10-2011

New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics

Leslie M. Decker
University of Nebraska at Omaha

Constantina O. Moraiti
University of Ioannina

Nicholas Stergiou
University of Nebraska at Omaha, nstergiou@unomaha.edu

Anastasios D. Georgoulis
University of Ioannina

Recommended Citation

Decker, Leslie M.; Moraiti, Constantina O.; Stergiou, Nicholas; and Georgoulis, Anastasios D., "New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics" (2011). *Journal Articles*. 89.
https://digitalcommons.unomaha.edu/biomechanicsarticles/89

New insights into anterior cruciate ligament deficiency and reconstruction through the assessment of knee kinematic variability in terms of nonlinear dynamics

Leslie M. Decker[1], Constantina Moraiti[2], Nicholas Stergiou[1,3,*], Anastasios D. Georgoulis[2]

[1]Nebraska Biomechanics Core Facility, University of Nebraska at Omaha, 6001 Dodge Street, Omaha, NE 68182-0216, USA.
[2]Orthopaedic Sports Medicine Center, Department of Orthopaedic Surgery, School of Medicine, University of Ioannina, Ioannina, Greece.
[3]Department of Environmental, Agricultural and Occupational Health Sciences, College of Public Health, University of Nebraska Medical Center, 987850 Nebraska Medical Center, Omaha, NE 68198-7850, USA.

*Corresponding author. Tel.: 402-5543247; fax: 402-5543693.
E-mail address: nstergiou@unomaha.edu (N. Stergiou).

Abstract

PURPOSE: Injuries to the anterior cruciate ligament (ACL) occur frequently, particularly in young adult athletes, and represent the majority of the lesions of knee ligaments. Recent investigations suggest that the assessment of kinematic variability using measures of nonlinear dynamics can provide with important insights with respect to physiological and pathological states. The purpose of the present article was to critically review and synthesize the literature addressing ACL-deficiency and reconstruction from a nonlinear dynamics standpoint.

METHODS: A literature search was carried out in the main medical databases for studies published between 1990 and 2010.

RESULTS: Seven studies investigated knee kinematic variability in ACL patients. Results provided support for the theory of “optimal movement variability”. Practically, loss below optimal variability is associated with a more rigid and very repeatable movement pattern, as observed in the ACL-deficient knee. This is a state of low complexity and high predictability. On the other hand, increase beyond optimal variability is associated with a noisy and irregular movement pattern, as found in the ACL-reconstructed knee, regardless of which type of graft is used. This is a state of low complexity and low predictability. In both cases, the loss of optimal variability and the associated high complexity leads to an incapacity to respond appropriately to the environmental demands, thus providing an explanation for vulnerability to pathological changes following injury.

CONCLUSION: Subtle fluctuations that appear in knee kinematic patterns provide invaluable insight into the health of the neuromuscular function after ACL rupture and reconstruction. It is thus critical to explore them in longitudinal studies and utilize nonlinear measures as an important component of post-reconstruction medical assessment.

LEVEL OF EVIDENCE: Level II

Introduction

Movement variability corresponds to the normal variations that occur in motor output across multiple repetitions of a task and has become a topic of major interest within the field of human movement sciences [107]. As introduced early by Bernstein in his seminal work [6], the generation of movement patterns consists of a “repetition without repetition” phenomenon in the sense that patterns never repeat exactly as themselves. Arrays of examples from daily life illustrate such phenomenon. When we walk, our footprints on sand or on snow never repeat themselves in the exact same fashion. In the same way, when we stand quietly, we continuously sway without being able to remain completely still. Until recently, such variations were considered as noisy variations, resulting from some random processes [30, 96, 97]. However, recent literature from different scientific domains has shown that many phenomena previously described as noisy are actually the results of nonlinear interactions and have deterministic origins, conveying important information regarding the system behavior [2, 30, 31].

Within this framework, many studies have investigated the complex fluctuations that appear in gait, with the aim of gaining deeper insights into this fundamental human activity [8, 15, 17, 18, 38-40, 60-62, 106, 120, 121]. Using tools from nonlinear dynamics, these studies demonstrated that the complex fluctuations are responsible for the flexible adaptations to everyday stresses placed on the human body during gait. They also established a clear link between complexity alteration and unhealthy states in gait. The aim of the present paper is then to review the major progress this approach has brought in terms of pathological knee understanding, with the ultimate goal of presenting working tracks with regards to rehabilitation programs that would slow down the development of long-term degenerative diseases.

The first section of the review will define the constructs of variability and complexity, illustrated briefly by means of a common human physiological rhythm: the heartbeat. The second section will focus on gait, investigating complexity under both healthy and unhealthy states and presenting different techniques of analyses. In the third section, the theory of “optimal movement variability”, which focuses on the benefits of having complex control of movement, with a balance between rigid control and randomness, will be presented. The last section will address thoroughly a widespread musculoskeletal injury, the anterior cruciate ligament (ACL) rupture, and then demonstrate that the examination of the subtle complex fluctuations that appear in gait provides invaluable insight into the health of the neuromuscular function after ACL rupture and reconstruction.

Nonlinear dynamics and its application to physiological rhythmicity

Physiological rhythms are central to life and concepts from fractals and chaos have provided a large body of knowledge into the nature of these rhythms [28], such as the fluctuations in heart rate [29, 34, 85, 98], systemic blood pressure [36, 37], and respiration [110, 119]. Under “normal” conditions, these rhythms are never strictly periodic but rather complex, fluctuating in a certain fashion over time [28]. On the other hand, alterations in these physiological rhythms, in the form of more regular or random fluctuations, have been associated to disease states [28] (See Appendix).

To illustrate these findings, let consider the beating of the heart, which is one of the most complex physiological rhythm in nature. This rhythm, which is evaluated through the beat-to-beat interval so-called R-R interval, results from the activity of the sinus node (i.e., the heart pacemaker), which is controlled by the autonomic portion of the nervous system. The autonomic system is composed of the sympathetic and parasympathetic branches with the former branch increasing the firing rate of the sinus-node cells and the latter branch inversely decreasing the firing rate. The pacemaker is then constantly under this tug-of-war between the two branches and as a result, the R-R interval which appears a-priori roughly constant is in fact highly variable over time [35]. Recently, different studies using concepts derived from the mathematical theory of chaos and fractals have plainly considered these fluctuations and provided deep insights into heart dynamics. In particular, fractal analyses were applied to the R-R interval and evaluated the dependence between fluctuations of the heartbeat on one time scale and those over multiple time scales [58, 84] (Figure 1). Fascinatingly, the presence of long-range correlations was revealed in the R-R interval time series, meaning that the interval at any instant depend on the interval at relatively remote times with this dependence decaying in a scale-free (fractal-like) power-law fashion. In other words, there is a long-memory process in the R-R series, with each value being dependent upon the global history of the series. In terms of biology, these long-range correlations have been proposed to accommodate for possible perturbations applied on the heart since they may prevent excessive “mode-locking” that would restrict its functional responsiveness (plasticity) [84]. Support for this inference is provided by findings obtained from severely pathologic states, such as heart failure, where the breakdown of long-range correlations is often accompanied by the emergence of a dominant frequency mode. Analogous transitions to highly periodic behavior have been observed in a wide range of other disease states, including certain malignancies, sudden cardiac death, epilepsy, and fetal distress syndromes [32, 33]. Moreover, many other techniques (e.g., approximate, sample, and multiscale entropies, largest Lyapunov and Hurst exponents, correlation dimension, recurrence quantification analysis) from nonlinear dynamics yielded invaluable insights into the pathophysiologic mechanisms associated with cardiac events [3, 21, 63, 82, 125]. Collectively, all these studies on heart dynamics confirmed the hypothesis that the properties of the heart behavior are of major importance for the maintenance of a healthy cardiovascular function and provided clinically important information on abnormal cardiovascular regulation that could not be uncovered using traditional analyses of heart rate variability.

[Insert Figure 1 about here]

Toward understanding complexity in gait

Concepts and methods described above to detect and quantify the behavior of the heartbeat time series can be applied to movements in human locomotion [83]. Locomotion is indeed a multifractal act arising from the couplings of multiple structures (e.g., motor cortex, cerebellum, basal ganglia, spinal cord) and inputs (e.g., information from vestibular, visual and peripheral receptors), and it has been shown that the locomotor outputs, as the stride interval, fluctuates over time under healthy/normal conditions. Although these subtle fluctuations between strides during walking appear to vary in a random manner (noise), with no correlation between the present and future strides, the healthy adult locomotor system actually possesses a kind of “motor memory”, such that the fluctuations from one stride to the next ones display a subtle, “hidden” temporal structure [39, 40, 120, 121]. The finding that these fluctuations are not random but rather contain such a structure has subsequently led to the idea that investigating this temporal organization may provide insight into how these movements are controlled to maintain a stable and flexible gait. Therefore, many investigations have examined whether key variables in walking, such as the linear or angular rhythmical motions of the joints and the stride time interval, display “hidden” properties [8, 15, 17, 18, 38-40, 60-62, 106, 120, 121]. In the next sections, we will focus our attention on two indicators from nonlinear dynamics, the largest Lyapunov exponent and the approximate entropy (ApEn), which are to our knowledge the only tools that have been used to investigate the fluctuations present during gait in patients with an anterior cruciate ligament injury.

