



# A Geometric Milieu Inside the Brain

Arturo Tozzi<sup>1</sup> · Alexander Yurkin<sup>2</sup> · James F. Peters<sup>3,4</sup>

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## Abstract

The brain, rather than being homogeneous, displays an almost infinite topological genus, since it is punctured with a high number of “cavities”. We might think to the brain as a sponge equipped with countless, uniformly placed, holes. Here we show how these holes, termed topological vortexes, stand for nesting, non-concentric brain signal cycles resulting from the activity of inhibitory neurons. Such inhibitory spike activity is inversely correlated with its counterpart, i.e., the excitatory spike activity propagating throughout the whole brain tissue. We illustrate how Pascal’s triangles and linear and nonlinear arithmetic octahedrons are capable of describing the three-dimensional random walks generated by the inhibitory/excitatory activity of the nervous tissue. In case of nonlinear 3D paths, the trajectories of excitatory spiking oscillations can be depicted as the operation of filling the numbers of octahedrons in the form of “islands of numbers”: this leads to excitatory neuronal assemblies, spaced out by empty areas of inhibitory neuronal assemblies. These mathematical procedures allow us to describe the topology of a brain of infinite genus, to represent inhibitory neurons in terms of Betti numbers and to highlight how spike diffusion in neural tissues is generated by the random activation of tiny groups of excitatory neurons. Our approach suggests the existence of a strong mathematical background subtending the intricate oscillatory activity of the central nervous system.

**Keywords** Arithmetic figures · Central nervous system · Nonlinear · Excitatory/inhibitory ratio · Neurons

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✉ Arturo Tozzi  
tozziarturo@libero.it; Arturo.Tozzi@unt.edu

Alexander Yurkin  
alv11yurkin@rambler.ru

James F. Peters  
james.peters3@umanitoba.ca

<sup>1</sup> Center for Nonlinear Science, University of North Texas, 1155 Union Circle, #311427, Denton, TX 76203-5017, USA

<sup>2</sup> Russian Academy of Sciences, Moscow, Puschino, Russia

<sup>3</sup> Department of Electrical and Computer Engineering, University of Manitoba, 75A Chancellor’s Circle, Winnipeg, MB R3T 5V6, Canada

<sup>4</sup> Mathematics Department, Adiyaman University, Adiyaman, Turkey

## 1 Introduction

The brain is a Riemannian manifold with genus zero. In other words, the brain does not contain holes: this tenet is implicitly assumed by the most influential accounts of the nervous activity (Friston & Ao, 2012; Telley et al., 2019). Genus is a particular topological invariant linked to the Euler characteristic that is generally used to classify 2D manifolds, but it can be generalized in higher dimensions too. In this paper, we will tackle the issue of a scarcely observed topological property of the brain that goes against the mainstream “genus zero opinion”. Come to think of it, it could be stated that the brain exhibits countless holes, because the neural tissue encompasses neurons devoid of excitatory spikes, i.e., the neural tissue displays transient neuronal “punctures” with inhibitory activity (Hodge et al., 2019). This means that the brain is equipped with a countless, or at least very high, number of holes surrounding the excitatory spiking neurons. We will term these holes “brain vortexes” (Don et al., 2020). Assuming that the brain is isotropic/homogeneous at very large scales and that the excitatory/inhibitory ratio is constant, the tissue concentration of these holes must be homogeneous too. To make a trivial example, we might think to the brain as a sponge equipped with countless and uniformly placed holes. Here we will try to answer to crucial questions: how are brain vortexes produced during nervous activity? Can they be described in mathematical terms, i.e., within the geometric dynamics on a 3D manifold of infinite genus? Is the brain depending on mathematical rules? What are the topological features, peculiarities and predictable physical consequences of a brain described in terms of a Riemannian manifold with high, almost infinite, genus? To answer these questions, we introduce a deterministic geometric model that permits visual constructions of linear (without any acceleration) and nonlinear (with the simplest uniformly acceleration) random walks in three-dimensional spaces. Our model is derived from the Pascal’s triangle, an array of the binomial coefficients widely used in numerous contexts. Its applications in mathematics extend to algebra, calculus, trigonometry, plane and solid geometry. Pascal’s Triangle is widely used in algebra and probability/combinatorics (Edwards, 2013), since it allows us to find without tedious computations the number of subsets of  $r$  elements that can be formed from a set with  $n$  distinct elements (Brothers, 2012). In the real world, this leads into the topic of graph theory, such as, e.g., turning mapping information into structures such as shortest paths, airplane routes and airport control, Dijkstra’s algorithm, computer graphics, engineering, search algorithms and data management. Other examples of the scientific utility of Pascal’s triangle can be provided. In a triangular portion of a grid, the number of shortest grid paths from a given node to the top node is the corresponding entry in Pascal’s triangle. Proton Nuclear Magnetic Resonance displays an inherent geometry in which Pascal’s triangles has a prominent role (Hore, 1983).

