e., every generator defines a unique nerve cluster $N := \{V(s)\}$, a collection of Voronoï regions
Input  : Read 2D fMRI image img.
Output: Gradient orientation-based Voronoï tiling on img.
$Pixels := \{pixel\ p : p \in img\}$;
$Generators := \{s : s \in Pixels\}$;
Select $p \in Pixels$;
$Pixels := Pixels \setminus p$;
/* Remove p from Pixels. */;
Compute gradient orientation angle $\theta_p$ of p;
$Generators := Generators \cup \{p\}$;
/* Add p to the set of mesh generators Generators. */;
while ($Pixels \neq \emptyset$) do
    select $pNew \in Pixels$;
    Compute $\theta_{pNew}$;
    /* Next, guarantee $\theta_{pNew}$ is not the same as $\theta_s$. */;
    if ($\theta_s \neq \theta_{pNew}$ for all s in Generators) then
        $Generators := Generators \cup \{pNew\}$ ;
        /* i.e., add pNew to the set of Generators */;
        Select $p \in Pixels$;
        $Pixels := Pixels \setminus p$;
        /* i.e., remove p from Pixels */;
        /* pNew defines a unique nerve cluster $N := V(pNew)$ */;
        Compute Voronoï tiling using the set of Generators;
    else
        Ignore pNew;
    /* Continue looking for a unique mesh generator pNew */;
Superimpose V(Generators) on img;
```

Figure 2. The steps in the method used to construct the mesh on an fMRI image shown in **Figure 1D**.

5 Rényi entropy as a Monotonic Function of Information for fMRI Nucleus Clusters.

The major new elements in the evaluation of fMRI images are nucleus clusters, maximal nucleus clusters, strongly near maximal nucleus clusters, convexity structures that occur whenever max nucleus clusters intersect (Peters and Inan, 2016). We showed in the above paragraphs that in a Voronoï tessellation of an fMRI image, of particular interest is the presence of ***maximal nucleus clusters*** (MNC), *i.e.*, clusters with the highest number of adjacent polygons. In this section, we now introduce a measure of the information that MNCs in fMRI images yield. We demonstrate that MNC reveal regions of the brain with higher levels of cortical information in comparison with non-MNC cortical regions, that uniformly yield less information.

In a series of papers, Rényi (Rènyi, 1961; Rènyi, 1966), introduced a measure of information of a set random events. Let X be a set random events such as the occurrence of polygonal areas in a Voronoï tessellation and let $\beta > 0, \beta \neq 1, p(x)$ the probability of the occurrence of x in X. Then Rényi entropy $H_\beta(X)$ is defined by

$$X = \{x_1, \cdots, x_n\},$$

$$H_\beta(X) = \frac{1}{1-\beta} \log_2 \sum_{i=1}^{n} p^\beta(x_i).$$

Because of the relationship between Rényi entropy of a set of events and the information represented by events, Rényi entropy and information are interchangeable in practical applications (Rènyi, 1982; Bromiley et al., 2010). In fact, it has been shown that Rényi entropy $H_\beta(X)$ is a monotonic function of the information associated with *X*. This means that Rényi entropy can be used as a measure of information for any order $\beta > 0$ (27).

Let X_{MNC}, X_{nonMNC} be sets of MNC polygon areas and non-MNC polygon areas in a random distribution of tessellation polygon areas. Also, let $p(x) = \frac{1}{x}, p(y) = \frac{1}{y}$ be the probability of occurrence of $x \in X_{MNC}, y \in X_{nonMNC}$. Notice that the nuclei in MNCs have the highest concentration of adjacent polygons, compared all non-MNC polygons. Based on measurements of Rényi entropy for MNC vs. non-MNC observations, we have confirmed that Rényi entropy of nucleus polygon clusters is consistently higher than the set of non-MNC polygons (**Figures 3** and **4**). This finding indicates that MNCs yield higher information than any of the polygon areas outside the MNCs.

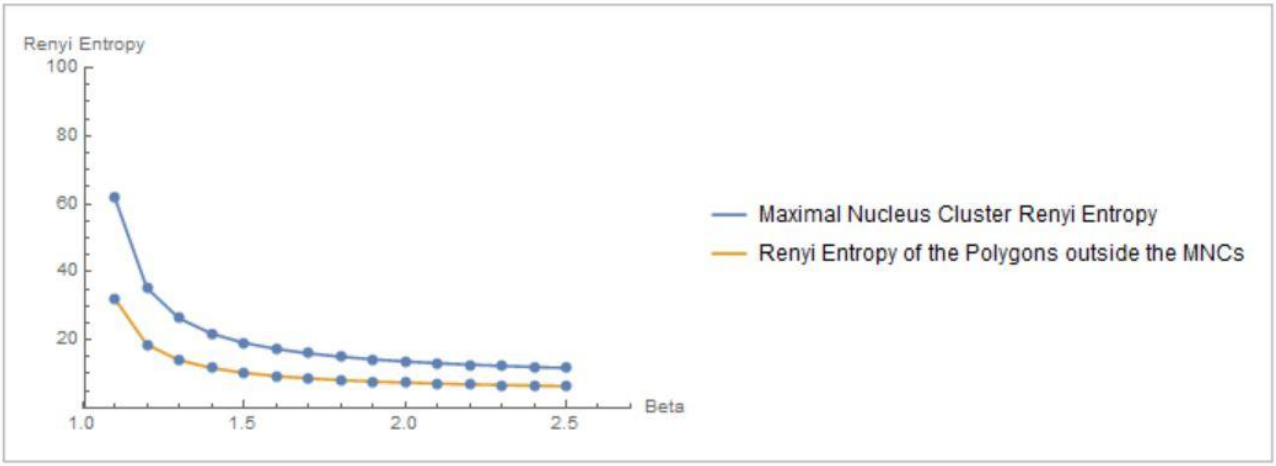


Figure 3. Rényi entropy values of maximal nucleus clusters, compared with the surrounding areas of fMRI images. The *x* axis displays the values of the Beta parameter for $1.1 \leq \beta \leq 2.5$.

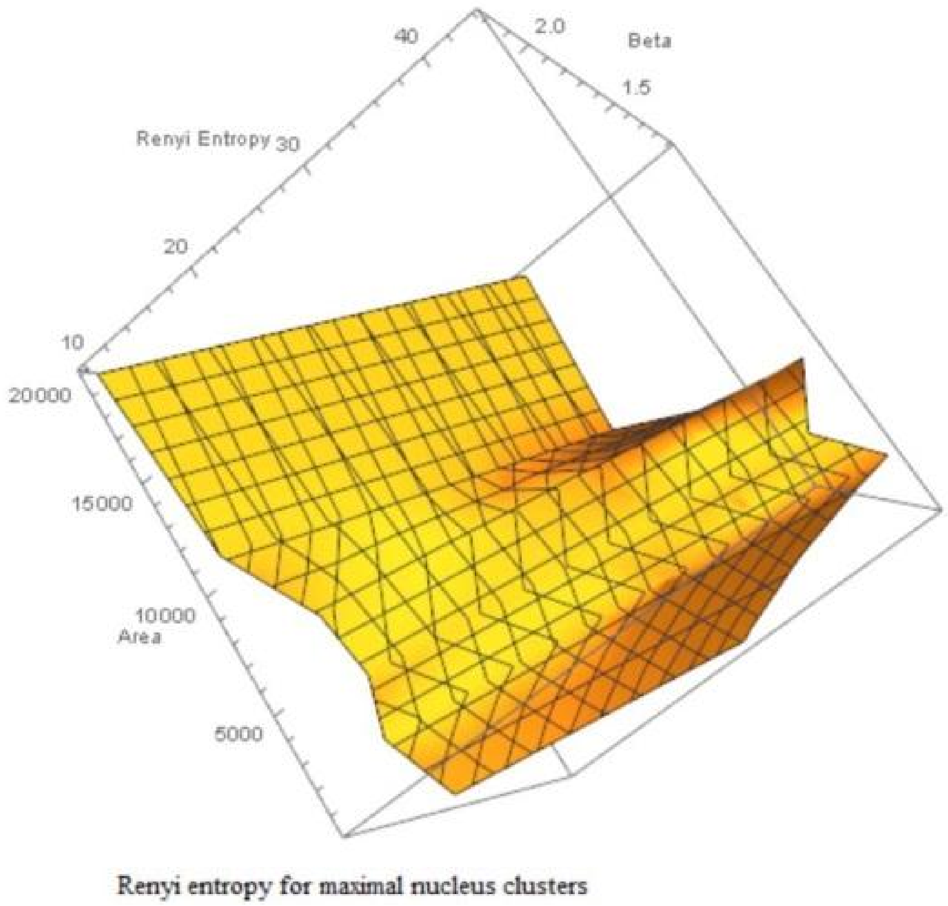


Figure 4. Rényi entropy values vs. number polygon areas vs. $1.1 \leq \beta \leq 2.5$ of maximal nucleus clusters in fMRI images. MNC Nuclei surround by polygons with smaller areas have higher Rényi entropy, which tells us that smaller MNC areas yield more cortical information than MNCs with larger areas.

In sum, Rényi entropy provides a measure of the information in maximal nucleus clusters and the surrounding zones of fMRI images. This means that the information from areas occupied by MNCs vs. non-MNC areas can be measured and compared. This also means that the maximal nucleus clusters are equipped with higher entropy values (and corresponding higher information), which contrasts with measure of information in the surronding non-MNC zones. Hence, MNCs make it possible to pinpoint the highest source of information in fMRI images.

6 Borsuk-Ulam theorem comes into play. The Borsuk-Ulam Theorem (Borsuk, 1933; Dodson and Parker, 1997) states that:

Every continuous map $f : S^n \to R^n$ *must identify a pair of antipodal points (on* S^n*).*

That is, each pair of antipodal points on an *n*-sphere maps to Euclidean space R^n (Beyer and Zardecki, 2004; Matousek, 2003). Points on S^n are *antipodal*, provided they are diametrically opposite (Weisstein, 2015; Marsaglia, 1972). For further details, see Tozzi and Peters (2016a and 2016b). The two antipodal points can be used not only for the description of simple topological points, but also for more complicated structures (Borsuk 1969), such spatial or temporal patterns functions, signals, movements, trajectories and symmetries (Saye and Sethian, 2011; Peters, 2016. If we simply evaluate CNS activity instead of "spatial signals", BUT leads naturally to the possibility of a region-based, not simply point-based, brain geometry, with many applications (Peters, 2014). We are thus allowed to describe nervous systems functions or shapes as antipodal points on a n-sphere (**Figures 3A, 3B**). It means that the activities under assessment (in this case, the 4D torus movements) can be found in the feature space derived from the descriptions (feature vectors) in a tessellated fMRI image.

If we map the two antipodal points on a n-1 –sphere, we obtain a single point. The signal shapes' functions can be compared (Weeks, 2002; Saye and Sethian, 2011): the two antipodal points representing systems features are assessed at one level of observation, while the single point is assessed at a lower level. Although BUT was originally described in terms of a natural number *n* that expresses a structure embedded in a spatial dimension, nevertheless the *n* value can stand for other types of numbers: it can be also cast as an integer, a rational or an irrational number (Tozzi and Peters, 2016b). We might regard functions or shapes as embedded in an *n*-sphere, where *n* stands for a temporal dimension instead of a spatial dimension. This makes it possible to use the *n* parameter as a versatile tool for the description of fMRI brain features (**Figure 5C**).

In sum, BUT and its variants say that:

a) There exist regional spatial fMRI patterns (shapes, functions, vectors) equipped with proximities, affine connections, homologies and symmetries.
b) We are allowed to assess the spatial patterns described by the MNC in terms of signals, temporal patterns (in our 4D case, movements and trajectories on the 3D brain), in order to achieve a real-time description of the movements of the hypersphere.

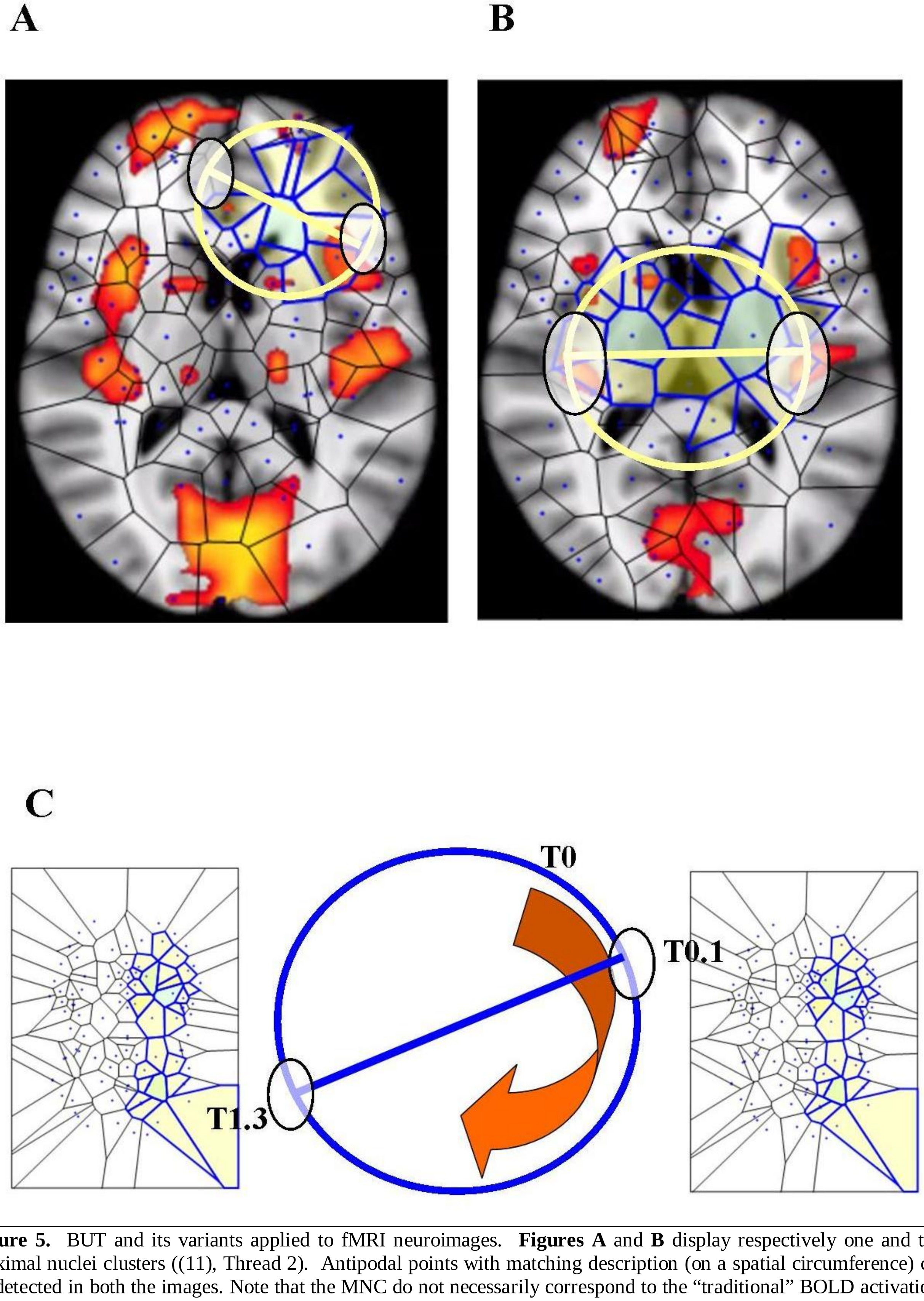


Figure 5. BUT and its variants applied to fMRI neuroimages. **Figures A** and **B** display respectively one and two maximal nuclei clusters ((11), Thread 2). Antipodal points with matching description (on a spatial circumference) can be detected in both the images. Note that the MNC do not necessarily correspond to the "traditional" BOLD activations (shown in red) detectable in fMRI neuroimaging studies. **Figure C** displays a temporal matching description between two maximal nuclei clusters at time T0.1 and T1.3 seconds. Note that, in this Figure, the n-sphere number n refers to the time, and not to a spatial dimension. The curved arrow depicts the time conventionally passing clockwise along the circumference of the n-sphere.

7 Quaternionic movements. In a previous study (Tozzia and Peters, 2016a), the presence of a hypersphere was detected invoking BUT: we viewed the antipodal points as brain signals opposite each other on a Clifford torus, *i.e.*, we identified the simultaneous activation of brain antipodal signals as a proof of a perceivable "passing through" of the fourth dimension onto the nervous 3D surface.

Here we evaluated instead, in resting-state fMRI series, a more direct hallmark of the presence of a hypersphere: the trajectory and the temporal evolution of the signals on the 2D brain surface, in order to see whether they match the predicted trajectories of the Clifford torus. To evaluate a hypersphere in terms of a framework for brain activity, we first needed to identify potential brain signal loci where quaternion rotations might take place: we thus embedded the brain in the 3D space of a Clifford torus and looked for its hallmarks or hints (**Figure 6**).

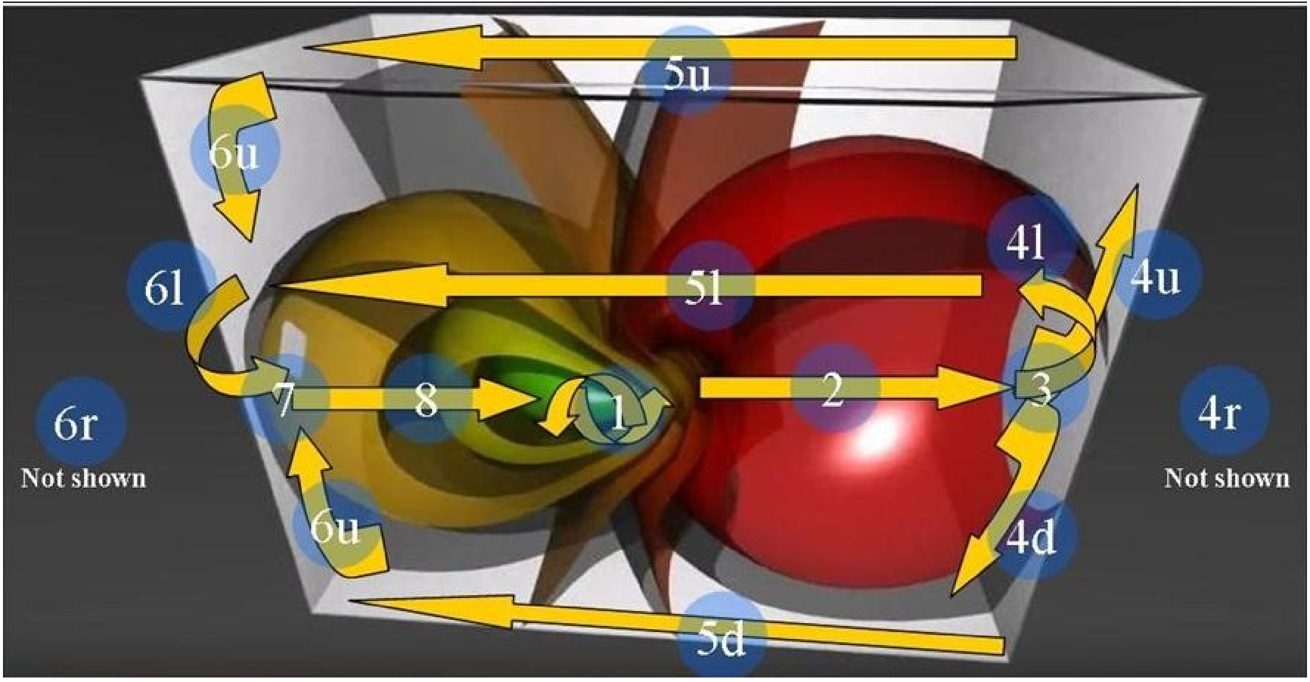


Figure 6 shows the 3D Stereographic projection of the "toroidal parallels" of a hypersphere (from https://www.youtube.com/watch?v=QlcSlTmc0Ts ; see also http://www.matematita.it/materiale/index.php?lang=en&p=cat&sc=2,745). The orange arrows illustrate the trajectories followed by the 4D quaternionic movements of a Clifford torus when projected onto the surface of the 3D space in which it is embedded. The circled numbers describe the trajectories, starting from the conventional point 1 (the letters u,d,r,l denote respectively the upper, down, right and left trajectories on the surface of the 3D paprallelepiped). Note that the arrows follow the external and medial surfaces of the 3D space in a way that is predictable. Just one of the possible directions of the quaternion movements is displayed: the flow on a Clifford torus may indeed occur in every plane. In this Figure, the spheres on the right grow in diameter, forming a circle of increasing circumference on the right surface of the 3D space. Conversely, on the opposite left side, the spheres shrink and give rise to a circle of decreasing circumference on the left surface of the 3D space.

RESULTS

We found that clusters of higher activity, which are equipped with higher Rényi entropy compared with the surrounding zones, are scattered throughout different brain areas. It means that some micro-areas of a specific anatomical zones contain more information than the adjacent ones. In other words, the MNC approach detects zones with higher Rényi entropy, compared with the surrounding ones. In various frames, more than one cluster is detectable. The image data analysis shows also that the MNC activity displays the typical features of the Clifford torus' movements, supporting the hypothesis that a functional hypersphere occurs during resting state brain activity (**Figure 7**). The temporal sequence also show the hypersphere moves on the brain, and it moves relatively slowly. At start, the trajectory follows the median sections (see timeframes 0.1-0.3 in **Figure 7**), then moves towards the posterior part of the brain, where a reflexion of four trajectories along the lateral surfaces occurs (0.4). This pattern closely matches the one predicted by the model illustrating the quaternionic movements on a Clifford torus. The hypersphere does not display a regular or continuous movement, rather it proceeds forward and then backward for a short time (time 0.5 and 0.6). From 0.7, the trajectory follows the patterns predicted by **Figure 6**.

The MNC activity follows a specular, repetitive temporal pattern of activation (**Figures 7, 8, 9**). For example, the pictures of the first and the last time have MNC activity with matching description. The MNC activity areas are different from those of BOLD activity (**Figure 9)**. The results can be summarized as follows: the movements of a hypersphere are clearly detectable, and the MNC activity clearly displays antipodal points in a temporal sequence, independent from fMRI activation.

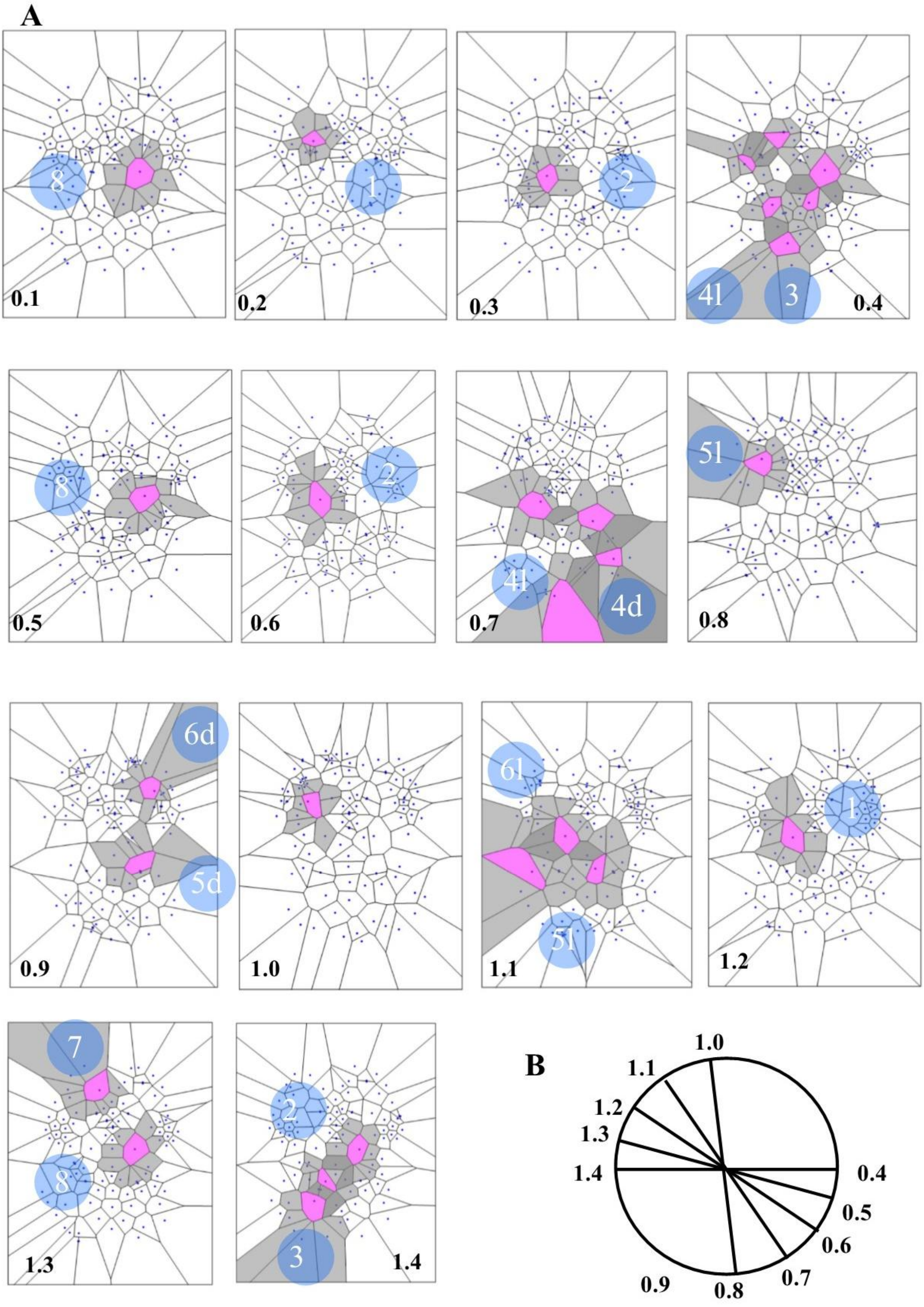


Figure 7A depicts a real pattern of maximal nuclei clusters temporal activation (from Mitra et al., 2015, Thread 4). Note that the typical trajectories of a Clifford torus are clearly displayed (see **Figure 6** for comparison). If you look at the parallelepipedal 3D projections of the 4D quaternionic movements (**Figure 6**), the MNC embedded in the 2D brain surface stand for the 4D movements INTERNAL to the parallelepiped, while the MNC lying outside of the 2D brain surface stand for the 4D movements on the SURFACE of the parallelepiped in **Figure 7B**. The movements described by maximal nucleus clusters are temporally specular. A matching description among temporal frames occurs, so that, for example, the frame 0.2 displays the same MNC features of 1.3. It means that the hypersphere moves in a stereotyped sequence and according a repetitive temporal sequence, following the trajectories predicted by the quaternionic model.

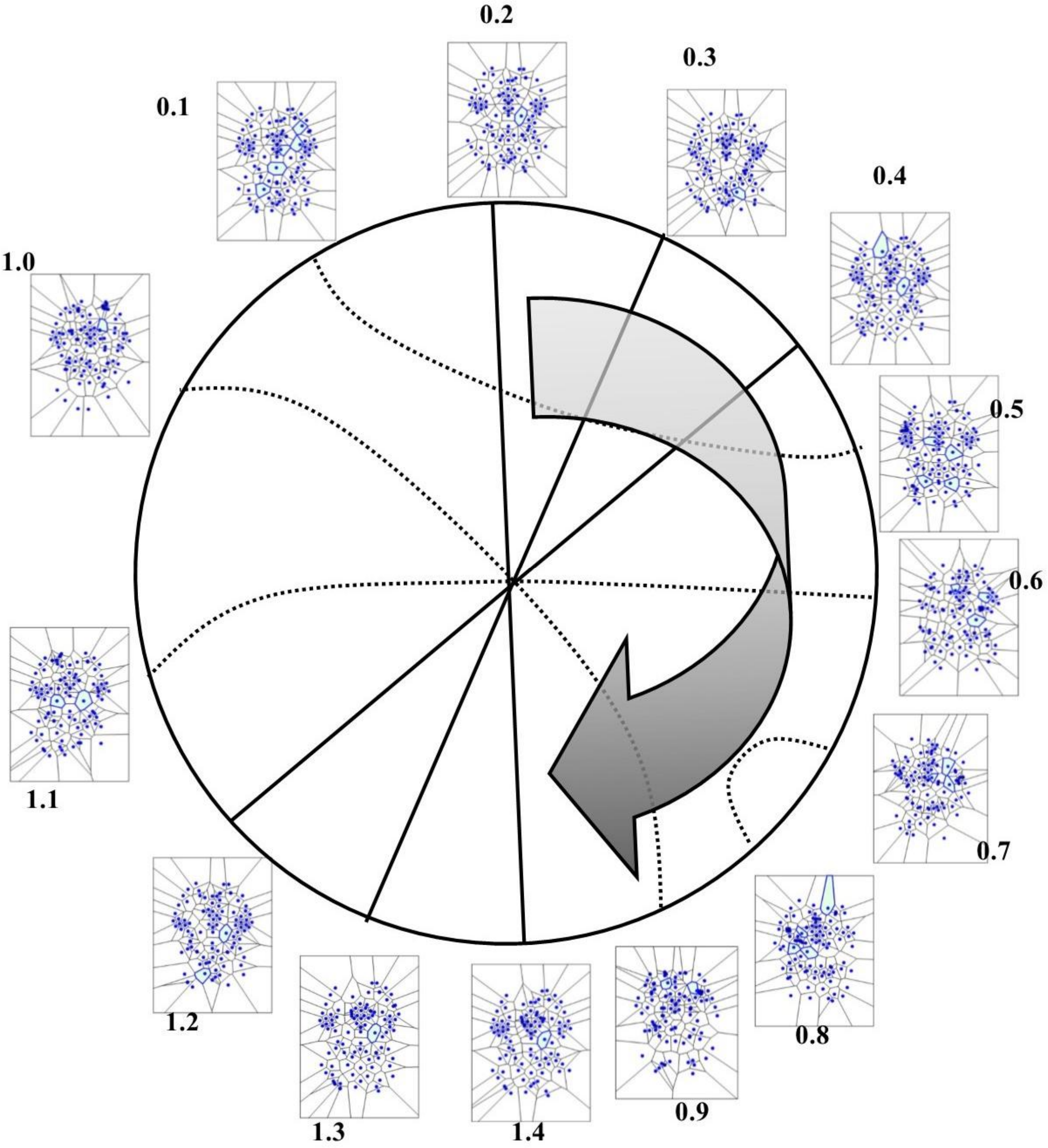


Figure 8. Temporal antipodal points (from Thread 2 frames). The straight lines connecting opposite points on the temporal circumference depict "pure" antipodal points, while the curved lines depict non-antipodal points with matching description.

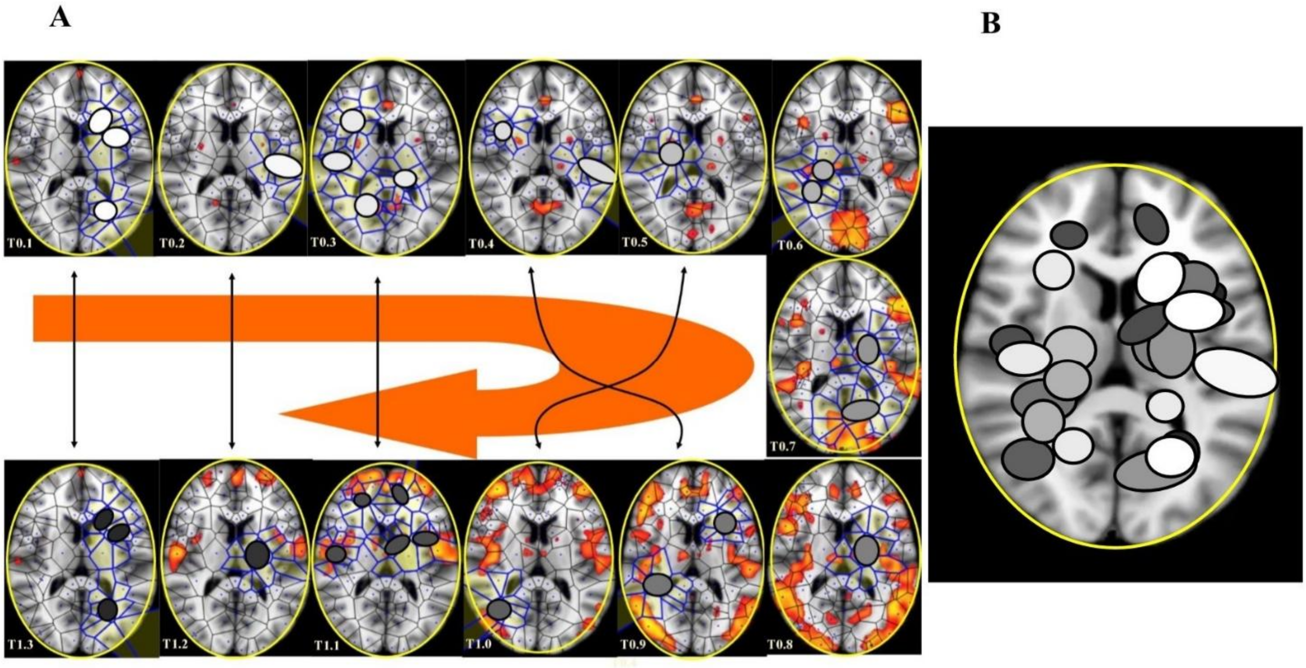


Figure 9A. This figure (from Thread 1 timeframes) illustrates another way to illustrate temporal antipodal points. The temporal sequences are displayed clockwise, from T=0.1 to T=1.3. The Voronoï regions embedded in MNC are depicted as circles. The white circles refer to the presence of mesh clusters at high activity in the initial times, the grey circles in the intermediate times and the darker circles in the later times. **Figure 9B**. MNC activity on 13 superimposed, consecutive brain images from Thread 1 (from time T0 to T13). Note that the areas of nuclei activation are scarcely superimposed to the "classical" zones of BOLD activation (shown in red).

CONCLUSIONS

There are two state-of-the-art approaches for understanding the communication among distributed brain systems using fMRI data. The first – dynamic causal modelling - uses models of effective connectivity, while the other - Granger causal modelling - uses models of functional connectivity (Friston, 2009; Friston, 2010). This paper introduces a novel method, the computational proximity, which is different: rather than being correlated with the "classical" BOLD activity, it shows how spatial regions are correlated through their "proximity". From the experiment done so far, we are beginning to see different forms of brain function represented by the MNC. We showed that computational proximity (i.e., strongly near nucleus mesh clusters) in 2D fMRI images is able to reveal hidden temporal patterns of Rényi entropy, enabling us to detect functional information from morphological data.

Here we have shown that a morphological analysis of simple 2D images taken from fMRI video frame sequences might give insights into the functional structure of neural processing. In a previous study, we evaluated the possible *hints* of a hypersphere on simple fMRI scans during resting state brain activity (Tozzi and Peters, 2016a). We showed how, due to the Borsuk-Ulam theorem (BUT), the fMRI activation of brain antipodal points could be a signature of 4D. The antipodal points predicted by BUT could be evaluated not just on images taken from fMRI studies, but also on datasets from other neurotechniques, such as, for example, EEG. In the current study we used a novel method, in order to confirm the data of the previous work with a completely different and more sophisticated approach. Indeed, looking at the sequences of maximal nucleus clusters and their entropy, we found experimental patterns compatible with the ones predicted by the hypersphere model. We detected on the 3D brain "shadows" of a 4D hypersphere rotating according to quaternion movements: these "hints" make it possible for us the possibility to visualize both the spatial arrangement and the movements of the corresponding Clifford torus. In other words, during spontaneous brain activity, the apparently scattered temporal changes in MNC follow a stereotyped trajectory which can be compared with the 4D movements of a hypersphere. Our study uncovered evidence of hypersphere during spontaneous activity, demonstrating that brain activity lies on a 3-sphere embedded in 4D space. How can be sure that the MNC reveals the presence of a brain hypersphere? Three cues talk in favor of this hypothesis. First, the MNC patterns in resting state fMRI closely resemble the theoretical trajectories predicted by Clifford torus movements. Second, temporal sequences of fMRI images display matching description, in agreement with the BUT dictates. Third, there is a difference in Rényi entropy between MNC and the surrounding zones, these data pointing towards diverse levels of activity. The reproducibility of the hypersphere movements suggests that this organizational feature is essential to normal brain function. Because the Clifford torus incessantly changes its intrinsic structure, due to the different transformations of the quaternionic group, it is reasonable to speculate that each mental state corresponds to a different hypersphere's topological space. The concept of a hypersphere in the brain is also more noteworthy, if we frame it in the general picture of nervous symmetries (Tozzi and Peters, 2016b). A shift in conceptualizations is evident in a brain theory of broken symmetries based on a hypersphere approach. It might be speculated that symmetries are hidden in a 3D dimension and restored in the higher dimension of the hypersphere, and vice versa. It means that brain functional and anatomical organization may be better assessed if one considers how certain hidden "symmetries", essential to shaping brain gradients and activity, may only appear under the lens of higher-dimensional neural representations (Tozzi and Peters, 2016b), i.e., the hypersphere. We anticipate our essay to be a starting point for further evaluation, both in physiological and pathological conditions, of a neural fourth spatial dimension where other brain functions, such as perception, memory retrieval, might take place. It is also possible that every brain function displays a peculiar temporal pattern of such a novel entropic "activity". In sum, we operationalized a novel, fairly inexpensive, image-analysis technique useful in detecting hidden temporal patterns in the brain. We can assess the spatial patterns described by MNC in terms of entropy variations. While, by our "subjective" and "private" viewpoint, we tend to watch an image inferring the semantic parts in order to give it a meaning, MNC allow the detection of the "objective", entropy, which do not necessarily correspond to the zones of the figure that we repute more significant. This means that MNC provide a basis for quantifying high-yield information areas in fMRI image features that are normally "hidden" from our attention.

Dedicated to the Memory of Som Naimpally

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MICRO AND MACRO-LEVELS OF NEURAL OBSERVATION DESCRIBE THE SAME BRAIN ACTIVITY

Brain activity can be assessed either at anatomical/functional micro-, meso- and macro- spatiotemporal scales of observation, or at intertwined levels with mutual interactions. We show, based on topological findings, that nervous activities occurring in micro-levels project to single activities at macro-levels. This means that brain functions assessed at the higher scale of the whole brain necessarily display a counterpart in the lower ones, and vice versa. Furthermore, we point out how it is possible for different functional and anatomical levels to be stitched together to become condensed brain activities, giving rise, for example, to ideas and concepts. Also, a topological approach makes it possible to assess brain functions in the general terms of particle trajectories taking place on donut-like manifolds. In physics, the term duality refers to a case where two seemingly different systems turn out to be equivalent. Our framework permits a topological duality among different neuro-techniques, because it holds for all the types of spatio-temporal brain activities, independent of their inter- and intra-level relationships, strength, magnitude and boundaries.

Many neuro-techniques have been developed throughout the years, in order to assess brain activity at different levels or dimensions of spatio-temporal observation. The rather general term “brain activity” stands here for a large repertoire of brain functions and mental faculties, such as attention and perception, emotions and cognition, memory and learning, higher cognitive processes (decision making, goal-directed choice, and so on) (Gazzaniga, 2009), mind wandering (Andrews-Hanna et al., 2014) and so on. Every technique is an observational domain of the whole neuro-scientific discipline, each one assessing an anatomical or functional scale different from the others. Some techniques assess brain activity at gross-grained levels of observation, such as EEG and lesion studies (Buszaki and Watson, 2012; Jensen et al., 2014). Others take into account a meso-level of observation, e.g., localized brain areas and sub-areas, such as diffuse tensor imaging, MEG analysis and fMRI resting state functional connectivity. Other approaches allow the assessment of more coarse-grained levels, e.g., microlumns (Opris and Casanova, 2014), or single-neuron function and structure. Further, more reductionist approaches focus on the molecular levels of brain activity: see, for example, Jacobs et al. (2007), Stankiewicz et al. (2013), Ekstrand et al. (2014), Gárate et al. (2014). The last, but not the least, other techniques favour an approach that involves more than a single functional and anatomical level, tackling the issue of brain functions in terms of non-boundary wall domains spanning over every observational dimensions and scales

(Friston, 2010; Sporns, 2013; Tozzi, 2015). Consciousness, for example, does not seem to be confined to a single level (Koch et al., 2016). This means that far apart levels must interact one each other too (Touboul, 2012).
Here we explore the possibility to assess dimensional scales as well as multilevel brain activity in terms of algebraic topology. We show, based on novel topological findings, how brain activities with matching descriptions embedded in higher anatomical or –functional levels map to single activities in lower scales. Therefore, activities encompassed in higher dimensional levels necessarily display a counterpart in the lower ones, and vice versa. This leads to a novel scenario, where different scales of brain activity are able to scatter, collide and combine, merging together in an assessable way. Our framework holds for all the types of approaches to the brain, independent of their peculiar features, resolution, magnitude and boundaries. This means that all the neuro-techniques are *dual* under topological transformation. The term *dual* refers to a situation where two seemingly different physical systems turn out to be equivalent. If two techniques or phenomena are related by a duality, it means that one can be transformed into the other, so that one phenomenon ends up looking just like the other one (Zwiebach and Barton, 2009). We also show how such duality permits brain activity assessment in the general terms of particle trajectories taking place on donut-like manifolds. Indeed, every brain model can be described in the guise of multi-dimensional tori, projecting and mapping among levels which display different spatio-temporal features.

TOPOLOGY AND BRAIN ACTIVITIES AT DIFFERENT ANATOMICAL/FUNCTIONAL LEVELS

Here we assess brain activities in terms of geometric structures. Brain physical spaces model regions, areas or shapes on the surface of abstract geometric spaces. Nervous activity are then modelled as paths followed by particles traveling through brain micro-, meso- or macro- areas, or through different levels. Lower-level brain activity can be depicted as a structure equipped with n-dimensions (e.g., a two-dimensional disk), while the higher-level one as a n+1 -dimensional structure (e.g., a three-dimensional sphere). Various continuous mappings from higher to lower dimensional structures lead to the Borsuk-Ulam theorem (BUT) (Borsuk 1933;Krantz, 2009; Tozzi and Peters, 2016a). BUT states states that a single point on a circumference maps to two antipodal points on a sphere, both characterized by the same description. Points on the sphere are *antipodal*, provided they are diametrically opposite (Weisstein, 2016). If we simply evaluate nervous activities instead of *points*, BUT leads naturally to the possibility of a region-based brain geometry. Indeed, the two opposite *points* could stand not just for the description of simple topological points (Marsaglia, 1972), but also of the signals detected by different neuro-techniques, such as spatial or temporal patterns, vectors, particle trajectories, entropies, free-energies (Peters, 2016). Therefore, we can describe brain features as antipodal points on *n*+1 –dimensional structures. Brain signals of different scales can be compared, because the two antipodal points can be assessed at higher-dimensional scales of observation (brain macro-levels), which can be pulled back to single points at lower-dimensional scales (brain micro-levels) (Tozzi and Peters, 2016b). The two points (or regions, or activities) do not need necessarily to be antipodal, in order to be described together (Peters, 2016). Indeed, BUT can be generalized also for the assessment of non-antipodal features, provided there are a pair of regions, either adjacent or far apart, with the same feature vector (Peters and Tozzi, 2016a). Even though BUT was originally described just for convex spheres, it is also possible for us to look for antipodal points on structures equipped with other shapes (Mitroi-Symeonidis, 2015; Tozzi, 2016). This means that, whether brain activity displays concave, convex or flat geometry, it does not matter, because we may always find the points with matching description predicted by BUT. Furthermore, an *n*+1 –dimensional structure might map straight to a corresponding lower-dimensional surface, instead of another *n*-dimensional structure. In other words, a brain area may map also just to itself (Weeks, 2002), so that the mapping of two antipodal points to a single point in a dimension lower becomes a projection internal to the same structure. For technical readers, see also: Dodson and Parker (1997), Matousek (2003), Crabb and Jaworowski (2013).

In the evaluation of brain activities at every spatio-temporal scale, here we assess antipodal *regions* instead of antipodal *points* (Peters and Naimpally, 2012; Lentzen, 1939; Disalle, 1995; Henderson, 1996; Di Concilio, 2013; Di Concilio and Gerla, 2006). A brain region is called a *worldsheet*, if everyone of its sub-regions contains at least one brain activity modelled as a string that describes a path followed by a moving particle. The term *worldsheet* designates a region of the brain space completely covered by nervous activities (Peters and Tozzi, 2016b) (**Figure 1**). A 2D plane worldsheet can be rolled up to form the lateral surface of a 3D cylinder, termed a *worldsheet cylinder* (Peters 2016b). Further, a worldsheet cylinder maps to a *worldsheet torus*, formed by bending the former until the ends meet. In sum, a flattened worldsheet maps to a worldsheet torus. This means that every brain activity can be described in terms of particle movements along the surface of multi-dimensional, donut-like toruses (**Figure 1**). Hence, BUT provides a way to evaluate changes of information among different anatomical and functional brain levels in a topological space, which is distinguished from purely functional or thermodynamical perspectives.
Next, consider Brouwer's fixed point theorem (FPT) (Volovikov and Yu, 2008). Su (1997) gives a nice illustration of the FPT: no matter how you continuously slosh the coffee around in a coffee cup, some point is always in the same position that it was before the sloshing began. And if you move this point out of its original position, you will eventually we move some other point in the sloshing coffee back into its original position. In BUT terms, this means

that not only we can always find a brain region containing an activity, but also that every activity comes together with another one, termed a *wired friend*. These observations lead to a *wired friend theorem*: every occurrence of a wired friend activity on the $n+1$ -dimensional structure maps to a fixed description, e.g. to another activity that belongs to an n-dimensional structure (**Figure 1**) (Peters and Tozzi, 2016b). The significance of this is that we can always find an activity, embedded in a higher-dimensional brain macro-level, which is the topological description of another activity, embedded in a lower dimensional brain micro-level. And vice versa.

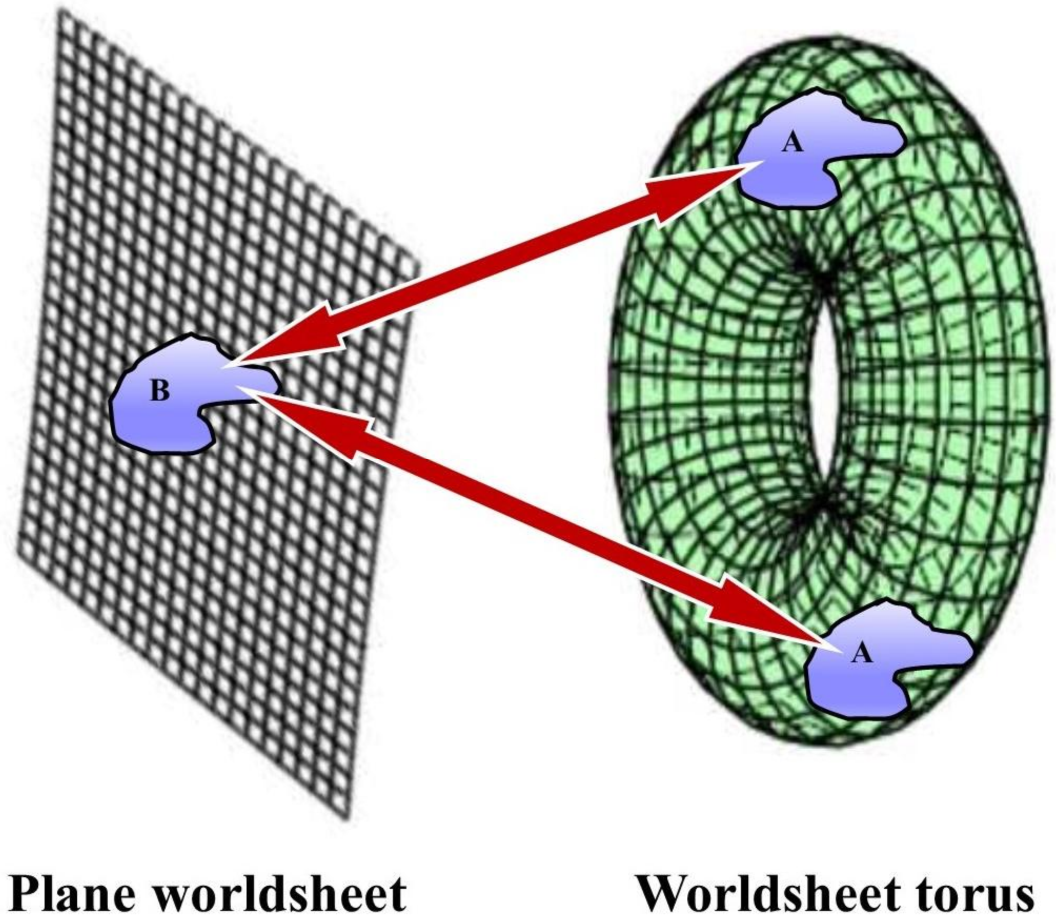

Figure 1. Samples of brain activities, illustrated in guise of geometrical shapes, are represented by the regions A and B on different structures with diverse dimensions. Regions A and B are examples of antipodal activities which lie on structures with various dimensions. See the text for further details.

THE MERGING OF BRAIN ACTIVITIES

In the previous paragraph, we showed how different brain activities, depicted in guise of geometrical shapes, necessarily have at least a feature in common. In topological terms, nervous activities/shapes are continually transforming into new homotopically equivalent nervous activities/shapes. They might influence each other by scattering, colliding and combining, to create bounded regions in the brain. Hence, it is possible for brain activities to stick together to become *condensed*, e.g., worldsheets (operationally assessable in terms of the torus described above), which are portrayed as a collection of interacting elements of geometrical shapes.

Eventually brain activity's shapes will deform into another, as a result of the collision of a pair of separate shapes. Let a brain activity be represented in **Fig. 2.A**. This brain activity evolves over time as it twists and turns through the outer reaches of another brain activity. An inkling twisting brain activity appearing in the neighbourhood of the first one is illustrated in **Fig. 2.B**. The two activities begin interacting, so that the first now has a region of space in common with the second (**Fig. 2.C**). In effect, as a result of the interaction, they are partially stitched together. The partial absorption of one brain activity in another is shown in **Fig. 2.D**. Here, a very large region of the total brain space occupied by the first activity is absorbed by the second. Therefore, we have the birth of a condensed brain activity. The two brain activities become at first concentric in **Fig. 2.E**., then a complete condensed shape is formed in Fig. **2.F**. When the two brain activities are completely transformed into a new one, we have instance of their homotopy of equivalence, with the second that has completely absorbed the first. To make an example, the idea of *cat* arises from the perception of many single cats of different size, colour, and so on. This is a further instance of the duality principle in brain theories. That is, one brain activity is the dual of another, provided the first can be deformed into the second there is no longer any difference between the cat I see and the cat I imagine.

Here we provide a short mathematical treatment for technical readers. Let $f, g : X \to Y$ be a pair of continuous maps. For example, let $f\left(X\right)$ and $g\left(X\right)$ be two localized brain activities. A *homotopy* (Cohen, 1973) between *f* and *g* is a continuous map $H : X \times [0,1] \to Y$ so that $H(x,1) = g(x)$ and $H(x,0) = f(x)$. It is possible to deform (transform) one brain activity with a particular shape into another with a different shape. It means that the birth of novel brain activities, that evolve out of the interaction of initially disjoint activities, is allowed. Let $id_X : X \to X$ denote an identity map defined by $id_X(x) = x$. Similarly, $id_Y : Y \to Y$ is defined by $id_Y(t) = y$. The composition $f \circ g(X)$ is defined by $f \circ g(X) = f\left(g(X)\right)$. Similarly, $g \circ f(X)$ is defined by $g \circ f(X) = g\left(f(X)\right)$. The sets *X* and *Y* are homotopically equivalent, provided there are continuous maps so that $g \circ f \simeq id_X(x)$ and $f \circ g \simeq id_Y(y)$. The sets *X* and *Y* are the same homotopy type, provided *X* and *Y* are homotopically equivalent (Peters and Inan, 2016; Peters and Naimpally, 2012). This leads to a comparison of brain activities, with seemingly varying shapes and sizes, that are homotopically equivalent. The brane in **Fig. 2.E** is an example of a Edelsbrunner-Harer nerve (Peters and Inan, 2016), which is a collection $Nrv\Im$ such that all nonempty subcollections of $Nrv\Im$ have a non-void common intersection, i.e.,

$$Nrv\Im = \left\{X \in \Im : \bigcap X \neq \emptyset\right\}.$$

Lemma 1. Brain activities of the same homotopy type are stitched together to form a condensed brain activity.

Proof. Let *G*, *H* be brain activities with the same homotopy type. Then brain activity *G* can be deformed into brain activity H. In effect, shape *H* absorbes *G*. By definition, brain activity *H* is a condensed brain activity. This phenomenon is true in general for homotopically equivalent brain activity that have the potential to be stitched together. To make a psychological example, the prolonged view of different cars gives rise to idea of traffic. Hence, the desired result follows.

Theorem 1. A condensed brain activity is an instance of an Edelsbrunner-Harer nerve.

Proof. From Lemma 1, a condensed brain activity is an instance of an Edelsbrunner-Harer nerve.

Theorem 2. Every brain activity is a Edelsbrunner-Harer nerve.

Proof. Let *G* be a macro-level brain activity. Every *G* is a collection of micro-level shapes, so that each of the shape has brain activity *G* in common. That is, all the micro-levels brain activities occurring in *G* have nonempty intersection. Consequently, *G* is an Edelsbrunner-Harer nerve. Hence, the desired result follows.

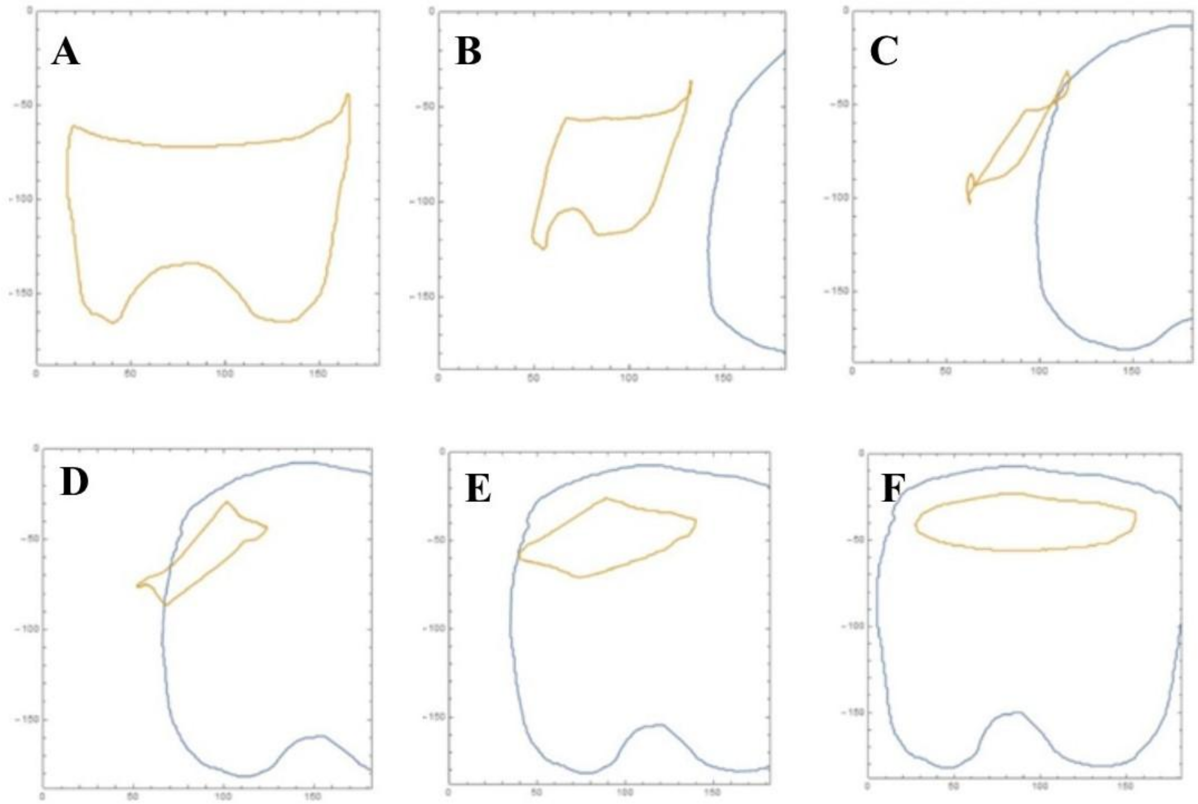

Figure 2. Homotopically equivalent shapes, standing for brain activities. **A**: a brain activity at a given spatiotemporal level. Such level could be differently coarse-grained, e.g., might stand for every micro-, meso- or macro-level. **B**: two brain activities at two different levels. **C**: interacting brain activities. **D**: dual brain activities. **E**: concentric brain activities. **F**: condensed brain activity. See the text for further details.

