THE UNLIKELIHOOD OF STOCHASTIC PATHS IN MULTIDIMENSIONAL PHASE SPACES

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The methodological/operational virtues of stochastic approaches allow us to assess biophysical phenomena in terms of random walks, Brownian motions, Markov chains, etc. We argue that these approaches are not profitable when stochastic paths occur in high-dimensional phase spaces. Indeed, contrary to the two-dimensional random walks, the higher-dimensional random walks do not resume to the starting point: the more the phase space's dimension, the more the (seemingly) stochastic paths are confined/constrained. The mathematical impossibility of high-dimensional random paths has numerous implications, both epistemological and operational. Stochasticity should no longer be used for the evaluation of real-world systems, since the experimental assessment of multifactorial biophysical phenomena requires numerous parameters, each one standing for a different dimension in the phase space. Furthermore, multidimensional trajectories cannot generate circular, recurrent paths returning to the starting point, making unnecessary powerful methodological weapons correlated with cyclic configurations such as the Jordan curve theorem and the Betti number. Since higher-dimensional trajectories are unable to cross all the microstates with the same probability, our account suggests the unlikelihood of ergodic paths in multidimensional phase spaces, casting also doubts on the Shannon's account of information entropy in the continuous case. Next, we describe how the memory of old events is preserved in high-dimensional phase spaces, since memoryless events disconnected from the past, e.g., stochastic resetting and Markov chains, are banned.

We want to end up with an epistemological consideration. The Heisenberg's uncertainty principle does not allow to measure at the same time both the position and the velocity of a quantum object. The chaotic logistic map does not allow to know exactly the particle location when the phase parameter is between 3 and 4. The Godel's theorem does not allow to find statements about natural numbers that are at the same time true and provable within a consistent formal system. In these three examples from quantum dynamics, nonlinear dynamics and mathematical foundations, the unfeasibility to reach a single univocal result and to express simultaneously well-defined conjugate properties by a single value does depend on neither technical difficulties, nor failures in the observational devices of the current technology, nor our ignorance of some fundamental property of reality, rather it stands for an insurmountable, irreducible, universal feature that is intrinsic to the system under evaluation and cannot be even in theory solved. In our case, too, the unfeasibility of random paths in high dimensions stands for an intrinsic mathematical feature of the system, an epistemological boundary that cannot be overtaken by methodological tricks. Once expunged the randomness from the evaluation of multiparametric phenomena, the sole approach to partially rescue its methodological/operational virtues is to limit ourselves to the study of oversimplified, lower-dimensional systems.

KEYWORDS: topology; phase space; Brownian motion; information entropy; Shannon.

Terms like "random walk" and "stochasticity" bring about different interpretations according to the context in which are implemented. Therefore, our first step will be to provide standardized definitions. In probability theory, a "random process" (in literature the term "random" is frequently interchangeable with "stochastic") is a sequence of variables whose outcomes do not follow a deterministic pattern, rather an evolution described by probability distributions (Paul and Baschnagel, 2013). Put in plain words, the state of a stochastic process cannot be accurately predicted by the knowledge of its previous and current states, since no preferential flow direction does exist. A "random walk" is a path consisting of a succession of random steps in a mathematical space (Codling et al., 2008). A "Brownian motion" depicts the random fluctuations of particles inside a fluid at thermal equilibrium (Blomberg et al., 2020). A "Markov chain" is a stochastic model describing a sequence of possible events such that each event's probability depends only on the state attained in the previous event (Rogers and Williams, 2000). "Ergodicity" is a random process in which all the accessible microstates in a phase space are equiprobable over a long period of time (Walters, 1982; Barth, 1898). The above-mentioned concepts of random processes, random walks, Brownian motion, Markov chains, ergodicity, are commonly used to approach classic, relativistic and quantum systems (Gong et al., 2021). Stochasticity has been used to cope with disparate scientific phenomena, such as, e.g., light, motion of liquids/gases, signal processing, gambling, evolution, ecology (Elowitz et al., 2002; Pontes-Filho et al., 2020; Casacio et al., 2021).

