THE CONQUEST OF HIGH DIMENSIONS: A SCIENTIFIC ACCOUNT

Arturo Tozzi (MD, PhD, AAP)

Center for Nonlinear Science, Department of Physics, University of North Texas, Denton, Texas 76203, USA
1155 Union Circle, #311427
Denton, TX 76203-5017 USA

Computational Intelligence Laboratory, University of Manitoba, Winnipeg, Canada
Winnipeg R3T 5V6 Manitoba
E-mail address: tozziarturo@libero.it

ASL Napoli 2 Nord, Distretto 45, Via Santa Chiara, 80023, Caivano, Naples, Italy

tozziarturo@libero.it

This is my story, the story of a family pediatrician and amateur neuroscientist/physicist. As an "outsider", I publish in some of the major scientific journals (also nuts in Nature and NEJM) and collaborate with worldwide universities and renewed scientists. My scientific field? Difficult to say, because I do not like at all to be on focus. Not regarding myself as a proper scientist, I feel free to (try to) publish in rather different disciplines (medicine, biology, physics, math, philosophy and, above all, neuroscience). Working in my room in Naples, Italy, without vis-à-vis contacts with true scientists, my favoured methodological approach is necessarily a "testable rationalism": sharp experimental previsions arising from top-down, deductive mathematical approaches. Joining together concepts from far-flung fields, I pursue the application of mathematic and physical theory to biology, especially to neural systems.
This manuscript encompasses all my published papers (2014- half 2018) in different fields: math, physics, biology, philosophy and, above all, neuroscience.

THE BRAIN IN HIGHER DIMENSIONS

Tozzi A, Peters JF. 2016. Towards a Fourth Spatial Dimension of Brain Activity. Cognitive Neurodynamics 10 (3): 189–199. doi:10.1007/s11571-016-9379-z.
Current advances in neurosciences deal with the functional architecture of the central nervous system, paving the way for general theories that improve our understanding of brain activity. From topology, a strong concept comes into play in understanding brain functions, namely, the 4D space of a "hypersphere's torus", undetectable by observers living in a 3D world. The torus may be compared with a video game with biplanes in aerial combat: when a biplane flies off one edge of gaming display, it does not crash but rather it comes back from the opposite edge of the screen. Our thoughts exhibit similar behaviour, *i.e.* the unique ability to connect past, present and future events in a single, coherent picture as if we were allowed to watch the three screens of past-present-future "glued" together in a mental kaleidoscope. Here we hypothesize that brain functions are embedded in a imperceptible fourth spatial dimension and propose a method to empirically assess its presence. Neuroimaging fMRI series can be evaluated, looking for the topological hallmark of the presence of a fourth dimension. Indeed, there is a typical feature which reveal the existence of a functional hypersphere: the simultaneous activation of areas opposite each other on the 3D cortical surface. Our suggestion - substantiated by recent findings - that brain activity takes place on a closed, donut-like trajectory helps to solve long-standing mysteries concerning our psychological activities, such as mind-wandering, memory retrieval, consciousness and dreaming state.

Tozzi A, Peters JF. 2016. A Topological Approach Unveils System Invariances and Broken Symmetries in the Brain. Journal of Neuroscience Research 94 (5): 351–65. doi:10.1002/jnr.23720.
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. BUTtells 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.

Peters JF, Ramanna S, Tozzi A, İnan E. 2017. Bold-Independent Computational Entropy Assesses Functional Donut-Like Structures in Brain fMRI Images. Front Hum Neurosci. 2017 Feb 1;11:38. doi: 10.3389/fnhum.2017.00038. eCollection 2017.

We introduce a novel method for the measurement of information level in fMRI (functional Magnetic Resonance Imaging) neural data sets, based on image subdivision in small polygons equipped with different entropic content. We show how this method, called maximal nucleus clustering (MNC), is a novel, fast and inexpensive image-analysis technique, independent from the standard blood-oxygen-level dependent signals. MNC 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. This approach befits the geometric character of fMRIs. The main purpose of this study is to provide a computable framework for fMRI that not only facilitates analyses, but also provides an easily decipherable visualization of structures. This framework commands attention because it is easily implemented using conventional software systems. 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.

Tozzi A, Peters JF. 2017. From abstract topology to real thermodynamic brain activity. Cognitive Neurodynamics, 11(3) 283–292. Doi:10.1007/s11571-017-9431-7.

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, may 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.

Peters JF, Tozzi A, Ramanna S, Inan E. 2017. The human brain from above: an increase in complexity from environmental stimuli to abstractions. Cognitive Neurodynamics,11(4), 391–394. DOI: 10.1007/s11571-0-17-9428-2.

Contrary to common belief, the brain appears to increase the complexity from the perceived object to the idea of it. Topological models predict indeed that: a) increases in anatomical/functional dimensions and symmetries occur in the transition from the environment to the higher activities of the brain, and b) informational entropy in the primary sensory areas is lower than in the higher associative ones. To demonstrate this novel hypothesis, we introduce a straightforward approach to measuring island information levels in fMRI neuroimages, via Rényi entropy derived from tessellated fMRI images. This approach facilitates objective detection of entropy and corresponding information levels 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. This suggests that the brain lies in dimensions higher than the environment and that it does not concentrate, but rather dilutes messages coming from external inputs.

Tozzi A, Peters JF, Fingelkurts AA, Fingelkurts AA, Marijuán PC. 2017. Topodynamics of metastable brains. Physics of Life Reviews, 21, 1-20. http://dx.doi.org/10.1016/j.plrev.2017.03.001.

The brain displays both the anatomical features of a vast amount of interconnected topological mappings as well as the functional features of a nonlinear, metastable system at the edge of chaos, equipped with a phase space where mental random walks tend towards lower energetic basins. Nevertheless, with the exception of some advanced neuro-anatomic descriptions and present-day connectomic research, very few studies have been addressing the topological path of a brain embedded or embodied in its external and internal environment. Herein, by using new formal tools derived from algebraic topology, we provide an account of the metastable brain, based on the neuro-scientific model of Operational Architectonics of brain-mind functioning. We introduce a "topodynamic" description that shows how the relationships among the countless intertwined spatio-temporal levels of brain functioning can be assessed in terms of projections and mappings that take place on abstract structures, equipped with different dimensions, curvatures and energetic constraints. Such a topodynamical approach, apart from providing a biologically plausible model of brain function that can be operationalized, is also able to tackle the issue of a long-standing dichotomy: it throws indeed a bridge between the subjective, immediate datum of the naïve complex of sensations and mentations and the objective, quantitative, data extracted from experimental neuro-scientific procedures. Importantly, it opens the door to a series of new predictions and future directions of advancement for neuroscientific research.

Tozzi A, Peters JF, Fingelkurts AA, Fingelkurts AA, Marijuán PC. 2017. Brain projective reality: novel clothes for the emperor. Reply to comments on "Topodynamics of metastable brains" by Tozzi et al. Physics of Life Reviews, 21, 46-55. https://doi.org/10.1016/j.plrev.2017.06.020.