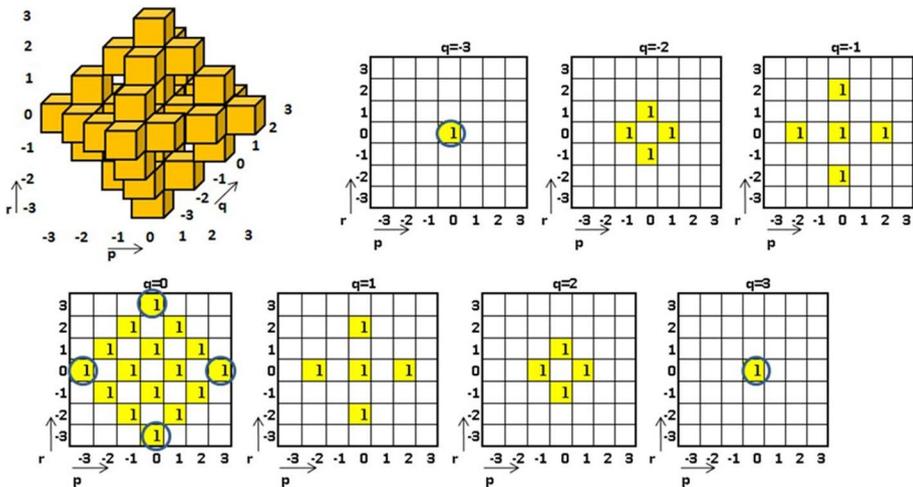
In the following, we will show how Pascal’s triangle-derived model may describe the paths of random walks that produce brain vortexes and short- and long-range nervous oscillations.

## 2 Geometric Models of Random Walks

Simple visual geometric models are required to make it easy to understand the description of complex phenomena (Klein, 1956; Sommerfeld, 1973). Recursive formulas to calculate the step-shaped Pascal’s triangle at various initial conditions and during random walks processes have been suggested.

Pascal’s arithmetic triangle, its analogues, generalizations and possible applications of visual geometric models have been thoroughly carried out (Yurkin, 2013, 2016, 2018; Yurkin et al., 2018). Novel, stepwise form for Pascal’s triangle (1D), two-sided (2D) and multi-dimensional generalizations can be achieved in linear models of random walks (Kolmogorov et al., 1995). Yurkin (1995) proposed an optical laser scheme standing for a nonlinear 1D walk in a system of rays; further, a real laser nonlinear 2D random walk in a system of rays was carried out. Nonlinear and non-Markovian random walks were described by Fedotov and Korabel (2015). Sarkar and Maiti (2017) portrayed a symmetric random walk on a regular tetrahedron, an octahedron and a cube. In the 1D case (along a straight line), a random walk (linear and nonlinear) can occur along two mutually perpendicular directions (right, left) inside an arithmetic triangle (the triangle has two corners on his base and one on his top) (Kolmogorov et al., 1995). In the 2D case, a random walk (linear and nonlinear) can be carried out in four different directions (forward, back, right, left) inside an arithmetic square (the square has four corners) (Yurkin, 2019a).

Linear and nonlinear 3D random walks has been described as visual linear and nonlinear 3D models in form of arithmetic octahedrons (Yurkin, ). In the 3D case of a Pascal’s triangle, random walks (both linear and nonlinear) can be carried out in six different directions (forward, backward, right, left, up, down) inside an arithmetic regular octahedron equipped with six vertices. For further details, see Yurkin (). Sequential iterations of octahedrons composed of small cubes describe the number of walks from the initial cell (initial cube) to the final cell (final cube). In the linear case, neighboring empty cells will densely fill the linear arithmetic octahedrons at the next iterations, without leaving any gaps or



**Fig. 1** The second iteration ( $n = 2$ ) of the nonlinear arithmetic octahedron consists of 36 cubes. The Figures  $q = \pm 1$  show the formation of separate structures of numbers (“islands of numbers”). Modified from: Yurkin (2019b, 2019c)

empty spaces. In turn, a 3D nonlinear random walk in a volume can be described as octahedrons not tightly filled with cubes (branching cells). See Fig. 1 for further details. Some empty cells inside the octahedrons (white cubes or gaps) will be filled with yellow cubes at the next iteration, some empty cells will be filled after every iteration, and so on. For big  $n$  numbers, the relative quantity of the empty cells or gaps (related to the general quantity of cells in nonlinear octahedron) decreases with increases in number  $n$ .

