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Review

Gait analysis under the lens of statistical physics

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ABSTRACT

Human gait is a fundamental activity, essential for the survival of the individual, and an emergent property of the interactions between complex physical and cognitive processes. Gait is altered in many situations, due both to external constraints, as e.g. paced walk, and to physical and neurological pathologies. Its study is therefore important as a way of improving the quality of life of patients, but also as a door to understanding the inner working of the human nervous system. In this review we explore how four statistical physics concepts have been used to characterise normal and pathological gait: entropy, maximum Lyapunov exponent, multi-fractal analysis and irreversibility. Beyond some basic definitions, we present the main results that have been obtained in this field, as well as a discussion of the main limitations researchers have dealt and will have to deal with. We finally conclude with some biomedical considerations and avenues for further development.

Contents

1. Introduction

Walking is the main way humans use for independent self-translation around the world. Normal human walking is a method of locomotion involving the use of the two legs, alternately, to provide both support and propulsion with at least one foot being in contact with the ground at all times [1]. Gait is a very individual trait in healthy subjects that can even be used for personal identification [2], but it changes with age [3,4] and can be modified by emotions [5], exercise-related or cognitive fatigue [6], or environmental factors [7]. Walking is formed by a sequence of gait cycles, its basic and fundamental unit. These can be defined as the combi-

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nation of motor phenomena that occur between two floor contacts (usually heel contacts) of the same foot, and is composed of two phases: 1) the stance one, in which the foot maintain contact with the ground; and 2) the swing one, in which the limb moves forward in a sort of pendular motion [1]. Walking then emerges from interleaving left and right gait cycles.

Bipedal walking is one of the main milestones in hominid evolution [8], and independent walking is the most relevant milestone in motor development during infancy [9]. This is because walking requires an extremely well coordinated, finely modulated activation of muscles by the central nervous system [10,11]. In contrast to a simplistic idea of quasi-automatic movements produced by spinal circuits, walking is an emergent property of the central nervous system; and, as any voluntary movement, it is determined by an intense neural control involving a complex network formed by cortical regions, basal ganglia, brainstem centres and spinal cord circuits [12].

In the field of basic neuroscience, walking has received significant attention as a model of human movement, due both to its functional relevance, and to the advantage of being a cyclic movement that can be measured and treated as a complex signal [13]. Similar attention can be found in medicine due to the impairment resulting from multiple disorders, such as highly prevalent musculo-skeletal diseases or devastating neurological disorders [14]. The analysis of gait patterns can tell us significant information about these disorders and help us in therapeutic decision making [15].

Many neurological and neurodegenerative diseases have a definitive effect on motor control. Subsequent movement impairments, in particular gait abnormalities, are very frequent, altering daily life and causing dependency. In normal healthy conditions, the coordination of joint movements during gait is tightly controlled by neural motor brain structures. As a whole, these brain structures regulate many factors contributing to the appropriate sequence of flexor–extensor muscle contractions, the final result being a precise movement of the joint chains and the translation of the body's center of gravity in bipedal posture [16]. Lesions in any of the various components of the cerebral motor system (including motor cortices, basal ganglia, thalamus, cerebellum, corticospinal pathways, and ascending somatosensory pathways) alter the output signals of the postsynaptic motor neuronal spinal cord circuitry and, therefore, the sequence of muscle contraction [17]. Gait motor performance is hence altered at first instance, impeding the correct translation of the body. However, gait is a cognitive propositive action of high importance for the brain, and the whole nervous system adapts its dynamics to achieve the target. Several plastic mechanisms are then triggered, including, for instance, the re-arrangement of synaptic connections [17]. This ultimately results in the generation of newly-configured sequences of muscle contractions, executing a sort of "maladaptive" gait. While the cognitive target is achieved, the movement might not properly be adjusted to the biomechanical properties of the joint's soft tissues, muscles and bones and to cellular metabolic needs, thus yielding torque-related deformities. Those newly-generated signals are a reflection of brain adaptation, and the quantitative evaluation of the differences between the neurological patients' and the control subjects' signals is essential for the interpretation of the prognosis of the disease and for the design of personalised therapies. Studying and understanding human gait is thus of major importance, both for guiding medical interventions and as a door for shedding light on the functioning of the nervous system. The advent of new technologies has made possible the quantification of the different motor phenomena involved in gait pattern configuration [18], and different mathematical tools have been applied to these data [19,20].

Within this large field, the application of statistical physics concepts has been receiving an increasing attention. It is not difficult to identify the reasons behind this surge. One of the main objectives of this branch of physics is the characterisation of the constituents of a system (i.e. the micro-scale), when only the emergent global dynamics (i.e. the macro-scale) is accessible and thus observable [21]. Making a parallelism with genetics, this is equivalent to trying to characterise the genotype, when only the phenotype of an organism (and changes thereof) can be observed. The same problem is found in gait, which is the result of a chain of interactions starting from the central nervous system and ending in the peripheral tissues; yet, only the final output, and not the intermediate steps, are easily observable. Among the many metrics that have been developed within statistical physics to this end, a few of them stands out for describing concepts well aligned with neuroscience: to illustrate, entropy is related to the predictability of a signal, and the lack of predictability can easily be associated to a lack of control by the lesioned brain; and the maximum Lyapunov exponent describes the response of the system to perturbations, which translates to the feedback control mechanisms acting during gait. On top of this, most statistical physics metrics are easy to compute, and are built on solid theoretical foundations.

In this review, we aim at creating a stronger bridge between clinical gait analysis and statistical physics, and at fostering the flow of ideas from the latter to the former. For that, physicists have to understand the idiosyncrasies and problems behind gait data; and, at the same time, physicians need to better understand what is assessed by statistical physics metrics, which at times can be quite abstract. We focuson how four fundamental statistical physics concepts have been applied to instrumental gait analysis, namely: entropy, maximum Lyapunov exponent, multi-fractal analysis and irreversibility. These have been chosen for being representative of basic statistical physics concepts (including predictability, fluctuations and time asymmetry); for being computationally affordable; and for having widely been used in gait analysis. We discuss how these concepts have been applied to different types of gait data, and the main results obtained in different pathologies. We finally close this review with a discussion of the limitations of the methods hitherto proposed, of some conceptual mistakes we have found in the literature, and of avenues for further development.

2. Basics of instrumented gait analysis

People has been interested in analysing walking since the earliest moments of science. Aristotle (384–322 BCE) is the author of the earliest recorded comments and theories on the movement of humans and animals [22]. Progress was afterwards made through the experiments and theories of Giovanni Borelli (1608–1679), on tendon biomechanics, and of Willhelm (1804–1891) and Eduard (1806–1871) Weber, on the anatomy and biomechanics of walking. Other notable contributors include Jules Etienne Marey (1830–1904), Eadweard Muybridge (1830–1904), and Gaston Carlet (1849–1892), who developed a shoe with three pressure transducers built into the sole; this was the first recording of the double bump of the ground reaction force vector [23]. The major developments in the early twentieth century were force plates and the understanding of kinetics [22]. It was not until the advent of modern computers that clinical gait analysis became widely available. Instrumented (or computerised) gait analysis (IGA) is now a complex discipline based on powerful systems of measurement with different degrees of complexity, strong neuro-scientific research and widely spread clinical application. Still, IGA has not reached its maximal technology capacity yet. In the years to come, better and cheaper systems may be incorporated to clinical care and will provide clinicians with a large quantity of precise informa-

Table 1
Different types of parameters in instrumented gait analysis.

	Question	Definition	Example
Spatiotemporal parameters	What?	Motion of the whole body	Walking speed, step cadence
Kinematic parameters	What?	Motion of individual joints	Knee flexion
Kinetic parameters	How?	Forces, work and power behind the motion	Knee flexor moment
Electromyographic parameters	Why?	EMG activation of individual muscles	Activation of the vastus lateralis
Individual muscle information	Why?	Data of muscle performance from inverse dynamic modelling	Force produced by vastus lateralis
Oxygen/ CO_2 consumption data	How much?	Energy consumption	Oxygen consumption during walking

tion of motor performance, which needs to be processed and presented in a useful way.

When it comes to the numerical analysis of IGA data, three aspects have to be clarified: the type of data; how these data are represented; and under which conditions they are recorded.

Regarding the first aspect, motor phenomena can be evaluated by means of different recordings - see Table 1. Spatiotemporal parameters are those that assess how the body moves as a whole (e.g. speed) or how the gait cycle is configured (e.g. stance time). Kinematic parameters assess how the displacement of particular body segments around the different joints is made in space (e.g. knee flexion). Kinetic parameters assess the forces that provoke the displacement of the body or particular body segments (e.g. power, torque), measured through force plates. By means of models, we can extract torques and powers for the different joints, and even for particular muscles. The muscle activity along gait cycle can be assessed by superficial electromyographic recordings. Finally, the metabolic cost of walking can be measured indirectly by calorimetry and metabolic cost measurements (e.g. CO_2).

Data from IGA can be analysed as scalar values, giving information of a particular feature in a precise moment of the cycle (e.g. knee flexion at initial contact), or averaged along the whole cycle (e.g. range of knee flexion). Alternatively, they can be analysed as vectors or matrices by multivariate statistical and machine-learning approaches [19,20,24] - the former being the focus of this review.

Finally, gait can be analysed in different environments. Traditional IGA uses laboratories in which highly precise systems quantify different aspects of human movement, for instance on instrumented aisles or treadmills. Additionally, virtual reality systems have been incorporated, allowing the integration of non-portable equipment into real environments [25]. Finally, systems like instrumented insoles, accelerometers, or even mobile phones, have allowed the assessment of gait in natural environments [26].