Largest Lyapunov exponent (LyE)

In order to estimate LyE in gait, a first step consists in reconstructing the state space of a certain joint or limb in an abstract, multidimensional space, where the coordinates represents simply the values of some state variables (e.g., joint or limb angular displacements) characterizing the joint or the limb [24, 50, 106, 109]. In such a space, the set of all possible states that can be reached corresponds to the state space. The sequence of such states over the time scale defines a trajectory in the state space and, as time increases, this trajectory converges towards a low-dimensional indecomposable subset called an “attractor” which gives information about the asymptotic behaviour (periodic, chaotic or random) of the joint [106]. Most of time, the state space is reconstructed based on the Takens' delay embedding theorem [95, 111]. The reconstruction process involves creating time-lagged copies of the original joint kinematic time series [1, 22, 50]. These time lag copies are used to reconstruct the attractor [55] (Figure 2A and 2B). Despite variations in the kinematics parameters used to reconstruct the state space, all highlighted appropriate embedding dimensions higher than two (most of time around five for walking-derived time series), indicating that the attractors underlying the joints movements during human walking exceed a periodic attractor, converging possibly towards a strange attractor and suggesting that the observed movement’s patterns fluctuate over time in a chaotic way [8, 15, 17, 18]. Once the state space is reconstructed, LyE is calculated to determine the nonlinear structure of the reconstructed attractor. Specifically, LyE measures the average exponential rate of divergence of neighbouring trajectories of the attractor [1, 50, 93] (Figure 2C). Hence, a strictly periodic time series will have no divergence of points in the attractor, while a chaotic time series will have some divergence between two neighboring points as time progresses. Several algorithms have been proposed to compute LyE with the most popular being Wolf et al. and Rosenstein et al. [7, 14, 16, 93, 122].

Even though previous results strongly favored a chaotic nature of the fluctuations present in the gait patterns, all are hindered by the fact that the identification of chaos in time series is a very difficult process since purely random signals can mimic chaos and have sometimes been misdiagnosed as chaotic or vice versa [92, 112]. Thus, methods known as surrogate analyses have been used in gait to prevent such misdiagnoses [8, 15, 72, 106]. Technically, these analyses consist in the creation of a random counterpart of the original time series, by destroying its nonlinear structure. This counterpart is then embedded in an equivalent state space as the one of the original time series and similar topological parameters as those obtained from the original time series are calculated (e.g., LyE). Accordingly, differences in the parameters evaluated from the original time series and its surrogate counterpart indicate that the fluctuations over time in the original data are veritably chaotic and not randomly derived. The surrogate algorithms of Theiler et al. [112] and Theiler and Rapp [113] has been used in the past and related results support the notion that fluctuations in human gait have a deterministic pattern [8, 15, 39]. However, these algorithms have been shown of limited utility when applied to time series with strong pseudo-periodic behaviors as it is the case in gait. Thus, Small et al. [100] have consequently proposed another algorithm, the so-called pseudo-periodic surrogate (PPS) algorithm, to preserve the inherent periodic components while destroying the inter-cycle dynamics (nonlinear structure). In their recent work, Miller et al. [72] showed that both the PPS [100] and Theiler algorithms [112, 113] attest for the presence of chaotic fluctuations in gait, with more robust and suitable results using the PPS algorithm. Hence, using the state space reconstruction approach, the fluctuations in the gait patterns have been found to be chaotic, attesting the complexity of human gait dynamics.

From an application standpoint, LyE analyses have been successfully applied to several populations and the entire age spectrum, including new walkers with and without Down syndrome [15, 101], elderly fallers and non-fallers [67], and patients suffering from peripheral arterial disease [78], peripheral neuropathy [17, 69], anterior cruciate ligament deficiency of the knee [75, 77, 108, 124], and knee osteoarthritis [123]. Thus, using the LyE, a measure from the mathematical theory of chaos, these investigations have collectively led to a better understanding of why the nonlinear gait pattern is altered under certain conditions.

[Insert Figure 2 about here]

Approximate entropy (ApEn)

ApEn is well known for its ability to discern regularity and predictability from a wide variety of systems, including deterministic, stochastic, and composite systems, while being applicable to noisy medium-sized time series [51, 86, 87-90]. ApEn is strictly speaking a “regularity statistics” that reflects the likelihood that “similar” patterns of observations will not be followed by additional “similar observations”. From a mathematical standpoint, ApEn, better identified as ApEn (N, r, m), requires the determination of three unknown parameters, m, r, and l. The parameter m determines the length of the segments to be compared. The second parameter r is the tolerance threshold for accepting similar patterns between two segments, and has been recommended to be within 0.1-0.2 times the standard deviation using gait data [86, 88, 89]. Note that ApEn values vary significantly within the recommended range of r values. The most appropriate r value is the one that provides the maximum ApEn value [68]. The third parameter l is the embedding lag (e.g., $l = 1$ then adjacent points are used), which is set to be the smallest lag at which the autocorrelation function of the time series is close to 0. Typical values for gait data analysis are $m = 2$, $r = 0.2$ to 0.25 times the standard deviation of the data, and $l = 1$ [9, 25, 54, 59, 117] (Figure 3).

If the time series is random there will be a lot fewer similar vectors of length $m+1$ than there are of length m. If the time series has a repeating pattern, then there will be just as many similar vectors of length $m+1$ as there are of length m (i.e., the length of the vector wouldn't make any difference in how many repeats are found). For the analysis of a time series with unknown structure, the idea is to compare the number of similar vectors of length m with the number of similar vectors of length $m+1$, and use the result as a measure of the randomness of the time series. The ApEn typically ranges from 0 to 2. Values closer to 0 are consistent with greater periodicity and regularity. Conversely, values nearing 2 represent greater unpredictability and irregularity [86-88]. The higher the unpredictability is in a time series, the larger the value of the ApEn. In gait, the ApEn values obtained from joint kinematics were found generally in the range [0.28-0.50] [106]. Accordingly, the probability that similar patterns are followed by additional similar patterns in the gait time series is high, reflecting a high level of predictability. An important point to mention, however, is that ApEn is not genuinely able to dissociate between chaotic and random fluctuations of the gait patterns. To counter such a limitation, Miller et al. [72] have also applied surrogation techniques to their ApEn calculations and obtained ApEn values from the surrogated gait data (both Theiler and PPS algorithms) larger than the original ApEn values, confirming the presence of subtle chaotic fluctuations in gait.

Since recently, a growing number of human gait studies use ApEn in the hope of gaining insight into the fluctuations presents in the walking pattern and factors that affect them. For instance, ApEn has been successfully applied to lower limb joint kinematics of preadolescent children with Down syndrome [9], patients with anterior cruciate ligament deficiency of the knee [25, 76], Parkinson's disease patients after levodopa therapy [59], as well as to minimum foot clearance of older adults with a history of falls [53, 57]. Together, these investigations have revealed that ApEn correlates well with pathology while, in some cases, it is predictive of subsequent clinical outcomes.

[Insert Figure 3 about here]

Conceptual framework of movement variability

Variability of human gait offers many functional benefits. Multiple cortical and subcortical sites contribute to functional gait, that is, the skills required to carry out difficult tasks and negotiate a wide range of conditions. Specifically, this plasticity allows the locomotor system to cope with the exigencies of an unpredictable and changing environment. A reduction or deterioration of the chaotic nature of these temporal variations of the gait pattern represents a decline in the "healthy flexibility and adaptability" that is associated with rigidity and inability to adapt to stresses [33, 45, 64-66, 104, 105].

Using this framework as a foundation, Stergiou et al. [107] have proposed a model to explain the rhythms complexity as it relates to health. Through the study of movement variability they proposed the theory of "optimal movement variability", which is pioneering in the sense that it relates in an inverted U-shape relationship the concept of *complexity* with the concept of *predictability*. Practically at this optimal state of movement variability the biological system is in a healthy state and is characterized by the largest possible effective complexity (i.e., the uppermost point along the inverted U-shaped function), attaining high values only in the intermediate region between excessive order (i.e., maximum predictability) and excessive disorder (i.e., no predictability). This variability has deterministic structure and specifically chaotic and reflects the adaptability of the system to environmental stimuli and stresses. Decrease or loss of this optimal state of variability renders the system more predictable and more rigid. However, Stergiou et al. [107] also added that an increase beyond optimal variability renders the system more noisy, unstable and unpredictable. Both situations result in decreased complexity, which means decreased flexibility and adaptability to perturbations, such as those associated with unhealthy states (Figure 4).

[Insert Figure 4 about here]

Addressing ACL injury through knee kinematic variability

A specific musculoskeletal injury that could benefit from the theory of optimal movement variability is anterior cruciate ligament (ACL) rupture, which is a very common sports injury. In fact, lesions of the ACL occur frequently, particularly in young adult athletes, and represent the majority of the lesions of knee ligaments [48, 73]. The ACL is an important stabilizer of the knee joint. This is due not only to the mechanical properties of the ligament but also to the afferent information provided to the central nervous system by the mechanoreceptors that exist in the ACL [47, 99, 103]. The loss of the ACL is associated with excessive anterior tibial translation and tibial rotation [26, 70, 71]. Furthermore, ACL deficiency has been related to alterations in joint movement patterns during locomotion [5, 12, 26] and increased amount of osteoarthritis and meniscal injuries in the knee joint [11, 41, 71]. However, the underlying neural mechanisms responsible for this behavior of the ACL-deficient knee have not been understood. Assessing the functional dynamic knee stability (i.e., the stability of the knee during gait) using a nonlinear dynamic approach can enhance our understanding of these mechanisms. In addition, no consensus exists on the optimal treatment of this injury. For instance, a great controversy exists regarding the superiority of the autografts used for ACL reconstruction and how the disruption of the proprioceptive information provided by the ACL can be restored. Thus, specific questions could be investigated with respect to ACL injury and treatment through the study of knee kinematic variability. Such questions are: (1) how knee kinematic variability is affected in ACL rupture?; (2) is knee kinematic variability restored after ACL reconstruction and which autograft is the most suitable for ACL reconstruction?; and (3) which mechanisms underlying gait are revealed by studying knee kinematic variability through this injury?

Below we will address these questions by (1) reviewing our previous research to assess knee kinematic variability in ACL-deficient and ACL-reconstructed patients (summarized also in Table 1), and (2) discussing proposed theories for movement variability and its relationship under the results obtained from ACL-related studies to identify future directions for investigations.