### 3 Brain Random Walks Come Into Play

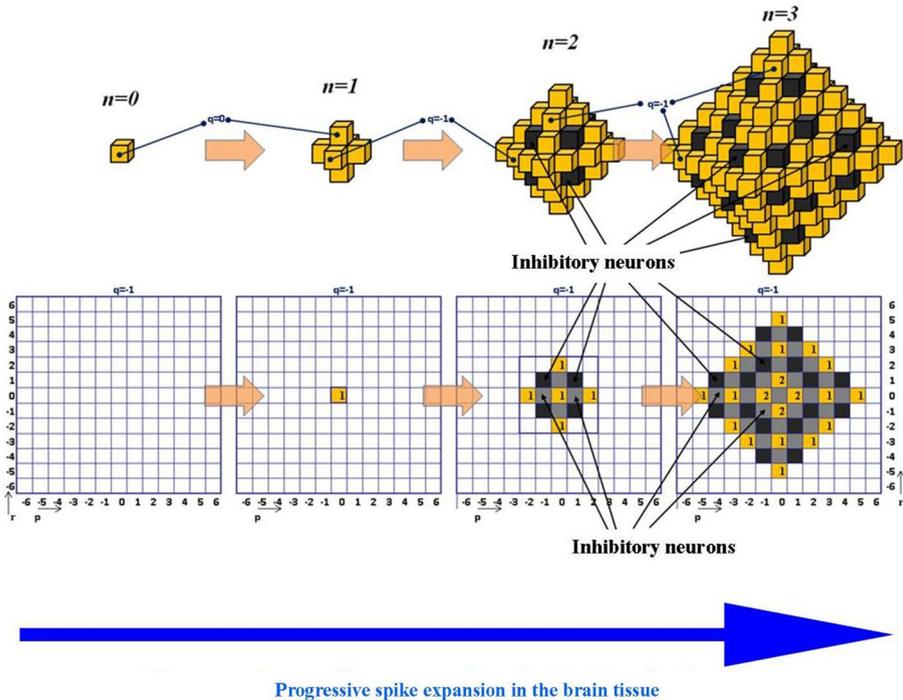
The iterations illustrated in in the previous paragraph permit the classification of different types of random walks in the form of the following table:

	<b>Linear random walk</b> (one unit steps, perpendicular each others)	<b>Nonlinear random walk</b> (first one unit steps, second two units steps, third three unit steps, etc., perpendicular each others)
3D case	<ul style="list-style-type: none"> <li>• Steps of constant length along six perpendicular directions in octahedron</li> <li>• Gaps and “islands of numbers” are absent in a linear arithmetic octahedron</li> </ul>	<ul style="list-style-type: none"> <li>• Steps of increasing length along six perpendicular directions in octahedron</li> <li>• Gaps and “islands of numbers” appear and disappear in different areas in a nonlinear arithmetic octahedron after several iterations. The relative quantity of the empty cells or gaps decreases with increases in <math>n</math></li> </ul>