This paper (formally a response to the comments of nine highly qualified commenters to our paper: " topodynamics of metastable brains ") introduces a novel paradigm in neuroscience, termed " projectionism " , which assesses projections and mappings among different functional brain dimensions and phase spaces. We describe recently published papers that confirm our general framework. Furthermore, we compare brain symmetries with the predictive coding that stands for a sort of Kant a priori located in in our brains. We illustrate the " unreasonable power " of topology in neuroscience, which allows a rationalistic but testable top-down inquiry of the brain activity, in order to mathematically assess the physical and biological dynamics of the human nervous system. We also propose possible biochemical correlates of a brain fourth dimension, with clues provided by… LSD intake. Also, we suggest fresh mathematical approaches to brain topological dynamics, introducing novel theorems and proposing complex functional nervous spaces very different from the classical Euclidean ones. We close our paper with a novel computational scenario that takes into account the tenets of neural Darwinism.

Tozzi A, Peters JF, Cankaya M. 2018. The informational entropy endowed in cortical oscillations. Cognitive Neurodynamics. https://doi.org/10.1007/s11571-018-9491-3.
A two-dimensional shadow may encompass more information than its corresponding three-dimensional object. Indeed, if we rotate the object, we achieve a pool of observed shadows from different angulations, gradients, shapes and variable length contours that make it possible for us to increase our available information. Starting from this simple observation, we show how informational entropies might turn out to be useful in the evaluation of scale-free dynamics in the brain. Indeed, brain activity exhibits a scale-free distribution that leads to the variations in the power law exponent typical of different functional neurophysiological states. Here we show that modifications in scaling slope are associated with variations in Rényi entropy, a generalization of Shannon informational entropy. From a three-dimensional object's perspective, by changing its orientation (standing for the cortical scale-free exponent), we detect different two-dimensional shadows from different perception angles (standing for Rènyi entropy in different brain areas). We show how, starting from known values of Rènyi entropy (easily detectable in brain fMRIs or EEG traces), it is feasible to calculate the scaling slope in a given moment and in a given brain area. Because changes in scale-free cortical dynamics modify brain activity, this issue points towards novel approaches to mind reading and description of the forces required for transcranial stimulation.

Tozzi A. 2018. The Hidden Dimensions of the Central Nervous System. viXra:1801.0089.
Brain activity takes place in three spatial-plus time dimensions. This rather obvious claim has been recently questioned by papers that, taking into account the big data outburst and novel available computational tools, are starting to unveil a more intricate state of affairs. Indeed, various brain activities and their correlated mental functions can be assessed in terms of trajectories embedded in phase spaces of dimensions higher than the canonical ones. In this review, I show how further dimensions may not just represent a convenient methodological tool that allows a better mathematical treatment of otherwise elusive cortical activities, but may also reflect genuine functional or anatomical relationships among real nervous functions. I then describe how to extract hidden multidimensional information from real or artificial neurodata series, and make clear how our mind dilutes, rather than concentrates as currently believed, inputs coming from the environment. Finally, I argue that the principle "the higher the dimension, the greater the information" may explain the occurrence of mental activities and elucidate the mechanisms of human diseases associated with dimensionality reduction.

Tozzi A. 2018. A Novel Procedure for the Assessment of Multidimensional Brain Activities. viXra:1804.0322.
The brain activity displays hidden functional dimensions, apart from the conventionally assessed three spatial ones (plus time). This finding, corroborated by a long sequence of recent experimental observations, requires novel methodological devices in order to provide a mathematical treatment for such elusive nervous extra-dimensions. Here we describe a novel, simple approach that makes feasible to extract hidden multidimensional information from real neurodata series, in order to detect, assess and quantify a fourth spatial dimension of cortical activity. Also, our technique might stand for the first step towards an artificial nervous network equipped with four spatial dimensions, instead of the classical three.

THE DIFFERENT FUNCTIONS OF THE BRAIN ACTIVITY

Tozzi A, Peters JF. 2017. Just One Brain Activity. bioRxiv, doi: https://doi.org/10.1101/147447.
The term "brain activity" refers to a wide range of mental faculties that can be assessed either on anatomical/functional micro-, meso- and macro- spatiotemporal scales of observation, or on intertwined cortical levels with mutual interactions. Our aim is to show that every brain activity encompassed in a given anatomical or functional level necessarily displays a counterpart in others, i.e., they are "dual". "Duality" refers to the case where two seemingly different physical systems turn out to be equivalent. We describe a method, based on novel topological findings, that makes different manifolds (standing for different brain activities) able to scatter, collide and combine, in order that they merge, condense and stitch together in a quantifiable way. We develop a computational tool which explains how, despite their local cortical functional differences, all mental processes, from perception to emotions, from cognition to mind wandering, may be reduced to a single, general brain activity that takes place in dimensions higher than the classical three-dimensional plus time. This framework permits a topological duality among different brain activities and neuro-techniques, because it holds for all the types of spatio-temporal nervous functions, independent of their cortical location, inter- and intra-level relationships, strength, magnitude and boundaries.

Tozzi A, Zare M, Benasich AA. 2016. New Perspectives on Spontaneous Brain Activity: Dynamic Networks and Energy Matter. Front Hum Neurosci. 10:247. doi: 10.3389/fnhum.2016.00247.
Spontaneous activity of the brain is generated in the absence of an explicit task and hence frequently associated to resting-state or default-network functions. Despite its recent discovery has shed new light on questions concerning the structural and functional architecture of the brain and how they are related to "mind", several issues still need to be assessed. In this review, we focus on the scarcely explored energetic requirements and constraints of spontaneous activity, taking into account both thermodynamical and informational standpoints. At first, we argue that the "classical" definitions of spontaneous activity do not take into account an important feature. Indeed, spontaneous brain activity is equipped with slower oscillations compared with the evoked, task-related one, hence it exhibits lower levels of enthalpy and free-energy. Therefore, noteworthy thermodynamic energetic differences occur between spontaneous and evoked brain activities. It means that the brain functions traditionally associated with spontaneous activity, such as mind wandering and so on, require less energy that other nervous activities. We also review recent empirical observations in neuroscience, in an attempt to capture how spontaneous brain dynamics and mental function can be embedded in a non-linear

dynamical framework, which talks about nervous activity in terms of phase spaces, particle trajectories, random walks, attractors and/or paths at the edge of the chaos. This takes us from the thermodynamic free-energy to the realm of variational free-energy, a theoretical construct pertaining to probability and information theory and able to explain several unexplored features of spontaneous brain activity.

Tozzi A, Peters JF. 2017. A Symmetric Approach Elucidates Multisensory Information Integration. Information 8,1. doi: 10.3390/info8010004.

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 an empirically assessable methodology. 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.

Tozzi A, Peters JF. 2017. Towards Topological Mechanisms Underlying Experience Acquisition and Transmission in the Human Brain. Integr Psychol Behav Sci. 51(2), 303–323. doi: 10.1007/s12124-017-9380-z.

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.

Tozzi A. 2015. Richard Avenarius' "Kritik Der Reinen Erfharung": the English Translation. viXra:1511.0251.