Randomness provides us with a soothing, manageable methodological approach that permits us to cope with (seemingly) mathematically untreatable phenomena. We will provide a few examples from biology. Using an isotope-guided random walk approach, Wooller et al. (2021) were able to reconstruct mobility and range of an Arctic woolly

mammoth that lived 17,100 years ago. The random behavior of gene expression in intracellular microenvironments leads to both heterogeneity in nuclear genome organization Finn and Misteli, 2019; Pang et al., 2020) and substantial fluctuations in protein concentrations (Klosin et al. 2020). Phenotypical/behavioral heterogeneity does not depend just on the conventional "Nature vs. Nurture" contraposition that emphasizes the individual differences in genes, epigenetic factors and environmental interactions (Kiviet et al., 2014). On the contrary, the phenotype is shaped by another underrated factor too, i.e., the nonheritable molecular stochasticity produced by developmental events. Therefore, variations in fitness do not depend just on genetic and/or epigenetic factors, but are also correlated with random, nonlinear, self-reinforcing components. Stochasticity inherent in biochemical gene expression and cellular structure contributes to a broad range of phenotypic/behavioral variations also in genetically identical entities, such as clones of Escherichia coli (Elowitz et al., 2002), of Poecilia Formosa (Bierbach et al., 2017), of crayfish (Vogt et al., 2008). Concerning neuroscience, the dynamical behavior of neuronal networks and their stochastic evolution towards criticality can be fruitfully studied through random Boolean networks (Kang et al., 2021). It has been suggested that the occurrence of intrinsic randomness during the nervous development generates individual diversity in Drosophila melanogaster's brain wiring. This means that anatomical sets of visual neurons can be wired up in variable stochastic ways, conferring to every fly a different ability to orient to the line (Linneweber et al., 2020).

Here we question the prominence of stochastic approaches in the assessment of dynamic systems' affairs. Departing from the common claim that undisturbed random walks stochastically return to the starting point, we stress that the higher the dimensions of the phase space, the less the possibility that random walks return to the starting point. We will proceed as follows: at first, we will describe why stochastic approaches are not profitable when random walks occur in phase spaces of dimensions higher than two. Next, appraising the mathematical, physical and biological consequences of our claim against stochasticity, we suggest that phenomena like random walks and Markov chains cannot be assessed when weighed in multidimensions. Then, we will answer to a few objections related with memoryless events such as stochastic resets and Markov chains. Finally, we will suggest an alternative methodological

"A DRUNK MAN WILL FIND HIS WAY HOME, BUT A DRUNK BIRD MAY GET LOST FOREVER"

framework to quantify real-life systems dynamics.

A random walk in a two-dimensional lattice has unity probability of reaching any point (say, the starting point) as the number of steps approaches infinity (McCrea and Whipple, 1940). However, when coping with random walks, an unappreciated factor must be regarded, i.e., the number of dimensions of the corresponding phase space. Consider a random walk on a lattice of dimension D^d . The probability $p^{(d)}$ that a random walk returns to the origin is: p(1) = p(2) = 1 (McCrea and Whipple, 1940). This means that a particle almost surely will get back to the starting point in case of two-dimensional random walks. To provide an example, a person (say a drunk man) erratically walking around the streets arranged in a square grid of an infinite city will always go back home. Yet, in case of random walks in phase spaces equipped with dimensions higher than two, the probability to reach the starting point decreases with the increase in the number of dimensions (Domb, 1954; Finch 2003). Indeed, p(d) < 1 for d > 2, so that, for example, p(3) = 0.3405, p(5) = 0.1351, p(8) = 0.079, and so on (Montroll, 1956). Therefore, a drunk bird, that, unlike the drunk man, can flight and move in three dimensions instead of just two, will not get back to its nest.