3. Entropy

Entropy, in its physical interpretation of the quantity of disorder, randomness, or uncertainty about the dynamics of a system, has a long history of applications in biology and medicine [27,28]. When applied to IGA, it allows to assess how repetitive and controlled the gait cycles are. As a lesioned system and its subsequent adaptive mechanisms can only provide a restricted number of possible movement patterns, and they can only enforce them through a weaker control, a reduction is to be expected in the entropy of a number of cinematic parameters. To the best of our knowledge, the first application of entropy measures to gait time series was proposed in 2003 [29], comparing healthy subjects walking in different conditions (spontaneous walking vs. walking paced by a metronome). Since then, the number of studies has exploded; not just in the number of conditions, but also in the number of applied entropy metrics. For the sake of completeness, the most important are sketched below.

- Shannon and symbolic entropies. Shannon's original formulation of the entropy [30] is calculated over a continuous probability distribution $f(x)$ as: $S[f(x)] = -\int f(x)\log_2 f(x)dx$. When the base of the logarithm is set to 2, it represents the information needed, in terms of number of bits, to describe the distribution. When continuous values are not available, and in general when it is convenient to discretise the signal to reduce noise and artefacts [31], the resulting entropy is known as symbolic [32].
- Approximate (ApEn) and Sample (SampEn) entropy. Building on the concept of Kolmogorov-Sinai entropy, ApEn measures the predictability of time series by assessing how probable are two sub-windows of it, which are similar between themselves, of also evolving in a similar manner [33]. The greater is this probability, the more regular (or predictable) is the time series, and hence the smaller the resulting ApEn value. SampEn is a further modification of the same idea, in which the comparison of a sub-window with itself is not taken into account; this reduces the bias of the metric, at the cost of not being a true information measure anymore [34]. More comprehensive comparisons of both metrics can be found in Refs. [35,36].
- Permutation entropy. Metric representing the information encoded in the permutation patterns associated to a time series, that is, in the order relations among consecutive values [37–39]. It is assessed by dividing the time series into short windows; by calculating the corresponding permutation pattern, i.e. the order required to sort the elements of such windows in ascending order; and finally by calculating the Shannon entropy of the resulting pattern probability distribution.
- Multiscale entropy. Previously described entropy metrics are calculated over all values available in the time series, thus inherently analysing the time scale induced by the temporal resolution of data. Healthy (and pathological) physiologic dynamics nevertheless develop over a multitude of scales, whose heterogeneity can be described by calculating a multiscale entropy. As originally proposed [40,41], this involves two steps: firstly, the reconstruction of consecutive coarse-grained time series $\{y^\tau\}$, such that $y^\tau(t) = \frac{1}{\tau}\sum_{i=(j-1)\tau+1}^{j\tau} x(i)$; in other words, the time series is splitted in non-overlapping sub-windows of size τ, which are represented by the corresponding average value. Secondly, any suitable entropy metric is calculated over the new time series $y^\tau(t)$, for then obtaining the evolution of the entropy as a function of τ. Many alternatives to this initial approach have been subsequently proposed, see for instance [42]. It can be appreciated that, more than to a specific metric, multiscale refers to a way of pre-processing the data; as such, this approach can be found in conjunction with SampEn [29,43–47], symbolic entropy [48–50], or approximate entropy [51].
- Control entropy. One assumption underlying all previously described entropy measures is that the analysed time series are stationary in a statistical sense, something not usually holding in biology and medicine. In order to tackle this issue, the concept of control entropy was introduced, as the entropy of

the differences between neighbouring values, as opposed to the values themselves [52]. Mathematically, given a time series $x(t)$, this can be calculated as: $CE[x(t)](t) = SampEn[\delta(\frac{dx}{dt}(t, t+w))]$, where δ and w are the parameters used to calculate the SampEn as described above.

Additional alternatives of entropy metrics, not reviewed here for the sake of conciseness, include the analysis of multi-scale entropy through Discrete Wavelet Transform [53]; quaternion entropy [54]; quantized dynamical entropy [55–57]; diffusion entropy, i.e. the entropy of the diffusion process generated by a time series [58,59]; intrinsic mode entropy [60,61]; differential entropy [62]; cross entropy [63,64]; and persistent entropy [65,66]. The precision and relevance of some of these metrics have directly been compared, as for instance in Refs. [48,61,67,68,50]; and analyses have been performed on the importance of different parameters [35,69,70,67]. There are nevertheless no guidelines about which metric is better for the analysis of a given system, leaving the doors open to multiple options.

The analysis of gait entropy should logically start with healthy subjects, as a way of shedding light on the mechanisms behind the normal control performed by the central nervous system; many studies have therefore focused on the effects of different walking speeds, either spontaneous, forced (through a metronome) or by means of slopes [71]. The influence of walking speed on the different explored metrics for entropy in IGA is complex. Higher walking speeds seem to be related with an increased entropy in kinematic time series [72,54], reflecting that the SNC might be either relaxing its otherwise tight control when increasing velocity to adapt to more spurious unexpected interferences, or because there is no time to imprint the same tight control as when walking slow. On the other hand, the entropy of the time of stride seems to evolve in the opposite direction, showing increased entropy with lower walking speeds [73,74]. Another study further showed no statistically significance difference for all paced walking speeds [29]. Such complexity may be the results of both the small differences induced by the walking speed, and of the use of different entropy metrics. It is finally worth noting two additional studies on healthy subjects, specifically runners [75] and toddlers [43].

Within the analysis of healthy individuals, a special place should be reserved to studies devoted to the analysis of gait of elderly people. The aim is usually to forecast, and eventually to understand the reasons behind, the risk of falling, as this is associated to major comorbidities and healthcare costs [76–78]. Obtained results are somewhat contradictory. Specifically, most of the works generally found an increased entropy in elderly individuals [79,80,45,57,81]. Moreover, this increase seems related with falls. This suggests that elders have lost their adaptive capacity due to the natural deterioration of the brain, with movement being less regulated, specifically the transmission of the somatosensory feedback to cerebellum that modulates the response to interferences of the external world to gait is altered, as well as the continuous control of antigravitation muscles by brainstem mechanisms like reticulospinal or vestibulospinal systems [82]; but some found statistically not significant differences [44,83]. Finally, Ref. [84] found a complex relationship with the minimum toe clearance (expression of somatosensory feedback deficit of joint positions to motor control in the swing phase), with elders usually having higher entropy, reflecting that the motor response is not regulated because of the impoverishment of somatosensory inputs; but a lower entropy when large values of the clearance are considered - an effect more marked when considering the falls risk group. It is also worth noting Ref. [64], which proposed a clinical classification model reaching an accuracy of 90%.

When moving to the analysis of the gait of patients suffering from specific diseases, a group of three stands out for being usually tackled together. These include Parkinson's Disease [85,53,86–88,51,46,89,90,47,66], Huntington's disease [85,53,86,91,51,46,90], and amyotrophic lateral sclerosis [85,53,86,51]. Note that, in spite of the similar results they yield, these pathologies are substantially different, the first two being related to the basal ganglia, which control the fine processing of movements temporally regulating the eccentric/concentric muscle contraction; and the latter one to the motor neurons of the cerebral cortex, brainstem and spinal cord, which control the concentric contraction of muscles and thus the force, power and joint torque. One would expect that after a lesion of motor neurons, the subsequent problems in agonist/antagonist concentric contraction and spasticity would initially decrease the entropy, and that it would remain lower while the system is compensating and fixing a new configured kinematic pattern that allows locomotion. Then, after larger lesions are produced (due to the degenerative nature of these pathologies), entropy should increase as a reflection of the loss of adaptive capability of finding a functional gait parameter configuration to walk. On the other hand, basal ganglia lesions should disrupt the fine control of movement, resulting in an increase of entropy due to a lack of adaptive capacity. These changes may vary, influenced both by the thresholds and scales in the entropy metrics. Most analyses indicate that patients suffering from these three diseases display higher entropy [89,90,47]; the only exception can be found in Ref. [51], where few significant differences were found between the amyotrophic lateral sclerosis (ALS) disease and control groups, and Ref. [85], where the entropy of the control group was higher. It is unfortunately difficult to understand where these differences come from, due to the multiple available entropy metrics, and to the different ways data have been pre-processed. In spite of this, having comparable data for these three diseases together has allowed the creation of classification models for predicting the specific condition of each patient, reaching accuracies of 85% [86], 91% [90], 98% [66], and above 99% [46].

Other diseases that have been studied in the literature include symptomatic knee osteoarthritis [92]; diabetic foot [93]; lumbar spinal stenosis [62]; hemiparetic patients following stroke [94,95]; multiple sclerosis [96]; Down syndrome [97]; cerebral palsy [98]; Alzheimer's Disease [99]; and peripheral arterial disease [100]. In almost all cases, a lower entropy has been detected in the gait of patients, when compared to control subjects [97,92,96,93]; the only exception is a higher entropy for ankle, knee, and hip in patients with peripheral arterial disease [100]. Additionally, entropy metrics have been proposed as features for training automatic classification models [62,95].

4. Maximum Lyapunov exponent

The maximum Lyapunov exponent (MLE) is based on the Lyapunov's theory of dynamic stability, initially formulated to assess the sensitivity of a mechanical system to small perturbations [101,102]. In short, given a dynamical system, it is based on calculating the evolution of two trajectories starting from very near points, and in assessing how much these trajectories diverge with time. Thus, large values of the MLE imply that small perturbation can result in a very different evolution, and a lack of control on the evolution of the system; the application to gait is thus only natural [103].