The French-Swiss Professor in inductive philosophy Richard Avenarius (Paris, 1843- Zurich, 1896) and also the father of empirio-criticism together with Ernst Mach, is one of the most underrated and misunderstood philosophers ever. Nevertheless, influenced by the most innovative proposals of his times of transition between the idealistic/rationalist legacies and the new materialistic/scientific interpretation of the reality – i.e, by cultural evolutionism, linguistics, biomechanics, entropy/energy theories and, above all, by the newborn experimental psychology -, he produced a complete and innovative system of philosophy, aiming at investigate the laws of knowledge. Chunks of his original ideas can be found not only in theories of mind/brain after him - such as Gestalt, phenomenalism, behaviourism, functionalism and cybernetics, autopoiesis, dynamical systems theory, embedded/embodied approaches – but also in current neuroscientific approaches – nervous transduction, electric spikes, neural code, multisensory integration, free-energy principle -. Our aim is to provide the first chronological English summary of his masterpiece, the German-written "Kritik", thus giving the possibility to the (almost) totally unaware English speakers to appreciate such a neglected and innovative thinker.

The two books of the "Kritik der reinen Erfahrung" (Critique of Pure Experience), published respectively in 1888 and 1890, comprise a prologue and three parts, divided in 1040 short paragraphs. Each quoted paragraph will be put in bracket [ ]. In order to avoid Avenarius' technicalities, we will use a simplified idiom. If he were alive today, I would have not agreed with such an oversimplification: indeed, the neologisms he used were partly necessary for the denomination of new phenomena, but partly resulted from the extreme care he took to prevent all possible changes as well in physiological as in psychological theories. We however hope he will forgive us: a better comprehension of his theory will make him a favour.

Tozzi A, Peters JF, Fingelkurts A, Fingelkurts A, Perlovsky L. 2018. Syntax meets semantics during brain logical computations. Progr Biophys Mol Biol. https://doi.org/10.1016/j.pbiomolbio.2018.05.010.

The discrepancy between syntax and semantics is a painstaking issue that hinders a better comprehension of the underlying neuronal processes in the human brain. In order to tackle the issue, we at first describe a striking correlation between Wittgenstein's Tractatus, that assesses the syntactic relationships between language and world, and Perlovsky's joint language-cognitive computational model, that assesses the semantic relationships between emotions and "knowledge instinct". Once established a correlation between a purely logical approach to the language and computable psychological activities, we aim to find the neural correlates of syntax and semantics in the human brain. Starting from topological arguments, we suggest that the semantic properties of a proposition are processed in higher brain's functional dimensions than the syntactic ones. In a fully reversible process, the syntactic elements embedded in Broca's area project into multiple scattered semantic cortical zones. The presence of higher functional dimensions gives rise to the increase in informational content that takes place in semantic expressions. Therefore, diverse features of human language and cognitive world can be assessed in terms of both the logic armor described by the Tractatus, and the neurocomputational techniques at hand. One of our motivations is to build a neuro-computational framework able to provide a feasible explanation for brain's semantic processing, in preparation for novel computers with nodes built into higher dimensions.

BRAIN ACTIVITY: NOT JUST SPIKES!

Tozzi A. 2015. Information Processing in the CNS: A Supramolecular Chemistry? Cognitive Neurodynamics 9 (5): 463–477.

How does central nervous system process information? Current theories are based on two tenets: a) Information is transmitted by action potentials, the language by which neurons communicate with each other – and b) homogeneous neuronal assemblies of cortical circuits operate on these neuronal messages where the operations are characterized by the intrinsic connectivity among neuronal populations. In this view, the size and time course of any spike is stereotypic and the information is restricted to the temporal sequence of the spikes; namely, the "neural code". However, an increasing amount of novel data point towards an alternative hypothesis: a) The role of neural code in information processing is overemphasized. Instead of simply passing messages, action potentials play a role in dynamic coordination at multiple spatial and temporal scales, establishing network interactions across several levels of a hierarchical modular architecture, modulating and regulating the propagation of neuronal messages. b) Information is processed at all levels of neuronal infrastructure from macromolecules to population dynamics. For example, intra-neuronal (changes in protein conformation, concentration and synthesis) and extra-neuronal factors (extracellular proteolysis, substrate patterning, myelin plasticity, microbes, metabolic status) can have a profound effect on neuronal computations. This means molecular message passing may have cognitive connotations. This essay introduces the concept of "supramolecular chemistry", involving the storage of information at the molecular level and its retrieval, transfer and processing at the supramolecular level, through transitory non-covalent molecular processes that are self-organized, self-assembled and dynamic. Finally, we note that the cortex comprises extremely heterogeneous cells, with distinct regional variations, macromolecular assembly, receptor repertoire and intrinsic microcircuitry. This suggests that every neuron (or group of neurons) embodies different molecular information that hands an operational effect on neuronal computation.

Peters JF, Tozzi A. Ramanna S. 2016. Brain Tissue Tessellation Shows Absence of Canonical Microcircuits. Neuroscience Letters 626: 99–105. doi:10.1016/j.neulet.2016.03.052.

We provide a novel, fast and cheap method for the morphological evaluation of simple 2-D images taken from histological samples. This method, based on computational geometry, leads to a novel kind of "tessellation" of every type of biological picture, in order to locate the zones equipped with the highest functional activity. 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 as usually believed, display scattered neuronal micro-clusters equipped with higher activity than the surrounding ones.

Tozzi A, Fla Tor, Peters JF. 2016. Building a minimum frustration framework for brain functions in long timescales. J Neurosci Res.94(8): 702–716.

The minimum frustration principle is a computational approach which states that, in the long timescales of evolution, proteins' free-energy decreases more than expected by thermodynamic constraints as their aminoacids assume conformations progressively closer to the lowest energetic state. Here we show that this general principle, borrowed from protein folding dynamics, can be fruitfully applied to nervous function too. Highlighting the foremost role of energetic requirements, macromolecular dynamics, and, above all, intertwined timescales in brain activity, the minimum frustration principle elucidates a wide range of mental processes, from sensations to memory retrieval. Brain functions are compared to trajectories which, in long nervous timescales, are attracted towards the low-energy bottom of funnel-like structures characterized both by robustness and plasticity. We discuss how the principle, as derived explicitly from evolution and selection of a funneling structure from microdynamics of contacts, is different from other brain models equipped with energy landscapes, such as the Bayesian and free-energy principle and the Hopfield networks. In sum, we make available a novel approach to brain function cast in a biologically informed fashion, with the potential to be operationalized and assessed empirically.

Tozzi A, Peters JF, Ori O. 2017. Fullerenic-topological tools for honeycomb nanomechanics. Towards a fullerenic approach to brain functions. Fullerenes, Nanotubes and Carbon nanostructures.25 (4): 282-288. http://dx.doi.org/10.1080/1536383X.2017.1283618.

