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Brains are Probabilistic, Electrophysiologically Intricate and Triune: A Biased-Random Walk Perspective on Computational Neuroscience

El Cerebro es probabilístico, electrofisiológicamente intrincado y trino: una perspectiva de la neurociencia computacional basada en caminatas aleatorias dirigidas

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**Abstract.**

The pursuit of a unified theory that captures the intricacies of the brain and mind continues to be a significant challenge in theoretical neuroscience. This paper presents a novel, triune framework that utilizes the concept of collective biased random walk (cBRW). Our approach strives to transcend biological specifics, offering a high-level abstraction that remains general and applicable across various neural phenomena. Despite the solid traditional foundation of computational neuroscience, the intricate delicacy of neural processes calls for a renewed probabilistic approach. We aim to utilize the intuitive nature of probability concepts—such as the probability of localization and state, and uniform probability distribution—to study the stochastic organization of electric charges and signals in the brain. This electrophysiological intricacy emerges from the seemingly paradoxical reality that tiny electric events, while random, collectively give rise to predictable, long-range oscillations. These oscillations manifest in three groups of activation states. Our framework categorizes the brain as a triune system, accommodating classical, semiclassical, and non-classical interpretations of both probabilistic phenomena and cBRW models, alongside three groups of states. We conclude that by appreciating, rather than overlooking, the tiny random walks of electric charges and signals in the brain, we can gain a triune mathematical foundation for theoretical brain science, the powerful capabilities of this organ, and the electromagnetic interfaces we can develop.

Resumen.

La búsqueda de una teoría unificada que capture las complejidades del cerebro y la mente sigue siendo un desafío significativo en la neurociencia teórica. Este artículo presenta un nuevo marco trino que utiliza el concepto de caminatas aleatorias dirigidas colectivas (cBRW). Nuestro enfoque busca trascender los detalles biológicos, ofreciendo una abstracción de alto nivel que sigue siendo general y aplicable a diversos fenómenos neuronales. A pesar de la sólida base tradicional de la neurociencia computacional, la delicadeza intrincada de los procesos neuronales requiere un enfoque probabilístico renovado. Nuestro objetivo es utilizar la naturaleza intuitiva de los conceptos de probabilidad, como la probabilidad de localización y estado, y la distribución de probabilidad uniforme, para estudiar la organización estocástica de las cargas y señales eléctricas en el cerebro. Esta complejidad electrofisiológica surge de la realidad aparentemente paradójica de que pequeños eventos eléctricos, aunque aleatorios, colectivamente dan lugar a oscilaciones predecibles y de largo alcance. Estas oscilaciones se manifiestan en tres grupos de estados de activación. Nuestro marco categoriza el cerebro como un sistema trino, acomodando interpretaciones clásicas, semiclásicas y no clásicas de fenómenos probabilísticos y modelos de BRW, junto con estos tres grupos de estados. Concluimos que, al apreciar, en lugar de pasar por alto, las pequeñas caminatas aleatorias de las cargas y señales eléctricas en el cerebro, podemos obtener una base matemática trina para la ciencia teórica del cerebro, las poderosas capacidades de este órgano y las interfaces electromagnéticas que podemos desarrollar.

Keywords.

Brain States, Brain Theory, Brain Electrophysiology, Neural Computations, Electroencephalography, Non-Classic Brains.

Palabras Clave.

Estados cerebrales, teoría del cerebro, computaciones neuronales, electroencefalografía, cerebros no-clásicos.

1. Introduction

The computational and mathematical exploration of the brain has garnered widespread interest. However, questions remain: is the brain another biophysical or engineering system? Can we classify the mind as a type of computational system?

In this context, the notion of probability is pivotal in science, engineering, and computation (Jaynes, 2003) as well as in many biological processes, such as random walks (Codling, 2008). Probability has also been suggested as a logic for modeling the measurement process (Rossi, 2023). Indeed, probability is a cornerstone concept in many mathematical and computational neuroscience textbooks. The statistical analysis of channel gating, for instance, involves probabilities associated with ion channel states (Dayan & Abbot, 2005; Johnston & Wu, 1995). The spontaneous release of neurotransmitter is a calcium-dependent process governed by probabilistic laws (Johnston & Wu, 1995). At the systemic level, probabilistic methods (frequentist, Bayesian, etc) are crucial for modeling significant neural phenomena, such as encoding and decoding of stimuli (Dayan & Abbot, 2005; Doya et al., 2007), predictive coding and motor control (Aitchison & Lengyel, 2017), Fisher information (Dayan & Abbot, 2005; Doya et al., 2007), the free energy principle in neuroscience (Friston, 2010) and the role of uncertainty (Knill, 2004) in neural computation.

Conversely, the brain's electrical nature is essential for the rapid and efficient transmission of information (Hille, 2001; Koch, 1999). This characteristic is present at various scales, from individual ions (Hille, 2001) to macromolecules (ion channels), membranes (both intracellular and extracellular), and system-level signals (local field potentials or LFP and Electroencephalography or EEG) (Nunes & Srinivasan, 2006; Buzsaki et al., 2012). More recently, direct electric communication (ep-haptic effects) has been acknowledged in numerous brain processes (Anastassiou & Koch, 2014).

In this paper, we present an approach that underscore the brain's probabilistic nature and how it contributes to the brain electrophysiological complexity. By “electrophysiologically intricate”, we refer to a complex system with diverse and interconnected phenomena that, nonetheless produce organized electrophysiological signals. We adopt the random walk (RW) paradigm as our primary mathematical and computational framework. A RW is a sequence of random steps taken by a *particle* (an ion in our case) in real space or by a *signal* (such as the LFP or the EEG) in a mathematical space (Codling et al., 2008). Despite its randomness, this process adheres to certain probabilistic rules. Biased random walks (BRWs), in contrast, exhibits directionality, showing a preference for movement in specific ways. It is within this triune nature of the brain—random, organized, and a blend of both—that its computational and cognitive powers may lie.

Finally, we address the necessity for generalization in our theoretical neuroscience approach. A generalized theoretical neuroscience seeks concepts applicable not only to a particular brain or nervous system (e.g., of a mammalian animal like a rodent or primate), but also to invertebrate brains, diminutive insects (where probabilistic models may be more suitable), neuromorphic artificial intelligence systems, and still unexplored or unknown neural-like systems. Social insects and their BRWs during foraging can also be models of “liquid brains” (Solé et al., 2019). Ant foraging behavior may provide insights into RW and collective BRWs (cBRWs) mechanisms that are challenging to investigate in more conventional brains.