From an algorithmic point of view, two main ways have been proposed to estimate the MLE: the algorithm of Wolf et al. [104] (also called the W-algorithm), and the algorithm of Rosenstein et al. [105] (the R-algorithm). While the latter is in principle more suitable for the analysis of short time series, the differences between both can be more complex [106]. Additionally, the computation of these metrics can be performed on a single or multiple

strides, called respectively short- and long-term MLE; while the former is more clearly related to the structure of the gait, and especially on the probability of falls, the latter has been found to yield complementary information [107]. Any result should therefore be interpreted with caution.

As expected, the maximum Lyapunov exponent has firstly been estimated in healthy subjects. Beyond several studies addressing the problems associated with its estimation [108–110,61], it is worth noting a study showcasing the use of this metric, by comparing the temporal variability between walking in unstable shoes and walking in a normal athletic-type control shoe [111]. Results indicate a higher maximum Lyapunov exponent when walking in unstable shoes, possibly reflecting the larger variability in walking patterns by them forced.

Several pathologies have also been studied, the most important being ageing [112,108,113,109]; correlations have been found between the capacity of maintaining dynamical stability and age, but also with strength and amount of physical activity. Other examples of conditions include claudication [107], cerebella damage [114], models of high falling risk [110], Down's syndrome [97], multiple sclerosis [115], peripheral arterial disease [100], reconstruction of the anterior cruciate ligament [116], and knee osteoarthritis [117]. In all of these, external interferences exist, including the noises induced by peripheral lesions of soft or hard tissues, like muscle, ligaments, bones or joint tissues, which introduce disturbances in the final response of the motor command and in the somatosensory feedback to the motor system [82]. This would promote modifications in the output signals. A metric also based on the analysis of the trajectory followed by a dynamical system, and thus related to the maximum Lyapunov exponent, is the correlation dimension [118–120]. Roughly speaking, it represents the probability of two arbitrary points to be closer than a given distance, as a function of such distance. While less attention has been devoted to this concept in the context of gait analysis, it is worth noting a few works that have applied this metric, usually in conjunction with the MLE. These include the analysis of healthy individuals [121,122], as well as patients suffering from osteoarthritis [123,124] and neurodegenerative diseases [125,126].

As a final note, it is worth considering Ref. [127]; beyond studying healthy subjects gait, it also offers a free software for Window® environment to compute several dynamical metrics, both on gait and other types of time series.

5. Multi-fractal analysis

Long-range correlations and fractal-like properties are present in a wide range of natural phenomena [128,129]. The Hurst exponent is one of the most reliable parameters to quantify the scaling law for these temporal correlations, specially when dealing with real-world time series [130,131]. In the simplest case, only one scaling index is necessary to characterise the global linear correlations in a sequence, namely, mono-fractal. However, when the scaling is not a global but a local property, one scaling exponent is not sufficient to unveil the interplay between a superposition of subsets, each characterised by a different scaling exponent, leading to what is known as multi-fractality [132]. It is important to point out that multi-scaling can be originated by the presence of non-linear correlations and heavy-tail distributions [133].

The most used methodology for estimating scaling exponents is the so-called Multifractal Detrended Fluctuations Analysis (MFDFA) [133]. Briefly, it studies the fluctuations on data sequences by systematically eliminating the mth-degree polynomial trends over windows of different sizes s. Then, the q-Generalised Fluctuation Function $F_q(s,m)$ is estimated, defined as the averaged variance of the detrended time series and weighted to a factor q. For long-term correlated data, $F_q(s,m)$ scales as $s^{h(q)}$ inside a certain range of s. For more details about the algorithm, see [133]. For $q=2$, the classical Hurst exponent is retrieved $h(2)=H$, $(0<H<1)$, that quantifies the linear correlations in the sequence. $H=1/2$ stands for memory-less fluctuations. Persistence, i.e. positive memory, is related to $H>1/2$, while negative memory or anti-persistent correlations correspond to $H<1/2$. For mono-fractal data, h is independent of q and equal to H, since only one scaling exponent is enough; on the other hand, h decreasing with q is a result of a multi-fractal nature, which can be described through a set of scaling parameters $\{h_q\}$. It has to be noted that other approaches are also sometimes used to study multi-fractal properties, including those based on wavelet transforms [134,135], and improved methods based on Fractal Analysis [136,137]. We start reviewing the application of this concept to gait data by initially focusing on long-range linear correlations, as measured by the Hurst exponent H, as these were historically the first to be considered. Primarily, long-range fractal-like correlations (extended over hundred of steps) were found in stride interval fluctuations from healthy young people [138,139]. One year later, it was shown that these correlations are stable up to thousand of strides at three walking rates (usual or self-selected, slow and fast) [140]. Additionally, Hausdorff and co-workers showed that during metronomic walking, the stride interval becomes uncorrelated independently of the walking rate [140]. Opposed to this result, Delignieres et al. [141] found anti-persistent fluctuations in metronomically constrained walking, and that slow walking can be considered an anti-persistent non-stationary walk rather than a strongly persistent noise. Subsequent studies found that long-range correlations are also present when healthy subjects run [142,143], or when treadmill locomotion is imposed [144], although correlations are reduced. These results provide evidence that long-range temporal correlations exist at a wide range of gait speeds in healthy young adults. Moreover, models are able to generate sequences reproducing the experimental long-range temporal correlations [145,146].

Further studies showed that long-range correlations are reduced with maturation [147] and in elderly healthy subjects [148], since there is age-related decline in the general chemical and electrical activity of the micro and macro circuitries of the basal ganglia, which affects mobility, imposing deconfigured neural motor commands that induce longer lasting movements. Besides, physiological ageing brings a decrease in muscle mass and strength [149,150], joint somatosensory inputs (conscient proprioception) might also be decreased [151,152], and there is a higher probability of suffering arthrosis and joint deformity [153]. All those factors might also reduce the longe range correlation of movements. On the other hand, Malatesta et al. [154] found no significant differences in the temporal correlations between healthy young, 65-yr-old and octogenarians subjects walking on a treadmill, which makes sense if we take into account that the treadmill is imposing its own rhythm as a pacemaker. An additional study by Herman and co-workers proposed to characterise the "cautious" gait of the elderly [155]. They considered subjects with High Level of Gait Disorder (HLGD, i.e. walking difficulty not attributable to a chronic condition or disability), and found that long-term correlations are significantly lower in fallers compared with non-fallers [155], suggesting that a decrease in the correlations is an indicator of fear of walking.

Pathological alterations on the motor system also induce a decrease in the long-range correlations in the stride interval fluctuations. Such correlations were lower compared with controls when subjects suffer from Huntington [148] and Parkinson's diseases

[156,144,157], both pathologies affecting the basal ganglia, whose disability in coordinating the appropriate sequence of muscle contraction introduces tremor or discoordinated movements that increase short range noise. However, stride interval fluctuations from subjects with advanced amyotrophic lateral sclerosis also showed lower degree of long-range correlations, as one would expect from a completely deconfigured neural command that hinder movement, although for this disease the basal ganglia is intact and does not generate short range noise. It was additionally found that treadmill walking reduced the scaling exponent in healthy controls but not in subjects with Parkinson's disease [144]. On the other hand, the use of medication in subjects suffering of Parkinson's can be identified when rest tremors are studied, through an increase in the correlations in the velocity signals [53,95]. Surprisingly, peripheral neuropathy does not alter the temporal correlations of stride intervals of gait, despite these patients tending to walk slowly [158]. Withinn the general context, these findings contribute to the idea that changes in the scaling laws, i.e. the reduction in the correlations, are largely a reflection of a deterioration of the central control of gait, and not simply a reflection of a slower walking speed [158].

Beyond the detection of long-range linear correlations, multi-fractal analysis allows assessing the presence of non-linear ones, which are described by the scaling parameters $\{h_q\}$. Note that the presence of non-linear correlations, multi-fractal scalings, or multi-fractal properties, are all synonyms and are here used interchangeably. Multi-fractal scaling was primarily observed from theoretical models, conjecturing a slightly multi-fractal fluctuations in several gait regimens [146] and its decrease with maturation [145]. Subsequently weak multi-scaling was experimentally confirmed in both free and metronomically triggered conditions in healthy subjects [135,159,160], being the unconstrained slow and fast paces the most multi-fractal, and the former one actually being an anti-persistent walk, possibly due to a non-stationarity generated by a loss of concentration while trying to follow the pace. Weak multi-fractality has also been reported by Ivanov et al. [161]. Most recently, Dutta et al. [162] experimentally showed that stride intervals from both healthy subjects and patients with neurodegenerative diseases (Huntington's and Parkinson's) present multi-fractal properties, as well as from subjects suffering amyotrophic lateral sclerosis [163], with healthy subjects having higher degree of multi-fractality compared to patients. As opposed to these results, in [164,165] it was reported that, compared to healthy controls, multi-fractality is higher in individuals with the aforementioned diseases. Further, they found a wider degree of multi-scaling in both children and healthy older adults. On the other hand, Ducharme and co-workers [166,167] found that healthy subjects generate mono-fractal stride-to-stride intervals for unperturbed walking, and multi-fractal when perturbed. This opposing multi-scaling feature is probably due to a different data acquisition procedure [167]. Moreover, multi-fractality has been also observed in the walking of patients with Parkinson's during a keystroke [168], and in velocity signals of rest tremors [53,95]. In most cases, the main source of the multi-scaling is the presence of long-range correlations, rather than the distribution. Remarkably, by comparing the multi-scaling of the correlations between the two feet of a patient, a discrimination between Huntington's and Parkinson's diseases is achieved [169]; and such correlation quantifies the degree of the neurodegenerative pathology [170]. Lastly, Ihlen and Vereijken [171] proposed to identify multi-scaling in human gait by analysing the interplay between local temporal correlations and local magnitude of the stride time variability. It is finally worth mentioning that a detailed analysis on the optimisation of the parameters of the fractal approach used in order to obtain reliable results for finite-size measurements can be found in [172].