We ought to define our terminology: what does "in higher dimensions" mean? Biophysical paths are generally described in terms of particles moving inside trivial three-dimensional phase spaces. In this simple case, the x, y and z axes stand for the three Euclidean spatial dimensions, while time passing stands for the particles' trajectories. If further axes are introduced in the phase space, the particles are allowed to move in further dimensions apart from the canonical three (plus time). The methodological step of increasing the phase space dimensions is computationally expensive but highly profitable, since the higher the number of dimensions, the more information can be achieved from the system under evaluation. A higher number of parameters, everyone standing for a further dimension, improves our comprehension of complex phenomena. The recent availability of big data boosts the number of evaluable dimensions and leads to fully novel strategies to tackle far-flung problems, from the dynamics of chemical compounds to the turbulent flows of plasma-like fluids (see, e.g., Dekker et al., 2017; Cardesa et al., 2017). To provide an example, neuroscientists use multidimensional nervous phase spaces to add parameters such as spike frequencies, synchronized oscillations, color perceptual spaces, tactile qualities (Victor et al., 2017; Stringer et al., 2019). The more experimental parameters we consider, the more the random walks will take place in higher dimensions. Since multidimensional random walks exhibit an extremely low probability to return by chance to the starting point, we are allowed to state that the (apparently stochastic) trajectories occurring in multidimensional phase spaces are actually hampered and constrained.

WHY ERGODICITY GETS LOST IN HIGH DIMENSIONS

Once established on mathematical grounds that random walks in higher dimensions are not so random as assumed, what are the physical and biological consequences of our claim?

The randomness underlying elusive biophysical phenomena allows their mathematical treatment in terms of circular, recurrent paths that are able to describe, e.g., cellular life cycles or biochemical pathways. When random walks take place inside simple mathematical spaces (say, the trivial set of all points in the two-dimensional plane with integer coordinates), they produce closed loops (Lawler et al., 2011). These ubiquitous, recurrent, cyclic configurations are methodologically required to assess, classify and quantify almost every physical/biological dynamical system. For example, a closed path is mandatory to elucidate autocatalysis, since the cyclic pattern of autocatalytic reactions brings energy into the system, which it exports back out to the surroundings (Agosta and Brooks, 2020). In turn, our account tells a different story: random walks in high-dimensional phase spaces do NOT form closed paths, since their trajectories are unable to close the loop by returning to the starting point. This means that the random paths taking place in high dimensions are not closed sets, rather they are open sets, incapable of generating recurrent paths and cyclic configurations.

The focus on circular paths suggests that the open multidimensional trajectories cannot be described by the usual methodological tools used for closed paths, <u>such as the Jordan curve theorem describing closed surface regions</u> and the Betti number counting the number of cyclic boundaries and generators (= number of holes) of closed surface regions (Don et al., 2020). The theory says that as the number of closed cycles increases in a system, so does the Betti number. However, in our framework things haven't gone so well: Betti number cannot be counted when we are coping with high-dimensional stochastic dynamical systems, because cyclic boundaries are very rare in multidimensions.

Another consequence is even more troublesome, raising concerns against the ergodic theory. Our account implies that random walks taking place in high dimensions cannot be fully ergodic, because every point (say, the starting point) cannot be easily crossed more than once. This means that the trajectories of multi-dimensional systems are unable to homogenously fill the whole phase space, leading to a loss of the same ergodicity provided in lower dimensions by random choices.

If ergodicity is not guaranteed, further difficulties are encountered in relation to Shannon's account of the entropy in the continuous case. We should remember that for Shannon the entropy for continuous stochastic processes has many properties analogous to the entropy for discrete stochastic processes. In chapter 21 of his seminal paper, Shannon (1948) describes the continuous case of the entropy of ergodic ensemble of functions (i.e., the entropy of a set of functions together with a probability measure).