Embracing this “universalist” view (see definition in Brugger, 1981), it is important to develop (i) general definitions akin to those utilized in biology (Bunge, 1979) and (ii) highly abstract models that dissect elementary mechanisms of action, such as those present in convergent and divergent networks or in nonlinear and simple logical operations with minimal or no dynamics (see for instance, Gutierrez et al., 2021).

With the concept of BRW, extended to several dimensions and scales—from ions to animal behavior—we want to modestly contribute to the intuitively transparent definitions that form the abstract foundation of theoretical neuroscience.

2. A Personal Proposal

Our proposal is founded on five elements: 1. Probability (encompassing the Probability of being in a state b and Probability of localization at x , $Ps(b)$ and $Pl(x)$), 2. electrophysiological intricacy, 3. triune character, 4. biased random walks (BRW) and a fifth, more subjective element: delicacy. The last honors the brain-mind relationship. This respect for the brain's delicate circuits is woven throughout the proposal (Gomez-Molina et al., 2013).

BRWs are posited as a fundamental characteristic that manifest not only in the brain's physical space, but also within more abstract spaces, such as the space state or the space of activation variables (e.g. membrane voltages or EEG-potentials). In virtue of these BRWs, electric charges and signals unpredictably transcend their borders and circuits interconnect in unnumerable ways, often exhibiting a certain bias or directional tendency.

We contend that the brain's electrophysiological complexity arises from a unique combination of stochastic behaviors and directional tendencies. This complexity is further enriched by the dynamic interplay between activation and inactivation processes, as well as the integration of traditional and non-traditional categories, what we refer to as the ‘triune approach’ to various concepts.

But why are BRWs apt for this role? Primarily because our brains are engineered to process movement, with locomotion being one of the most fundamental movements. The brain and body's bilateral architecture likely

stems from the need to compute straightforward locomotion, reflecting a biased or asymmetric pattern. This bilateral symmetry, with left and right organs, sensors and muscles arrayed around locomotion, suggests that symmetries and asymmetries have been influential in our evolutionary history (Corballis, 2017).

Thus, we possess abundant neural resources capable of comprehending, encoding, and orchestrating BRWs. With this foundation, we can anticipate to the brain's behavioral nucleus but also an engagement of computational resources within ourselves that are apt for this interpretation.

3. Sketch of the Paper, its Methods, and Algorithms

In section 4, we classify probabilistic and RW approaches into three categories and define probabilities of activation and localization. Section 5 present computational examples of BRWs for one and two dimensions and illustrate how a collective of three signals in BRWs can give rise to a simple electrophysiological signal. The potential to scaling up to a greater number of signals or particles in real brains is discussed in section 6. Finally, we recognize the need to have classic, semiclassical and non-classic approaches to understand the full electrophysiological intricacy of the real brain.

We use theoretical methods. Computational methods are only illustrative. The general algorithm we use can be called the *recursive uniform distribution method* and it is inspired by Fisher information. It can be schematically presented in Figure 1.

The recursive uniform distribution method evaluates how random walk behaviors are influenced by parameters that are themselves randomly determined. It mirrors Fisher information's focus on parameter sensitivity and the quantification of information, extending these concepts to a dynamic model where parameter uncertainty is inherent.

In Fisher information, the intricacies arise from the need to understand how small changes in parameters affect the likelihood function (Dayan & Abbot, 2005; Doya et al., 2007). In our recursive model, complexities arise from the need to understand how the distribution of the parameters (a and b), which are themselves random variables, affect the behavior of the BRW.

Our goal here is to illustrate different types of BRWs in a way that students in a course of Theoretical Neuroscience can understand intuitively. Computer simulations, when used, are mainly for illustrative purposes. They are written in Python 3.11.5.

If a future goal is to derive exact properties or to prove certain behaviors of the model, then a more nuanced theoretical approach would be necessary. Extending the rigorous analysis found in Fisher information studies to random parameters can be one way to do it.

4. Theoretical Results: Probabilities

4.1 States and a Triune Classification Framework for them

A triune approach to probabilities based on a state classification for the whole brain, cortical modules, neurons, and ion channels has been proposed before (Gomez & Lopera, 1999; Gomez-M, 2000). A threefold method aims to reconcile strongly polarized or dichotomic views.

The more general thing we can say about an entity is that it presents states. Even information systems that are harder to describe or imagine, like those in psychology or cybernetics can be approached with this notion.

In a multi-scale approach, states can be defined in terms of electrophysiological activation (Andreassi, 2007; Duffi, 1972) or indicators of neural activity, like those associated with depolarizing currents, spiking, calcium levels (Denizot et. al., 2019; Gomez-M., 2000; Koch, 1999; Malmivuo & Plonsey, 1995). EEG high frequency activity or other forms proposed in EEG-source localization also involve the notion of electrophysiological activation (Malmivuo & Plonsey, 1995).

Activation states can be continuous or discrete. For a continuous description of states in terms of order relations, functions and space states see Bunge (1979).

For a discrete classification of states, the minimal number of states we can study is two (e.g. ON and OFF). However, we use here a previous classification based on three states (including one intermediate state) to avoid radical dichotomies (Gomez & Lopera, 1999; Gomez-M, 2000).

The 3 states classes are:

Activation. A state of high electrophysiological activity associated with excitation, depolarization, high calcium levels, local EEG activity of high frequencies or alert state.