6. Irreversibility

Time irreversibility is formally defined as the lack of invariance of the statistical properties of a system (or a time series) under the operation of time reversal; more intuitively, it can be described as whether a time series can or cannot be recognised from its time-reversed version. To illustrate, imagine watching a movie of an ideal pendulum: it would not be possible to decide whether the movie is played forward or backward, as both would be identical (except for a change in the sign of the velocity). On the other hand, the classical example of an irreversible movie is the one depicting ice cubes melting in a glass; its time-reversed version, with water solidifying in regular structures, is unnatural at best. Time irreversibility is a fundamental property of non-equilibrium systems, and stems from two properties observed in many real-world systems: the presence of non-conservative forces, i.e. of memory [173,174], and of non-linear dynamics [175]. It is not surprising that irreversibility metrics and tests have been applied to many medical problems, including the characterisation of Parkinson's disease tremors [176]; of brain dynamics through corresponding electroencephalographic (EEG) recordings [177–180]; and of cardiac dynamics in different conditions [181–183]. Nevertheless, and as opposed to what seen for other metrics, irreversibility has mostly been neglected by the gait community - some reasons for this will be discussed in Section 7.

It is intuitive that gait should be an irreversible dynamics, as brain signals to the muscles that provoke joint movement must be continuous and coordinated; in other words, they are the result of a computation in which memory (the past position and movements of the body) plays an important part. This idea was firstly used in 2003 by Ref. [184], and later by Ref. [185] along similar lines; this was nevertheless not numerically checked, and was only used to justify the application of Left-to-Right Hidden Markov Models. More recently, two papers explored the use of irreversibility as marker of pathology. Firstly, Ref. [186] analysed time series of patients with peripheral arterial disease; a statistically significant lower irreversibility was found in patients on the Y axis of both legs with respect to the control group, reflecting a reduced repertoire of possible responses to an otherwise healthy normal neural command. The next year, Ref. [99] analysed gait kinematic time series for patients with mild cognitive decline and early Alzheimer's dementia; a more complex scenario was depicted, with some joint movements displaying an increased irreversibility (e.g. ankle rotation in mild cognitive decline patients, reflecting an adaptation to dynamically correct the ankle to increase the base of support [187]), while others a marked decrease (e.g. pelvic tilt in both pathologies, which tends to be fixed in a mid flexo/extension position with lower movement range, in order to increase stability during load transfer).

7. Conclusions and challenges ahead

Instrumented gait analysis (IGA) is steadily increasing in importance, both for understanding the inner mechanisms of brain computation, and the effects that different pathologies have on this essential aspect of everyday's life. IGA is nevertheless only as useful as the metrics extracted therefrom, hence the importance of defining and assessing suitable quantifiers. In this contribution we have reviewed how four statistical physics concepts, namely entropy, maximum Lyapunov exponent, multi-fractal analysis, and irreversibility, have been used to characterise human gait, both in health and pathologies. While coming from the same scientific field, these four concepts are substantially different, both in terms of the property of the system they assess, and of the requirements on the analysed data. A synthesis of these differences is proposed

Table 2
Main characteristics of the metrics considered in this study; see main text for details.

	Entropy	MLE	MFA	Irreversibility
Characterised property	Predictability	Recovery from perturbations	Linear/non-linear correlations	Computation, memory
Min. time series length	> 20	> 50	$> 1,000$	> 200
Computational cost	Low	High	Medium to high	Medium to high
Free parameters	Medium	Few	Few	Medium

Table 3
Synthesis of the main results observed in the Literature for five major pathological conditions. Acronyms in italic and superscript indicate the type of data analysed by each work. *jap*: joint angles and positions; *ac*: accelerations; *mtc*: minimum toe clearance; *si*: stride intervals; *f*: forces.

Ageing		
Metric:	*Main trend:*	*Exceptions:*
Entropy	Increased entropy [79]^{jap}, [80,45,57,81]^{ac}	[84]^{mtc}, [44,83]^{ac}
MLE	Reduced stability [112]^{jap}, [113]^{si}, [108,109]^{ac}	-
MFA	Reduced correlations [148,155]^{si}	[154]^{si}
Irreversibility	-	-
Parkinson's Disease		
Metric:	*Main trend:*	*Exceptions:*
Entropy	Increased entropy [53,86,87,90,66]^{si}, [88,46,47]^{f}, [89]^{ac}	[85]^{si}
MLE	-	-
MFA	Reduced correlations [156,144,157]^{si}, [95]^{f}. Multi-fractal scaling [162,168]^{si}	[164,165]^{si}
Irreversibility	-	-
Huntington's Disease		
Metric:	*Main trend:*	*Exceptions:*
Entropy	Increased entropy [85,53,86,91,90]^{si}, [46]^{f}	[51]^{f}
MLE	-	-
MFA	Reduced correlations [148]^{si}. Multi-fractal scaling [162]^{si}	[164,165]^{si}
Irreversibility	-	-
Alzheimer's Disease		
Metric:	*Main trend:*	*Exceptions:*
Entropy	Increased entropy [99]^{jap}	-
MLE	-	-
MFA	-	-
Irreversibility	Mixed [99]^{jap}	-
Amyotrophic Lateral Sclerosis		
Metric:	*Main trend:*	*Exceptions:*
Entropy	Increased entropy [53,86]^{si}, [51]^{f}	[85]^{si}
MLE	-	-
MFA	Reduced correlations [156]^{si}. Multi-fractal scaling [163]^{si}	[164,165]^{si}
Irreversibility	-	-

in Table 2. It has nevertheless to be taken into account that this is a simplification, as for instance different algorithms, e.g. for estimating entropy, have different requirements in terms of time series length, and also have different numbers of parameters that have to be tuned. Additionally, Table 3 reports a synthesis of the obtained results for five major pathologies, organised in main trends and exceptions for each metric, and further reporting the gait data used in the analysis.

The attentive reader will already have identified some common patterns: pathologies usually increase entropy, and reduce stability and correlations. This is not completely surprising, as one may expect a weaker control by the central nervous system, and hence a less controlled gait. There are nevertheless exceptions, which point towards a more complex scenario. Any metric showing a more controlled system could be pointing at the deployment of adaptive mechanisms in the brain (while this is not too lesioned), to create a successful cinematic and kinetic configuration maintaining a functional walk. However, this control will fail as soon as the adaptive mechanisms fail, leading to a completely uncontrolled system. This is known to happen in motor neuron degenerative diseases, such as Amyotrophic Lateral Sclerosis and Multiple Sclerosis. Depending on the evolution of the desease, one can thus find a wide spectrum, from lower to higher entropy, when comparing against healthy subjects. Lesions in the basal ganglia may start with some increase in control at the debut of disease; yet, as basal ganglia are a very important part of the adaptive mechanism itself, the progression of the lesion will result in an intensifying lack of control.

Results here reported also highlights some challenges that will have to be overcome, in order to ensure that IGA will have a prominent role in clinical practice.

First of all, observing differences between e.g. control subjects and patients is not necessarily tantamount to obtaining useful clinical knowledge and tools. On the one hand, as the described metrics are related with the output of the motor system, their changes cannot directly be interpreted as causal mechanisms. Abnormalities in motor output can emerge as secondary adaptations of the system, requiring additional and tailored experiments to confirm any causal hypothesis. On the other hand, while most research works have focused on the statistical significance of results, only few have used such differences to build classification models [62,86,169,95,64,46,90,66]. The importance of having such models, and specifically explainable ones, is nevertheless obvious, and is especially relevant in the case of pathologies for which early diagnosis is hindered by a lack of reliable and affordable early biomarkers - e.g. Parkinson's and Alzheimer's diseases.

Secondly, as illustrated in Table 3, many contradictory results have been observed for multiple pathologies, or even for control subjects in comparable conditions. On one hand, this may point towards an evolution of the underlying control strategy by part

of the central nervous system; something that can only be confirmed through longitudinal studies. Yet, and on the other hand, this may also be the spurious result of using different techniques to record gait; of heterogeneous (and not easily comparable) data recording procedures and conditions; and of the use of different variants of the four metrics, of different algorithms to calculate them, or of different parameters. In spite of some efforts in the Literature [107,68,48,35,61,67,50,69,70,67,188], more comparative studies are needed to clarify which metrics, algorithms and parameter values ought to be used, possibly by relying on numerical models of gait [145,146,110].

Thirdly, one must acknowledge that creating bridges between different scientific fields is challenging at best, as concepts and ideas that are standard in one of them may be hard to grasp in another one. The case here reviewed is not exception, resulting in some widespread technical and conceptual fallacies. To illustrate, different metrics have different requirements in terms of minimum time series length - some very broad guidelines are included in Table 2. Yet, the Hurst exponent has been estimated on time series as short as 20 values [148], something that is known to lead to overestimations; interestingly, results were then confirmed with longer time series [162]. We have also found many examples of research works claiming that the complexity of the time series was calculated, for then using entropy metrics [29,75,68,189,26,49,71,57,50,61,190,90]. While entropy and complexity are undoubtedly related concepts, they are not interchangeable, as well known in statistical physics [191–193]. This highlights the importance of relying on mixed teams, in which people with different background (medical on one hand, physics on the other) can interact.