The self-organized brain oscillations in the central nervous system encompass spontaneous excitability that produce bifurcations. Indeed, the brain is a non-linear electromagnetic-activation oscillatory system at the edge of chaos with inter-dependent modules (Fraiman & Chialvo, 2012; Tognoli & Kelso, 2013; Tozzi et al., 2016; Wang et al., 2017; Xu & Wang, 2014). The occurrence of genetic-driven spontaneous oscillations during the brain development has been widely studied in both real and syntetic models. It is well-known that spontaneous cortical electric fluctuations occur before the 35th week of gestation (Krueger & Garvan, 2014) and are more frequently detectable in immature synapses (Kavalali et al., 2011). The neocortical circuits not just display rich spontaneous dynamics engaged by sensory inputs but are also able to generate outputs independent of external stimuli (Yuste et al., 2005). Trujillo et al. (2019) highlighted how structural and transcriptional changes in network activity spontaneously follow fixed genetic programming in human neocortical organoid models, producing random phase-amplitude coupling that resembles human neonatal EEG features. The transcriptional or epigenetic heterogeneity related to early biases in cell fate choices can be stochastic in nature (Soldatov et al., 2019; Velasco et al., 2019; Wang et al., 2019). These data highlight the critical role of spontaneous electromagnetic induction in the formation of an economical self-organized neuronal network. Given the predominant role of nonlinear stochastic paths in brain dynamics, the above-described Pascal’s triangle-framed recursive formulas of geometric linear/nonlinear assemblies may find application to understand the nonlinear activity of neuronal oscillations’ 3D random walks. In touch with the framework theorized by Pascal’s triangle iterations, it is well-known that neural crest cells differentiate through a series of stereotypical lineage-restriction binary decisions that involve coexpression/competition of genes driving alternative fate programs (Soldatov et al., 2019). During migration, multipotent neural crest cells follow a

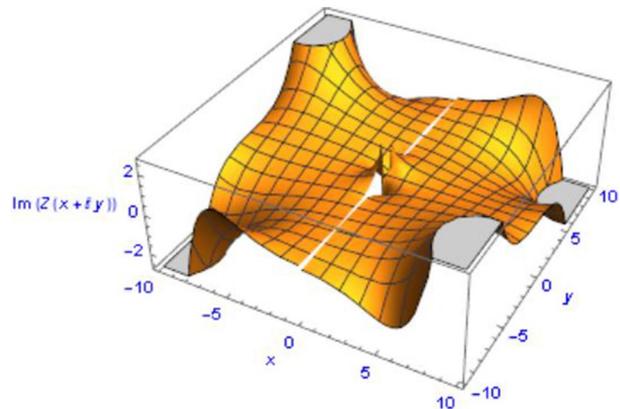
progression of fate bifurcations that can be formalized as a series of sequential binary decisions assessable in terms of Pascal's triangle.

The spatiotemporal balance of the brain activity is kept equalized by varying the strengths of neuronal excitation (E) and inhibition (I) (Haider et al., 2006; Xue et al., 2014). A constant, steady E/I ratio does exist between the total amount of excitatory and inhibitory stimulation, both in vitro and in the intact cortex, both at the single neuron level and at the network excitability level (Sengupta & Stemmler, 2014; Sengupta et al., 2013). Excitation and inhibition are deeply matched: an optimal E/I ratio across neurons is always retained, despite the fluctuations in cortical levels' activity. E/I ratio stands for a homeostatic mechanism between strengthening and weakening processes in the adaptation of real synapses. Homeostasis triggers a discrepancy between inhibitory and excitatory connections that could contribute to symmetry breaking and leads to directed coupling and information transfer (Tognoli). E/I ratio could be regarded as the whole symmetry of the intact cerebral cortex. In terms of the Pascal's triangle model, the filled cells stand for single excitatory neurons, while the empty cells produced inside the octahedrons stand for inhibitory neurons (Fig. 2). After a few iterations, the empty cells will be progressively filled with yellow cubes: this means that areas of inhibition and excitation continuously appear and disappear when further iterations take place during the expansion of the spike oscillation.



**Fig. 2** Neural oscillation expansion and neuronal excitatory/inhibitory occurrence in terms of random walks taking place inside a 3D lattice. In our nonlinear octahedron model, inhibitory neurons look like dark gaps, while excitatory neurons like yellow filled cubes. Modified from: Yurkin (2019b, 2019c)

**Fig. 3** A Riemannian surface with the center of the surface punctured with a hole



### 3.1 Vortex Cycles in Brain Spikes

A punctured manifold is analogous to a physical/biological space with holes. This means that we need to work on a manifold that is Riemannian. Briefly, a manifold is a topological space that is locally Euclidean (i.e., around every point, there is a neighborhood that is topologically the same as the open unit ball in  $\mathbb{R}^n$ ). A Riemann surface is a surface-like configuration that covers the complex plane with several, and in general infinitely many, “sheets”. A sample Riemannian surface is shown in Fig. 3. It is easy to notice that the center of the surface is punctured with a hole, which stands, in our framework, for a rupture of neuronal excitability due to inhibitory components. Inhibitory neurons can be modelled as vortex cycles (Don et al., 2020; Peters, 2018, 2020) with induced order proximity of spiraling hole vortices (Ahmad & Peters, 2019). The rim of this brain vortex cycle represents the edge of an inhibitory neuronal assembly. The inner cycles for a vortex reaching inward represent excitatory brain pull. Therefore, the brain can be depicted as nesting, non-concentric vortex cycles embedded in a punctured Riemann surface (Weyl, 1955).