Fullerenic structures equipped with Stone-Wales transformations have been successfully utilized in the study of macromolecular assemblies. Here we show that this approach could be useful in the assessment of issues from a far-flung research area, i.e., neuroscience. Indeed, the basic morphological and functional unit of the brain, called the human microcolumn, is a tubular structure that can be flattened in the guise of a fullerene-like two-dimensional lattice. We describe this procedure in order to build a fullerene-like microcolumn, in which neuronal firing and electric signal propagation are assessed in terms of topological neural network modifications, instead of the canonical logic circuits. Every node stands for a neuron, where neural computations take place. This means that nervous activity, other than logic circuits, could instead depend on topological transformations and symmetry constraints dictated by Stone-Wales transformations occurring in the upper cortical layers. A two-dimensional fullerene-like lattice not only simulates the real microcolumn's microcircuitry, but also makes it possible to build artificial networks equipped with robustness, plasticity and fastness. In this note, electric signal propagation is investigated in terms of pure topological modifications of the neural honeycomb network.

Tozzi A, Peters JF, Ori O. 2017. Cracking the barcode of fullerene-like cortical microcolumns. Neurosci Letters,644, 100–106. http://dx.doi.org/10.1016/j.neulet.2017.02.064.

Artificial neural systems and nervous graph theoretical analysis rely upon the stance that the neural code is embodied in logic circuits, *e.g.*, spatio-temporal sequences of ON/OFF spiking neurons. Nevertheless, this assumption does not fully explain complex brain functions. Here we show how nervous activity, other than logic circuits, could instead depend on topological transformations and symmetry constraints occurring at the micro-level of the cortical microcolumn, *i.e.*, the embryological, anatomical and functional basic unit of the brain. Tubular microcolumns can be flattened in fullerene-like two-dimensional lattices, equipped with about 80 nodes standing for pyramidal neurons where neural computations take place. We show how the countless possible combinations of activated neurons embedded in the lattice resemble a barcode. Despite the fact that further experimental verification is required in order to validate our claim, different assemblies of firing neurons might have the appearance of diverse codes, each one responsible for a single mental activity. A two-dimensional fullerene-like lattice, grounded on simple topological changes standing for pyramidal neurons' activation, not just displays analogies with the real microcolumn's microcircuitry and the neural connectome, but also the potential for the manufacture of plastic, robust and fast artificial networks in robotic forms of full-fledged neural systems.

Tozzi A, Peters JF, Jausovec N. 2016. A repetitive modular oscillation underlies human brain electric activity. Neurosci Lett, 653, 234-238. 10.1016/j.neulet.2017.05.051.
The modular function j, central in the assessment of abstract mathematical problems, describes elliptic, intertwined trajectories that move in the planes of both real and complex numbers. Recent clues suggest that the j-function might display a physical counterpart, equipped with a quantifiable real component and a hidden imaginary one, currently undetectable by our senses and instruments. Here we evaluate whether the real part of the modular function can be spotted in the electric activity of the human brain. We assessed EEGs from five healthy males, eyes-closed and resting state, and superimposed the electric traces with the bidimensional curves predicted by the j-function. We found that the two trajectories matched in more than 85% of cases, independent from the subtending electric rhythm and the electrode location. Therefore, the real part of the j-function's peculiar wave is ubiquitously endowed all over normal EEGs paths. We discuss the implications of such correlation in neuroscience and neurology, highlighting how the j-function might stand for the one of the basic oscillations of the brain, and how the still unexplored imaginary part might underlie several physiological and pathological nervous features.

Deli E. Tozzi A, Peters JF. 2017. Relationships between short and fast brain timescales. Cognitive Neurodynamics, 11(6), 539-552.DOI: 10.1007/s11571-017-9450-4.
Brain electric activity exhibits two important features: oscillations with different timescales, characterized by diverse functional and psychological outcomes, and a temporal power law distribution. In order to further 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 mirror each other over time via a sinusoid relationship and provide, through the Bloch theorem from solid-state physics, the possible equation which links the two timescale activities. We show that, based on topological findings, nervous activities occurring in micro-levels are projected to single activities at meso- and 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. Our topological approach makes it possible to assess brain functions both based on entropy, and in the general terms of particle trajectories taking place on donut-like manifolds. Condensed brain activities might give rise to ideas and concepts by combination of different functional and anatomical levels. Furthermore, cognitive phenomena, as well as social activity can be described by the laws of quantum mechanics; memories and decisions exhibit holographic organization. In physics, the term duality refers to a case where two seemingly different systems turn out to be equivalent. This topological duality holds for all the types of spatio-temporal brain activities, independent of their inter- and intra-level relationships, strength, magnitude and boundaries, allowing us to connect the physiological manifestations of consciousness to the electric activities of the brain.

Peters JF, Tozzi A, Deli E. 2017. Towards Equations for Brain Dynamics and the Concept of Extended Connectome. SF J Neuro Sci 1:1.
The brain is a system at the edge of chaos equipped with nonlinear dynamics and functional energetic landscapes. However, so far no connection has been found between the electric activities of the brain and the physiological repertoire of behavior. Recent work suggests the integrated nature of information processing in the brain not only via synaptic connectivity, but a wholesome physical organization, which takes the shape of a toroidal particle trajectories, chaotic attractors or standing waves. The characterization of brain activities concerning the type of attractors or the trajectories of the nervous phase space is also missing. Starting from a system governed by differential equations in which a dissipative strange attractor coexists with an invariant conservative torus, we developed a 3D model of brain phase space which has the potential to be operationalized and assessed empirically. We achieved a system displaying either a torus or a strange attractor, depending just on the initial conditions. Further, the system generates a funnel-like attractor equipped with a fractal structure. Changes in three brain phase parameters lead to modifications in the funnel's breadth or in torus/attractor superimposition. We have found that the higher frequencies of evoked activities are more deterministic because the greater funnel breadth reduces the degrees of freedom. Thus, evoked activities are more deterministic. In contrast, the resting state corresponds to lower frequencies and represents greater degrees of freedom, which engender daydreaming, mind wandering and other liberal, often arbitrary mental associations. Our model connects the physiological manifestations of consciousness with the electric activities of the brain and it also powerfully explains the differences in motivation between evoked and resting activities based on energy use. This idea might point to the origin of a large repertoire of brain functions, such as sensations/perceptions, memory and self-generated thoughts.

Tozzi A, Peters JF, Deli E. 2018. Towards plasma-like collisionless trajectories in the brain. Neurosci Lett. 662:105-109. https://doi.org/10.1016/j.neulet.2017.10.016.
Plasma studies depict collisionless, collective movements of charged particles. In touch with these concepts, originally developed by the far-flung branch of high energy physics, here we evaluate the role of collective behaviors and long-range functional couplings of charged particles in brain dynamics. We build a novel, empirically testable, brain model which takes into account collisionless movements of charged particles in a system, the brain, equipped with oscillations. The model is cast in a mathematical fashion with the potential of being operationalized, because it can be assessed in terms of McKean-Vlasov equations, derived from the classical Vlasov equations for plasma. A plasma-like brain also elucidates cortical phase transitions in the context of a brain at the edge of chaos, describing the required order parameters. In sum, showing how the brain might exhibit plasma-like features, we go through the concept of holistic behavior of nervous functions.

Tozzi A. 2018. Einstein and the physics of the mind: Comment on "Physics of mind: experimental confirmations of theoretical predictions" by Felix Schoeller et al.Phys Life Rev, https://doi.org/10.1016/j.plrev.2018.01.009.
In touch with the Authors' strong physicalist claims, we take a step further: to encompass the dynamics described by the Queen of physics, i.e., special relativity, into the fruitful framework of dynamic logic. Indeed, the subjective perception of time could be assessed through the objective reference frame described by Einstein's four-dimensional spacetime in special relativity.