ACL-deficient knees

In our first study [108], we investigated the effect of walking speed on kinematic variability of the ACL-deficient knee. The LyE was calculated from the knee joint flexion-extension time series (Table 1; Figure 2). The deficient knee had significantly more divergence in the knee flexion-extension movement trajectories over time than the contralateral intact knee. Furthermore, increases in walking speed did not affect the knee flexion-extension movement patterns for our subject population. Therefore, we proposed that the altered dynamical properties of the ACL-deficient knee lead to lack of ability to cope with various perturbations. Clinically, the ACL-deficient knee is less able to adjust to the unpredictable and ever changing environmental demands. Thus, the ACL-deficient knee over time develops further knee pathology possibly in terms of osteoarthritis and meniscal damage.

In a follow-up study [25], we sought to further verify that differences between the ACL-deficient and the contralateral intact knee do exist (Table 1). To this end, we used a different metric, the ApEn to examine the knee joint flexion-extension time series. Findings revealed that the ACL-deficient knee exhibited more regular patterns than the contralateral intact knees and verified the results of our first study. This clinically means that the loss of afferent proprioceptive input in the ACL-deficient knee resulted in a decrease in the adaptability of the system rendering it less able to adjust to perturbations. Furthermore, as walking speed increased the knee joint flexion-extension pattern became more irregular. This is probably due to the fact that faster walking requires the recruitment of additional resources (e.g., motor units), resulting in increased possibility of error (randomness) within the system.

In both previously reported studies, the ACL-deficient knee was compared to the contralateral intact knee. There is biomechanical evidence, however, that after ACL rupture, adaptations occur not only in the ACL-deficient knee but also in the intact contralateral knee, when compared to healthy controls [5, 20, 116]. Therefore, it was unclear if the results of the above mentioned studies could be generalized in terms of ACL deficiency and comparisons with healthy controls. Thus, in a follow-up study [75] we compared individuals diagnosed with ACL rupture using MRI criteria and matched healthy controls that walked with the same speed (Table 1). The LyE was calculated from the knee joint flexion-extension time series of both groups. As predicted, the results revealed that the ACL-deficient knee had a more rigid behavior as it was the case when was compared with the intact contralateral knee. Clinically, this increased rigidity means that the exact same areas of the articulating bones are loaded without any dispersion or distribution of pressure, providing a possible explanation why the ACL-deficient knee over time develops further injury and osteoarthritis.

Lastly, because backward walking is used by physical therapists to strengthen the hamstring muscles and thus improve the function of the knee joint of ACL-deficient patients, we recently investigated kinematic variability of the deficient knee during backward walking [124]. The results further verified the above findings since ACL deficiency resulted in more rigid movement patterns as compared to healthy controls that walked at the same speed. Thus, we verified that these findings are present regardless of direction of walking (forwards vs. backwards). Clinically, this could imply diminished functional responsiveness to the environmental demands for both knees of ACL-deficient patients, which may result in knees more susceptible to injury.

Collectively, all the above findings proved unequivocally that ACL deficiency causes altered variability in the knee flexion-extension movement patterns. These alterations may be due to altered muscular activity in the ACL-deficient patients to compensate for the loss of the ligament. Actually, it has been shown that the ACL plays an important role in knee stability because of its mechanical properties and the mechanoreceptors that exist in it [47, 103]. For instance, using both animal and human models, it has been demonstrated that the activation of the ACL mechanoreceptors induces hamstring contraction resisting anterior tibial translation (ACL-hamstring reflex) [19, 23, 114]. The loss of proprioceptive input from the mechanoreceptors that exist in the ACL may lead to changes in the central nervous system, which in turn leads to the development of altered muscular patterns and postural synergies [10, 13, 81]. For instance, Courtney et al. [17] showed that ACL-deficient patients exhibit altered somatosensory evoked potentials as well as different gastrocnemius and hamstrings activity during treadmill walking. Di Fabio et al. [13] reported the activation of a long loop, capsular hamstring reflex due to increased mechanical laxity at the ACL-deficient knee. In addition, it has been shown that there are indeed changes in the central nervous system after ACL rupture [118]. The above changes are reflected in alterations in variability in the knee flexion-extension movement patterns during walking implying diminished functional responsiveness to the environmental demands which could result in the deficient knees being more susceptible to future pathology. Recently, Tzagarakis et al. [115] suggested that a chronic ACL rupture generates less variability during walking than an acute ACL rupture, because of the adaptation mechanisms that are developed. Gradually progressing or chronic conditions allow an individual to adapt their gait patterns. This might explain the difference in results from their study [115] compared with our results obtained in chronic ACL rupture [25, 75, 108]. This should be a topic of further investigation in the future where longitudinal studies will provide critical insights.

The above also pointed towards another very important clinical question. If ACL reconstruction could restore variability in the knee flexion-extension movement patterns during walking to the normative levels of the healthy controls.

After ACL reconstruction

The purpose of ACL reconstruction is to restore the function of the knee to normal and prevent the development of any future pathology in the joint. Is this accomplished with respect to variability in the knee flexion-extension movement patterns during walking? Which of the two most commonly used autografts (bone-patellar tendon-bone [BPTB] and quadrupled semitendinosus-gracilis [ST/G]) is the most effective in restoring this variability after ACL reconstruction?

In order to answer these questions, we investigated the functional outcome after ACL reconstruction using either BPTB or quadrupled ST/G autografts [76] by evaluating the regularity of the knee joint flexion-extension motion patterns using

ApEn. Findings revealed that patients at two years after ACL reconstruction, using either BPTB or quadrupled ST/G, exhibited a more noisy and unpredictable knee flexion-extension movement patterns as compared to uninjured healthy matched controls who walked at the same speed. It is important clinically that there were no differences between the two grafts. As suggested in the literature, these results could be related to the altered neuromuscular activity found in the ACL-reconstructed knee. Hiemstra et al. demonstrated that there is both a knee extensor and knee flexor strength deficit [42], while there are also changes in the agonist/antagonist neuromuscular balance in the ACL-reconstructed knee using an ST/G autograft [43]. Practically, it has been shown that BPTB reconstructed knees exhibit an increased quadriceps strength deficit while the ST/G reconstructed knees have an increased hamstrings strength deficit [20]. These changes in muscular performance could be neural in origin. Specifically, the lack of afferent proprioceptive input due to the replacement of the natural ACL or the alterations at the harvesting site result in changes the neural control of the knee [46, 102]. Moreover, due to the different mechanics of the joint, the afferent input from the mechanoreceptors around the knee joint may be different from those of a healthy knee [56]. This is reflected in the variability analysis of the knee flexion-extension movement patterns during walking.

In our first study on ACL reconstruction [76], no data on the contralateral limb was reported; although it has been shown that after ACL reconstruction there are also biomechanical adaptations in the intact knee [20, 44]. We therefore used the LyE to investigate the variability in the knee flexion-extension movement patterns during walking after ACL reconstruction using either a BPTB or a quadrupled ST/G autograft [77]. Findings revealed that ACL reconstruction also altered the variability in the knee flexion-extension movement patterns during walking in the intact contralateral leg. We propose that this alteration is a compensatory mechanism in order to maintain some degree of symmetry between the two legs. This is consistent with previous studies that have identified bilateral lower extremity accommodations in gait biomechanics and muscular performance in ACL-reconstructed patient [20, 44]. Specifically, Hiemstra et al. [44] showed that there are strength deficits in the knee extensors and knee flexors also in the intact limb after ACL reconstruction, when compared to uninjured control group.

As mentioned earlier, ACL-deficient subjects exhibited decreased LyE and ApEn values (i.e., increased rigidity and regularity of the knee flexion-extension movement patterns). On the other hand, increased values were found after ACL reconstruction. In addition, no difference was found between the two grafts, which indicate a lack of superiority of one graft over the other with respect to knee kinematic variability.

Clinically, these results can be explained by the following hypothesis. An individual that now knows that the ACL is reconstructed feels “secure” to increase and add extra motion. However, since the proper proprioceptive channels are not there, knee motion variability and knee function are not restored to normative levels. On the contrary, ACL-deficient knee patients are more “careful” in the way they walk trying to eliminate any extra motion, and thus their walking is more rigid. Our results also signify that the present reconstruction techniques or the grafts used (i.e., single graft bundle, typical transtibial drilling of femoral tunnel) are not sufficient in restoring knee kinematic variability to normal. A possible explanation for the inability is the absence of complete reinstatement of the actual anatomy of the ACL [27, 52]. Cadaver and in vivo studies have highlighted limitations of current surgical approaches for restoring normal knee anatomy and function, and led to a surge of interest in anatomical ACL reconstructions that attempt to better reproduce the two-bundle anatomy and its insertion sites. Another possible explanation is that ACL reconstruction cannot restore the proprioceptive pathways found in a healthy knee [46, 102]. Accordingly, an ACL injury should be regarded as a neurophysiological dysfunction, not being a simple musculoskeletal injury [49]. Therefore, it is critical to improve our current reconstruction techniques to better replicate the actual morphology of the ACL and improve the ability of the joint to provide proprioceptive information via new rehabilitation techniques.

A new model to explain movement variability in ACL deficiency and reconstruction

The results from our studies provided support for the optimal movement variability proposition (Figure 4). Specifically, healthy gait is characterised by an optimal state of movement variability, which offers maximum complexity, where complexity is defined as highly variable fluctuations in physiological processes resembling chaos. This state allows for flexibility, adaptability, and ability to respond to unpredictable stimuli and stresses. In our above experiments this is the state that is exhibited by our healthy controls. Decrease or loss of this optimal state of movement variability is associated with a system that is more rigid and very repeatable, as we demonstrated in the ACL-deficient knee. This is a state of decreased complexity and high predictability (Figure 4). Increase beyond optimal variability is associated with a system, which is noisy and irregular, as we demonstrated in the ACL reconstructed knee. This is a state of decreased complexity and low predictability (Figure 4).