In this context, a novel formulation of the Borsuk Ulam theorem (BUT) might be of great help: the Vortex-BUT, which works on a manifold with holes. There are three forms of vortexBUT:

- Physical geometry vortex BUT (pevBUT): each pair of antipodal vortex hypersphere surface points  $S^{n-1}(\mathbb{R}^n)$  maps to the Euclidean space  $\mathbb{R}^n$ .
- Region-based vortex BUT (revBUT): each pair of antipodal vortex hypersphere surface regions in  $2^{S^{n-1}}(2^{\mathbb{R}^n})$  region points map to the Euclidean space  $2^{\mathbb{R}^n}$  (Peters, 2016).
- Descriptive vortex BUT (phivBUT): each pair of antipodal vortex surface points OR regions maps to  $\mathbb{R}^k$ ,  $k \geq 1$ .

Each glial structure is an example of a massive vortex cycle. A punctured physical surface is a surface populated by vortices: this allows us to start viewing punctured brain surfaces using vortexBUT. The one very different thing about the new form of BUT is that we replace the Borsuk-Ulam use of  $S^n$  with  $V^n$ , a vortex in  $n$ -dimensional space. Then the simplest form of vortexBUT is defined by a continuous function

$$f : V^n \rightarrow \mathbb{R}^n$$

so that  $f(x) = f(-x)$  for antipodal points  $x, -x$  on  $V^n$ .

Several variants of BUT have been provided in the very last years to assess brain functions (Tozzi et al., 2017). Why do we need another BUT variant? The answer is straightforward, if we consider that single neurons may have an impact on surround firing statistics and even on simple behaviors. Exploiting the advantages of a simple cortex, Hemberger et al. (2019) examined the influence of single pyramidal neurons on their surrounding cortical circuits. Brief activations of single neurons triggered reliable sequences of firing in tens of other excitatory/inhibitory cortical neurons, reflecting cascading activity through local networks. The evoked pyramidal patterns extended over hundreds of micrometers from their source over up to 200 ms. In touch with a vortexBUT account of the brain, simultaneous activation of pyramidal cell “pairs” (i.e., neuronal activities with matching description as dictated by BUT) stand for balanced control of population activity, preventing paroxysmal amplification. Single cortical pyramidal neurons can generate rapidly evolving and non-random firing sequences, in touch once again with our Pascal triangle’s model (Hemberger et al., 2019).

## 4 Conclusions

Our account of deterministic models equipped with visual constructions of linear and non-linear 3D random walks through arithmetic figures displays interesting geometric and algebraic topological properties. The minuscule regions between brain cells have the appearance of cavities or holes in donut-shaped activation regions. From (Don et al., 2020), we know that brain activation regions have vortical structures defined by nested, possibly intersecting brain signal cycles resulting from the activity of inhibitory neurons. Here we observe that these brain activation region vortexes reside in a Riemannian space, since each brain vortex cycle does not have a sub-cycle that resides in the vortex. The brain, rather than being homogeneous, embodies a real, smooth Riemannian manifold in the sense that at each cell  $p(x, y, z, t)$  (point in a 4D spacetime setting) we can describe a piecewise smooth mapping  $f : \mathbb{R}^n \rightarrow \mathbb{R}$  defined by  $\nabla f = \frac{\partial f}{\partial x} + \frac{\partial f}{\partial y} + \frac{\partial f}{\partial z} + \frac{\partial f}{\partial t}$  that maps the rate of change of  $p$  to a real number. In effect, a collection of brain cells has its own differential geometry. In 4D spaces, the rate of change of brain activity oscillates piecewise continuously in spiraling vortexes represented by  $\nabla f$ , encompassing linear random walks, in which the achieved arithmetic octahedron is densely filled with numbers. Each of these vortexes has its own  $\nabla f$  represented by a free group providing its seeds in fMRI videos quantified with Betti numbers. In this context, a Betti number equals the number of generators of a free group representation (Munkres, 1984) of basin activation vortexes. These cortical Betti numbers arise naturally at a varying pace over spatio-temporal episodes in brain activity. In a Riemannian model of brain activity,  $f(p)$  and  $f(p')$  loom as fixed points inasmuch as  $f(p) = p$  and  $f(p') = p'$  for the varying brain cell rates of change of  $\nabla f(p)$ ,  $\nabla f(p')$ . This view of brain cell activations residing on a Riemannian manifold represents a straightforward extension of the 2D view of a Riemannian surface (Weyl, 1955). Due to our lack of knowledge, we cannot specify whether our nervous Riemannian manifold with genus zero displays compactness or non-compactness. In case of compactness, we are in front of algebraic geometry rather than just geometry and our title should be “An Algebraic, topological and Geometric Milieu Inside the Brain” instead of just “A Geometric Milieu Inside the Brain”.