DISCUSSION

Neuro-techniques evaluate different types and forms of brain activity, displayed at micro-, meso-, or macro-levels of observation. Here we evaluate topological concepts that makes it possible for us to correlate the features of different neurotechniques' setups. We achieve generalizations that allow the assessment of every possible brain activity, independent on its scale, magnitude, specific features and local boundaries. Brain activities, equipped either with antipodal or non-antipodal matching description and embedded in higher-dimensional nervous structures, map to a single activity in lower-dimensional ones, and vice versa. In other words, there exists an assessable and quantifiable correspondence between micro-, meso- and macro-levels of brain activities. We could conceive brain activities that are too far apart ever to communicate with one another, so that activities bounded on distant brain regions would never have direct contact: for example, two apparently opposite brain activities such as emotions and abstraction have apparently very few in common. However, our topological investigation reveals that this scenario is unfeasible, because there must be at least one element in common also among brain activities that are very distant one each other. Brain activities will always have some element in common: they do not exist in isolation, rather they are part of a large interconnected whole, with which they interact. Whether you experience pain or pleasure, or chomp on an apple, or compute a mathematical expression, or quote a proverb, or remember your childhood, or read Wittgenstein's *Tractatus*, it does not matter: the large repertoire of your brain functions can be described in the same topological fashion. The distinction among different coarse-grained levels of nervous activity does not count anymore, because nervous function at small, medium and large scales of neural observation turn out to be topologically equivalent.

In our brain scenario, particle movements are described as functions occurring on structures displaying different possible geometric curvatures, either concave, convex or flat. Such generalization encompasses the brain models that claim for different curvatures of the brain phase space (see, for example, Sengupta et al., 2016). This means that such theories are DUAL: e.g., their topological description is the same, despite the huge difference in the subtending hypothesized curvature. It allows a useful simplification in the assessment of brain activity. Furthermore, the level of observation is not significant in the evaluation of brain activities, because such levels are fully interchangeable. Because projections between dimensions describe neural phenomena spanning from the smallest to the highest scales, the distinction among different coarse-grained scales does not count anymore, because nervous activity is topologically the same, at small, medium and large scales of observation. This means, for example, that that all the types of cognitive studies assess the same topological activity, regardless of their different protocols and procedures.

Brain theories predict the existence of long-range connexions, e.g., paths equipped with two ends lying on physical separated brain zones. An appropriate projection mapping shows that, if the two ends have matching features (e.g., the intensity, or length, or pairwise entropy), the two activities are the same. In sum, two activities with matching description, embedded in two brain zones of different levels, display the same features. Activities with matching ends (regions) in different cortical areas might also help to throw a bridge, for example, between sensation and perception. In the same guise, the relationships between the spontaneous and the evoked activity of the brain (Tozzi et al., 2016b) take now a new significance: they become just two sides of the same coin, made of topologically-bounded dynamics.

Our results also entail that every kind of high-dimensional brain activity can be described in terms of donut-like structures (Peters and Tozzi, 2016b). Lower-dimensional features can be assessed in the generic terms of particle trajectories traveling on higher-dimensional, donut-like toruses. This methodological advance, already used in limited trials (Stemmler et al., 2015) could be useful in order to achieve a unvarying operationalization of the countless theories describing brain function (Marijuan et al., 2013). In sum, the paths described by BUT and FPT variants elucidate how the tight coupling among different neural activities gives rise to brains that are in charge of receiving and interpreting signals from other cortical zones, in closely intertwined relationships at every spatio-temporal level. Therefore, topology becomes one of the central information processing strategies of the nervous system.

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A TOPOLOGICAL APPROACH UNVEILS SYSTEM INVARIANCES AND BROKEN SYMMETRIES IN THE BRAIN

Symmetries are widespread invariances underlining countless systems, including the brain. A symmetry break occurs when the symmetry is present at one level of observation, but "hidden" at another level. In such a general framework, a concept from algebraic topology, namely the Borsuk-Ulam theorem (BUT), comes into play and sheds new light on the general mechanisms of nervous symmetries. BUT tells us that we can find, on an *n*-dimensional sphere, a pair of opposite points that have same encoding on an *n*-1 sphere. This mapping makes it possible to describe both antipodal points with a single real-valued vector on a lower dimensional sphere. Here we argue that this topological approach is useful in the evaluation of hidden nervous symmetries. This means that symmetries can be found when evaluating the brain in a proper dimension, while they disappear (are hidden or broken) when we evaluate the same brain in just one dimension lower. In conclusion, we provide a topological methodology for the evaluation of the most general features of brain activity, *i.e*., the symmetries, cast in a physical/biological fashion that has the potential to be operationalized.

SIGNIFICANCE STATEMENT

We provide a theoretical/methodological framework based on simple topological concepts which make possible the evaluation of brain parameters in terms of their dimensionality, symmetries and symmetry breaking. The brain functional and anatomical organization may be better assessed if one considers how certain hidden "symmetries", essential to shaping brain gradients and activity, may only appear under the lens of higher-dimensional neural representations. We explain the computational and thermodynamical interest of such topologies and offer concrete examples of their possible applications to neuroscience. This paper emphasizes the role of a rigorous mathematical apparatusin unifying and operationalizing deep multi-disciplinary theoretical questions.

Symmetry is a type of invariance occurring when a structured object does not change under a set of transformations (Weyl). Symmetries hold the key to understanding many of nature's intimate secrets, because they are the most general feature of countless types of systems. Huge swathes of mathematics, physics and biology, including the brain, can be explained in terms of the underlying invariance of the structures under investigation. In physics, symmetries can be "broken". Symmetry breaking consists of sudden change in the set of available states: the whole phase space is partitioned into non-overlapping regions (Roldàn), so that small fluctuations acting on a system cross a critical point and decide which branch of a bifurcation is taken. In particular, in spontaneous symmetry breaking (SSB), the underlying laws are invariant under a symmetry transformation, but the system as a whole changes. SSB is a process which allows a system cast in a symmetrical state to end up in an asymmetrical one. SSB describes systems where the equations of motion or the Lagrangian obey certain invariances, but the lowest-energy solutions do not exhibit them. "Hidden" is perhaps a better term than "broken", because the symmetry is always there in such equations (Higgs). In case of finite systems with metastable states, the confinement is not strict: the system can "jump" from a region to another (Roldàn). Concerning the brain, its activity is an example of an open system, partly stochastic due to intrinsic fluctuations, but containing islands at the edge of the chaos, which maintains homoeostasis or allostasis in the face of environmental fluctuations (Friston 2010). The brain retains the characteristics of a complex, non-linear system with non-equilibrium dynamics (Fraiman et. al., 2012), equipped with random walks (Afraimovich et.al., 2013); it operates at the edge of chaos (Tognoli et.al., 2014;) and lives near a metastable state of second-order phase transition, between micro- and macro-levels (Beggs et.al., 2012), characterized by infinite correlation length, countless dimensions, slight non-ergodicity, attractors (Deco et.al., 2012) and universal power laws, testified by the presence of spontaneous neuronal avalanches (De Arcangelis).

In such a multifaceted framework, the Borsuk-Ulam theorem is useful. This theorem tells us that, if a sphere is mapped continuously into a plane set, there is at least one pair of antipodal points having the same image; that is, they are mapped in the same point of the plane (Beyer and Zardecki, 2004). Here we show that brain symmetries, hidden at a lower level, are detectable at a higher level of analysis, and vice versa. In other words, a symmetry break occurs when the symmetry is present at one level of observation, but "hidden" at another level.

This theoretical paper comprises six sections. In the first section we show how brain symmetries can be studied in a topological fashion, i.e. in terms of antipodal points on a hypersphere. If we enclose symmetries, equipped with antipodal self-similar points, into the abstract spaces of *n*-spheres, they can be evaluated in guise of projections on S^{n-1}, where they stand for the broken symmetry. Sections two-four explain how we are allowed to generalize the BUT to the study of all the types of brain symmetries. In particular, section two illustrates how the symmetries do not need to be framed just as antipodal points on spatial n-spheres, as stated by the "classical" BUT, but can be also embedded in every kind of n-spheres equipped with other types of dimensions. Section three further enlarges the possible use of BUT in the study of symmetries, by showing that they can also occur between two non-antipodal points embedded in a n-sphere. Section four is devoted to extend the concept of symmetries from systems formed by convex spheres to the concave, hyperbolic manifolds which are thought to be the natural frame of brain activity. The fifth section lists the best candidates that may represent a symmetry (and Lagrangian) to formulate a BUT theory for the nervous system. Throughout sections one-five, we provide also concrete examples of applications of symmetry and symmetry breaking in neuroscience, in order to show our theory can be operationalized in the study of brain anatomy, function and dynamics. In the final sixth section, we describe the methodological advantages of the topological approach to nervous symmetries.

1) NERVOUS SYMMETRIES AS ANTIPODAL POINTS ON AN *n*-SPHERE

The Borsuk-Ulam Theorem (BUT) is a remarkable finding by K. Borsuk (Borsuk 1933) about Euclidean n-spheres and antipodal points. It states that (Dodson 1997):

Every continuous map $f : S^n \to R^n$ *must identify a pair of antipodal points (on* S^n*).*(**Figure 1**).

The sphere S^n maps to R^n, which is a*n*-dimensional Euclidean space. Another less technical definition is: if a sphere is mapped continuously into a plane set, there is at least one pair of antipodal points having the same image; that is, they are mapped in the same point of the plane (Beyer 2004). For other definitions of BUT and its countless proofs, see (Matoušek, 2003; Peters, 2016).

The notation S^n denotes an n-sphere, which is a generalization of the circle (Weeks). An *n*-sphere is an n-dimensional structure embedded in an *n*+1 space. For example, a 1-sphere (S^1) is the one-dimensional circumference surrounding a 2-dimensional disk, while a 2-sphere (S^2) is the 2-dimensional surface of a 3-dimensional ball (a beach ball is a good example). An *n*-hypersphere (briefly, n-sphere or S^n) is formed by points which are constant distance from the origin in (*n*+1)-dimensions (Marsaglia 1972). For example, a 3-sphere (also called *glome*) of radius *r* (where r may be any positive real number) is defined as the set of points in 4D Euclidean space at distance *r* from some fixed center point **c** (which may be any point in the 4D space) (Moura 1996). A 3-sphere is a simply connected 3-dimensional manifold of constant, positive curvature, which is enclosed in a Euclidean 4-dimensional space called a 4-ball. A 3-sphere is thus the surface or boundary of a 4-dimensional ball, while a 4-dimensional ball is the interior of a 3-sphere, in the same way as a bottle of water is made of a glass surface and a liquid content.

Points on S^n are *antipodal*, provided they are diametrically opposite (Weisstein). Examples of antipodal points are the endpoints of a line segment, or the opposite points along the circumference of a circle, or the poles of a sphere. Further, every continuous function from an n-sphere S^n into Euclidean n-space R^n maps some pair of antipodal points of S^n to the same point of R^n. To make an example, if we use the mapping f : $S^3 \to R^3$, then $f(x)$ in R^3 is just a signal value (a real number associated with x in S^3) and $f(x) = f(-x)$ in R^3. Furthermore, when g: $S^2 \to R^2$, the $g(x)$ in R^2 is a vector in R^2 that describes the x embedded in S^2. In other words, a point embedded in a R^n manifold is projected to two opposite points on a S^{n+1}-sphere, and vice versa. In the next chapters we will highlight the versatility of the three main ingredients of the BUT: the antipodal points with matching description, the n-sphere and the possibility to map into a n-1 sphere.

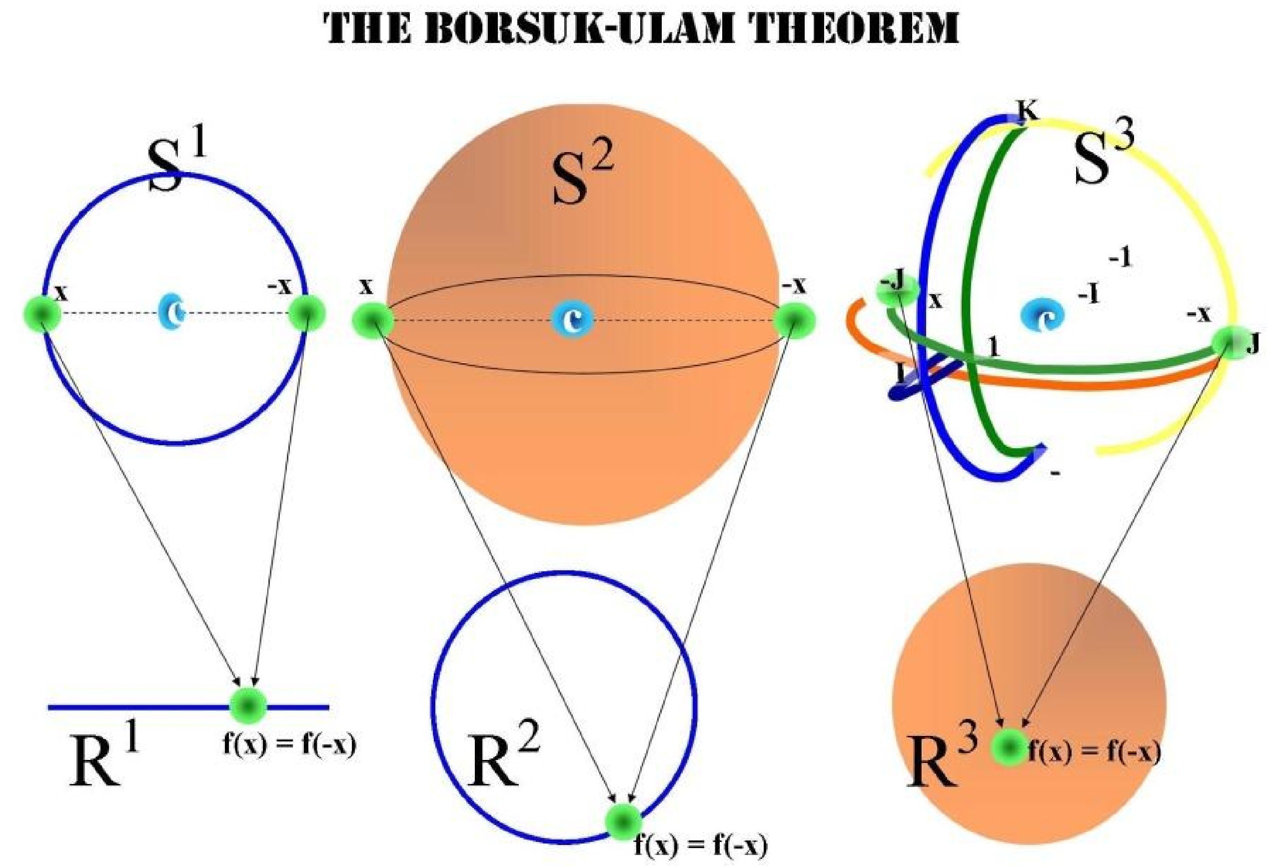

Figure 1. The Borsuk-Ulam theorem for different values of S^n. Two antipodal points in S^n project to a single point in R^n, and vice versa. Remind that every S^n is embedded in a n+1-ball, and thus every S^n is one-dimension higher than the corresponding R^n.

Description of a signal through BUT. In terms of activity, a feature vector $x \in R^n$ models the description of a signal. To elucidate the picture in the application of the BUT in signal analysis, we view the surface of a manifold as a n-sphere and the feature space for signals as finite Euclidean topological spaces. The BUT tells us that for description $f(x)$ for a signal x, we can expect to find an antipodal feature vector $f(-x)$ that describes a signal on the opposite (antipodal) side of the manifold S^n. Thus, the pair of antipodal signals have matching descriptions on S^n.

Let X denote a nonempty set of points on the surface of the manifold. A topological structure on X (called a topological space) is a structure given by a set of subsets τ of X, having the following properties:

(Str.1) Every union of sets in τ is a set in τ

(Str.2) Every finite intersection of sets in τ is a set in τ

The pair (X,τ) is called a topological space. Usually, X by itself is called a topological space, provided X has a topology τ on it. Let X, Y be topological spaces. Recall that a function or map $f : X \rightarrow Y$ on a set X to a set Y is a subset $X \times Y$ so that for each $x \in X$ there is a unique $y \in Y$ such that $(x, y) \in f$ (usually written $y = f(x)$). The mapping f is defined by a rule that tells us how to find $f(x)$. For a good introduction to mappings, see (Willard 1970).

Shapes and homotopies. A mapping $f : X \rightarrow Y$ is continuous, provided, when $A \subset Y$ is open, then the inverse $f^{-1}(A) \subset X$ is also open. For more about this, see (Krantz). In this view of continuous mappings from the signal topological space X on the manifold's surface to the signal feature space R^n, we can consider not just one signal feature vector $x \in R^n$, but also mappings from X to a set of signal feature vectors $f(X)$. This expanded view of signals has interest, since every connected set of feature vectors $f(X)$ has a shape. The significance of this is that signal shapes can be compared.

A consideration of $f(X)$ (set of signal descriptions for a region *X*) instead of $f(x)$ (description of a single signal x) leads to a region-based view of signals. This region-based view of the manifold arises naturally in terms of a comparison of shapes produced by different mappings from X (object space) to the feature space R^n. An interest in continuous mappings from object spaces to feature spaces leads into homotopy theory and the study of shapes.

Let $f, g : X \to Y$ be continuous mappings from X to Y. The continuous map $H : X \times [0,1] \to Y$ is defined by $H(x,0) = f(x),\ H(x,1) = g(x),$ for every $x \in X$.

The mapping *H* is a *homotopy*, provided there is a continuous transformation (called a deformation) from *f* to *g*. The continuous maps *f, g* are called homotopic maps, provided $f(X)$ continuously deforms into $g(X)$ (denoted by $f(X) \to g(X)$). The sets of points $f(X)$, $g(X)$ are called shapes. For more about this, see (Manetti 2015, Cohen 1973).

It was Borsuk who first associated the geometric notion of shape and homotopies. There are natural ties between Borsuk's result for antipodes and mappings called homotopies. The early work on n-spheres and antipodal points eventually led Borsuk to the study of retraction and homotopic mappings (Borsuk 1958-59, Borsuk 1969, Borsuk 1980). This leads into the geometry of shapes and shapes of space (Collins). A pair of connected planar subsets in Euclidean space R^2 have equivalent shapes, provided the planer sets have the same number of holes *(22).* For example, the letters e, O, P and numerals 6, 9 belong to the same equivalence class of single-hole shapes. In terms of signals, it means that the connected graph for $f(X)$ with, for example, an *e* shape, can be deformed into the 9 shape. This suggests yet another useful application of Borsuk's view of the transformation of a shape into another, in terms of signal analysis. Sets of signals not only will have similar descriptions, but also dynamic character. Moveover, the deformation of one signal shape into another occurs when they are descriptively near (Peters 2014).

In sum, the concept of antipodal points can be generalized to countless types of systems' signals. The two antipodal points can be indeed used not just for the description of simple topological points, but also of more complicated structures, such as shapes of space (spatial patterns), of shapes of time (temporal patterns), thermodynamical parameters, movements, trajectories, and also general symmetries (Peters 2014).

If we simply evaluate central nervous system activity instead of "signals", BUT leads naturally to the possibility of a region-based, not simply point-based, brain geometry, with many applications. A brain region can have indeed features such as area, diameter, average signal value, trajectories, and so on (Peters 2016). We are thus allowed to describe brain symmetries as antipodal points on a n- sphere. If we map the two points on a n-1 –sphere, we obtain a single point. Here the symmetry is "hidden", i.e. is not visible in dimension n-1. A spontaneous symmetry breaking occurs when a symmetry is not a property of the individual states of a system, but is a property of the mathematical structure that models the physical system. This is the case with the antipodal points on *n*-sphere that can be mapped to the same signal value. To restore the apparently broken symmetry, we need just to evaluate the single point in a dimension higher, where the two antipodal points will appear and the symmetry, "hidden" in the lower dimension, will be "refurbished". In conclusion, if we enclose brain symmetries, equipped with antipodal self-similar points, into the abstract spaces of *n*-spheres, the former can be evaluated in guise of projections on S^{n-1}. The two antipodal points standing for symmetries are assessed at one level of observation, while the single point standing for the broken symmetry are assessed at a lower level of observation.

An example: interpretation of a tessellation of an fMRI. Here we specify the nature of the observables and the mapping of signals into the feature space used for the analysis of brain activity and we show an application to available datasets to explain why our proposed approach offers an advance over the current set of tools. To do this, we include an application showing a graphical analysis of a brain fMRI (a so called "Delaunay tessellation") to better understand some aspects of brain computation and/or function viewed in the context of the predictions of the BUT.

We need at first to build a Delaunay tessellation. Each keypoint signal is chosen based on its feature values, which sharply contrast with its neighbouring signal values. The Delaunay triangulation connects with pair of nearest keypoints with a straight edge, resulting in a collection of triangles covering an image (Edelsbrunner). In its simplest form, a keypoint is chosen based on dominant color intensity and pixel gradient. That is, the gradient orientation of pixel is the angle of the tangent to the pixel. A pixel gradient dominates, provides the gradient differs sharply from its neighbours. Consider **Figure 2,** which contains tessellations of four fMRI images from Fox (2015). The triangle vertices in the four Delaunay triangulation fMRI images are dominant (keypoint) brain signals in a collection of 1-sphere surface values. The upper half of the Figure contains a Delaunay mesh in situ (**Figure 2A**) and a Delaunay mesh projected onto a 1-sphere **(Figure 2B)**. The lower half of this Figure contains the Delaunay mesh plot by itself (**Figure 2C**) and the Delaunay mesh projected onto a 2-sphere by itself (**Figure 2D**) (Frank). If we look at this keypoint-based Delaunay mesh in the **Figure 2**, we have:

1. keypoints associated with brain signals with high intensity and gradient orientation differ from those of neighbouring fMRI pixels.
2. the Delaunay mesh connects each pair of fMRI keypoint pixels nearest each other.
3. the Delaunay mesh includes connections between keypoints between the pairs of fMRI images.
4. the connections between the four fMRI images represent mappings predicted by BUT, i.e., at least one pair of fMRI keypoints map (are connected to) a keypoint on another image.
5. fMRI pixel intensity and gradient orientation of a fMRI keypoint constitute a feature vector in R^n (**Figure 2D**).

In sum, we are able to predict the occurrence of antipodal points on different fMRI images, by knowing just the activated points on one of them. In effect, this means that we can know in advance which brain areas are activated at the same time. Novel patterns of simultaneous (or sequential) activities of different (smaller or bigger) brain zones could be discovered and transferred to a lower dimension R^n manifold.

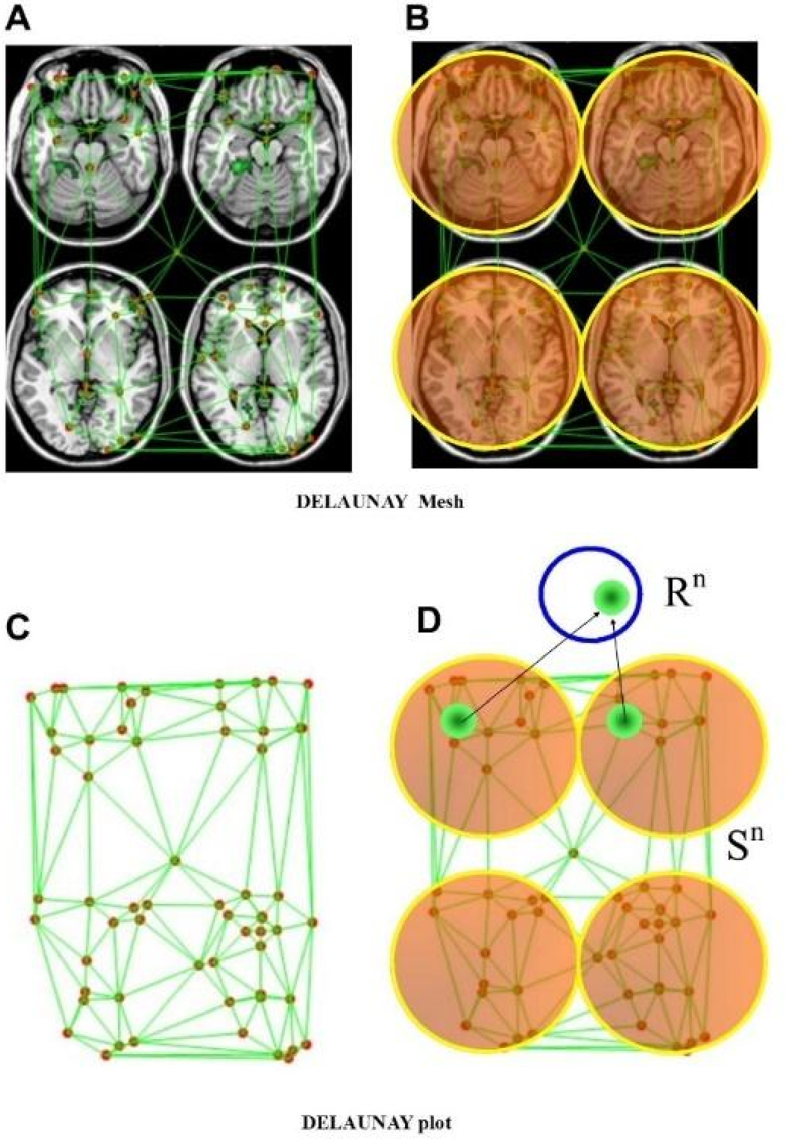

Figure 2. Meta-analytic activations associated with mind-wandering and related spontaneous thought processes throughout the entire brain. Horizontal slices presented with 3 mm skip (modified from Fox 2015). The right Figures (**A** and **C**) depict Delaunay tessellation, while the left Figures (**B** and **D**) depict the same images embedded in S^n spheres, according to the BUT dictates. See text for further details.

2) SYMMETRIES CAN BE EMBEDDED IN DIFFERENT KINDS OF n-SPHERES

The BUT can be generalized to all the types of brain symmetries. Although BUT has been originally described just in case of n being a natural number which expresses a spatial dimension, nevertheless the value of n in the brain S^n can also stand for a fractional or an irrational number. The n exponent does not need necessarily either to be a natural number or embedded in a spatial dimension. We are allowed to modify the BUT's the exponent on an n-sphere, and to change a natural number into a rational or irrational one, in order to describe n in a brain symmetric system equipped with two antipodal points. We are allowed indeed, if we take into account a BUT on d-spheres with Hausdorff dimension d, which is a fraction between 0 and 1 and is an expression of the fractal dimension.

We used the following terminology:

1) **Metric space**: Let X be a metric space with the metric $\mu_d(X)$ defined on it. This means that $\mu_d(X) \geq 0$ and μ_d has the usual symmetry and triangle inequality properties for all subsets of X.
2) **Hausdorff measure**: Let d be either 0 or a positive real number in R_0^+. The Hausdorff measure $\mu_d(\mathrm{X})$ equals a real number for each number d in $X = R^d$.
3) **Hausdorff dimension (informal)**: The threshold value of d denoted by $\dim_H(\mathrm{X})$ is the Hausdorff dimension of X, provided $\mu_d(X) = 0$, if $d > \dim_H(X)$, and $\mu_d(X) = \infty$, if $d < \dim_H(X)$.

Lemma. Schleicher Boundedness Lemma. Let d be any real number in R_0^+ and let Y be a metric space. If $X \subset Y$, then:

$\dim_H (X) \leq \dim_H (Y)$.

Proof. Immediate from the definition of the Hausdorff dimension of a nonempty set.

Assume that X is a nonempty subset (inner sphere) of an n-sphere and having the same center as S^n with the Hausdorff measure $\mu_d(X)$ defined on it and assume that $\mu_d(X)$ satisfies the Schleicher Lemma conditions. The inner sphere S^d of an n-sphere S^n can be any sub-sphere in S^n, including S^n itself. Then, the inner sphere S^d has dimension $d = \dim_H (X)$, $d \leq n$. In addition, assume that R^d is a d-dimensional space which is a subset of the n-dimensional Euclidean space R^n, $d<n$. This gives us new form of the BUT (Borsuk 1933).

Theorem. Hausdorff-Borsuk-Ulam Theorem. Let S^d with Hausdoff dimension d be an inner sphere of an n-sphere and let $f : S^d \rightarrow R^d$ be a continuous map. There exists a pair of antipodal points on S^d that are mapped to the same point in R^d.

Proof. A direct proof of this theorem is symmetric with the proof of the Borsuk-Ulam Theorem is given by Su (1997), since we assume that S^d is an inner sphere of S^n symmetric about the center of S^n and, from the Schleicher Boundedness Lemma, $\dim_H (S^d) \leq \dim_H (S^n)$.

In summary, the Borsuk-Ulam theorem can be used not only for the description of "spatial" dimensions equipped with natural numbers, but also for the description of antipodal points on brain d-spheres equipped with (fractal) Hausdorff dimension d. The same mechanism also stands for other kinds of n-spheres'dimensions other than fractals. It allows us to use the n parameter as a versatile tool for the description of central nervous system's symmetries. The n exponent of S^n can be casted as an integer, a rational (the above mentioned case of self-similarity and fractal dimensions: see also paragraph 5), or an irrational number (in case we want to evaluate nonlinear, chaotic brain as embedded in a Feigenbaum constant's dimension: see the example 2 below) (Smith). The n exponent could stand for completely different parameters: for example, we might regard brain circadian rhythms as embedded in a sphere in which n stands for the time, and not for a spatial dimension. In such a vein, we may also regard the temporal symmetries in EEG as antipodal points characterized by similarities in time occurrence, and not in shape.

Example 1: from stimuli to brain responses. The brain, in a topological framework, might stand for a system formed by two variables connected in a way such that when one changes, the other changes. The initial state occurs before the variation, the final state afterwards (**Figure 3**). The changes can be either real or merely possible. The final state depends on two settings: the initial state of the system and the external factors acting on the system. Note that in this case, in touch with dictates of the BUT variant, the system is formed by n-spheres equipped with time-, and not spatial-dimensions.

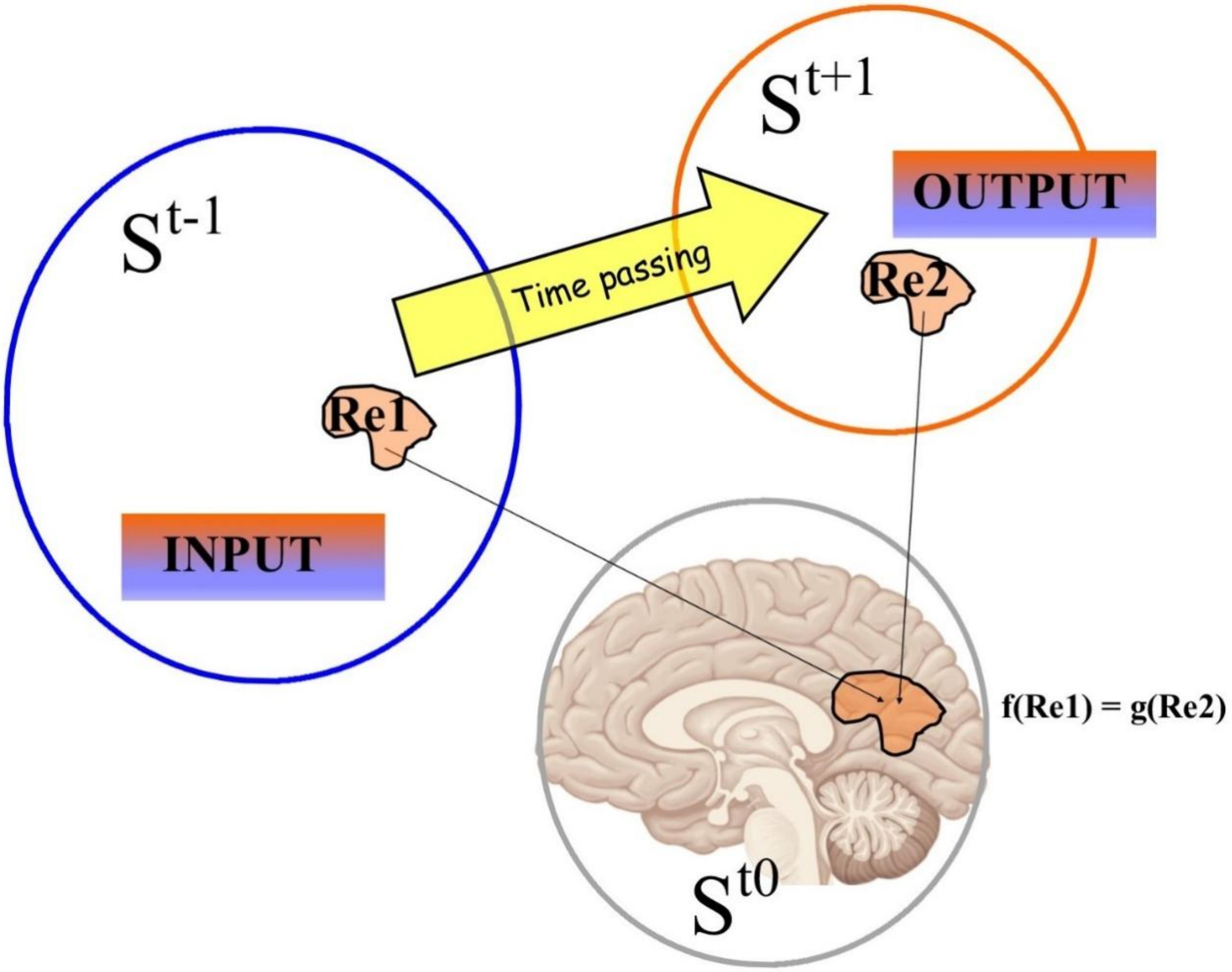

Figure 3. A system formed by n- spheres in which n stands for a time dimension. The antipodal points Re1 and Re2 are located respectively onto a sphere equipped with a dimension of time T-1 (the past) and with a dimension of time T+1 (the future). The brain, equipped with time T0, stands for the present.

Example 2: phase transitions and nonlinear dynamics in the brain. The brain is believed to be open system which maintains a non-equilibrium steady-state (i.e., homoeostasis or allostasis) in the face of continuous environmental fluctuations (Friston; Van de Ville). It displays complex, non-linear dynamical features and is equipped with a large number of interacting and inter-dependent components, with random walks (Perkins), circular causality (Fraiman), and self-organized criticality (Bak). The brain is also said to operate at the edge of chaos (a regime charachterized by dependence from initial conditions, positive Lyapunov exponents and attractors) and tends to live near a metastable state of second order phase transition (Afrahimovich; de Arcangelis). Sequential, hierarchical self-organization on an increasing scale leads to passage beyond reversibility in space as well as in time, and to the emergence of novel features and properties at each level (Beggs; Taylor). In this complex framework, the BUT variant is able to elucidate (at least some) of the dynamics underlying the nonlinear brain. We need at first to introduce, the “logistic map”, which is a one-dimensional nonlinear difference equation widely used to study equations in the field of dynamic systems theory. To make an example, take into account the coupled equations (Richardson):

$$X_{(t+1)} = r_1 x_{(t)} \left(1 - x_{1(t)}\right) + \alpha r_2 x_{2(t)} \frac{\left(1 - x_{2(t)}\right)}{1+\alpha},$$

$$X_{2(t+1)} = r_2 x_{2(t)} \left(1 - x_{2(t)}\right) + \alpha_1 r_1 x_{1(t)} \frac{\left(1 - x_{2(t)}\right)}{1+\alpha},$$

where *x* is a generic variable representing some observable behavior, *r* is a fixed behavioral parameter (the phase parameter) and *t* equals time from step 0 to step n. A logistic map may be simply plotted and visualized on a one-parameter bifurcation diagram, as a function of the scaled parameter *r* (**Figure 4A**). At the edge of criticality, a so called "Hopf bifurcation" occurs. In general, every chaotic system that corresponds to a one-dimensional map with a single quadratic maximum will bifurcate at the same rate (Alligood): the limiting ratio of each bifurcation interval to the next between every period doubling is 4.6692.... This value is called the first universal "Feigenbaum constant" (Smith): note that that such constant is a transcendental number (Jordan).

Through our BUT variant, we achieve a *n*-sphere with a *n* exponent corresponding to the Feigenbaum number. The next step is to locate the n-sphere on the above mentioned logistic map, in order to embed the topological antipodal points into the bifurcation diagram (**Figure 4A**). Once achieved two antipodal points for every bifurcation, we are allowed to map them in the concentric layers of another *n*-sphere (**Figure 4B**). We obtain a novel topological n-sphere which summarizes the whole behaviour of a nonlinear system in phase transition, such as the brain. Note that the center of the sphere stands for a completely linear system, while, when we move along the circumference towards the sphere surface, we achieve antipodal points representing a progressively more chaotic system. In such a vein, the knowledge of just the single central point and the first Feigenbaum constant leads to predictions about the temporal development of the phenomena occurring into the brain at the edge of chaos.

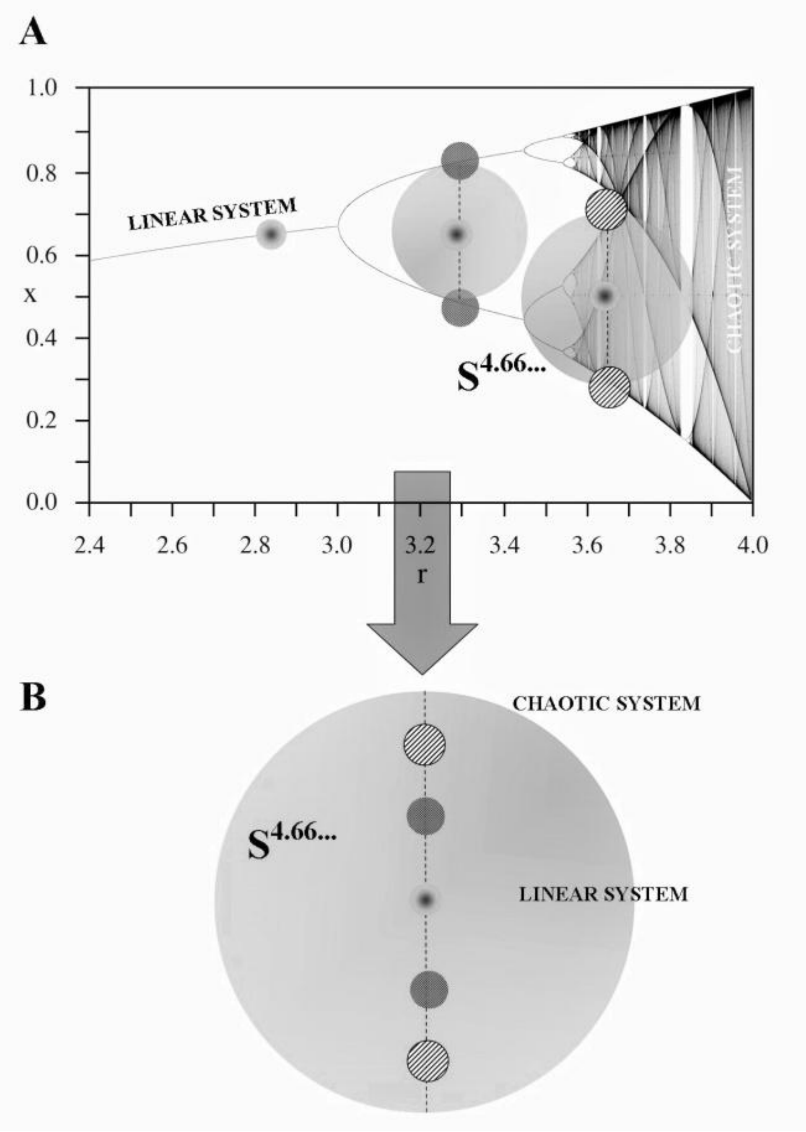

Figure 4A. Bifurcation diagram of a logistic map's nonlinear dynamical equation. The axis x displays the phase parameter. At the first Hopf bifurcation, the exponent n of the n-sphere corresponds to the first Feigenbaum constant. The same operation can be repeated at each of the following bifurcations: just the first and the second ones are displayed in Figure. Each sphere is equipped with two antipodal points which intersect the curves of the corresponding bifurcation and which display the same value on the axis x.

Figure 4B. The antipodal points described in Figure A are projected onto a single sphere, which stands for the Figure A's spheres cast in a concentric way, so that the center is the same for all of them.

3) SYMMETRIES DO NOT NEED TO BE ANTIPODAL POINTS ON *n*-SPHERES

The applications of BUT can be generalized not just for the evaluation of brain symmetries as antipodal points on a *n*-sphere, but also of non-antipodal points. Indeed, a theorem derived from BUT, called the Re-BUT (Region based version of BUT), sounds as follows:

Let 2^{Sn} be a family of regions on an n-sphere. A region can have features such as area, diameter, average signal value, and so on.

Theorem (Re-BUT). Iff : $2^{Sn} \rightarrow R^n$ is a continuous function, then f(Re1) = f(Re2) for a pair of regions Re1, Re2 on 2^{Sn}. (Peters, 2016).

Proof. Given Re1 in 2^{Sn}, we that know that there many possible regions Re2 with matching feature values. The value of f(Re1) is a feature value of region Re1. From the fact that there is at least one other region Re2 descriptively the same as Re1 in 2^{Sn}, we have f(Re1) = f(Re2).

Example. Let f(Re1) equal the area of Re1 on an n-sphere. Since there are many regions of an *n*-sphere with area the same as Re1, let Re2 be one of those regions. Then f(Re1) = f(Re2). (**Figure 5**)

This means the antipodal points restriction from the "classical" BUT is no longer needed. We can also consider homotopic brain regions on an *n*-sphere that are either adjacent or far apart. And ReBUT applies, provided there are a pair of regions on *n*-sphere with the same feature values. We are thus allowed to say that the two points do not need necessarily to be antipodal, in order to be described together. This makes it possible, for example, to evaluate matching signals from neuroimaging techniques, even if they are not "opposite", but "near" one each other.

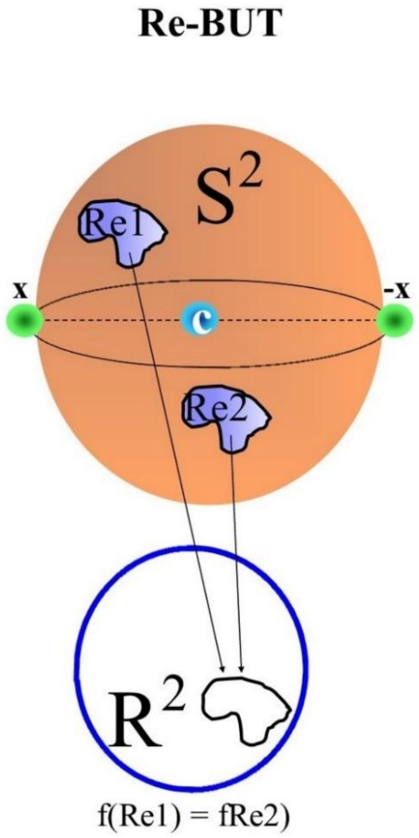

Figure 5. *A simplified sketch of the RE-BUT. The functions with matching description do not need necessarily to be antipodal. Thus, two signals, if equipped with a signal matching, may be embedded in every zone of the n-sphere.*

An example based on multisensory integration: hierarchical structures of the brain. The re-BUT nicely applies to multisensory integration (Klemen): two environmental stimuli from different sensory modalities display similar features, when mapped into cortical neurons. To make an example, an observer stands in front of the surrounding environment (**Figure 6**). A guitar player is embedded in the environment. The observer perceives, through his different sense organs such as ears and eyes, the sounds and the movements produced by the player. The guitar player stands for an object embedded in a three dimensional sphere. The two different sensory modalities produced by the player (sounds and movements) stand for non-antipodal points on the sphere's circumference. Even if objects belonging to different regions can either be different or similar, depending on the objects features (Peters, 2016), however the two non-antipodal points must share the same features. In our case, both sounds and movements come from the same object embedded in the sphere, i.e. the guitar player. The two non-antipodal points project to a n-1-dimensional layer, the brain cortex - where multisensory neurons lie - and converge into a single multimodal signal. According to the dictates of the Re-BUT, such a single point contains a "melted" messages from the two modalities, which takes into account the features of both.

The sequential processing of information is thought to be hierarchical, such that the initial, low-level inputs are transformed into representations and integration emerges at multiple processing cortical stages (Werner; Van den Heuvel). Such processes of progressive message convergence could be fruitfully studied in terms of symmetries and antipodal points which converge towards a single manifold (**Figure 6**). The observable brain anatomy would reside in the n-dimensional space (antipodal points are not glued), but, if we apply the BUT, we could hypothesize that there exists, at a certain level of abstraction, a functional space in which these homotopic regions are "mapped" as one single point/region, which could, for instance, make transparent the resilient redundancy of the homotopic regions at the relevant level of processing.

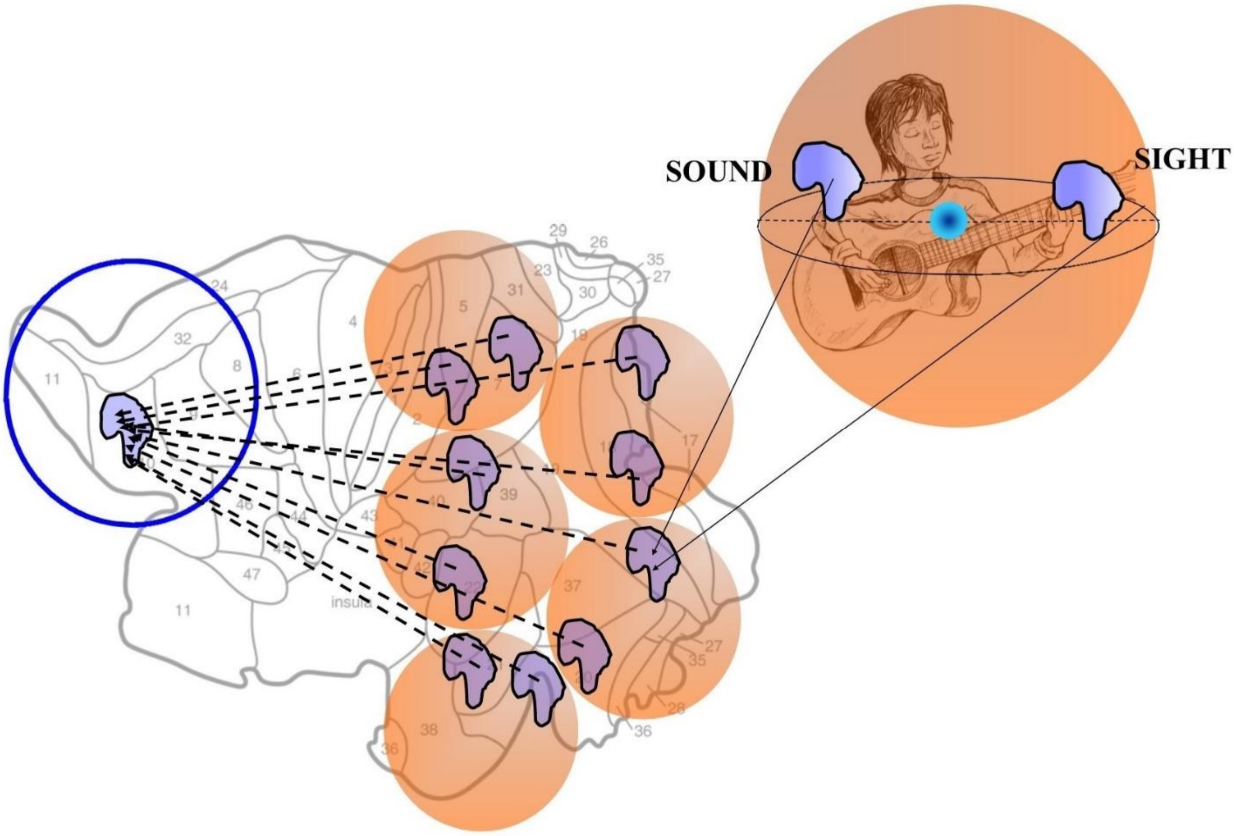

***Figure 6**. Convergence of n-spheres' antipodal points with the same matching description. Cerebral hemispheres were unfolded and flattened into a two-dimensional reconstruction by computerized procedures (Van Essen, 2005). The final, pure abstractions achieved in the frontal lobes encompass countless different matching points from different, closely packed, n-spheres coming from the sensory areas. The ideas (abstractions) link together antipodal points embedded in different n-spheres. Their projections to the "higher" areas give rise to the abstract concepts. See the main text for further details.*

4) GENERALIZATION OF BORSUK-ULAM THEOREM TO SYMMETRIES OCCURRING ON HYPERBOLIC MANIFOLDS

The original formulation of the BUT describes the presence of antipodal points on spatial manifolds in every dimension, provided the n-sphere is a convex, positive-curvature manifold. However, many symmetry breakings described in physics and biology (and, in particular, in the brain!) occur on manifolds equipped with another type of geometry: the hyperbolic one. The latter encloses complete Riemannian *n*-manifolds of constant sectional curvature -1 and concave shape. The models of hyperbolic space (i.e., the Klein model) share the same geometry, in the sense that any of them can be related to others by a transformation that preserves the geometrical properties of the space, including isometry, though not with respect to the metric of a Euclidean embedding. From differential geometric treatments of probability measures, it is easy to see that brain manifolds traced out by sufficient statistics of a probability measure are negative-curved in nature (Watanabe), and therefore endowed with a hyperbolic geometry. Hyperbolic manifolds allow the study of energy gradients in brain energetic landscapes, because they describe the descent to the lower energetic basins. For example, the proteins' final folded conformation is dictated by the minimum frustration principle on long timescales: proteins' energy decreases more than expected by thermodynamical claims, as they assume conformations progressively more like the native state (Bryngelson; Sutto; Fla). Now the question is whether the antipodal points predicted by BUT can be detected not also on positive-curvature manifolds as stated by Borsuk, but also on manifolds equipped with negative curvature. In other words, is possible to transport the BUT's antipodal points onto riemannian manifolds with NEGATIVE curvature? The answer is positive, if we perform a parallel transport of the two antipodal points of S^n onto the hyperbolic manifold (Hairer 2004; Mitroi-Symeonidis 2015). There are different routes one can take to achieve the goal. We need to resort to one of the following generic transport procedures: Ehresmann connection (Ehresmann, 1950), Levi-Civita connection (Boothby 1986), Laplace-Beltrami operator (Jost 2002). Also, we can retain a first-order approximation and formulate descent directions that are orthogonal to the previous descent ones, through numerical analysis with the conjugate gradient-descent algorithm (Snyman 2005). Routinely used in optimization, conjugate gradient descent methods have been used in neuroimaging for gradient descent on manifolds traced out by energy functions (Sengupta 2014b). After a connection has been performed and the vectors corresponding to the antipodal points have been achieved on the hyperbolic manifold M^n, the standard projection method (Hairer 2004) allows us to use the Riemann exponential map $\exp(\omega)$ to map the vector from $S^n \rightarrow M^n$, and the logaritmic map $\log(\omega)$ for the opposite mapping $M^n \rightarrow S^n$. Once achieved the center of the hyperbolic manifold M^n through the "ham-sandwich" theorem, we are allowed to map the two antipodal points from S^n to M^n, and vice versa (Peters 2016).

In summary, the BUT can be generalized also to symmetries occurring on concave manifolds. We are thus allowed to look for antipodal points and hidden symmetries also on structures equipped with a negative curvature, as it occurs for the most of brain symmetries and nervous energy landscapes.

5) LOOKING FOR SYMMETRIES IN BRAIN

The search for symmetry in central nervous system is not an easy task: due to our lack of knowledge of the brain function, we do not know exactly what (and where) the hidden symmetries are. Furthermore, it is unrealistic to think to obtain in biology the mathematical accuracy of a physics experiment, i.e., while a physical experiment isolates the object of study and excludes the surrounding confounding features, a biological trial must take into account countless hidden variables. As a matter of fact, recent studies suggest that cognitive functions do not depend solely on electrical pulses, but also on intra- and extra-neuronal causes, involving supramolecular interactions among biologically active macromolecules (Tozzi 2015). Thus, the overwhelming complexity of the factors involved is beyond our current computational comprehension. It is also important to warn that descriptions cannot unambiguously characterize the etiology of fluctuation assets, as similar symmetric properties may stem from qualitatively different generators that may be difficult to distinguish with our finite amount of data (Papo).

Power laws. It has been demonstrated that the frequency spectrum of cerebral activity exhibits a scale-invariant behavior $S(f)= 1/f^n$, where **S(f)** is the power spectrum, **f** is the frequency and n is the power spectral density, the so-called "dimension" of the fractal (that equals the negative slope of the line in a log power versus log frequency scatter plot) (Milstein; Pritchard). Interestingly, the brain generates fluctuations with complex scaling properties even in the absence of exogenous perturbations or changes in parameters controlling its activity (Papo) and the scale-invariant behavior involves not only the cortical electric activity, but also spontaneous neurotransmitter release (Fox). Indeed, studies suggest that a universal scaling is a spatio-temporal property of the brain, characterizing a large class of cerebral models and physiological signal (De Arcangelis 2006). The emergence of power law distributions has been interpreted in terms of self-organized criticality (Lubeck), a successful framework that refers to a mechanism of slow energy accumulation and fast energy redistribution, driving the system toward a critical state (De Arcangelis 2010). Analyzing the scaling properties, it has been proposed that cognitive processes can be framed in terms of complex generic properties of brain activity at rest and, ultimately, of functional equations, limiting distributions, symmetries, and possibly universality classes characterizing them (Sengupta 2014). Power law distributions contain information on how large-scale physiological and pathological outcomes arise from the interactions of many small-scale processes (Jirsa). The above mentioned fractal dimension gives rise to a dimension greater than the "classical" one-dimension which is generally attributed to the "normal" curves embedded in a standard Euclidean space (Mandelbrot). More importantly, the fractal dimension encourages us to have another look at the mechanisms which give rise to the brain's power law distributions. As stated above, the BUT variants can be used for the description of antipodal points on d-spheres equipped with Hausdorff (fractal) dimension d. It is thus suitable to make use of a rational numbers, instead of integer ones, as n exponents in S^n. The mechanism of a slope corresponding both to the α exponent and the n-dimension is valid both for "spatial" fractals (**Figure 7A**) and for "temporal" power laws' plot (**Figure 7B**).