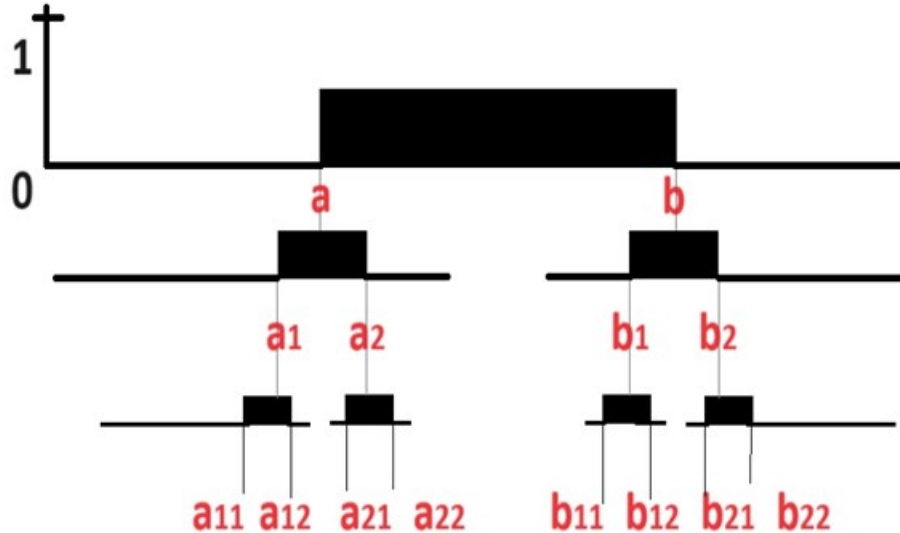
Semiaction. A state of middle level electrophysiological activity associated with resting membrane potentials (including values close to spike threshold), alpha EEG activity or relaxed global state. Due to its mixed properties, between sleep and activation, this state may possess the most surprising computational abilities (Gomez-Molina, 2022).

Inactivation. A state of minimal or reduced electrophysiological activity associated to inhibition, hyperpolarization, EEG activity at low frequencies and the deep sleep state of the whole brain.

This definition bears resemblance to, but is distinct from, the one employed in neuroimaging by Lin et al. (2022). In their framework, only two states are delineated, and an event is classified as activated (or deactivated) upon the execution of a cognitive function (Lin et al., 2022). However, it is important to note that while the latter condition may be met in certain instances, our criteria for activation do not exclusively hinge on the execution of a cognitive function. These states can be de-

Figure 1

The Recursive Uniform Distribution Method: an Intuitive Form to Understand BRWs and the Complexities of the Electrophysiological Signals in the Brain



Note. Changes in probability distributions, probability functions, probability densities, and waves of probability, and how they create collective Bias Random Walks (cBRWs) in real or mathematical spaces, form the basis of storing (memory) and processing (thinking, intelligence) information in the brain.

finer for ion channels, neurons, brain regions, and the whole brain itself (Gomez & Lopera, 1999; Gomez-M, 2000; Gomez-Molina, 2003; Gomez-Molina et al., 2015).

4.2 Probability of state b $P_s(b)$ and Probability of localization at x $Pl(x)$

A system —such as a neuron or a cortical module— has a certain probability of being in a specific state b , $P_s(b)$, if its activation signal, like membrane potential or local field potential, satisfies the criteria for that state b (for instance, exceeding a threshold for spiking or being within a high frequency range when active). Similarly, a particle has a probability to occupy, or be found in, a particular region x , known as $Pl(x)$.

$Pl(x)$ for particles moving in BRW in real space are equivalent to $P_s(b)$ for signals changing in BRW in state space. Neurons compute in cBRW in state space similarly to how ants (using swarm intelligence) or ions move in cBRW in real space. This parallel allows us to extend the classification of activation to probabilities in general.

4.3 Extending the Triune Classification Framework for Probability and RWs

Like the classification we presented above for states, we propose here a triune classification framework for probabilistic approaches and RWs, consisting of three main classes. Two of these classes are dichotomous, exhibiting opposite characteristics, while the third class serves as an intermediate category, embodying features from both dichotomous classes. Each main class may contain

sub-classes, and there is a possibility for overlap between classes and sub-classes.

Classic Class. In this category we include the empirical probability (also called the relative frequency probability, the long-run probability or the “objective or frequentist probability”). It is defined as a ratio $P = \frac{PA}{AP_0}$, where PA represents all the cases associated with a particular outcome, and AP_0 represents all possible cases. This probability is in the range between zero and one, including these extreme values. It can be continuous or discrete (Doya et. al., 2007; Jaynes, 2003).

Classic Random Walks involve Gaussian distributions and conventional diffusion processes. They can be analyzed in one, two, or three spatial dimensions. The behavior is characterized by a mean squared displacement that is proportional to time. BRWs that behave without the bias according to a gaussian distribution, can belong to this class.

In the **semiclassic class**, probabilities such as Bayesian (interpreted as a degree of belief) or subjective probabilities are included. These probabilities are updated as new evidence is acquired. $P_s(b)$ for $b = \text{semiactivation}$ might belong to this class.

Semiclassic Random Walks are associated with non-gaussian distributions but still retaining some properties of the classical class. Levy-flights (Codling, 2008) will be classic in the sense that they retain some classic properties but because they are non-gaussian they belong to this class.

Non-classic class. Non-classic probabilities are those that indicate a clear distinction with classical properties. For instance, if we emphasize some physical propensity or tendency over long-run behavior, we are in the framework of propensity theory. Probabilities calculated using the Schrodinger equation (Abers, 2004) are other sub-class of this class. Exotic probabilities (with a range outside 0 or 1 (Yousef, 2001), or those linked with fuzzy mathematics (Gomez-Molina, 2003) can also belong to different sub-classes of this class.

Non-classic random walks can include self-avoiding walks (Madras & Slade, 1996), random walk that never crosses itself (Lawler, 1996), and quantum walks (Kempe, 2009).

4.4 A Minimalist Scenario

To give a minimalist example, let's imagine a 1D encephalon of length L with sensors located at $x = 0$ and $x = L$. We can divide it in N segments and assume initially that the source has equal location probability to be in any of them. We can assume that the source emits two walkers (signals like ionic currents or magnetic fields, or particles) that attenuate with the distance to the sensor. Each one has, however, a probability to go the right or to the left (to account for source orientation and anisotropy) and to leave with certain magnitude in each direction (to account for medium parameters, like conductivity and permittivity). The problem is: for a given recording of these signals for the sensors, what is the location probability of the source or the sources? What is the probability of activation that each position has?

To go deeper into this problem, we need to study RW and BRWs in these simplified scenarios.

5. Computational Results: RWs and BRWs in Electrophysiology

Locomotion is one of the most fundamental behaviors the brain controls. The trajectory the animals describe in space form a sequence of steps or paths with some bias (a goal) but also with randomness (exploratory turnings). This trajectory is called biased random walk (BRW) and it can be described in some physical and/or state space.