Tozzi A, Peters JF. 2017. Quantifying Mental Ideas Through Special Relativity and Bekenstein-Hawking Formulas. viXra:1703.0171.
When perceived by the human mind, an object might encompass diverse content according to different observers. Further, subjectively experienced time is encoded in the later entorhinal cortex. Starting from these two observations concerning mental perception of space and time, and considering Einstein's accounts, we show how, in terms of special relativity, imagination's content is not stationary and fixed, rather depends on the observer's standpoint. We elucidate how the subjective phenomenon of time (perceived by our mind as static) might give rise to changes in quantifiable content between the real and the imagined object. We describe how to correlate the quantifiable content of the sensed object embedded in the environment with the corresponding internal thought (subjective percept). In particular, based on recent neuroscientific literature, we show how changes in our mental time windows are able to squeeze the information content of the subjective percepts, compared with their matching environmental objects. Further, we elucidate how this novel framework could be able to confirm or reject a recently raised hypothesis, which suggests that the brain activity takes place in functional dimensions higher than our usual four-dimensional spacetime.

Tozzi A, Peters JF. 2018. Multidimensional brain activity dictated by winner-take-all mechanisms. Neuroscience Letters, 678 (21):83-89. https://doi.org/10.1016/j.neulet.2018.05.014.
A novel demon-based architecture is introduced to elucidate brain functions such as pattern recognition during human perception and mental interpretation of visual scenes. Starting from the topological concepts of invariance and persistence, we introduce a Selfridge pandemonium variant of brain activity that takes into account a novel feature, namely, demons that recognize short straight-line segments, curved lines and scene shapes, such as shape interior, density and texture. Low-level representations of objects can be mapped to higher-level views (our mental interpretations): a series of transformations can be gradually applied to a pattern in a visual scene, without affecting its invariant properties. This makes it possible to construct a symbolic multi-dimensional representation of the environment. These representations can be projected continuously to an object that we have seen and continue to see, thanks to the mapping from shapes in our memory to shapes in Euclidean space. Although perceived shapes are 3-dimensional (plus time), the evaluation of shape features (volume, colour, contour, closeness, texture, and so on) leads to n-dimensional brain landscapes. Here we discuss the advantages of our parallel, hierarchical model in pattern recognition, computer vision and biological nervous system's evolution.

Tozzi A, Peters JF, Jaušovec N. 2018. EEG dynamics on hyperbolic manifolds. Neurosci Lett. https://doi.org/10.1016/j.neulet.2018.07.035.

Biological activities, including cellular metabolic pathways, protein folding and brain function, can be described in terms of curved trajectories in hyperbolic spaces which are constrained by energetic requirements. Here, starting from theorems recently-developed by a deceased Field Medal young mathematician, we show how it is feasible to find and quantify the shortest, energy-sparing functional trajectories taking place in nervous systems' concave phase spaces extracted from real EEG traces. This allows neuroscientists to focus their studies on the few, most prominent functional EEG's paths and loops able to explain, elucidate and experimentally assess the rather elusive mental activity.

PURE PHYSICS

Peters JF, Tozzi A. 2016. Quantum Entanglement on a Hypersphere. Int J Theoret Phys, 1–8. doi:10.1007/s10773-016-2998-7.
A quantum entanglement's composite system does not display separable states and a single constituent cannot be fully described without considering the other states. We introduce quantum entanglement on a hypersphere - which is a 4D space undetectable by observers living in a 3D world -, derived from signals originating on the surface of an ordinary 3D sphere. From the far-flung branch of algebraic topology, the Borsuk-Ulam theorem states that, when a pair of opposite (antipodal) points on a hypersphere are projected onto the surface of 3D sphere, the projections have matching description. In touch with this theorem, we show that a separable state can be achieved for each of the entangled particles, just by embedding them in a higher dimensional space. We view quantum entanglement as the simultaneous activation of signals in a 3D space mapped into a hypersphere. By showing that the particles are entangled at the 3D level and un-entangled at the 4D hypersphere level, we achieved a composite system in which each local constituent is equipped with a pure state. We anticipate this new view of quantum entanglement leading to what are known as qubit information systems.

Tozzi A, Peters JF. 2016. Symmetries, Information and Monster Groups before and after the Big Bang. Information 7(4), 73; doi:10.3390/info7040073.
The Monster group, the biggest of the sporadic groups, is equipped with the highest known number of dimensions and symmetries. Taking into account variants of the Borsuk-Ulam theorem and a novel topological approach cast in a physical fashion that has the

potential to be operationalized, the Universe can be conceived as a lower-dimensional manifold encompassed in the Monster group. Our Universe might arise from spontaneous dimension decrease and symmetry breaking that occur inside the very structure of the Monster Module. We elucidate how the energetic loss caused by projection from higher to lower dimensions and by the Monster group's non-abelian features is correlated with the present-day asymmetry in thermodynamic arrow. By linking the Monster Module to theoretical physical counterparts, we are allowed to calculate its enthalpy and Lie group trajectories. Our approach also reveals how a symmetry break might lead to a Universe based on multi-dimensional string theories and CFT/AdS correspondence.

Tozzi A. 2015. How to Turn an Oscillation in a Pink One. Journal of Theoretical Biology 377, 117–18. doi:10.1016/j.jtbi.2015.04.018.

Scale-free dynamics - also called $1/f^n$ behavior, pink noise, power law, fractal-like distribution (Newman, 2005) - are an intrinsic feature of a large class of natural models, from earthquakes to brain activity (He et al., 2010). Assessing a geometrical/mathematical model of synthetic power law oscillations, we noticed that a wave containing a fractal-like structure can be produced by summing a random oscillation to a carefully chosen one. Here follows the procedure we carried out. First, we generated random numbers with power law distribution, obtaining a series of oscillations **1** in a log amplitude versus log frequency scatter plot. The series exhibited a pink noise behavior: $A(f)= 1/f^n$, where **A** was the amplitude of the oscillation, **f** was the frequency and **n** was the power exponent (Milstein et al. 2009). Second, we produced a non scale-free oscillation **2** equipped with a random point $\mathbf{O_2}$. Third, we chose the point $\mathbf{O_1}$ characterized by the same frequency of $\mathbf{O_2}$, but a different amplitude. Fourth, we extrapolated the sine waves corresponding to the points $\mathbf{O_1}$ and $\mathbf{O_2}$. Fifth, we looked for the required oscillation $\mathbf{O_3}$ which we had to superimpose upon $\mathbf{O_2}$, in order that the combination might be equal to the oscillation $\mathbf{O_1}$. We handled the sinusoidal oscillations through the classical formula (Booker, 1965) reported in Figure B, where t denotes time. In summary, we demonstrated that a pink noise can be obtained by adding a random sine wave to a proper one. This observation gives rise to countless applications: a "hidden" oscillation may cause a scale-free behavior in a random noise; a fractal system can be produced by simply choosing the appropriate oscillation to bring in; if power laws are involved in random walks, phase transitions and self-organized criticality (Bak et al., 1987), then the superimposition of a carefully chosen oscillation may lead to systems of increased complexity; "nested" waves from the central nervous system's spontaneous networks (Fox and Raichle, 2007) may be the source of the scale-free dynamics seen in EEG and fMRI; in the event of brain 1/f scaling disruption caused by illnesses such as Alzheimer's disease, an external wave - for instance, via transcranial stimulation (Reato et al., 2013) - could restore the broken symmetry.