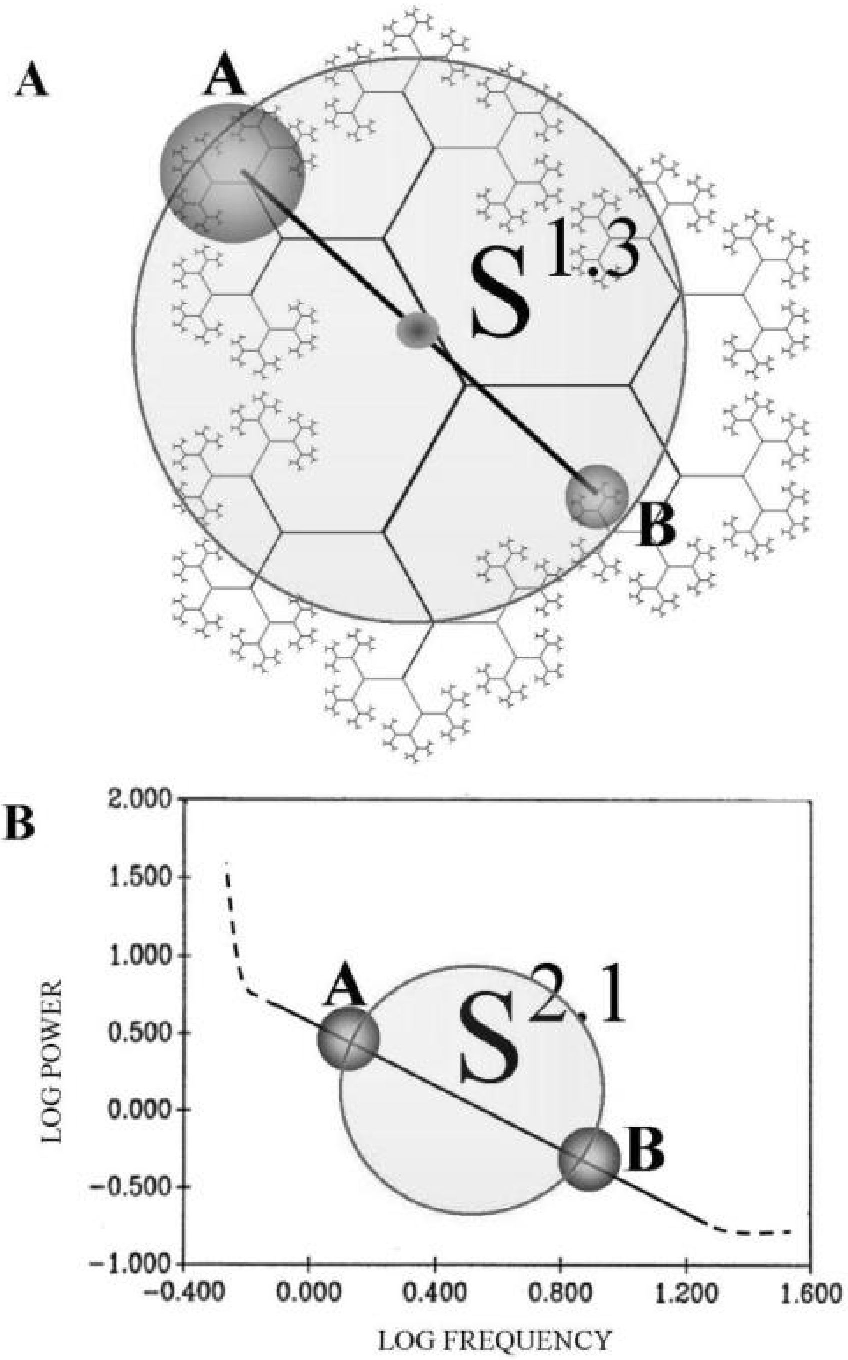

Figure 7. Antipodal points on self-similar structures.

Figure 7A. Spatial fractals embedded in a n-sphere equipped with n corresponding to a rational number (in this case, 1.3). The black circles A and B depict fractals at lower and higher magnification, respectively. They have matching description.

Figure 7B. The plot displays log power versus log frequency of an electric wave, along with the regression line (modified from Pritchard 1992). The regression line's slope (in this case, $\alpha = 2.1$) is the linear alignment of the data points reflecting the dominant power law. The plot displays an example of the "temporal" variant of scale-free behavior (the so called power laws), in the framework of the BUT: if we take into account a system with, i.e., a fractal dimension D = 2.1, we may regard the spatial $1/f^{\alpha}$ structure (equipped with antipodal points A and B) as embedded in a sphere $S^{2.1}$ which is equipped with a value of n corresponding to the fractal dimension α. Note that the BUT is not valid at the slope's tails, where the α exponent is lost (dotted lines on the right and left of the main slope).

Equalizing excitation–inhibition ratios across cortical neurons. Another symmetry has been recently found in the CNS. An unexpected degree of order has been revealed in the spatial distribution of synaptic strengths. It is a mechanism by which the neurons equalize the strengths of excitation (E) and inhibition (I) and the brain maintains its internal balance, not only in time, but also in space (Xue). Specifically, there is a constant E/I ratio between the total amount of excitatory and inhibitory stimulation (Sengupta 2013; Sengupta 2014). E/I ratio is stable, both in vitro andin the intact and spontaneously active cerebral cortex, not only for individual pyramidal neurons at a given time (Haider), but also across multiple cortical neurons (Xue) and during neural avalanches (Lombardi). Excitation and inhibition are always matched: an optimal E/I ratio across neurons is maintained, despite fluctuating cortical activity levels, through the appropriate strengthening or weakening of inhibitory synapses, carried out by an increased recruitment ofparvalbumin-expressing inhibitory neurons (Xue). The relationship between the two opposing forces in the mammalian cerebral cortex affects many cortical functions, such as feature selectivity and gain (Sengupta 2013a), or memory of past activity (Lombardi). It may allow for rapid transitions between relatively stable network states (Sengupta 2013b), permitting the modulation of neuronal responsiveness in a behaviourally relevant manner. E/I ratio could be interpreted as the evidence of a homeostatic mechanism between strengthening and weakening processes in the adaptation of real synapses, both at the single neuron level and at the network excitability level. Homeostatic systems induce a distinction between inhibitory and excitatory connections that could contribute to symmetry breaking, leading to directed coupling and information transfer (Tognoli). E/I ratio could be thus regarded as the symmetry of the intact and spontaneously active cerebral cortex.

A matter of energy? An issue of central importance in this context is the recently proposed free-energy principle for adaptive systems, which tries to provide a unified account of action, perception and learning (Friston 2010). Any self-organizing system at equilibrium with its environment must minimize its (variational) free energy, thus resisting a natural tendency to disorder/entropy. The bayesian probability of sensory states (interoceptive and exteroceptive) must have low entropy and, because entropy is also the average self-information or "surprise", the brain must avoid surprises. The feasibility of a calculation based on entropy has been demonstrated useful for the basic understanding of neural function (Friston 2008). The variational free-energy principle separates the environment (the external states) from the agent (the internal states) (Friston 2013). Agents can suppress free energy (or surprise) by changing the two things that it depends on: either they can change sensory input by acting on the world, or modify their internal states via different perceptions (Sengupta 2013b). **Figure 8** elucidates the process of perception in Bayesian and topological terms. The brain uses Bayesian beliefs in order to evaluate if a matching description takes place. If it occurs, we achieve the "known" (i.e., "I see a cat"). When the description is instead not matching, a Kullback-Leibler divergence takes place and we attain the "unknown" (i.e., "I'm not sure whether I'm seeing a cat, or a lynx"). There are two possible ways to compensate and achieve once again the "known": either the R^n sphere moves, say, to the right (change in mental priors) or it moves to the left (body movements, in search of the expected signals in the environment). Variations can thus be removed either through peripheral action (practical behavior) or through brain action (theoretical behavior).

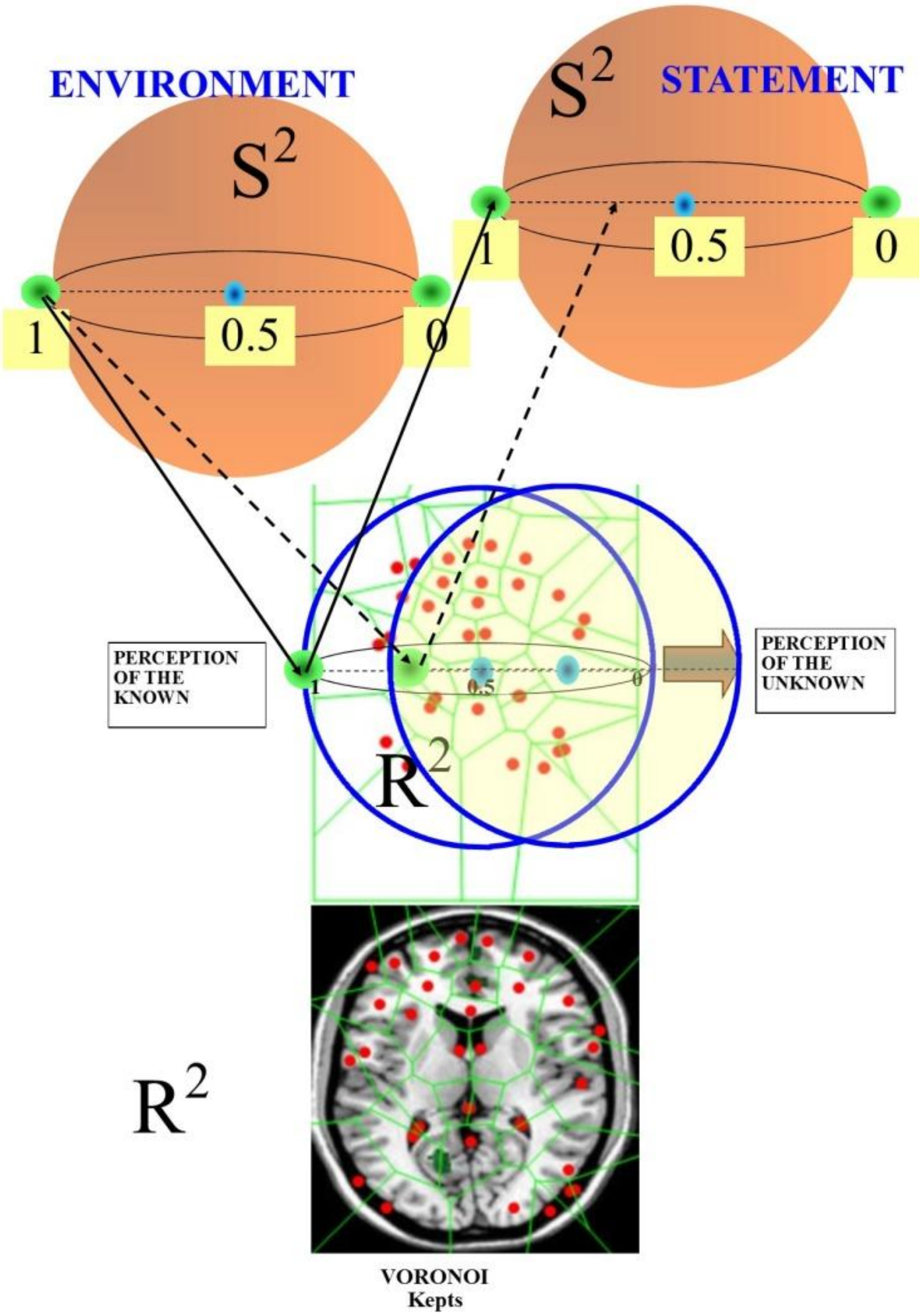

FIGURE 8. The "oscillating" R^n manifold. The inputs (the environment) and outputs (in this case, the statement correlated with the environmental input) are located onto two spatial n-spheres, each one equipped with antipodal points corresponding to 1 (ON state) and 0 (OFF state) and with a center corresponding to 0.5 (fuzzy, uncertain state). The two antipodal points map to a point located on the diameter of a Euclidean manifold R^n which, in this case, stands for groups of neurons equipped with logic gates (prepared through another type of tessellation, the Voronoi's). An input 1 is projected to R^n and then maps, for the Re-BUT theorem, to the output n-sphere in position 1. However, when the output (say 0.3) is different from the input (say 1), it means that the R^n sphere has moved horizontally and its center has moved. In this case, the input 1 does not map anymore to 1 on R^n, but to 0.3, so that R^n projects to the output 0.3, even if the input is 1. If the input and the output are known (respectively 1 and 0.3), we can calculate the change occurring in the R^n projection. In order to compare the two different projections on R^n, we just need to know how much the center of the R^n sphere has moved. We can thus predict, given a known input, which cortical areas was activated when the output

has changed: we just need to look at the R^n tessellation and to see where the novel position of the point (corresponding to an activated zone) is located.

In touch with the “ancient” Richard Avenarius (Avenarius) and Ernst Mach (Mach), the relation of the “I” (the corporeal presence of the human being) to the environment (the spatial presence of the object) is determined in such a way that both are present as common and inseparable elements. The “I” is found to be present just as much as the environment. This interconnection and inseparability of the “I” and its surrounding constitutes an essential association and homogeneity of the two coordinated values, setting in motion a circular process, from any point within which the whole complex of changes may start. In sum, the ideal point of rest, about which the life of the organism moves in constant oscillations, has also a logical-mathematical significance when framed as a topological theory.
The viability of the CNS is influenced by a balance between the metabolic cost incurred (in terms of ATP) by its operation and the information theoretic benefits realized by energy expenditure (Sengupta 2014). The metabolic activity of the brain is remarkably constant over time (Raichle 2002) and the energy budget (that is the energy use by various neuronal processes) has been calculated (Sengupta 2010). Minimizing variational free energy necessarily entails a metabolically efficient encoding that is consistent with the principles of minimum redundancy and maximum information transfer (Sengupta 2013b). Maximizing mutual information and minimizing metabolic costs are two sides of the same coin: by decomposing variational free energy into accuracy and complexity, one can derive the principle of maximum mutual information as a special case of maximizing accuracy, while minimizing complexity translates into minimizing metabolic costs. Despite an apparent resistance to the natural tendency to increase entropy, nonequilibrium steady-state is maintained (Sengupta 2014). To solve this problem, one uses a (bayesian) information theoretic construct, called the “variational free energy”, that is a proxy for entropy: minimising entropy production corresponds to the principle of minimising “variational free energy” at each point in time. The variational free energy may be considered a sort of symmetry for systems that attain nonequilibrium steady-state: accordingly, we can treat it exactly as a Lagrangian and, implicitly, as a way of minimizing entropy. Thus, the variational free energy is the Lagrangian, which is the expression of the underlying brain symmetry.

Quantum mind theories. Thus far, “symmetrical” theories of CNS have been proposed in the framework of quantum mind theories (Freeman). Some of these models resemble lattice gauge theory of high-energy physics, whilst others are quantum systems not in the sense that they constitute of quantum components (like any physical system), but that their macroscopic properties cannot be explained without recourse to an underlying quantum dynamics. Since it is not possible to test these hypotheses due to our lack of knowledge of the quantum effects in the brain, we will not go through these theories, but will briefly summarise the most interesting concepts. Many models are based on the notion of spontaneous breakdown of symmetry (Freeman). The dynamical symmetry that gets broken is the rotational symmetry of the electric dipole vibrational field of the water molecules and other biomolecules present in the brain structures. The external input or stimulus acts on the brain as a trigger for the breakdown of the dipole rotational symmetry. When the system is not in the least energy state, mathematical consistency requires the existence of massless particles, the Nambu-Goldstone quanta, that are normally observed in solid state physics. It has been hypothesized that long-range correlations established by the coherent condensation of bosons may have a role in memory storage, learning and consciousness (Matsui).

6) CONCLUSIONS: WHAT FOR?

We provided a general topological mechanism which explains the phenomenon of broken symmetries in brain. The model is casted in an experimental fashion which has the potential of being operationalized. The question here is: what for? What does a topologic reformulation add in the evaluation of brain hidden symmetries? First of all, it must be emphasized that the symmetries are widespread at every level of organization and may be regarded as the most general feature of systems, perhaps more general than free-energy and entropy constraints too. Indeed, recent data suggest that thermodynamic requirements have close relationships with symmetries. The novel, interesting observation that entropy production is strictly correlated with symmetry breaking in quasistatic processes paves the way to use system invariances for the estimation of the brain metastable states’ free-energy and the energy requirements of neural computations and information processing (Roldán 2014). Thus, giving insights into symmetries provides a very general approach to every kind of brain function and dynamics. A shift in conceptualizations is evident in a brain theory of broken symmetries based on a BUT approach: the symmetries, in this framework, are hidden in a dimension and restored in a dimension higher, and vice versa. To make an example, beyond the critical value, the “death” of complexity occurs and the system falls into a supercritical regime or regularity (Zare). In such a vein, the fractal dimension characterizing the low-frequency spikes of the spontaneous brain activity is lost, when high-frequency spikes are activated by sensations and perceptions (Buszaki; Allegrini).

Further, the invaluable opportunity to treat the brain elusive phenomena as topological structures allows us to describe symmetries in the language of powerful analytical tools, such as combinatorics, hereditary set systems (Matoušek), simplicial complexes, homology theory, functional analysis. Also generalizations of the BUT, such as, for example, the Grassmann manifolds (Dol'nikov 1992) and the Bourgin-Yang-type theorems (Yang 1954) could be fruitfully used in the study of nervous hidden symmetries. Embracing the BUT approach to symmetries means that the "real" brain activities can be described as paths or trajectories on "abstract" structures (called topological manifolds). This takes us into the powerful realm of algebraic topology, where the abstract metric space (a projection of the environment's real geometric space) constitutes sufficient statistics. Moreover, attempts are being made to provide a systematic way to characterize symmetries in the network structures of the connectome – by inspecting the eigenvalues of different types of connectivity matrices (Esposito).

We would like to bring to an end with a "semantic" consideration: the terms "symmetry" and "symmetry breaking" might appear somewhat arbitrary, because it could be argued that the n^{-1} space is more symmetrical than the n-dimensional space it maps (in terms of group theory/theoretical physics), since the antipodal gluing does not lead to opposite infinities/limits, but only to a circular "continuum" which erases a discontinuity. We want to anticipate such possible hermeneutical confusion in some of the readership, by emphasizing that our use of "symmetries" displays the invaluable advantage not only to treat the characteristic occurrence in cortical dynamics of complex fluctuations as a physical object (Tononi), but also to classify measurable cognitive functions as operators acting on symmetries (Papo). By changing physical space into the dialectics "symmetry/topology", paradoxes of nervous activity are more easily exposed: the BUT language opens up a virtual window onto spaces beyond our brain's physical three-dimensional structure.

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FROM ABSTRACT TOPOLOGY TO REAL THERMODYNAMIC BRAIN ACTIVITY

Recent approaches to brain phase spaces reinforce the foremost role of symmetries and energy requirements in the assessment of nervous activity. Changes in thermodynamic parameters and dimensions occur in the brain during symmetry breakings and transitions from one functional state to another. Based on topological results and string-like trajectories into nervous energy landscapes, we provide a novel method for the evaluation of energetic features and constraints in different brain functional activities. We show how abstract approaches, namely the Borsuk-Ulam theorem and its variants, display real, energetic physical counterparts. When topology meets the physics of the brain, we arrive at a general model of neuronal activity, in terms of multidimensional manifolds and computational geometry, that has the potential to be operationalized.

The brain is a complex, non-linear system operating at the edge of chaos, formed by inter-dependent components which exhibit spontaneous self-organization and emergent properties (Tognoli and Kelso, 2013; Fraiman and Chialvo, 2012; Zare and Grigolini, 2013). In such a vein, the brain is equipped with phase spaces where particle movements take place (Watanabe et al., 2013; Yan et al., 2013). Such trajectories may display different paths. It has been suggested that the brain is equipped with funnel-like locations in phase space where trajectories converge as time progresses, following the shortest path (Tozzi et al., 2016a; Sengupta et al., 2016). Others proposed that brain function does not exhibit erratic brain dynamics nor attractors, but a stable sequence, the so-called transient heteroclinic channel (Afraimovich et al., 2013) and that a multidimensional functional torus might be displayed during spontaneous brain activity (Tozzi and Peters, 2016a). Furthermore, crucial concepts like communication-through-coherence (Deco and Jirsa, 2012) and *plasma-like* collisionless collective movements (Touboul 2012) must be taken into account. In sum, different functional regimes occurring in the brain phase space have been described, both in central nervous systems and in artificial neural networks, and they have been correlated with different brain functions (Tozzi et al., 2016a).

Despite the large number of possible trajectories, the processes governing brain paths may be unified when we take just into account energetic requirements and constraints. Indeed, the second law of thermodynamics states that e*very process occurring in nature proceeds in the sense in which the sum of the entropies of all bodies taking part in the process is increased* (Planck's formulation). This paper aims to evaluate brain energetic constraints in the framework of algebraic topology, namely the Borsuk-Ulam theorem (BUT) (Borsuk 1933). We will take into account also another important topological ingredient, e.g., the symmetries, widespread at every level of nervous organization. Symmetries may be regarded as the most general feature of biological systems (including the brain), perhaps more general also than energetic requirements, so that giving insights into them might provide a general approach to nervous activities (Tozzi and Peters, 2016b). Here we show how BUT and its variants provide powerful insights into brain functioning, especially if we assess the noteworthy relationships between symmetry breaks, changes of neural dimensions, thermodynamic free-energy and informational entropy.

ABSTRACT TOPOLOGY COMES INTO PLAY

The *standard* version of the Borsuk-Ulam theorem (BUT). BUT states that (Dodson 1997):

Every continuous map $f: S^n \to R^n$ *must identify a pair of antipodal points (on* S^n*).*

In other words, if a sphere S^n is mapped continuously into a *n*-dimensional Euclidean space R^n, there is at least one pair of antipodal points on S^n which map onto the same point of R^n. For further details, see Tozzi and Peters (2016a).

Examples of antipodal points are the opposite points along the poles of a sphere (Matousek, 2003). The notation S^n denotes an n-sphere of convex curvature, which is embedded in a *n*+1 euclidean space (Weeks, 2002; Marsaglia, 1972). BUT variants provide a topological methodology for the evaluation of the most general features of brain activity, cast in an empirical fashion that has the potential to be operationalized. This is a quantitative way to give a physical meaning to the otherwise *abstract* concept of BUT. Many BUT variants, useful for the evaluation of brain functions, have been recently described (Tozzi and Peters, 2016b; Peters and Tozzi, 2016a).

Systems' symmetry breaking (Sym-BUT): changes in brain dimensions. Symmetries are invariances underlining physical and biological systems (Weyl, 1982). A symmetry break occurs when the symmetry is present at one level of observation, but "hidden" at another level (Roldàn et al., 2014). BUT tells us that we can find, on an *n*-dimensional sphere, a pair of opposite points that have the same encoding on an *n*-1 sphere. This means that symmetries can be found when evaluating the system in a proper dimension, while they disappear (are hidden or broken) when we assess the same system in just one dimension lower (Tozzi and Peters, 2016b).

There are two different ways to define and assess brain dimensions. Indeed, the term *dimension* may reflect either functional relationships of brain activities, or anatomical connections between cortical areas. The first approach takes into account the dimensionality of the neural space. Connectivity and complex network analyses of neural signals allow the assessment of the complex dynamics of brain activity, providing a novel insight into the multidimensionality of various neural functions' representations (Kida et al., 2016). From a dynamical system perspective, one would expect that brain activities are represented as, for example, some scalar quantity measured at different brain locations (say N locations) at different points in time. Then one could describe nervous dynamics as trajectories and/or manifolds in a N-dimensional phase space (Lech et al., 2016). Mazzucato et al (2016) demonstrated that stimuli reduce the dimensionality of cortical activity. Clustered networks, such as default mode network, have instead a larger dimensionality, because the latter grows with ensemble size: the more neurons are recruited, the more the dimensions (Mazzucato et al, 2016). Apart from giving insights in neural dynamics in the *canonical* three dimensions (space, time, and frequency), complex network analyses are also able to evaluate other functional dimensions, e.g. categories of neuronal indices such activity magnitude, connectivity, network properties and so on (Kida et al., 2016). It must be taken into account that dimension reduction and symmetry breaking display close relationships, so that symmetries are correlated with changes in functional dimensions in the brain. Indeed, a key feature of dynamical approaches is that the dynamics they predict are characterized by nonequilibrium phase transitions, and therefore breaks of symmetries (Scholz et al., 1987). Many studies emphasized how different levels of behavioral dynamics' organization take place in neural ensembles. To make some examples, Jirsa et al. (1998), focusing on the cortical left-right symmetry, derived a bimodal description of the brain activity that is connected to behavioral dynamics, while Jirsa et al. (1994) demonstrated that, when an acoustic stimulus frequency is changed systematically, a spontaneous transition in coordination occurs at a critical frequency, in both motor behavior and brain signals.

Concerning the second approach to brain dimensionality, it has been recently suggested that brain trajectories, at least during spontaneous activity, might display four spatial dimensions, instead of three (Tozzi and Peters 2016a). Brain symmetric states display dimensions higher than asymmetric ones, so that, in this case, the space of interest does not refer to dynamical neural spaces, but to detectable physical cortical locations. In such a vein, Stemmler et al. (2015) proposed that animals can navigate by reading out a simple population vector of grid cell activity across multiple spatial scales. Combining population vectors at different microscopic dimensions predicts indeed neural and behavioral correlates of multiscale grid cell readout, that transcend the known link between entorhinal grid cells and hippocampal place cells. While the spatial activity of a single grid cell does not constitute a metric, an ensemble of hierarchically organized grid cells does provide instead a distance measure (Stemmler et al., 2015). In our paper, the mapping of trajectories from high dimensional manifold to lower dimensions refers to both the above described definitions of dimensionality.

In sum, the study of changes in brain dimensions is a promising novel methodology. We need to take into account that, despite neural networks modelling complex systems are known to exhibit rich, lower-order connectivity patterns at the level of individual nodes and edges, however higher-order organization remains largely unknown. Benson et al. (2016) recently developed an algorithmic framework for studying how complex networks are organized by higher-order connectivity patterns, revealing unexpected hubs and geographical elements. In such a vein, Kleinberg et al. (2016) demonstrated that real networks are not just random combinations of single networks, but are instead organized in specific ways dictated by hidden geometric correlation between layers. Such correlations allowed the detection of multidimensional communities, e.g., sets of nodes that are simultaneously similar in multiple layers. Crucial for our topological arguments, such multidimensionality also enables accurate trans-layer link prediction, meaning that connections in one layer can be predicted by observing the hidden geometric space of another layer. For example, when the geometric correlations are sufficiently strong, a multidimensional framework outperforms navigation in the single layers, allowing efficient targeted navigation simply by using local multilayer knowledge (Kleineberg et al., 2016).

General BUT (Gen-BUT). Here we provide also a generalized version of BUT, which allows a topological study of the brain in the context of physics. Gen-BUT states that:

Multiple sets of objects with matching descriptions in a d-dimensional manifold M^d *are mapped to a single set of objects in* M^{d-1} *and vice versa.* The sets of objects, which can be mathematical, physical or biological features, do not need to be antipodal and their mappings need not to be continuous. The term *matching description* means the sets of objects display common feature values or symmetries. *M* stands for a manifold with any kind of curvature, either concave, convex or flat. M^{d-1} may also be a part of M^d. The projection from a sphere to an Euclidean space in not anymore required, just M is required. The notation *d* stands for a natural, or rational, or irrational number. This means that the need for spatial dimensions of the classical BUT is no longer required. Note that a force, or a group, an operator, an energetic source, is needed, in order to project from one dimension to another. The process is reversible, depending on energetic constraints.

String-BUT: a topological approach to brain paths. Another foremost BUT variant is the string-based BUT (briefly, **strBUT**) (Peters and Tozzi, 2016b). The usual continuous function required by BUT (Peters and Tozzi, 2016a; Peters, 2016) is replaced by a proximally continuous function, which guarantees that, whenever a pair of strings (regions that are called *world lines*) are close (near enough to have common elements), then we always know that their mappings will be also be close. A string is a region of space with either bounded or unbounded length. As a particle moves through space following a world line (Olive and Landsberg, 1989), interactions occur at the junctions of world lines. A string is then a part of a hypersphere surface, over which a particle travels. Put another way, a string is path-connected and its path is defined by a sequence of adjacent surface points. The points can be physical, as opposed to abstract geometric points. In other words, a string is a thin region of space that has describable features such as connectedness, length, open-ended or closed-ended, and shape. Strings are antipodal, provided they are disjoint and yet have the same description (Petty, 1971). In terms of nervous theory, a string is a path which stands for a moving particle into either the functional or anatomical spaces of the brain.

In order to map S^n to S^{n-1}, we need to work with lower dimensional spaces containing regions where each point in S^{n-1} has one less coordinate than a point in S^n. Let X be a topological space equipped with Lodato proximity δ (Peters, 2016). $\mathrm{str}A\ \delta\ \neg\mathrm{strA}$ reads $\mathrm{str}A$ and $\neg\mathrm{strA}$ are close. Dochviri and Peters (2016) introduce a natural approach in the evaluation of the nearness of sets in topological spaces. The objective is to classify levels of nearness of sets relative to each given set. The main result is a proximity measure of nearness for disjoint sets in an extremely disconnected topological space. Let $\mathrm{int}(\mathrm{str}A)$ be the set of points in the interior of $\mathrm{str}A$. Another result is that if strings $\mathrm{str}A, \neg\mathrm{strA}$ are nonempty semi-open sets such that $\mathrm{str}A\ \delta\ \neg\mathrm{strA}$, then $\mathrm{int}(\mathrm{str}A)\ \delta\ \mathrm{int}(\neg\mathrm{strA})$.

An important feature is that the manifolds M^d and M^{d-1} are topological spaces equipped with a strong descriptive proximity relation. Recall that in a topological space M, every subset in M and M itself are open sets. A set *E* in *M* is open, provided all points sufficiently near *E* belong to *E* (Bourbaki, 1966). The description-based functions in genBUT are strongly proximally continuous and their domain can be mathematical, physical or biological features of world line shapes. Let *A*,*B* be subsets in the family of sets in *M* (denoted by 2^M) and let $f: 2^M \rightarrow R^n, A \in 2^M, f(A) =$ a feature vector that describes *A*. That is, $f(A), f(B)$ are descriptions of *A* and *B*. Nonempty sets are *strongly near*, provided the sets of have elements in common. The function *f* is strongly proximally continuous, provided A strongly near B implies $f(A)$ is strongly near $f(B)$. This means that strongly near sets have nonempty intersection. From a genBUT perspective, multiple sets of objects in M^d are mapped to $f\left(A\cap B\right)$, which is a description of those objects common to *A* and *B*. In other words, the functions in genBUT are set-based embedded in a strong proximity space. In particular, each set is set of contiguous points in a path traced by a moving particle. The path is called a world line. Pairs of world lines have squiggly, twisted shapes opposite each other on the surface of a manifold. Unlike the antipodes in a conventional hypersphere assumed by the BUT, the antipodes are now sets of world lines that are discrete and extremely disconnected. Sets are extremely disconnected, provided: a) the closure of every set is an open set (Dochviri and Peters, 2016), b) the closure of every set is embedded in the discrete space, and c) the intersection of the closure of the intersection of every pair of antipodes is empty. The shapes of the antipodes are separated and belong to a computational geometry. That is, the shapes of the antipodal world lines approximate the shapes in conventional homotopy theory (Peters, 2016). The focus here is on the descriptions (sets of features) of world line shapes. Mappings onsets with matching description, or, in other words, mappings on descriptively strongly proximal sets, here means that such mappings preserve the nearness of pairs of sets. The assumption made here is that antipodal sets live in a descriptive Lodato proximity (DLP) space. Therefore, antipodal sets satisfy the requirements for a DLP (Peters, 2016). Let δ be a DLP and write $A\ \delta\ B$ to denote the descriptive nearness of antipodes *A* and *B*. And let f be a DLP continuous function. This means $A\ \delta\ B \text{ implies } \mathrm{f}(A)\ \delta\ \mathrm{f}(B) = \mathrm{f}(A) \cap \mathrm{f}(B) \neq \emptyset.$

Example: Assume that antipodes A and B have symmetries (shape, bipolar, overlap, path-connectedness), and f is DLP strongly continuous function, then $A\ \delta\ B \ \Rightarrow\ \mathrm{f}(A)\ \delta\ \mathrm{f}(B)$

This means that, whenever A and B are descriptively close, then A is mapped to $f(A)$ and B is mapped to $f(B)$ and $\mathrm{f}(A)\ \delta\ \mathrm{f}(B)$. If we include in the description of A and B the location of the discrete points in A and B, then the DLP mapping is invertible. That is, $f(A)$ maps to *A*, $f(B)$ maps to *B*and $f(A)\ \delta\ f(B) \text{ implies } A\ \delta\ B.$

To make an example, in nervous functional terms we may state that the paths followed by nervous trajectories in brain phase spaces are closed and can be described in guise of moving strings.

ABSTRACT TOPOLOGY MEETS *REAL* PHYSICS: BRAIN ENERGETIC REQUIREMENTS

A BUT variant, termed **energy-BUT**, is particularly useful in our context. There exists a physical link between the abstract concept of BUT and the energetic features of the system formed by two manifolds M^d and M^{d-1}. We start from a manifold M^d equipped with a pair of antipodal points, standing for a symmetry according to Sym-BUT. When these opposite points map to a n-Euclidean manifold (where M^{d-1}lies), a symmetry break/dimensionality reduction occurs, and a single point is achieved (Tozzi and Peters 2016b). However, it is widely recognized that a decrease in symmetry goes together with a decrease in entropy and free-energy, at least in a closed system. This means that the single mapping function on M^{d-1}displays energy parameters lower than the two corresponding antipodal functions on M^d. Therefore, decreases of dimensions give rise to decreases of energy and energy requirements **(Figure 1**). In such a way, BUT and its variants yield physical quantities, because we achieve a system in which energetic changes do not depend anymore on thermodynamic parameters, rather on affine connections and homotopies.

It must be taken into account that energy-BUT concerns not just energy, but also information. Indeed, two antipodal points contain more information than their single projection in a lower dimension. Dropping down a dimension means that each point in the lower dimensional space is simpler, because each point has one less coordinate. In sum, energy-BUT provides a way to evaluate decreases in energy and information in topological, other than thermodynamic, terms.

An example. Here we provide an example in order to calculate the energy requirements of different functional states in the central nervous system. We start from a nervous closed system, shaped in guise of a M^{d-1}equipped with a single physical function A characterized, say, by a free-energy =1 and an entropy =2. For gen-BUT, when we project the function to M^d, we achieve two antipodal functions B and C with matching description, forming a symmetric system. The question here is: which are the free-energy and the entropy of each one of the two antipodal (symmetric) functions on M^d? And what happens to enthalpy? This question is crucial, because it calls attention to energy conservation and symmetries. In effect, this question leads to the Noether theorem (Noether, 1918), which gives us a physical, testable counterpart to the otherwise *algebraic* topological BUT. Indeed, if we do not take into account the changes in free energy from A to B and C, there is no possibility to translate the abstract BUT to the physics of brain activity, and we have to use the BUT, as we already did, simply as a useful methodological tool (Peters et al., 2016).

The following scenario can be depicted. The projection (mapping) of the description of a pair of physical points (or regions, or functions) on M^d into a point in M^{d-1} occurs because we have found a continuous function between the two manifolds. This is a flexible situation, because we can vary the description of the pair physical points (regions, or functions) and achieve a mapping to various Euclidean spaces, depending on the number of features of the antipodes. From the gen-BUT perspective, the entropy of antipodal regions would be part of the description of the antipodes and would be the same for each antipode. This works for regions, since informational entropy is defined in terms of a set of events. Each regional antipode would be the culmination of a set of random events, leading to each antipode. Similarly, the free energy of each antipode would be the same. In sum, if the region A is characterized by free-energy =1 and an entropy =2, the regions B and C are both characterized by a free-energy =1 and an entropy =2. The total free energy of the system $B+C$ is doubled, compared with A.

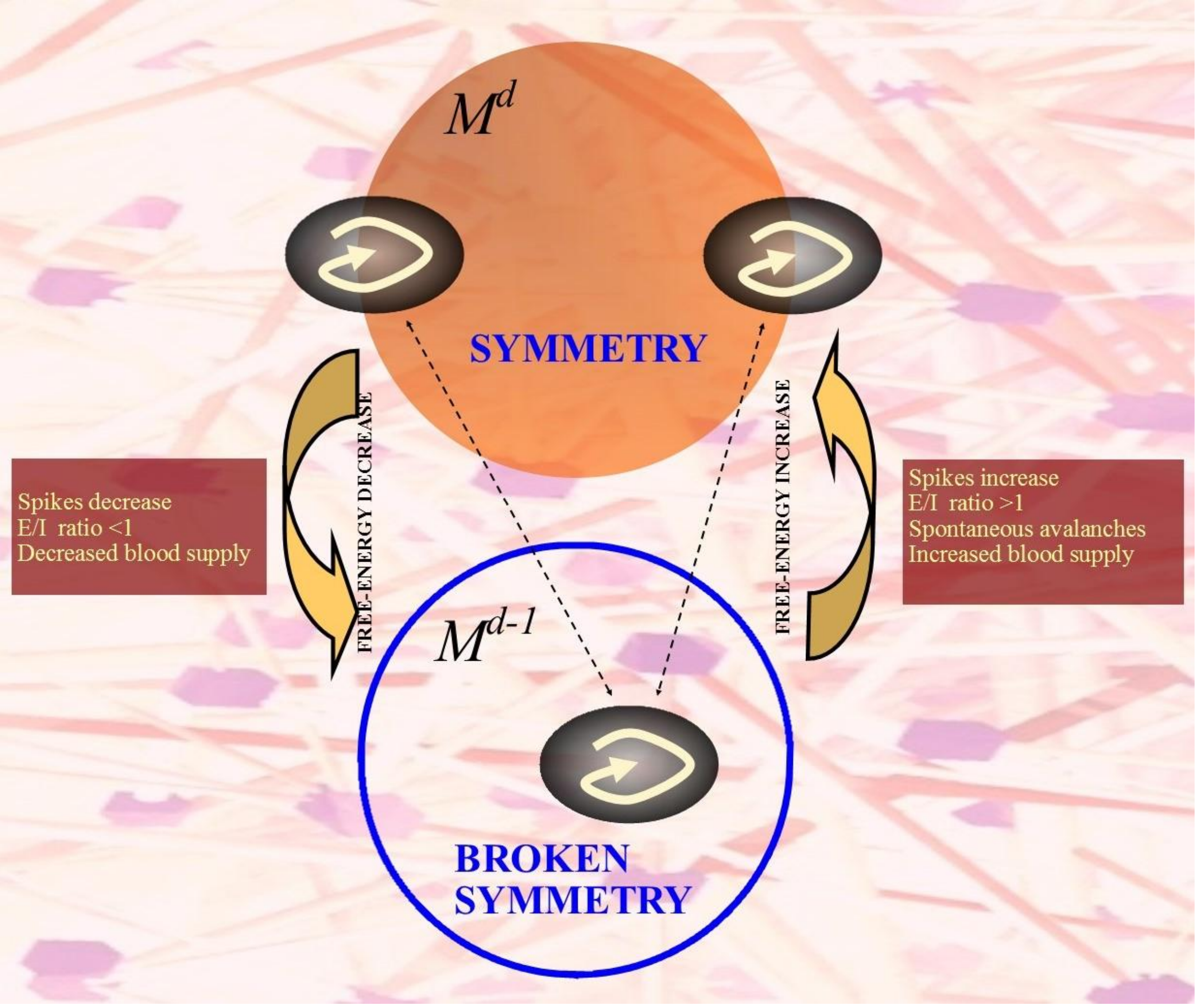

Figure 1. The manifold M^d displays two antipodal points with matching description. It this case, according to strBUT dictates, the antipodal points stand for two symmetric functions equipped with the same energetic conformation (black ovals containing curved arrows). When a symmetry break occurs, the manifold M^{d-1}displays just a single function, equipped with an energetic level lower than the sum of the antipodal functions' ones. Therefore, dimension loss occurs with a decrease of energy. The lateral dark boxes illustrate some hypothetical but plausible conditions which might cause increase or decrease of energy in the brain. In sum, the system displays a configuration with higher energy in M^d, and with lower energy when a symmetry break occurs. The background stands for a schematized structure of the brain phase space.

BRAIN THERMODYNAMIC PARAMETERS: WHEN BUT ENCOMPASSES A PHYSICAL QUANTITY

In the previous paragraph, our discussion on energetic requirements assumed that the brain is a closed system. Changing the state of system necessarily entails a modification in thermodynamic free-energy, which is equivalent to the work done on the system, and which can be regarded as the average uncertainty, or the information we have about the system's microscopic states (Sengupta et al. 2013a). However, we need to take into account that the brain is an open, non-equilibrium biological system. As thermodynamic entropy measures the dispersion over microstates of a thermodynamic canonical ensemble, informational entropy plays the same role, but over some phase functions or macroscopic variables that change with time (Sengupta et al. 2013a). It means that symmetry breaking in the brain may occur through the widely described phenomena of critical fluctuations and critical slowing (Scholz et al, 1987). In such a vein, this paragraph aims to correlate classical thermodynamical parameters with brain dynamical features, in order to analyze and quantify them.

Free-energy. The brain represents 2% of the human body mass yet it accounts for about 20% of total energy consumed, a substantial proportion (Attwell and Laughlin, 2001). The metabolic brain activity, influenced by a balance between the energy cost incurred by its operation and the benefits realized by energy expenditure, is therefore high and constant over time (Sengupta et al., 2013a). Why does the brain consume such remarkable amounts of energy, despite the fact that evolution is geared toward minimizing very high metabolic costs? Almost 20–60% of the energy allocated for the brain is used to support the metabolic rate of the cortical grey matter and for synapses and action potentials (Sengupta et al., 2013b). For our purposes, we limit our analysis to spike frequency. It easy to see that the free energy roughly corresponds to the electric spike frequency. See Tozzi et al. (2016b) for a technical explanation. It means that the increase in thermodynamic free-energy during brain activity is mostly due to spikes, and that we are allowed to evaluate variations in thermodynamic free-energy during brain activity just in terms of electric spiking. In the context of ongoing fluctuations with complex properties caused by variations in thermodynamic parameters, a foremost issue is the *free-energy principle* (Friston 2010). A self-organizing system like the brain, at non-equilibrium steady-state with its environment, needs to minimize its free-energy (and associated entropy), in order to resist a tendency towards disorder/entropy. The key thrust is that energy expenditure is balanced by homeostatic mechanisms, in an effort to minimize free-energy, and in an interplay between neuronal structure and activity at many different spatiotemporal scales. A subtle equilibrium takes place among actual sampled sensations, brain's predictions (e.g, the expected energy), expectation (e.g., the best possible guess), surprise (e.g. an improbable outcome caused by unknown quantities), accuracy (e.g., the surprise about the sensations that are expected) and complexity (e.g., the beliefs before and after observing data through sensory inputs). Such different mechanisms tend towards a main goal: minimising entropy production, which corresponds to minimising the so called *variational free-energy*. There is a strict correspondence between concepts in Friston's formalism and that of the thermodynamics. For example, the Gibb's thermodynamical free-energy stands, in Friston's framework, for the entropy of recognition density, or in other words, for the above mentioned actual sensation sampled by the brain. Further, because variational and thermodynamic free-energy share a common minimum, we are also allowed to link information processing (e.g., Bayesian belief updating) to metabolic efficiency (Sengupta et al., 2013b), so that the average time of variational free-energy becomes a proxy for entropy.

Temperature. The cortical temperature is not a stable parameter as currently believed. The brain displays instead thermal gradients observed at many spatiotemporal scales (Wang H. et al., 2014). Local temperature fluctuations may act as a dynamic variable, modulating presynaptic and postsynaptic events, sensory stimuli, behavioral changes, memory encoding and fine-tune activity-dependent processes (Kalmbach and Waters, 2012; Long and Fee, 2008). In terms of symmetry breakings achieved during nervous second order phase-transitions, temperature might stand for one of the critical control parameters which dictates how the brain evolves from one coordinated state to another. Therefore, brain temperature can be used as an order parameter to monitor the dynamics of the nervous collective state and deviations from the symmetrical state. Indeed, in terms of informational entropy, cortical temperatures contain information about how large-scale physiological and pathological outcomes arise from the interactions of many small-scale processes, in order that thermal brain variations may lead to different probability outcomes. In sum, non-stationary thermal cortical fluctuations, an underrated general mechanism of nervous function able to modify the energy of the brain and to influence psychophysical characteristics, can be assessed in topological terms.

Entropies. Entropies are evaluated in fMRI functional studies through different techniques, e.g., pairwise entropy (Schneidman et al., 2006; Watanabe et al., 2014; Wang Z. et al., 2014), Granger causality index, phase slope index, and so on (Kida et al., 2016). Such approaches also make it possible to analyse how the complexity of an adaptive system like the brain is best understood as a dynamic network that aims to decrease its free-energy, for example via entropy transfer. Here we propose a novel topological way to assess, in brain fMRI functional studies, changes in informational entropies. The method, referred here to changes in cortical spatial dimensions, is described in **Figure 2**. The Figure shows how, by knowing just the entropy values for each BOLD-activated brain area, we are allowed to correlate two different brain states, e.g., a state with symmetry breaking and a state with preserved symmetries.

During a symmetry break or vice versa, the brain may use different mechanisms in order to modify thermodynamic parameters. The possible mechanisms are displayed in **Figure 1**. For example, when the system goes from symmetry to symmetry break, the enthalpy must be reduced of the half, via, e.g., a decrease of local blood flow (enthalpy), or a decrease of spike frequency (free-energy). When the system goes from a symmetry break towards a restored symmetry, the brain requires a surplus of *external* energy to *inject* into M^d, and vice versa. Brain spikes, in this framework, could stand for one of the thermodynamic parameters able to give rise to different attractors, and to supply the required enthalpy, in order to proceed from a symmetry to a symmetry breaking and vice versa.

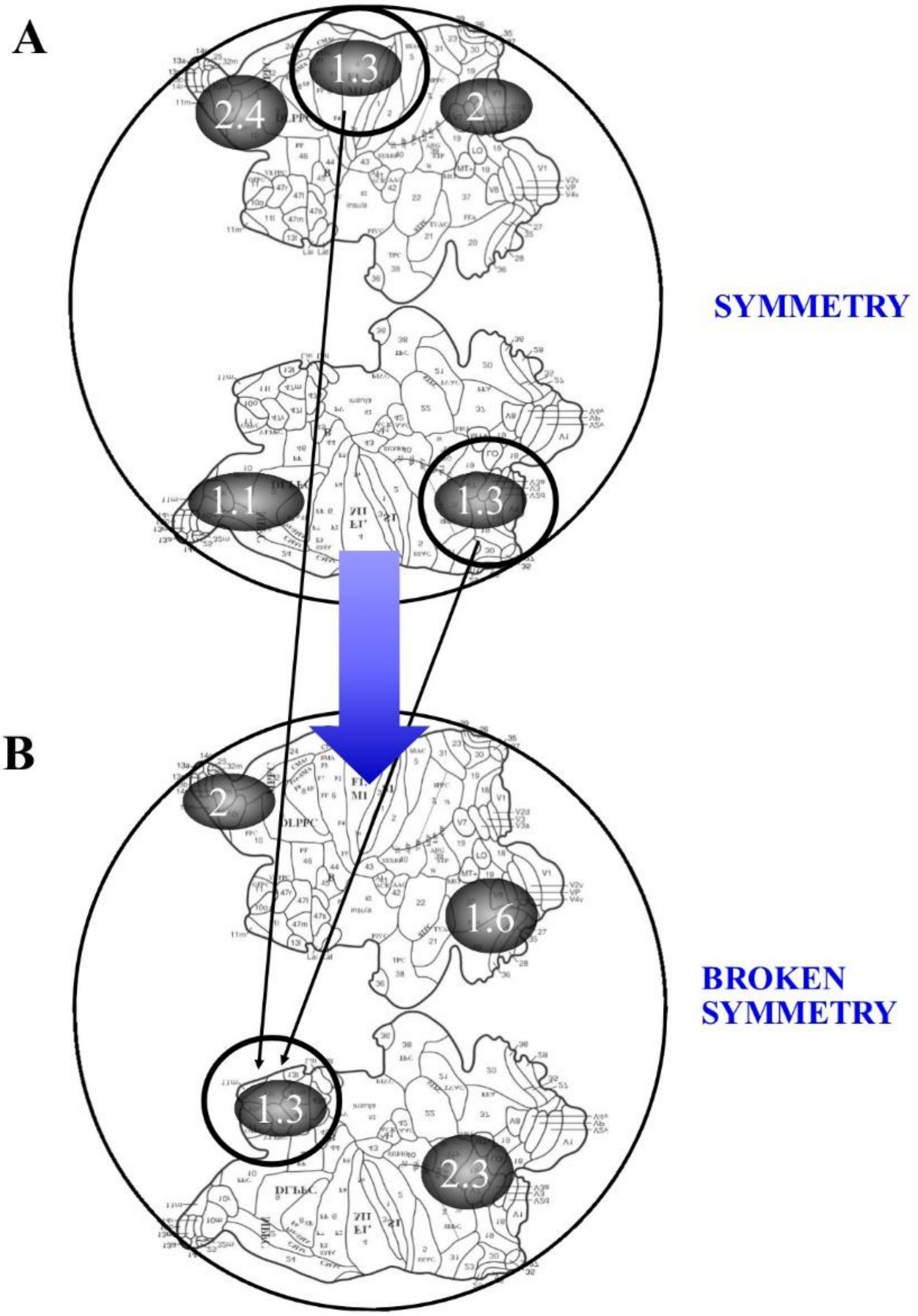

Figure 2. The two brain hemispheres are flattened and displayed in 2D, according to Van Essen (2005). The black circles, depicting hypothetical micro-areas of BOLD signal during fMRI functional studies, contain a number which stands for the corresponding entropy value. **Figure A** displays a functional state with preserved symmetry (e.g., mind wandering), while **Figure B** one with symmetry breaking (e.g., a task-related activity). Note that two micro-areas with the same entropy values in **Figure A** stand for two points with matching description. The latter necessarily project to a single point, in case the brain symmetry is broken, according to the dictates of gen-BUT. It means that in **Figure B** there must be a micro-area with the same entropy value of the two matching points in **Figure A**. It allows us to recognize which zones of the brain could be correlated during symmetry breaks.

CONCLUSIONS

We showed how, from an *abstract* topological assessment of brain activity, we may achieve *real* thermodynamic parameters, in order to evaluate and correlate different cortical functions. BUT and its novel variants display very useful general features which help us to explain a wide-range of brain phenomena. By satisfying the requirements for BUT, it is possible for us to quantify increases and decreases of free-energy/entropy/enthalpy when going from one functional brain conformation to another, *e.g*., from the functional 4D sphere of the default mode network during spontaneous brain activity (Tozzi and Peters, 2016a), to the lower dimensional 3D manifold during evoked brain activity (Papo, 2014). Therefore, the existence of one pair of mappings implies an overall change in thermodynamic and informational parameters. Despite BUT theorem states that it exists *at least a pair* of antipodal point that maps a dimension lower, nevertheless it does not say that *every antipodal pair* will be mapped to a single set, nor that *all* the two sets of objects in higher dimensions display matching descriptions with *all* the single sets of objects in lower dimensions. It means that we would neither specifically assess if a recorded brain state or a set of trajectories is the image of any antipodes, nor the accurate matching of the mapping from higher-dimension manifolds to lower-dimension ones. However, BUT is still very informative about brain dynamics in practice. Indeed, there exist some trajectories, even if we don't know which, that are mapped to a lower-dimensional space and imply a predictable energetic change. Because the brain functional micro-zones are countless, the use of BUT is helpful in achieving a drastic reduction and simplification of the areas to investigate. Instead of looking for a needle in a haystack, BUT makes it possible for neuro-researchers to remove the most of the straw and to increase the number of needles. The BUT approach also overtakes the claim of Simas et al. (2016), who suggested that the algebraic topological approach of embedding a brain network on metric spaces (of different dimensions) may reveal regions that are members of large areas or subsystems, rather than regions with a specific role in information processing. In sum, contrary to the classical averaging of connectivity matrices and to the recent algebraic topological methodologies, the BUT approach reveals brain areas with a specific role in information processing.

A shift in conceptualizations is evident in a methodological approach based on BUT. That is, the opportunity to treat brain dynamics as topological structures gives us the invaluable chance to describe them through the tools of functional analysis (Dol'nikov, 1992). The BUT perspective enunciates a symmetry property located in the physical space (the environment and the brain) to be translated to an abstract space and *vice-versa,* enabling us to achieve maps from one system to another. This approach is in touch with recent proposals, which provide a rigorous way of measuring distance on brain manifolds (Sengupta et al., 2016). We might imagine the brain as a manifold, equipped with a high number of symmetries and with an internal, mathematically structured, holistic generative model of the external world. Depending on external stimuli (Tozzi et al., 2016a) and on individual background, symmetry breaks occur, giving rise to phase spaces equipped with a lower number of dimensions. This takes us into the realm of metric algebraic topology (Willard, 1990), where multidimensional manifold describe the structural order of the relationships between nervous anatomical components and their functional paths.

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ENTROPY IN PRIMARY SENSORY AREAS LOWER THAN IN ASSOCIATIVE ONES: THE BRAIN LIES IN HIGHER DIMENSIONS THAN THE ENVIRONMENT

(the human brain from above: an increase in complexity from environmental inputs to abstractions)

The brain, rather than integrate sensory inputs and concentrate them into concepts as currently believed, appears to increase the complexity from the perceived object to the idea of it. Topological models predict indeed that an increase in dimensions and symmetries occurs from the environment to the higher activities of the brain, and that informational entropy in the primary sensory areas must be lower than in the higher associative ones. In order to demonstrate the novel hypothesis, we introduce a method for the measurement of information in fMRI neuroimages, *i.e.*, nucleus clustering's Rényi entropy derived from strong proximities in feature-based Voronoï tessellations, *e.g.*, maximal nucleus clustering. The technique facilitates the objective detection of entropy/information in zones of fMRI images generally not taken into account. We found that the Rényi entropy is higher in associative cortices than in the visual primary ones. It suggests that the brain lies in dimensions higher than the environment and that it does not concentrate, but rather dilutes the message coming from external inputs.