Furthermore, the impaired variability noted in the deficient or reconstructed knee using either graft could imply inability to respond to the environmental demands. It could therefore be speculated that this is the reason that both situations linked to susceptibility to further injury and development of future pathology. Indeed, long follow-up studies have shown an increased incidence of osteoarthritis in the ACL-deficient and reconstructed knees [4, 79, 80, 91]. However, and as we mention below, it is critical to explore variability in the knee movement patterns during walking in longitudinal studies and utilize nonlinear measures as an important component of post-reconstruction medical assessment.

Considerations for future works

Based on the above it is evident that the examination of knee kinematic variability can provide us with useful information concerning the changes that are introduced in the neuromuscular function after ACL rupture and reconstruction. However, much research work remains. We certainly need longitudinal studies with large numbers of patients enrolled where nonlinear variability measures of knee kinematics will be correlated to clinical and radiological findings. In addition we have not explored differences in knee kinematic variability between patients with complete ACL rupture that have instability with activities of daily living (non-copers) and those that had returned to all pre-injury activity without limitation (copers) [74, 94].

In addition, as stated earlier, the results on knee kinematic variability may signify the improvement of the current reconstruction techniques in order to better replicate the actual morphology of the ACL, and development of new rehabilitation techniques, which will improve the ability of the joint to provide proprioceptive information, may be needed. Thus, it is imperative to examine knee kinematic variability once new techniques have been developed.

Clinically, we believe that the examination of knee kinematic variability using nonlinear methodology can eventually become a routine examination among orthopaedic surgeons and sports medicine specialists to examine the functional outcome of an ACL reconstruction, or any disorder that affects gait, or even of rehabilitation programs. This practically will be for these clinicians what exactly cardiologists do with heart rate variability using the Holter devices. Similarly, we anticipate this to be an easy procedure, which will be based on the usage of a handheld and a wearable device that can acquire data from the patient while walking. The data from the wearable device (i.e. adhesive electrogoniometer) will be downloaded seamlessly to the handheld via wireless technology for evaluation. The software loaded on the handheld will be capable to analyze the data with nonlinear methodology and provide with comparisons to a normative database. In this fashion, the surgeon will be able to assess the complexity and repeatability of the knee movement patterns during walking. Based on this evaluation, recommendation can be made for further rehabilitation or return to sports.

Conclusion

Future sports medicine investigations should attempt to determine (1) the reliability of nonlinear measures in athletes with ACL reconstruction; (2) how long the values of nonlinear measures remain altered after ACL reconstruction; (3) what surgical techniques can lead to the eventual return of nonlinear values to normative levels; and (4) what neurophysiological or mechanical mechanisms explain the changes in nonlinear measures after ACL reconstruction. Ideally, these investigations would lead to the determination of whether altered values of the nonlinear measures after reconstruction are associated with an increased risk for subsequent injury recurrence and future knee pathology.

Acknowledgements

This work is supported by the NIH (K25HD047194 and 1K99AG033684), the NIDRR (H133G040118 and H133G080023), and the Nebraska Research Initiative.

References

[1] Abarbanel HDI (1996) Analysis of observed chaotic data. Springer, New York.

[2] Amato I (1992) Chaos breaks out at NIH, but order may come of it. Science 256:1763-1764.

[3] Baillie RT, Cecen AA, Erkal C (2009) Normal heartbeat series are nonchaotic, nonlinear, and multifractal: new evidence from semiparametric and parametric tests. Chaos 19:028503.

[4] Barrance PJ, Williams GN, Snyder-Mackler L, Buchanan TS (2006) Altered knee kinematics in ACL-deficient non-copers: a comparison using dynamic MRI. J Orthop Res 24:132-140.

[5] Berchuck M, Andriacchi TP, Bach BR, Reider B (1990) Gait adaptations by patients who have a deficient anterior crutiate ligament. J Bone Joint Surg Am 72:871-877.

[6] Bernstein NA (1967) The coordination and regulation of movements. Pergamon Press, Oxford.

[7] Bruijn SM, van Dieen JH, Meijer OG, Beek PJ (2009) Statistical precision and sensitivity of measures of dynamic gait stability. J Neurosci Meth 178:327-333.

[8] Buzzi UH, Stergiou N, Kurz MJ, Hageman PA, Heidel J (2003) Nonlinear dynamics indicates aging affects variability during gait. Clin Biomech 18:435-443.

[9] Buzzi UH, Ulrich BD (2004) Dynamic stability of gait cycles as a function of speed and system constraints. Motor Control 8:241-254.

[10] Courtney C, Rine RM, Kroll P (2005) Central somatosensory changes and altered muscle synergies in subjects with anterior cruciate ligament deficiency. Gait Posture 22:69-74.

[11] Daniel DM, Stone ML, Dobson BE, Fithian DC, Rossman DJ, Kaufman KR (1994) Fate of the ACL-injured patient. A prospective outcome study. Am J Sports Med 22:632-644.

[12] Devita P, Hortobagyi T, Barrier J, Torry M, Glover KL, Speroni DL, Money J, Mahar MT (1997) Gait adaptations before and after anterior cruciate ligament reconstruction surgery. Med Sci Sports Exerc 29:853-859.

[13] Di Fabio RP, Graf B, Badke MB, Breunig A, Jensen K (1992) Effect of knee joint laxity on long-loop postural reflexes: evidence for a human capsular-hamstring reflex. Exp Brain Res 90:189-200.

[14] Dingwell J, Robb R, Troy K, Grabiner M (2008) Effects of an attention-demanding task on dynamic stability during treadmill walking. J Neuroeng Rehabil 5:12.

[15] Dingwell JB, Cusumano JP (2000) Nonlinear time series analysis of normal and pathological human walking. Chaos 10:848-863.

[16] Dingwell JB, Cusumano JP, Cavanagh PR, Sternad D (2001) Local dynamic stability versus kinematic variability of continuous overground and treadmill walking. J Biomech Eng 123:27-32.

[17] Dingwell JB, Cusumano JP, Sternad D, Cavanagh PR (2000) Slower speeds in patients with diabetic neuropathy lead to improved local dynamic stability of continuous overground walking. J Biomech 33:1269-1277.

[18] Dingwell JB, Marin LC (2006) Kinematic variability and local dynamic stability of upper body motions when walking at different speeds. J Biomech 39:444-452.

[19] Dyhre-Poulsen P, Krogsgaard MR (2000) Muscular reflexes elicited by electrical stimulation of the anterior cruciate ligament in humans. J Appl Physiol 89:2191-2195.

[20] Ferber R, Osternig LR, Woollacott MH, Wasielewski NJ, Lee JH (2004) Bilateral accommodations to anterior cruciate ligament deficiency and surgery. Clin Biomech (Bristol, Avon) 19:136-144.

[21] Ferrario M, Magenes G, Campanile M, Carbone IF, Di Lieto A, Signorini MG (2009) Multiparameter analysis of heart rate variability signal for the investigation of high risk fetuses. Conf Proc IEEE Eng Med Biol Soc 2009:4662-4665.

[22] Fraser AM, Swinney HL (1986) Independent coordinates for strange attractors from mutual information. Phys Rev A 33:1134-1140.

[23] Fujita I, Nishikawa T, Kambic HE, Andrish JT, Grabiner MD (2000) Characterization of hamstring reflexes during anterior cruciate ligament disruption: in vivo results from a goat model. J Orthop Res 18:183-189.

[24] Gates DH, Dingwell, JB (2009) Comparison of different state space definitions for local dynamic stability analyses. J Biomech 42:1345-1349.

[25] Georgoulis AD, Moraiti C, Ristanis S, Stergiou N (2006) A novel approach to measure variability in the anterior cruciate ligament deficient knee during walking: The use of the Approximate Entropy in Orthopaedics. J Clin Monit Comput 20:11-18.

[26] Georgoulis AD, Papadonikolakis A, Papageorgiou CD, Mitsou A, Stergiou N (2003) Three-dimensional tibiofemoral kinematics of the anterior cruciate

ligament-deficient and reconstructed knee during walking. Am J Sports Med 31:75-79.

[27] Girgis FG, Marshall JL, Monajem A (1975) The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. Clin Orthop Relat Res 106:216-231.

[28] Glass L (2001) Synchronization and rhythmic processes in physiology. Nature 410:277-284.

[29] Glass L (2009) Introduction to controversial topics in nonlinear science: is the normal heart rate chaotic? Chaos 19:028501.

[30] Glass L, Mackey MC (1988) From clocks to chaos: The rhythms of life. Princeton University Press, Princeton, NJ.

[31] Gleick J (1987) Chaos: Making a new science. Viking Penguin, Inc., New York, NY.

[32] Goldberger AL (1996) Non-linear dynamics for clinicians: chaos theory, fractals and complexity at the bedside. Lancet 347:1312-1314.

[33] Goldberger AL (1997) Fractal variability versus pathologic periodicity: complexity loss and stereotypy in disease. Perspect Biol Med 40:543-561.

[34] Goldberger AL, Amaral LA, Hausdorff JM, Ivanov PCh, Peng CK, Stanley HE (2002) Fractal dynamics in physiology: alterations with disease and aging. Proc Natl Acad Sci U S A 99:2466-2472.

[35] Goldberger AL, Rigney DR, West BJ (1990) Chaos and fractals in human physiology. Sci Am 262:42-49.

[36] Griffith TM, Edwards DH (1994) EDRF suppresses chaotic pressure oscillations in isolated resistance artery without influencing intrinsic complexity. Am J Physiol 266:H1786-H1800.

[37] Griffith TM, Edwards DH (1994) Fractal analysis of role of smooth muscle Ca2+ fluxes in genesis of chaotic arterial pressure oscillations. Am J Physiol 266:H1801-H1811.

[38] Hausdorff JM, Mitchell SL, Firtion R, Peng CK, Cudkowicz ME, Wei JY, Goldberger AL (1997) Altered fractal dynamics of gait: Reduced stride-interval correlations with aging and Huntington’s disease. J Appl Physiol 82:262-269.

[39] Hausdorff JM, Peng CK, Ladin Z, Wei JY, Goldberger AL (1995) Is walking a random walk? Evidence for long-range correlations in the stride interval of human gait. J Appl Physiol 78:349-358.