When we deal with physical spaces in the brain, the walking entity can be an ion like calcium (Denizot et al., 2019; Malmivuo & Plonsey, 1995), a small molecule (Nicholson, 2005; Postnikov et al., 2022) or an axonal extension (Staa, 2023). The walking entity can also be an electric signal fluctuating within the state-space of its values. In this case we have a BRW in a mathematical space. When we talk about organisms or animals, in neuroethology for example, the walking entity is the animal itself. The way an ant or animal searches for food can be modeled as a random walk or a BRW in real space (Codling et al., 2008). Part of our efforts in

this paper is present a general, "universalist" (Brugger, 1981) approach for all these situations.

5.1 Random Walks in one Dimension (1D)

For x_i , representing the electrical signal of a cell or an average signal of a group of cells- three distinct tendencies emerge:

- *Upward Tendency (UP)*: signifies activation or excitation.
- *Downward Tendency (DOWN)*: represents inactivation or inhibition.
- *Stabilizing Tendency (stay)*: The signal tends to hover near its preceding value, x_{i-1} , fluctuating slightly upwards or downwards, or remaining at x_{i-1} itself, indicative of a resting state.

Each tendency is going to have a probability, $P(UP)$, $P(DOWN)$, $P(stay)$ such that they satisfy:

$$P(UP) + P(DOWN) + P(stay) = 1$$

To have a better intuition, we are going to use only a uniform distribution Z over the interval (a, b) . In this distribution, all the corresponding z values have the same probability. If we want to generate 3 mutually exclusive outcomes from this uniform distribution, we need to subdivide it in 3 different subintervals (a, c) , (c, d) and (d, b) . We make the length of the subinterval proportional to the probability we want to have for each one of these 3 outcomes or events. For instance, if we want that $P(UP) = P(DOWN) = P(stay)$ all the subintervals are going to be the same length but if $P(UP) > P(DOWN) > P(stay)$ then $c - a > d - c > b - d$. We can have more than three mutually exclusive behaviors, like "going UP SLOWLY", or "going DOWN FASTLY". Compound behaviors can also be defined, like "going UP fast, then stay and, finally, going DOWN Fastly". In this way we can simulate, for instance, a burst of spikes.

The advantages of uniform distributions in any of these cases are multiple. According to the principle of indifference, when we do not have any reasons to give credence to one alternative over other, the best option is giving the same (Jaynes, 2003). They can be handled easier by intuition, and therefore we can estimate more clearly subjective probabilities. There are mathematical advantages too. For instance, for the three behaviors mentioned above, the expectancy of the UP tendency is:

$$E(UP) = E(Z) = \frac{a+c}{2}$$

and its variance is:

$$Var(UP) = Var(Z) = \frac{(c-a)^2}{12}$$

The probability for Z to be in any subinterval of (a, b) is proportional to the length of the subinterval:

$$P(a < Z < c) = \frac{c-a}{b-a}$$

Where the constant of proportionality is simply $\frac{1}{b-a}$. This method can have applications in several scenarios. For instance, to model the random walk of a small molecule in the brain or the behavior of an animal foraging for food in the wild. If the random walk is completely random and without any directional preference (unbiased random walk), then the subintervals are all equal and the next step is to determine the distance of the next position of the walking entity. We can assume that the distance is constant (as it is usually the case) or generated for other random distribution. However, if the walker is in some kind of field that makes it go preferentially to the left (or to the right) —or to stay around— then the subintervals should have a length proportional to this field or preference. It can even be more realistic to make the distance longer in the preferred direction, to simulate the effect of other walkers that also go in that direction. Obstacles can also be simulated as fields (Codling et al., 2008; Gomez-Molina et al., 2017).

We can see an example of the electrical signals in the membrane of two neurons with different ongoing activity but having a strong common input that dominates the tendency of the signal. To illustrate our proposal, a simple uniform distribution is enough. However, see Figure 2, we have generated the distribution parameters with other uniform probability distribution, as indicated before. In circles we represent the “decision points about the next turning direction”. They coincide in time for both cells because the common input arrives to them simultaneously.

For the minimalist 1D scenario of section 4.4, the configuration of a sensor (natural or artificial) with a threshold of 10 units (and m signals) illustrates how intricate and delicate electrophysiological propagation processes can be when described as cBRWs, even in simplified models. In Figure 2, the sensor responds to the blue signal ($m = 1$) when it crosses the threshold upward at around 60-time units and until it crosses downward at around 80-time units.

A second potential application is for modeling single ion channel behavior (Johnston & Wu, 1995) or UP and DOWN states in neurons (Wilson, 2008). In the first case, the mean open time or the mean closed time can be introduced to estimate $P(UP)$ and $P(DOWN)$.

The length of the subintervals can be adjusted based on the distance source-sensor. The source might exhibit repulsive or attractive forces, move and/or switch polarity once reached by the walker. Such a model allows for the assessment of the electrophysiological intricacy of real dipoles, sources, sinks and oscillatory signals in one dimension. While a minimalist uniform distribution is a significant oversimplification, it serves as a useful tool for fostering intuition in students about cBRWs. This approach’s primary advantage lies in its simplicity.

In Figure 3 we have three BRWs, simulated like in Figure 2. They represent a simple case of collective

BRW, or cBRW, generating an electrophysiological signal, in red. This is calculated as a single point source in an unbounded isotropic conductor (Buzsaki et al. 2012; Malmivuo & Plonsey, 1995).

5.2 Probability Distributions and Random Walk in two Dimensions (2D)

In this kind of random walk the walker can present the following motions: Vertical (UP, DOWN, STAY) and Horizontal (LEFT, RIGHT, STAY). We can apply to the Horizontal motion the same considerations we applied to the vertical motion in the previous section. In Figure 4 we show all the possible positions that two particles have occupied during 100 time units. Time evolution is not shown but some idea of the possible trajectories can be estimated. The density of circles can be used to calculate the total probability of location in these 100 steps.

An example for 14 particles, discriminated by color and symbol, is shown in Figure 5. Each particle starts in a different position and has a particular bias. The figure tries to give us an intuition of what can be a cBRW with many walkers, with the hope that they can help to build a picture of how intricate the movement and probability of localization of electrical charges in the brain and its associated electrophysiological processes are.

