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# ACL deficiency affects stride-to-stride variability as measured using nonlinear methodology

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**Abstract** Previous studies suggested that the small fluctuations present in movement patterns from one stride to the next during walking can be useful in the investigation of various pathological conditions. Previous studies using nonlinear measures have resulted in the development of the "loss of complexity hypothesis" which states that disease can affect the variability and decrease the complexity of a system, rendering it less able to adjust to the ever changing environmental demands. The nonlinear measure of the Lyapunov Exponent (LyE) has already been used for the assessment of stride-to-stride variability in the anterior cruciate ligament (ACL) deficient knee in comparison to the contralateral intact knee. However, there is biomechanical evidence that after ACL rupture, adaptations are also present in the contralateral intact knee. Thus, our goal was to investigate stride-to-stride variability in the ACL deficient knee as compared to a healthy control knee. Seven subjects with unilateral ACL deficiency and seven healthy controls walked at their self-selected speed on a treadmill, while three-dimensional knee kinematics was collected for 80 consecutive strides. A nonlinear measure, the largest LyE was calculated from the resulted knee joint flexion-extension data of both groups. Larger LyE values signify increased variability and increased sensitivity to initial conditions. Our results showed that the ACL deficient group exhibited significantly less variable walking patterns than the healthy control. These changes are not desirable because they reflect decreases in system's complexity, which indicates narrowed functional responsiveness, according to the "loss of complexity hypothesis." This may be related with the increased future pathology found in ACL deficient patients. The methods used in the present paper showed great promise to assess the gait handicap in knee injured patients.

**Keywords** Gait analysis · Stride-to-stride variability · Nonlinear methods · Anterior cruciate ligament deficiency

## Introduction

In 1967 Bernstein used the term "repetition without repetition" to describe subsequent repetitions of a certain motor task [5]. Indeed, kinematics, kinetics, and patterns of muscle activation are different each time a specific motor task is performed. This also seems to be the case for able-bodied gait as fluctuations among subsequent strides have been observed [39, 54]. This stride-to-stride variability has been attributed not only to measurement noise (i.e., movement artifacts), but also to the underlying mechanisms that produce human gait in both healthy and pathological conditions.

Thus, several studies using both the traditional linear (i.e., standard deviation, coefficient of variation) and nonlinear (i.e., Lyapunov Exponent (LyE), Approximate Entropy, Detrended Fluctuation Analysis) tools, have shown that variability is altered with aging and pathology [7, 23, 24, 31, 40]. However, the usage of the traditional

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linear tools to investigate stride-to-stride variability has been questioned by researchers [45]. Specifically, linear tools can mask the true structure of variability, since strides are averaged to generate a "mean" picture of the subject's gait. In this averaging procedure, which is usually accompanied with normalization, the temporal variations of the gait pattern are lost. Nonlinear measures can overcome these problems since they can measure the behavior of a continuously changing system over time, such as the human locomotor system during gait.

Furthermore, nonlinear measures have been able to provide important insight regarding the structure of stride-to-stride variability [22, 45]. In particular, they have showed that stride-to-stride variability exhibits chaotic properties which can provide the neuromuscular system with the capacity to respond to unpredictable stimuli and stresses [22, 35, 45] (Appendix 1). In addition, gait studies in aging and diseased states such as Huntington's disease, Parkinson's disease, amyotrophic lateral sclerosis [7, 23, 24] have shown that stride-to-stride variability is altered by these processes. Such alterations have also been noted in other medical domains such as cardiology (assessment of heart rate variability), neurology (assessment of electroencephalographic data variability), pediatrics (assessment of pulse oximetry signals in preterm newborns for the prediction of histologic chorioamnionitis), and endocrinology (assessment of hormone secretion variability) [2, 6, 8, 12, 16, 34, 50, 51]. Thus, it has been proposed that chaotic properties characterize healthy systems, where the variability observed provides flexibility to adapt to everyday stresses placed on the human body [41]. On the contrary, pathology is associated with altered variability, decreased system complexity, increased rigidity, and reduced functional responsiveness (loss of complexity hypothesis) [20].