[40] Hausdorff JM, Purdon PL, Peng CK, Ladin Z, Wei JY, Goldberger AL (1996) Fractal dynamics of human gait: Stability of long-range correlations in stride interval fluctuations. J Appl Physiol 80:1448-1457.

[41] Hawkins RJ, Misamore GW, Merritt TR (1986) Follow-up of the acute non-operative isolated anterior cruciate ligament tear. Am Sports Med 14:205-210.

[42] Hiemstra LA, Webber S, MacDonald PB, Kriellaars DJ (2000) Knee strength deficits after hamstring tendon and patellar tendon anterior cruciate ligament reconstruction. Med Sci Sports Exerc 32:1472-1479.

[43] Hiemstra LA, Webber S, MacDonald PB, Kriellaars DJ (2004) Hamstrings and quadriceps strength balance in normal and hamstring anterior cruciate ligament-reconstructed subjects. Clin J Sport Med 14:274-280.

[44] Hiemstra LA, Webber S, MacDonald PB, Kriellaars DJ (2007) Contralateral limb strength deficits after anterior cruciate ligament reconstruction using a hamstring tendon graft. Clin Biomech (Bristol, Avon) 22:543-550.

[45] Hong SL (2007) The dynamics of structural and functional complexity across the lifespan. Nonlinear Dynamics Psychol Life Sci 11:219-234.

[46] Johansson H, Sjölander P, Sojka P (1990) Activity in receptor afferents from the anterior cruciate ligament evokes reflex effects on fusimotor neurones. Neurosci Res 8:54-59.

[47] Johansson, H., Sjolander, P., Sojka, P (1991) A sensory role for the cruciate ligaments. Clin Orthop 268:161-178.

[48] Johnson R (1983) The anterior cruciate ligament problem. Clin Orthop Relat Res 172:14-18.

[49] Kannus P, Järvinen M (1987) Conservatively treated tears of the anterior cruciate ligament: long term results. J Bone Joint Surg Am 69:1007-1012.

[50] Kantz H, Schreiber S (1997) Nonlinear time series analysis. Cambridge University Press, Cambridge, UK.

[51] Kaplan DT, Furman MI, Pincus SM, Ryan SM, Lipsitz LA, Goldberger AL (1991) Aging and the complexity of cardiovascular dynamics. Biophys J 59:945-949.

[52] Kapreli E, Athanasopoulos S (2006) The anterior cruciate ligament deficiency as a model of brain plasticity. Med Hypotheses 67:645-650.

[53] Karmakar CK, Khandoker AH, Begg RK, Palaniswami M, Taylor S (2007) Understanding ageing effects by approximate entropy analysis of gait variability. Conf Proc IEEE Eng Med Biol Soc 2007:1965-1968.

[54] Katsavelis D, Mukherjee M, Decker L, Stergiou N (2010) Variability of lower extremity joint kinematics during backward walking in a virtual environment. Nonlinear Dynamics Psychol Life Sci 14:165-178.

[55] Kennel MB, Brown R, Abarbanel HD (1992) Determining embedding dimension for phase space-reconstruction using a geometrical construction. Phys Rev A 45:3403:3411.

[56] Khalsa PS, Grigg P (1996) Responses of mechanoreceptor neurons in the cat knee joint capsule before and after anterior cruciate ligament transection. J Orthop Res 14:114-122.

[57] Khandoker AH, Palaniswami M, Begg RK (2008) A comparative study on approximate entropy measure and poincaré plot indexes of minimum foot clearance variability in the elderly during walking. J Neuroeng Rehabil 5:4.

[58] Kobayashi M, Musha T (1982) 1/f fluctuation of heartbeat period. IEEE Trans Biomed Eng 29:456-457.

[59] Kurz MJ, Hou JG (2010) Levodopa influences the regularity of the ankle joint kinematics in individuals with Parkinson's disease. J Comput Neurosci 28:131-136.

[60] Kurz MJ, Stergiou N (2005) An artificial neural network that utilizes hip joint actuations to control bifurcations and chaos in a passive dynamic bipedal walking model. Biol Cybern 93:213-221.

[61] Kurz MJ, Stergiou N (2007) Do horizontal propulsive forces influence the nonlinear structure of locomotion? J Neuroeng Rehabil 15:4-30.

[62] Kurz MJ, Stergiou N (2007) Hip actuations can be used to control bifurcations and chaos in a passive dynamic walking model. J Biomech Eng 129:216-222.

[63] Liebovitch, LS, Todorov, AT, Zochowski M, Scheurle D, Colgin L, Wood MA, Ellenbogen, KA, Herre JM, Bernstein RC (1999) Nonlinear properties of cardiac rhythm abnormalities. Physical Review E 59:3312-3319.

[64] Lipsitz LA (2002) Dynamics of stability: the physiologic basis of functional health and frailty. J Gerontol A Biol Sci Med Sci 57:B115-B125.

[65] Lipsitz LA (2004) Physiological complexity, aging, and the path to frailty. Sci Aging Knowledge Environ 2004:pe16.

[66] Lipsitz LA, Goldberger AL (1992) Loss of “complexity” and aging. Potential applications of fractals and chaos theory to senescence. JAMA 267:1806-1809.

[67] Lockhart TE, Liu J (2008) Differentiating fall-prone and healthy adults using local dynamic stability. Ergonomics 51:1860-1872.

[68] Lu S, Chen X, Kanters JK, Solomon IC, Chon KH (2008) Automatic selection of the threshold value R for approximate entropy. IEEE Trans Biomed Eng 55:1966-1972.

[69] Manor B, Li L (2009) Characteristics of functional gait among people with and without peripheral neuropathy. Gait Posture 30:253-256.

[70] Marans HJ, Jackson RW, Glossop ND, Young C (1989) Anterior cruciate ligament insufficiency: a dynamical three dimensional motion analysis. Am J Sports Med 17:325-332.

[71] McDaniel Jr WJ, Dameron Jr TB (1980) Untreated ruptures of the anterior cruciate ligament. A follow-up study. J Bone Joint Surg Am 62:696-705.

[72] Miller DJ, Stergiou N, Kurz MJ (2006) An improved surrogate method for detecting the presence of chaos in gait. J Biomech 39:2873-2876.

[73] Miyasaka KC, Daniel DM, Stone ML, Hirshman P (1991) The incidence of knee ligament injuries in the general population. Am J Knee Surg 4:3-8.

[74] Moksnes H, Snyder-Mackler L, Risberg MA (2008) Individuals with an anterior cruciate ligament-deficient knee classified as noncopers may be candidates for nonsurgical rehabilitation. J Orthop Sports Phys Ther 38:586-595.

[75] Moraiti C, Stergiou N, Ristanis S, Georgoulis AD (2007) ACL deficiency affects stride-to-stride variability as measured using nonlinear methodology. Knee Surg Sports Traumatol Arthrosc 15:1406-1413.

[76] Moraiti CO, Stergiou N, Ristanis S, Vasiliadis HS, Patras K, Lee C, Georgoulis AD (2009) The effect of anterior cruciate ligament reconstruction on stride-to-stride variability. Arthroscopy 25:742-749.

[77] Moraiti CO, Stergiou N, Vasiliadis HS, Motsis E, Georgoulis A (2010) Anterior cruciate ligament reconstruction results in alterations in gait variability. Gait Posture 32:169-175.

[78] Myers SA, Johanning JM, Stergiou N, Celis RI, Robinson L, Pipinos II (2009) Gait variability is altered in patients with peripheral arterial disease. J Vasc Surg 49:924-931.

[79] Noyes FR, Matthews DS, Mooar PA, Grood ES (1983) The symptomatic anterior cruciate-deficient knee, part II: the results of rehabilitation, activity modification and counseling on functional disability. J Bone Joint Surg Am 65:163-174.

[80] Noyes FR, Mooar PA, Matthews DS, Butler DL (1983) The symptomatic anterior cruciate-deficient knee, part I: the long term functional disability in athletically active individuals. J Bone Joint Surg Am 65:154-162.

[81] Pailhous J, Bonnard M (1992) Steady-state fluctuations of human walking. Behav Brain Res 47:181-189.

[82] Patangay A, Zhang Y, Lewicke A (2009) Measures of cardiac contractility variability during ischemia. Conf Proc IEEE Eng Med Biol Soc 4198-4201.

[83] Peng C-K, Hausdorff JM, Goldberger AL (2000) Fractal mechanisms in neural control: Human heartbeat and gait dynamics in health and disease. In: Walleczek J (ed) Self-organized biological dynamics and nonlinear control. Cambridge University Press, Cambridge, UK.

[84] Peng C-K, Mietus J, Hausdorff JM, Havlin S, Stanley HE, Goldberger AL (1993) Long-range anticorrelations and non-Gaussian behavior of the heartbeat. Phys Rev Lett 70:1343-1346.

[85] Pikkujämsä SM, Mäkikallio TH, Sourander LB, Räihä IJ, Puukka P, Skyttä J, Peng CK, Goldberger AL, Huikuri HV (1999) Cardiac interbeat interval dynamics from childhood to senescence: comparison of conventional and new measures based on fractals and chaos theory. Circulation 100:393-399.

[86] Pincus SM (1991) Approximate entropy as a measure of system complexity. Proc Natl Acad Sci U S A 88:2279-2301.

[87] Pincus SM (2000) Irregularity and asynchrony in biologic network signals. Methods Enzymol 321:149-182.

[88] Pincus SM, Gladstone IM, Ehrenkranz RA (1991) A regularity statistic for medical data analysis. J Clin Monit 7:335-345.

[89] Pincus SM, Viscarello RR (1992) Approximate entropy: a regularity measure for fatal heart rate analysis. Obstet Gynecol 79:249-255.

[90] Pincus, SM, Keefe, DL (1992) Quantification of hormone pulsatility via an approximate entropy algorithm. Am J Physiol 262:E741-E754.

[91] Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J (2007) A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: A controlled, prospective trial. Am J Sports Med 35:564-574.