As a good approximation, the movement of ions in the brain obeys the basic equations proposed in the Hodgkin-Huxley model (Johnston & Wu, 1995; Malmivuo & Plonsey, 1995). However, part of these movements is random, and these ions also behave probabilistically. Classical, semiclassical, and non-classical approaches to probability and BRWs each provide essential insights that are, in some ways, complementary.

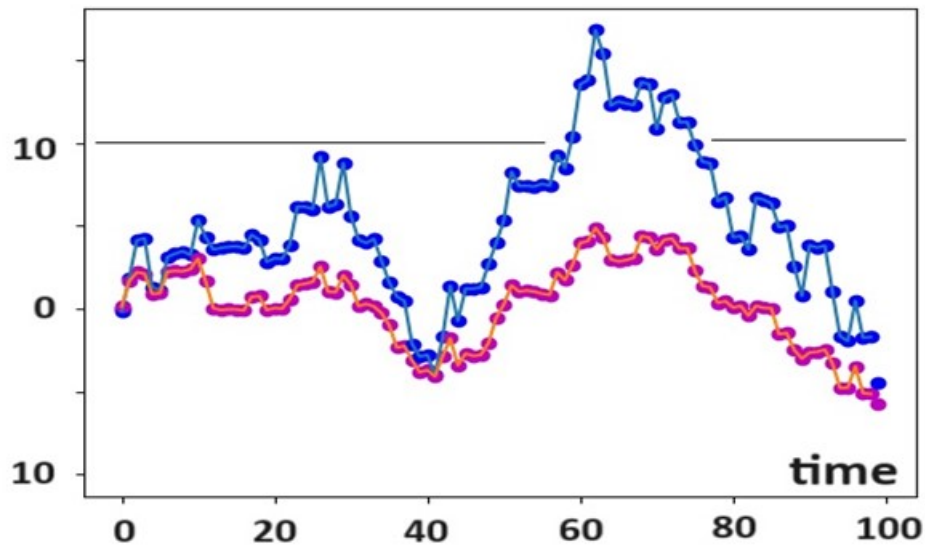
6. Discussion

In this paper we have illustrated with theoretical models and simulations the probabilistic nature of brain electrophysiology using the tools of BRWs at essentially two different scenarios: the analysis of *electrical signals within a state space* (Figure 2 and 3) and the examination of actual *electric brain charges (ions) in physical space* (Figure 4 and 5). We explore the utilization of uniform distribution as the fundamental model to generate BRWs. This approach is rooted in the desire to comprehend intricate electrophysiological systems using minimalistic assumptions, akin to the way Fisher information encapsulates the essence of a variable’s informativeness with respect to a parameter.

In the methods section, we propose a recursive application of the uniform distribution, where the parameters of one uniform distribution are determined by another, creating a layered structure that enriches the behavior of the BRW.

Figure 2

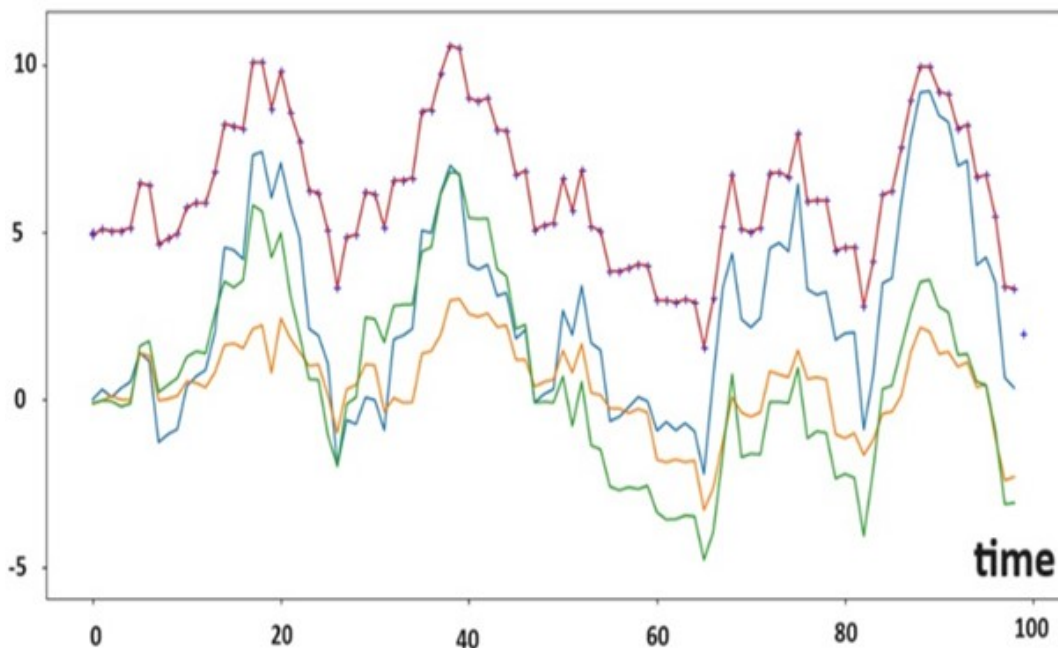
Trajectories (100 steps) for two Particles in a Coherent Random Walk Sharing the same Qualitative Event (showed in blue and red circles for clarity: UP, DOWN and STAY events, according to the recursive uniform distribution method), but Responding to them with Different Magnitudes



Note. This effect can be observed at high resolution but disappears at low resolution. These simulation tools can be used as a method of analysis of evoked responses at two sensory or field stimulation conditions, where the parameters are unknown. Similarly, they can be used to simulate two homologous brain areas under similar and synchronous inputs.