Tozzi A, Peters JF, Navarro J, Marijuán PC. 2017. Heidegger's being and quantum vacuum. Progress in biophysics and molecular biology. https://doi.org/10.1016/j.pbiomolbio.2017.07.009.

A dialogue between Martin Heidegger and a theoretical physicist, namely Richie, unveils the striking relationships between the Eastern and Western philosophical concepts of Being and the experimentally detectable quantum vacuum. We provide an account of long-standing theoretical issues, such Being, Entity, Existence and the unique role of the human Thoughts in the world, and expound their possible physical counterparts.

Tozzi A, Peters JF. 2018. A Groupoid for Commutative and Noncommutative Operations: a Step Towards Quantum/relativity Unification. viXra:1802.0100.

The unexploited unification of general relativity and quantum physics is a painstaking issue that prevents physicists to properly understanding the whole of Nature. Here we propose a pure mathematical approach that introduces the problem in terms of group theory. Indeed, we build a cyclic groupoid (a nonempty set with a binary operation defined on it) that encompasses both the theories as subsets, making it possible to join together two of their most dissimilar experimental results, *i.e*., the commutativity detectable in our macroscopic relativistic world and the noncommutativity detectable in the quantum, microscopic world. This approach, combined with the Connes fusion operator, leads to a mathematical framework useful in the investigation of relativity/quantum mechanics relationships.

Tozzi A, Peters JF. Entangled Antipodal Points on Black Hole Surfaces: the Borsuk-Ulam Theorem Comes Into Play. viXra:1804.0014.

The entangled antipodal points on black hole surfaces, recently described by t'Hooft, display an unnoticed relationship with the Borsuk-Ulam theorem. Taking into account this observation and other recent claims, suggesting that quantum entanglement takes place on the antipodal points of a S^3 hypersphere, a novel framework can be developed, based on algebraic topological issues: a feature encompassed in an S^2 unentangled state gives rise, when projected one dimension higher, to two entangled particles. This allows us to achieve a mathematical description of the holographic principle occurring in S^2. Furthermore, our observations let us to hypothesize that a) quantum entanglement might occur in a four-dimensional spacetime, while disentanglement might be achieved on a motionless, three-dimensional manifold; b) a negative mass might exist on the surface of a black hole.

Tozzi A. 2018. Information and thermodynamic entropy from the standpoint of local observers in an expanding universe. viXra:1804.0346.

We describe cosmic expansion from the standpoint of an observer's comoving horizon. When the Universe is small, the observer detects a large amount of the total cosmic bits, which number is fixed. Indeed, information, such as energy, cannot be created or destroyed in our Universe, i.e., the total number of cosmic bits must be kept constant, despite the black hole paradox. When the Universe expands, the information gets ergodically "diluted" in our isotopic and homogeneous Cosmos. This means that the observer can perceive just a lower number of the total bits, due the decreased density of information in the cosmic volume (or its surrounding surface, according to the holographic principle) in which she is trapped by speed light's constraints. Here we ask: how does the second law of thermodynamics enter in this framework? Could it be correlated with cosmic expansion? The correlation is at least partially feasible, because the decrease in the information detected by a local observer in an expanding Universe leads to an increase in detected cosmic thermodynamic entropy, via the Bekenstein bound and the Laudauer principle. Reversing the classical scheme from thermodynamic entropy to information entropy, we suggest that the quantum vacuum's cosmological constant, that causes cosmic expansion, could be one of the sources of the increases in thermodynamic entropy detected by local observers.

GAUGE THEORIES FOR BIOLOGY

Sengupta B, Tozzi A, Coray GK, Douglas PK, Friston KJ. 2016. Towards a Neuronal Gauge Theory. PLOS Biology 14 (3): e1002400. doi:10.1371/journal.pbio.1002400.

Given the amount of knowledge and data accruing in the neurosciences, is it time to formulate a general principle for neuronal dynamics that holds at evolutionary, developmental, and perceptual timescales? In this paper, we propose that the brain (and other self-organized biological systems) can be characterized via the mathematical apparatus of a gauge theory. The picture that emerges from this approach suggests that any biological system (from a neuron to an organism) can be cast as resolving uncertainty about its external milieu, either by changing its internal states or its relationship to the environment. Using formal arguments, we show that a gauge theory for neuronal dynamics—based on approximate Bayesian inference—has the potential to shed new light on phenomena that have thus far eluded a formal description, such as attention and the link between action and perception.

Tozzi A, Sengupta B, Peters JF, Friston KJ. 2017. Gauge Fields in the Central Nervous System.193-212. In: The Physics of the Mind and Brain Disorders: Integrated Neural Circuits Supporting the Emergence of Mind, edited by Opris J and Casanova MF. New York, Springer; Series in Cognitive and Neural Systems. Pages 193-212. ISBN: 978-3-319-29674-6. DOI10.1007/978-3-319-29674-6_9.

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.

Tozzi A, Peters JF, Navarro J, Kun W, Lin B, Marijuán PC. 2017. Cellular Gauge Symmetry and the Li Organization Principle. Progress in Biophysics and Molecular Biology. https://doi.org/10.1016/j.pbiomolbio.2017.06.004.

Based on novel topological considerations, we postulate a gauge symmetry for living cells and proceed to interpret it from a consistent Eastern perspective: the *li* organization principle. Gauge theories had a tremendous impact in particle physics and have been recently proposed in order to assess nervous activity too. Herein, taking into account novel claims from topology, the mathematical branch that allows the investigation of the most general systems activity, we aim to sketch a gauge theory addressed to the fundamentals of cellular organization. In our framework, the reference system is the living cell, equipped with general symmetries and energetic constraints standing for the intertwined biochemical, metabolic and signaling pathways that allow the global homeostasis of the system. Abstractly, these functional movements would follow donut-like trajectories. Environmental stimuli stand for forces able to locally break the symmetry of metabolic and signaling pathways, while the species-specific DNA is the gauge field that restores the global homeostasis after external perturbations. We show how the Borsuk-Ulam Theorem (BUT), which states that a single point on a circumference maps two points on a sphere, allows an inquiry on the evolution from inorganic to organic structures as well as the comparison between prokaryotic and eukaryotic metabolisms and modes of organization. Furthermore, using recently developed BUT variants, we operationalize a methodology for the description of cellular activity in terms of topology/gauge fields and discuss about the experimental implications and feasible applications. We converge on the strategic role that second messengers have played regarding the emergence of such a unitary gauge field for the cell, and the subsequent evolutionary implications for multicellulars. A new avenue for a deeper investigation of biological complexity looms. Philosophically, along this overall exploration of cellular dynamics and biological complexity, we might be reminded of the duality between two essential concepts proposed by the great Chinese synthesizer Zhu Xi (in the XIII Century). His explanatory scheme epitomizes a feasible philosophical interpretation of the present proposal: on the one side, the *li* organization principle, which may be taken as equivalent to the dynamic interplay between symmetry and information; and on the other side, the *qi* principle, which can be interpreted as the energy participating in the process, and which always appears as interlinked with the former. In contemporary terms, it would mean the required interconnection between information and energy, and at the same time it would be pointing at essential interpretive principles of information philosophy.