[92] Rapp PE (1994) A guide to dynamical analysis. Integr Psychol Behav 29:311-327.

[93] Rosenstein MT, Collins JJ, De Luca CJ (1993) A practical method for calculating largest Lyapunov exponents from small data sets. Physica D 65:117-134.

[94] Rudolph KS, Eastlack ME, Axe MJ, Snyder-Mackler L (1998) Movement patterns after anterior cruciate ligament injury: a comparison of patients who compensate well for the injury and those who require operative stabilization. J Electromyogr Kinesiol 8:349-362.

[95] Ruelle D, Takens F (1971) On the nature of turbulence. Commun Math Phys 20:167-192.

[96] Schmidt RA (2003) Motor schema theory after 27 years: Reflections and implications for a new theory. Res Q Exerc Sport 74:366-375.

[97] Schmidt RA, Lee TD (2005) Motor control and learning: A behavioral emphasis. Human Kinetics Publishers, Champaign, IL.

[98] Shiogai Y, Stefanovska A, McClintock PV (2010) Nonlinear dynamics of cardiovascular ageing. Phys Rep 488:51-110.

[99] Sjölander P, Johansson H, Djupsjöbacka M (2002) Spinal and supraspinal effects of activity in ligament afferents. J Electromyogr Kinesiol 12:167-176.

[100] Small M, Yu D, Harrison RG (2001) Surrogate test for pseudoperiodic time series data. Phys Rev Lett 87:8101-8104.

[101] Smith BA, Stergiou N, Ulrich BD (2010) Lyapunov exponent and surrogation analysis of patterns of variability: profiles in new walkers with and without down syndrome. Motor Control 14:126-142.

[102] Solomonow M, Baratta R, Zhou BH, Shoji H, Bose W, Beck C, D'Ambrosia R (1987) The synergistic action of the anterior cruciate ligament and thigh muscles in maintaining joint stability. Am J Sports Med 15:207-213.

[103] Solomonow M, Krogsgaard M (2001) Sensimotor control of knee stability. A review. Scand J Med Sci Sports 11:64-80.

[104] Sosnoff JJ, Newell KM (2008) Age-related loss of adaptability to fast time scales in motor variability. J Gerontol B Psychol Sci Soc Sci 63:P344-P352.

[105] Sosnoff JJ, Voudrie SJ (2009) Practice and age-related loss of adaptability in sensorimotor performance. J Mot Behav 41:137-146.

[106] Stergiou N, Buzzi UH, Kurz MJ, Heidel J (2004) Nonlinear tools in human movement. In: Stergiou N (ed) Innovative analyses of human movement. Human Kinetics, Champaign, IL, pp 63-90.

[107] Stergiou N, Harbourne RT, Cavanaugh JT (2006) Optimal movement variability: A new theoretical perspective for neurologic physical therapy. J Neurol Phys Ther 30:120-129.

[108] Stergiou N, Moraiti C, Giakas G, Ristanis S, Georgoulis AD (2004) The effect of the walking speed on the stability of the anterior cruciate ligament deficient knee. Clin Biomech (Bristol, Avon) 19:957-963.

[109] Strogatz SH (1994) Nonlinear dynamics and chaos: With applications to physics, biology, chemistry, and engineering. Addison-Wesley, Reading, MA.

[110] Szeto HH, Cheng PY, Decena JA, Cheng Y, Wu DL, Dwyer G (1992) Fractal properties in fetal breathing dynamics. Am J Physiol 263:R141-R147.

[111] Takens F (1981) Detecting strange attractors in turbulence. In: Rand D, Young LS (eds) Lecture notes in mathematics: Dynamical systems and turbulence. Springer-Verlag, Berlin, Vol. 898, pp 366-381.

[112] Theiler J, Eubank S, Longtin A, Galdrikian B, Farmer JD (1992) Testing for nonlinearity in time series: the method of surrogate data. Physica D 58:77-94.

[113] Theiler J, Rapp PE (1996) Re-examination of the evidence for low-dimensional, nonlinear structure in the human electroencephalogram. Electroen Clin Neuro 98:213-222.

[114] Tsuda E, Okamura Y, Otsuka H, Komatsu T, Tokuya S (2001) Direct evidence of the anterior cruciate ligament-hamstring reflex arc in humans. Am J Sports Med 29:83-87.

[115] Tzagarakis GN, Tsivgoulis SD, Papagelopoulos PJ, Mastrokalos DS, Papadakis NC, Kampanis NA, Kontakis GM, Nikolaou PK, Katonis PG (2010) Influence of acute anterior cruciate ligament deficiency in gait variability. J Int Med Res 38:511-525.

[116] Urbach D, Nebelung W, Weiler HT, Awiszus F (1999) Bilateral deficit of voluntary quadriceps muscle activation alter unilateral ACL tear. Med Sci Sports Exerc 31:1691-1696.

[117] Vaillancourt DE, Newell KM (2000) The dynamics of resting and postural tremor in Parkinson's disease. Clin Neurophysiol 111:2046-2056.

[118] Valeriani M, Restuccia D, DiLazzaro V, Franceschi F, Fabbriciani C, Tonali P (1996) Central nervous system modifications in patients with lesion of the anterior cruciate ligament of the knee. Brain 119:1751-1762.

[119] Wessel N, Riedl M, Kurths J (2009) Is the normal heart rate "chaotic" due to respiration? Chaos 19:028508.

[120] West BJ, Griffin L (1998) Allometric control of human gait. Fractals 6:101-108.

[121] West BJ, Griffin L (1999) Allometric control, inverse power laws and human gait. Chaos Solitons Fractals 10:1519-1527.

[122] Wolf A, Swift JB, Swinney HL, Vastano JA (1965) Determining Lyapunov exponents from a time series. Physica D 16:285-317.

[123] Yakhdani HR, Bafghi HA, Meijer OG, Bruijn SM, van den Dikkenberg N, Stibbe AB, van Royen BJ, van Dieën JH (2010) Stability and variability of knee kinematics during gait in knee osteoarthritis before and after replacement surgery. Clin Biomech (Bristol, Avon) 25:230-236.

[124] Zampeli F, Moraiti CO, Xergia S, Tsiaras VA, Stergiou N, Georgoulis AD (2010) Stride-to-stride variability is altered during backward walking in anterior cruciate ligament deficient patients. Clin Biomech (Bristol, Avon) 25:1037-41.

[125] Zbilut JP, Thomasson N, Webber CL (2002) Recurrence quantification analysis as a tool for nonlinear exploration of nonstationary cardiac signals. Med Eng Phys 24:53-60.

APPENDIX

The behavior of a continuously changing system can be periodic, random or chaotic. Periodic systems are organized and are repeatable and predictable **(Figure A)**. Random systems, on the other hand, contain no order and are unpredictable. Their behavior is never repeated **(Figure B)**. Chaotic systems have characteristics of both. They seem to be random but they contain order and are deterministic in nature. They are unpredictable, very flexible and can operate under various conditions **(Figure C)**.

Figure A

Graphic representation of a periodic system [sin(1/10)] **(a)** and the corresponding phase plane plot **(b)**, where the time series data is plotted versus the first derivative. The LyE and ApEn value for this system are 0.1 and 0 respectively.

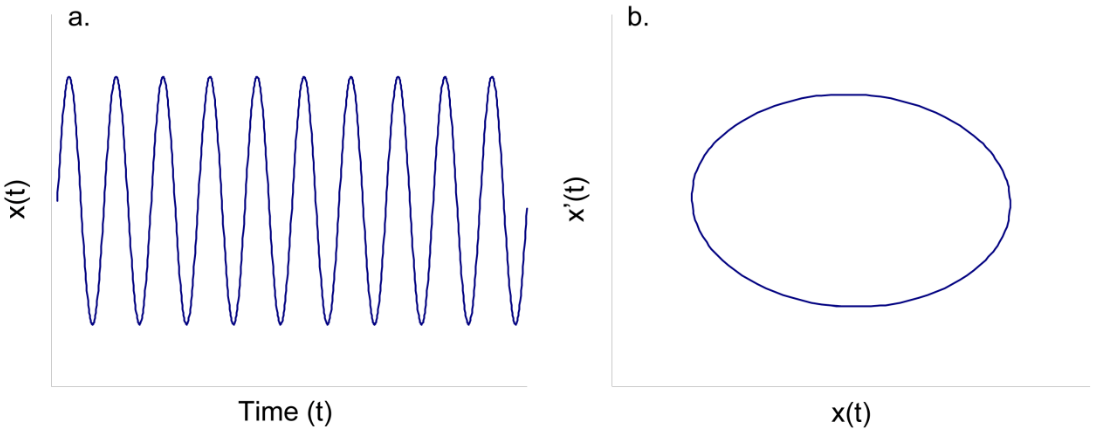

Figure B

Graphic representation of a random system (Gaussian noise centered on zero and a standard deviation of 1.0) **(a)** and the corresponding phase plane plot **(b)**. The LyE and ApEn value for this system are 0.1 and 0.45 respectively.

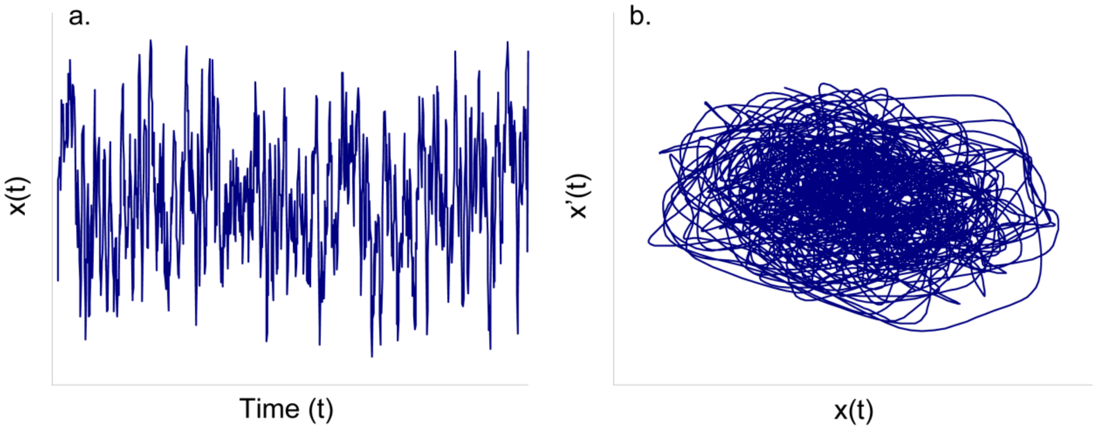

Figure C

Graphic representation of a chaotic system (the Lorentz attractor) **(a)** and the corresponding phase plane plot **(b)**. The LyE and ApEn value for this system are 0.469 and 2 respectively.