According to Shannon, there are two cases:

- 1) The entropy in the discrete case is related to the logarithm of the PROBABILITY of long sequences of samples and to the NUMBER of the probable sequences of long length.
- 2) the entropy in the continuous case is related to the logarithm of the PROBABILITY DENSITY of long sequences of samples and to the VOLUME of the probable sequences of long length in the function space.

The technical difference between the two cases is due to a strict requirement, i.e., the key feature of the Shannon's account of both discrete and continuous entropies: the system under assessment must be ergodic. Indeed, the occurrence of ergodicity is the tenet that explains a few essential properties required by the Shannon's account of information entropies:

- a) Every generated sequence must display the same statistical properties.
- b) The continuous space can be split into more manageable small cells.
- c) If an ensemble is ergodic, each function is the set typical of the ensemble, i.e., each function can be expected to go through all the convolutions of any of the functions of the set.

To sum up, the occurrence of system's ergodicity leads to the statistical homogeneity required by Shannon to treat the entropy of his three channels: the discrete noiseless, the discrete with noise and the continuous channel.

Shannon states that, in the case of continuous entropy with white noise and large n, there is a well-defined volume (at least in the logarithmic sense) of high probability, and within this volume the probability density is relatively uniform (in the logarithmic sense). Shannon demonstrates that the region of high probability is a sphere of radius \sqrt{nN} in the discrete case, while in the continuous case the volume of high probability is the squared radius of a sphere having the same volume. This leads us to a further factor to ponder: the curse of dimensionality (Barbour 2019). It is well-known that the more the dimensions of the sphere, the less its volume. Consider a n-sphere with fixed positive curvature embedded in a n+1 Euclidean space: the more the n-dimensions of the sphere, the less its volume (Matousek, 2003; Kůrková 2019). Paradoxically, this means that the volume of different hyperspheres with the same radius tends towards

zero as their dimensionality tends to infinity (Wang 2005). In higher-dimensional spheres, the ball volume tends to be squeezed and clustered near the equator, approaching the zero as their dimensionality tends to infinity. Summarizing, (random) walks inside a high dimensional hypersphere are constrained by a few factors:

- 1) Stochastic paths cannot return to the starting point.
- 2) Stochastic paths tend to converge near the borders (near the equator), leaving aside the poles and traveling in a volume which becomes smaller and smaller with progressive increase in number of dimensions.
- 3) Multidimensional random walks tend to be compressed in small spaces.

If the volume of high-dimensional balls is progressively "shrunken" inside the sphere, this means once again that the system's ergodicity gets lost, since the random trajectories are constrained in small volumes and cannot cross the whole sphere. This also means that the volume of the probable sequences of long length in the function space, which is a crucial parameter of Shannon's entropy in the continuous case, does not hold anymore in multidimensions.

In conclusion, since the ergodicity of multidimensional random paths cannot be guaranteed, the operation performed by Shannon of dividing the continuum of messages and signals into a large but finite number of homogeneous small regions is doomed to failure outside the context of his three (low-dimensional) channels. The real world is made of a high number of functional dimensions, a number that is much higher than the dimensions assessable via the Shannon's channels.

THE (MISLEADING) PROBLEMS OF STOCHASTIC RESETTING AND MARKOV CHAINS

We stated that "the more the dimensions, the more the (seemingly) stochastic paths are constrained", because their trajectories cannot resume to the starting point. It might be objected that our statement is wrong, since there are at least two stochastic processes with many returns to the starting point:

- A) The stochastic processes with resetting, i.e., a sudden transition to a single preselected state or region in the phase space.
- B) The Markov chains, i.e., the sequence of possible events such that each event's probability depends only on the previous state (Kirchhoff et al., 2018).