Yurkin A, Tozzi A, Peters JF, Marijuan PC. 2017. Quantifying Energetic Dynamics in Physical and Biological Systems Through a Simple Geometric Tool and Geodetic Curves. Addendum to: Cellular Gauge Symmetry and the Li Organization Principle. Progress in Biophysics and Molecular Biology. https://doi.org/10.1016/j.pbiomolbio.2017.06.007.

The present Addendum complements the accompanying paper "Cellular Gauge Symmetry and the Li Organization Principle"; it illustrates a recently-developed geometrical physical model able to assess electronic movements and energetic paths in atomic shells. The model describes a multi-level system of circular, wavy and zigzag paths which can be projected onto a horizontal tape. This model ushers in a visual interpretation of the distribution of atomic electrons' energy levels and the corresponding quantum numbers through rather simple tools, such as compasses, rulers and straightforward calculations. Here we show how this geometrical model, with the due corrections, among them the use of geodetic curves, might be able to describe and quantify the structure and the temporal development of countless physical and biological systems, from Langevin equations for random paths, to symmetry breaks occurring ubiquitously in physical and biological phenomena, to the relationships among different frequencies of EEG electric spikes. Therefore, in our work we explore the possible association of binomial distribution and geodetic curves configuring a uniform approach for the research of natural phenomena, in biology, medicine or the neurosciences.

BUT AND BIOLOGY

Tozzi A. 2014. Evolution: Networks and Energy Count. Nature 515: 343. doi:10.1038/515343c.

First draft: Trofim Lysenko, the ominous Stalin's agronomist and enthusiastic supporter of Lamarkism, suggested with bitterness the heritability of acquired characteristics. His heretic ideas were dismissed with disgust in favor of the "post-Darwinist" standard evolution theory (SET), one of the most pervasive paradigms of the modern science. However, after half a century of oblivion, the debate is once again an hot topic of current research (Laland K, et al., Does evolutionary theory need a rethink? Nature. 2014 Oct 9;514(7521):161-4). In particular, the possible epigenetic inheritance within organisms have been suggested as neo-Lamarckian in nature and talks about a picture different from SET, despite Wray's skeptical claims. If we examine the problem from the novel perspective of the supramolecular chemistry, we notice that the epigenetic information involves the storage of information at the molecular level and its retrieval, transfer and processing at the supramolecular level, via transitory processes that are self-organized, self-assembled and dynamic. SET does not keep into account that the complexity of adaptive evolving systems (including species, niches and environment) is best understood as dynamic networks of relationships, aiming to decrease their free energy via entropy transfer. The DNA is just one of the countless functional tasks of interest in the study of evolution: changes propagate through interlinked levels of organization, inducing connectivity and interaction on all scales of the multilevel system, with no preferred level of granularity. Models of fitness attractors intended to capture the process of natural selection are starting to be developed, taking into account power laws, non-equilibrium steady-state at the edge of the chaos and energetic landscapes made of basins, valleys, floors, ridges and saddle points. In conclusion, it would be useful to investigate SET in the framework of dynamical system theories.

Tozzi A. 2015. Oral Propranolol for Infantile Hemangioma. The New England Journal of Medicine 373 (3): 284–85. doi:10.1056/NEJMc1505699.

The article by Léauté-Labrèze et al. (Feb. 19 issue)1 emphasizes the therapeutic efficacy and the short-term safety of propranolol in the treatment of infantile hemangiomas. However, recent studies raise concerns about potential long-term neurodevelopmental or cognitive effects of the highly lipophilic propranolol.2 Indeed, lipophilic beta-blockers cross the blood–brain barrier, leading to sleep and memory disturbance.3 For example, sleep disturbance, somnolence, and irritability have been observed in many infants treated with propranolol,4 and this drug has been shown to decrease specific memory functions in adults.5 A recent review suggested the possibility that blockage of neural pathways critical for learning and memory could be an unrecognized long-term side effect of propranolol in infants.6 Further long-term studies are thus needed before clinicians routinely suggest the use of propranolol in the treatment of infantile hemangiomas.

Tozzi A, Peters JF. 2017. The multidimensional world. Lambert Academic Publishing, Saarbrücken, Germany. ISBN-13: 978-3-330-03530-0.

Recently introduced versions of the Borsuk-Ulam theorem (BUT) reveal that a feature vector on a n-manifold projects two feature vectors (matching descriptions of a single object) onto an n+1 manifold. Starting from this rather simple, yet far-reaching, computational topology observation, we build a fruitful general framework, able to elucidate disparate "real" physical and biological phenomena, from quantum entanglement to gauge theories. Summarizing this novel topological approach, we take into account projections among functional or real dimensions. We achieve a system of mappings that fit very well with experimental results, making it possible to assess countless systems in far-flung scientific branches. This book highlights the computational character of matching descriptions (arising from descriptively proximal objects) that display a widest range of possible uses. Such observations point to BUT not just from the standpoint of a novel interpretation of almost all the biological and physical phenomena, but also as suitable tools in evaluating the slight (objective and subjective) differences that make our world an astonishing realm of rich heterogeneity.

HIGHLIGHTS:
A novel theorem
Natural projections and evolution
Gravitational lensing
Pauli exclusion principle
Small world networks
Ergodicity
Group theory
Thermodynamic entropy: the arrow of time
Shannon, Rényi entropy
The dimensions of living beings
How to detect hidden dimensions?

Tozzi A. 2016. Borsuk-Ulam Theorem Extended to Hyperbolic Spaces. In Computational Proximity. Excursions in the Topology of Digital Images, edited by J F Peters, 169–171. doi:10.1007/978-3-319-30262-1.

Peters JF, Tozzi A. 2016. Region-Based Borsuk-Ulam Theorem. arXiv.1605.02987.
This paper introduces a region-based extension of the Borsuk-Ulam Theorem (denoted by reBUT). A region is a subset of a surface on a finite-dimensional n-sphere. In topology, an n-sphere is a generalization of the circle. For a continuous function on an n-sphere into n-dimensional Euclidean space, there exists a pair of antipodal n-sphere regions with matching descriptions that map into Euclidean space Rn. The main results include a number of different region-based forms of the classical Borsuk-Ulam Theorem as well as the Straecker digital Borsuk-Ulam Theorem and the Burak-Karaca digital Borsuk-Ulam Theorem. Applications of reBUT are given in the evaluation of brain activity and quantum entanglement.