Recently, this approach has been utilized to investigate how anterior cruciate ligament (ACL) deficiency affects variability. It has been found that the ACL deficient knee exhibits differences in stride-to-stride variability when compared to the contralateral intact knee [19, 46]. Specifically, it has been shown that the ACL deficient knee is more sensitive to initial conditions as compared to the intact contralateral knee [46]. However, this study is limited because the ACL deficient knee was compared only to the intact contralateral knee. There is biomechanical evidence 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 [4, 17, 48]. Thus, it is unclear whether the results of the above mentioned studies [19, 46] can be generalized in terms of ACL deficiency and comparisons with healthy controls.

Therefore, the purpose of this study was to investigate if alterations exist in stride-to-stride variability in the ACL deficient knee as compared to healthy control. The nonlinear measure of LyE was utilized to answer this question. This measure provides an estimate of the sensitivity of the system to initial conditions with larger LyE values signifying increased variability, and increased sensitivity to initial conditions. We hypothesized that the ACL deficient knee will exhibit different LyE values than the healthy control knee.

## Methods

### Subjects

Seven subjects (five males, two females; mean age 34 ± 9 years, mean mass 75 ± 6 kg, mean height 1.70 ± 0.08 m) diagnosed with ACL rupture by MRI criteria volunteered for ACL deficient group. In six patients, the diagnosis was later confirmed under direct visualization arthroscopically. The mean time from injury to testing was 33.5 months. All patients suffered from giving way episodes. Clinically, the level of deficiency was evaluated using Lysholm scores (66 ± 15) and static measurements of tibial translation using the KT-1000 (side-to-side differences more than 3.5 mm) (KT 1000; Medmetric Corp., San Diego, CA, USA). Seven healthy subjects (five males, two females; mean age 29 ± 4.2 years, mean mass 69.2 ± 8 kg, mean height 1.71 ± 0.09 m) with no history of neuromusculoskeletal injury volunteered as the control group (Lysholm score 98 ± 2; KT-1000 score less than 3 mm). All subjects signed an informed consent according to the University Institutional Review Board.

### Protocol

The subjects walked on a motorized treadmill (SportsArt 6005; SportsArt America, Woodinville, WA, USA). A six-camera optoelectronic system (Peak Motus 4.33; Peak Performance Technologies, Inc., Englewood, CO, USA) was used to capture the three-dimensional movements of 15 reflective markers placed on the selected bony landmarks of the lower limbs and the pelvis using the model described by Davis [11]. The reflective markers were placed on the skin surface of both anterior superior iliac spines, mid thighs, lateral femoral epicondyles, mid tibias, lateral malleolus, outsole of the shoes approximately at the second metatarsal heads, heels, and the sacrum [11]. All markers were positioned on the participating subjects by the same examiner.

Using the algorithms described by Davis [11] that combine anthropometric measurements and the position of the reflective markers, we calculated the three-dimensional knee joint angular displacement. In the present study we only examined the sagittal angular displacement (flexion-extension) of the knee. We also collected three-dimensional data instead of two-dimensional to minimize measurement error due to perspective error.

All subjects were given ample time to warm up and familiarize themselves with walking on the motorized treadmill at a self-selected pace. This pace represented their natural walking speed. By using a self-selected pace, walking speed was reduced as a potential cause of changes in variability. Thus, any variability changes detected were due to the ACL deficiency and not to potential discomfort that may be associated with using a predetermined speed for all subjects [14, 53]. Furthermore, the group mean values for the walking speeds were 0.74 ± 0.19 m $s^{-1}$ for the control group and 0.75 ± 0.16 m $s^{-1}$ for the ACL deficient group. A statistical comparison indicated that there were no significant differences ($P = 0.900$) in the walking speed between the two groups. Once subjects were comfortable walking on the treadmill at their self-selected pace, data were collected continuously for 2 min at 50 Hz. The collected data represented at least 80 continuous walking strides.