Sequential processing of information is hierarchical, such that the initial, low-level inputs of primary sensory areas are transformed into representations and integration emerges at multiple processing associative cortical stages (Werner and Noppeney 2009; Nieuwenhuys et al. 2008). Brain functions organize in global gradients of abstraction and a spatially progressive increases in amalgamation of representation or function emerge as cortical distance from the input increases (Taylor et al., 2016). In sum, the current paradigm talks about a brain that, through the limited human sensory repertoire, extractsand concentrates information from the environment (**Figure 1A**). However, recent topological advances talk about a different scenario.The Borsuk-Ulam theorem (BUT) states that (Borsuk 1933):

Every continuous map $f: S^n \to R^n$ *must identify a pair of antipodal points (on* S^n*).*

This means that the positive-curvature sphere S^n maps to the Euclidean space R^n, which stands for an *n*-dimensional Euclidean space (Matoušek, 2003). Many BUT variants have been recently proposed(Peters and Tozzi, 2016; Tozzi and Peters, 2016a; Tozzi and Peters, 2016b; Peters et al., 2016). A generalized version of BUT states that:
Multiple sets of objects with matching descriptions in a d-dimensional manifold M^d *are mapped to a single set of objects in* M^{d-1} *and vice versa*. The sets of objects, which can be physical or biological features, do not need to be antipodal and their mappings need not be continuous. The term *matching description* means the sets of objects display common feature values. *M*might stand for manifolds with any kind of curvature, either concave, convex or flat. M^{d-1}may also be a part of M^d. The projection from S^n to R^n in not required anymore. Instead, just *M* is required. The notation *d*

stands for a natural, rational, or irrational number. This meansalso that the need for natural number and spatial dimensions of the classical BUT is no longer required. There exists a physical link between the abstract concept of BUT and the real energetic features of systems formed by two manifolds M^d and M^{d-1}. M^d is equipped with two matching points, standing for symmetries. When the two points map to a n-Euclidean manifold where M^{d-1} lies, a symmetry breakanddimensionality reduction occurs, and a single pointis achieved in the image space. It is widely recognized that a decrease in symmetry goes together with a reduction in entropy and free-energy (in a closed system)(Roldán et al., 2014). This means that the single mapping function on M^{n-1}displays energy parameters lower than the sum of the two corresponding matching functions on M^d. Therefore, a decrease in dimensions gives rise to a decrease of energy and energy requirements, and vice versa. This *energy-BUT* variant concerns not just energy, but also information. Indeed, two antipodal points contain more information than their single projection in a lower dimension. Dropping down a dimension means each point in the lower dimensional space is simpler, because each point has one less coordinate. In sum, energy-BUT provides a way to evaluate the decrease of energy in topological, other than thermodynamical, terms.

Given the recent claims of brain higher dimensionality (Tozzi and Peters, 2016a), we propose a novel framework where the environment displays less dimensions and symmetries than the central nervous system, so that external inputs progressively increase their complexity when spikes cross the brain towards higher associative cortices (**Figure 1B**). In order to demonstrate our hypothesis, we evaluated, through a novel neuroimaging technique, the entropy values in different cortical areas after visual stimuli presentation.

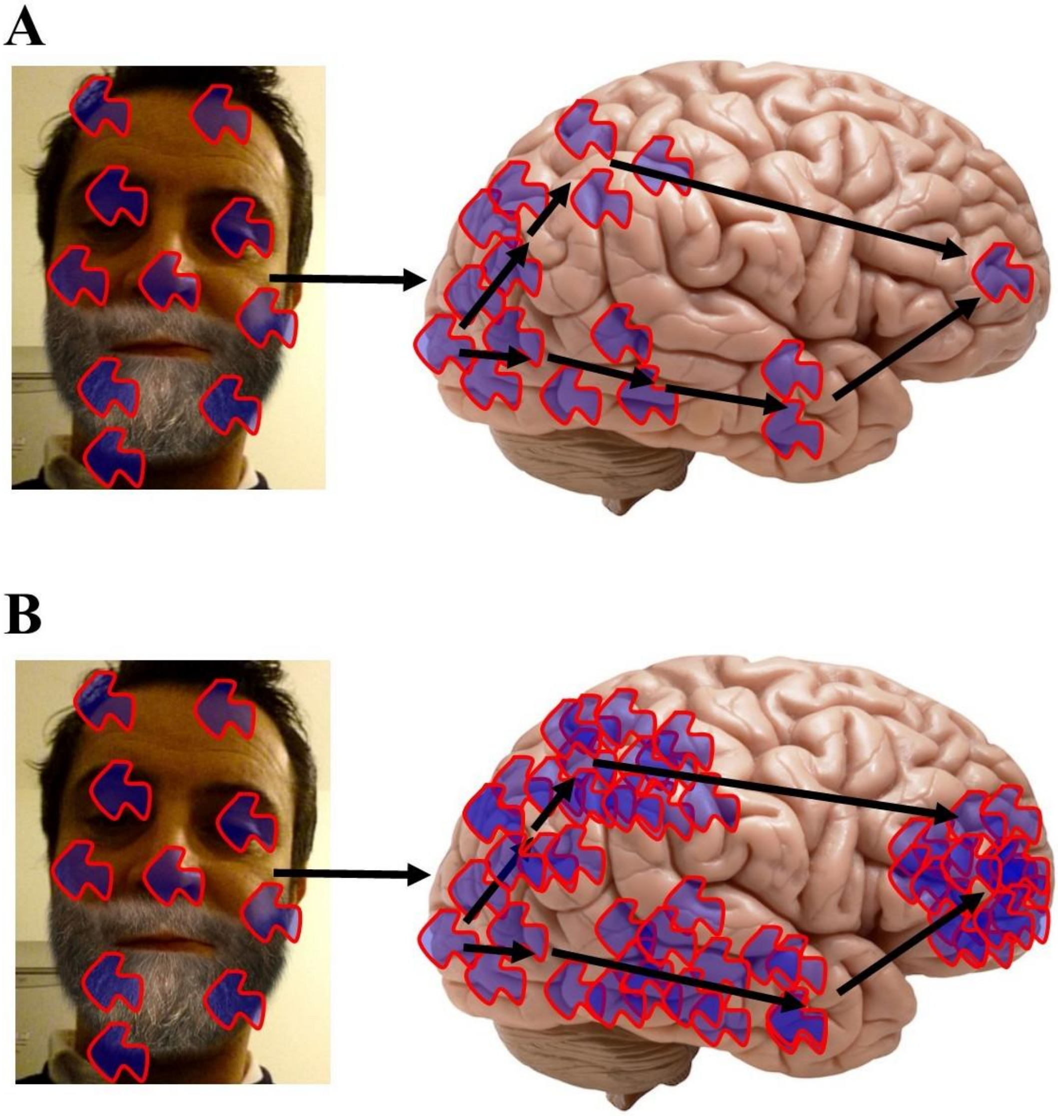

Figure 1. Two models of information processing in the brain. The current paradigm (**Figure 1A**) states that the sensory input is progressively concentrated by areas far from the primary sensory ones. In the higher associative areas,

a general concept related to the visual percept is achieved. Therefore, starting from the overwhelming complexity of the environment, the brain focuses just on what it is useful for the individual preservation. The alternative scenario hypothesizes that the sensory input is progressively diluted when passing from the lower sensory areas to the higher associative ones (**Figure 1B**). In other words, the novel hypothesis states that the concept is more complex than the inputs from the external world. The brain activity leads to increases, and not decreases, of complexity, compared with the surrounding environment.

MATERIALS AND METHODS

Samples. We evaluated 16 fMRI images from visual tasks experiments, which illustrate the activity of different brain areas during vision. The images, taken from Mandelkow et al. (2016), display a widely distributed fMRI response throughout the brain, elicited by basic vision and object recognition (**Figure 2A**). A voxel-wise ANOVA F-statistic map (threshold $p < 1\%$, uncorrected) was superimposed on the T1 -weighted anatomical MRI of one representative subject (16 axial slices in radiological convention). Each tessellated image leads to the MNC mesh clustering described in the next paragraph.

Nucleus Clustering in Voronoï Tilings. A Voronoï tessellation is a tiling of a surface with various shaped convex polygons ((Peters 2016; Edelsbrunner, 2006; Duyckaerts and Godefroy, 2000; Frank and Hart, 2010). A Voronoï region is the set of all points on the plane surface that are nearer to the generating point than to any other generating point on the surface (**Figure2B**) (Peters et al. 2016). In this investigation of fMRI images, each of the generating points in a particular Voronoï tessellation has a different description. Each description of generating point *s* is defined by the gradient orientation angle of *s*, *i.e.*, the angle of the tangent to the point. A *nucleus cluster* in a Voronoï tiling is a collection of polygons that are adjacent to (share an edge with) a central Voronoï region, called the cluster nucleus. In this work, the focus is on maximal nucleus clusters, which highlight singular regions of fMRI images (**Figure 2C**). A pair of Voronoï regions are considered *strongly near*, provided the regions have an edge in common (Peters and Inan, 2016; Peters, 2016). A *maximal nucleus cluster* contains a nucleus polygon with the highest number of strongly near (adjacent) Voronoï regions (**Figure2D**). In order to build aVoronoï tiling, every generating point has gradient orientation angle that is different from the angles of each of the other points used in constructing the tiling on an fMRI image (see **Figure 2B**). The focus in this form of Voronoï tiling is on guaranteeing that each nucleus of a mesh cluster is derived from a unique generating point. The end result is a collection of Voronoï regions that highlight different structures in a tessellated fMRI image. Taking this a step further, we identify maximal nucleus clusters on a tessellated fMRI image. In effect, each maximal nucleus tells us something different about each region of a tiled fMRI image, since we include, in the description of a maximal nucleus, the number adjacent regions as well as the orientation angles of the nucleus generating point. In sum, in a Voronoï tessellation of an fMRI image, of particular interest is the presence of *maximal nucleus clusters*(MNC), *i.e.*, clusters with nuclei having the highest number of adjacent polygons.

Rényi entropy as a Monotonic Function of Information for fMRI Nucleus Clusters. We introduce a measure of the information that MNCs in fMRI images yield. We show how MNC reveal brain regions with higher levels of cortical information in comparison with non-MNC cortical regions, that uniformly yield less information. Rényi (1961; 1966), introduced a measure of information of a set random events. Let *X* be a set random events such as the occurrence of polygonal areas in a Voronoï tessellation and let $\beta > 0, \beta \neq 1, p(x)$ the probability of the occurrence of *x* in *X*. Then Rényi entropy $H_\beta(X)$ is defined by

$$X = \{x_1, \cdots, x_n\},$$

$$H_\beta(X) = \frac{1}{1-\beta} \log_2 \sum_{i=1}^{n} p^\beta(x_i).$$

Rényi entropy and information are interchangeable in practical applications (Rènyi, 1982; Bromiley et al., 2010). In fact, Rényi entropy $H_\beta(X)$ is a monotonic function of the information associated with *X*. This means that Rényi entropy can be used as a measure of information for any order $\beta > 0$. The nuclei in MNCs have the highest concentration of adjacent polygons, compared all non-MNC polygons. Based on measurements of Rényi entropy for MNC vs. non-MNC observations, we have confirmed that Rényi entropy of nucleus polygon clusters is consistently higher than the set of non-MNC polygons (**Figures 2 E-G**). This finding indicates that MNCs yield higher information than any of the polygon areas outside the MNCs. Therefore, Rényi entropy provides a measure of the information in MNCs and the surrounding zones of fMRI images. This means that the MNCs are equipped with higher entropy values (and corresponding higher information), which contrasts with the measure of information in the surrounding non-MNC zones.

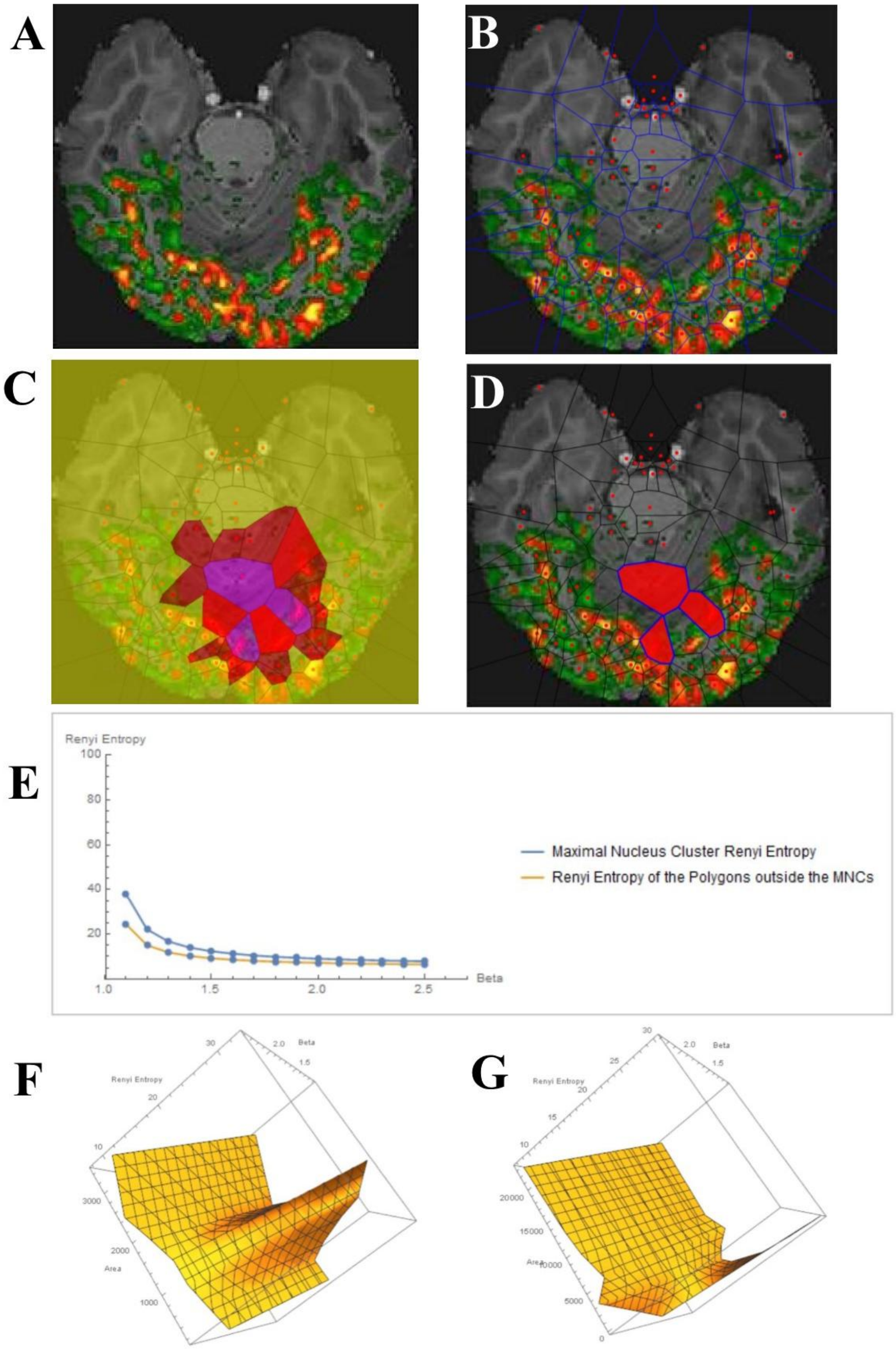

Figure 2. An fMRI image (**Figure 2A**), taken from Mandelkow et al. (2016), underwent Voronoï tessellation (**Figure 2B**). Each • in the tiling represents a generating point with particular features, such gradient orientation and brightness. There are no two • that have the same description. For this reason, every Voronoï region has a slightly different shape.

Figure 2C displays areas with the higher number of adjacent polygons, in this case three. **Figure 2D** shows a sample maximal nucleus cluster for a particular generating point represented by the dot • in N. In this Voronoï tiling, the nucleus has several adjacent (strongly near) polygons. Since the nucleus has the highest number of adjacent polygons, it is maximal. This nucleus is of particular interest, since the generating point • in N has a gradient orientation that is *different from the gradient orientation of any other generating point in this particular tiling.* **Figure 2E** shows Rényi entropy values of maximal nucleus clusters, compared with the surrounding areas of fMRI images. The *x* axis displays the values of the Beta parameter for $1.1 \leq \beta \leq 2.5$. **Figures 2F and G** display Rényi entropy values vs. number polygon areas vs. $1.1 \leq \beta \leq 2.5$ of, respectively, MNC and polygons outside the MNC. MNC Nuclei surrounded by polygons with smaller areas have higher Rényi entropy, which tells us that smaller MNC areas yield more cortical information than MNCs with larger areas.

RESULTS

Each frame from Mandelkow et al. (2016) showed that stimulus-correlated fMRI activity is widespread in the occipital and ventral temporal cortices, consistent with their established involvement in basic vision and object recognition. For each frame, we produced tessellated images with one or more maximal mesh regions. Furthermore, we generated tessellated images showing one or more MNC. The MNC were found to be located in anterior or central brain zones, far from the posterior primary visual sensory areas. The entropy values are higher in the associative zones than in the primary sensory ones. It means that the associative area, during vision, display more activity than the surrounding ones, including the primary visual area. See **Figure 3** for further details.

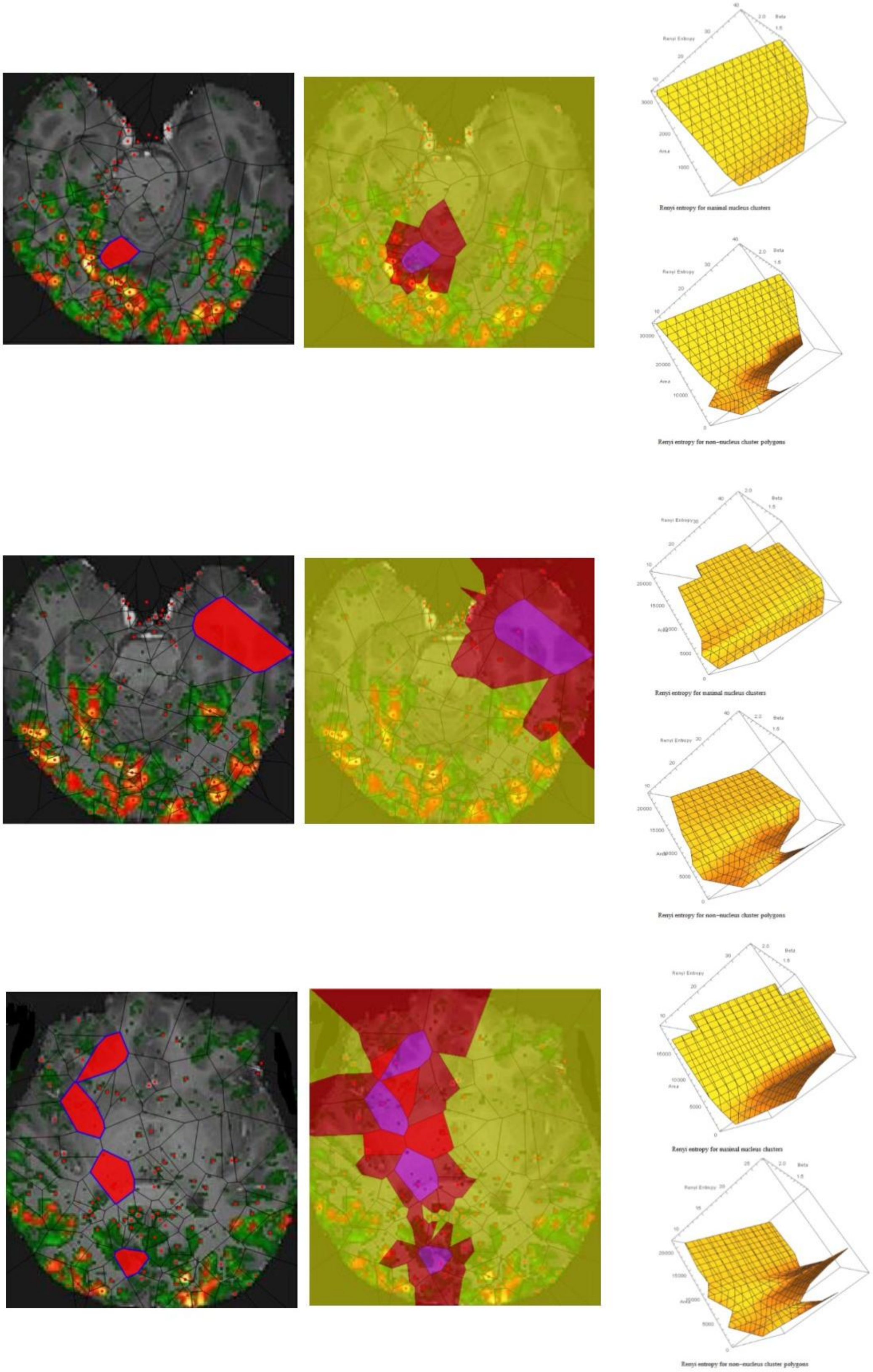

Figure 3. The left side of the Figure depicts MNC tessellations of three samples taken from Mandelkow et al. (2016). The right part displays, for every sample, the Rényi entropy values vs. number polygon areas of MNC (upper part) and outside MNC (lower part).

DISCUSSION

The current paradigm describes an objective hierarchical landscape of cognition, where a relatively linear and continuous increase in simboli content occurs over network-depth. A continuum of stratified landscapes takes place in a hierarchically ordered connectome, where a graded order of class is represented by a diagram of connected nodes. Starting from external inputs, an emergent aggregation of functions and representations gives rise to hierarchical abstractions processing, where *abstraction* is defined as a process creating general concepts of representation, by emphasizing common features (Taylor et al., 2015). A structural pyramid of the human connectome with gross network-depth directionalitycan be sketched. *Concrete* regions at the base of pyramid, connected to the outside world, are related to simple perceptions, sensory processing or physical actions. *Abstract* regions at the pinnacle of the pyramid, which are deepest in the brain network and least connected with the outside world, are related to more abstract concepts and symbols. Behavioral elements are conceptualized as brain functions, tasks or behaviors. It means that even abstract behaviors start with sensory inputs and the information representation flow converges towards less complex schemes, e.g., the ideas (Pexman et al. 2016). Unified concepts tend to compress and amalgamate the information content of an idea or an observable event, in order to retain only information which is relevant for an individualized goal or action (Taylor et al., 2015).

Here we proposed and tested an alternative hypothesis, where the above mentioned pyramid of complexity is inverted. The abstract concepts are more intricate and contain more information than the external world. The brain does not *extract* and concentrate the meaning of external objects in simple ideas, rather it *dilutes* the meaning of external objects in complicated ideas. The information is not *aggregated*, rather it is *scattered* in the brain. Recent papers suggest that the brain activity might be multidimensional and shaped in guise of a donut-like structure. It means that the brain function lies in a dimension higher than the environment. Brain activity can be compared to a phase space where projections take place among regions temporarily equipped with different functional dimensions, each one mapping the other.In the powerful topologic framework of BUT and its variants, the world external to the observer *is* a single set of objects, while the world internal to the observer *is* many sets of objects with matching description. Biologically significant, environmental inputs'single descriptions become matching descriptions in our thoughts. The object's concept lies in a dimension higher than the object. It means that, e.g., mental images of cats are not pale copies of cats. While mental images are matching descriptions, cats are single descriptions. Thus, contrary to common belief, the object's concept is more intricate than the object. The brain contains more dimensions and symmetries than the environment andencompasses all the concepts its symmetries might display. We might speculate that such species-specific pool of central nervous system's symmetries, despite their finite number, can be arranged in countless, versatile modular structures, giving rise to therange of possibilities available for the human brain.

According to the BUT dictates, single descriptions grasp less information and entropy than matching descriptions. Indeed, the energy-BUT variant describes an increase of energy from single descriptions to higher projections. It means that, if our model is true, the primary sensory areas might display less entropy than the associative areas. Therefore, to test our hypothesis, we needed to evaluate the changes in entropy values in fMRI images, in given timescales and in different areas. We used a novel image analysis technique. The major new elements in the evaluation of fMRI images are nucleus clusters, maximal nucleus clusters, strongly near maximal nucleus clusters, convexity structures that occur whenever max nucleus clusters intersect. We showed that in a Voronoï tessellation of an fMRI image, of particular interest is the presence of *maximal nucleus clusters* (MNC), *i.e.*, clusters with the highest number of adjacent polygons. We demonstrated that MNC reveal regions of the brain with higher levels of cortical information in comparison with non-MNC cortical regions, that uniformly yield less information. We showed that, in touch with our hypothesis, such brain zones with higher levels of cortical information correspond to associative areas.

In sum, a progressive symmetry reconstruction might occur in human brain from the lower-dimensional single features of the *concrete* periphery to the higher dimensional matching features of the *abstract* center. It means that brain concepts and ideas are from *above*, not from *below.*

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TOWARDS A PHYSICAL CORRELATION BETWEEN SLOW AND FAST BRAIN TIMESCALES

Brain electric activity exhibits two important features: oscillations with different timescales, characterized by diverse functional and psychological outcomes, and a temporal power law distribution, which appears as a straight line when plotted on logarithmic scales in a log power versus log frequency plot. In order to investigate the relationships between low- and high- frequency spikes in the brain, we used a variant of the Borsuk-Ulam theorem which states that, when we assess the nervous activity as embedded in a sphere equipped with a fractal dimension, we achieve two antipodal points with similar features (the slow and fast, scale-free oscillations). We demonstrate that slow and fast nervous oscillations are correlated and provide, through the Bloch theorem from solid-state physics, the possible equation which links the two timescale activities.

Brain electric activity displays a mean action potential rate of 4 Hz (Sengupta 2013). However, this is just a mean value which accounts for the diverse timescales of nervous activity. Indeed, the coexistence of very low-frequencies (<2 Hz) and high frequencies (>10) can be found in the brain (Buszaki). It is thought that these two timescales are associated with unrelated functional activities (Raichle 2010). It has been proposed that the anatomical, functional and psychological correlates of the slow cortical potentials are respectively the spontaneous brain activity (Raichle 2010) the default mode networks and the unconstrained, conscious cognition (i.e. mind-wandering or day dreaming propensities) (Andrews-Hanna; Kucyi) or the dreaming state (Fox, 2015). Many observations confirm the hypothesis that spontaneous fluctuations are the basic, “intrinsic,” standard architecture of functional brain organization (Krueger; Yuste). Spontaneous low-frequency fluctuations of cerebral activity cannot be simply reduced to a background noise uncorrelated to the system response (de Arcangelis; de Pasquale), rather they occur during unconstrained “resting’ states” (subjects left to themselves in a scanner, with no explicit task instruction, lying quietly with eyes closed or fixating on a cross) and thus represent neuronal activity that is intrinsically generated by the brain (Fox 2007). Spontaneous fluctuations have been observed not only in electric activity, but also in various haemodynamic and metabolic parameters, as well as spontaneous fluctuations in the membrane potential, spontaneous spikes (O‘Donnell) and neurotransmitter release (Kavalali). Among the networks exhibiting coherent fluctuations in spontaneous activity during rest, of particular interest is the “default-mode network” (DMN), *i.e.*, functionally and structurally connected regions that show high metabolic activity and blood flow at rest, but deactivate when specific goal-directed behavior or cognition is needed (Damoiseaux). On the other side, during stimuli-evoked activity or cognitive demands, the brain transitorily exhibits functional conformations - other than the spontaneous ones -, which are linked with specific psychological correlates (Cole). The high frequency activity has been correlated, *i.e.*, with perceptual binding and feedback/feedforward waves which improve the perception of external inputs (Buszaki). The (environmental and internal) inputs cause changes in spike frequency in diverse cortical areas: the brain thus exhibits a high number of possible source configurations, such as gamma oscillations in somatomotor cortex during states of enhanced vigilance, or alpha waves in posterior zones with eyes open, and so on (Bastos).

In this paper we ask whether there is a correlation between the functionally heterogeneous low and high frequencies, and evaluate whether it is true that, when the former changes, the latter also changes. To assess this possibility, we bring to the table three powerful concepts from far-flung branches: the ubiquitous power laws, the Borsuk-Ulam theorem (BUT) from algebraic topology and the Bloch theorem from solid-state physics.

METHODS

Brain activity observed at both low and high temporal scales exhibits a $1/f^{\alpha}$ -like power spectrum (Newman), including not just macroscopic electric oscillations, electroencephalography, magnetoencephalography and functional magnetic resonance imaging signals (Heemail), but also microscopic membrane potentials and fluctuations in neurotransmitter release (Fox 2007, Milstein; Linkenkaer-Hansen). In particular, the temporal frequency spectrum of cerebral electric activity displays a scale-invariant behaviour $S(f)= 1/f^{\alpha}$, where $S(f)$ is the power spectrum, f is the frequency and α is an exponent that equals the negative slope of the line in a log power versus log frequency plot (Van de Ville; Pritchard). Pink noise can be regarded as an intrinsic property of the brain characterizing a large class of neuronal processes (Fraiman; He), suggesting the possibility that power law distributions contain information about how large-scale physiological and pathological outcomes arise from the interactions of many small-scale processes (de Arcangelis). The emergence of power law distributions in the brain has been also correlated with the spontaneous appearance of high frequency neuronal avalanches (Papo; Tinker; Beggs).

Therefore, both slow and fast oscillations are equipped with a power law structure. Now BUT and its variants come into play. The Borsuk-Ulam Theorem (Borsuk 1933; Dodson) points out that, if a sphere S^n is mapped continuously into a n-dimensional Euclidean space R^n, there is at least one pair of antipodal points on S^n which map onto the same point of R^n (Beyer). See Tozzi 2016a and Tozzi 2016b for further details about BUT and its variants. The notation S^n stands for an n-sphere, which is a generalization of the circle (Weeks). An n-sphere is a n-dimensional structure of constant curvature, embedded in a convex n+1 space (Marsaglia; Henderson). For example, a 2-sphere (S^2) is the 2-dimensional surface of a 3-dimensional ball (a beach ball is a good illustration). Examples of antipodal points are the poles of a sphere (Matousek). Tozzi (2016a) provides a mathematical treatment for technical readers.

The concept of antipodal points can be can be used not just for the description of simple topological points, but also of more complicated features, such as shapes of space (spatial patterns, i.e., area and diameter), of shapes of time (temporal patterns), vectors or tensors, functions, signals (Borsuk 1958-59; Borsuk 1969; Peters 2016). If we simply evaluate systems activity instead of “signals”, BUT leads naturally to the possibility of a region-based, not simply point-based, geometry. We are thus allowed to describe systems features as antipodal points on a n-sphere. If we map the two points on a n-1 sphere, we obtain a single point. This means that signal shapes can be compared (Weeks; Peters 2016): the two antipodal points standing for systems features are assessed at one level of observation, while the single point at a lower level (Tozzi 2016a). The BUT can be used not just for the evaluation of antipodal, but also of non-antipodal points on an n-sphere. We can consider regions on an n-sphere that are either adjacent or far apart (Tozzi 2016a). And this BUT variants applies, provided there are a pair of regions on n-sphere with the same feature value. Therefore, the two points (or regions) do not need necessarily to be antipodal, in order to be described together (Peters 2016). This makes it possible to evaluate matching signals, even if they are not “opposite”, but “near” each other: the antipodal points restriction from the “standard” BUT is no longer needed. Although BUT was originally described just in case of n being a natural number which expresses a structure embedded in a spatial dimension, nevertheless the value of n can stand for other types of numbers. The n value of S^n can be also cast as an integer, a rational or an irrational number (Tozzi 2016a). For example, we might regard functions or shapes as embedded in a sphere in which n does not stand for a spatial dimension, but for a fractal one. This makes it possible to use the n parameter as a tool for the description of nervous power laws.

In sum, the widespread brain scale-free can be evaluated in terms of algebraic topology. **Figure 1** illustrates an example of nervous temporal power laws embedded in a n-sphere, in which n stands for the brain power slope. The n-sphere, in this case, is equipped with a n-value corresponding to the fractal dimension α (which could be detected by several neurofunctional techniques: see (Pritchard; He). The figure clearly shows that the low- and high- frequency brain oscillations exhibit a matching description: indeed, the scale-free distribution of the brain spikes allows us to consider the slow and fast frequencies as homotopies or affine connections. Embracing brain fractals in the framework of algebraic topology (Willard; Dodson) means that power laws at different timescales (the antipodal points) can be described as functions on “abstract” structures: the BUT perspective permits the nervous scale-free property located in the real space (the brain geometric space) to be translated to an abstract space and *vice-versa*, enabling us to achieve maps from one level to another.

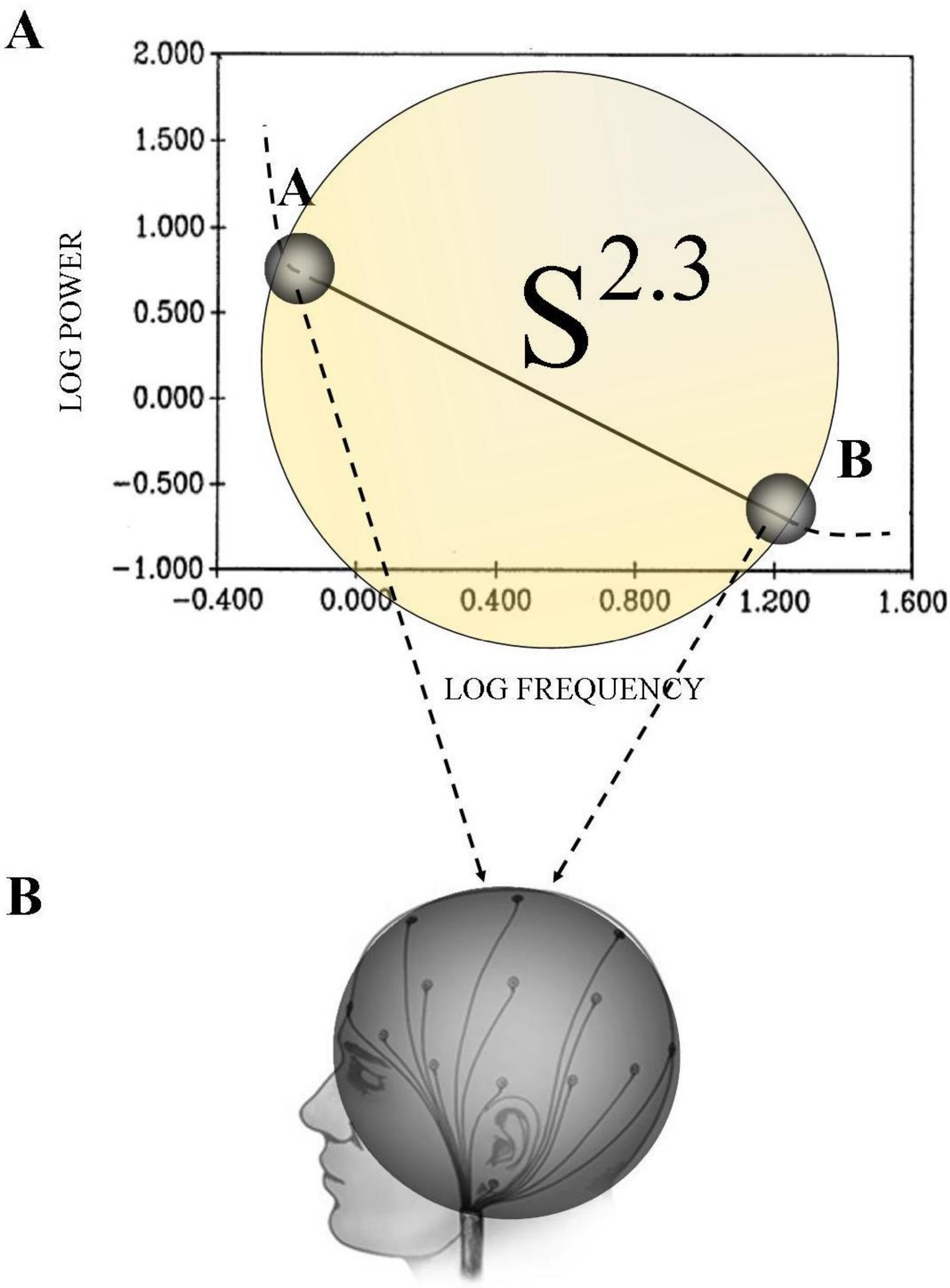


Figure 1A. Log amplitude versus log frequency scatter plot of brain spikes detected by EEG techniques (modified from Pritchard). The Figure displays on the x axis the frequency (in Hz) and on the y axis the power (in μV^2) of the electric spikes. Note that the scale is logarithmic: it means that on the x axis, for example, -0.400 = 0,39 Hz, 0 =1 Hz, 0.4 = 2.52 Hz, 1.2 = 16 Hz and so on. In turn, on the y axis, -1.000 = 0,1 μV^2, -0.5 = 0,32 μV^2, 0.000 = 1 μV^2, 1.000 = 10 μV^2, and so on. The figure also depicts a fractal dimension, in this case equipped with the slope $\alpha = 2.3$.

The BUT now comes into play: the black circles A and B, which respectively depict power laws at low- and high- brain frequency, stand for two antipodal points with matching description, embedded in a n-sphere with fractal exponent α (in this case, 2.3). Note that the Borsuk-Ulam theorem is not valid at the slope's tails, where the α exponent is lost (dotted lines on the right and left of the main slope).

Figure 1B. The total fractal activity detected by different functional neurotechniques stands for the projection of the two antipodal points on a n-1 -manifold. Ah head mounted EEG is showed for sake of simplicity.

RESULTS

In sum, our topological approach showed that low- and high-frequency fractal spikes are correlated in the brain, because they display the same features. By knowing the values of an antipodal points, the other one can be detected and measured on the opposite side of the diameter (corresponding to the fractal slope). Once established that a matching description occurs between slow and fast brain oscillations, we looked for a feasible equation able to link their reciprocal activities. A theory from an apparent far-flung branch, solid-state physics, might indeed help us to improve our knowledge of different nervous oscillations' relationships.
In a periodically repeating environment (such as a lattice), the Bloch wave is a linear oscillation obtained by the product of (Floquet, Taversa, Ahn):

a) a periodic function with the same periodicity as the lattice,
b) a plane wave.

In such a solid-state physics' system, the wavefunction Ψ for a particle has the form:

$$\Psi(x) = e^{ikr} u(x).$$

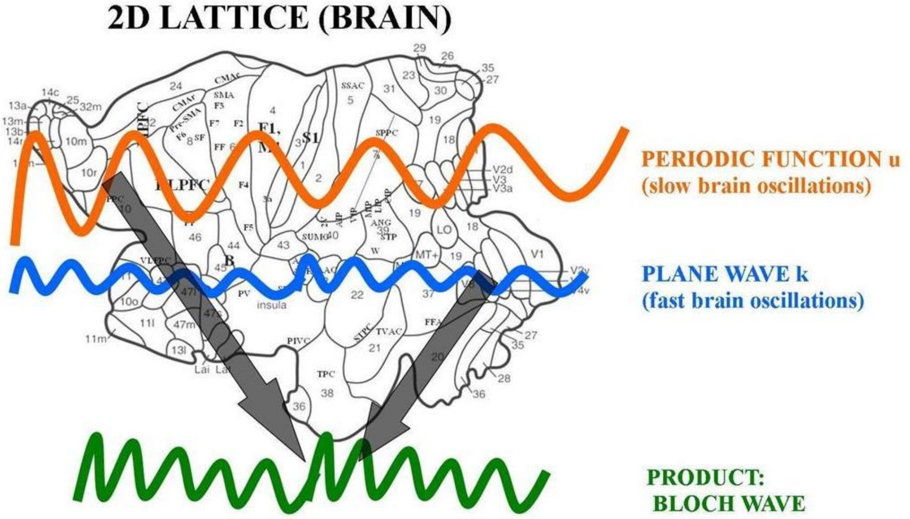
In which Ψ is called a Bloch wave, x is its position, e^{ikr} is a plane wave (in which e is the Euler's number, i is the imaginary unit, k is a vector of real numbers called the *crystal wave vector*), and $u(x)$ is a periodic function with the same periodicity as the lattice. A mathematical treatment for technical readers is provided in the **Appendix**.

In a brain framework, we are allowed to look for the nervous correlates of the Bloch wave's equation (**Figure 2A**):

1) We may consider just the real part and put aside the imaginary part of the Bloch theorem.
2) The brain stands for a 2-D lattice. We are indeed allowed to unfold and flatten cerebral hemispheres into a two-dimensional reconstruction by computerized procedures (Van Essen, 2005).
3) The periodic functions u stand for the spontaneous, slow brain oscillations which take place on the 2D brain lattice. We may conventionally state that u has the same periodicity of the brain lattice, because it corresponds to the nervous spontaneous oscillations.
4) The plane waves (the vectors of real numbers k) stand for the fast, task-evoked brain oscillations.
5) The Bloch waves stand for an unknown brain parameter able to link together the parameters u and k.

Figure 2B provides a simulation of the Bloch theorem applied to brain function. The picture shows that a change in slow oscillations leads to a change in fast oscillations, and vice versa.

A



B

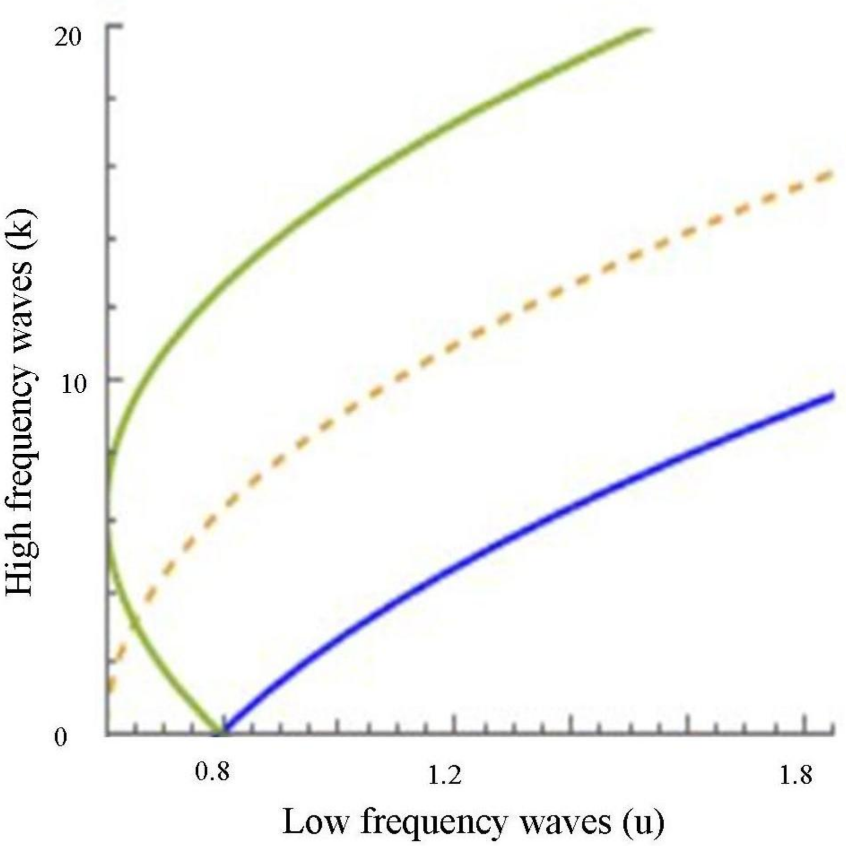


Figure 2A. A rough sketch depicting the brain correlates of the Bloch theorem. See the text for further details.
Figure 2B. Relationships between slow and fast brain oscillatory activity, according to the Bloch Theorem. A plot of Bloch wave forms, for *k* (high frequency waves) on the *y*-axis, and *u* (low frequency waves) on the *x*-axis, is displayed. The brain spike frequencies are expressed in Hz (note that this time the scale is non-logaritmic). The different lines correspond to diverse values of the Bloch wave. Just the slow frequencies included in the fractal range are displayed, while the non-fractal slope tail on the left of **Figure 1A** is excluded.

CONCLUSIONS

The aim of this paper was to investigate the possible functional relationships between slow and fast brain oscillations. We elucidated the correlations between nervous fluctuations with different timescales and functional activity (the low- and the high- frequency spikes) and proposed a possible equation, based on the Bloch theorem, in order to quantify their connections. Indeed, if we replace the periodic function with the scale-free ultra-slow waves of the default mode networks, and the plane wave with the fast brain spikes, we obtain a Bloch wave function which takes into account their correlations. In such a way, the increase in frequency of the slow electric oscillations leads to a predictable increase of the fast electric ones. Our simulation showed that spontaneous fluctuations in cortical excitability might have a remarkable effect on the field potentials activity frequency spectrum as well as the spiking activity of neurons. This coupling, which serves an important coordinating role, provides a logical structure for the integration of brain functional activity (Buszaki; Raichle). Recent results demonstrate indeed that gamma-band activity in the alert monkey is largely an emergent property of cortex from the resting state waves (Bastos). This hypothesis is made more salient by the observation that many types of behavioral variability follow a 1/*f* frequency distribution similar to that of spontaneous BOLD, meaning that there is increasing power at lower frequencies (Fox).
The Bloch theorem might shed new light on the interpretation of the data from functional neuroimaging. If we were able to calculate the Bloch wave from the experimental records, we could obtain a simple factor which summarizes the behaviour of the brain's dynamical system - and which could also be compared with the real data from pairwise entropy studies (Watanabe) -. We thus achieve a sort of single “order parameter” which could allow a better comprehension of cortical dynamics. This method could be used in the study of EEGs as well as fMRI neuroimaging. We also suggest other feasible applications of the Bloch theorem in different fields of neuroscience: for example, if we replace the brain with a lattice, we might evaluate the first Brillouin zone and quantify the Bloch waves in different functional states (for further details, see **Appendix**). The fact that the same Bloch wave may be obtained from different types of oscillations could explain the apparently chaotic behaviour of cortical fluctuations. If the Bloch waves change in different functional states (i.e., sensations, perceptions, emotions, mind wandering and so on), we might be able detect the underlying activity, starting just from the knowledge of the Bloch wave. Furthermore, the well-known relationships between Bloch waves, Floquet multipliers, Lyapunov exponents and limit-cycle attractors (see **Appendix**) allow us to evaluate the brain oscillations’ spatial fractals/temporal power laws in the context of dynamical system theories. To make an example, starting from the Lyapunov exponents endowed in the metastable brain at the edge of chaos (Beggs) - , we might achieve a more manageable linear system, which depends just on the various brain timescales.

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APPENDIX: BLOCH WAVES AND FLOQUET THEOREM

The Bloch theorem states that, if you multiply a plane wave by a periodic function, you obtain a Bloch wave, which expresses the energy eigenstates for a particle in a lattice, written as ψn_k, where *n* is a discrete index.

There are different Bloch waves with the same *k*, each one with a different periodic component *u*. Further, the same Bloch wave can be built in different ways, involving different vectors *k* and different periodic functions *u*. However, if we take into account just the first Brillouin zone of our lattice, we obtain that every Bloch state has a unique *k*.

The concept of Bloch theorem from solid-state physics - a second order differential equation - is about crystals in any number of spatial dimensions and deals in particular with the Schrödinger equation. However, it can be also applied in theory of ordinary differential equations, through the Floquet theorem. Indeed, the two theorems are almost equivalent (Floquet). The Floquet theorem, through a coordinate change in the lattice, transforms the original periodic system into a more manageable traditional linear system with constant, real coefficients. In other words, we map a fundamental matrix solution into a matrix function depending on the time, giving rise to a time-dependent change of coordinates. The Floquet theorem holds for any homogeneous, linear system of first order differential equations with a periodic coefficient matrix. Through a coordinate change in the lattice, the Floquet's theorem transforms the periodic system into a traditional linear system with constant, real coefficients.

We start from a linear first order differential equation:

$$x = A(t)x,$$

where $x(t)$ is a column vector of length n, and $A(t)$ is an $n \times n$ periodic matrix with period T.

Then, for all $t \in R$:

$$\Phi(t+T) = \Phi(t)\Phi^{-1}(0)\Phi(T),$$

In which $\Phi(t)$ is a fundamental matrix solution of the above differential equation $x = A(t)x$, and $\Phi^{-1}(0)\Phi(T)$ is the monodromy matrix.

Now let's consider the $n \times n$ matrices: *B, P, Q, R*:

For each matrix B such that:

$$E^{TB} = \Phi^{-1}(0)\Phi(T),$$

there is a periodic (period *T*) matrix function $t \rightarrow P(t)$ such that:

$\Phi(t) = P(t)\, E^{tB}$ for all $t \in R$. This representation is the Floquet normal form for the fundamental matrix $\Phi(t)$.

There is also a real matrix R and a real periodic function (period -2T) matrix function $t \rightarrow Q(t)$ - which is continuous and periodic - such that:

$$\Phi(t) = Q(t)E^{tR} \text{ for all } t \in R.$$

The latter mapping gives rise to a time-dependent change of coordinates:

$$y = Q^{-1}(t)x,$$

under which the original system becomes a linear system with real constant coefficients $y = Ry$. The mapping of a fundamental matrix solution for such a differential equation into a (time-dependent) matrix function gives rise to a time-dependent change of coordinates, under which the original periodic system becomes a linear system with real constant coefficients $y = Ry$.

The eigenvalues of e^{TB} are called the characteristic multipliers of the system, while the characteristic exponent, called the Floquet exponent, is a complex μ such that $e^{\mu T}$ is a characteristic multiplier of the system. Floquet exponents are not unique and their real parts correspond to the Lyapunov exponents.

The linear differential equations with periodic coefficients have been widely used in many scientific fields. In particular, they provide a versatile tool for the stability analysis of physical systems equipped with a periodic steady-state and infinite memory, such as Brownian particles and circuit resonators (Traversa). The Floquet multipliers have been also used to assess the stability of periodic motion in natural rhythmic - movements in humans and machines -, not just in linear systems, but also in stochastic noise and in limit-cycle, nonlinear oscillators (Ahn).

A TOPOLOGICAL THEORY OF KNOWLEDGE IN THE HUMAN BRAIN
(Towards topological mechanisms underlying experience acquisition and transmission in the human brain)

Experience is a process of awareness and mastery of facts or events, gained through actual observation or second-hand knowledge. Recent findings reinforce the idea that a naturalized epistemological approach is needed to further advance our understanding of the nervous mechanisms underlying experience. This essay is an effort to build a coherent topological-based framework able to elucidate particular aspects of experience, *e.g.*, how it is acquired by a single individual, transmitted to others and collectively stored in form of general ideas. Taking into account concepts from neuroscience, algebraic topology and Richard Avenarius' philosophical analytical approach, we provide a scheme which is cast in an empirically testable fashion. In particular, we emphasize the foremost role of variants of the Borsuk-Ulam theorem, which tells us that, when a pair of opposite (antipodal) points on a sphere are mapped onto a single point in Euclidean space, the projection provides a description of both antipodal points. These antipodes stand for nervous functions and activities of the brain correlated with the mechanisms of acquisition and transmission of experience.

Current advances in human neurosciences shed new light on questions concerning the status of mental activity and its relation to physical function. Promising innovations such as transcranial stimulation (Filmer et al., 2014) and mind-to mind communication (Grau et al., 2014) call for broad methodological investigations in order to further advance our understanding of the brain. In this essay we will focus on *experience*, an active process of understanding, knowledge and mastery of facts or events which encompasses a different range of brain functions, such as thought, perception, memory, emotion, will, imagination, inter-individual communication and scientific theories (Cavell, 2002). Experience is gained through: a) the direct, actual observation of immediately perceived events and subsequent interpretation, b) or records or summaries from first-hand observers or experiencers c) or from instruments (Popper and Eccles, 1997).

In such a framework, simple concepts from algebraic topology, namely the Borsuk-Ulam theorem (BUT) and its variants, come into play, giving rise to a different approach that makes it possible to evaluate mental activities correlated with experience. In this essay, we will limit our topological evaluation to specific features of experience, *e.g.*, its acquisition and transmission. We will start from the pure, unmediated experience of the single individual and will proceed towards objects categorization and social experience through a plurality of shared experiences. In other words, we will investigate the knowledge acquisition by an individual, a community and mankind at large. We will pursue the inductive approach introduced by the French Swiss philosopher Richard Avenarius (1843-1896). His *Kritik der reinen Erfahrung* (*Critique of Pure Experience*) (Avenarius, 1908) provides a useful high-level interpretation of physiological functions and psychological behavior, which works well in building a topological framework for experience (Russo Krauss, 2013; Russo Krauss, 2015).

This paper comprises six sections. In the first section, we introduce BUT and its variants. The second section analyzes the experiences of the single individual, who includes no other standpoint than that where he stands. As the case of the Greek philosopher, he is in the turmoil of the market-place, not as buyer or seller, in order that he may just observe. Particular cases are provided in sections three and four, in order to establish the psychological correlates of experience acquisition and transmission. In section five, we extend the experience onto social groups and a general human setting, where the most general concepts may arise. Section six aims to answer the crucial question: what does a topological approach bring to the table, in the experimental evaluation of physiological mechanisms of experience?

1) THE BORSUK-ULAM THEOREM AND ITS VARIANTS

The Borsuk-Ulam Theorem (BUT) states that, if a sphere S^n is mapped continuously into an *n*-dimensional Euclidean space R^n, there is at least one pair of antipodal points on S^nwhich map onto the same point of R^n (Borsuk, 1933; Dodson, 1997; Beyer, 2004) (**Figure 1A**). See Tozzi and Peters (2016a) for further details and a mathematical treatment. The notation S^n stands for an *n*-sphere (Weeks, 2002), which is an *n*-dimensional, circular structure, embedded in an $n+1$ space (Marsaglia, 1972). For example, a 2-sphere (S^2) is the 2-dimensional surface of a 3-dimensional space (the exterior of a beach ball is a good illustration). Antipodal points are, *e.g.*, the poles of a sphere (Matousek, 2003; Collins, 2004).

We can consider regions on an *n*-sphere that are either adjacent or far apart (**Figure 1B**). This means that pairs of points need not be antipodal, in order to have matching descriptions (Peters, 2016). This BUT variant has utility, provided there are a pair of regions on an *n*-sphere which are *similar*. The concept of antipodal points can be used not just for the description of points, but also for more complicated structures, such as shapes of space (object contours), temporal intervals (temporal oscillations), functions, vectors and symmetries (Borsuk, 1958-59; Borsuk, 1969; Peters, 2014; Tozzi and Peters 2016b) (**Figure 1C**). This leads to a particularly useful region-based BUT, dubbed reBUT (Peters, 2016). We are thus allowed to describe brain features on an *n*-sphere either as antipodal points, or antipodal regions. It means that antipodal signal shapes can be compared (Weeks, 2002; Peters, 2016). That is, feature-based descriptions of antipodes can be assessed at one level of observation, while their projections into a single shape can be analyzed at a lower level (Tozzi and Peters, 2016b).

Although BUT was originally limited to an *n*-sphere where *n* is a natural number, nevertheless *n* can also be regarded as rational or irrational number (Tozzi and Peters, 2016b). For example, we might regard functions or shapes as embedded in a sphere in which *n* stands for number of instants in time. Hence, the parameter *n* becomes useful in the description of dynamical systems such as the brain.

In sum, the BUT displays four versatile ingredients which can be modified in different guises: a continuous mapping, two antipodal (or non-antipodal) points (or functions) with matching description, an *n*-sphere where the *n* value may change and, last but not least, the mapping of antipodal points into the lower level of a *n-1* sphere.