Let's start with "stochastic resetting", a rather common event: when one unsuccessfully searches his misplaced glasses at home, a spontaneous tendency is to return to the starting point and recommence the search (Evans et al., 2011). Another example comes from population dynamics, where resets correspond to catastrophic events (Allegrini et al., 2007; Fuchs et al., 2016; Culbreth et al., 2019). Many influential papers investigated the consequences of stochastic resetting. Fuchs et al. (2016) derived the first and second law of thermodynamics for continuous and discrete stochastic dynamics with resetting and identified its contribution to the total entropy production. However, their noteworthy account concerns stochastic dynamics taking place just in low dimensional phase spaces. Indeed, they studied an overdamped colloidal particle along a SINGLE spatial coordinate x, immersed in a heat bath at a given temperature. Since the particle experiencing a systematic force is randomly reset to a fixed position x_0 , we can state that Fuchs et al.'s model concerns just a very simple, low-dimensional path. To make another example, Evans et al. (2011), who successfully assessed diffusion with stochastic resetting, explored just the commonest (and simplest) process in nature, namely, the diffusion of a single (or multi-) particle system in VERY LOW dimensions. They assessed only the schematic space-time trajectory of a one-dimensional Brownian motion starting at x_0 and resetting stochastically at rate r to its initial position. In recent years, the Markovian processes of Lévy flights, i.e., a mix of long trajectories and short random movements with power-law distributions of step lengths with diverging variance, has become prominent. Lévy flights are useful for modeling faster-than-Brownian dynamics in a variety of complex systems, such as travels of humans within cities, immune cells' trajectories in the brain, displacements of animals and hunter-gatherers in their environments (Boyer and Pineda, 2016). Nevertheless, it must be emphasized that the most of these approaches with Lévy flights use simplified low-dimensional models. Take the foremost paper by Boyer and Pineda (2016). They described how long-range memory processes exhibiting slow diffusion are path dependent, such that anomalous motion emerges from frequent relocations to already visited sites. Once again, they assessed just discrete, one-dimensional walks, leaving apart the study of complex, multidimensional systems.

To sum up, these three examples from prominent works suggest that memoryless events disconnected from the past, such as stochastic resetting and Lévy flights, are technically difficult to assess when coping with high number of phase spaces' dimensions. Therefore, we conclude that the memoryless events disconnected from the past able to guarantee the return to the starting point can be achieved and assessed just in very simple, lower-dimensional models.

Another important consequence of our account involves the Markov chains. As one increases the discrete-time steps in the stochastic Markov chains, there exists a probability measure at next future step that is independent of the probability distribution at the past steps (Feller, 1971; Ramstead et al., 2017). However, our framework suggests that the trajectories of Markov chains in high dimensions are not fully independent from the initial steps, because the random possibility to return to a single point (say, the starting point) is severely restricted. Therefore, when a system is evaluated in multidimensions, memoryless events are forbidden. This means that a sort of "memory" of the previous states must exist, a "memory" that prevents multidimensional walks to return to already crossed points (say, the starting point). Therefore, stochastic activities in multidimensions are incapable of producing Markov chains. In touch with our claim, recent neuroscientific accounts suggest that the brain fluctuations are not properly ergodic. It has been proposed that the brain fluctuations are weakly non-ergodic, since a few nervous phase space regions may take extremely long times to be visited (Bianco et al, 2007; Fraiman and Chialvo, 2012). We are tempted to speculate that this slight non-ergodicity of the brain activity might depend on the recently described existence of functional multidimensional phase spaces in the central nervous system (Tozzi, 2019). An increase in functional brain dimensions might produce an anomalous diffusion of stochastic flows, constraining the random nervous trajectories in confined zones of the multidimensional nervous phase space.

Summarizing, the existence of constrained trajectories in high dimensional phase spaces runs counter the occurrence of memoryless processes such as stochastic resetting and Markov chains.

CONCLUSIONS: NOT ALWAYS ALL ROADS LEAD TO ROME

We discussed the role of stochasticity in the scientific evaluation of biophysical systems, inferring that this approach is not profitable when particles' trajectories occur in phase spaces of dimensions higher than two. We showed how the particles' random trajectories, when assessed from the perspective of high-dimensional phase spaces, are not properly stochastic, rather they are constrained.