In cortical 4D spaces encompassing nonlinear random walks, the achieved arithmetic octahedron is not fully filled with numbers, since it contains gaps. Gaps, “islands of numbers” and separate structures of numbers appear and disappear inside the octahedron in the nonlinear 3D case after many iterations (Figs. 1 and 2). For high  $n$  numbers, the relative quantity of the empty cells or gaps (relative to the total number of cells in the nonlinear octahedron) decreases with increases in  $n$ . In sum, for nonlinear 3D cases, we can speak of filling the numbers of the arithmetic octahedron in the form of “islands of numbers” or separate structures of numbers, until a given threshold is reached. This leads us into the realm of a nonlinear brain punctured with inhibitory components that break the topological order of the neuronal tissue and propagating oscillations. The fact that physical constraints, such as the ones described by Pascal’s triangle permutations, limit the range of brain activity has been largely recognized in brain growth. Tripathy et al. (2018) reported that Mast1, expressed just in postmitotic neuronal dendritic and axonal compartments, is associated with the microtubule cytoskeleton. Mice with Mast1 microdeletions display peculiar macroscopic features, such as enlarged corpus callosum and smaller cerebellum, in absence of megalencephaly. These opposite findings (abnormal increase vs abnormal reduction) let us to hypothesize that the macroscopic growth of the brain tissue is regulated by physical constraints: keeping invariant the brain size (i.e., in absence of megalencephaly), the central nervous tissue of animals harboring Mast1 microdeletions undergoes a general rearrangement. In physical/mathematical terms, a three-dimensional lattice (standing for the whole brain mass) harbors vectors and tensors which product (including excitatory and inhibitory neurons) must be held constant. When lattice perturbations occur (e.g., the case of cytoskeleton’s genetic Mast1 alterations), one of the tensors modifies. To keep invariant the tensor product, another tensor need to vary: in simpler words, the fact that more axons cross the midline in Mast1 Leu278 del mice means that the size of other structures (in this case, the cerebellum) must decrease. In touch with this observation, Tripathy et al. (2018) report that, in animals harboring Mast1 microdeletions, the PI3K/AKT3/mTOR pathway is unperturbed, whereas Mast2 and Mast3 levels are diminished, indicative of a dominant-negative mode of action.

In our framework, the combinatorial properties of the Pascal’s triangle are correlated with the mathematical operations leading to brain spikes, through iterated random walk patterns. The occurrence of inhibitory cells in terms of “hollows” in the very structure of the brain tissue permits us to consider the topological features of a high-genus manifold, compared with genus-zero manifolds. What does the occurrence of a neural manifold of very high genus physically mean? There are many ways to generalize the notion of genus to higher dimensions, e.g., Heegaard genus in algebraic topology, arithmetic and geometric genus in algebraic geometry (Almgren & Thurston, 1977). Feldman et al. (1996) tackled the issue of the topological properties of infinite genus Riemann surfaces. They introduced a class of infinite genus Riemann surfaces, specified by means of a few geometric axioms, to which the classical theory of compact Riemann surfaces up to and, including the Torelli Theorem, extends. The axioms are flexible enough to encompass many interesting examples, such as the heat curve and a connection to the periodic Kadomcev–Petviashvilli equation. Apart from the mentioned accounts, our results suggest the feasibility of another intriguing operational approach, which allows us to generalize the notion of genus to higher dimensions through another powerful weapon: the Betti number. The brain might stand for a manifold equipped with a Betti number corresponding to the number of inhibitory neurons. Betti numbers are topological objects proved to be invariants by Poincaré that are used to extend the polyhedral formula to higher dimensional spaces. Informally, the  $k$ th Betti number refers