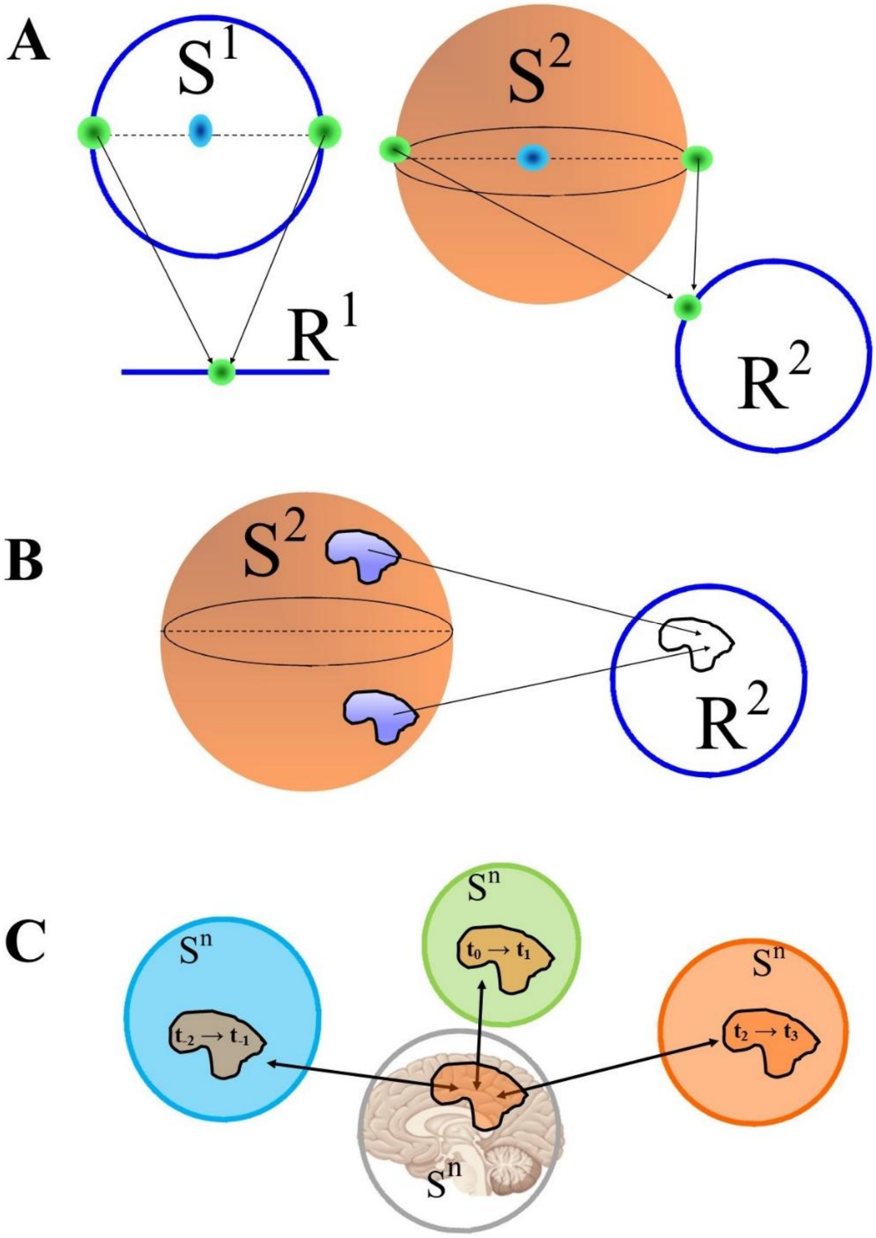

Figure 1A. *The Borsuk-Ulam theorem in case of S^n being a circle and a sphere. Two antipodal points in S^n project to a single point in R^n, and vice versa.* ***Figure 1B.*** *Simplified sketch of a BUT variant. Two functions with matching* *description do not need either to be antipodal (shown here), or embedded in the same n-sphere (shown in* **Figure 1C***), in order to be described together.* ***Figure 1C*** *displays an example of brain oscillations in a topological framework. In this case, the antipodal regions are three temporal intervals, embedded in different spatial n-spheres, which project to the brain surface. Therefore, the concept of similar antipodal signals can be used not just for the description of points or spatial features, but also of temporal sequences. This means that BUT allows us to compare not just motionless points or shapes, but also events.*

2) EXPERIENCE ACQUISITION AT THE INDIVIDUAL LEVEL

Every human individual originally accepts:

a) an ever-changing spatial environment composed of manifold parts dependent on one another,
b) other human individuals making manifold describable statements and
c) these statements are dependent upon the environment.

When an individual becomes aware of some of the manifold parts of the environment outside him, he states he is having an experience. In a topological framework, we embed the environment in an *n*-sphere, the cortical layers in a *n*-Euclidean space and the describable statements in another *n*-sphere (**Figure 2**). The environmental *n*-sphere contains an object detected by the human individual, *e.g.*, manifold parts perceived together, while the other *n*-sphere contains statements which are not simple sounds or noises, but words (or gestures, such as the lacrimal secretions which point to crying or mimic movements) describing the object. A triad is accomplished, where a person is the only one of the three member who is a witness. The object and its verbal counterpart stand for two antipodal points, while their matching description is achieved in the brain of the human individual. It is noteworthy that the topological relationships among the three members do not exist out of the triad (**Figure 3**). We cannot perceive the thoughts and the sensations of other people, but just assign them thoughts and sensations analogous to ours. In topological words, we project our thoughts, emotions and statements to other people embedded in further environmental n-spheres.

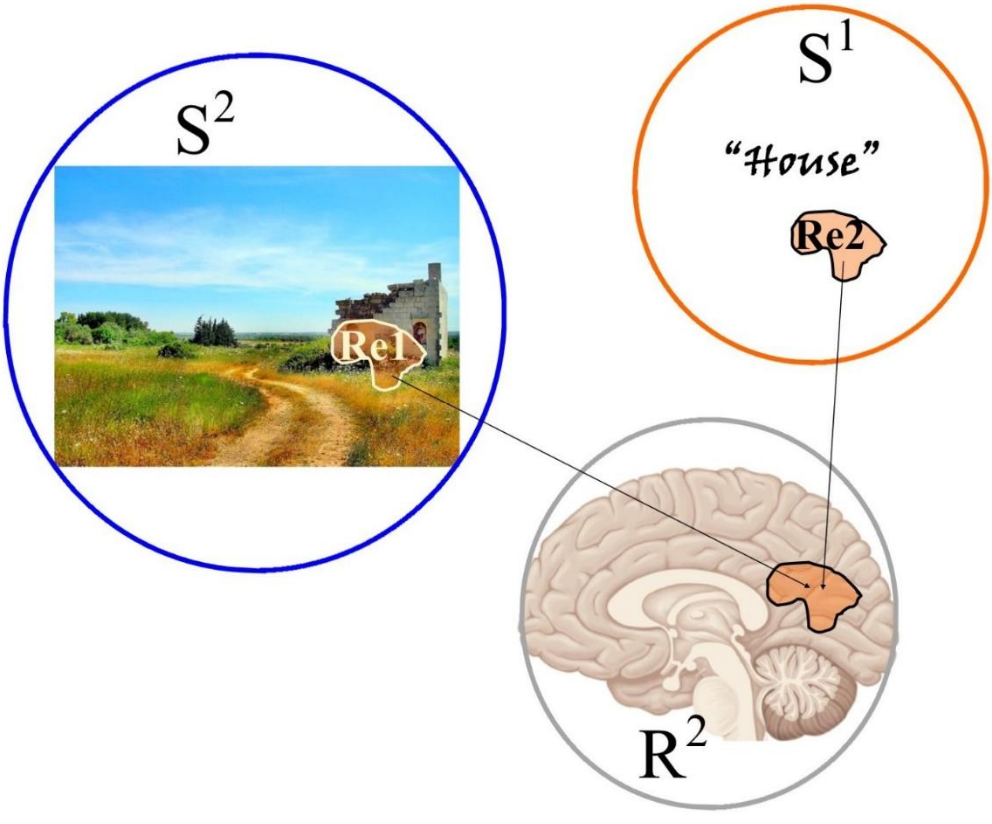

Figure 2*. Topological view of the individual experience evaluated through BUT variants. The environment is embedded in a S^n sphere, where the signal Re1, standing for an object, displays matching description with the signal*

Re2 embedded in a S^{n-1} sphere, standing for the word corresponding to the object. Both Re1 and Re2 project to a single signal, embedded in a manifold R^n, e.g., the brain.

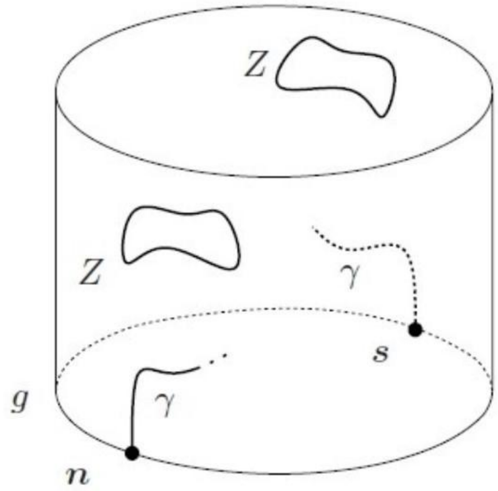

***Figure 3**. The two figures Z with matching description project to the two functions γ on the g plane. It easy to see that the if we follow the two functions γ from n and s on, their ends cannot meet (modified from Matousek, 2003). Likewise, the two figures Z display similar features, but are disjoint.*

Consider two (apparently) interchangeable propositions:

a) if a statement comes from the environment, then the statement is an experience;
b) if a statement is an experience, then the statement comes from the environment.

Indeed, the link between environment and statements is very dynamical. Sometimes, when environment changes, *e.g.*, during a chemo-physical experiment, a variation in statement follows. Other times statements may vary even if environment does not change, and vice versa: *e.g*., over time, a child watching the same figure could detect modifications in the image, or the the same name may refer to different people. Statements may also change due to differences in the cultural background of individuals.
From this, we can ask the following three questions.

1) In what sense does an experience come from the environment?
2) In what sense is a statement an experience?
3) Do these two questions collimate or diverge?

The next Sections will be devoted to the answers of these three questions, via topological tools. The concepts of matter, substance, soul, consciousness, necessity, freedom, reality will not be included in our answers, nor the long-standing issue of causality. Indeed, the topological concept of proximity helps in elucidating the cause-and-effect problem in observing phenomena. Current scientific experience is grounded on the tenets of causality, *e.g.*, the relation between two processes where the first, the cause, is assumed to be responsible for the second, the effect. It is believed that the brain infers the causes underlying sensory events (Parise et al., 2011), or, in other words, is able to understand the causes when just the effects are known. This inferencing is not limited to conscious and high-level cognition, but it is also performed continually and effortlessly in unconscious perception (Körding et al. 2007). We argue that, if we evaluate different spatial and temporal (neural) phenomena in the light of the “sameness” and projections instead of causality, we achieve a novel view of brain events which has the potential to be operationalized and cast in an empirical way. Inference is replaced by affine connections, proximities, mappings and homotopies (i.e., perceived shapes are mapped into others, such as a coffee cup mapped to a torus). This is in touch with some philosophers (Hume, 1739-40) and scientists (Libet et al, 1987; Bengson et al., 2014) who believe that inference is just a trick of the mind, *i.e*., the cause-effect relationships do not exist, but are merely apparent correlations among events dictated by our natural, evolutionary instinct of mental association among conjoined events. In Hume's words, we tend to believe that things behave in a regular manner to the extent that behavior patterns of objects seem to persist into the future, and throughout the unobserved present. Chicharro and Ledberg (2012) noticed that, because subsystems in the brain are often bidirectionally connected (Friston, 2008; Barrett and Simmons, 2015;), it means that interactions rarely should be quantified in terms of cause-and-effect.

3) EXPERIENCE MECHANISMS: BRAIN OSCILLATIONS TOWARDS UNSTABLE ENERGETIC EQUILIBRIA

A *system* is formed of two variables connected in a way such that when one changes, the other changes. The initial state occurs before the variation, the final state afterwards. **Figure 4** provides an example of how a topological formulation of a system allows an objective quantification of empirically testable features. The changes can be either real or merely possible. The final state depends on two settings, namely, the initial state of the system and the external factors acting on the system.

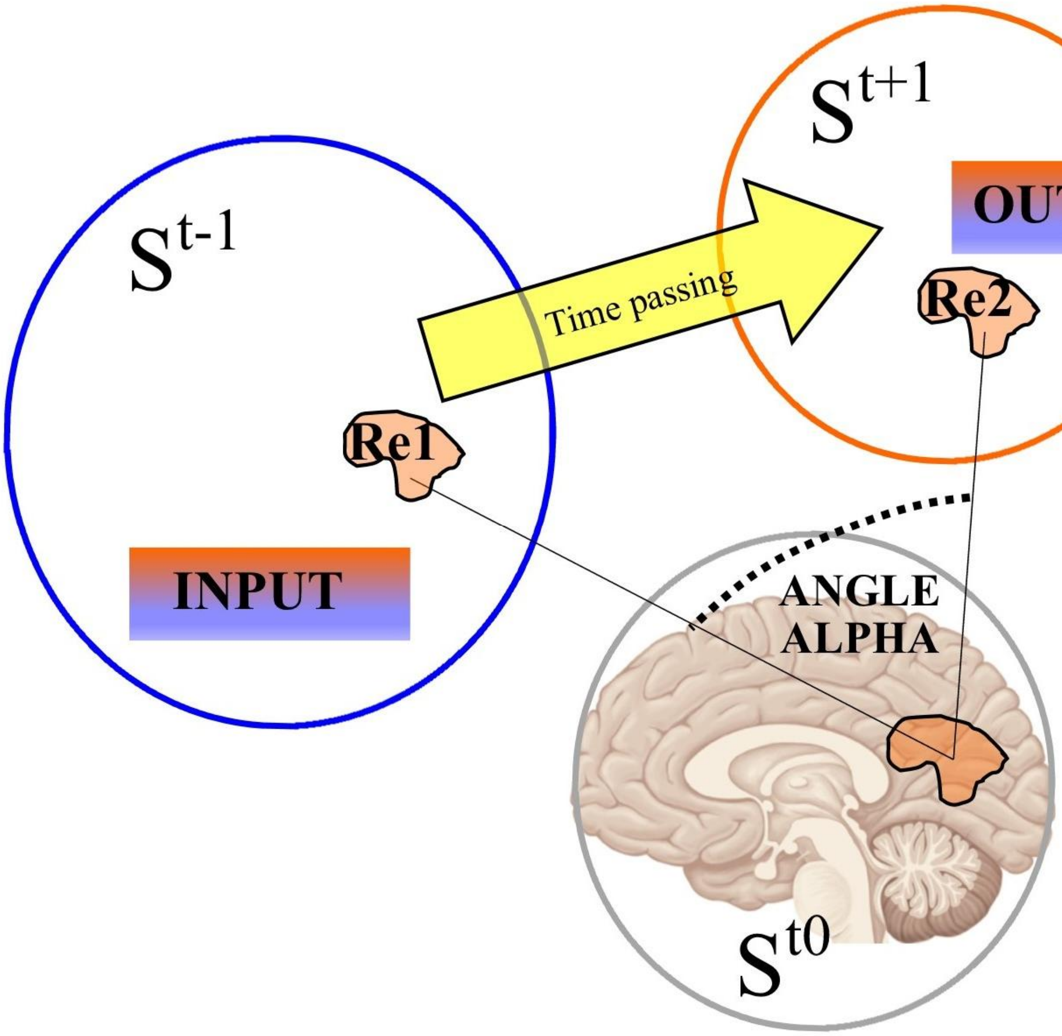

Figure 4*. A system formed by n- spheres made of time dimensions, according to one of the BUT variant. The antipodal regions Re1 and Re2 are located respectively onto a sphere equipped with a dimension of time T-1 (the past) and T+1 (the future). The brain occupies the present time T0. The angle alpha, corresponding to the temporal distance between the presentation of the stimulus and its word retrieval, can be measured. Modified from Tozzi and Peters (2016b).*

The environment of a single individual is also a system that can be divided into spatial and social environments. The environment acts on organisms in two ways, namely, impinging on an organism causing a material change, or stimulating the nerves. A human individual is the source of a peculiar environment, having both non-nervous and nervous systems. The nervous system, in turn, can be divided in peripheral and central nervous system (Nieuwenhuys et al, 2008). The statements made by human beings do not depend on the environment, nor by the peripheral nerves. Indeed, when nerves are damaged, it is still possible to have sensations such as phantom limb syndrome and visual hallucinations during optic nerve atrophy. Is there a part of the CNS which provides a basis for statements? We need not care about the precise anatomical and physiological structure, since experimental evidence has not sufficiently localized brain functions. Therefore, it makes sense to agree that there is a division of functional subsystems in the brain, irrespective of differences in morphological development and functional relationships. From this point forward, the term *brain* refers to unidentified subsystems that are the source of statements.

Acceptance that statements depend on the environment is tantamount to accepting that they depend on the brain and, particularly, on changes in brain. Statements depend on the environment just in the sense that the environment is able to modify the brain. While variations of the environment are studied by the special sciences, we will focus instead on variations of an individual, and in particular, of his brain. Statements do not directly depend on the environment but rather on brain variations. An entire psychical life is a function of self-preservation of the organism within certain limits. The highest levels of conservation are achieved when an energetic equilibrium occurs in the brain between two opposite dynamical forces, namely, brain activity and energy requirements. The brain alternates between these states of equilibrium and breaks into a process that consists of *oscillations* between the two phases, in the deviation from a preliminary value and in approximating to it again. When changes take place, the equilibrium of a brain is disturbed and conditions that annul the changes occur, so that the brain approximates once again to its maximum-maintenance. The functional phenomenon termed brain *oscillation* might encompass different mechanisms, *e.g.*, attractors (Tozzi, Fla, Peters 2016), transient heteroclinic channels (Afraimovich et al., 2013), networks with collective computational abilities (Hopfield 1982; Izhikevich, 2010), nervous oscillators (Zlotnik et al., 2016) and so on. Despite the countless possible scenarios, the processes governing the brain *oscillations* may be generalized, when we take into account the second law of thermodynamics, which states that *every process occurring in nature proceeds in the sense in which the sum of the entropies of all bodies taking part in the process is increased* (Planck's formulation). An issue of central relevance in this context is the *free-energy principle* (FEP) (Friston, 2010). The brain is a self-organizing system at non-equilibrium steady state with its environment (Tognoli and Kelso, 2014) which has to minimize its free-energy, in order to resist a natural tendency towards disorderly state and high entropy. This formulation reduces the physiology of brain to its homeostasis, namely, the maintenance of system states confronted with a constantly changing environment. The brain is regarded as an active inference machine that works according to Bayesian principles: sensory inputs constrain estimates of prior probability from past experience, to create the posterior probabilities that serve as beliefs about the causes of such inputs in the present (Sengupta et al., 2013; Sengupta et al, 2014: Sengupta et al., 2016). The probability of sensory states must have low entropy and, since entropy is also the average self-information or "surprise", the brain implicitly avoids surprises (Friston et al, 2015). Agents suppress free-energy (or surprise) by changing: a) the sensory input, though an action on external states (the environment), or b) their internal brain states, through perception or attention. The imperative to maintain a non-equilibrium steady-state through exchanges with the environment acquires a logical-mathematical framework when evaluated through topological lenses. Indeed, one can regard belief-updating as free-energy minimisation in terms of energetic gradients and information flows (Sengupta et al., 2016) occurring in brain phase spaces embedded in n-spheres. We will be back on the operationalization of this energetic argument in Section five. The concepts of *proximity* (spatial as well as descriptive closeness) and affine connections are also helpful in solving one of the problems raised by *oscillations, e.g.,* how cooperation among so many "distant" sub-networks occurs seamlessly in real time. Thanks to the continuous mapping provided by BUT, we achieve a quantifiable explanation to the speed and balance of a system characterized by hierarchical and cross-hierarchical cooperating modules (Linkenkaer-Hansen et al., 2001).

4) VITAL TRAINS, CHARACTERS, ELEMENTS

In the previous Section, we argued that the elementary physiological processes consist of a state of disturbance of the equilibrium of the brain, followed by a restoration of the difference. All the changes which lie between this beginning and end of a physiological process are termed *vital train.* This is a complex three-stages process. The initial section emerges from a quiet state in which the oscillation, *e.g.*, a disturbance which breaks the equilibrium, is introduced. Follows then an intermediate section, where compensation mechanisms are activated via variations counteracting the oscillations. The final state is such that the oscillation is suppressed, with return to the quiet and maximum preservation state. The removal of the alteration, in order to achieve the highest level of conservation, may occur in two ways, namely, return to the original stable state or to a different stable state. Here we give an example which illustrates how mental life is arranged in three sections. At start, there is the expected value, stated by the individual as sure, true, known. When a statement is perceived as the same, long chains of oscillations lead to *all together*, *always*, *everywhere*, progressively reaching more general concepts. When the *identical* becomes a rule, the rules become laws and the truths become sure, existing, while the *different* becomes exception. Then enters a variation, stated as different, diverging, doubtful, unexpected. It comes together with the feeling of pain, opposition, or uncertainty, dissatisfaction. The second, following section is an effort to suppress the anomaly: the brain strives to remove the unpleasant experience. In touch with FEP, variations can be removed either through peripheral action (practical behavior), or through brain action (theoretical behavior). There are two ways to suppress the variations: (1) reduction of the unknown to the known; (2) gradual habituation to a change, so that the unknown becomes known. In the fifth Section we will describe how topology helps in elucidating these ways to suppress variations. A value is achieved in the final section which leads to feelings of rest, satisfaction, certainty, truth and quiet. It must be stressed that each statement is influenced by type and magnitude of an individual's background (Betzel et al., 2014). Although every vital train of thoughts ends with phase three, the ideal equilibrium of the brain can be never achieved, due to the continuous dynamics of infinite, superimposed, cross-linked, hierarchical vital trains. Indeed, the brain operates at the edge of chaos and tends to live near a metastable state of second-phase transition (Papo, 2014; Deco and Jirsa, 2012; Beggs and Timme, 2012; de Arcangelis and Herrmann, 2010). In other words, the brain displays nonlinear dynamics. As we will see in Section five, BUT and its variants give us the possibility to achieve linear dynamics from nonlinear ones.

A vital train is a process that progressively removes useless terms, approximating to the final pure stages equipped with: a) minimum energy and maximum stability, b) higher spatial and temporal unrestriction. The evolution of vital trains is towards more perfect series, *i.e.*, the lowest energetic basins, where the gradient descent values can be calculated by comparing angles between n-spheres.

The role of habituation and its changes is crucial, because they give rise to the *identity* and the *difference*. The more the same oscillation is repeated, the more the sensation is perceived as usual, and the same, certain, the known, the familiar. In an energetic context, habituation stands for the state equipped with the lowest possible energy (Tozzi et al., 2016). The final state of the brain is a physiological configuration which is unvaried towards every changing component of the environment. However, this final state embeds not just the final pure state, but also other accidental factors, which need to be progressively abolished. This occurs because minimal energy is difficult to reach. The answer to the first question in Section 2 is thus the following: the environment is at the base of the experience just in case it leads to variations in the individual brain, and just in case a statement depends on environmental variations. However, such values are valid just for a given individual, in a given moment: the individual final state varies from individual to individual, and also from place to place and from epoch to epoch (Barttfeld et al., 2015; Gorgolewski et al., 2014; Vuksanovic and Hövel, 2014).

In sum, the general scheme is the following: when an individual makes a statement, a change in oscillations occurs in brain. The statements depend upon the characteristics of the physiological variations in brain and its oscillations. Of utmost importance is the sensation of prevalence and perception of finer details (discrimination), in which some sensations are highlighted by the attention, compared with the faded background sensations. In topological terms, the prevalence plays an important role in deciding which parts of the environmental n-sphere must be taken into account: it means that the brain chooses from the external inputs the complex of elements of biological significance and marks them as *signals*. A possible role for visual attention and prevalence in an energetic gradient descent context has been recently hypothesized (Sengupta et al., 2016). Consciousness can be linked to our first BUT ingredient, namely, a continuous mapping. Indeed, brain activity needs continuous inputs from a source of enduringly active neurons. The ascending arousal system is a good candidate, because it contains tonic active neurons which guarantee a continuous electric stream towards the cortex, at least during alertness (Nieuwenhuys et al., 2008). In such a framework, consciousness stands both for physiological tonic neurons and for the continuous mapping required by BUT.

Human statements can be partitioned into characters (qualifications like pleasant, nice, beneficial, unpleasant) and elements (such as green, cold, hard, sweet). The difference between characters and elements is that the former are mutable and can be defined as forms, while the latter are permanent and can be defined as contents. At first, we examine experience regarded as character, *i.e.* the variable form (emotions, sensations, perceptions and so on), in which we experience anything. The question is not what individuals mean by an experience, but rather what individuals state is an experience. Many examples can be listed in which statements are referred as experience, *e.g.*, the appearance of the sun, perceived temporal relationships among events, the difference between sleep and arousal, travel in far countries during dreams, miracles, presages of death, causal connections, footprints of animals, calculations and mathematical theorems. So, what is an experience? Is it always linked to the external environment? Does it refer to entities, or simply to the cognition of their existence, or is it pure cognition without existence? No one of the solutions proposed in answer to these questions is satisfactory, because experience cannot be defined in only in one way. The individual simply bumps into the components of the environment, and then describes what he has encountered. When a little girl states that she has seen angels, then the angels are an experience for her. The individual who states "it is an experience", is equivalent to coalescing a plurality of single perceptions, explainable thanks to BUT and its variants.

Thus, a better although incomplete definition of experience could be: *something perceived.* Also the ego, the I, is a statement, in which perception is felt as the individual's own perception. The more an observable and the individual are separated, the more the observable is perceived as active and a factum of experience, while the individual perceives selfhood as a passive percipient. Now we evaluate experience regarded as content, *i.e*., everything which is felt, sensed, perceived and so on. When individuals state they have an experience, what is the content of their experience? That content depends on modifications in the brain and on the current state and education of each individual. Regardless whether statements are about existing or non-existing entities, all the values perceived in a given moment as experience are indeed the content of experience, and may vary with individual changes. The answer to the second question raised in Section 2 is thus the following: experience, in a narrower definition, is the perception from the brain's standpoint of the things extracted from the environment. A wider definition of experience does not involve things, but ideas. Ideas can also appear to be about existing, simply there or given entities, so that, even if a centaur is not an experience, its idea is an experience. Thus, a *continuous* flow occurs from the perceived thing (the narrower concept of experience) to the represented idea (the wider concept of experience). *Continuos*, in touch with one of the BUT ingredients.

5) EXPERIENCE TRANSMISSION AT INTER-INDIVIDUAL LEVELS

Brains of different individuals join together in higher order systems formed by social assemblies. The whole mass of human experience tends to become adapted as much as possible to the surrounding world. Humanity stands, as a whole, for a kind of ultra-human organism, following the same basic rules of self-preservation of the individual. When the geographical and social environment widens to include the entire Earth surface and all mankind, the brain removes the accidental factors via a process of progressive elimination. However, due to the differences of initial conditions among individuals, the ideas achieved in the third section could lead, after a while, once again from a known to an unknown. The ultimate suppression of variations occurs via the search for universal laws. Over time, individuals and the generations project faster, simpler and unavoidable concepts. This ongoing conceptualization of our experience is an approximation process that always tends towards identical highly generalized, unlimited concepts characterized by simple, complete descriptions, by qualitative differences expressed in many ways and by formal equivalences expressed in different forms.

The highest concepts, i.e. the final states corresponding to all the possible environment manifold parts, are equipped with the maximum possible frequency and embrace all the possible historical contents of the statements. For a topological explanation, see **Figure 5A**. Godel's suggestion of abstract terms more and more converging to the infinity in the sphere of our understanding take us straight to a comparison with systems equipped with BUT antipodal points and regions. The highest concept, expressed by the statement the *whole is this* is the *concept of the world* (e.g., an abstract idea). In terms of BUT, we achieve a progressive symmetry decrease. Starting from the countless symmetries endowed in the environment, we accomplish into the brain their substantial decrease (Tozzi and Peters, 2016b).

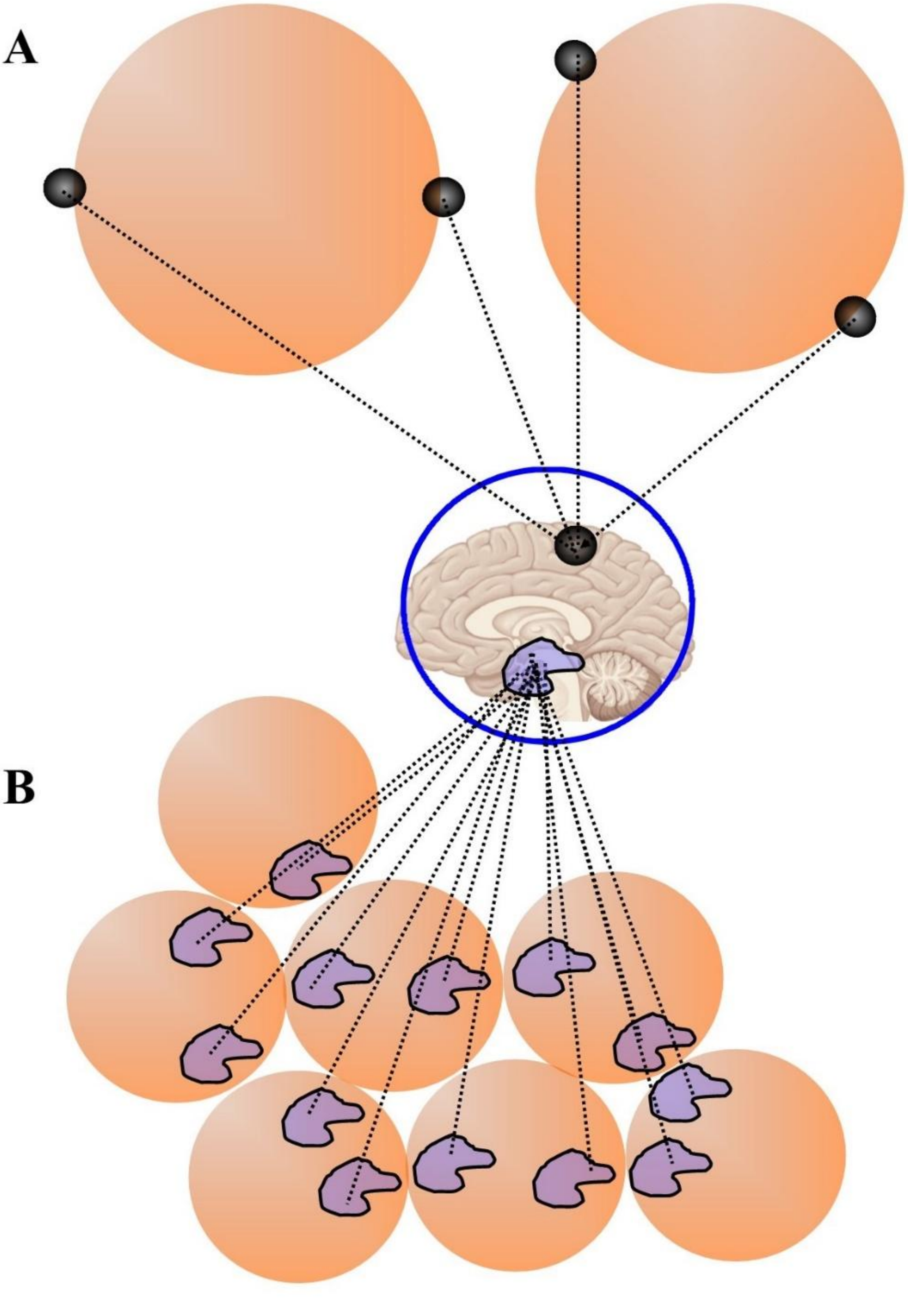

Figure 5. *Convergence of n-spheres' antipodal points with matching description.* ***Figure A****: the ideas (abstractions) link together antipodal points embedded in different environmental n-spheres. Their projections to the brain give rise to abstract concepts.* ***Figure B****: the final, pure abstractions encompass countless different matching functions from different, closely packed, environmental n-spheres.*

However, the concept of the world still embraces more general concepts as well as superfluous ones. Indeed, many different conceptualizations of the world result from genetic constraints, social groups and historical background. The concepts of the world are still incomplete, because they also include unnecessary components and their historical development has not ended at this time.

The concept of the world is preserved by individuals and left to posterity via communication and conditioning. If a concept is transmitted unchanged over generations, its strength decreases with the time due to habituation, until it cannot be recognized anymore. The transformation of the concepts of the world leads from certainty to doubts about them. Thus arises the *enigma* of the world, in place of the concept of the world. Confronted with the enigmas of our environment, the more perplexity increases, the more urgent is the need to solve the problems as soon as possible and several new different satisfying concepts of the world may arise. Solutions are however transitory and changing with the time, both within individuals and communities. Every concept of the world is characterized by residual unneeded concepts, depending on the education of the individuals. The number of superfluous concepts may either remain the same, or decrease, or increase. Provisional solutions to the enigma of the world are countless and the only way to find more general concepts is to expunge the surplus components. The more the concept of the world is spatially enlarged, the more the solution is general and definitive, approximating an exclusive experience. Increasingly over space and time, concepts of the world tend towards the higher level concepts and the brain is satisfied. During cultural evolution, the concepts of the world are at first regarded as a positive experience, a perceived thing, an empiric experience. However, in a following phase of removal, they weaken and are regarded as non-empirical experience, pseudo-problems, until they gradually vanish and disappear. The last phase is their reappearance in a distilled form, just as pure descriptions (**Figure 5B**). More mature, pure concepts of the world allow the brain to be entirely conditioned by the environment and mature statements are regarded as complete experience. There is an answer to the third question raised in Section 2. That is, a primitive experience (experience=naturally perceived) leads to addition of non-experience (either experience=perceived and experience=not perceived) until a definitive, just described, exclusive experience takes place (experience=purified perceived). More advanced social groups, *e.g.,* scientists, may be closer than others to pure concepts of the world, at least in some fields of experience. Indeed, evolution does not proceed linearly nor uniformly. Small groups of individuals have an important role in pushing forward changes that lead to possible solutions of the problems.

6) WHY BRING TOPOLOGY INTO THE ASSESSMENT OF EXPERIENCE?

The question here is: what does a topologic reformulation add in the evaluation of the nervous processes of experience? BUT and its extensions provide a methodological approach which makes it possible for us to study experience in terms of projections from real to abstract phase spaces. The importance of projections between environmental spaces, where objects lie, and brain phase spaces, where mental operations take place, is also suggested by a recent paper, which provides a rigorous way of measuring distance on concave neural manifolds (Sengupta et al., 2016). The real, measurable nervous activity can be described in terms of paths occurring on n-spheres. It leads to a consideration of affinities among nervous signals, characterized as antipodal points on multi-dimensional spheres embedded in abstract spaces. To provide an example, **Figure 4** shows how embedding brain activities in n-spheres allows the quantification of geometric parameters, such as angles, lengths, and so on, that could be useful in neuroimaging data optimization. BUT and its ingredients can be modified in different guises, in order to assess a wide range of nervous functions. Although this field is nearly novel and still in progress, with several unpublished findings, we may provide some examples. Such a methodological approach has been proved useful in the evaluation of brain symmetries, which allow us to perform coarse- or fine-grained evaluation of fMRI images and to assess the relationships, affinities, shape-deformations and closeness among BOLD activated areas (Tozzi and Peters, 2016b). Further, BUT has been proved useful in the evaluation of cortical histological images previoulsy treated with Voronoi tessellation (Peters et al., 2016).

A wide range of brain dynamics, ranging from neuronal membrane activity to spikes, from seizures to spreading depression (Wei; Bernard; Richardson), lie along a continuum of the repertoire of the neuronal nonlinear activities which may be of substantial importance in enabling our understanding of central nervous system function and in the control of pathological neurological states. Nonlinear dynamics are frequently studied through logistic maps equipped with Hopf bifurcations, where intervals are dictated by Feigenbaum constants. Tozzi and Peters (2016b) introduced an approach that offers an explanation of nervous nonlinearity and Hopf bifurcations in terms of algebraic topology. Hopf bifurcation transformations (the antipodal points) can be described as paths or trajectories on abstract spheres embedded in n-spheres where n stands for the Feigenbaum constant's irrational number (Kim; Schleicher). Although the paper takes into account just Hopf bifurcations among the brain nonlinear dynamics, this is however a starting point towards the "linearization" of other nonlinear dynamics in the brain. In sum, BUT makes it possible for us to evaluate nonlinear brain dynamics, which occur during knowledge acquisition and processing, through much simpler linear techniques.

BUT and its variants are not just a *methodological* approach, but also display a *physical*, quantifiable counterpart. To make an example, although anatomical and functional relationships among cortical structures are fruitfully studied, *e.g.*, in terms of dynamic causal modelling, pairwise entropies and temporal-matching oscillations (Friston, 2010; Watanabe et al., 2014), nevertheless *proximity* among brain signals adds information that has the potential to be operationalized. For example, based on the ubiquitous presence of antipodal cortical zones with co-occuring BOLD activation, it has been recently suggested that spontaneous brain activity might display donut-like trajectories (Tozzi and Peters 2016a).

BUT allows the evaluation of energetic nervous requirements too. There exists a physical link between the two spheres S^n and S^{n-1} and their energetic features. When two antipodal functions a n-sphere S^n, standing for symmetries, project to a *n*-Euclidean manifold (where S^{n-1} lies), a single function is achieved and a symmetry break occurs (Tozzi and Peters 2016b). It is known that a decrease in symmetry goes together with a decrease in entropy. It means that the single mapping function on S^{n-1} displays energy parameters lower than the sum of two corresponding antipodal functions on S^n. Therefore, in the system S^n and S^{n-1}, a decrease in dimensions gives rise to a decrease in energy. We achieve a system in which the energetic changes do not depend anymore on thermodynamic parameters, but rather on affine connections, homotopies and continuous functions. A preliminary example is provided by a recent paper, where BUT allows the detection of Bayesian Kullback-Leibler divergence during unsure perception (Tozzi and Peters, 2016b).

CONCLUSIONS

In conclusion, we have provided a topological approach to experience features which makes it possible to evaluate the interactions among environment, brain and human statements. A shift in conceptualizations is evident in the BUT approach. The interaction of neural signals is described in terms of *sameness, closeness* and their *feature value vectors* (*e.g.*, amplitude, duration, and so on). The invaluable opportunity to treat elusive mental activities in terms of topological structures makes it possible for us to describe experience in the language of powerful analytical tools. Embracing the approach provided by BUT and its variants in characterizing brain interactions means that the *real* neuronal activity can be described as paths or trajectories on *abstract* structures. This takes us into the realm of computational topology, a realm endowed with abstract metric spaces, *e.g.* projections of environmental spaces into geometric ones. It supplies us with richly sufficient statistics, that helps us to elucidate the mechanisms of human experience.

We conclude with a methodological remark. The symbolic logic approach to scientific experience, prevailing in the beginning of the twentieth century after Whitehead and Russell's influential book (1910) and the rise of logical positivism, was dismissed in the following decades. Our novel approach is paradoxically a return to the past, because it leads once again to emphasize the old weapons of logic thinking as methodologies able to inspire scientists in their experimental evaluation of physical/biological counterparts of human experience.

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TOPOLOGY UNDERLYING GIBSON'S ECHOLOGICAL THEORY OF PERCEPTION

(a topological/ecological theory of perception)

During the exploration of the surrounding environment, the brain links together external inputs, giving rise to perception of a persisting object. During imaginative processes, the same object can be recalled in mind even if it is out of sight. Here, Borsuk's theory of shape and the Borsuk-Ulam theorem provide a mathematical foundation for Gibson's notion of persistence perception. Gibson's ecological theory of perception accounts for our knowledge of world objects by borrowing a concept of invariance in topology. A series of transformations can be gradually applied to a pattern, in particular to the shape of an object, without affecting its invariant properties, such as boundedness of parts of a visual scene. High-level representations of objects in our environment are mapped to simplified views (our interpretations) of the objects, in order to construct a symbolic representation of the environment. The representations can be projected continuously to an ecological object that we have seen and continue to see, thanks to the mapping from shapes in our memory to shapes in Euclidean space.

Theoretical physics teaches us that the intimate micro-structure of the world consists of elements in perpetual movement, interacting with each other in a framework of probabilities, energy fields and vacuum. However, when we see a segment in a visual scene in the environment, we perceive elements seemingly melted together in a single complex of sensations. To make an example, we are able to detect, in the indistinctness of a rural scene at sunrise time, an increasingly distinct world of trees, hills, valleys and moving particles, e.g., birds flying from one tree to another. In effect, we appear to be sewing pieces of a changing scene together. How does the brain join different significant elements, giving rise to a single, stable perception of a scene? How does the brain imagine or recall objects that are out of sight? These two problems need to be tackled not at the microscopic atomic or sub-atomic level, nor at the galactic level, but at an intermediate macroscopic level where living beings stand. A noteworthy approach to understanding the mechanisms of direct perception is to start at the ecological level. Indeed, this article introduces a shape-based explanation of J.J. Gibson's theory of persistence perception (Gibson, 1950). Throughout the second half of the twentieth century, James J. Gibson (1966, 1971, 1979) developed a unique theory in perceptual science, namely the ecological theory of perception (ETP), which stresses the importance of the relationships of the individual and the environment (Heft, 1997). The foundation for perception is ambient, ecologically available, direct information, as opposed to peripheral or internal sensations. The human (and/or animal) individual is embedded in the surrounding environment and the perception is strictly linked to searching movements, because changing awareness of the connectedness of the components of a scene occurs *in situ*, and not in a static context. The environment contains real, perceivable opportunities (called “affordances”) for an individual’s actions. Affordances are properties of the perceived environment (Gibson, 1979; Gibson, 1986; Lu, 2013) that provide paths to merged structures, shapes and actions. For example, the more chances children are given to directly perceive and interact with their environment, the more affordances they discover, and the more accurate their perceptions become over the passage of time. –Perceiving is essentially exploratory (Heft, 1997). It consists in the acquisition of objective knowledge, by assembling diverse views of an object to form its abstract representation. In effect, a perceptual system is formed by vision, movements of the eyes, head and entire body. Gibson argued that perception of persisting surfaces depends on the perception of specific structures, invariant over time.   Recognition (perceiving) objects entails continuous mappings between our representations of objects and in-the-world ones. In effect, perception can be explained by our discovery of equivalent configurations (form, shapes) of objects (Heft 1997; Rock, 1983).

Visual information is carried in two separate pathways in our brain (Mishkin et al., 1983). Visual identification of objects is enabled by the multisynaptic corticocortical ventral pathway, which interconnects the striate, prestriate, and inferior temporal areas. On the other side, visual location of objects is made possible by the dorsal pathway, which runs dorsally, interconnecting the striate, prestriate, and inferior parietal areas. Therefore, the visual system separates processing of an object’s form and color (“what”) from its spatial location (“where”) (Rao et al., 1997).   Recent findings suggest that nervous structures process information through topological as well as spatial mechanisms. For example, it is has been hypothesized that hippocampal place cells create topological templates to represent spatial information (Dabaghian, 2014; Arai, 1014; Chen, 2014). Developments in studies which consider the role of embodied cognition and action in psychology can be seen to support this basic position about hippocampal place cells. In particular, in this article, we show that novel incarnations of the “classical” Borsuk-Ulam theorem lead to a better comprehension and assessment of several features of direct perception and imagination.

BORSUK-ULAM THEOREM AND ITS VARIANTS

Borsuk-Ulam theorem. Topology, which assesses the properties that are preserved through deformations, stretchings and twistings of objects, is a underrated methodological approach with countless possible applications (Willard, 1970; Krantz, 2009; Manetti, 2015). The Borsuk-Ulam theorem or BUT, cast in a quantitative fashion which has the potential of being operationalized, is a universal principle underlying a number of natural phenomena. In particular, we will show that BUT and its variants allow the assessment of perceptual features in terms of affinities and projections from real spaces to representations in feature spaces. It is noteworthy that BUT and its variants talk about projections, connections, not about cause-and-effect relationships (Tozzi and Peters, 2016a). Briefly, BUT states that, if a single point on a circumference projects to a higher spatial dimension, it gives rise to two antipodal points with matching description on a sphere, and vice versa (**Figure 1A**) (Borsuk, 1933; Marsaglia, 1972; Matoušek, 2003; Beyer, 2004). This means that the two antipodal points are assessed at one level of observation in terms of description, while a single point is assessed at a lower level (Tozzi 2016b), i.e., point location vs. point description.   Points on a sphere are “antipodal”, provided they are diametrically opposite (Henderson, 1996). Examples of antipodal points are the poles of a sphere. This means, e.g., that there exist on the earth surface at least two antipodal points with the same temperature and pressure. BUT looks like a translucent glass sphere between a light source and our eyes: we watch two lights on the sphere surface instead of one. But the two lights are not just images, they are also real with observable properties, such as intensity and diameter.

Variants of the Borsuk-Ulam theorem. The concept of antipodal points can be generalized to countless types of system signals. The two opposite points can be used not just for the description of simple topological points, but also of lines, or perimeters, areas (**Figure 1B**), regions, spatial patterns, images, temporal patterns, movements, paths, particle trajectories (**Figure 1C**) (Borsuk, 1969; Peters and Tozzi, 2016b), vectors (**Figure 1D**), tensors, functions (**Figure 1E**), algorithms, parameters, groups, range of data, symbols, signs, thermodynamic parameters (**Figure 1F**), or, in general, signals. If we simply evaluate nervous activity instead of “signals”, BUT leads naturally to the possibility of a region-based, not simply point-based, brain geometry, with many applications. A region can have indeed features such as area, diameter, illumination, average signal value, and so on. We are thus allowed to describe system features as antipodal points on a sphere (Weeks, 2004; Peters, 2016).

Descriptively similar points and regions do not need necessarily to be opposite, or on the same structure (**Figures 2A** and **2B)** (Peters, 2016; Peters and Tozzi 2016a).   Therefore, the applications of BUT can be generalized also on non-antipodal neighbouring points and regions on an sphere. In effect, it is possible to evaluate matching signals, even if they are not “opposite”, but “near” each other. As a result, the antipodal points restriction from the “standard” BUT is no longer needed, and we can also consider regions that are either adjacent or far apart.   And this BUT variant applies,

provided there are a pair of regions on the sphere with the same feature value. We are thus allowed to say that the two points (or regions, or whatsoever) do not need necessarily to be antipodal, in order to be labeled together (Peters 2016).
The original formulation of the BUT describes the presence of antipodal points on spatial manifolds in every dimension, provided the manifold is a convex, positive-curvature structure (*i.e*, a ball). However, many brain functions occur on manifolds endowed with other types of geometry: for example, the hyperbolic one encloses complete Riemannian *n*-manifolds of constant sectional curvature -1 and concave shape (*i.e*, a saddle) (Sengupta et al., 2016). We are thus allowed to look for antipodal points also on structures equipped with kinds of curvature other than the convex one (**Figure 2C**) (Mitroi-Symeonidis, 2015). Or, in other words, whether a system structure displays a concave, convex or flat appearance, does not matter: we may always find the points with matching description predicted by BUT (Tozzi, 2016). A single description on a plane can be projected to higher dimensional donut-like structures (**Figure 2D**), in order that a torus stands for the most general structure which permits the description of matching points. For further details, see Peters and Tozzi (2016b).
Although BUT has been originally described just in case of *n* being a natural number which expresses a structure embedded in a spatial dimension, nevertheless the value of *n* in the brain sphere can also stand for other types of numbers. The BUT can be used not just for the description of "spatial" dimensions equipped with natural numbers, but also of antipodal regions on brain spheres equipped with other kinds of dimensions, such as a temporal or a fractal one. This means, e.g., that spherical structures can be made not just of space, but also of time. The dimension *n* might stand not just for a natural number, but also for an integer, a rational, an irrational or an imaginary one. For example, *n* may stand for a fractal dimension, which is generally expressed by a rational number. This makes it possible for us to use the *n* parameter as a versatile tool for the description of systems' features.
Furthermore, matching points (or regions) might project to lower dimensions on the same structure (**Figure 3A**). A sphere may map on itself: the projection of two antipodal points to a single point into a dimension lower can be internal to the same sphere. In this case, matching descriptions are assessed at one dimension of observation, while single descriptions at a lower one, and vice versa. Such correlations are based on mappings, e.g., projections from one dimension to another. In many applications (for example, in fractal systems), we do not need the Euclidean space (the ball) at all: a system may display an intrinsic, *internal* point of view, and does not need to lie in any dimensional space (Weeks, 2002). Therefore, we may think that the system just does exist by - and on – itself.

The foremost role of symmetries. Symmetries are real invariances that underline the world and occur at every level of systems' organization (Weyl, 1982). Bilinear forms of geometrical structures manifest symmetrical properties (Weyl, 1918). In other words, affine structures preserve parallel relationships. Symmetries are the most general features of mathematical, physical and biological entities and provide a very broad approach, explaining also how network communities integrate or segregate information. It must be emphasized that symmetries are widespread and may be regarded as the most general feature of systems, perhaps more general than free-energy and entropy constraints too. Indeed, recent data suggest that thermodynamic requirements have close relationships with symmetries. The interesting observation that entropy production is strictly correlated with symmetry breaking in quasistatic processes paves the way to use system invariances for the estimation of both the free energy of metastable states, and the energy requirements of computations and information processing (Roldán, 2014). Thus, giving insights into symmetries provides a very general approach to every kind of systems function. A symmetry break occurs when the symmetry is present at one level of observation, but "hidden" at another level. A symmetry break is detectable at a lower dimension of observation (**Figure 3B**). Thus, we can state that single descriptions are broken (or hidden) symmetries, while matching descriptions are restored symmetries. In other words, a symmetry can be hidden at the lower dimension and restored when going one dimension higher. If we assess just single descriptions, we cannot see their matching descriptions: when we evaluate instead systems one dimension higher, we are able to see their hidden symmetries. In sum, symmetries, single descriptions and matching descriptions are the common language among different real sciences.

In sum, BUT displays versatile formulations that can be modified in different guises, in order to achieve a wide range of uses in neuroscience, such as multisensory integration, neural histological images tessellation, brain symmetries, Kullback-Leibler divergence during perception, detection of a brain functional 3-sphere. For further details, see Tozzi (2016a and 2016b). In the next paragraphs, we will focus on the role of BUT and its variants in direct perception and object recalling, taking into account Gibson's incisive observations.

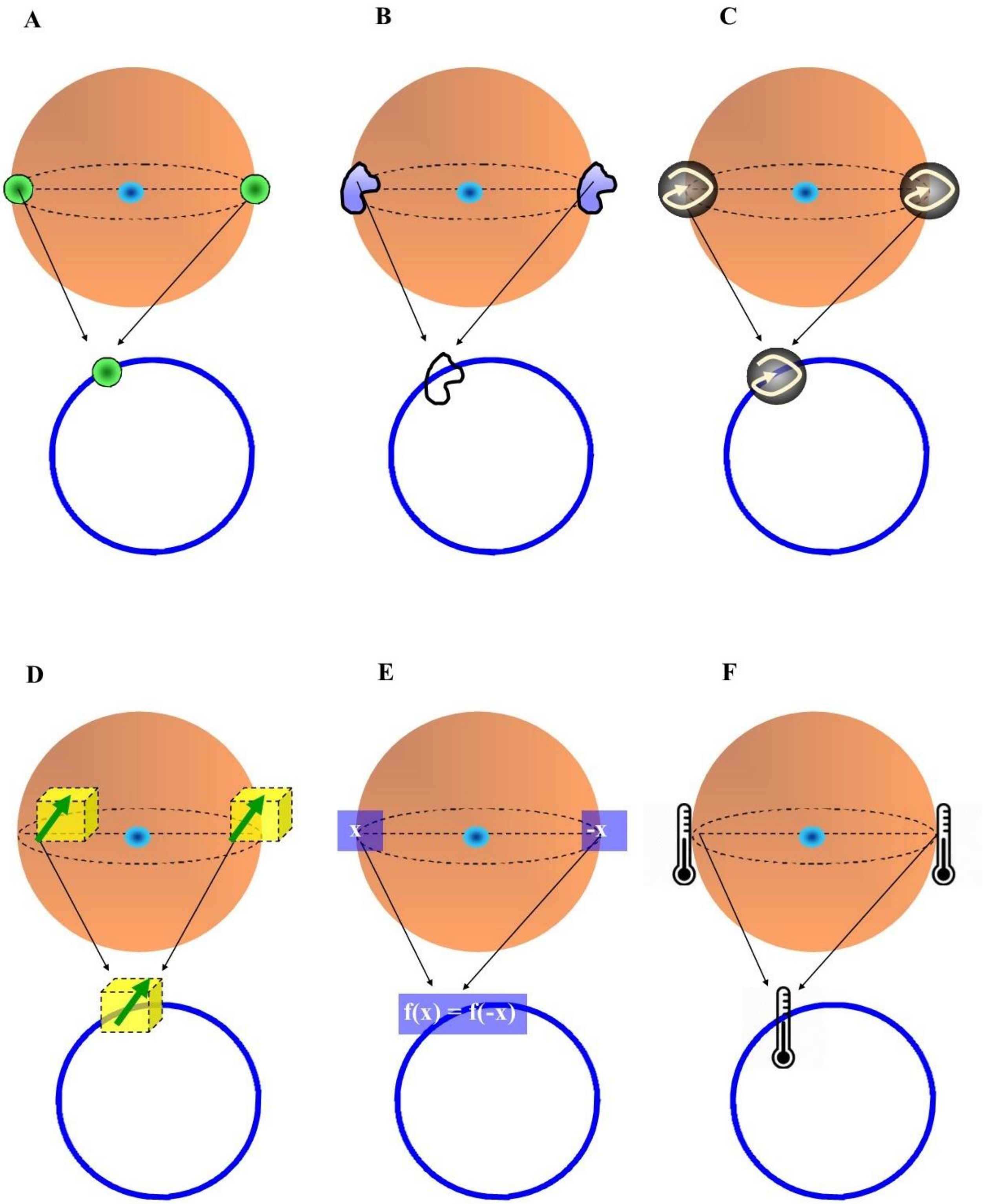

Figure 1. Possible types of antipodal features in Borsuk Ulam theorem (BUT). The original formulation of the BUT, with two antipodal points, is illustrated in **Figure 1A**. **Figures 1B-1F** display, respectively, two antipodal shapes, trajectories, vectors, functions and temperatures. Each set of antipodal features on a sphere stands for a single feature on a circumference, if we evaluate it just one dimension lower.