As a final point, Table 3 (or even the length of the different sections) suggests that the four concepts here analysed, while being complementary in nature, have not equally been considered. Specifically, the use of entropy and MFA can be considered as widespread in gait analysis; but only two research works have focused on the irreversibility of gait time series. This may be the results of several factors. First of all, computational approaches to irreversibility are relatively recent, with the first metric being proposed by Yves Pomeau in 1982 [194] - entropy, in contrast, is a concept known in information theory since 1948 [30]. Additionally, while many more metrics have been proposed in the last decade, choosing the best one for a given real-world problem is not trivial [188]; the computational cost is usually much higher, when compared to entropy metrics [188]; and the understanding of the theoretical meaning of irreversibility is challenging.

In spite of these challenges ahead, it is clear that the instrumental analysis of gait can strongly benefit from statistical physics concepts; and that existing studies have helped in understanding the mechanisms behind some major pathologies and how they affect gait, from Parkinson's to Alzheimer's. It would be far from surprising to see an increase in the number of published papers on this topic; and even the adoption of those metrics in a clinical context in the near future.

CRediT authorship contribution statement

Massimiliano Zanin: Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Supervision. **Felipe Olivares:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing. **Irene Pulido-Valdeolivas:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing. **Estrella Rausell:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing. **David Gomez-Andres:** Conceptualization, Investigation, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

Irene Pulido-Valdeolivas has received travel reimbursement from Roche Spain, Novartis and Genzyme-Sanofi, and she is a founder and holds stock in Aura Robotics SL. She is an employee at UCB Pharma since July 2020 and all the work in this paper is based on her previous work at Universidad Autónoma de Madrid.

David Gómez Andrés has received honoraria as an advisor from Biogen and Lupin Neuroscience and as a speaker from Biogen, PTC, and Shire. He has also received travel reimbursement from Roche, PTC, Shire and Laboratorios Rubio. He was founder and holds stock in Aura Robotics SL. He is/was an investigator in clinical trials founded by Pfizer, Biogen, Avexis, Roche, Fibrogen and Santhera.

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References

[1] Levine D, Richards J, Whittle MW. Whittle's gait analysis. Elsevier Health Sciences 2012.
[2] Badiye A, Kathane P, Krishan K. Forensic Gait Analysis. Treasure Island (FL): StatPearls Publishing; 2021.
[3] Dewolf AH, Sylos-Labini F, Cappellini G, Lacquaniti F, Ivanenko Y. Emergence of different gaits in infancy: relationship between developing neural circuitries and changing biomechanics. Front Bioeng Biotechnol 2020;8:473.
[4] Dewolf AH, Sylos-Labini F, Cappellini G, Ivanenko Y, Lacquaniti F. Age-related changes in the neuromuscular control of forward and backward locomotion. PloS one 2021;16(2):e0246372.
[5] S. Xu, J. Fang, X. Hu, E. Ngai, Y. Guo, V. Leung, J. Cheng, B. Hu, Emotion recognition from gait analyses: Current research and future directions, arXiv preprint arXiv:2003.11461 (2020)..
[6] P.C.R. d. Santos, F.A. Barbieri, I. Zijdewind, L.T.B. Gobbi, C. Lamoth, T. Hortobágyi, Effects of experimentally induced fatigue on healthy older adults' gait: A systematic review, PloS one 14 (12) (2019) e0226939..
[7] Ebersbach G, Sojer M, Müller J, Heijmenberg M, Poewe W. Sociocultural differences in gait. Movement Disorders 2000;15(6):1145–7.
[8] Pontzer H, Raichlen DA, Sockol MD. The metabolic cost of walking in humans, chimpanzees, and early hominins. J Hum Evol. 2009;56(1):43–54.
[9] W.M.G.R.S. GROUP, M. de Onis, Who motor development study: Windows of achievement for six gross motor development milestones, Acta Paediatrica 95 (S450) (2006) 86–95..
[10] Lacquaniti F, Ivanenko YP, Zago M. Patterned control of human locomotion. J Physiol 2012;590(10):2189–99.
[11] Sylos-Labini F, Zago M, Guertin PA, Lacquaniti F, Ivanenko YP. Muscle coordination and locomotion in humans. Current Pharmaceutical Design 2017;23(12):1821–33.
[12] Takakusaki K. Functional neuroanatomy for posture and gait control. J Movement Disorders 2017;10(1):1.
[13] Bronstein A, Brandt T. Clinical disorders of balance, posture and gait. CRC Press; 2004.
[14] Kirtley C. Clinical gait analysis: theory and practice. Elsevier Health Sciences 2006.
[15] Chia K, Fischer I, Thomason P, Graham HK, Sangeux M. A decision support system to facilitate identification of musculoskeletal impairments and propose recommendations using gait analysis in children with cerebral palsy. Front Bioeng Biotechnol 2020. 1342.
[16] Shumway-Cook A, Woollacott MH. Motor control: translating research into clinical practice. Lippincott Williams & Wilkins; 2007.
[17] Marret S, Vanhulle C, Laquerriere A. Pathophysiology of cerebral palsy. Handbook Clinical Neurol 2013;111:169–76.
[18] Muro-de-la Herran A, Garcia-Zapirain B, Mendez-Zorrilla A. Gait analysis methods: An overview of wearable and non-wearable systems, highlighting clinical applications. Sensors 2014;14(2):3362–94.
[19] Chau T. A review of analytical techniques for gait data. part 1: fuzzy, statistical and fractal methods. Gait Posture 2001;13(1):49–66.
[20] Chau T. A review of analytical techniques for gait data. part 2: neural network and wavelet methods. Gait Posture 2001;13(2):102–20.
[21] Gnesotto FS, Mura F, Gladrow J, Broedersz CP. Broken detailed balance and non-equilibrium dynamics in living systems: a review. Rep Prog Phys 2018;81(6):066601.