Figure 3

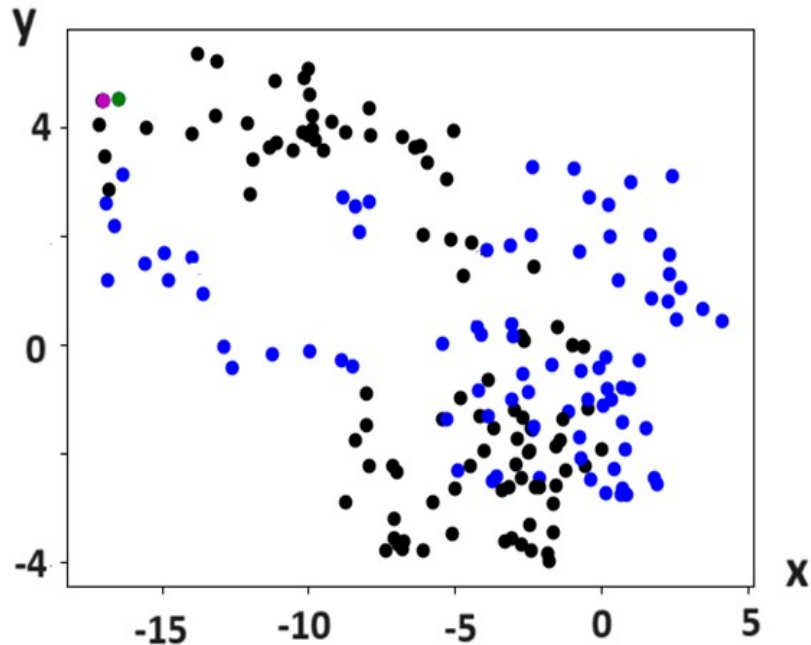
Three Electrical Signals Associated to Cell Membranes Describing a cBRW



Note. An electrophysiological signal (such as a local potential or EEG) is shown at the top (red, +), representing the weighted sum of the signals below.

Figure 4

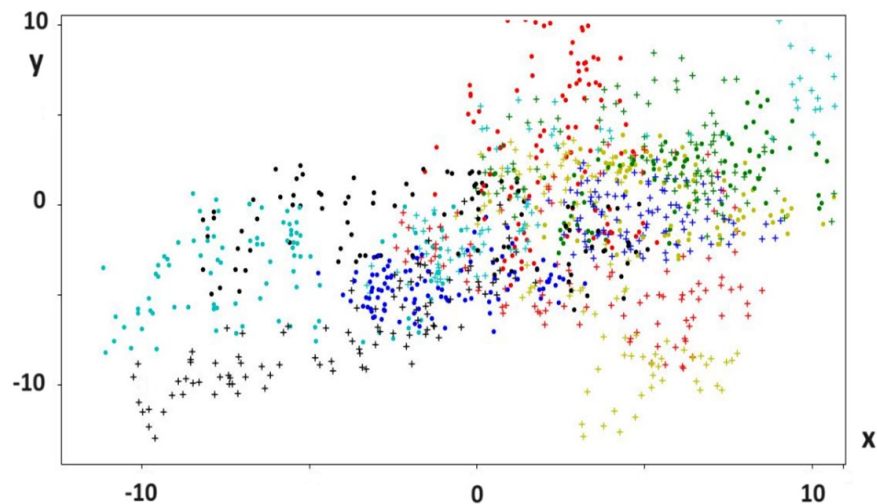
Two simulations of two Particles (black and blue). They perform a Biased Random Walk in two Dimensions



Note. The positions of each particle are shown for all 100 steps. The final position after 100 steps is indicated in green for the blue particle and in magenta for the black particle. Both particles start at the position (0,0). The density of circles in a given area x indicates the probability of finding the particle in that location, $Pl(x)$.

Figure 5

A Collective Biased-Random Walk (cBRW) Involving 14 Particles in a Two-dimensional Space, Defined by the X and Y axes



Note. Despite utilizing shared algorithms, the presence of local heterogeneity —represented by specific random values drawn from uniform distributions— can result in a diverse array of position sequences, density patterns, and location probability values across different regions and time intervals. Some measures of central tendency and parametric statistics might not be appropriate for real cBRW, where ephaptic effects and the delicate nature of electrophysiological interactions make parameter estimation difficult.

For example, by changing the parameters a and b of a distribution, the associated subintervals (e.g., (a, c) and (d, b) ; see section 5.1) can be modified as well as the associated state probabilities. In this way, the discrete distribution can switch itself probabilistically between uniform, gaussian, bimodal, monotonically increasing and monotonically decreasing distributions. This method preserves the intuitive clarity of the uniform distribution, which is often obscured in more complex distributions. By doing so, this work demonstrates that even the simplest of distributions can be harnessed to model rich and varied behaviors.

6.1 BRWs between Sources and Sinks in Real Brains

In the extracellular or intracellular space, as well as in the walls of ion channel pores, ions moving under fields encounter various small and large macromolecules, such as water, metabolites, and proteins, in addition to cellular structures like cell membranes, vesicles, and cytoskeletal proteins. While the mesoscopic trajectories of ions generally exhibit a certain tendency or bias, they cannot be fully described in a smooth (classical) manner using Maxwell's equations at the molecular level. This is because we cannot have a detailed description of the exact locations of all the molecules in the brain. In this complex organ we cannot possibly know all the molecular and cellular details (Nunes & Srinivasan, 2006). The heterogeneity of the brain can only be approached statistically (probabilistically). Therefore, the trajectories of ions, instead of being smooth, break with each collision forming a sequence of positions that can be described as a BRW. See Figure 6 for the case of one source and sink.

The number of electrophysiological biased random walks (BRWs) occurring throughout the entire brain is staggeringly large, potentially surpassing 10^{17} per second. This calculation considers that each ion moving through an ion channel generates a distinct single-ion-BRW trajectory while the channel remains open. Moreover, a multitude of BRWs take place adjacent to the cell membranes, rendering this estimate quite conservative. Nonetheless, it is astonishing that long-range oscillatory activity exhibits such macroscopic and coherent organization of circuit currents across the scalp, given the collective behavior of countless BRWs at the nanoscopic level.

6.2 Activation, Dipoles and RWs

The increase in depolarization and the associated inward cation currents that characterize activation states suggest that the total number of state-switching events of the ion channels (channel opening and closing) per unit of time is a characteristic of activated regions. It is then expected that there are changes in the parameters of the random walks of cations (Ca^{2+} , Na^{+} , K^{+} or H^{+}) during activation. This situation can be of interest to new scanner techniques (Gomez-Molina, 2003, 2008; Toi, 2022). In other words, the regions of the brain

where we have activation, can be characterized by an abundance of BRW. A particularly significant particle to describe activation at many levels is the ion calcium (Gomez-Molina, 2022). Importantly, calcium signaling is not only present on neurons but also in other cells whose role has been largely ignored in activation processes, like glia and astrocytes (Denizot et al., 2019).