Peters JF, Tozzi A. 2016. String-Based Borsuk-Ulam Theorem. arXiv:1606.04031.
This paper introduces a string-based extension of the Borsuk-Ulam Theorem (denoted by strBUT). A string is a region with zero width and either bounded or unbounded length on the surface of an n-sphere or a region of a normed linear space. In this work, an n-sphere surface is covered by a collection of strings. For a strongly proximal continuous function on an n-sphere into n-dimensional Euclidean space, there exists a pair of antipodal n-sphere strings with matching descriptions that map into Euclidean space Rn. Each region M of a string-covered n-sphere is a worldsheet (denoted by wshM). For a strongly proximal continuous mapping from a worldsheet covered n-sphere to Rn, strongly near antipodal worldsheets map into the same region in Rn. An application of strBUT is given in terms of the evaluation of Electroencephalography (EEG) patterns.

Tozzi A. Peters JF. 2017. Critique of pure free energy principle: Comment on "Answering Schrödinger's question: A free-energy formulation" by Maxwell James Désormeau Ramstead et al. Physics of Life Reviews. DOI: 10.1016/j.plrev.2017.10.003.
The paper by Ramstead et al. reminds us the efforts of eminent scientists such as Whitehead and Godel. After having produced influential manuscripts, they turned to more philosophical issues, understanding the need for a larger formalization of their bounteous scientific results. In a similar way, the successful free-energy principle has been generalized, in order to encompass not only the brain activity of the original formulation, but also the whole spectrum of life. Here we go through philosophical (the principle of identity) and physical (temperature, Pandemonium architecture, time reversal entropy) issues that might be correlated with the free energy principle.

Tozzi A, Peters JF. 2018. What it is like to be "the same"? Progress in Biophysics and Molecular Biology. 133, 30-35. https://doi.org/10.1016/j.pbiomolbio.2017.10.005.
A unifying principle underlies the organization of physical and biological systems. It relates to a well-known topological theorem which succinctly states that an activity on a planar circumference projects to two activities with "matching description" into a sphere. Here we ask: what does "matching description" mean? Has it something to do with "identity"? Going through different formulations of the principle of identity, we describe diverse possible meanings of the term "matching description". We demonstrate that the concepts of "sameness", "equality", "belonging together" stand for intertwined levels with mutual interactions. By showing that "matching" description is a very general and malleable concept, we provide a novel testable approach to "identity" that yields helpful insights into physical and biological matters. Indeed, we illustrate how a novel mathematical approach derived from the Borsuk-Ulam theorem, termed bio-BUT, might explain the astonishing biological "multiplicity from identity" of evolving living beings as well as their biochemical arrangements.

Koczkodaj WW, Magnot J-P, Mazurek J, Peters JF, Rakhshani H, Soltys M, Strzałka D, Szybowski J, Tozzi A. 2017. On normalization of inconsistency indicators in pairwise comparisons. International Journal of Approximate Reasoning.86, 73–79. http://doi.org/10.1016/j.ijar.2017.04.005.
In this study, we provide mathematical and practice-driven justification for using [0, 1] normalization of inconsistency indicators in pairwise comparisons. The need for normalization, as well as problems with the lack of normalization, is presented. A new type of paradox of infinity is described.

Tozzi A, Peters JF, Chafin C, De Falco D, Today J. 2018. A timeless biology. Progr Biophys Mol Biol. 134, 38-43. doi: 10.1016/j.pbiomolbio.2017.12.002.
Contrary to claims that physics is timeless while biology is time-dependent, we take the opposite standpoint: physical systems' dynamics are constrained by the arrow of time, while living assemblies are time-independent. Indeed, the concepts of "constraints" and "displacements" shed new light on the role of continuous time flow in life evolution, allowing us to sketch a physical gauge theory for biological systems in long timescales. In the very short timescales of biological systems' individual lives, time looks like "frozen" and "fixed", so that the second law of thermodynamics is momentarily wrecked. The global symmetries (standing for biological constrained trajectories, i.e. the energetic gradient flows dictated by the second law of thermodynamics in long timescales) are broken by local "displacements" where time is held constant, i.e., modifications occurring in living systems. Such displacements stand for brief local forces, able to temporarily "break" the cosmic increase in entropy. The force able to restore the symmetries (called "gauge field") stands for the very long timescales of biological evolution. Therefore, at the very low speeds of life evolution, time is no longer one of the four phase space coordinates of a spacetime Universe: but it becomes just a gauge field superimposed to three-dimensional biological systems. We discuss the implications in biology: when assessing living beings, the underrated role of isolated "spatial" modifications needs to be emphasized, living apart the evolutionary role of time.

Tozzi A. 2018. Cause/effect correlations through the Borsuk-Ulam theorem and Kneser graphs. viXra: 1801.0117. PLUS: Tozzi A. 2018. Nervous Oscillations on a Twisted Cylinder. viXra:1803.0284.

Nervous dynamics display long range correlations, recurring paths, circular dynamics of activity that can be assessed through the Borsuk-Ulam theorem (BUT), which states that two points on a sphere map to a single point on a circumference. However, when evaluating neurodata extracted from EEG and fMRI, the BUT-related methods, based on projections and mappings among different functional brain dimensions, are impractical and computationally expensive. Here we show that BUT is correlated with graph theory, and in particular with the so-called Kneser graphs. This means that the combinatory features of brain activity can be described in terms of dynamical mappings and closed paths taking place on well-established abstract structures. We suggest that physical and biological systems' dynamics make predictable moves into peculiar phase spaces, following constrained trajectories that can be experimentally quantified. Further, we show that such long-range, recurring nervous trajectories described by the BUT's matching antipodal features (say, two far apart brain areas that are activated simultaneously and display the same value of entropy) can be described in terms of closed paths on a Möbius strip. In sum, Kneser graphs and Möbius strips allow the evaluation of nervous system's dynamics in terms of constrained trajectories taking place onto the well-established, easily manageable phase space of a twisted cylinder.

Tozzi A, Peters JF. 2018. Killing the fathers: a biology-framed skepticism. Researchgate. DOI: 10.13140/RG.2.2.17316.99208. PLUS: Tozzi A, Peters JF. 2017. With a little help by Nicholas de Cusa: erasing infinity from physical teories. viXra:1711.0201.

Starting from the tenets of human imagination, *i.e.*, the concepts of lines, points and infinity, we provide a biological demonstration that the skeptical claim "human beings cannot attain knowledge of the world" holds true. We show that the Euclidean account of the point as "that of which there is no part" is just a conceptual device, untenable in our physical/biological realm: terms like "lines, surfaces and volumes" label non-existent, arbitrary properties. We also elucidate the psychological and neuroscientific features hardwired in our brain that lead us humans to think to points and lines as truly occurring in our environment. Therefore, our current scientific descriptions of objects' shapes, graphs and biological trajectories in phase spaces need to be revisited, leading to a proper portrayal of the real world's events. In order to provide also a positive account, we view miniscule bounded physical surface regions as the basic objects in a biological context in a traversal of spacetime instead of the usual Euclidean points. Our account makes it possible to erase a painstaking problem that causes many theories to break down and/or being incapable of describing extreme events: the unwanted occurrence of infinite values in equations, such as singularity in the description of black holes. We propose a novel approach, based on point-free geometrical standpoints, that banishes infinitesimals and leads to a tenable physical/biological geometry. We conclude that points, lines, volumes and infinity do not describe the world, rather they are fictions introduced by ancient surveyors of land surfaces.