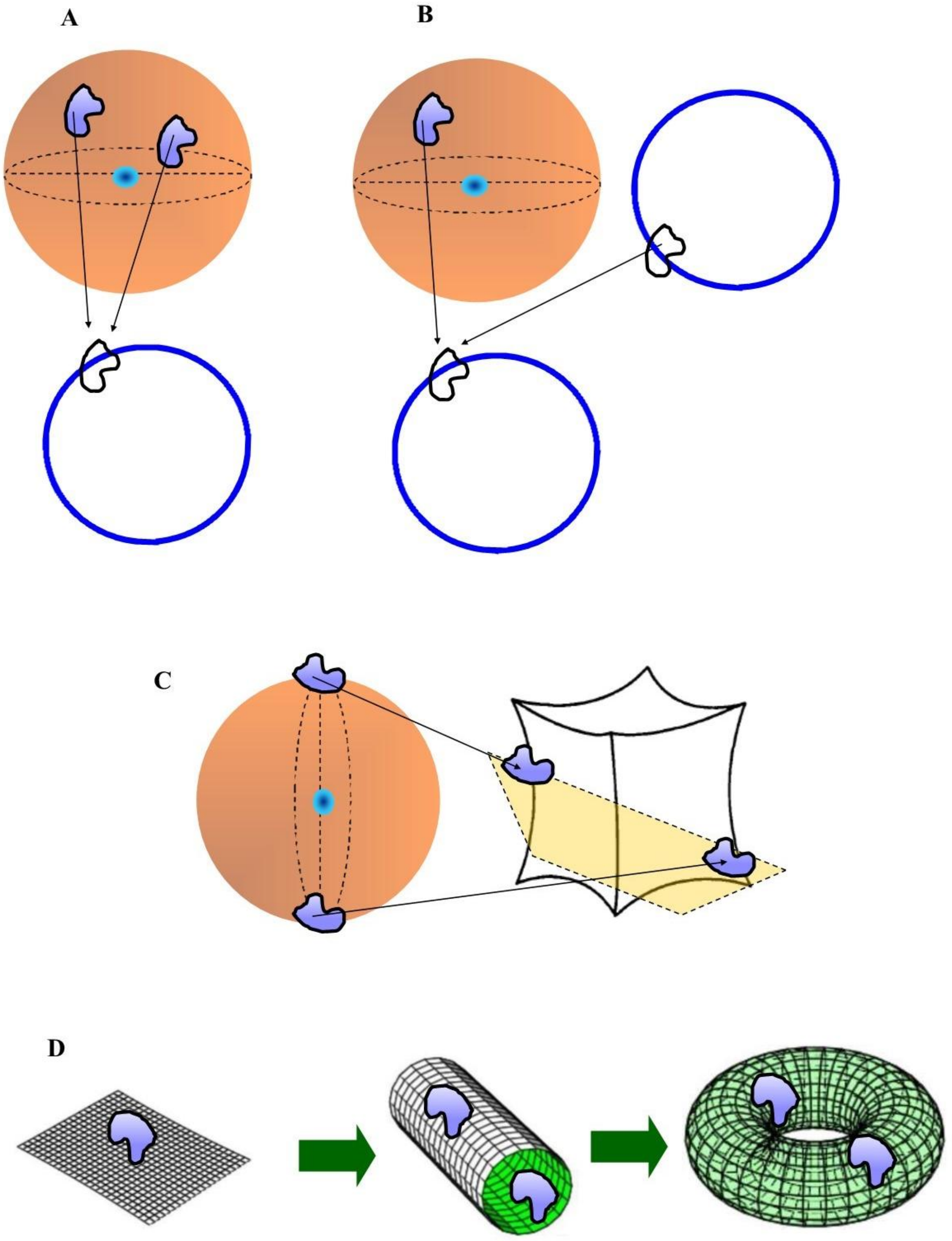

Figure 2. Two features with signal matching do not need necessarily to be antipodal. Indeed, the applications of the BUT can be generalized also on non-antipodal points on the same sphere (**Figure 2A**), of non-antipodal points lying on two different structures (**Figure 2B**). **Figures 2C** and **2D**: BUT applies for structures with different types of curvatures. See the main text for further details.

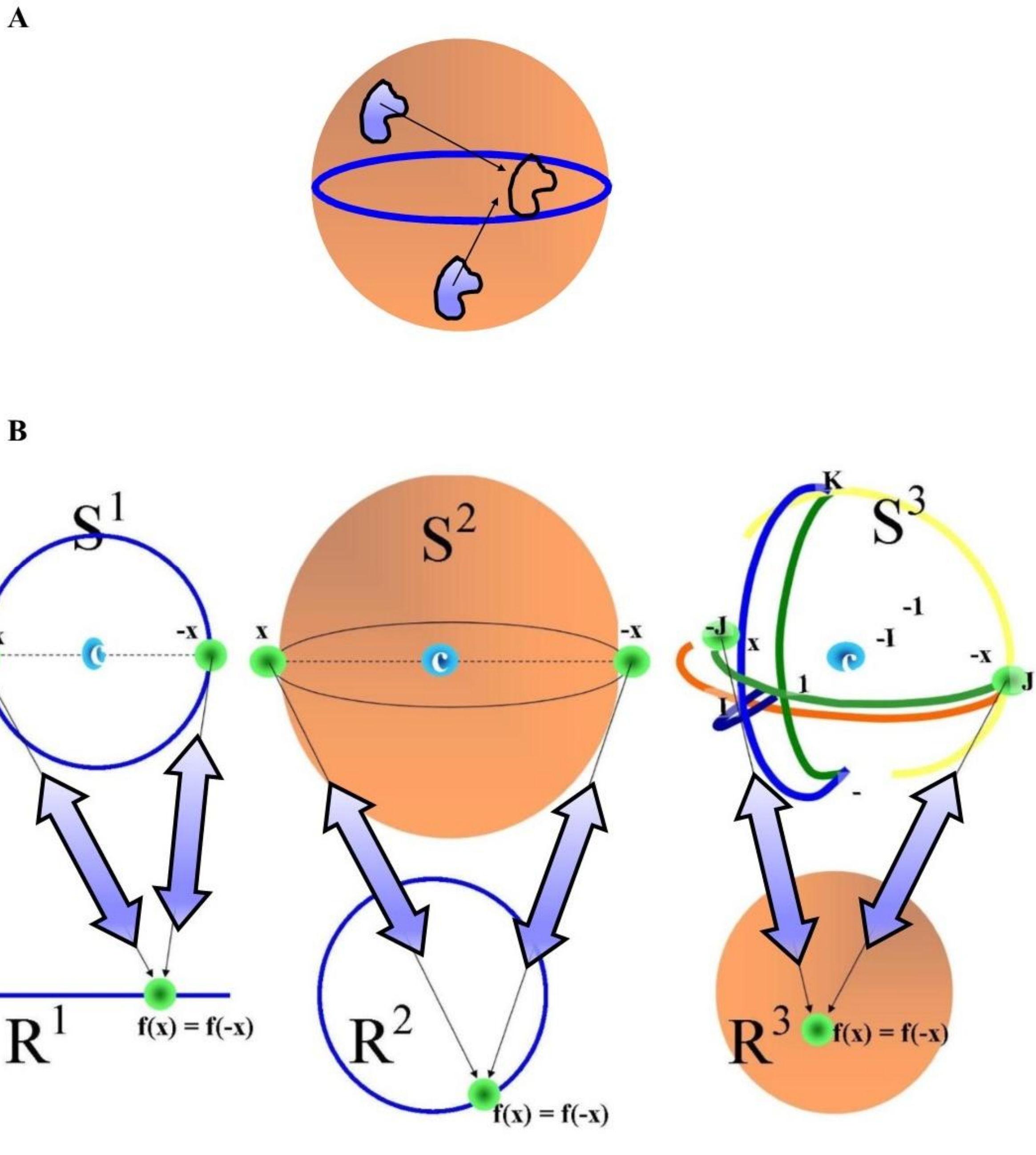

Figure 3A shows how a sphere may map on itself. See the main text for further details. **Figure 3B** displays the BUT acting on structures of different dimensions: a 2-D circle, a 3-D sphere and a 4-D hypersphere. A symmetry, e.g., two antipodal points in higher dimensions, is said to be "broken" when it maps to a single point in one dimension lower. Note that the mapping is reversible from higher to lower dimensions, and vice versa (blue double-sided arrows).

PERCEPTION OF SHAPES AND PERCEPTION AS SHAPE MAPPING

In such a theoretical context of perception, the Borsuk-Ulam theorem helps elucidate the tenets of the ETP and explains how we see an object and how we imagine it (Tozzi and Peters, 2016b). Briefly, BUT explains how high-level representations of objects in our environment are typically mapped to simplified views (our interpretations and coalescences) of the objects. And these mappings described by BUT can sometimes be reversed (*inversed*) to achieve a form of pullback from descriptions to sources of descriptions, from a simplified view to multiple views of the same object. Indeed, a new form of shape theory (called homotopy) discovered by K. Borsuk makes it possible to assess the properties that are preserved through deformation, stretching and twisting of objects (Beyer, 2004; Manetti, 2015). Homotopy is a theory of shape deformation (Borsuk, 1971; Borsuk and Dydak, 1980), e.g., how some shapes can be deformed into other shapes. In this context, the term "shape" means "exterior form" and a "deformation" is a mapping from shape into another one. A classical example is the deformation of a coffee cup into a torus. The combination of various forms of BUT and homotopy theory provides a methodological approach with countless possible applications, especially in helping us understand perception and how we acquire visual imagination. The theory of shape, in simple terms, focuses on the global properties of geometric objects such as polyhedra and tori, neglecting the complications of the local structures of the objects (Borsuk and Dydak, 1980). What shape theory and BUT tell us about visual image acquisition echoes the Gibsonian view of perception: *cognitive processes relating to perception, storage, retrieval and reorganization interact with memory structures and construct a symbolic representation of the environment*. For example, mesh view in **Figure 4** can be viewed as visualization of one among many symbolic views of Leonardo Da Vinci's Mona Lisa painting. In effect, an individual perceives [constructs] the features and events of the environment specified by this [pickup] information from the environment (Heft, 1997).

In particular, BUT variants and Borsuk's theory of shapes are closely allied to Gibson's view of *persistence of perception* (Gibson, 1979; Natoulas, 1992). That is, our perception of an object continues, even when the object is out of sight. This can concisely explained by viewing regions on the surface of a hypersphere as multiple representations of object shapes, mapped continuously to an ecological object that have seen and continue to see. It occurs thanks to the continuous mapping from shapes in our memory to shapes in Euclidean space. In effect, persistence perception can be viewed as signals matching, real-scene visual signals that are collectively the umbra of physical shapes. To make an example, **Figure 4** displays the Mona Lisa painting impinging on the optic nerves: we map it to similar shape representations, such as the Mona Lisa mesh. Gibson accounted for our knowledge of world objects by borrowing a concept of invariance in topology: a series of transformations can be endlessly and gradually applied to a pattern without affecting its invariant properties (Gibson,1950). And, principal among the properties of world objects, is shape and the acquisition of persistent perception of object shapes, which we nicely explain with BUT variants.

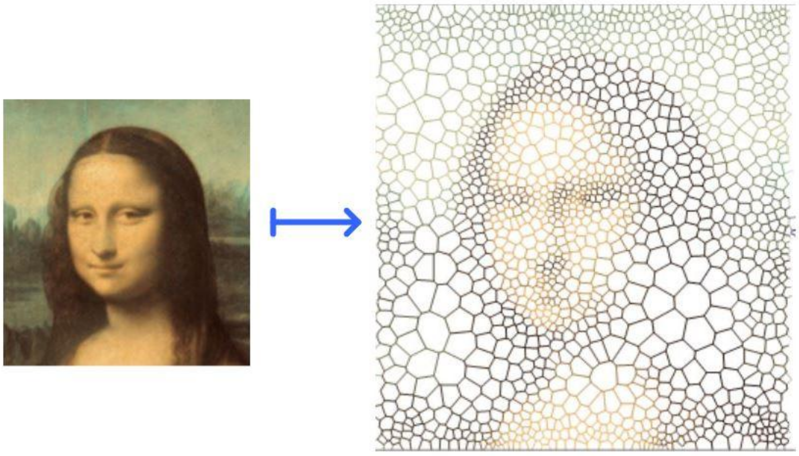

Figure 4. Mona Lisa shape deformably mapped to Mona Lisa Exterior Mesh Shapes. This mapping illustrates nascent Gibsonian persistence perception: we abstract away from the very complex structures in Da Vinci's painting to arrive a simpler, geometric view of the image as a collection of familiar convex polygons.

A TOPOLOGICAL APPROACH TO GIBSON'S "ASK NOT WHAT'S INSIDE YOUR HEAD, BUT WHAT YOUR HEAD'S INSIDE OF"

We start from the simplest and most natural standpoint: an individual (either human or animal) embedded in his environment (Russo-Krauss, 2015). The environment stands for what surrounds the organisms that perceive and behave, in order that both are joined together in a inseparable couple. In topological terms, we may say that the individual is embedded in a spatial three-dimensional ball. Thus, the individual stands in front of the surrounding spatial environment, shaped in guise of a sphere. The environment is not the one of the "traditional" physics: indeed, it can be described through – and is made of - the triad of "medium", "substance" and "surfaces" perceived by the individual. The ecological surface stands for the "classical" geometric plane, while the ecological medium for the standard geometrical space. In such a guise, the object features that the individual perceives are just the interface between surfaces, in order that information is embedded into the light (natural or artificial) surrounding them. The most stable, long-lasting perception of the individual is the base upon which he stands, e.g., the ground, the horizontal surface under his feets. When the individual raises his eyes, he perceives the sky, or the ceiling. The middle zone between the ground and the sky is the medium. The objects, e.g., something which can be handled, stand vertically in the medium. The permanent objects are just surface features which can be perceived on long timescales. For our purposes, it is noteworthy that the human (and also animal) individual splits the environment, in which he moves and finds novel affordances, in three components: the ground and the sky, which join together at the horizon, and the intermediate zone, the medium. We are thus allowed to split the three-dimensional ball into three slices: the sky on the top, the ground on the bottom and the intermediate zone in the middle. In topological terms, the brain splits the environment in different closed subsets. In this framework, a theorem, closely linked to the Borsuk-Ulam theorem, comes into play: the Lusternik–Schnirelmann theorem (LST). It states that, if a sphere is covered by n+1 open sets, then one of them contains a pair of antipodal points. In other words, every time you split a sphere in three parts, there is always one of them which contains an entire diameter, where the antipodal points lie (**Figure 5A**). With this theorem, we are guaranteed at least a pair of exactly opposite points on a sphere (Dodson and Parker, 1997). According to LST, one of the three slices must necessarily contain some antipodal points, e.g., surface features with matching description. When an individual moves around and looks for something (i.e., an object), his brain focuses on one of the three slices of the n-sphere. If we state that the individual attention is driven by one of the slices, we may term such slice as the one containing antipodal points. In other words, the individual needs to find, in one of the three slices in which he separates his environment (the sky, the ground and the medium), a pair of antipodal points equipped with matching description. The latter, by an ecological point of view, share something perceivable in common. Note that, according to the forms of the BUT, the points do not need necessarily to be antipodal. It means that two points embedded in one of the three closed sets do not need to be opposite to be described together. The antipodal points, according to one of the BUT variants, do not need to be simple *points*, but they could have different features. They could be spatial objects or shapes, but also matching movements, or they may display a temporal scale. In the latter case, the shapes are not called objects, but events.

Once we have established a topological framework for objects in the environment, how does the process of perception occur in our brain (mind)? When two antipodal points (or functions) are joined together according to BUT or its variants, they are perceived together, in order that the individual sees (or hears, or touches) a complex of sensations representing the object. According to one of the BUT features (the mapping from an higher to a lower dimension), the dimensions of the surrounding environment need to be reduced when they "enter" our brain. To make an example, we will take into account the multisensory integration, a mental phenomenon occurring when two stimuli from different cues are perceived together (e.g., the view of a running ambulance and the sound of its siren, **Figure 5A**). In a topological view, BUT (and its variants) nicely applies to multisensory integration: two environmental stimuli from different sensory modalities display similar features, when mapped into cortical neurons. To make an example, an observer stands in front of the surrounding environment. An ambulance is embedded in the environment. The observer perceives, through his different sense organs such as ears and eyes, the sounds and the movements of the ambulance. The latter stands for an object embedded in the three-dimensional sphere. The two different sensory modalities (sounds and movements) stand for non-antipodal points on the sphere's circumference. Even if objects belonging to opposite regions can either be different or similar, depending on their features (Peters, 2016), however they must share the same features. In our case, both sounds and movements come from the same object embedded in the sphere, i.e., the ambulance. The two non-antipodal points project to a two-dimensional layer, the brain cortex - where multisensory neurons lie - and converge into a single multisensory signal (**Figure 5B**). According to the dictates of the BUT, such a single point contains a "melted" messages from the two modalities, which takes into account the features of both (Tozzi and Peters, 2016b).

Contrary to the standard theories of perception, which emphasize the input processing and an helmotzian distinction between fixed, innate sensations and variable, learned perceptions, ETP proposes a novel approach. A mutual relationship occurs between the individual and the environment. The perceptive experience is direct and immediate.

Informations are directly taken from the environment, with no mediations. According to ETP, the real word is the phenomenic one. The ETP concept of a smart mechanism able to extract the invariants from the input stream means that the active subject puts in relationships and connexions the objects through his senses, with no need for mental processing in order to build them. The truth corresponds to the immediate perception, which is a *datum* in our brain. Topology nicely explains this interesting feature which is common not just to perceptions, but also to higher mental activities. Indeed, the antipodal point do not stand just for spatial features, such as an object, but also for temporal sequences. It means that the brain is constrained to link together not just spatial elements in an object, but also temporal events in a concept, an idea, a proposition, a hope, a desire and so on. Furthermore, the individual can be embedded not just in a spatial n-sphere, but also in a n-sphere in which n stands for the time, according to the dictates of the BUT variants. Also many spheres with different times are possible: it means that the individual is "constrained" to link past and future events, it is not a choice of his own.

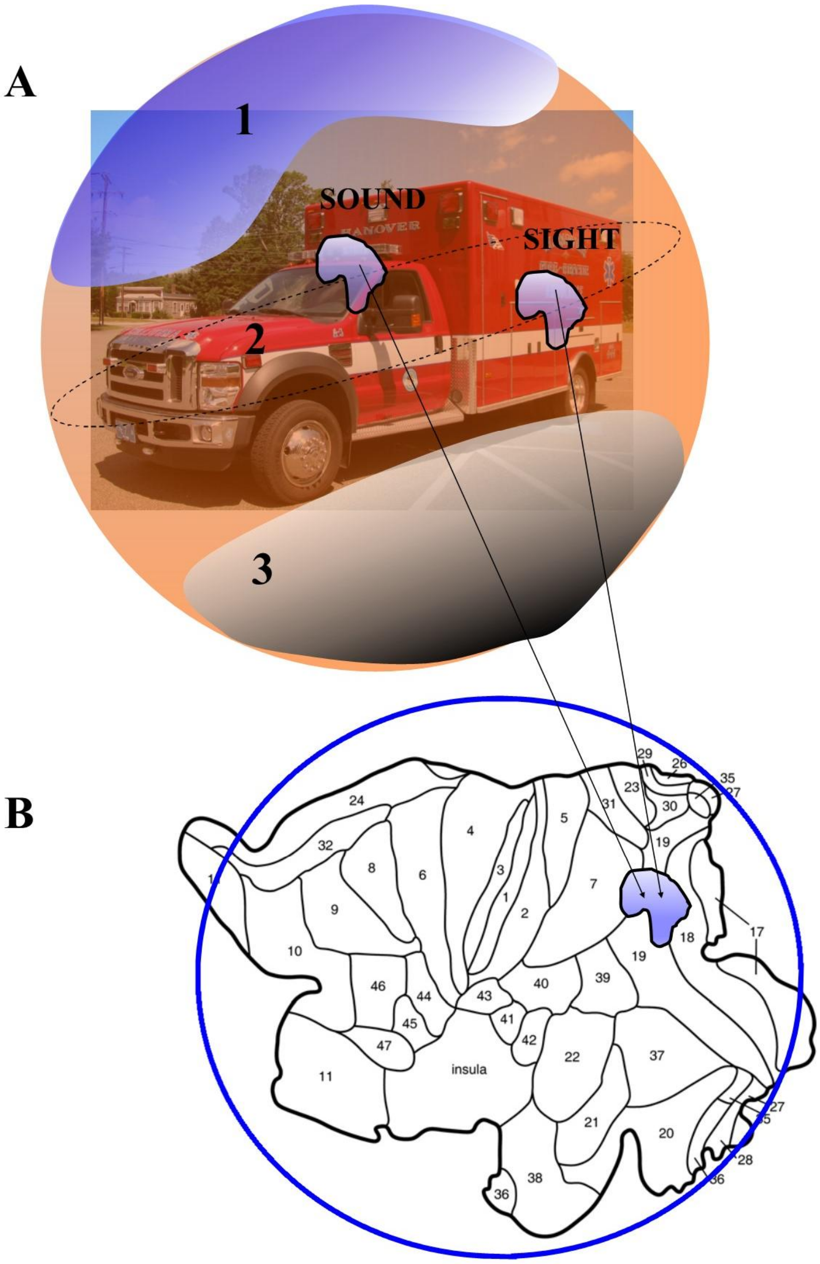

Figure 5A. The three closed regions predicted by the Lusternik–Schnirelmann theorem are named 1, 2 and 3. Once achieved two points with matching description embedded into one of the three closed regions (in this case, the region 2), they can be projected (**Figure 5B**) to a single point onto a 2D brain model (modified from Van Essen, 2005).

CONCLUSIONS

Our paper provides a link between the Ecological Theory of Perception (Gibson ETP) and the topological framework of BUT and its variants, able to explain the mechanisms of perception. Although Gibson stated that space is a myth, a ghost, a fake produced by geometry, a topological approach sheds new light on his own theory. According to this novel conception, the individual's brain (or mind) is forced to coalesce together some components of the environment, in a complex interaction between external affordances and the motivated humans who perceive them. The melting of parts of the environment into a single perception is thus compelled, and is not a free choice made by the individual. The brain needs to perceive different elements together and cannot split them, because the perception may occur and operate just in this way.

The evolutionary advantage is self-evident: the perception of different elements is useless by itself, while the perception of a complete object, or of a concept or an idea, is mandatory in order to survive in an explorable environment, full of possibilities, but also of dangers. In sum, the need to join things together in a single perception is mandatory for our brain (mind). It is important to emphasize that the antipodal points with matching description do not need to be causally correlated: their relationship is a topological one, meaning that the surface features of an object are "linked" together in a single complex of sensations by projections, affine connexions and proximity. In other words, the concept of *connexion* means that the joined parts if the environment are not necessarily in causal relationship, rather they are simply functionally correlated. The individual, with the habituation, learns, from childhood forward, to join together the elements which are more useful for his surviving.

"Perception is based on information, not on sensations" (Gibson, 1979). This means that ETP, rather than sensation-based, is information-based, because emphasizes an analysis of the environment (in terms of affordances), and the concomitant specificational information that the organism detects about such affordances. The human behaviour is radically situated. In other words, you cannot make predictions about human behaviour unless you know what situation or context or environment the human in question was in. Individuals stand in an ecological relation to the environment, such that to adequately explain some behaviour it is necessary to study the environment or niche in which it took place and, especially, the information that "epistemically connects" the organism to the environment. Thus, an appropriate analysis of the environment, made in terms of BUT and its variants, becomes crucial for an explanation of perceptually guided behaviour.

Gibson's work strengthens and brings to the front the primary question of "what" is perceived, before questions of mechanisms and material implementation are introduced (Rao et al., 1997). Together with a contemporary emphasis on dynamical systems theory as a necessary methodology for investigating the structure of ecological information, the Gibsonian approach, particulary in the light of the modern tools of algebraic topology, has maintained its relevance and applicability to neuroscience.

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A SYMMETRIC APPROACH ELUCIDATES MULTISENSORY INFORMATION INTEGRATION

Recent advances in neuronal multisensory integration suggest that the five senses do not exist in isolation of each other. Perception, cognition and action are integrated at very early levels of central processing, in a densely coupled system equipped with multisensory interactions occurring at all temporal and spatial stages. In such a novel framework, a concept from the far-flung branch of topology, namely the Borsuk-Ulam theorem, comes into play. The theorem states that when two opposite points on a sphere are projected onto a circumference, they give rise to a single point containing their matching description. Here we show that the theorem applies also to multisensory integration: two environmental stimuli from different sensory modalities display similar features when mapped into cortical neurons. Topological tools not only shed new light on questions concerning the functional architecture of mind and the nature of mental states, but also provide a general methodology which as the advantage to be assessed empirically. We argue that the Borsuk-Ulam theorem is a general principle underlying nervous multisensory integration, resulting in a framework that has the potential to be operationalized.

> *"A color is a physical object when we consider its dependence upon its luminous source; regarding, however, its dependence upon the retina, it becomes a psychological object, a sensation. Not the subject, but the direction of our investigation, is different in the two domains" (Mach 1885).*

Current advances in human neurosciences shed new light on questions concerning the status of the mental and its relation to the physical. Multisensory neurons (we will also term them "heteromodal" or "multimodal") receiving convergent inputs from multiple sensory modalities (independent sources of information called "cues") integrate information from the five different senses (Krueger et al. 2009). When cues are available, combining them facilitates the detection of salient events and reduces perceptual uncertainty, to improve reactions to immediate dangers and to rapidly varying events (Fetsch et al. 2010). Multisensory neurons are able as well to carry outcomplex brain activities, such as object categorization (Werner and Noppeney 2010). Heteromodal integration displays complicated temporal patterns: absent in the superior colliculus of newborn's brain, it arises in the earlier weeks/months of postnatal life (Stein and Rowland 2011, Royal et al. 2010). As time goes on, neurons develop their capacity to engage in multisensory integration, which determines whether stimuli are to be integrated or treated as independent events. Multisensory integration's development is due to early sensory experience, extensive experience with heteromodal cues and, above all, maturation of cooperative interactions between superior colliculus and cortex (Burnett et al. 2007, Stein et al. 2009). The ability to engage in multisensory integration specifically requires cortical influences (Stein 2014; Johnson et al 2003): without the help of cortical activity, neurons become responsive to multiple sensory modalities, but are unable to integrate different sensory inputs (Xu et al. 2012). To make the picture more intricate, multisensory experience is a plastic capacity depending on dynamical brain/environment interactions (Porcu 2014): neurons retain indeed sensitivity to heteromodal experience well past the normal developmental period, in order that the brain learns a multisensory principle based on the specifics of experience and is able to apply it to novel incoming stimuli (Yu et al. 2010).

In such a multifaceted framework, the Borsuk-Ulam theorem (BUT) from topology, comes into play. This theorem tells us that two opposite points on a sphere, when projected on a one-dimension lower circumference, give rise to a single point displaying a matching description (Borsuk 1933). In this review, we will elucidate the underrated role of topology in multimodal integration, illustrating how simple concepts may be applied to brain processes of cues integration. This paper comprises four sections and an appendix. In the first sections, we will compare the traditional hierarchical view of multisensory integration with the very last developments: the latter talk about the nervous system as a sum of multisensory neurons that form extensive forward, backward and lateral connections at the very first steps of integration in the primary sensory areas. The second section provides a description of the Borsuk-Ulam theorem and its role in multisensory integration. Section three will go through the BUT's theoretical and experimental consequences in theory of knowledge and in the explanation of mental states' nature. The last section will elucidate what the BUT brings on the table, when applied to multimodal neurons. We also will provide a technical appendix as supporting information: this material will show how the BUT theory for brain can be operationalized, unpacking topological concepts afforded by a mathematical point of view.

CLASSICAL VS CURRENT VIEW

Traditional research on the basic science of sensation asks what types of information the brain receives from the external world. To elucidate the classical view, as an example we will go through the visual system, the best known and the most relevant among sensory systems in Primates. The retinal receptors are sensitive to simple signals related to the external world. The message is sent to the primary visual cortex V1, where specific aspects of vision such as form, motion or color are segregated in different parallel pathways. V1 projects to the associative areas termed "unimodal", since they are influenced by a sole sensory modality (in this case, the vision) (Nieuwenhuys et al 2008). The visual unimodal associative cortex (secondary visual cortex) is arranged in two streams, devoted to the control of action and objects perception. Processing channels, each serving simultaneously specialized functions, are also present in the central auditory and somatosensory systems. The message is then conveyed from unimodal to associative areas termed "heteromodal", since they are influenced by more than one sensory modality (visual, auditory, somatosensory, and so on) (Pollmann 2014). Ahigh-order heteromodalarea, the prefrontal cortex, collects the highly processed inputs conveyed by other associative areas. In this classical view, the sequential processing of information is hierarchical, such that the initial, low-level inputs are transformed into representations and multisensory integration emerges at multiple processing cortical stages (Werner and Noppeney 2010). The hierarchical view is also embraced by the most successful model of cognitive architecture, the connectome, where hubs/nodes are characterized by preferential railways of information flows (Van den Heuvel and Sporns 2011).

In the last decade, neuroscience has witnessed major advances, emphasizing the potentially vast underestimation of multisensory processing in many brain areas. New mechanisms, such as the "unimodal multisensory neurons" (Allman et al. 2009), have been demonstrated. In addition, multisensory interactions have been reported at system levels traditionally classified as strictly unimodal: both primary and secondary sensory areas receive substantial inputs from sources that carry information about events impacting other modalities (Hackett and Schroeder 2009; Shinder 2014; Reig 2014; Kuang 2014; Kim 2015). In particular, this can now be considered established in the case of the human V1, which is inherently multisensory (Murray 2015). In adult mice, vision loss through one eye leads whiskers to become a dominant nonvisual input source which attains extensive visual cortical reactivation (Nys 2015). In blind individuals, when visual inputs are absent, occipital ("visual") brain regions respond to sound and spoken language (Bedny 2015). There is a growing number of studies reporting the presence of connectivity between V1 and primary auditory cortex (as well as other higher-level visual and auditory cortices). Non-visual stimuli have been shown to enhance the excitability of low-level visual cortices within the occipital pole. Research into crossmodal perception has also linked senses other than vision, such as taste with audition (Yan 2015). Escanilla et al (2015) demonstrated odor-taste convergence in the nucleus of the solitary tract of the awake freely licking rat. A multisensory network for olfactory processing, via primary gustatory cortex connections to primary olfactory cortex, once again suggests that sensory processing may be more intrinsically integrative than previously thought (Maier 2015).

In sum, the current broad consensus is that the multimodal model is widely diffused in the brain and that most, if not all, higher, as well as lower level neural processes are in some form multisensory. Information from multiple senses is integrated already at very early levels of processing, leading to the concept of the whole neocortex as multisensory in function. Forward, backward and lateral extensive connections support communication in a densely coupled system, where multisensory interactions occur at all temporal and spatial stages (Klemen and Chambers 2012). The content of the single neuronal outputs turns out to be increasingly complex. The functional wheel has come full circle when the highest polymodal areas send feedback messages to the primary sensory cortices. From now on, a ceaseless pathway of feedbacks and feedforwards takes place among cortical areas. The functional importance of the so called "backward" connections is worth of mention. The effects of the projections from higher areas to multimodal neurons play an important role both in multisensory's development and in complex brain functions, providing meaningful adjustments to the ongoing activity of a given area. It has been argued that backward connections might embody the causal structure of the world, while forward connections just provide feedback about prediction errors to higher areas (Bastos 2015). That is, anatomical forward connections are functional feedback connections. For backward connections to effectively modulate lower level processing, higher order areas would need to begin their processing at approximately the same time as lower areas. While this was originally thought not to be the case, we know now that the cross-modal interactions' processing latencies are highly similar to the latencies at which initial sensory processing occurs in the respective primary cortices (Klemen and Chambers 2012).

A TOPOLOGICAL MODEL OF MULTISENSORY INTEGRATION

The Borsuk-Ulam Theorem (BUT) is a remarkable finding by K. Borsuk (Borsuk 1933; Dodson 1997; Matoušek, 2003) about the topological concepts of Euclidean n-spheres and antipodal points. Put simply, BUT states that a sphere displays two antipodal points that emit matching signals. When they are projected on a circumference, they give rise to a single point which contains the features of both antipodal points (**Figure 1A**). To say that points on the sphere are *antipodal* means that they are diametrically opposite (Weisstein). Examples of antipodal points are the endpoints of a line segment, or the opposite points along the circumference of a circle, or the poles of a sphere (Moura 1996). Here “opposite points” means two points on the surface of a three-dimensional sphere (the surface of a beach ball is a good example) which share some characteristics in common and are at the same distance from the center of the beach ball (Marsaglia 1972). To make an example, on the earth’s surface there always exist two opposite points with the same pressure and temperature. For a mathematical treatment of BUT, see Tozzi and Peters (2016a) and Tozzi and Peters (2016b). Two opposite points embedded in a sphere project onto a single point on a circumference, and vice versa: it means that the projection from a higher dimension (equipped with two antipodal points) to a lower one gives rise to a single point (equipped with the characteristics of both the antipodal points). It is worth to be mentioned again that the two antipodal points display similar features: we will go through this central issue in the very next paragraph.

What does BUT mean, in a physical/biological context? How could BUT be helpful in the evaluation of multisensory integration? The answer is positive. Here follows the key to solve the question: the two antipodal points can be used not just for the description of simple topological points, but also for the description of broad-spectrum phenomena: *i.e*., either two antipodal shapes, or functions, or signals, or vectors. For example, a “point” may be described as a collections of signals or a surface shape, where every shape maps to another antipodal one. This expanded view of signals has interest, since every connected couple of antipodal points has a shape. This means that signal shapes can be compared. If you evaluate physical and biological phenomena instead of “signals”, BUT leads naturally to the possibility of a region-based, not simply point-based, geometry, with many applications. In terms of activity, two antipodal points model the description of a signal. For a given signal on a sphere, we can expect to find an antipodal point that describes a signal with matching description. In sum, the mapping from the sphere to the circumference is defined by a rule which tells us how to find a single point (Willard 1970; Krantz 2009). The region-based view of the manifold arises naturally in terms of a comparison of shapes produced by different mappings from the sphere to the circumference (Peters and Tozzi, 2016). An interest in continuous mappings from object spaces to feature spaces leads into homotopy theory and the study of shapes: it means that antipodal points on a sphere have the same shape (Manetti 2015, Cohen 1973). It was Borsuk who first associated the geometric notion of antipodal shapes and mappings called homotopies (Borsuk 1958-59, Borsuk 1969, Borsuk 1980). This leads into the geometry of shapes and shapes of space (Collins 2000; Weeks 2002).

BUT can be used not just for the description of topological abstract spaces, but also for a general description of biological and physical systems. In our case, multisensory integration could easily be evaluated in terms of antipodal points. **Figure 1B** depicts an example of multisensory integration in the BUT framework. An observer stands in front of the surrounding environment. A guitar player is embedded in the environment. The observer perceives, through his different sense organs such as ears and eyes, the sounds and the movements produced by the guitar player. According to the BUT dictates, the guitar player stands for an object embedded in a three-dimensional sphere. The two different sensory modalities produced by the guitar player (sounds and movements) stand for the antipodal points on the sphere’s circumference. Even if objects belonging to antipodal regions can either be different or similar, depending on the features of objects (Peters 2016), however the two antipodal points must share the same features. Both sounds and movements come indeed from the same object embedded in the sphere, i.e. the guitar player. The two antipodal points are not true points, but instead shapes, or functions, which can also be portrayed as vectors containing all the features of the stimulus: in the case, for example, of the visual inputs, the vector contains information about the colours, the shape, the movements of the guitar player. The two antipodal points at first project to a two-dimensional layer, the brain cortex - where multisensory neurons lie -, then are integrated into a single multimodal signal, which takes into account the features of both. Cerebral hemispheres can be indeed unfolded and flattened into a two-dimensional reconstruction by computerized procedures (Van Essen 2005). We may think to a single vector, embedded in the two-dimensional brain, which contains the features of all the information from the two inputs.

A variant of the BUT theorem, called RE-BUT (Peters and Tozzi, 2016), states that the two points (or regions, or vectors or whatsoever) with similar description do not need necessarily to be antipodal, in order to be described together (**Figure 2A**). It means that different inputs from different modalities do not need to be perfectly antipodal on the n-sphere (the environment). Sets of signals not only will have similar descriptions, but also dynamic character; moveover, the deformation of one signal shape into another occurs when they are descriptively near (Peters 2014). It elucidates another important feature of multisensory integration. Although multisensory interactions’ simulations at the neuronal level clearly show that the simple effect of heteromodal convergence is sufficient to generate multimodal properties (Lim 2011), nonetheless the multisensory integration’ occurrence almost never could be predicted on the basis of a simple linear addition of their unisensory response profiles: the interactions may indeed be superadditive, subadditive, or display inverse effectiveness and temporal changes (Krueger 2009, Royal 2009; Perrault et al. 2011; Benson 2014). In the BUT’s topological framework, this apparently bizarre behaviour is explained by the dynamical changes occurring at the antipodal points (Peters 2016). There is indeed the possibility that two inputs from different cues are not perfectly integrated. It means that the mapping of the two cues on the S^{n-1} sphere does not match perfectly, and the sensation is doubtful (**Figure 2B**). A superimposition of two spheres with slightly different center occurs. The brain thus might “move” its spheres, in order to restore the coherence between the two signals. It means, by an operational point of view, that we might be able to evaluate the distance between the central points of the two spheres, in order to achieve the value of discrepancy between the two multisensory signals projected from the environment to the brain.

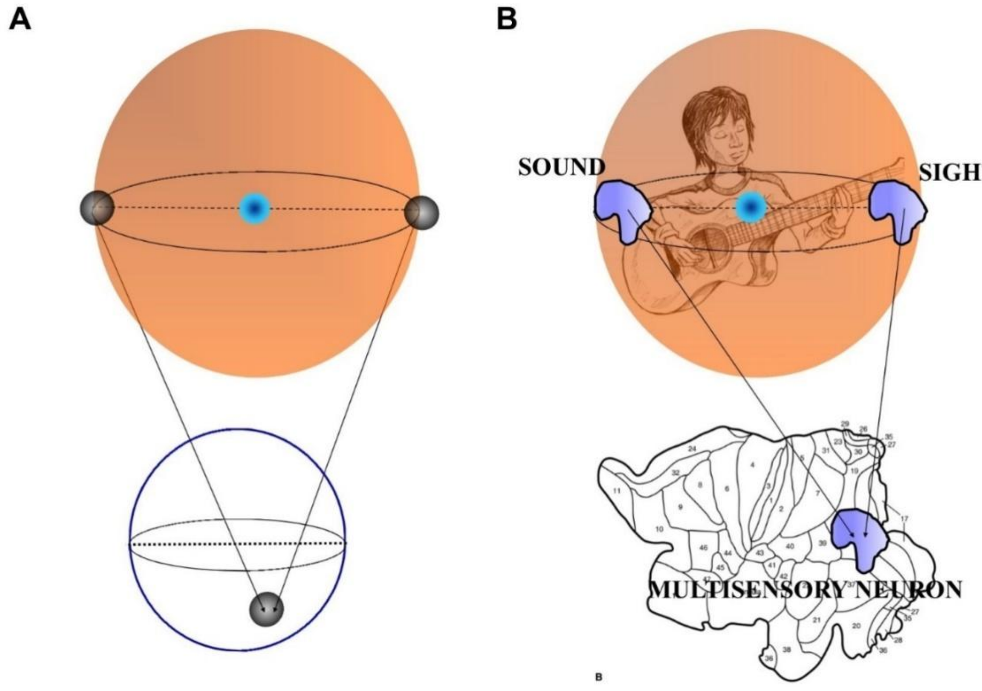

Figure 1A. A simplified sketch of the Borsuk-Ulam theorem: two antipodal points (black spheres) on a three-dimensional sphere project to a single point on a two-dimensional circumference.
Figure 1B shows what happens when an observer is in front of a guitar player. The environmental inputs from different sensory modalities (in this case sound and sight are depicted, in guise of shapes instead of points) converge on a single group of multisensory neurons in the cortical layers of brain's observer. Note that the brain is depicted as a two-dimensional layer. According to the dictates of the Borsuk-Ulam theorem, the single shape contains a "melted" messages from the two modalities. Modified from Tozzi and Peters (2016b).

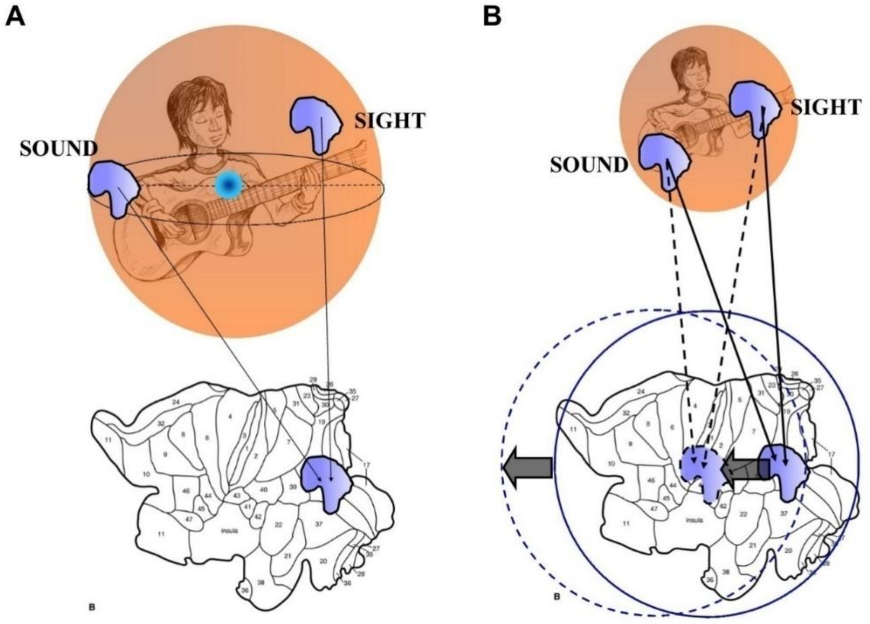

Figure 2A. A simplified sketch of the RE-BUT. The functions with matching description do not need inevitably to be antipodal. Thus, the two inputs from different sensory modalities, if equipped with a signal matching, may come from every point of the environment. **Figure 2B.** When the two inputs from different modalities do not perfectly match on the 2-D brain surface, it occurs a discrepancy between two brain spheres which can be quantified, by evaluating the distance between their two centers. Modified from Tozzi and Peters (2016b).

AN ANSWER FOR CURRENT ISSUES

In this section we will go through the issues of the nature of mental states and theory of knowledge, through the lenses of topology. The BUT model takes into account the content-bearing properties of physical neural networks,by reducing representational states to construct of observables and by providing a mechanistic account of the neural processes which underlie the mental processes of knowledge. BUT integration works not just at the low-level processes - such as perception, motor control and simple mnemonic processing - (Sutter 2014), but also at the high-levels - such as planning and reasoning - (Drugowitsch 2014). In the above-described recent model of multisensory integration, sensory modalities outline a broadly interconnected network with multiple forward, backward and lateral connections, rather than a hyerarchical system of parallel sensory streams that converge at higher levels. The key difference between the traditional and the novel view is whether the hierarchy comprises distinct and parallel streams that converge at higher levels, or whether there are dense interactions between all sensory streams, even at lower levels (Klemen and Chambers 2012). The BUT approach supports a model that assume rich cross-modal interconnectedness at all processing levels, suggesting that functional interplay between the senses occurs at all anatomical levels and across a varied time course. To make an example, the connections between the two secondary cortex's visual pathways (the "where" and the "what" systems) provides**evidence for a common and simultaneous neural substrate for action and perception.**

The BUT allows us to establish the "metaphor" in a general cognitive theory. If a metaphor is a linguistic expression in which at least one part of the expression is transferred from one domain of application (source domain), where it is common, to another (target domain) in which it is unusual (Bailer-Jones 2002), there are striking formal analogies with the topological concept of antipodal points. We hypothesize that the metaphor is produced by the convergence on a multisensory neurons' assembly of both literal and figurative messages (corresponding to the antipodal points located in the environment). The heteromodal integration, aiming to gain insight through the metaphor that no literal paraphrase could ever capture, links together in a linguistic expression the domain of intuitive common-sense understanding of the "literal", and the domain of application of the "figurative". The peculiar nature of multisensory integration leads to a radical rethinking of mental representations. It takes into account the "cognitive" needs of theoretical representational states and provides a neuroanatomical frame to cognitive semantics. Can a single neuronal output contain more information than each of its countless inputs? The answer to this crucial question implies cognitive theoretical conclusions, concerned both with information and knowledge.

Multimodal neurons utilize the salient, meaningful information from different sensations and "melt" them into a novel message, which holds a "semantic" content. Consider the classical "leg of the table". The leg "appears to us at first a single, indivisible whole. One name designates the whole". But "the apparently indivisible thing is separated into parts" (Mach 1885): the world "leg" is not strictly a literal source domain, because it already contains the "merging" and integration of several features, such as the color, the shape, the temperature, the evoked feelings. In the framework of BUT, mental processes are not just cortical networks' computations operating on the "syntax" of representation (i.e., boolean logic), but they also throw a bridge between the latter and the "semantic" notion of mental content. The countless inputs become thus able to solve not-computable functions and to "fabricate" a cognitive process. BUT mechanisms underlying multisensory integration let us hypothesize that our "naïve" thoughts are semantic (van Ackeren 2014), rather than syntactic, and that, during mental processes, the metaphor goes before the axiomatization and the formal syntax rulesof thefirst-order predicate logic. Scientific data confirm heteromodal integration as "semantic" and show which cortical networks are most likely to mediate these effects, with the temporal area being more responsive to semantically congruent, and the frontal one to semantically incongruent audio-visual stimulation (Doehrmann and Naumer 2008). It has been suggested that multisensory facilitation is associated with posterior parietal activity as early as 100 ms after stimulus onset; as participants are required to classify heteromodal stimuli into semantic categories, multimodal processes extend in cingulate, temporal and prefrontal cortices 400 ms after stimulus onset (Diaconescu et al. 2011).

The BUT model displays astonishing connections with the Gärdenfors' (2011) "cognitive semantics", which states that meanings are in the head, but are not independent of perception and bodily experience. Topology provides a conceptual bridge between "realistic" semantics (the meaning of an expression is something out there in the world) and "cognitive" semantics (meanings are expressions of mental entities independent of truth). Gardenfors states that semantic elements are based on spatial or topological rules (Gärdenfors 2000, Kuhn 2003), not on symbols: in touch also with BUT multisensory integration, cognitive models are primarily image-schemas transformed by metaphoric and metonymic operations (Gardenfors2011). Experimental data provide evidence for a complex interdependency between spatial location and temporal structure in determining the ultimate behavioral and perceptual outcome associated with a paired multisensory stimulus (Stevenson 2012).This experience of time and two- or three-dimensional spatial configurations, together with the expressions pertaining to higher level of conceptual organization, can be easily explained by a topological mapping of the components onto the multisensory. The blending, a standpoint of cognitive semantics (Langacker 2008), refers to a "mental" space configuration in which elements of two input spaces are projected into a third space, the blend, which thus contains elements of both (Fauconnier 1997). If we figure this space not as "mental" but as "biological", the blend turns out to be the BUT. Rather than just combining predicates, the semantic model/BUT structure blends behaviors from multiple (mental or anatomical) spaces and explains "apparently" emergent phenomena (Kim 1999).

Inferring which signals have a hypothetical common underlying cause - and hence should be integrated -is a primary challenge for a perceptual system dealing with multiple sensory inputs. The brain is able to efficiently infer the causes underlying our sensory events. Experiments demonstrate that we use the similarity in the temporal structure of multisensory cue combinations to infer from correlation the causal structure as well as the location of causes (Parise and Spence 2012). This capacity is not limited to the high-level cognition; it is performed recurrently and effortlessly in perception too (Körding 2007).In case of abnormal multisensory experience (visual-auditory spatial disparity), an atypical multisensory integration takes place (Stein 2009). We hypothesize that inferences form a sort of "niche construction", which shapes the common sense of a neural machinery operating in embodied/embedded interaction with the environment (Friston 2010). Our brain is also able of abstraction, i.e. to create its own representational endowment or potential, without recourse to external objects or states of affairs, such as causal antecedents or evolutionary history (Grush 2002). Truth conditions are not crucial for such a kind of representational content. How could multisensory neurons' outputs abstract both causal and not causal events, in order to introduce new multifaceted elements into the thinking process? Perhaps heteromodal neurons are able to re-evoke complex data also in absence of the original external stimulus, by comparing and integrating the countless novel semantic messages included in the single bi-dimensional point predicted by BUT, in order that the brain is able to "look without seeing, listen without hearing" (Leonardo da Vinci) (McLean 2006). The role of the highest cortical areas could be crucial in activating cortical multisensory neurons of lower levels, also in absence of external stimuli. Data from literature suggest this possibility. Two important temporal epochs have been described in the visual, auditory and multimodal response to stimuli: an early phase during which there is weak or no unisensory responses yet a defined multisensory response, and a late period after which the unisensory responses have ended and the multisensory response remains (Royal 2010). In sum, in view of the BUT principles, the higher brain activities may be explained by a sole factor: the presence of a three-dimensional structure equipped with antipodal points. It astonishingly resembles Godel's suggestion of abstract terms more and more converging to the infinity in the sphere of our understanding.

WHAT DOES TOPOLOGY BRINGTO THE TABLE?

In conclusion, we provided a general topological mechanism which explains the elusive phenomenon of multisensory integration. The model is casted in a physical/biological fashion which has the potential of being operationalized and experimentally tested. A shift in conceptualizations is evident in a theory of knowledge based on BUT multisensory integration: it is no longer the default position to assume that perception, cognition and motor control are unisensory processes (Méndez 2014). In agreement with Ernst Mach (1885) objects are "combinations or complex of sensations". Our senses do not exist in isolation of each other and, in order to fully answer to epistemological queries, the processes in question must be studied in a multimodal context (Klemen and Chambers 2012). The question here is: what for? What does a topologic reformulation add in the evaluation of multimodal integration? The invaluable opportunity to treat elusive mental phenomena as topological structures takes us into the realm of algebraic topology, allowing us to describe brain function in the language of powerful analytical tools, such as combinatorics, hereditary set systems (Matoušek), homology theory and functional analysis. BUT and its extensions provide a methodological approach which makes it possible for us to study multisensory integration in terms of projections from real to abstract phase spaces. The importance of projections between environmental spaces, where objects lie, and brain phase spaces, where multimodal operations take place, is also suggested by Sengupta et al. (2016), who provide a way of measuring distance on concave neural manifolds. Such a methodological approach has been proved useful in the evaluation of brain symmetries and to assess the relationships and affinities among BOLD activated areas (Tozzi and Peters, 2016b) and in the evaluation of cortical histological images (Peters et al., 2016)._BUT and its variants are not just a *methodological* approach, but also display a *physical* meaning. Based on the antipodal cortical zones with co-occuring BOLD activation, it has been recently suggested that brain trajectories might display donut-like trajectories (Tozzi and Peters 2016a).

The different animals' senses capture only bits and selected aspects of reality and display the world from limited points of view (Holldobler and Wilson 2002). "The development of the human mind has practically extinguished all *feelings*, except a few sporadic kinds, *sound*, *colours*, smells, warmth, etc." (Peirce 1892). However, a realistic fraction, albeit incomplete, reaches our brain from outside and gives rise, thanks to the BUT, to an isomorphism between sensations and perceptions. As stated above, the BUT perspective allows a symmetry property located in the real space (the environment) to be translated to an abstract space, and *vice-versa,* enabling us to achieve a map from one dynamical system to another. “A *truth* is like a *map*, which does not copy the ground, but uses signs to tell us where to find the hill, the stream and the village” (Goodman 2005). If symmetry transformations (antipodal points) can be evaluated, we are allowed to use the pure mathematical toolsof topological group theory. Symmetry transformations therefore furnish us with a topologic family of models able to explain the data. In the study of multisensory integration, promising empiric advances are forthcoming: cutting edge methods have been recently proposed, from oscillatory phase coherence, to multi-voxel pattern analysis as applied to multisensory research at different system levels,to the TMS-adaptation paradigm (for a review, see Klemen and Chambers 2012). The last but not the least, two computational frameworks that account for these multisensory integration have been recently established (Magosso et al. 2008, Ohshiro et al. 2012). In the framework of BUT theorem, such advances might provide a considerable experimental support and a unifying computational account of multisensory neurons’ features.

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A TOPOLOGICAL BRAIN ELUCIDATES SYNTACTIC AND SEMANTIC PROCESSING

When facing a proposition, the brain straightforwardly understands its grammar and discriminates whether it is true or false. Unlike computers, the brain is able to identify signs of sequences in terms of both syntactic symbols and semantic meaning. We show, based on the current literature, that a testable algebraic topological approach gives helpful insights into brain’s computational activity during semantic recognition. Indeed, recent suggestions allow us to hypothesize that the semantic properties of a proposition are processed in brain dimensions higher than the syntactic ones. Furthermore, we show how, in a fully reversible process, the syntactic elements embedded in Broca’s area might project to scattered semantic cortical zones, where the presence of higher functional dimensions gives rise to an increase in proposition’s information content. Taking into account the dictates of novel versions of the Borsuk-Ulam and the fixed-point theorems, we build a framework that provides a feasible explanation for semantics processing in the brain, and also paves the way to novel computers which nodes are built in higher dimensions.

Syntax assesses the relationships among the elements of linguistic expressions (Carnie, 2006). A property relative to a proposition is syntactic if it depends just on the symbols by themselves. In philosophical language, syntax stands for grammar, which includes also phonology and orthography, e.g., sounds, spellings and so on (Martinich, 1996). In mathematical logic, a concept related to a symbols sequence is syntactic if it depends just on the symbols forming the sequence, not taking into account the *meaning*. The ambiguous term *meaning* will stand here for the truth or the falseness of an expression or a sequence of symbols. On the other side of the coin, *semantics* assesses the relationships between expressions and extra-linguistic truths (Nerbonne, 1996; Cruse, 2004). A property relative to a proposition is semantic if it depends on the meaning, *e.g.*, if the proposition is true or false. In philosophical language, semantics stand for the study of the meanings of linguistic expressions. A concept related to a symbols sequence is semantic if it depends on the meaning transmitted by the sequence.

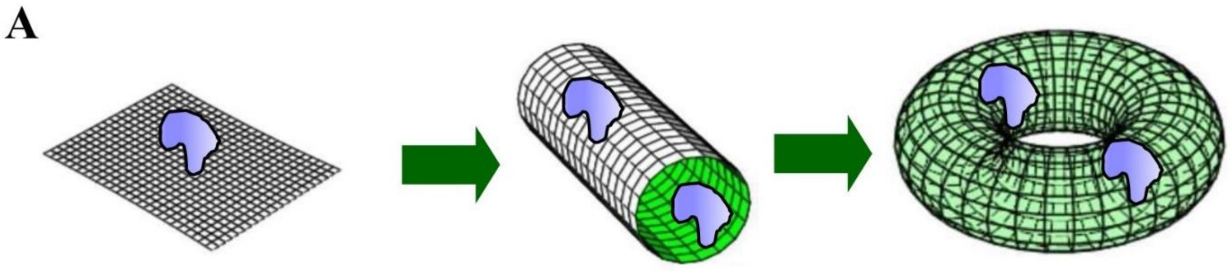
While syntactic properties are algorithmically verifiable by computers, semantic ones are not, because the latter are based on the notion of truth, a task that cannot be pursued by current computers. Furthermore, Godel's first incompleteness theorem (Godel, 1931) demonstrates that, if we limit ourselves to syntactic approaches, we will never be able to reach truths. To make an example, Godel states that the phrase: "this enunciate is not demonstrable" could be either a) false, and in this case it absurd, because is false and demonstrable, b) or could be true, and is this case is not demonstrable. Given a group of arithmetical axioms, there is always a true arithmetic proposition that cannot be demonstrated starting from the axioms, if we admit just the syntactic methods dictated by the Hilbert's program (Mancosu, 1998). Therefore, syntactic methods are inadequate in order to understand the whole properties of the same model that we easily understand through semantics. In sum, while the human brain is able to grasp the semantic notion of truth, the latter cannot be verified by computers. Furthermore, Godel's second incompleteness theorem states that is not possible to verify the truth of a group of arithmetic axioms (Godel, 1931). Such problem might be overtaken, because every true arithmetic proposition can be demonstrated starting from Peano axioms (Segre 1994), which use semantic methods. However, we cannot never be sure that the semantic methods we used were truthful. The existence of axioms is based on our extremely questionable intuition that such axioms are true. Therefore, if we use just the unquestionable and consistent syntactic methods, as proposed by Hilbert, we cannot proof all the truths. Vice versa, if we rather use the uncertain semantic methods, we could possibly know all the arithmetic truths, but we cannot be sure that such methods are correct. Here we propose a topological computational method able to throw a bridge between syntactic and semantic expressions, in order to overtake the Godel's incompleteness theorems and to build semantics-solving machines.