Physical and biological phenomena are nearly always complex and multifactorial: this means that the experimental assessment of real dynamics must consider a large number of parameters, each one standing for a different dimension of the phase space. To provide an example, how the central nervous system represents large-scale, navigable space has been the topic of countless investigations (Jeffery et al. 2015). Though, these studies are performed in uncomplicated experimental settings where animals explore small, two-dimensional, flat arenas. On the contrary, the real world explored by animals encompasses large, three-dimensional volumetric spaces (Jeffery et al. 2015). It has been demonstrated that the flying bats' hippocampus displays a multiscale representation of very large environments up to 32 meters (Eliav et al., 2021). Therefore, the study of real dynamical systems requires multidimensional approaches. Though the addition of further dimensions to the experimental setting poses technical and computational challenges, the operation is welcomed, being the biophysical world made of multifactorial dynamics. We stated that high-dimensional paths cannot be stochastic: this means that the real (multidimensional) systems can be described without resorting to concepts such as ergodicity, randomness, Markov chains, closed paths, Betti numbers, and so on. Take the example of evolution. At the simplest level of the genes, evolution is believed to follow random processes of mutation and drift (Baquero et al., 2021). However, at the higher levels (e.g., plasmids, microbiotas, etc.), the systems' degrees of freedom decrease, constrained by the dictates of other factors such as, e.g., complex environments and shifting niches. Therefore, the evolutionary trajectories, subjected to random variations at the lower levels of observation, display preferential frequented paths (highways) at the highest levels (Baquero et al., 2021), where randomness is rather hampered by the complexity of the multidimensional influences.

Our critical approach involves a few aspects of the renowned Shannon's information entropy too. Shannon (1948) explicitly portrayed his (low-dimensional) stochastic ergodic system in terms of random walks and Markov paths. We showed that Shannon's approach is not profitable when random walks occur in phase spaces of dimensions higher than two. Further, we argued that the high-dimensional, multiparametric tracks ubiquitous in the real world of biophysical phenomena cannot be operationally treated in terms of loops and closed paths, since the more parameters are inserted in a scientific model, the more the random paths are constrained to be open. This means, to provide an example, that the circular, biochemical pathways stochastically occurring inside a living cell cannot be assessed in terms of multidimensional phase spaces.

Once formulated a mathematical critique of stochasticity in high dimensional phase spaces, our next step is to suggest a feasible procedure for the operational treatment of random walks in real biophysical affairs. During the scientific assessment of the countless multiparametric systems surrounding us, the only methodological way to preserve stochasticity and its useful topological weapons (such as, e.g., the Jordan curve theorem and the Betti numbers) is to make things easier. Real dynamical phenomena can be treated in terms of stochasticity, Markov chains, etc., just in one case: when the multifactorial system under evaluation is abridged and reduced to an extremely poor number of

parameters, each one standing for a different dimension of the phase space. Since stochasticity can be evaluated just in low dimensions, random walks can be analyzed in only one way: leaving apart multidimensional assessment.

We want to end up with an epistemological consideration. The Heisenberg's uncertainty principle does not allow to measure at the same time both the position and the velocity of a quantum object (Heisenberg 1927). The chaotic logistic map does not allow to know exactly the particle location when the phase parameter is between 3 and 4 (May 1976; Richardson et al., 2014). The Godel's theorem does not allow to find statements about natural numbers that are at the same time true and provable within a consistent formal system (Godel 1931). In these three examples from quantum dynamics, nonlinear dynamics and mathematical foundations, the unfeasibility to reach a single univocal result and to express simultaneously well-defined conjugate properties by a single value does depend on neither technical difficulties, nor failures in the observational devices of the current technology, nor our ignorance of some fundamental property of reality, rather it stands for an insurmountable, irreducible, universal feature that is intrinsic to the system under evaluation and cannot be even in theory solved. In our case, too, the unfeasibility of random paths in high dimensions stands for an intrinsic mathematical feature of the system, an epistemological boundary that cannot be overtaken by methodological tricks.

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