[22] Baker R. The history of gait analysis before the advent of modern computers. Gait Posture 2007;26(3):331–42.
[23] Braun M. Picturing time: the work of Etienne-Jules Marey (1830–1904). University of Chicago Press; 1992.
[24] Figueiredo J, Santos CP, Moreno JC. Automatic recognition of gait patterns in human motor disorders using machine learning: A review. Med Eng Phys 2018;53:1–12.
[25] Soczawa-Stronczyk AA, Bocian M. Gait coordination in overground walking with a virtual reality avatar. R Soc Open Sci 2020;7(7):200622.
[26] Chen M-S, Jiang BC. Resistance training exercise program for intervention to enhance gait function in elderly chronically ill patients: multivariate multiscale entropy for center of pressure signal analysis. Comput Math Methods Med 2014;2014.
[27] Brody H. The systems view of man: Implications for medicine, science, and ethics. Perspectives Biol Med 1973;17(1):71–92.
[28] Smith CJ. Problems with entropy in biology. Biosystems 1975;7(2):259–65.
[29] Costa M, Peng C-K, Goldberger AL, Hausdorff JM. Multiscale entropy analysis of human gait dynamics. Physica A: Stat Mech Appl 2003;330(1–2):53–60.
[30] Shannon CE. A mathematical theory of communication. Bell Syst Tech J 1948;27(3):379–423.
[31] Beim Graben P. Estimating and improving the signal-to-noise ratio of time series by symbolic dynamics. Phys Rev E 2001;64(5):051104.
[32] Daw CS, Finney CEA, Tracy ER. A review of symbolic analysis of experimental data. Rev Sci Instruments 2003;74(2):915–30.
[33] Pincus SM. Approximate entropy as a measure of system complexity. Proc Nat Acad Sci 1991;88(6):2297–301.
[34] Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol-Heart Circulatory Physiol 2000.
[35] Yentes JM, Hunt N, Schmid KK, Kaipust JP, McGrath D, Stergiou N. The appropriate use of approximate entropy and sample entropy with short data sets. Ann Biomed Eng 2013;41(2):349–65.
[36] Delgado-Bonal A, Marshak A. Approximate entropy and sample entropy: A comprehensive tutorial. Entropy 2019;21(6):541.
[37] Bandt C, Pompe B. Permutation entropy: a natural complexity measure for time series. Phys Rev Letters 2002;88(17):174102.
[38] Amigó J. Permutation complexity in dynamical systems: ordinal patterns, permutation entropy and all that. Springer Science & Business Media; 2010.
[39] Zanin M, Zunino L, Rosso OA, Papo D. Permutation entropy and its main biomedical and econophysics applications: a review. Entropy 2012;14(8):1553–77.
[40] Costa M, Goldberger AL, Peng C-K. Multiscale entropy analysis of complex physiologic time series. Phys Rev Letters 2002;89(6):068102.
[41] Costa M, Goldberger AL, Peng C-K. Multiscale entropy analysis of biological signals. Phys Rev E 2005;71(2):021906.
[42] Humeau-Heurtier A. The multiscale entropy algorithm and its variants: A review. Entropy 2015;17(5):3110–23.
[43] Bisi MC, Riva F, Stagni R. Measures of gait stability: performance on adults and toddlers at the beginning of independent walking. J Neuroeng Rehabilitation 2014;11(1):1–9.
[44] Bisi M, Stagni R. Complexity of human gait pattern at different ages assessed using multiscale entropy: from development to decline. Gait Posture 2016;47:37–42.
[45] Bizovska L, Svoboda Z, Vuillerme N, Janura M. Multiscale and shannon entropies during gait as fall risk predictors - a prospective study. Gait Posture 2017;52:5–10.
[46] Nam Nguyen QD, Liu A-B, Lin C-W. Development of a neurodegenerative disease gait classification algorithm using multiscale sample entropy and machine learning classifiers. Entropy 2020;22(12). 1340.
[47] Hsieh Y-L, Abbod MF. Gait analyses of parkinson's disease patients using multiscale entropy. Electronics 2021;10(21):2604.
[48] Qumar A, Aziz W, Saeed S, Ahmed I, Hussain L. Comparative study of multiscale entropy analysis and symbolic time series analysis when applied to human gait dynamics. In: 2013 International Conference on Open Source Systems and Technologies. IEEE; 2013. p. 126–32.
[49] Yu J, Cao J, Liao W-H, Chen Y, Lin J, Liu R. Multivariate multiscale symbolic entropy analysis of human gait signals. Entropy 2017;19(10):557.
[50] Risso W. Symbolic time series analysis and its application in social sciences, Time Series Analysis and Applications. Zagreb. Croatia: InTech; 2018. p. 107–26.
[51] Liu A-B, Lin C-W. Multiscale approximate entropy for gait analysis in patients with neurodegenerative diseases. Entropy 2019;21(10):934.
[52] Bollt EM, Skufca JD, McGregor SJ. Control entropy: A complexity measure for nonstationary signals. Math Biosci Eng 2009;6(1):1.
[53] Liao F, Wang J, He P. Multi-resolution entropy analysis of gait symmetry in neurological degenerative diseases and amyotrophic lateral sclerosis. Med Eng Phys 2008;30(3):299–310.
[54] Szczęsna A. Quaternion entropy for analysis of gait data. Entropy 2019;21(1):79.
[55] Leverick G, Szturm T, Wu CQ. Using entropy measures to characterize human locomotion. J Biomech Eng 2014;136(12):121002.
[56] Leverick G, Wu C, Szturm T. Coarse quantization in calculations of entropy measures for experimental time series. Nonlinear Dyn 2015;79(1):93–100.
[57] Ahmadi S, Wu C, Sepehri N, Kantikar A, Nankar M, Szturm T. The effects of aging and dual tasking on human gait complexity during treadmill walking: a comparative study using quantized dynamical entropy and sample entropy. J Biomech Eng 2018;140(1).
[58] Scafetta N, Grigolini P. Scaling detection in time series: Diffusion entropy analysis. Phys Rev E 2002;66(3):036130.
[59] Cai S-M, Zhou P-L, Yang H-J, Zhou T, Wang B-H, Zhao F-C. Diffusion entropy analysis on the stride interval fluctuation of human gait. Physica A 2007;375(2):687–92.
[60] Amoud H, Snoussi H, Hewson D, Doussot M, Duchene J. Intrinsic mode entropy for nonlinear discriminant analysis. IEEE Signal Process Lett 2007;14(5):297–300.
[61] Raffalt PC, Denton W, Yentes JM. On the choice of multiscale entropy algorithm for quantification of complexity in gait data. Computers Biol Med 2018;103:93–100.
[62] Papadakis N, Christakis D, Tzagarakis G, Chlouverakis G, Kampanis N, Stergiopoulos K, Katonis P. Gait variability measurements in lumbar spinal stenosis patients: part a. comparison with healthy subjects. Physiol Meas 2009;30(11):1171.
[63] Rubinstein R. The cross-entropy method for combinatorial and continuous optimization. Methodol Computing Appl Probability 1999;1(2):127–90.
[64] Zhou Y, Romijnders R, Hansen C, van Campen J, Maetzler W, Hortobágyi T, Lamoth CJ. The detection of age groups by dynamic gait outcomes using machine learning approaches. Sci Rep 2020;10(1):1–12.
[65] Chintakunta H, Gentimis T, Gonzalez-Diaz R, Jimenez M-J, Krim H. An entropy-based persistence barcode. Pattern Recogn 2015;48(2):391–401.
[66] Tong J, Zhang J, Dong E, Du S. Severity classification of parkinson's disease based on permutation-variable importance and persistent entropy. Appl Sci 2021;11(4):1834.
[67] Yentes JM, Denton W, McCamley J, Raffalt PC, Schmid KK. Effect of parameter selection on entropy calculation for long walking trials. Gait Posture 2018;60:128–34.
[68] McGregor SJ, Bollt E. Control entropy: what is it and what does it tell us? Clinical Kinesiology (Online) 2012;66(1):7.
[69] McCamley JD, Denton W, Arnold A, Raffalt PC, Yentes JM. On the calculation of sample entropy using continuous and discrete human gait data. Entropy 2018;20(10):764.
[70] Ahmadi S, Sepehri N, Wu C, Szturm T. Sample entropy of human gait center of pressure displacement: a systematic methodological analysis. Entropy 2018;20(8):579.
[71] M.F. Vieira, F.B. Rodrigues, G.S. d. S. e Souza, R.M. Magnani, G.C. Lehnen, N.G. Campos, A.O. Andrade, Gait stability, variability and complexity on inclined surfaces, Journal of biomechanics 54 (2017) 73–79..
[72] McGregor SJ, Busa MA, Skufca J, Yaggie JA, Bollt EM. Control entropy identifies differential changes in complexity of walking and running gait patterns with increasing speed in highly trained runners, Chaos: An Interdisciplinary. J Nonlinear Sci 2009;19(2):026109.
[73] Abbasi AQ, Loun WA. Symbolic time series analysis of temporal gait dynamics. J Signal Processing Syst 2014;74(3):417–22.
[74] Thomas KS, Russell DM, Van Lunen BL, Colberg SR, Morrison S. The impact of speed and time on gait dynamics. Human Movement Sci 2017;54:320–30.
[75] McGregor SJ, Busa MA, Parshad R, Yaggie JA, Bollt E. Control entropy of gait: does running fitness affect complexity of walking? Clinical Kinesiology (Online) 2011;65(1):9.
[76] Siracuse JJ, Odell DD, Gondek SP, Odom SR, Kasper EM, Hauser CJ, Moorman DW. Health care and socioeconomic impact of falls in the elderly. Am J Surgery 2012;203(3):335–8.
[77] Gelbard R, Inaba K, Okoye OT, Morrell M, Saadi Z, Lam L, Talving P, Demetriades D. Falls in the elderly: a modern look at an old problem. Am J Surgery 2014;208(2):249–53.
[78] Jørgensen TSH, Hansen AH, Sahlberg M, Gislason GH, Torp-Pedersen C, Andersson C, Holm E. Falls and comorbidity: the pathway to fractures. Scandinavian J Public Health 2014;42(3):287–94.
[79] Kurz MJ, Stergiou N. The aging humans neuromuscular system expresses less certainty for selecting joint kinematics during gait. Neurosci Letters 2003;348(3):155–8.
[80] Arif M, Ohtaki Y, Nagatomi R, Inooka H. Estimation of the effect of cadence on gait stability in young and elderly people using approximate entropy technique. Measurement Sci Rev 2004;4(2):29–40.
[81] Ihlen EA, Van Schooten KS, Bruijn SM, Van Dieen JH, Vereijken B, Helbostad JL, Pijnappels M. Improved prediction of falls in community-dwelling older adults through phase-dependent entropy of daily-life walking. Front Aging Neurosci 2018;10:44.
[82] E.R. Kandel, J.H. Schwartz, T.M. Jessell, S. Siegelbaum, A.J. Hudspeth, S. Mack, et al., Principles of neural science, Vol. 4, McGraw-hill New York, 2000..
[83] Huijben B, Van Schooten K, Van Dieën J, Pijnappels M. The effect of walking speed on quality of gait in older adults. Gait Posture 2018;65:112–6.
[84] Karmakar CK, Khandoker AH, Begg RK, Palaniswami M, Taylor S. Understanding ageing effects by approximate entropy analysis of gait variability. In: 2007 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE; 2007. p. 1965–8.
[85] Aziz W, Arif M. Complexity analysis of stride interval time series by threshold dependent symbolic entropy. Eur J Appl Physiol 2006;98(1):30–40.
[86] Baratin E, Sugavaneswaran L, Umapathy K, Ioana C, Krishnan S. Wavelet-based characterization of gait signal for neurological abnormalities. Gait Posture 2015;41(2):634–9.