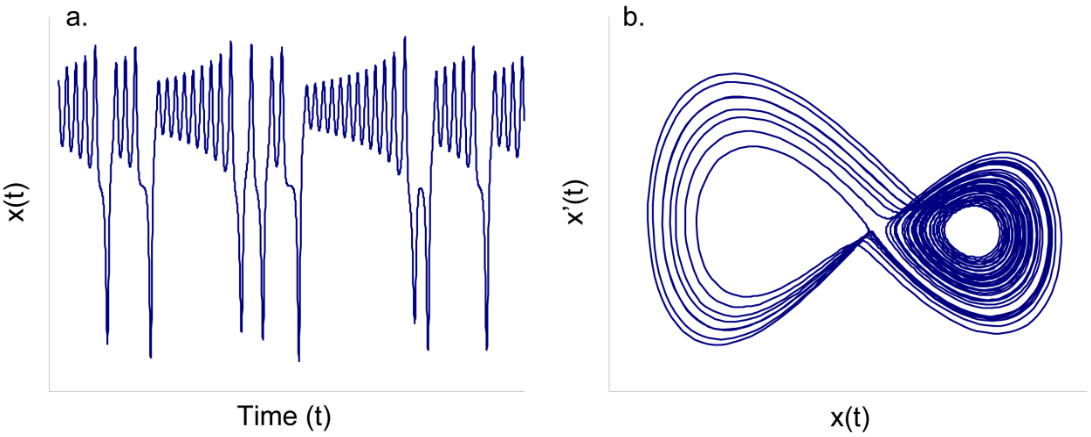

FIGURE LEGENDS

Figure 1. **(A)** An electrocardiogram (ECG) record, representing the electrical activity of the heart over time. The R-R interval represents the time duration between two consecutive R waves. **(B)** R-R interval time series. Even though the interval is fairly constant, it fluctuates about its mean (solid line) in an apparently erratic manner. The data used for the traces (A) and (B) were obtained from the free web resources available on Physionet (http://www.physionet.org).

Figure 2. Illustration of the calculation of the largest Lyapunov exponent (LyE) from the phase plane of an ACL-deficient knee motion. **(A)** An original ACL-deficient knee angle flexion-extension time series. The time series has been shorten to only a few strides for a clarity purpose. **(B)** The corresponding phase plane, with x(t) the angular position and x'(t) the angular velocity. **(C)** A section of the state space where the divergence of neighboring trajectories is outlined. The LyE is calculated from the exponential divergence of nearest neighbors of the attractor over time.

Figure 3. Illustration of the calculation procedure of the Approximate Entropy (ApEn) from an original ACL-deficient knee angle flexion extension time series. The time series has been shorten to only a few strides for a clarity purpose. **(A)** The time series is first divided up into short vectors of similar length m. One of these vectors is represented on the figure by the arrow between the points u(44) and u(45). Then, for each of the vectors, the procedure consists of counting up how many of the other vectors are similar. Vectors are considered similar to the original vector when their tails and tips are contained within a band of width r above and below those of the original vector, here u(44) ± r and u(45) ± r. The vectors that have been found similar to the original vector [u(44);u(45)] are represented by the other arrows. Note that the input parameters m and r have been set to 2 and 0.6 x standard deviation of the time series as it is commonly done in gait studies. **(B)** Such a procedure is then repeated for vectors that are one longer, i.e. length of m+1. ApEn is then obtained by calculating the natural logarithm of the relative prevalence of repetitive patterns of length m compared with those of length m+1.

Figure 4. Theoretical model of optimal movement variability as it relates to health. Adapted from Stergiou et al. [107]. In this theoretical model, greater complexity is characterized by chaotic fluctuations and is associated with a healthy state of the underlying system while lesser decreased complexity is associated with both periodic and random fluctuations where the system is either too rigid or too unstable. Both

situations characterize systems that are less adaptable to perturbations, such as those associated with unhealthy states. The notion of predictability has also been implemented in the model, mainly to differentiate between the random (too unstable) and periodic (too rigid) rhythms. Indeed, low predictability is associated with random/noisy and unstable systems, while high predictability is associated with periodic systems that are highly repeatable and rigid in their behaviors. In between there are chaotic, highly complex, based behaviors where the systems are neither too noisy nor too rigid. The individual signals are presented in Appendix.

Figure 1

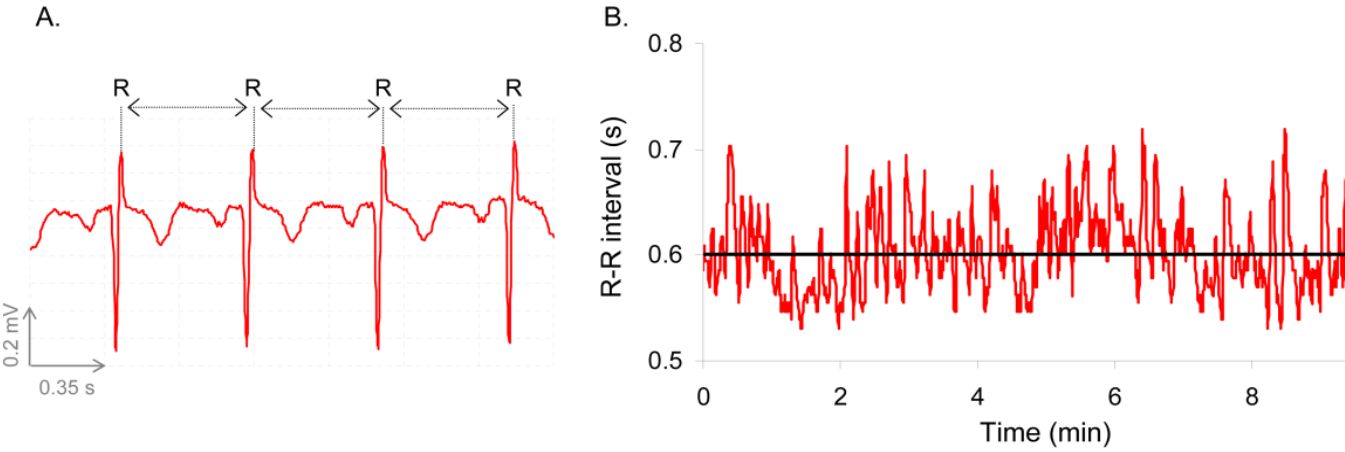

Figure 2

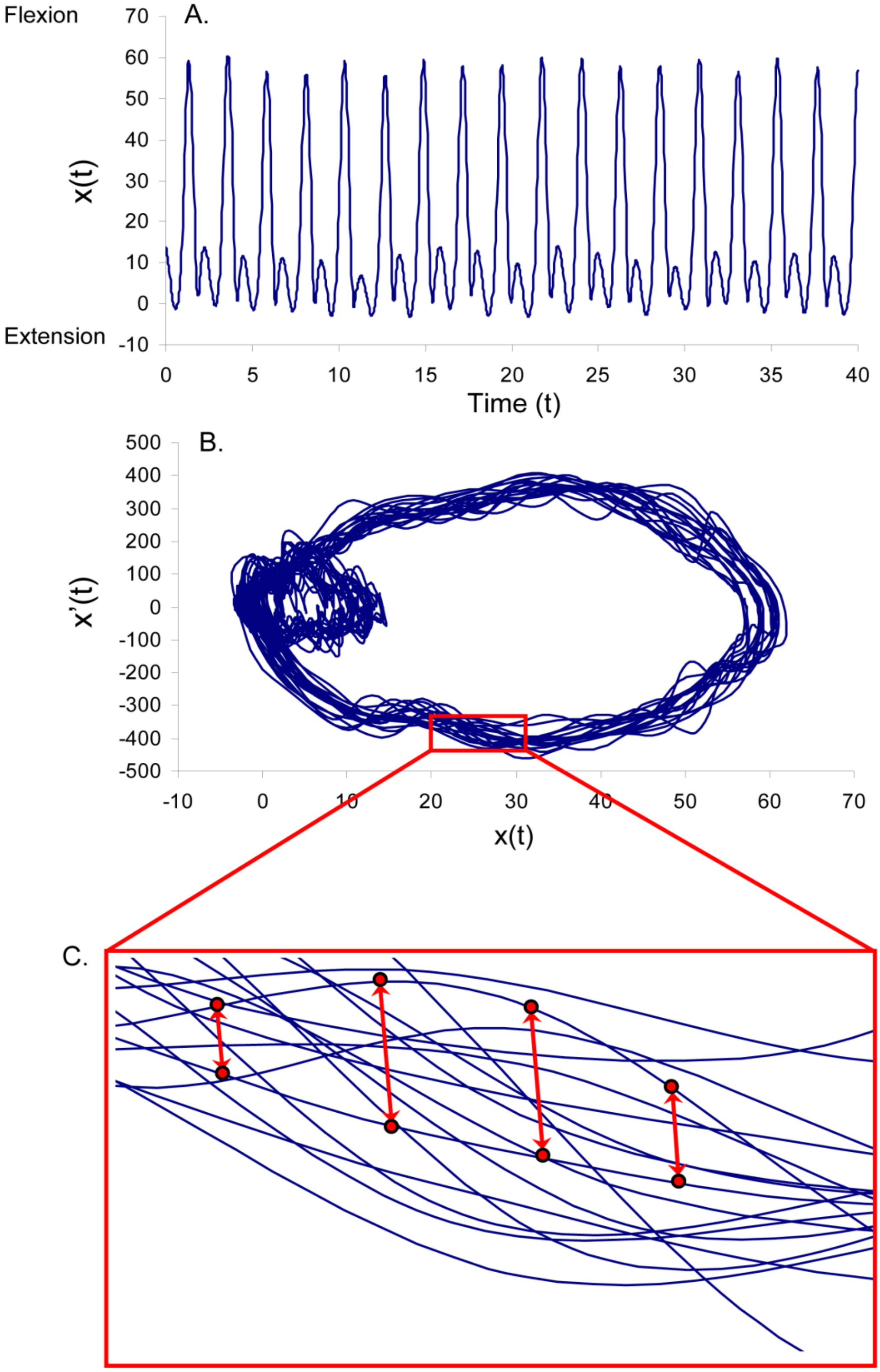
A.
Flexion
Extension
x(t)
70
60
50
40
30
20
10
0
-10
0
5
10
15
20
25
30
35
40
Time (t)
B.
x'(t)
500
400
300
200
100
0
-100
-200
-300
-400
-500
-10
0
10
20
30
40
50
60
70
x(t)
C.