TOPOLOGY COMES INTO PLAY

StringBUT. Here we introduce a string-based extension of the Borsuk-Ulam theorem, denoted *strBUT* (Peters and Tozzi, 2016a). The Borsuk-Ulam Theorem (BUT) states that a single point on a circumference maps on a sphere to two points equipped with matching description. For technical readers, see: Borsuk (1933), Matousek (2003), Crabb and Jaworowski (2013), Peters (2016), Peters and Tozzi (2016b), Tozzi and Peters (2016a). Continuous projections from an n-dimensional sphere to a n-dimensional Euclidean space lead to a string-based incarnation of the BUT. We consider a geometric structure that has the characteristics of a *string*. By definition, a string on the surface of an n-sphere is a line that represents the path traced by a particle moving along its surface. In an abstract geometric space, a string, also termed *worldline* (Olive, 1987; Olive and Landsberg, 1989) stands for a region of space with either bounded or unbounded lengths. In evaluating a string-based BUT, we take into account antipodal sets instead of antipodal points (Petty, 1971). Indeed, in a point-free geometry (Di Concilio, 2013; Di Concilio and G. Gerla, 2006), regions replace points as the primitives. If we assess a worldline in terms of a spatial region on the surface of an n-sphere, or in an n-dimensional normed linear space, strings can be defined as *antipodal* (**Figure 1**). Strings are antipodal, provided the regions encompassing the strings belong to disjoint parallel hyperplanes: put simply, they have no points in common. A region is called a *worldsheet* if that everyone of its subregions contains at least one string. In other words, the term worldsheet designates a nonempty region of a space completely covered by strings, in which every member is a string. A 2d plane worldsheet can be rolled up to form the lateral surface of a 3d cylinder, termed a worldsheet cylinder. Further, a worldsheet cylinder maps to a worldsheet torus, formed by bending the former until the ends meet (**Figure 1**). In sum, a flattened worldsheet maps to a worldsheet cylinder and a flattened worldsheet cylinder maps to worldsheet torus. It means that a bounded worldsheet cylinder is homotopically equivalent to a worldsheet torus. The strings on different wordsheets are antipodal and descriptively near, e.g., they share matching description. There is however a difference between the strings embedded in wordsheets of diverse dimensions. The higher the dimension of the wordsheet, the more the information encompassed in strings on the same region, because of the higher number of coordinates. Strings contain more information than their projections in a lower dimensions. It means that strBUT allows us to evaluate systems features in higher dimensions, in order to increase the amount of detectable information. To make an example, you might extract the three-dimensional shape of a cat, just looking at its shadow. Vice versa, dropping down a dimension means that each point in the lower dimensional space is simpler. In sum, strBUT provides a way to evaluate changes of information in a topological, other than thermodynamical, fashion.

Now a problem arises. Take the example of a string, say str1, on a n manifold (say a 2D worldsheet). Such str1 is antipodal to str2, e..g. the string embedded on a n+1 manifold (say a 3d worldsheet rolled up into a cylinder). Hovever, for the classical BUT, it must exist on the worlsheet cylinder ALSO another string, say str3, which has matching description with str2. This is because, as BUT dictates, going one dimension higher, a single feature needs to project to TWO matching features. It means that a projection mapping contains multiple mappings in higher levels.

Brouwer's fixed point theorem. Next, consider Brouwer's fixed point theorem (FPT) (Brower, 1906). In simple words, every continuous function from a n-sphere of every dimension (e.g. a disk, or a ball) to itself has at least one fixed point. FPT applies, for example, to any disk-shaped area, where it guarantees the existence of a fixed point, which behaves like a sort of whirlpool attracting moving particles. Su (1997) gives a coffee cup illustration of the FPT. No matter how you continuously slosh the coffee around in a coffee cup, some point is always in the same position that it was before the sloshing began. And if you move this point out of its original position, you will eventually move some other point in the sloshing coffee back into its original position. In strBUT terms, it means that we can always find a n-sphere containing a string. Also, each string has a particular shape and come together with another string, which is termed a *wired friend*. These observations lead to a *wired friend theorem*: every occurrence of a wired friend string with a particular shape on the structure S^n maps to a fixed description, e.g. another string that belongs to another structure. Every wired friend is recognizable by its shape, because the shape of a string is the silhouette of a wired friend string. We achieve a maps of wired friend strings, projecting from the 2D wordsheet, to the cylinder wordsheet, to the woldsheet torus. In sum, we can always find a structure containing a string which is a description of another string in a lower dimensional structure, and vice versa. In the next paragraphs we will discuss how this theorem has important consequences in the study of syntactic and semantic brain processing.



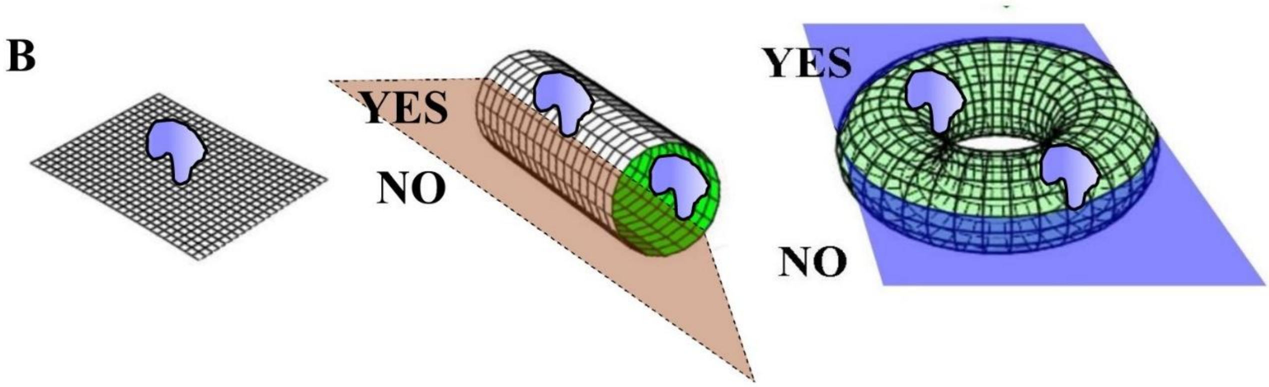


Figure 1A. String mappings according to StrBUT. A string (blue spot) maps to higher dimensions, from 2D sheets to 3D cylinders or toruses. The strings in the three different structures are equipped with matching description and are thus said to be antipodal. Note that, for the classical BUT, a single string in the 2D sheet maps to two opposite strings on the 3D structures.

Figure 1B. Syntactic and semantic counterparts of strBUT. On the left, the blue spot stands for a bidimensional syntactic construct. Going one dimension higher, we achieve a third dimension. This further dimension stands for the semantic concept of truth value (YES or NO). In sum, strings gain novel information when projected into higher-dimensional structures.

WHEN TOPOLOGY MEETS LOGIC

In this section, a sample application of strBUT and FTP is given in terms of syntactics and semantics. We hypothesize that the syntactic elements of a language lie on a n-manifold, while the semantic ones lie on an n+1 manifold. A syntactic proposition becomes semantic when brain mechanisms projects the former one dimension higher, and vice versa. In logical terms, we may state that p=q is syntactic, while $(p=q)^{n+1}$ is semantic. The higher dimension stands for the truth function, e.g., whether a proposition in true or false. To make an example, consider the syntactic preposition: "the-skin-is-tender" and the semantic one, equipped with a truth value of TRUE (or YES): "*the skin is tender*". The truth value, of course, could be FALSE (or NOT), in case of a disease affecting the skin. We write $(\text{the-skin-is-tender})^n$ and $(\textit{the skin is tender})^{n+1}$, where n stands for the abstract dimensions in which the proposition is embedded. The two prepositions also stand for two groups, where the n+1 group encompasses the n-group. The n+1 group, equipped with a truth function (YES and NOT), cannot be fully detected if we just look at the n-group, because the latter displays less dimensions. A part of information is lost in syntactics, due to the lower number of coordinates. It means that the whole semantic group can be assessed just in case we are in dimensions higher that the syntactic ones. In topological terms, syntactic operations take place when strings, e.g, linguistic prepositions, are placed in a 2D wordsheet, while semantic operations take place when strings are placed in wordsheet cylinders and toruses lying in higher dimensions. Therefore, a group equipped with the further dimensions of TRUE or FALSE is formed through a projective, continuous mechanism (**Figure 1B**).

For the classical BUT, semantic elements encompass not just one, but two antipodal strings, equipped with matching description. Such framework will be useful in the next paragraphs, when we will assess the cortical counterparts of propositions. Are there differences between the two points lying in higher dimensions and the single, lower-dimensional point? The foremost distinction is that the two antipodal points, lying one dimension higher, form a group by themselves. It means that semantic processing can be studied just in a context equipped with dimensions higher than syntactic symbols. Furthermore, when n increases, syntactic structures can be compared with models existing one dimension higher. What does the dimension n stand for? The n exponent might simply stand for a further spatial brain dimension. In this case, computers equipped with nodes endowed in higher spatial dimensions might be able to understand semantics.

SYNTACTICS AND SEMANTICS IN TOPOLOGICAL BRAINS

In touch with predictions from the above mentioned linguistic-topological model, we hypothesize that our brain processes syntactic and semantic elements through a change in functional or spatial dimensions. The syntactic processing that occurs at one level of brain activity is projected to a higher level, giving rise to semantic recognition, which encompasses more information. In the next paragraphs, taking into account the recent literature, we will go through possible physical brain counterparts.

Brain dimensions. In the novel framework, syntax displays less dimensions than semantics in the central nervous system, so that semantic inputs have increased complexity. The first step is to evaluate whether the brain encompasses different dimensions. The term brain *dimension* may reflect either functional activity, or anatomical connections between cortical areas. The functional approach, based on complex network analysis of brain signals, assesses neural space's multidimensionality in a brain conceived as a complex dynamical system (Kida et al, 2016; Giusti et al., 2016; Simas et al., 2015). It allows us to describe nervous dynamics as vectors or tensors in pluri-dimensional phase spaces. Apart from the *canonical* three dimensions, the technique is also able to assess other neural features, such as, e.g., frequency and magnitude, each one standing for other possible dimensions (Kida et al, 2016).

The anatomical approach to brain dimensionality evaluates cortical locations. Tozzi and Peters (2016a; 2016b) recently suggested that brain trajectories might display four spatial dimensions, instead of the canonical three, during cortical spontaneous activity. Such trajectories can be described in terms of torus-shaped structures. Stemmler et al. (2015) showed how animals can navigate by reading out a simple population vector of grid cell activity across multiple spatial scales. It means that the behavior of population vectors, each one lying in different anatomical dimensions embedded on functional toruses, predicts neural and behavioral correlates of grid cell readout. Benson et al. (2016) developed an algorithmic framework for studying how complex networks are organized by higher-order connectivity patterns, revealing hubs and geographical elements not readily achievable by other methods. They showed that information propagation units exhibit rich higher-order organizational structures. In such a vein, Kleinberg et al. (2016) recently proposed that real networks are not just random combinations of single network layers, but are instead organized in specific ways dictated by hidden geometric correlations between layers, which allow the detection of multidimensional communities. Crucial for our strBUT arguments, such multidimensionality enables trans-layer link prediction, in order that connections in one layer can be predicted by observing the hidden geometric space of another (Kleineberg et al, 2016).

Localizations. The brain localizations of syntactic and semantic processing described in literature seem to confirm our topological framework. The left anterior language areas, e.g. Broca's area (left Brodmann area 44), is crucial for syntactic processing in speech production and perception (Skeide and Friederici, 2016; Stromswold et al, 1996), despite the wide variability between individuals and the presence of diverse circuits, not dedicated just to a single kind of linguistic information processing (Sahin et al., 2009). While syntax seems to be localized in relatively fewer and smaller brain areas, semantics is instead scattered throughout vaste areas of the cortical surface (Huth et al, 2016). It is in touch with a model encompassing StrBUT and the fixed-point theorem, which regards semantic concepts as multiple antipodal strings on a torus surface and syntactic concepts as single strings located in specific brain zones (**Figure 2**). It also means that syntactic elements lie on brain dimensions higher than syntactic ones.

According to strBUT dictates, single strings grasp less information than their matching descriptions embedded in higher projections. Note also that semantic information is not aggregated, rather it is scattered in the brain. Syntactic symbols stand for single sets of objects, while semantic meanings for numerous sets of objects with matching description.

Recent suggestion let us hypothesize that, during human brain development, semantic processes precede syntactic ones. Indeed, Skeide and Friederici (2016) demonstrated in children a slow developmental segregation of syntax from semantics. The human embryo can already distinguish vowels *in utero*, but grammatical complexity is usually not fully mastered until at least 7 years. In the first three years, children rapidly acquire bottom-up processing skills, primarily implemented in the temporal areas. In a further stage, until the adolescence, top-down processes emerge gradually with the increasing structural connectivity of the left inferior frontal cortex. It means that childen are equipped with more semantics than adults, in touch with the hypothesis of decrease of functional brain dimensions with time passing. In a topological framework, it might be hypothesized that the FPT holds with time passing, leading to convergence of semantic concepts into fully developed syntactic ones.

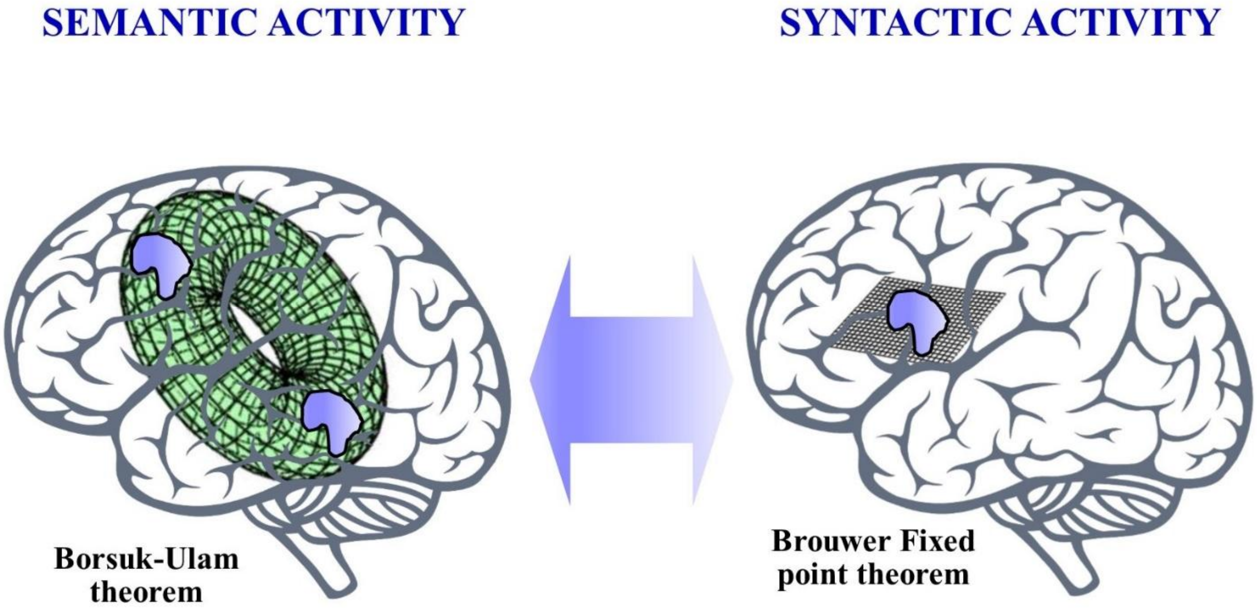


Figure 2. Semantic and syntactic brain activity in a topological framework. Mappings occur among brain regions which are temporarily equipped with different functional dimensions. According to the strBUT dictates, higher dimensional activities lie on a wordsheet torus, where scattered antipodal strings stand for the cortical areas activated during semantic activity. On the other side, syntactic processes lie on a 2D wordsheet, where the movements of the more localized strings endowed in the Broca's area are dictated by the FPT. Note that the process is full reversible, depending on the direction of the continuous mapping from one dimension to another.

CONCLUSIONS

We showed how semantic and syntactic brain abilities can be investigated in terms of algebraic topology, in particular through strBUT and FPT. Our data gave some understanding of how the connectivity among the brain active centres might change during syntactic or semantic inputs. These findings pave the way to novel computational and logic approaches to brain functions. Semantic concepts are based on the notion of truth; consequently, computers which carry inputs just on a 2D surface cannot evaluate whether a preposition is true or false. Despite massively parallel computers have become available (Angel and Leong, 2014), such kind of multidimensionality does not tackle the long-standing problem of semantics. Indeed, current multidimensional efforts just concern either access methods, in which sets of multidimensional points give computers support at the physical level (Gaede and Günther, 1998), or digital signal processing (Pastizzo et al, 2002) and data sampling (Mersereau and Speake, 1983). Multiple dimensions are merely used as representational devices for data analysis, limiting the potential of the current artificial intelligence studies. The fact that brain nodes can be embedded in higher dimensional spaces suggests the possibility to build computers equipped with pluridimensional nodes endowed in 3D geometric spaces. Indeed, a computer can be hypothesized having connections that are topologically 4D, even if embedded in a simple 3D space. Such computers, implemented in ordinary 3D space, but equipped with nodes with the same number of neighbors as a points in a 4D cube, could be able to perform semantic operations, due to the more degrees of freedom. Recent studies explored this approach. For example, Ursino et al. (2009; 2010; 2011; 2014) investigated how complex semantics can be extracted from the statistics of input features, using attractor neural networks. They focused on how similarity among objects, feature dominance and distinctiveness can be naturally coded using Hebbian training. Their model includes a lexical network, representing word-forms, and a semantic network composed of several areas, each one coding for a different feature. They use a simple taxonomy of schematic objects, i.e., a vector of features, with shared features (categories) and distinctive features (individual members) (Ursino et al., 2014). However, their framework differs from ours, because the former takes into account the hypothesis, opposite to ours, that concepts are represented in memory as a collection of features that *shrinks* the sum of previous sensory, motor and emotional experiences.

In logic, our framework elucidates several previous suggestions by various Authors. Hilbert's program states that every true proposition must be demonstrated starting from one of the available axioms. Except for the axioms, no other proposition can be considered true by itself, but must be necessarily assessed through algorythms and computational processing. It means that a demonstrable proposition is syntactic, because it could be verified by inspecting every symbol, with no need to keep into account its meaning. However, the Godel's first incompleteness theorem states that, given a group of arithmetical axioms, there will always be a true arithmetic enunciate that cannot be demonstrated starting from the axioms, if we just admit the methods suggested by the Hilbert's program. The theorem states that, if we limit ourselves to syntactic methods of reasoning, there will always be truths that are not accessible to us. Syntactic methods are inadequate in order to understand all the properties of an otherwise semantically understandable model. To make an example, our mental model of natural numbers cannot be completely characterized through syntactic methods. Furthermore, how can we be sure that all the axioms are true? Their truth depends just on the discourse universe, because the concept of truth has to do with semantics. According to formalists, axioms are indeed just starting points of linguistic jokes (Wittgenstein, 1953): the choice of an axiom looks like writing the rules of a table game. Therefore, every proposition, even if entirely false, is theoretically demonstrable, if we start from an erratic group of axioms. Our topological model sheds new light on some of these issues. While Hilbert describes real objects in terms of mathematical axioms, we describe them in terms of projections and mappings. Maps from the lower syntactic dimensions to the higher semantic ones ride out the caveats cast by Godel's theorems. In a language, paraphrasing Charles Ball, groups of words and expressions are correlated both with their shapes and meanings, which pertain to the same conceptual sphere, but to different dimensions. We could imagine that syntax works with individual symbols, while semantics works instead with groups of symbols.

For sake of brevity, here we did not tackle the issue of the third linguistic subfield (together with syntax and semantics), e.g., *pragmatics*, that investigates the ways in which context and use contributes to meaning (Mey 2001). However, our data pave also the way to a forthcoming interpretation of pragmatics, in terms of dimensions even higher than the semantic ones. We would like to bring to an end with a few excerpts from Wittgenstein's Philosophical Investigations (1953), where the author seems to foresight the topological framework in which propositions are embedded: "*I said to myself "I wonder what time it is?"—And if this sentence has a particular atmosphere, how am I to separate it from the sentence itself? It would never have occurred to me to think the sentence had such an aura if I had not thought of how one might say it differently—as a quotation, as a joke, as practice in elocution, and so on...* (I, 607). *Suppose someone said: every familiar word, in a book for example, actually carries an atmosphere with it in our minds, a 'corona' of lightly indicated uses.—Just as if each figure in a painting were surrounded by delicate shadowy drawings of scenes, as it were in another dimension, and in them we saw the figures in different contexts* (II_{VI}). *But how is it possible to see an object according to an interpretation? — The question represents it as a queer fact; as if something were being forced into a form it did not really fit. But no squeezing, no forcing took place here. When it looks as if there were no room for such a form between other ones you have to look for it in another dimension. If there is no room here, there is room in another dimension* (II_{XI}).

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INFORMATIONAL ENTROPIES FOR NON-ERGODIC BRAINS

Informational entropies, although proved to be useful in the evaluation of nervous function, are suitable just if we assume that nervous activity takes place under ergodic conditions. However, widespread claims suggest that the brain operates in a non-ergodic framework. Here we show that a topological concept, namely the Borsuk-Ulam theorem, is able to wipe away this long-standing limit of both Shannon entropy and its generalizations, such as Rényi's. We demonstrate that both ergodic and non-ergodic informational entropies can be evaluated and quantified through topological methods, in order to improve our knowledge of central nervous system function.

The most successful entropy-based theories of brain function – e.g., the free-energy principle (Friston 2010) – require that the brain activity takes place in an ergodic phase space. In physics and thermodynamics the ergodic hypothesis states that, over long periods, the time spent by a system in a region of the microstates' phase space with the same energy is proportional to the region's volume, so that all accessible microstates are equiprobable over a long period of time (Barth). In other words, ergodicity is a random process characterized by the time average of one sequence of events being the same as the ensemble average (Walters; Alaoglu). It also means that, in case of a Markov chain, as one increases the steps, there exists a positive probability measure at step n that is independent of the probability distribution at initial step 0 (Feller 1971). The Shannon informational entropy (1948) is able to link choice, uncertainty and thermodynamic entropy in a coherent picture able to explain macroscopic systems' behaviour such as the brain, if one just knows the statistical properties of the microscopic constituents. In the context of nervous function, it has been shown that variations in entropy are correlated with different psychological and cognitive states. As an example, analysis performed on emotionally online dialogues demonstrated the tendency towards a growing entropy (Sienkiewicz et al, 2013). Further, ensemble of supervised maximum entropy classifiers can accurately detect and identify sentiments expressed in notes (Wicentowski and Sydes, 2012), perceptual functions are correlated with thermodynamical entropy and free energy (Freeman et al., 2011) and Shannon entropy is able to predict task performance (Guastello et al., 2013). Finally, the entropy has been recently proposed as a measure of semantic and syntactic information of multidimensional discrete phenomena (Štys et al., 2015). Shannon entropy H requires some properties to be applied, because it should be:

a) continuous in the p_i, b) a monotonic increasing function of n and c) the weighted sum of the individual values of H. The most important limitation to the use of Shannon entropy is the need to operate under ergodic conditions. However, widespread claims suggest that the brain is not ergodic. Many authors suggest that the properties of brain fluctuations are inconsistent with the Markvian approssimation (Fraiman and Chialvo 2012), the mean-square distance travelled by brain particles displays anomalous diffusion (Bianco et al., 2007)) and the brain is weakly non-ergodic, as some phase space region may take extremely long times to be visited (Papo).

This paper aims to answer to the question whether it is possible to use informational entropies for the evaluation of non-ergodic systems (Rebenshtok and Barkai, 2008) and questions the validity of informational entropies under non-ergodic conditions. In such a framework, an underrated theorem from algebraic topology comes in help: the Borsuk-Ulam theorem and its variants. The theorem states that two opposite points on a sphere, when projected on a one-dimension lower circumference, give rise to a single point displaying a matching description (Borsuk 1933). We here show how Shannon and its generalized variants, both ergodic and non-ergodic, may be treated in terms of algebraic topology. We will discuss the mechanisms and the consequences for brain studies of such an "unification" between concepts from far-flung branches.

SHANNON ENTROPY ON A CIRCLE

Shannon entropy and its links with thermodynamical entropy. Shannon entropy (denoted by H(X), X a random variable with values $x_1, \ldots, x_n$) is a measure of the unpredictability of information content (Shannon 1948). Entropy is defined by:

$$X = \{x_1, \ldots, x_n\}.$$

$$H(X) = \sum_{i=1}^{n} p(x_i)\log_2[p(x_i)].$$

$$H(X) = \begin{cases} 0, \; if \;\; p(x) \;\; = 1, \\ 0, \; if \;\; p(x) \;\; = 0, \text{ by definition.} \end{cases}$$

Shannon entropy states that, under ergodic conditions, if we know the values of *p*, we may obtain the values of S(*p*). In other words, S(*p*) is a function(al) of a generic probability distribution *p* such that, if we modify *p*, we achieve a different value of entropy on the Shannon's curve. The connection with informational entropies' thermodynamical counterpart - i.e. the Boltzman-Gibbs entropy - is given by a standard procedure of MaxEnt distribution and thermodynamical limit ($N \to \infty$), which leads to the relation:

$S(P) = k_B H(P)$,

where k_B is the Boltzmann constant.

The Borsuk-Ulam theorem (BUT). The (BUT) is a remarkable finding by K. Borsuk about Euclidean n-spheres and antipodal points. It states that (Dodson):

Every continuous map $f: S^n \rightarrow R^n$ *must identify a pair of antipodal points.*

In other words, the sphere S^n maps to the euclidean space R^n, which stands for an *n*-dimensional Euclidean space. Note that the function needs to be continuous and that n must be a natural number (although we will see that it is not completely true) (Matoušek; Tozzi 2016a; Tozzi 2016b).

The notation S^n denotes an n-sphere, which is a generalization of the circle (Weeks). A *n*-sphere is a n-dimensional structure embedded in a *n*+1 space. For example, a 2-sphere (S^2) is the 2-dimensional surface of a 3-dimensional ball (a beach ball is a good example). An n-sphere is formed by points which are constant distance from the origin in (*n*+1)-dimensions (Marsaglia). For example, a 3-sphere (also called *glome* or *hypersphere*) of radius *r* (where r may be any positive real number) is defined as the set of points in 4D Euclidean space at distance *r* from some fixed center point **c** (which may be any point in the 4D space) (Henderson). A3-sphere is a simply connected 3-dimensional manifold of constant, positive curvature, which is enclosed in an Euclidean 4-dimensional space called a 4-ball. A 3-sphere is thus the surface or boundary of a 4-dimensional ball, while a 4-dimensional ball is the interior of a 3-sphere. From a geometer's perspective, we have different n-spheres, starting with the perimeter of a circle (S^1) and advancing to S^3, which is the smallest hypersphere, embedded in a 4-ball (**Figure 1**). Points on S^n are *antipodal,* provided they are diametrically opposite (Weisstein). Examples of antipodal points are the poles of a sphere. Further, every continuous function from an n-sphere S^n into Euclidean n-space R^n maps some pair of antipodal points of S^n to the same point of R^n. To make an example, if we use the mapping f: $S^3 \rightarrow R^3$, then f(x) in R^3 is just a signal value (a real number associated with x in S^3) and f(x) = f(-x) in R^3. Furthermore, when g: $S^2 \rightarrow R^2$, the g(x) in R^2 is a vector in R^2 that describes the x embedded in S^2. In other words, a point embedded in a R^n manifold is projected to two opposite points on a S^{n+1}-sphere, and vice versa.

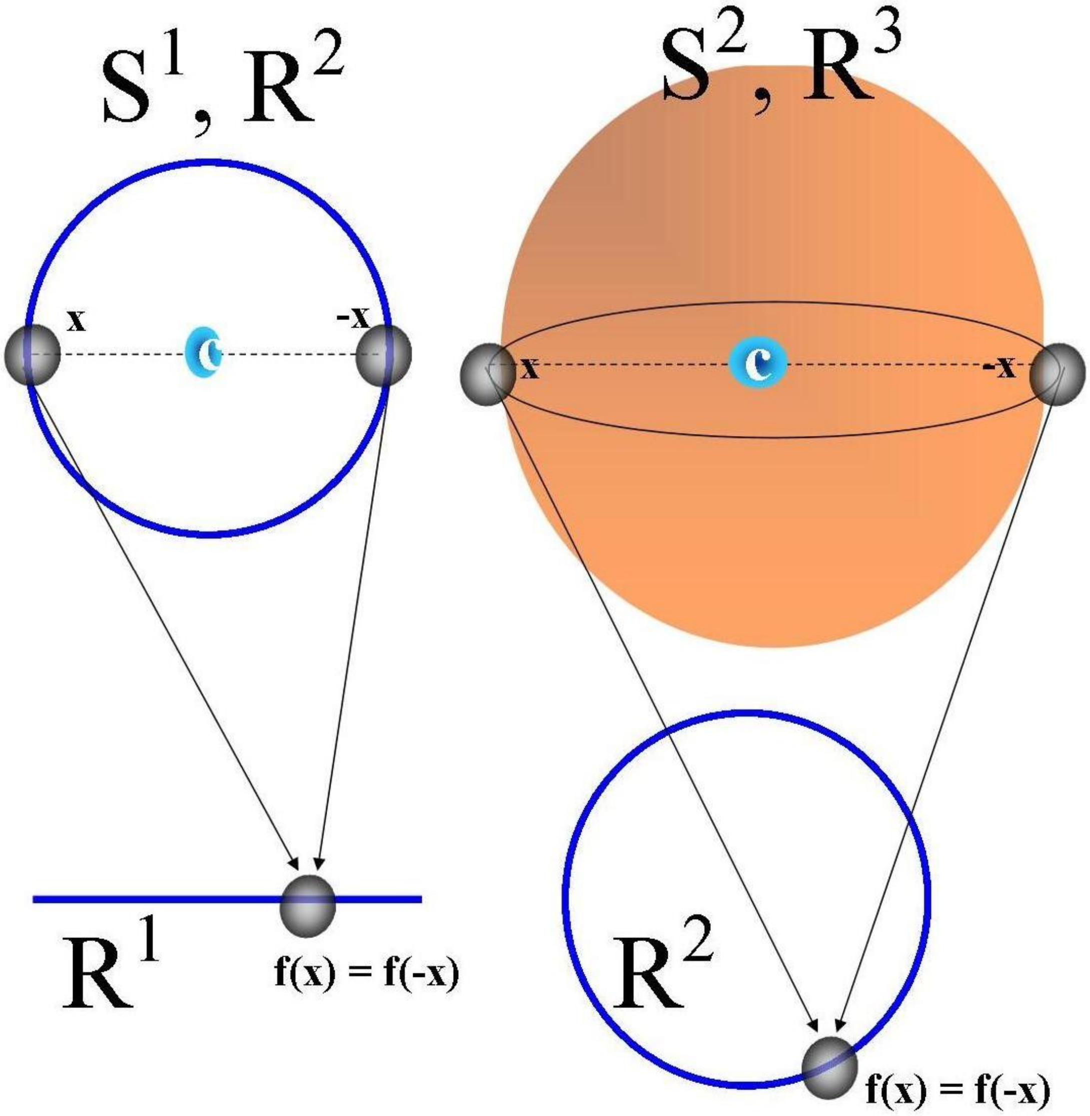


Figure 1. *The Borsuk-Ulam theorem for different values of* S^n*. Two antipodal points in* S^n *project to a single point in* R^n*, and vice versa.Remind that every* S^n *is embedded in a n+1-ball, and thus every* S^n *is one-dimension higher than the corresponding* R^n*.*

Application of BUT to signal analysis: shapes and homotopies. In terms of activity, a feature vector $x \in R^n$ models the description of a signal. To elucidate the picture in the application of the BUT in signal analysis, we view the surface of a manifold as a n-sphere and the feature space for signals as finite Euclidean topological spaces. The BUT tells us that for description f (-x) for a signal X, we can expect to find an antipodal feature vector f (-x) that describes a signal on the opposite (antipodal) side of the manifold S^n. Thus, the pair of antipodal signals have matching descriptions on S^n.

Let X denote a nonempty set of points on the surface of the manifold. A topological structure on X (called a topological space) is a structure given by a set of subsets τ of X, having the following properties:

(Str.1) Every union of sets in τ is a set in τ

(Str.2) Every finite intersection of sets in τ is a set in τ

The pair (X, τ) is called a topological space. Usually, X by itself is called a topological space, provided it has a topology τ on it. Let X,Y be topological spaces. Recall that a function or map $f : X \rightarrow Y$ on a set X to a set Y is a subset XxY so that for each x ∈*X*there is a unique *y*∈*Y*such that (x,y) ∈ f (usually written y =f (x)). The mapping *f* is defined by a rule that tells us how to find *f*(x). For a good introduction to mappings, see (Willard).

A mapping f : *X*→*Y* is continuous, provided, when $A \subset Y$ is open, then the inverse $f^{-1}(A) \subset X$ is also open. For more about this, see (Krantz). In this view of continuous mappings from the signal topological space X on the manifold's surface to the signal feature space R^n, we can consider not just one signal feature vector $x \in R^n$, but also mappings from *X* to a set of signal feature vectors *f*(*X*). This expanded view of signals has interest, since every connected set of feature vectors *f*(*X*) has a shape. The significance of this is that signal shapes can be compared.

A consideration of *f*(*X*) (set of signal descriptions for a region *X*) instead of *f*(*x*) (description of a single signal *x*) leads to a region-based view of signals. This region-based view of the manifold arises naturally in terms of a comparison of shapes produced by different mappings from *X* (object space) to the feature space R^n. An interest in continuous mappings from object spaces to feature spaces leads into homotopy theory and the study of shapes.

Let $f, g : X \to Y$ be continuous mappings from *X* to *Y*. The continuous map $H : X \times [0,1] \to Y$ is defined by:

$H(x,0) = f(x),\ H(x,1) = g(x),$ for every *x*∈*X*.

The mapping *H* is a *homotopy*, provided there is a continuous transformation (called a deformation) from *f* to *g*. The continuous maps *f*, *g* are called homotopic maps, provided *f*(*X*) continuously deforms into *g*(*X*) (denoted by $f(X) \to g(X)$). The sets of points *f*(*X*),*g*(*X*) are called shapes. For more about this, see (Manetti; Cohen).

For the mapping $H : X \times [0,1] \to R^n$, where *H*(*X*,0) and *H*(*X*,1) are *homotopic*, provided *f*(*X*) and *g*(*X*) and have the same shape. That is, *f*(*X*) and *g*(*X*) are homotopic, provided:

$\| f(X) - g(X) \| < \| f(X) \|$, for all*x*∈*X*.

There are natural ties between Borsuk's result for antipodes and mappings called homotopies. The early work on n-spheres and antipodal points eventually led Borsuk to the study of retraction and homotopic mappings (Borsuk 1958-59, Borsuk 1969, Borsuk 1980), pavin the way to the geometry of shapes and shapes of space (Collins). A pair of connected planar subsets in Euclidean space R^2 have equivalent shapes, provided the planer sets have the same number of holes. For example, the letters e, O, P and numerals 6, 9 belong to the same equivalence class of single-hole shapes. In terms of signals, it means that the connected graph for *f (X)* with, for example, an *e* shape, can be deformed into the 9 shape. This suggests yet another useful application of Borsuk's view of the transformation of a shape into another, in terms of signal analysis: sets of signals not only will have similar descriptions, but also dynamic character. Moveover, the deformation of one signal shape into another occurs when they are descriptively near (Peters 2014). It means that we are allowed to embed the Shannon entropy onto a n-sphere and to treat its values in terms of antipodal points. Therefore, we can deduce an optimization scheme that enables us to transport the two Shannon's antipodal points x and –x from S^n onto a S^{n-1}abstract manifold. The next two paragraphs will be devoted to illustrate how the Shannon entropy can be embedded in a n-sphere, both in ergodic and non-ergodic conditions.

Shannon entropy under ergodic conditions. For random numbers in the range from 0 to 1, we obtain the Shannon plot (**Figure 2A**). By embedding the Shannon plot in a hypersphere S^1 (the perimeter of a circle) with diameter F^1, a continuous function $\pi : S^1 \to R^1$ maps the BUT antipodal points *x* and -*x* to the same extreme entropy value, namely, H(1) = 0. In other words, both antipodal points have the same information content, since both are mapped to the same Shannon value, namely, 0. The center of the straight line segment $\overline{x(-x)}$ between the antipodal points (at the center of S^1) is mapped to the highest entropy, namely, H(0.5) = 1 (**Figure 2B**). The intermediate points on either side of the center of $\overline{x(-x)}$ are mapped to intermediate entropy values between 0 and 0.5. It easy to observe that the projection π : $(x_1, ..., x_{n+1}) \to (x_1, ..., x_n)$ is a homeomorphism from the Shannon curve U to S^1 with diameter F^1(**Figure 2B**). In such a vein, the points along one of the S^1 circles are homeomorphic to the Shannon entropy, under ergodic conditions. As a result, BUT provides a model for the computation of Shannon entropy, by evaluating the divergence of the probability of an event from the antipodal points on a hypersphere.

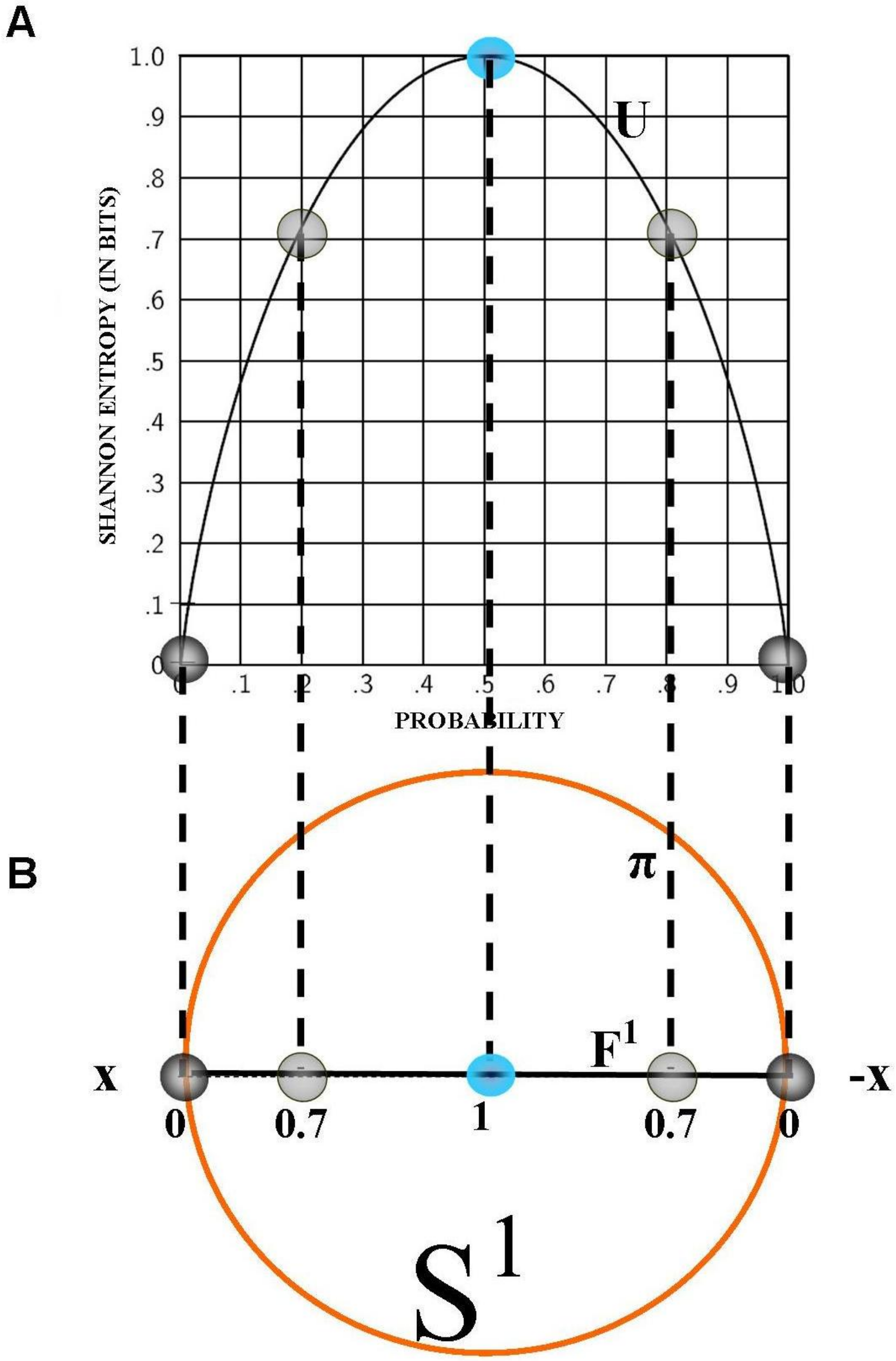


Figure 2. Figure 2A. Shannon entropy for probability distribution $P = (p, 1 - p)$, under ergodic conditions (from the original Shannon's graph). The entropy is plotted as a function of the random variable p, in the case of two possibilities with probabilities p and $(1-p)$. **Figure 2B.** Shannon (ergodic) entropy in the framework of the BUT theorem. Note that the entropy follows the circle diameter, e.g., the line which connects (maps to) the two antipodal points on S^1.

Shannon entropy under non-ergodic conditions. What happens in case of non-ergodic informational entropy? For example, take the case of a point λ on the S^1 sphere illustrated in Figure 1, which lies on a 1- circle forming the angle φ with the diameter F^1 of the ergodic Shannon entropy (**Figure 3**). If we find its antipodal point $-\lambda$, we achieve their homeomorphisms which can be projected on the Shannon plot, where we obtain the two points τ and $-\tau$. We can easily calculate the values of entropy and probability of τ and $-\tau$ (which are outside the classical Shannon curve), thus achieving the values of Shannon entropy in non-ergodic conditions. A bundle of lines (through the center of S^1) with different values of φ cover all the possibilities of non-ergodic entropy, just by embedding them in our n-sphere S^1. (**Figure 4**). In such a way, we achieve a circle equipped with countless diameters: one of them displays the Shannon entropy under ergodic conditions, the others display instead the informational entropies under non-ergodic condition. This simple operation allows a quantitative evaluation of informational entropies under non-ergodic assumptions.

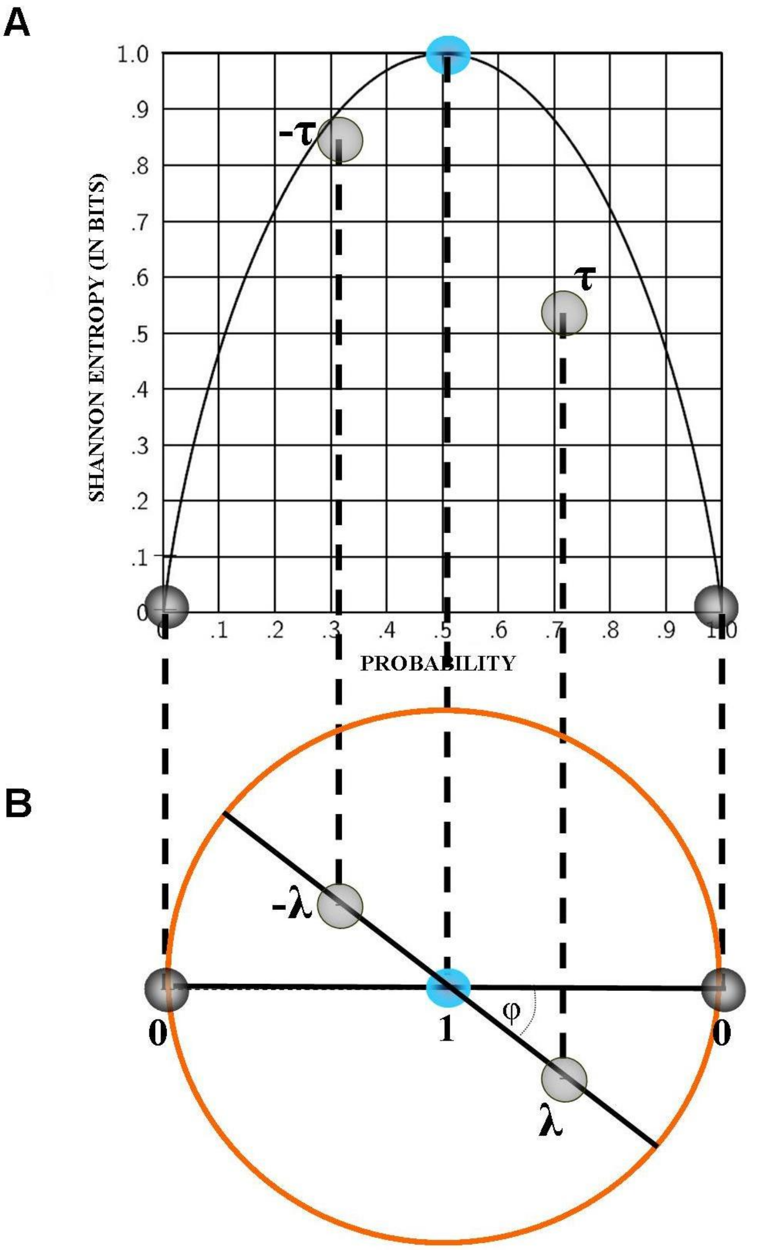


Figure 3. Non-ergodic probabilistic entropies in the framework of the BUT theorem. **Figure 3A**: Shannon entropy under non-ergodic conditions. Note that, while the ergodic Shannon entropy follows the diameter which connects the two antipodal points on S^1, non-ergodic entropies follow other quantifiable diameters along the "circumference" of S^1 (**Figure 3B**). Into the circle S^1, the points external to the Shannon entropy's diameter display all the possible values of non-ergodic entropy, i.e. the possibilities which does not fall into the Shannon plot's entropy curves. See text for further details.

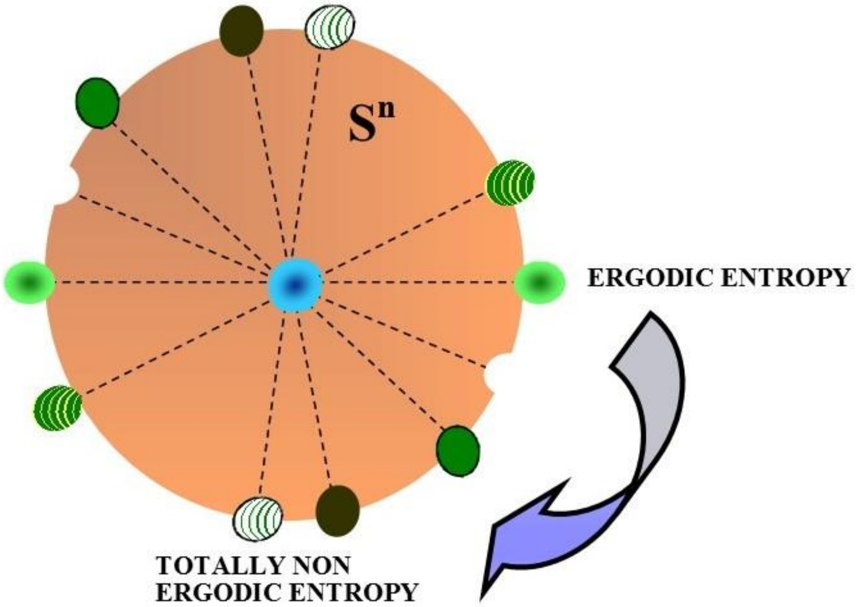


Figure 4. Bundle of lines on a n-sphere which illustrates the position of antipodal points for different non-ergodic conditions. The bundle can be used to evaluate the corresponding values of p and informational entropy on the Shannon plot.

RÉNYI ENTROPY ON A CIRCLE

The Shannon entropy is just a case of a family of more generalized entropies, such as Tsallis, and in particular, Renyi entropies, which also work just in an ergodic context. Indeed, the basic thermodynamic properties of many systems (i.e., multifractals) may be discussed by extending the notion of the information Shannon entropy into the more general framework of the Rényi entropy. Let *X* be a random variable with values in the range from 1 to *n*. Rényi entropy $H_n(X)$ of order *n* (Bialas et al, 2006) is defined by

$$H_n(X) = \frac{\log C(n,X)}{1-n}, \text{ where } C(n,X) = \sum_{i=1}^{m} p^n(x_i).$$

The Rényi entropy approaches the Shannon entropy as β approaches 1. By now, for sake of simplicity, we will termthe Rényi entropy order *n* with the greek letter β, so that β=1 (i.e., the limit for $\beta \to 1$) is defined to be the Shannon entropy:

$$Lim_{\beta\to 1} H_\beta(X) = \sum_i p_i \ln p_i.$$

The Rényi entropy is also closely related to the thermodynamical Gibbs entropy,via the thermodynamic free energy *F*, through the formula:

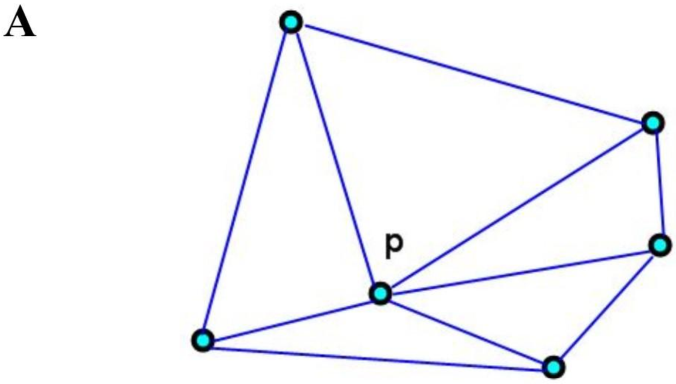
$F = (1 - T) H_\beta(X)$

In which T is the temperature. Mathematically, it is expressed as follows: the Rényi entropy of a system is minus the “1/β-derivative” of its free energy with respect to a quantity.

Because of its built–in predisposition to account for self–similar systems, the Rényi entropy is an effective tool to describe multifractal systems (Jizba and Arimitsu, 2001). It has been demonstrated that the Rényi entropy and generalized fractal dimension **α**are interchangeable: the Rényi’s parameter β is connected via a Legendre transformation with the multifractal singularity spectrum **α**. It means that, from the maximum entropy point of view, the power law

exponent n and Rényi’s parameter β exhibit a straight relation (see Jizba, 2001 for further details) and changes in power law exponents*n* lead to changes inRényi’s parameter β, and vice versa (Słomczynski et al, 2000).
In the next paragraphs, we will describe two different ways to embed the Rényi entropy on a n-sphere, both in touch with BUT dictates.

The first way: Rényi entropy-Based Friendship Theorem. The correlation between Rényi entropy and thermodynamic free energy can be explained via the Friendship Theorem introduced by Rényi and his coauthors in terms of the vertices of a particular graph (Havrda-Charvat, 1967, Rényi, 1966). It is C. Huneke’s simplified version of the Friendship Theorem (Huneke, 2002) that we give next.
Friendship Theorem:
if G is a graph in which any two vertices have exactly one common neighbour, then G has a vertex joined to all other vertices in the graph.
This theorem can be reformulated in terms of points and regions in the following way. In this reformulation, points x,y are connected, provided there is a straight edge whose endpoints are x,y.
Point-Based Friendship Theorem:
*if X is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.*This situation is illustrated in **Figure 5A**.
It is now a straightforward step to obtain a Rényi entropy-based Friendship Theorem:
if X maps to is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.
The situation described by the Rényi entropy-Based Friendship Theorem is illustrated in **Figure 5B**. If *X* is a region on an *n*-sphere and $H_{\alpha_1}(X), H_{\alpha_2}(X)$ are Rényi entropies of region *X* with respect to parameters α_1, α_2, respectively. In addition, it is assumed that *X* is a smooth manifold and $f : H_\alpha(X) \to X \in 2^{\mathbb{R}^n}$ is a homeomorphism that maps $H_{\alpha_1}(X), H_{\alpha_2}(X)$ to a region X in Euclidean space R^n. The vectors in X represent observations such as cortical temperatures that give rise to the n-sphere entropies shown in Figure 2B. We know from BUT that, whenever there is a continuous function f on n-sphere, a pair of antipodal points is mapped by *f* to a value in R^n, which has a region-based extension (Peters, 2016). In particular, given the homeomophism *f* which is a continous function on an *n*-sphere S^n whose surface values are Rényi entropies, then we know there is a pair of Rényi entropies that are mapped by *f* to $X \in 2^{Rn}$. In effect, we arrive at a reversal of Rényi entropies.



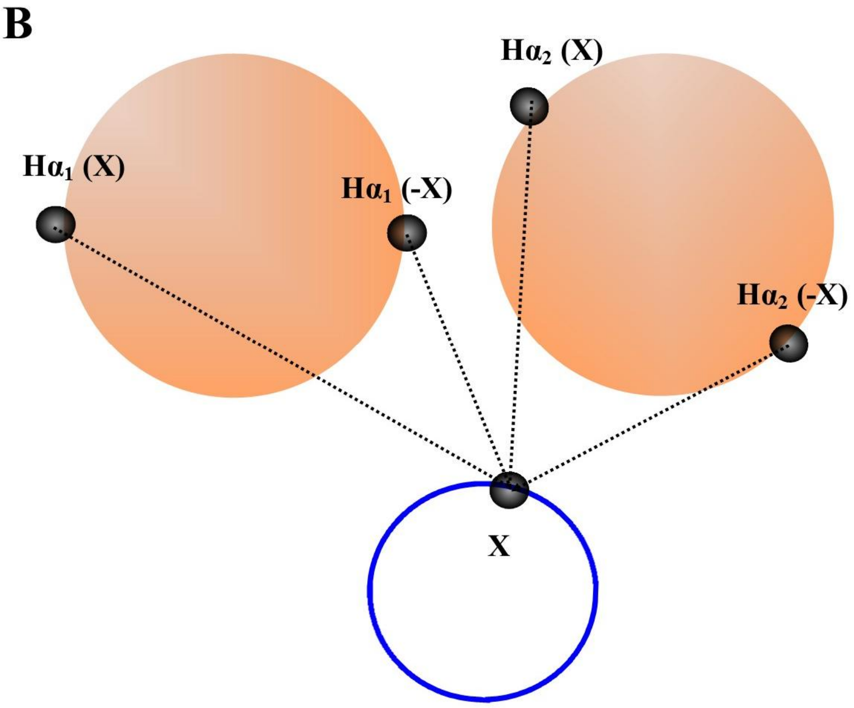


Figure 5A. Point-Based Friendship Theorem. See the main text for further details.