During activation the ions move in Brownian motion but with the typical parameters of the multiple RW that characterize activation. These parameters should depend on the microanatomy of the brain region (Nunes & Srinivasan, 2006). We suggest that by estimating the parameters of a distribution of probability as if they were, recursively, dependent on another distribution of probability, we can simulate the dynamics of the drivers of the BRWs (usually, differences of potential). In other words, by focusing on the probability of the parameters of a uniform probability distribution, rather than in the probability itself associated with such distribution, we can capture more discrete probability distributions for the possible events (see section 5.1).

cBRW may presumably contain many sources and sinks. More precisely, they may be thought of as a set of microsources and microsinks (Nunes & Srinivasan, 2006) but moving and rotating, like some early models of the depolarization wave of the heart (Malmivuo & Plonsey, 1995). One action potential can be conveniently understood as a traveling dipole (Rodriguez-Falces, 2015) or, more simply, as a moving activation or probability waves (Gomez-Molina et al., 2015).

If we have several axons running in parallel, and they activate simultaneously, one possible way to study this phenomenon is by using diffusion weighted imaging (DWI) that could potentially detect water particles flowing in the open channels of the axons (Gomez-M, 2000). The collective activation of ion channels can, theoretically, modify the apparent diffusion of water and this process can be detected with DWI.

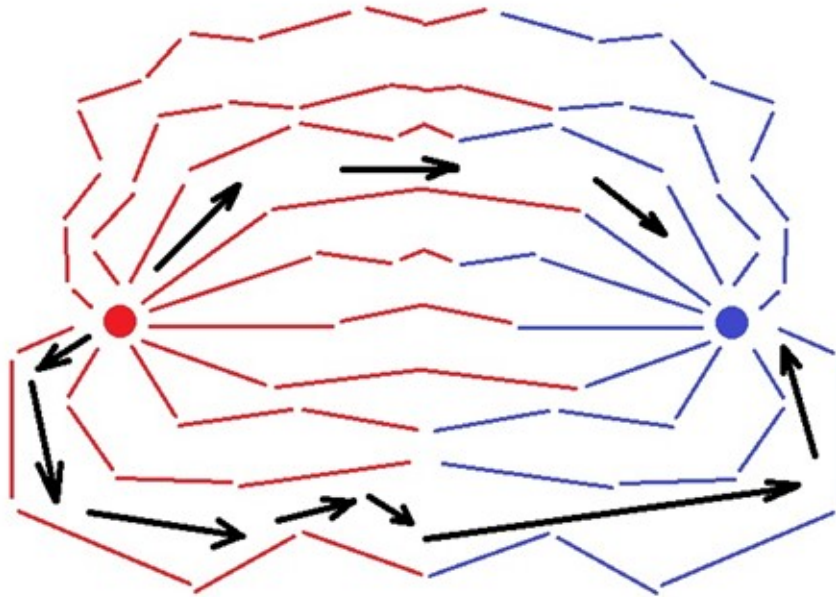
An increase in dipole density can also be a characteristic of activated regions (Michel, 2019; Nunes & Srinivasan, 2006). The probability distribution of the number, position, orientation, and magnitude of these dipoles should differ from what characterize non-activated regions. Many should be not far from the size of a compartment of an apical pyramidal neuron in layers II/III and V/VI. Biggest dipoles (equivalent dipoles) have been proposed in EEG/MEG solutions (Malmivuo & Plonsey, 1995; Michel & Brunet, 2019).

6.3 Transient Charge Unbalances and Conservation Laws

Long-range electric signals have probabilistic relationships with the open and location probability of the channels (Gomez-Molina, 2003), but most likely they are not simple or easy to reduce to a dipole model. In this context, the acceptance of equivalent dipoles as EEG-sources, for instance, has been a long debate in electro-

Figure 6

A Schematic Illustration of Biased Random Walks (BRWs) between a Source (in red) and a Sink (in blue) within a Heterogeneous Medium



Note. The biases (e.g. black arrows) and the red-blue transitions are irregular. The paths are depicted as a series of segments, intentionally elongated, and deviating from the ideal smooth trajectory. A fascinating aspect of the brain's electrophysiological complexity is how the nanoscopic randomness of billions of sinks and sources within such a diverse medium can lead to the relatively organized EEG/MEG patterns that we measure on the scalp. The interrelation of these sinks, sources and BRWs in a coherent whole is what we call cBRW.

physiology (Malmivuo & Plonsey, 1995). Point-current sources in gray matter are a better approximation but we still need to estimate P_s or Pl for ion channels.

Part of the electrophysiological intricacy we have studied arises because ephaptic effects can introduce a slight bias in various ions, including calcium. Additionally, physiological activations may induce a charge imbalance in certain brain regions, leading to the formation of both dipolar and monopolar components (Riera et al., 2013, 2012). Calcium ions are instrumental in representing neural network activity within entire organisms (Nietz et al., 2022). Developing methods to capture natural behaviors using these techniques is crucial.

In BRW models, calcium ions can be conserved, maintaining their quantity and presence. However, they may also bind to other entities, leading to their phenomenological 'annihilation' or disappearance. Conversely, they may dissociate from buffers or molecules, re-emerging as if they were phenomenologically generated anew (Gomez-Molina et al., 2017).

The conservation of mass is implicit when we study multiple particles in a random walk (if these particles do not react chemically with others). The conservation of charge is fundamental in electrophysiology as well

as the principle of electroneutrality (Johnston & Wu, 1995) although the last has controversial issues (Riera et al., 2013, 2012). Ion diffusion might introduce current sources (Halnes et al., 2016, 2017). Again, all of this is part of the electrophysiological intricacy of the brain.