to the number of path-connected edges (Kaczynski et al., 2004) embedded in surface holes. In case of a brain tissue with  $n$  vortex cycles and  $k$  edges attached between each of the cycles, the Betti number  $= n + k$  (Don et al., 2020; Manschot et al., 2012). The brain is a dynamical system where the genus continuously changes because inhibitory cells' activity may vary. If the brain displays a high genus, the population of excitatory neurons cannot increase beyond a given threshold because, in topological terms, the potential squeezing leaves always holes that cannot be reduced to a single point. Our model provides another way to generate inhibitory activity: the progressive iterations of random walks in an expanding excitatory neural activity lead to the production of hollows. These hollows stand for places that can be filled by inhibitory neurons. Therefore, inhibitory structures might spontaneously appear when nonlinear excitatory random walks start to occur in the nervous structures.

Experimental data achieved from the available neurotechniques suggest that our brain oscillations are balanced through a persistent excitatory/inhibitory (E/I) ratio. Here the concept of hyperuniformity comes into play. In amorphous cellular structures of ordered and disordered materials, anomalous suppression of density fluctuations takes place on large length scales (Klatt et al., 2019). A set of initial points evolves through Lloyd iterations since each point can be replaced by the centre mass of its Voronoi cell. A gradient descent algorithm is produced that permits a progressive convergence towards a minimum in the potential energy surface. Klatt et al. (2019) discovered that systems equipped with different initial configurations converge towards the same degree of uniformity after  $10^5$  Lloyd iterations. This means that, independent of the initial conditions, adult brain's cell volumes become uniform and the dimensionless total energy converges towards values comparable to the local energy minima. Therefore, we propose to describe brain oscillation expansion in terms of Lloyd iterations. In the nervous case, the seeds stand for the initial point sets (i.e., one or few excited neurons) which are converted into centroidal Voronoi diagrams. The tiny perturbations in the brain oscillations that seed the ensuing development of excitatory macro-structures might stand for the starting spots of the process described by Klatt et al. (2019) in terms of Voronoi cells and described by us in terms of Pascal's triangle models. Since every system must converge towards an hyperuniform state after a finite number of iterations (Tozzi & Peters, 2019), the brain starts from countless different possible spike conformations and then achieves the extremely high degree of uniformity typical of its neuronal E/I ratio.

In sum, we showed how relatively simple geometric and mathematical concepts might subtend the very mechanisms of intricate and nonlinear brain activities.

**Author Contributions** All the Authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All the Authors equally contributed to: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, statistical analysis, obtained funding, administrative, technical, and material support, study supervision.

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**Human rights** This research does not contain any studies with human participants or animals performed by any of the Authors.

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**Arturo Tozzi** is a M.D., Pediatrician in Naples Italy. He also works with The Center for Nonlinear Science, Denton Texas, USA. He does not like to be on focus. Looking for unexpected, hidden multidisciplinary relationships, he publishes in rather different Journals (e.g., nuts in Nature, New England Journal of Medicine, Physics of Life Reviews, PLOS Biology, Cognitive Neurodynamics, etc) and fields (biology, physics, math, philosophy, history, medicine, and, above all, neuroscience).

**Alexander Yurkin** is a member of Russian Academy of Sciences. Pupil of the mathematicians Vladislav Mikhalevich and Vasily Dikumar, he is a leading expert in geometric accounts of physical and biological processes. In particular, he studies linear and nonlinear systems' dynamics in terms of iterations of geometric figures, such as octahedrons and Pascal's triangles.

**James F. Peters** is Professor at Department of Electrical and Computer Engineering, University of Manitoba, Winnipeg, Canada. His research focuses on establishing frameworks for the study of the closeness of structures on triangulated finite bounded surface regions filled with holes in a space  $K$  endowed with a spatial or descriptive proximity relation. In Alexandroff-Hopf-Whitehead CW (Closure finite Weak) complexes on  $K$ , e.g., this leads to the discovery of proximal sub-complexes and proximal nerve structures that are close to each other either spatially or descriptively. Of particular interest is the detection, characterization, analysis, measurement, rate of change, energy, and classification of shapes of nesting, non-overlapping skeletal vortexes, forming what are known as optical vortex nerves.

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