Figure 5B. Rényi entropy-Based Friendship Theorem.

The second way: a fractional dimension. In the framework of Rényi entropy, we introduce a quantity called the *entropy difference:*

$$\Delta_{\alpha,\alpha_0}(P) = H_\alpha(P) - H_{\alpha_0}(P).$$

If we assume that $\alpha \rightarrow \alpha_0$, we can use the expansion of $H_\alpha(P)$ around a_0, obtaining the *differential entropy difference,* which is proportional to entropy derivative with respect to Rényi parameter:

$$\Delta_{\alpha,\alpha_0}(P) \approx \frac{d\,H_{\alpha_0}(P)}{d\alpha_0}(\alpha - \alpha_0).$$

Rényi entropy $H_n(X)$ of order *n* correlates with a hypersphere S^n and, applying BUT, we can predict entropy values assocated antipodal points on each *n*-sphere. That is, for a range of Rényi entropy orders $1,\ldots,n$, we map each n-sphere to Rényi entropy values in R^n. See **Figure 6** for an example.

Indeed, hyperspheres of order n can to extended to fractional values of n, giving rise to an enlarged of hyperspheres susceptible to treatment by BUT. To see this, consider the following introduction to the Hausdorff dimension.

4) **Metric space**: Let X be a metric space with the metric $\mu_d(X)$ defined on it. This means that $\mu_d(X) \geq 0$ and μ_d has the usual symmetry and triangle inequality properties for all subsets of X.
5) **Hausdorff measure**: Let d be either 0 or a positive real number in R_0^+. The Hausdorff measure $\mu_d(X)$ equals a real number for each number d in $X = R^d$.
6) **Hausdorff dimension (informal)**: The threshold value of d denoted by $\dim_H(X)$ is the Hausdorff dimension of X, provided $\mu_d(X) = 0$, if $d > \dim_H(X)$, and $\mu_d(X) = \infty$, if $d < \dim_H(X)$.

Hausdorff Dimension- To arrive at the Hausdorff (fractional) dimension of a subset X in a metric space, we need to consider the Hausdorff measure of X.

Definition 1. Hausdorff measure. Let X be a subset of a metric space M and let d any real number in R_0^+ $\varepsilon \in R_0^+$(a real number that is either positive or zero) a nonempty subset of X, U_i, $i \in \{1, . . . ,n\}$ is a cover of X, i.e., X is a subset of $X \subseteq C_i$ for all i (Schleicher 2007). Here n is any positive integer. Also, let diam(Ui) $<\varepsilon$ be the diameter of the cover U_i. The d-dimensional Hausdorff measure $\mu_d(X)$ is defined by:

$$\mu_d(X) = \lim_{\varepsilon \to 0}\left[\inf_{U_i \supseteq X} \sum_{i=1}^{n} n\left(diam\left(U_i\right)\right)^d\right].$$

The basic idea is to cover X with sets U_i with small diameters and estimate the d-measure of X as the sum of the $(\mathrm{diam}(U_i))^d$, i.e., the sum of the U_i diameters raised to the power d.

Lemma 1. Schleicher Lemma. Let d be any real number in R_0^+. For every bounded set X in a metric space, there is a unique value of $d := \dim_H(X)$ in $R_0^+ \cup \{\infty\}$ such that:

$\mu_d^I(X) = 0$, if $d^I > d$.

$\mu_d^I(X) = \infty$, if $d^I < d$.

Definition 2. Hausdorff dimension. The value of $d = \dim_H(X)$ in R_0^+ called the Hausdorff dimension of X. With $d = \dim_H(X)$, the Hausdorff measure $\mu_d(X)$ may be zero, positive or infinite.

Lemma 2. Schleicher Boundedness Lemma. Let d be any real number in R_0^+ and let Y be a metric space. If $X \subset Y$, then:

$\dim_H(X) \leq \dim_H(Y)$.

Proof. Immediate from the definition of the Hausdorff dimension of a nonempty set.

Assume that X is a nonempty subset (inner sphere) of an n-sphere and having the same center as S^n with the Hausdorff measure $\mu_d(X)$ defined on it and assume that $\mu_d(X)$ satisfies the Schleicher Lemma 1 conditions. The inner sphere S^d of an n-sphere S^n can be any sub-sphere in S^n, including S^n itself. Then, the inner sphere S^d has dimension $d = \dim_H(X)$, $d \leq n$. In addition, assume that R^d is a d-dimensional space which is a subset of the n-dimensional Euclidean space R^n, $d < n$. This gives us new form of the Borsuk-Ulam Theorem.

Theorem 1. Hausdorff-Borsuk-Ulam Theorem. Let S^d with Hausdoff dimension d be an inner sphere of an n-sphere and let $f : S^d \longrightarrow R^d$ be a continuous map. There exists a pair of antipodal points on S^d that are mapped to the same point in R^d.

Proof. A direct proof of this theorem is symmetric with the proof of the Borsuk-Ulam Theorem is given by Su (1997), since we assume that S^d is an inner sphere of S^n symmetric about the center of S^n and, from the Schleicher Boundedness Lemma 2, $\dim_H(S^d) \leq \dim_H(S^n)$.

We can thus evaluate how changes of Rényi parameter influence the structure of information measures in the probability space (**Figure 6**). To make an example, starting from a value of Renyi exponent (i.e., 0.4), it is possible to calculate the entropy values in case one wants to evaluate other exponents (**Figure 6**). The Figure 6 shows that the antipodal points corresponding to the exponent 2 are indeed in an exact position on the diameter corresponding to the 0.4 exponent. If one knows the position of all the Rényi exponents projected on a n-sphere, it is feasible to achieve all the corresponding values of Rényi entropies.

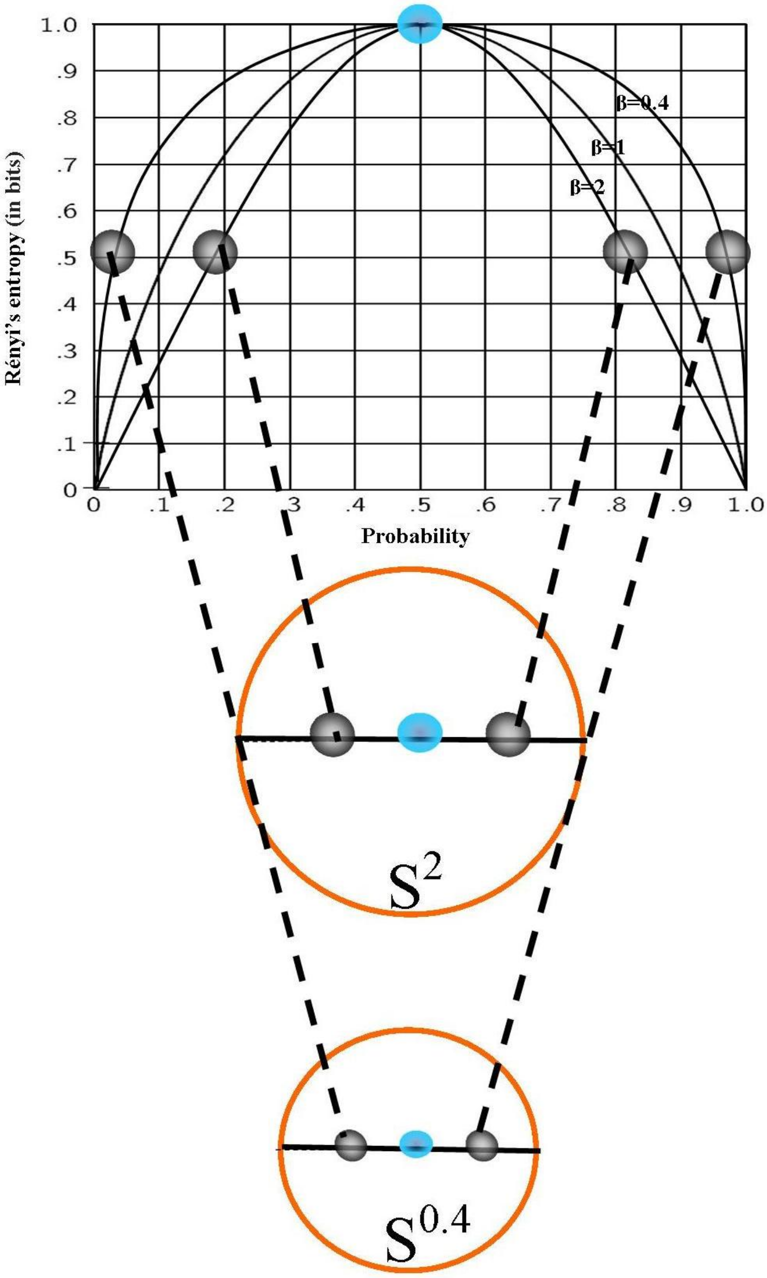


Figure 6. Generalized Renyi entropy. Note that $S^{0.4}$ has a smaller diameter than S^2 and the dotted lines are tangent to S^2. We achieve a mapping of antipodal points in $S^{0.4}$ to the Rényi entropy values associated with antipodal points on S^2.

CONCLUSIONS

We demonstrated that ergodic and non-ergodic informational entropies can be solved in terms of algebraic topology, by embedding the Shannon's plot in a n-sphere and by applying the Borsuk-Ulam theorem. Further, we provided an effort to insert informational entropies in the framework of group theory, by considering probabilities in guise of permutations on a n-sphere. The question now is: which are the advantages of such a "treatment"? For example, what does the use of Hausdorff-Borsuk-Ulam Theorem give us for different applications of Rényi entropy? The Borsuk-Ulam theorem and its variants display very useful general features which help us to explain a wide-range of phenomena, including brain activity. When a single point is embedded in just one dimension higher, it gives rise to two antipodal points. Thus, by adding just a further dimension to a biological system, we are allowed to study it in terms of antipodal points

(Tozzi 2016b). Furthermore, the two antipodal points on a S^n-sphere display homotopy and have matching descriptions. If we evaluate biological dynamics instead of "signals", BUT leads naturally to the possibility of a region-based, not simply point-based, geometry. In such a vein, a collections of brain signals could be viewed as surface shapes (or functions, or signals), where one shape maps to another antipodal one. We are also allowed to use the parameter n - a versatile tool which can be used both for integer and rational numbers - not just for the description of topological manifolds, but of biological systems too.

Why Rényi entropy? Rényi entropy and generalized diversity functions have shown to be proper indicators to quantify systems over time: from to plant communities (De Luca et al., 2011) to urban mosaics (Carranza et al., 2007). The use of Rényi entropy– unlike the many diversity measures for summarizing landscape structure based on Shannon entropy (Patil & Taillie, 2001) – allows the description of the ecosystem status at a specific moment and its trend over time (Müller, Hoffmann-Kroll, & Wiggering, 2000). Rényi entropy offers a "continuum of possible diversity measures" (Ricotta et al., 2003) at diverse spatial scales, which differ in their sensitivity to rare and abundant picture indexes, becoming increasingly regulated by the commonest when β gets higher. The change in β exponent can be regarded as a scaling operation that takes place not in the real, but in the data space (Podani, 1992). The aim of using the Rényi entropy does not consist in selecting the most appropriate parameter, rather in constructing 'diversity profiles': the Rényi's parameter β is particularly important, since it is not redundant and allows us to consider several measures at a time, by varying just the β parameter therein. The opportunity to treat Rényi entropies as topological structures gives rise to the possibility to evaluate brain phenomena with novel analytical tools, such as algebraic topology, combinatorics, hereditary set systems (Matoušek), simplicial complexes, homology theory, functional analysis and with generalizations of the Borsuk-Ulam theorem, such as, for example, the Bourgin-Yang-type theorems (Yang) and the Grassmann manifolds (Dol'nikov). If the dimension in which the sphere is embedded takes into account also non-ergodic conditions, we have a tool which is feasible for a calculation of both ergodic and non-ergodic entropies. In conclusion, we provided a very general topological mechanism which solves long-standing problems of non-ergodic and general informational entropies, casted in a physical/biological fashion which has the potential of being operazionalized and experimentally tested in the evaluation of brain dynamics.

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ENERGETIC LINK BETWEEN SPIKE FREQUENCIES AND BRAIN FRACTAL DIMENSIONS
(brain fractal slopes dictate spike frequencies, via informational entropy)

Oscillations in brain activity exhibit a power law distribution which appears as a straight line when plotted on logarithmic scales in a log power versus log frequency plot. The line's slope is given by a single constant, the power law exponent. Since a variation in slope may occur during different functional states, the brain waves are said to be multifractal, i.e., characterized by a spectrum of multiple possible exponents. A role for such non-stationary scaling properties has scarcely been taken into account. Here we show that changes in fractal slopes and oscillation frequencies, and in particular in electric spikes, are correlated. Taking into account techniques for parameter distribution estimates, which provide a foundation for the proposed approach, we show that modifications in power law exponents are associated with variations in the Rényi entropy, a generalization of Shannon informational entropy. Changes in Rényi entropy, in turn, are able to modify brain oscillation frequencies. Therefore, results point out that multifractal systems lead to different probability outcomes of brain activity, based solely on increases or decreases of the fractal exponents. Such approach may offer new insights in the characterization of neuroimaging diagnostic techniques and the forces required for transcranial stimulation, where doubts still exist as to the parameters that best characterize waveforms.

SIGNIFICANCE STATEMENT

The generalized informational entropy called "Rényi entropy" does not select the most appropriate probabilistic parameter as Shannon's, rather it builds diversity profiles. By offering a continuum of possible diversity measures at many spatiotemporal levels, it is very useful in the evaluation of the fractal scaling occurring in the brain. Rényi entropy elucidates how power laws behaviours in cortical oscillations are able to modify electric spike frequencies. Through its links with the scale-free behavior of cortical fluctuations, Rényi entropy suggests that the brain changes its fractal exponents in order to control free-energy and scale the entropy of different functional states.

INTRODUCTION

The brain activity observed at many spatiotemporal scales exhibits fluctuations with complex scaling behavior (Newman, 2005), including not only cortical electric oscillations, but also membrane potentials and neurotransmitter release (Linkenkaer-Hansen et al., 2001; Fox and Raichle, 2007; Milstein et al., 2009). In particular, the frequency spectrum of cerebral electric activity displays a scale-invariant behaviour $S(f) = 1/f^{\mu}$, where $S(f)$ is the power spectrum, f is the frequency and μ is an exponent that equals the negative slope of the line in a log power versus log frequency plot (Pritchard, 1992; Van de Ville et al., 2010). The (spatial) fractals and (temporal) power laws can be regarded as intrinsic properties of the brain and characterize a large class of neuronal processes (de Arcangelis and Herrmann, 2010; He et al., 2010); moreover, pink noise distributions contain information about how large-scale physiological and pathological outcomes arise from the interactions of many small-scale processes (Jirsa et al., 2014). The fractal slope is not invariant in the brain, rather is characterized by multiple possible exponents, summarized in a single value, the so called "generalized fractal dimension" γ. It has been demonstrated that different functional states - spontaneous fluctuations, task-evoked, perceptual and motor activity (Buszaki and Watson, 2012), cognitive demands (Buiatti et al., 2007; Fetterhoff et al., 2014), ageing (Suckling et al., 2008) - account for variations in power law exponents across cortical regions (Tinker and Velazquez, 2014; Wink et al., 2008). Accordingly, we may view brain activity as an ensemble of intertwined (mono)fractals, each with its own dimension and scaling slope, each marking dynamical transitions between different response regimes (Papo, 2014). The aim of this review is to evaluate the relationship among scaling exponents, free-energy/spike frequency and generalized informational entropies in the brain. Starting from Rényi entropy, and introducing a link with the power law behavior of cortical fluctuations, we show how the brain might change its fractal exponents, in order to control free-energy and scale the entropy of different functional states.

RÉNYI ENTROPY AND ITS THERMODYNAMICAL COUNTERPARTS

Here, we show how a generalization of informational entropies, e.g., the Rényi entropy, may turn out to be a useful tool in the evaluation of multifractal dynamics. The classical informational Shannon entropy is (Shannon, 1948):

$$S(X) = -\sum_{i=1}^{N} p_i \ln p_i . \qquad (1)$$

where X is a random variable with n possible outcomes and $p_i = P$ (for $i = 1,2,3, \dots n$) is the probability distribution P on a finite set. In other words, $S(P)$ is a function of a generic probability distribution p such that, if we modify p, we achieve a different value of entropy on the Shannon's curve. Natural generalizations of the Shannon entropy have been proposed. Among the available ones (e.g., Tsallis, 1988), it is convenient for our purposes to work with the one-parameter class of Rényi entropies with parameter α (Rényi, 1966), a flexible and underestimated information-theory based index. From the standpoint of information theory, Rényi entropy is a measurable quantity with operational definition, as it represents the minimal cost of a message, under the assumption that the cost is an exponential function of the code-length (Cambell, 1965). Rényi entropy can be defined as:

$$H_\alpha(X) = \frac{1}{1-\alpha} \ln \sum_{i=1}^{N} p_i^\alpha . \qquad (2)$$

where$0 \leq \alpha < \infty$. Rényi entropy approaches Shannon entropy as α tends to 1, so that, for $\alpha \to 1$, we recover the classical Shannon entropy.

Rényi entropy has applications in dynamical systems (Hentschel and Proccacia, 1983), coding (Cambell, 1965), information transfer (Jizba et al., 2012), theories in quantum mechanics (Jizba et al., 2015) and black holes' mutual information (Dong, 2016). Rényi entropy and generalized diversity functions have also been used to quantify ecosystems dynamics: from land cover types (Carranza et al., 2007; De Luca et al., 2011), to coastal dunes environments (Drius et al., 2013), from urban mosaics (Carranza et al., 2007) to species diversity in large areas (Rocchini et al., 2013). Multiscale entropy methods have been found to be suitable for the assessment of human heartbeat fluctuations and coding and noncoding DNA sequences analysis too (Costa et al., 2005).

Unlike the many diversity measures for summarizing landscape structure based on Shannon entropy, Rényi entropy makes it possible to describe the system's status at a specific moment as well as its time-varying trend (Müller et al., 2000; Patil and Taillie, 2001). Diversity cannot be reduced to a single index information, since all its aspects cannot be captured in a single statistics (Gorelick, 2006). A complete characterization of landscape diversity can be achieved if, instead of a single index, a parametric family of indices is used, whose members have varying sensitivities to the presence of rare and abundant elements, as in the case of the Rényi entropy (Jost, 2007). Diversity profiles are flat when the landscape is even, and steeply decrease as the landscape turns uneven (Jost, 2010). Therefore, Rényi's formulation allows a continuum of possible diversity measures which differ in their sensitivity to the rare and abundant elements in a landscape. Because of its build-in predisposition to account for self-similar systems, Rényi entropy is an effective tool to describe multifractal systems (Jizba and Arimitsu, 2001). Although fractal dimension does not encompass the full information of the Rényi entropy for arbitrary distribution, the former is a scaling exponent of the latter. Therefore, the generalized fractal dimension γ and the Rényi exponent α can be thought of as interchangeable. In particular, the Rényi parameter is connected via a Legendre transformation with the multifractal singularity spectrum. This in particular means that, from the maximum entropy point of view, Rényi entropy and power law exponent μ (expressed by the generalized fractal dimension γ) are strictly correlated. See Jizba and Arimitsu (2001) and Jizba and Korbel (2014) for technical details on mathematical proof. Therefore, changes in n and in γ lead to changes in the Rényi parameter α, and vice versa (Słomczynski et al., 2000). Variations in α, in turn, modify the probability distribution on finite sets. Thus, multifractal systems lead to different probability outcomes based solely on increases or decreases of $1/f^\mu$ exponents. In sum, the "probabilistic" virtues of Rényi entropy represent a novel physics-based approach to probe neural scale-free dynamics, with the potential to lead to new insights into brain systems at all space-time scales and all levels of complexity.

On the other hand, informational entropies are closely related to thermodynamic entropy. Because thermodynamic variables and Rényi parameter are in straight relation (Baez, 2011), changes in thermodynamic parameters lead to different probability outcomes. The connection between informational entropies and their thermodynamical counterparts, e.g., the Boltzmann-Gibbs entropy, is given by a standard procedure of maximum entropy (MaxEnt) distribution and thermodynamical limit ($N \to \infty$). The significance of entropy in statistical physics lies in the fact that the distribution which maximizes entropy under given constraints is the preferred one. The so-called MaxEnt principle, introduced by Jaynes (1957), leads to the classical distribution $p(E) = 1/Z\, e^{-\beta E}$, where $\beta = 1/k_B T$ is the inverse temperature.

A "TOP-DOWN" APPROACH TO RÉNYI ENTROPY

Here, we introduce a different approach to Rényi entropy and show how to use it for the assessment of thermodynamical parameters. Shannon entropy elucidates how changing the probabilities usually occurs when we have prior information. But suppose we address the issue from the reverse perspective: when the entropy changes, how does its variation influence the distributions? Given a distribution P, what information content is measured by a given entropy? Which factors are able to modify the entropy and to lead to different probability distributions? In the case of information entropy, we have a function $y = f(x)$, in which x is the input (the probability) and y is the output (the entropy). However, if we change y with y', can we find an y' such that $y' = f(x')$? We know that when p changes, S changes, but is the reverse true? is it possible the opposite, such that if S changes, p changes? Further, if we are hypothetically able to change S, is it possible to achieve the corresponding values of probability distribution p? Are there cases in which changes in S are known *a priori*, without a previous knowledge of p?

The "reversal" of Rényi entropy is easily explainable in topological terms, as a straightforward extension of the point-based Rényi Friendship Theorem (Huneke, 2002). Indeed, the above mentioned correlation between Rényi entropy and thermodynamic free-energy can be elucidated via the Friendship Theorem, in terms of the vertices of a particular graph (Havrda and Charvat, 1967, Rényi, 1966), illustrated in **Figure 1A**. It is Huneke's simplified version of the Friendship Theorem (Huneke, 2002) that we give next.

Friendship Theorem. *If G is a graph in which any two vertices have exactly one common neighbour, then G has a vertex joined to all other vertices in the graph.*

This theorem can be reformulated in terms of points and regions. In this reformulation, points x, y are connected, provided there is a straight edge whose endpoints are x, y.

Point-based Friendship Theorem. *If X is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.*

This situation is illustrated in **Figure 1A**.

It is now a straightforward step to obtain a Rényi entropy-based Friendship Theorem.

Rényi Entropy-based Friendship Theorem. *If X maps to is a nonempty set of points in which any two points are connected to a common point, then X has a point p that is connected to every other point in the set.*

The situation described by the Rényi Entropy-Based Friendship Theorem is illustrated in **Figure 1B**. If X is a region on an n-sphere, $H_{\alpha_1}(X), H_{\alpha_2}(X)$ are Rényi entropies of region X with respect to parameters α_1 and α_2. In addition, it is assumed that X is a smooth manifold and $f : H_\alpha(X) \to X \in 2^{Rn}$ is a homeomorphism that maps $H_{\alpha_1}(X), H_{\alpha_2}(X)$ to a region X in Euclidean space R^n. The vectors in X represent observations such as thermodynamical parameters (in our case, free-energy) that give rise to the n-sphere entropies shown in **Figure 1B**. We know from the Borsuk-Ulam Theorem (Borsuk, 1933; Tozzi and Peters, 2016a and 2016b) that, whenever there is a continuous function f on n-sphere, a pair of antipodal points is mapped by f to a value in R^n, which has a region-based extension (Peters, 2016). In particular, given the homeomophism f which is a continuous function on an n-sphere S^n whose surface values are Rényi entropies, then we know there is a pair of Rényi entropies that are mapped by f to $X \in 2^n$. In fact, we arrive at a reversal of Rényi entropies, in the sense that, starting from known values of entropy, we are able to achieve single probability values in lower dimensions.

Summarizing, our aim was to describe a case of "reverse" Rényi entropy: instead of the customary "bottom-up approach" (given known values of p, we obtain S), we can start from a "top-down" approach (given known changes in S, we obtain the unknown values of p). In technical terms, we consider entropy as a functional for an arbitrary distribution p and investigate its modifications, when a change in parameter α occurs, but the entropy S_α as a number remains the same. Let us have a distribution $P = (p_1, \dots, p_n)$ and entropy $H_\alpha(P)$. We would like to find a distribution Q s.t. $H_\alpha(P) = H_{\alpha'}(Q)$ for given α'. There are many possible distributions Q, but there is one special class Q_t, for which is $q_i = \frac{1}{n} + \left(p_i - \frac{1}{n}\right)t$. It is easy to show that $\sum_{i=1}^{n} q_i = 1$. The main advantage is that such class of distribution is partially ordered by the operation of majorization. Finally, parameter t can be obtained from the equation: $H_\alpha(P) = H_{\alpha'}(Q_t)$.

Is this a counterintuitive operation useful? Under which circumstances prior information on the level of entropy S is able to influence the probabilities? In the next chapter, we will point up that a clear correlation does exist between free-energy, multifractal spectrum and brain functions, when evaluated in terms of the probability states of spike frequencies dictated by "top-down" Rényi entropy.

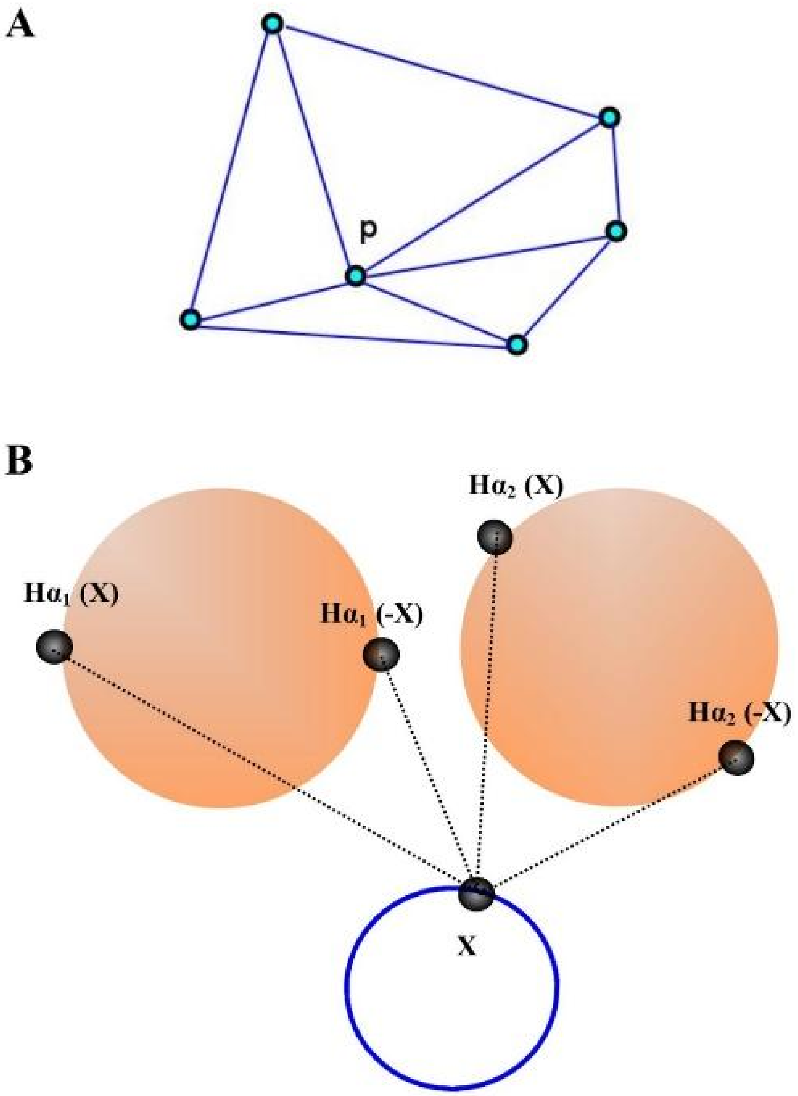

Figure 1A. Point-Based Friendship Theorem. See the main text for further details. **Figure 1B**. Rényi entropy-Based Friendship Theorem. It is grounded on the original Borsuk-Ulam theorem, which states that every continuous map $f : S^n \to R^n$ must identify a pair of antipodal points (on S^n). Another less technical definition of the Borsuk-Ulam theorem is: if a sphere is mapped continuously into a plane set, there is at least one pair of antipodal points having the same image; that is, they are mapped in the same point of the plane (Borsuk, 1933; Tozzi and Peters, 2016a).

THE "TOP-DOWN" APPROACH TO RÉNYI ENTROPY AND CORRELATIONS BETWEEN THERMODYNAMIC PARAMETERS AND POWER LAWS IN THE BRAIN

Here we correlate the "top-down" formulation of Rényi entropy with brain dynamics. In particular, we show how such Rényi entropy allows us to establish a connection between cortical power laws and spike frequencies.

Scale-free behavior is related to the frequency of brain oscillations, in particular to the frequency of electric spikes. Recent papers, starting to uncover connections between the exponent of a fractal scaling in escape paths from energy basins and the activation free-energy (Perkins et al., 2014), point towards cortical fluctuations in power law exponents that are able to modify the brain energy. Furthermore, exponential power law distribution can be described in terms of a skewness parameter controlling frequencies peakedness (Çankaya et al., 2015). It means that spike frequency's intrinsic asymmetry can be efficiently modelled too. Throughout the increases in free-energy, the $1/f^{\mu}$exponent varies across brain regions. The ongoing fluctuations with complex scale-free properties can thus be absorbed into a free-energy framework: the critical slowing implicit in power law scaling of dynamics is mandated by any system that minimizes its energetic expenditure (Friston, 2015). In turn, brain free-energy is correlated with the frequency of electric spikes. Indeed, each spike has a specific metabolic cost of 6.5 μmol/ATP/gr/min (Attwell and Laughlin, 2001; Sengupta et al., 2013). A recent study suggests that, because of the Ohm's law, energy consumption due to the "amplitude" of the oscillation is negligible, as compared with energy consumption due to the "frequency" of the oscillation (Tozzi et al., 2016). It means that electric spike frequency is correlated with brain fractal dimensions.

When generating a synthetic multifractal system in a log amplitude versus log frequency scatter plot, different series of free-scale oscillations with diverse power law exponents are achieved (**Figure 2A**). For sake of clarity, **Figure 2A** displays just the slope $\gamma = 2.1$. In order to correlate the probability p with log frequency, the values of log frequency can be projected to the x-axis of the Shannon's plot. The procedure is displayed in **Figure 2B**, where the two possibilities with probabilities $p = 0$ and $p = 1$ stand for $p = 0.2$ Hz and 16 Hz, respectively, and the intermediate values for the in-between frequencies, each one characterized by its probability p. **Figure 2B** displays the values of Rényi entropy (where $\alpha = 1$ corresponds to the slope $\gamma = 1$) on the y-axis, plotted as a function of p (and thus of log frequency) on the x-axis.

Once plotted the log frequency on the x-axis of the probabilities, modifications of the α exponent lead to different values of brain oscillations. The curves in **Figure 3** illustrate, as an example, the case of the "classical" Rényi entropy. At a given fixed value of p on the x-axis, changing the exponent α leads to an increase in Rényi entropy, and vice versa. In the "reverse" example depicted in **Figure 3B**, at a given fixed value of Rényi entropy on the y-axis, a variation in Rényi exponent modifies the probabilities, leading to a different probability distribution (and thus a different oscillation frequency). In other words, at each given value of Rényi entropy, a simple variation in power law exponent n modifies the value of p. Therefore, changes in α exponent are correlated with the occurrence of different spike frequencies.

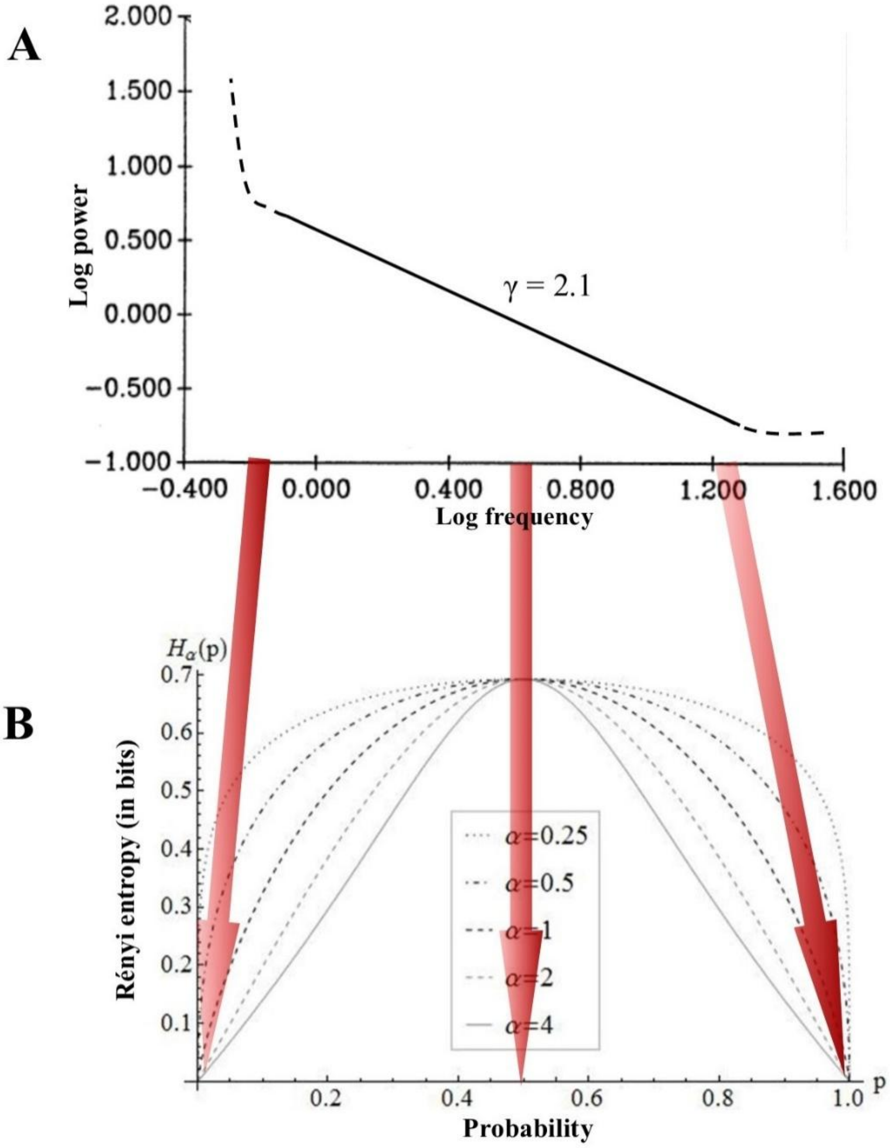

Figure 2A. Log amplitude versus log frequency scatter plot of brain spikes detected by EEG techniques (modified from Pritchard, 1992). The Figure displays on the x-axis the frequency (in Hz) and on the y-axis the power (in μV^2) of the electric spikes. Note that the scale is logarithmic: this means that on the x axis -0.400 = 0,39 Hz, 0 =1 Hz, 0.4 = 2.52 Hz, 1.2 = 16 Hz, and so on. In turn, on the y axis, -1.000 = 0,1 μV^2, -0.5 = 0,32 μV^2, 0.000 = 1 μV^2, 1.000 = 10 μV^2, and so on. The figure also depicts a possible fractal dimension, equipped with slope γ = 2.1. Note that the γ exponents, together with scale-free behavior, are lost at the slope's tails (dotted lines on the right and left of the main slope). **Figure 2B.** The Rényi entropy is plotted as probability distribution $P = (p, 1 - p)$ for different values of the Rényi parameter α. The solid curves show five cases of Rényi entropy, with exponents α=0.25, α=0.5, α=1 α=2 and α=4. The curve α=1 stands for the Shannon entropy (under ergodic conditions). The three arrows depict how the frequency parameter of **Figure 2A** can be embedded into the Rényi's plot of **Figure 2B**, via affine connections.

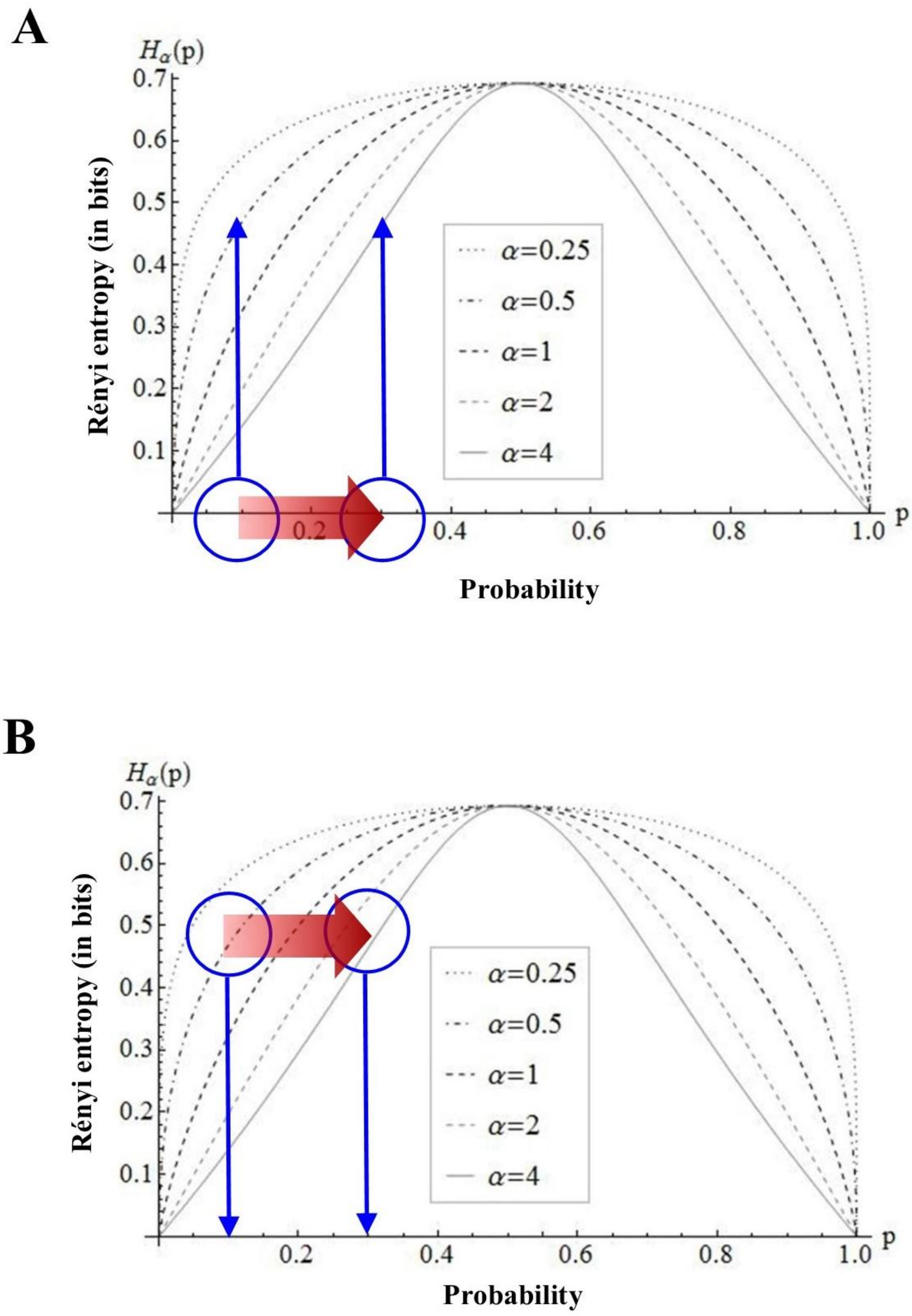

Figure 3A. Schematic representation of the "classical" Rényi entropy. The large arrow depicts how, at a fixed value of entropy (in this example, 0.45) on the y-axis, when p changes (from 0.1 to 0.3) on the x-axis, also the corresponding values of α change (from 0.5 to 4). **Figure 3B.** Schematic representation of the "reverse" Rényi entropy, illustrating the virtues of "top-down" entropy in the evaluation of probability distributions: at the fixed value of Rényi entropy=0.45 on the y-axis, when α changes from 0.5 to 4, we achieve a different value of p (from 0.1 to 0.3) on the x-axis.

CONCLUSIONS

We showed how increases or decreases in the $\frac{1}{f^{\mu}}$ power slope in the brain multifractal system might play a role in oscillations frequency. In other words, are we allowed to link probability outcomes with cortical electric spikes. Primitive changes in a sole parameter (the power law slope) lead to different probability distributions in cortical spike frequencies, through modifications in Rényi entropy. The "inverse" top-down approach to Rényi entropy (e.g., starting from known entropy changes, we achieve the unknown probability distributions) allows us to evaluate nervous system's macro-states based on a sole order parameter, although lacking knowledge of micro-states. The rationale for using the Rényi entropy does not lie in selecting the most appropriate parameter, rather in constructing "diversity profiles" (Patil and Taillie, 2001). Rényi entropy offers a "continuum of possible diversity measures" (Ricotta and Avena, 2003) at diverse spatiotemporal scales, which differ in their sensitivity to rare and abundant picture indexes, becoming increasingly regulated by the commonest when α gets higher. The change in α exponent can be regarded as a scaling operation that takes place not in the real, but in the data space (Podani, 1992). In sum, the Rényi α parameter is not redundant and allows us to consider several measures at a time. We can thus evaluate how changes in the Rényi parameter influence the structure of information measures in the probability space of brain activity. Rényi parameter's interpretation becomes clearer if we think that, in touch with thermodynamics, for values of α closer to the central spike frequencies: a) the entropy is sharply peaked around the maximal state, b) the entropy of non-maximal states rapidly decreases, and c) the most probable state is just one, whereas the other ones are suppressed. On the contrary, for values of α closer to the lowest and the highest spike frequencies, the distribution of near-optimal states is much broader and the entropy is flatter around the maximal value. Therefore, many energy states are occupied with high probability.

We hypothesize that, in order to optimize its activity, the brain displays an intrinsic mechanism of fluctuations equipped with complex temporal and spatial scaling properties. In this framework, changes in power law exponents play a crucial role in information processing, leading to variations not only in entropy and probability, but also in spike frequency. Complex scale-free statistics are thus fixed points of renormalization flows and can be understood as asymptotic behaviors emerging as the system is rescaled (Fraiman and Chialvo, 2012). Cognitive tasks are modulated by the $1/f^{\mu}$ exponents of the brain fluctuation probability function, leading either to a shrinking of multifractal spectrum, or transitions from mono- to multi-fractal distributions (Popivanov et al., 2006). The values corresponding to different distributions of oscillation frequencies and brain multifractal spectrum can be calculated in real neuroimaging data. Pairwise entropy methods in neuroimaging techniques (Watanabe et al., 2014) might benefit of such a reverse Rényi entropy-based approach. Indeed, the changes in Rényi α exponent (caused by variations in multifractal exponents), might lead to modification not just in electric spikes' frequency, but also in the frequency of other types of brain oscillations, such as neurotransmitter release, and so on.

Because scale-free behaviour is able to modify spike frequencies, we suggest that brain electric streams could be modulated through the superimposition of external electric currents characterized by carefully chosen power law exponents. Therefore, we suggest that transcranial electrical stimulation's techniques might take into account not just amplitudes and frequencies of the applied waveforms (Reato et al., 2013), but also their scaling slopes. A possible field of application are diseases such as Alzheimer's disease, depression, attention deficit hyperactivity disorder, autism (Fox and Raichle, 2007; Sunderam et al., 2009). They could be ameliorated, or even removed, by artificial fields of appropriate power law exponents, that could be able to "recovery" and restore physiological brain functions .

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GAUGE FIELDS IN THE CENTRAL NERVOUS SYSTEM

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Recent advances in neuroscience highlight the complexity of the central nervous system (CNS) and call for general, multidisciplinary theoretical approaches. The aim of this chapter is to assess highly organized biological systems, in particular the CNS, via the physical and mathematical procedures of gauge theory – and to provide quantitative methods for experimental assessment. We first describe the nature of a gauge theory in physics, in a language addressed to an interdisciplinary audience. Then we examine the possibility that brain activity is driven by one or more continuous forces, called *gauge fields*, originating inside or outside the CNS. In particular, we go through the idea of *symmetries*, which is the cornerstone of gauge theories, and illustrate examples of possible gauge fields in the CNS. A deeper knowledge of gauge theories may lead to novel approaches to (self) organized biological systems, improve our understanding of brain activity and disease, and pave the way to innovative therapeutic interventions.

….A possible role for gauge fields (Sengupta et al., 2016a) and symmetries (Tozzi and Peters 2016a) has been recently proposed in order to elucidate physiological and pathological features of brain activity. In the search for a dynamic interplay, a cross-over of the physics of elementary particles and cortical brain dynamics, gauge theory takes into account the possibility that brain activity is driven by one or more continuous forces represented by gauge fields, originating inside or outside the CNS. Three main ingredients are required to sketch gauge theory of the CNS:

- A system equipped with a symmetry and a correlated, measurable Lagrangian
- A continuous Lie group of local forces (transformations) which break the symmetry locally.
- 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 transformations.

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2) IN SEARCH FOR SYMMETRIES IN THE CNS

In this section, we focus on the key problem in sketching a gauge theory for the CNS. To do this, we need a continuous symmetry to break and restore. The search for nervous symmetries is not easy. Due to our incomplete knowledge of brain function, we do not know exactly which, and how many, symmetries are hidden in the CNS. Furthermore, symmetries need to be constrained and it is unrealistic to seek – in biology – the mathematical simplicity of physics. Even if we knew the requisite symmetries, it is doubtful if our current technology would be able to calculate all the necessary variables at each point in the CNS. For example, recent studies suggest that cognitive functions do not depend solely on electrical pulses, but on multifactorial intra- and extra-neuronal causes, involving supramolecular interactions among biologically active macromolecules (Tozzi, 2015). It is also important to remember that any hypothetical descriptions cannot unambiguously characterize the etiology of fluctuation properties, as similar symmetric properties may stem from qualitatively different generators, which may be difficult to distinguish with finite data (Papo 2014).
Despite these limitations, gauge theories could pave the way to a novel approach to organized living systems. The prevalence of complex fluctuations would allow not only treating the brain as a physical system, but also help classify cognitive processes as operators acting on symmetries. Moreover, the computational neuroscience community is currently undertaking an effort to provide a systematic way to characterize symmetry and asymmetry in the network structures of the connectome – by inspecting the eigenvalues of different types of connectivity matrices (Esposito et al., 2014). Gauge theories for the brain are reminiscent of a mechanism of homeostasis, in which: a) the conserved variable is a symmetry, often hidden from our observation, and b) the *balancing* force must be continuous. In what follows, we present a brief list of known symmetries in CNS that could be tested in the frame of a gauge theory. The following treatment reprises Tozzi and Peters (2016a).

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3) GAUGE THEORIES: WHAT ARE THEY GOOD FOR?

…Gauge theories also allow the projection from a *real*, external space onto an *abstract*, more manageable space equipped with sufficient statistics. However, a gauge framework is much more powerful and accurate. Gauge fields have a practical advantage: their forces may be exactly calculated through a difficult, but feasible experimental energy-based variational approach. Gauge theories can be evaluated through topological tools too, in particular through the Borsuk-Ulam theorem (BUT). BUT states that (Borsuk 1933; Dodson, 1997):

Every continuous map $f : S^n \rightarrow R^n$ *must identify a pair of antipodal points (on* S^n*).*

This means that the sphere S^n maps to an *n*-dimensional, Euclidean space R^n (Tozzi and Peters, 2016b). Points on S^n are *antipodal*, provided they are diametrically opposite. For the use of BUT and its variants, see Peters and Tozzi (2016). It has been recently proposed that symmetries lie on the S^n sphere in guise of antipodal points, while the broken symmetries lie on the corresponding R^n manifold (Tozzi and Peters, 2016a). Here, the gauge field stands for the continuous function required to go from a level to another (**figure 3**). This approach allows us to assess vector and tensor projections also by using the powerful tools of algebraic topology (Peters 2016).

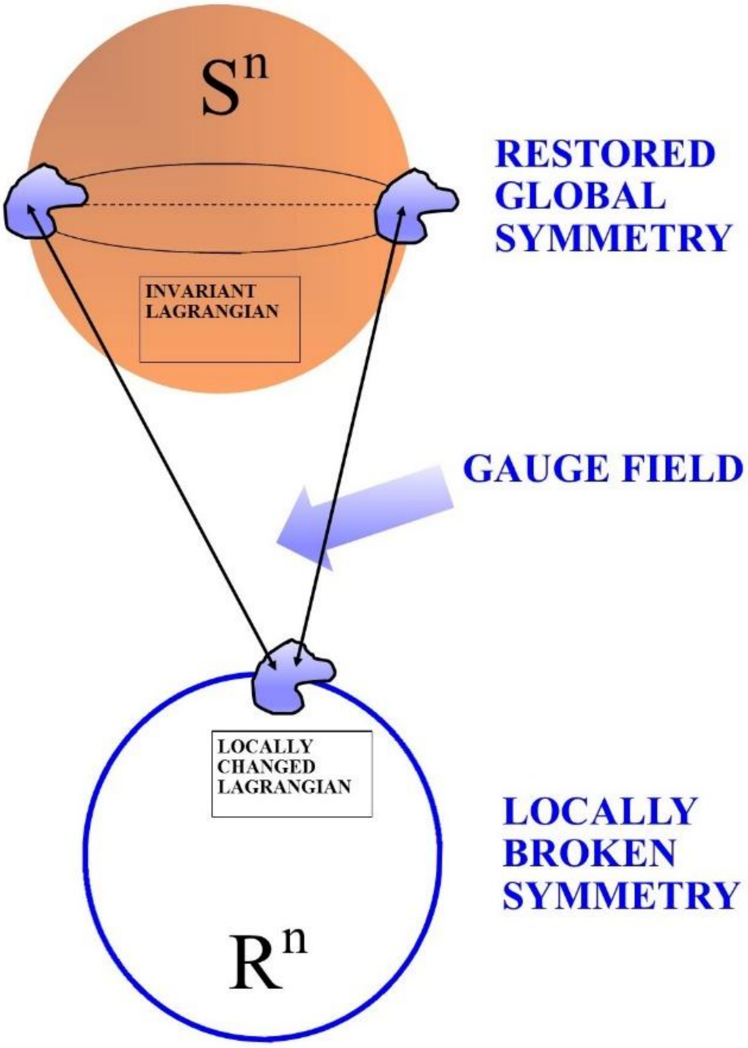

Figure 3. Borsuk-Ulam theorem and gauge fields. BUT and its variants require a function which needs to be continuous. In the same way, a gauge theory requires a gauge field which needs to be continuous.

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5) CANDIDATES FOR BRAIN GAUGE THEORIES

…to sketch a CNS gauge theory, we require the neuronal homologues of the three ingredients: i.e., a system equipped with a symmetry, local forces and one or more gauge fields. Depending on our initial gauge choice, the three ingredients can be assessed in different combinations. Many possibilities arise, whose feasibility can be experimentally verified. In closing, we provide some discussion of further candidates for gauge fields.

Consciousness. In the search of the neural correlates of consciousness (Koch et al., 2016), gauge theories may provide a novel method to investigate this challenging phenomenon. In particular, when embedded in a gauge framework, consciousness no longer stands for unspecified brain activity, but for a quantifiable parameter that can be expressed in terms of vectors or tensors. Indeed, consciousness might correspond to a Levi-Civita connection; e.g., the gauge field. In absence of consciousness, the external states do not produce sensory perturbations; from the perspective of the free energy principle, this means, the symmetry of the variational free energy, e.g., the sensory entropy, cannot be restored. As an example, during sleep, in which consciousness is altered, a response to local sensory perturbations does not occur. In such a vein, if we assume that the system stands for the cortex, ascending arousal systems are potential candidates for gauge fields. The midbrain contains tonic neurons that ensure a continuous cortical neuromodulation. Tonic neurons are located in the locus coeruleus, in the dorsal raphe and central superior nuclei; e.g., along the pathway of the ventral branch of ascending arousal system, and in the reticular thalamic nucleus, which is the final step of the dorsal branch of the ascending arousal system (Nieuwenhuys et al., 2008). Recent data suggest that the neural correlates of consciousness might be associated with posterior cortical hot zones (Koch et al, 2016). If this was the case, we could be allowed to assimilate qualitative notions of conscious level into the quantitative gauge theoretic framework of cortical function.

Blood flow. If we hypothesize that the system is the entire CNS and the gauge field is located in other bodily systems, it is possible that local forces stand for the cortical oscillations evoked by the stimuli from the external environment, while the continuous gauge field stands for haemodynamic fluctuations. The idea that blood circulation influences brain activity dates back to the pioneering work of Angelo Mosso (1896) and is still evident in brain mapping studies that predominate in modern neuroscience (Nieuwenhuys et al., 2008; Friston et al, 2014). A recent paper is particularly intriguing in this regard (Park et al., 2014). In humans, cardiovascular fluctuations underlie behaviourally relevant activation in multifunctional cortical areas. Neuronal events locked to heartbeats before stimulus onset predict the detection of a faint visual grating in the posterior right inferior parietal lobule and the ventral anterior cingulate cortex. Heartbeats therefore shape visual conscious experience, by contributing to neuronal representations. Similar coupling in the interoceptive domain would mean that the introception of autonomic signals might underlie subjectivity and sense of self (Park et al., 2014). Furthermore, emotions can be influenced by cardio-circulatory mechanisms. It has been demonstrated that short-term interoceptive fluctuations enhance perceptual and evaluative processes related to the processing of fear and threat. The processing of brief fear stimuli is selectively gated by their timing in relation to individual heartbeats and these interoceptive signals influence the detection of emotional stimuli at the threshold of conscious awareness, altering emotional judgments of fearful and neutral faces (Garfinkel et al., 2014). Resembling a novel version of Fechner law, gauge theories might quantitatively correlate stimuli and perceptual processing.

Environmental stimuli. In an *autopoietic* account of the gauge framework, the system might stand for the brain, equipped with self-sustained continuous forces producing local, self-generated perturbations. In this case, the best candidate for a gauge field is the continuous afference from the external world. In such a framework, the spontaneous activity of the brain cannot be simply reduced to background noise, uncorrelated to the system's response (Lombardi et al., 2012). We are presented with an auto-referential system, in which the role of spontaneous fluctuations is to preserve brain's internal symmetry. Homeostatic plasticity ensures that neuronal networks assume a sub-critical state, independently of the initial configuration. Surprisingly, increasing the external stimuli modifies the network set-point towards criticality (Priesemann 2015).

Time. It has been recently suggested that some brain functions could be dictated by the principle of minimum frustration, a concept borrowed from energetic landscapes of protein folding (Tozzi et al, 2016). The brain is equipped with many timescales, ranging from nanoseconds to several days. According to this novel formulation, structural changes in the brain lead to energy decrease at very long CNS timescales. With the passage of time, the trajectories of neuronal processes, such as memory and perceptual recognition, tend towards the low-energy basins of narrow funnel-like attractors. As with the free energy principle, the minimum frustration principle states that the gradient descent (energy decrease) dictated by Langevin equations takes place over long brain timescales. In such a vein, time becomes a gauge field. Indeed, at least at the non-relativistic scales typical of biological systems, time is a continuous function. This function can restore the global symmetry; e.g., the lowest possible variational free energy, which has been broken by local forces, e.g., environmental inputs. Time stands in this case for a known parameter, which affords the possibility to evaluate unknown parameters. …

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