[87] Afsar O, Tirnakli U, Kurths J. Entropy-based complexity measures for gait data of patients with parkinson's disease, Chaos: An Interdisciplinary. J Nonlinear Sci 2016;26(2):023115.
[88] Wu Y, Chen P, Luo X, Wu M, Liao L, Yang S, Rangayyan RM. Measuring signal fluctuations in gait rhythm time series of patients with parkinson's disease using entropy parameters. Biomed Signal Process Control 2017;31:265–71.
[89] Coates L, Shi J, Rochester L, Del Din S, Pantall A. Entropy of real-world gait in parkinson's disease determined from wearable sensors as a digital marker of altered ambulatory behavior. Sensors 2020;20(9):2631.
[90] Huang H-P, Hsu CF, Mao Y-C, Hsu L, Chi S. Gait stability measurement by using average entropy. Entropy 2021;23(4):412.
[91] Pham TD, Yan H. Spatial-dependence recurrence sample entropy. Physica A 2018;494:581–90.
[92] Tochigi Y, Segal NA, Vaseenon T, Brown TD. Entropy analysis of tri-axial leg acceleration signal waveforms for measurement of decrease of physiological variability in human gait. J Orthop Res 2012;30(6):897–904.
[93] Khalaf K, Al-Angari HM, Khandoker AH, Lee S, Almahmeed W, Al Safar HS, Jelinek HF. Gait alterations in the uae population with and without diabetic complications using both traditional and entropy measures. Gait Posture 2017;58:72–7.
[94] Rhea CK, Wutzke CJ, Lewek MD. Gait dynamics following variable and constant speed gait training in individuals with chronic stroke. Gait Posture 2012;36(2):332–4.
[95] Li M, Tian S, Sun L, Chen X. Gait analysis for post-stroke hemiparetic patient by multi-features fusion method. Sensors 2019;19(7):1737.
[96] Busa MA, Jones SL, Hamill J, van Emmerik RE. Multiscale entropy identifies differences in complexity in postural control in women with multiple sclerosis. Gait Posture 2016;45:7–11.
[97] Buzzi UH, Ulrich BD. Dynamic stability of gait cycles as a function of speed and system constraints. Motor Control 2004;8(3):241–54.
[98] Zanin M, Gómez-Andrés D, Pulido-Valdeolivas I, Martín-Gonzalo JA, López-López J, Pascual-Pascual SI, Rausell E. Characterizing normal and pathological gait through permutation entropy. Entropy 2018;20(1):77.
[99] J.-A. Martín-Gonzalo, I. Pulido-Valdeolivas, Y. Wang, T. Wang, G. Chiclana-Actis, M. d. C. Algarra-Lucas, I. Palmí-Cortés, J. Fernandez Travieso, M.D. Torrecillas-Narváez, A.A. Miralles-Martinez, et al., Permutation entropy and irreversibility in gait kinematic time series from patients with mild cognitive decline and early alzheimer's dementia, Entropy 21 (9) (2019) 868..
[100] Myers SA, Stergiou N, Pipinos II, Johanning JM. Gait variability patterns are altered in healthy young individuals during the acute reperfusion phase of ischemia-reperfusion. J Surg Res 2010;164(1):6–12.
[101] Lyapunov AM. The general problem of the stability of motion. Int J Control 1992;55(3):531–4.
[102] Cencini M, Vulpiani A. Finite size lyapunov exponent: review on applications. J Phys A: Math Theor 2013;46(25):254019.
[103] Mehdizadeh S. The largest lyapunov exponent of gait in young and elderly individuals: a systematic review. Gait Posture 2018;60:241–50.
[104] Wolf A, Swift JB, Swinney HL, Vastano JA. Determining lyapunov exponents from a time series. Physica D: Nonlinear Phenomena 1985;16(3):285–317.
[105] Rosenstein MT, Collins JJ, De Luca CJ. A practical method for calculating largest lyapunov exponents from small data sets. Physica D 1993;65(1–2):117–34.
[106] Cignetti F, Decker LM, Stergiou N. Sensitivity of the wolf's and rosenstein's algorithms to evaluate local dynamic stability from small gait data sets. Ann Biomed Eng 2012;40(5):1122–30.
[107] Myers SA, Johanning JM, Stergiou N, Celis RI, Robinson L, Pipinos II. Gait variability is altered in patients with peripheral arterial disease. J Vascular Surgery 2009;49(4):924–31.
[108] Terrier P, Reynard F. Effect of age on the variability and stability of gait: a cross-sectional treadmill study in healthy individuals between 20 and 69 years of age. Gait Posture 2015;41(1):170–4.
[109] Hussain VS, Spano ML, Lockhart TE. Effect of data length on time delay and embedding dimension for calculating the lyapunov exponent in walking. J R Soc Interface 2020;17(168):20200311.
[110] Bruijn SM, van Dieën JH, Meijer OG, Beek PJ. Statistical precision and sensitivity of measures of dynamic gait stability. J Neurosci Methods 2009;178(2):327–33.
[111] Federolf P, Tecante K, Nigg B. A holistic approach to study the temporal variability in gait. J Biomech 2012;45(7):1127–32.
[112] Buzzi UH, Stergiou N, Kurz MJ, Hageman PA, Heidel J. Nonlinear dynamics indicates aging affects variability during gait. Clinical Biomech 2003;18(5):435–43.
[113] Hamacher D, Liebl D, Hödl C, Heßler V, Kniewasser CK, Thönnessen T, Zech A. Gait stability and its influencing factors in older adults. Front Physiol 2019;9:1955.
[114] Hoogkamer W, Bruijn SM, Sunaert S, Swinnen SP, Van Calenbergh F, Duysens J. Toward new sensitive measures to evaluate gait stability in focal cerebellar lesion patients. Gait Posture 2015;41(2):592–6.
[115] Huisinga JM, Mancini M, George RJS, Horak FB. Accelerometry reveals differences in gait variability between patients with multiple sclerosis and healthy controls. Ann Biomed Eng 2013;41(8):1670–9.
[116] Moraiti CO, Stergiou N, Vasiliadis HS, Motsis E, Georgoulis A. Anterior cruciate ligament reconstruction results in alterations in gait variability. Gait Posture 2010;32(2):169–75.
[117] Alkjaer T, Raffalt PC, Dalsgaard H, Simonsen EB, Petersen NC, Bliddal H, Henriksen M. Gait variability and motor control in people with knee osteoarthritis. Gait Posture 2015;42(4):479–84.
[118] Grassberger P, Procaccia I. Characterization of strange attractors. Phys Rev Letters 1983;50(5):346.
[119] Grassberger P, Procaccia I. Measuring the strangeness of strange attractors. Physica D Nonlinear Phenomena 1983;9(1–2):189–208.
[120] Dingwell JB, Cusumano JP. Nonlinear time series analysis of normal and pathological human walking, Chaos: An Interdisciplinary. J Nonlinear Sci 2000;10(4):848–63.
[121] Tarnita D, Catana M, Tarnita D. Nonlinear analysis of normal human gait for different activities with application to bipedal locomotion, The Romanian Journal of Technical Sciences. Appl Mech 2013;58(1–2):177–90.
[122] S. DelMarco, Y. Deng, Detection of chaotic dynamics in human gait signals from mobile devices, in: Mobile Multimedia/Image Processing, Security, and Applications 2017, Vol. 10221, SPIE, 2017, pp. 43–56..
[123] Tarnita D, Georgescu M, Tarnita D. Application of nonlinear dynamics to human knee movement on plane and inclined treadmill. In: New Trends in Medical and Service Robots. Springer; 2016. p. 59–73.
[124] Tarnita D, Marghitu D. Nonlinear dynamics of normal and osteoarthritic human knee. Proc Romanian Acad 2017;18(4):353–60.
[125] Iqbal S, Zang X, Zhu Y, Jie Z. Nonlinear time-series analysis of human gaits in aging and parkinson's disease. In: 2015 international conference on mechanics and control engineering (MCE 2015).
[126] Elden RH, Al-Atabany W, Ghoneim VF. Gait variability analysis in neurodegenerative diseases using nonlinear dynamical modelling. In: 2018 9th Cairo International Biomedical Engineering Conference (CIBEC). IEEE; 2018. p. 41–4.
[127] Perc M. The dynamics of human gait. Eur J Phys 2005;26(3):525.
[128] Mandelbrot BB, Mandelbrot BB. The fractal geometry of nature, Vol. 1. WH freeman New York; 1982.
[129] R.A. Meyers, et al., Encyclopedia of complexity and systems science, Vol. 9, Citeseer, 2009..
[130] Hurst HE. Long-term storage capacity of reservoirs. Trans Am Soc Civil Eng 1951;116(1):770–99.
[131] Kantelhardt JW, Koscielny-Bunde E, Rego HH, Havlin S, Bunde A. Detecting long-range correlations with detrended fluctuation analysis. Physica A 2001;295(3–4):441–54.
[132] Tabar R. Analysis and data-based reconstruction of complex nonlinear dynamical systems, Vol. 730. Springer; 2019.
[133] Kantelhardt JW, Zschiegner SA, Koscielny-Bunde E, Havlin S, Bunde A, Stanley HE. Multifractal detrended fluctuation analysis of nonstationary time series. Physica A 2002;316(1–4):87–114.
[134] Muzy J-F, Bacry E, Arneodo A. The multifractal formalism revisited with wavelets. Int J Bifurcation Chaos 1994;4(02):245–302.
[135] Scafetta N, Griffin L, West BJ. Hölder exponent spectra for human gait. Physica A 2003;328(3–4):561–83.
[136] Gao J, Hu J, Tung W-W. Facilitating joint chaos and fractal analysis of biosignals through nonlinear adaptive filtering. PloS one 2011;6(9):e24331.
[137] Zhou W-X et al. Multifractal detrended cross-correlation analysis for two nonstationary signals. Phys Rev E 2008;77(6):066211.
[138] Hausdorff JM, Peng C-K, Ladin Z, Wei JY, Goldberger AL. Is walking a random walk? evidence for long-range correlations in stride interval of human gait. J Appl Physiol 1995;78(1):349–58.
[139] West BJ, Griffin L. Allometric control, inverse power laws and human gait. Chaos, Solitons Fractals 1999;10(9):1519–27.
[140] Hausdorff JM, Purdon PL, Peng C-K, Ladin Z, Wei JY, Goldberger AL. Fractal dynamics of human gait: stability of long-range correlations in stride interval fluctuations. J Appl Physiol 1996;80(5):1448–57.
[141] Delignières D, Torre K. Fractal dynamics of human gait: a reassessment of the 1996 data of hausdorff et al. J Appl Physiol 2009;106(4):1272–9.
[142] Jordan K, Challis JH, Newell KM. Long range correlations in the stride interval of running. Gait Posture 2006;24(1):120–5.
[143] Jordan K, Challis JH, Newell KM. Speed influences on the scaling behavior of gait cycle fluctuations during treadmill running. Human Movement Sci 2007;26(1):87–102.
[144] Frenkel-Toledo S, Giladi N, Peretz C, Herman T, Gruendlinger L, Hausdorff JM. Treadmill walking as an external pacemaker to improve gait rhythm and stability in parkinson's disease. Movement Disorders 2005;20(9):1109–14.
[145] Ashkenazy Y, Hausdorff JM, Ivanov PC, Stanley HE. A stochastic model of human gait dynamics. Physica A 2002;316(1–4):662–70.
[146] West BJ, Scafetta N. Nonlinear dynamical model of human gait. Phys Rev E 2003;67(5):051917.
[147] Hausdorff J, Zemany L, Peng C-K, Goldberger A. Maturation of gait dynamics: stride-to-stride variability and its temporal organization in children. J Appl Physiol 1999;86(3):1040–7.
[148] Hausdorff JM, Mitchell SL, Firtion R, Peng C-K, Cudkowicz ME, Wei JY, Goldberger AL. Altered fractal dynamics of gait: reduced stride-interval correlations with aging and huntington's disease. J Appl Physiol 1997;82(1):262–9.
[149] Clark BC, Manini TM. Sarcopenia ≠ dynapenia, The. J Gerontol Series A: Biological Sci Med Sci 2008;63(8):829–34.
[150] Chang K-V, Wu W-T, Huang K-C, Jan WH, Han D-S. Limb muscle quality and quantity in elderly adults with dynapenia but not sarcopenia: an ultrasound imaging study. Exp Gerontol 2018;108:54–61.