Figure 3

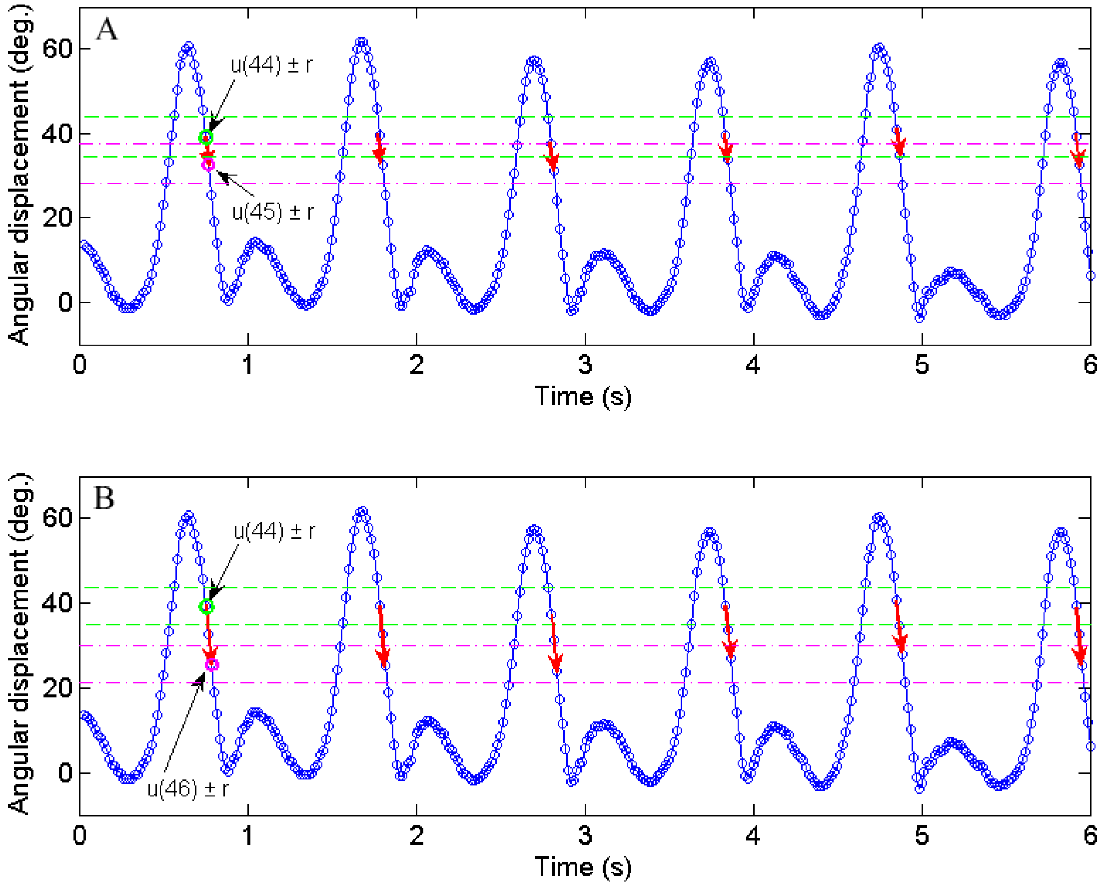
A
u(44) ± r
u(45) ± r
B
u(44) ± r
u(46) ± r
Angular displacement (deg.)
60
40
20
0
Time (s)
0
1
2
3
4
5
6

Figure 4

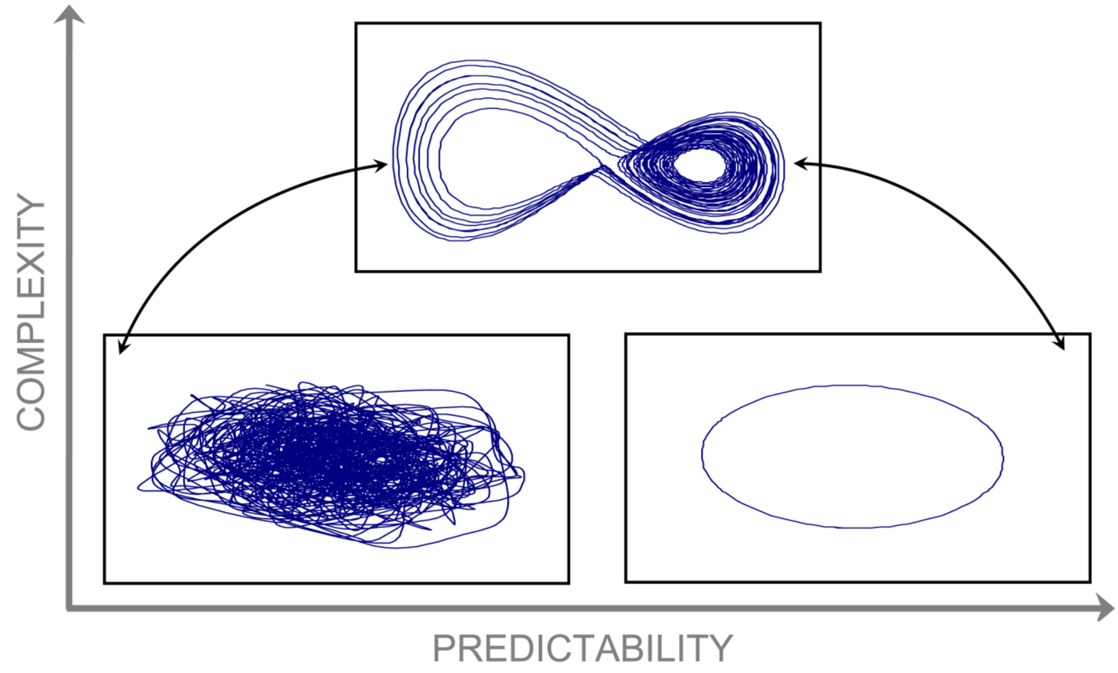

Table 1. Summary of main results.

Authors	Comparisons/Metrics	Results
	ACL DEFICIENCY	
Stergiou et al. Clin. Biomech. [64]	Patients with unilateral ACL-deficiency (deficient vs. intact knee) Metric: LyE of knee angular displacement	The ACL-deficient knee exhibited larger LyE values than the contralateral intact knee. Increases in walking speed did not alter the LyE values for either knee (deficient and intact).
Georgoulis et al. J. Clin. Monit. Comput. [76]	Patients with unilateral ACL-deficiency (deficient vs. intact knee) Metric: ApEn of knee angular displacement	The ACL-deficient knee exhibited lower ApEn values (greater regularity) than the contralateral intact knee. ApEn values increased with increases in walking speed, regardless of deficiency status.
Moraiti et al. Knee Surg. Sports Traumatol. Arthrosc. [65]	Patients with unilateral ACL-deficiency vs. healthy controls Metric: LyE of knee angular displacement	Patients exhibited lower LyE values than healthy controls.
Tzagarakis et al. J Int. Med. Res. [110]	Patients with acute isolated ACL rupture vs. healthy controls Metric: GEDEM index of medio-lateral trunk acceleration	Patients exhibited higher GEDEM index than healthy controls. A ROC analysis was used to assess the diagnostic value of the method and to determine a cut-off entropy value. The GEDEM cut-off value had a 95.6% probability of separating patients from controls.
Zampeli et al. Clin. Biomech. [66]	Patients with unilateral ACL-deficiency vs. healthy controls (backward walking) Metric: LyE of knee angular displacement	Both knees of the patients exhibited lower LyE values than those of healthy controls, revealing more rigid motion pattern. The intact knee of the patients showed lower LyE values than their deficient knee. These results hold regardless of walking direction (forwards in [65] vs. backwards in [66]).
	ACL RECONSTRUCTION	
Moraiti et al. Arthroscopy [80]	Patients with BPTB vs. with quadrupled ST/G ACL-reconstruction vs. healthy controls Metric: ApEn of knee angular displacement	Both patient groups had larger ApEn values (greater irregularity) than healthy controls. No significant differences were found between the two autografts.
Moraiti et al. Gait Posture [67]	Patients with BPTB vs. with quadrupled ST/G ACL-reconstruction vs. healthy controls Metric: LyE of knee angular displacement	Both patient groups had larger LyE values than healthy controls, although clinical outcomes indicated complete restoration. No significant differences were found between the two autografts. The intact contralateral knee had larger LyE than the ACL-reconstructed knee in both patient groups.

LyE: Largest Lyapunov exponent
ApEn: Approximate entropy
GEDEM: Gait Evaluation Differential Entropy