The conservation of charge is the paradigm for all conservation laws in electrodynamics, like the conservation of energy, momentum, and angular momentum in electrodynamics (Griffiths, 2014). This conservation principle has been the model for more complex conservation phenomena in non-classic physics: the conservation of probability and the flow of probability (probability current) (Abers, 2004). This perspective gives some real presence to the notion of probability since the flow of probability is analogous to the flow of an electric current or a fluid (Griffiths, 2014). It is well established that a single photon can evoke an electrical response in a rod (Gentili, 2021). It is possible that other neural processes, neural prostheses, or electromagnetic brain-computer interfaces such as EEG/MEG, electric/magnetic stimulation, MRI, or near-infrared spectroscopy (NIRS) might detect or exploit the non-classical probabilities of cBRWs in significant ways. The computational abilities of the mind, future computers (Aaronson, 2013) or brain-com-

puter hybrids can be due to the non-classic nature of Ps (semiactivation). Particles, including membrane currents or ion channels, at this state might be “cloudy” so $Ps(b) \times Pl(x) \times$ driving forces (Gomez-Molina, 2003) might represent powerful non-classical and fuzzy computations of cBRWs.

7. Conclusions

In this study, we endeavor to demonstrate how triune methodologies —classical, semi-classical, and non-classical— for probability and BRWs, alongside activation, semi-activation, and inactivation for activation states, each uniquely contribute to elucidating the complex electrophysiological phenomena observed in the brain. While the term ‘classical’ varies across disciplines, within mathematics, it denotes an approach grounded in logic and set theory, devoid of paradoxes, as characterized by Shapiro (Shapiro, 2005). In our proposed classification, the adherence to binary concepts, the law of excluded middle, and the law of non-contradiction distinguish classical mathematics.

7.1 Electric Charge: A Minimalist Concept in Electrophysiology

The earliest, simplest, and more fundamental concept of electrophysiology has been the concept of electric charge. Therefore, can we attempt to describe the brain’s electrophysiological complexity solely in these terms?

The concept of electric charge has been problematic from the beginning: an electric charge is not an “intrinsic property” that is carried inside an electric object. We need to place it inside an “EM field” to generate a force. Ronald Giere, an advocate of propensity in probability theory, has pointed out —to support his view— that electric charges can only be defined by their tendencies to interact with other charges, such as attracting or repelling them (Giere, 1973).

Moreover, when we try to construct the more elemental descriptions of electric current (e.g. a simple current = $\frac{dq}{dt}$, or a current density) in saline water we need to realize that we are not dealing only with a local flow of mass particles in RW in a passive media. All the molecules and particles of the media can rotate, be polarized, activated, and modify their Pl or Ps . The water molecules, for instance, are incredible dynamic, creating and annihilating charges in nanoseconds. The media became nonlinear, active, and anisotropic, forming more flows. There is something else around all the time: the “fields”, that forms incredible complex cBRW. Water protons, for their small mass and spin, can respond in ways that evolution might have exploited to increase the efficiency of ion channels (Hille, 2001).

It is well known that pH and water ions influence gating, opening probabilities and many other properties of ion channels (Hille, 2001). We suspect that conventional

approaches to probability might not work in all cases. We have explored the use of exotic probability by combining it with fuzzy logic (Gomez-Molina, 2003). Fuzzy logic is an important approach that captures many linguistic structures (Kerre, 2005) and it has been also applied to neuroscience (Gentili, 2021).

One goal of the paper is maximizing understanding of electrophysiological intricacy from minimal complexity in the probabilistic approach. In doing so, I took inspiration on a previous probabilistic/Bayesian approach to EEG/“ionic-current MRI” using Fisher information (Gomez-Molina, 2008; see current developments in Toi et al., 2022). Fisher information measures the sensitivity of a variable to parameter changes in the most economical terms. Similarly, the recursive uniform distribution method (Figure 1) seeks to generate a deep understanding of intricate electrophysiological signals from the simplest of distributions, in the realm of BRWs.

7.2 The Brain is a Delicate and Fragile System

We employ the term ‘delicate’ to underscore the profound reverence warranted by the brain’s intricate electrophysiology and its probabilistic behavior, which render it exquisitely sensitive, both in our study and engagement (invasive and non-invasive) with its interconnected circuits (Gomez-Molina et al., 2013).

In the realm of computational neuroscience, which grapples with intricate electrophysiological challenges, certain philosophical quandaries of computational complexity theory become salient (Aaronson, 2013). Definitions of intractable problems, logical omniscience, and the dichotomy of pure/mixed states offer fresh insights into the algorithmic discourse contrasting classical and non-classical mathematics. Pure states epitomize entities with a comprehensive informational profile, whereas mixed states denote systems shrouded in state-related uncertainty. These states may be delicate —acutely sensitive to measurement and research protocols— or, following Aaronson’s terminology (Aaronson, 2013), fragile —prone to environmental perturbations, noise, and distortion—. Real-world computations are inherently discrete, bounded by finite resources, and presuppose a circumscribed assessment of potential outcomes, thereby circumventing logical omniscience, where agents are presumed capable of discerning all logical ramifications.

In the real world, physicians, psychologists, conservationists, and bioethicists may hesitate to equate biological entities with the policies and rules designed for machines and industrial artifacts. Furthermore, when addressing diseases, it would be inappropriate to rely solely on an optimization-engineering approach, disregarding humane and ethical considerations. Living tissues, within clinical or bioethical contexts, should not be reduced to terms like “highly heterogeneous media”, “condensed matter”, or “biological machines”. Biological systems possess unique and significant qualities that

transcend such descriptions.

Through the concept of collective Biased Random Walks (cBRWs), we aim to reexamine rigorously these matters in brain electrophysiology and theoretical computational neuroscience. Nonetheless, our intention is not to introduce a new “ghost in the machine” or stray from meticulous brain research. The emphasis remains on the brain. Contemporary physics compels us to adopt new probabilistic models to elucidate the complexities of electrophysiological phenomena. The objective of this research is to ascertain the precise characteristics of cBRWs and to demystify the complexities of electrophysiological signals in relatively intuitive terms.

A blend of classical, semiclassical, and non-classical perspectives on probability and BRWs is indispensable. Cutting-edge technologies, such as electron paramagnetic resonance, MRI spectroscopy, diffusion-weighted imaging, near-infrared spectroscopy, EEG, MEG, brain-computer interfaces, and neuroprosthetic implants, encourage a deeper examination of electrical charge movements in the brain, while still valuing existing methodologies. Future research will reveal the scientific, technological, and philosophical boundaries and opportunities inherent in these inquiries.

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