[151] Ribeiro F, Oliveira J. Aging effects on joint proprioception: the role of physical activity in proprioception preservation. Eur Rev Aging Phys Activity 2007;4(2):71–6.
[152] Langan J. Older adults demonstrate greater accuracy in joint position matching using self-guided movements. Hum Mov Sci 2014;36:97–106.
[153] Finney A, Dziedzic KS, Lewis M, Healey E. Multisite peripheral joint pain: a cross-sectional study of prevalence and impact on general health, quality of life, pain intensity and consultation behaviour. BMC Musculoskeletal Disorders 2017;18(1):1–8.
[154] Malatesta D, Simar D, Dauvilliers Y, Candau R, Borrani F, Préfaut C, Caillaud C. Energy cost of walking and gait instability in healthy 65-and 80-yr-olds. J Appl Physiol 2003;95(6):2248–56.
[155] Herman T, Giladi N, Gurevich T, Hausdorff J. Gait instability and fractal dynamics of older adults with a 'cautions' gait: why do certain older adults walk fearfully? Gait Posture 2005;21(2):178–85.
[156] Hausdorff JM, Lertratanakul A, Cudkowicz ME, Peterson AL, Kaliton D, Goldberger AL. Dynamic markers of altered gait rhythm in amyotrophic lateral sclerosis. J Appl Physiol 2000.
[157] Kirchner M, Schubert P, Liebherr M, Haas CT. Detrended fluctuation analysis and adaptive fractal analysis of stride time data in parkinson's disease: stitching together short gait trials. PloS one 2014;9(1):e85787.
[158] Gates DH, Dingwell JB. Peripheral neuropathy does not alter the fractal dynamics of stride intervals of gait. J Appl Physiol 2007;102(3):965–71.
[159] Scafetta N, Moon RE, West BJ. Fractal response of physiological signals to stress conditions, environmental changes, and neurodegenerative diseases. Complexity 2007;12(5):12–7.
[160] Scafetta N, Marchi D, West BJ. Understanding the complexity of human gait dynamics, Chaos: An Interdisciplinary. J Nonlinear Sci 2009;19(2):026108.
[161] Ivanov PC, Ma QD, Bartsch RP, Hausdorff JM, Amaral LAN, Schulte-Frohlinde V, Stanley HE, Yoneyama M. Levels of complexity in scale-invariant neural signals. Phys Rev E 2009;79(4):041920.
[162] Dutta S, Ghosh D, Chatterjee S. Multifractal detrended fluctuation analysis of human gait diseases. Front Physiol 2013;4:274.
[163] Chatterjee S. Analysis of the human gait rhythm in neurodegenerative disease: A multifractal approach using multifractal detrended cross correlation analysis. Physica A 2020;540:123154.
[164] A. Muñoz-Diosdado, J. del Rio Correa, A. Brown, Multifractality in time series of human gait, in: Proceedings of the 25th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (IEEE Cat. No. 03CH37439), Vol. 2, IEEE, 2003, pp. 1792–1795..
[165] A. Muñoz-Diosdado, A non linear analysis of human gait time series based on multifractal analysis and cross correlations, in: Journal of Physics: Conference Series, Vol. 23, IOP Publishing, 2005, p. 010..
[166] S.W. Ducharme, Quantifying gait adaptability: Fractality, complexity, and stability during asymmetric walking. doctoral dissertations 1075 (2017)..
[167] Ducharme SW, van Emmerik RE. Multifractality of unperturbed and asymmetric locomotion. J Mot Behav 2018.
[168] Madanchi A, Taghavi-Shahri F, Taghavi-Shahri SM, Rahimi Tabar MR. Scaling behavior in measured keystroke time series from patients with parkinson's disease, The. Eur Phys J B 2020;93(7):1–8.
[169] Dutta S, Ghosh D, Chatterjee S. Multifractal detrended cross correlation analysis of neuro-degenerative diseases - an in depth study. Physica A 2018;491:188–98.
[170] D. Ghosh, S. Samanta, S. Chakraborty, Multifractal study of parkinson's and huntington's diseases with human gait data, in: Multifractals and Chronic Diseases of the Central Nervous System, Springer, 2019, pp. 117–147..
[171] Ihlen EA, Vereijken B. Detection of co-regulation of local structure and magnitude of stride time variability using a new local detrended fluctuation analysis. Gait Posture 2014;39(1):466–71.
[172] Phinyomark A, Larracy R, Scheme E. Fractal analysis of human gait variability via stride interval time series. Front Physiol 2020;11:333.
[173] Zwanzig R. Memory effects in irreversible thermodynamics. Phys Rev 1961;124(4):983.
[174] Puglisi A, Villamaina D. Irreversible effects of memory. EPL (Europhysics Letters) 2009;88(3):30004.
[175] Lawrance A. Directionality and reversibility in time series. Int Stat Rev/Revue Internationale de Statistique 1991:67–79.
[176] Timmer J, Gantert C, Deuschl G, Honerkamp J. Characteristics of hand tremor time series. Biol Cybern 1993;70(1):75–80.
[177] Van der Heyden M, Diks C, Pijn J, Velis D. Time reversibility of intracranial human eeg recordings in mesial temporal lobe epilepsy. Phys Lett A 1996;216(6):283–8.
[178] Schindler K, Rummel C, Andrzejak RG, Goodfellow M, Zubler F, Abela E, Wiest R, Pollo C, Steimer A, Gast H. Ictal time-irreversible intracranial eeg signals as markers of the epileptogenic zone. Clinical Neurophysiol 2016;127(9):3051–8.
[179] Yao W, Dai J, Perc M, Wang J, Yao D, Guo D. Permutation-based time irreversibility in epileptic electroencephalograms. Nonlinear Dyn 2020;100(1):907–19.
[180] Zanin M, Güntekin B, Aktürk T, Hanoğlu L, Papo D. Time irreversibility of resting-state activity in the healthy brain and pathology. Front Physiol 2020;10:1619.
[181] Costa M, Goldberger AL, Peng C-K. Broken asymmetry of the human heartbeat: loss of time irreversibility in aging and disease. Phys Rev Letters 2005;95(19):198102.
[182] Costa MD, Peng C-K, Goldberger AL. Multiscale analysis of heart rate dynamics: entropy and time irreversibility measures. Cardiovasc Eng 2008;8(2):88–93.
[183] Yao W, Yao W, Wang J. Equal heartbeat intervals and their effects on the nonlinearity of permutation-based time irreversibility in heart rate. Phys Lett A 2019;383(15):1764–71.
[184] K. Iwamoto, K. Sonobe, N. Komatsu, A gait recognition method using hmm, in: SICE 2003 Annual Conference (IEEE Cat. No. 03TH8734), Vol. 2, IEEE, 2003, pp. 1936–1941..
[185] Zhang D, Wang Y, Bhanu B. Age classification base on gait using hmm. In: 2010 20th International Conference on Pattern Recognition. IEEE; 2010. p. 3834–7.
[186] Orellana JN, Sixto AS, Torres BDLC, Cachadina ES, Martín PF, de la Rosa FB. Multiscale time irreversibility: Is it useful in the analysis of human gait? Biomed Signal Process Control 2018;39:431–4.
[187] Osoba MY, Rao AK, Agrawal SK, Lalwani AK. Balance and gait in the elderly: A contemporary review. Laryngoscope Investigative Otolaryngology 2019;4(1):143–53.
[188] Zanin M, Papo D. Algorithmic approaches for assessing irreversibility in time series: Review and comparison. Entropy 2021;23(11):1474.
[189] Torres BDLC, López MS, Cachadiña ES, Orellana JN. Entropy in the analysis of gait complexity: A state of the art. British J Appl Sci Technol 2013;3(4):1097.
[190] Yentes JM, Raffalt PC. Entropy analysis in gait research: methodological considerations and recommendations. Ann Biomed Eng 2021:1–12.
[191] Rosso OA, Larrondo H, Martin MT, Plastino A, Fuentes MA. Distinguishing noise from chaos. Phys Rev letters 2007;99(15):154102.
[192] Zurek WH. Complexity, entropy and the physics of information. CRC Press; 2018.
[193] Sethna J. Statistical mechanics: entropy, order parameters, and complexity, Vol. 14. USA: Oxford University Press; 2021.
[194] Pomeau Y. Symétrie des fluctuations dans le renversement du temps. Journal de Physique 1982;43(6):859–67.