## Data analysis

Stride-to-stride variability was assessed by examining how knee flexion-extension changes over time by calculating the largest LyE. This measure provides an estimate of the sensitivity of the system to initial conditions with larger LyE values signifying increased variability and increased sensitivity to initial conditions (Fig. 1).

Each knee angle data set consisted of 5,750 points, which is considered sufficient for this type of analysis [45]. The data were analyzed unfiltered so as to get a more accurate representation of the variations within the system (Fig. 1a) [33]. Furthermore, it was assumed that since the same instrumentation was used for all subjects, the level of measurement noise would be consistent for all subjects and that any differences could be attributed to changes within the system itself [42, 55]. Therefore, filtering the data may have eliminated important information and provided a skewed view of the system's inherent variability [42].

The application of nonlinear measures is based on examining the structural characteristics of the investigated data set that is embedded in an appropriately constructed state space. An appropriate state space is a vector space where the dynamical system can be defined at any point in time [1] (Appendix 2). Investigation of the characteristics of the state space is a powerful tool for examining a dynamic system because it provides information that is not apparent by just observing the data [1, 3].

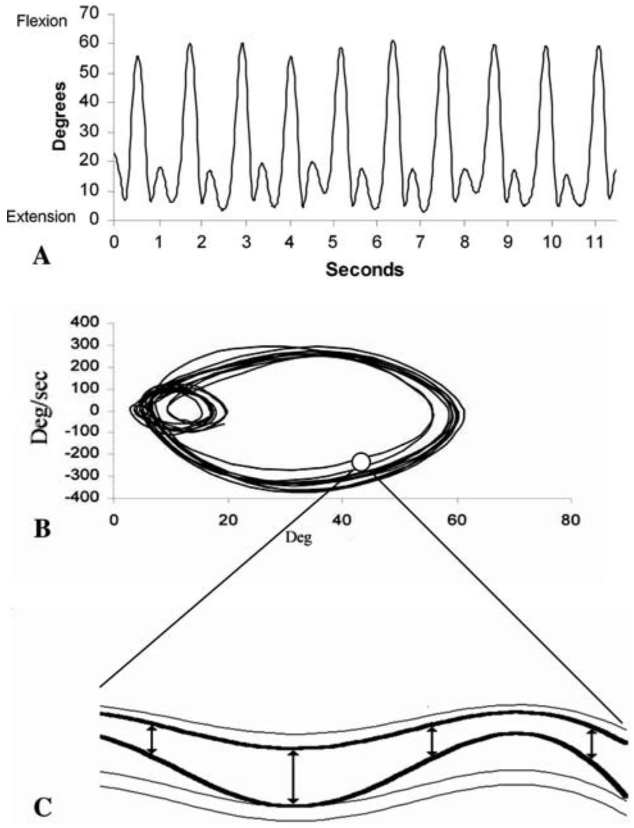

**Fig. 1** A graphical representation of the state space and the calculation of the LyE. **a** An original knee angle data set from several strides from an ACL deficient knee. **b** A two-dimensional state space generated from this entire data set using every single point, where knee flexion-extension (deg) is plotted versus angular velocity (deg/s). **c** A section of the state space where the divergence of neighboring trajectories is outlined. The LyE is calculated as the slope of the average logarithmic divergence of the neighboring trajectories, for the entire data series

The LyEs quantify the exponential separation of nearby trajectories in the reconstructed state space (Fig. 1). As nearby points of the state space separate, they diverge rapidly and can produce instability. LyEs from a stable system with little to no divergence will be 0 (e.g., sine wave). Alternatively, LyEs for an unstable system that has a high amount of divergence will be positive (e.g., random data). A chaotic system will have both positive and negative LyEs. Although a positive LyE indicates instability, the sum of the LyEs for a chaotic system remains negative and allows the system to maintain stability [1]. In this study, we calculated the largest LyE for each knee angle data set, using the Chaos Data Analyzer Professional Version (Physics Academy Software, Raleigh, NC, USA) software.

## Statistical analysis

Statistical analysis was performed on the LyE group means using an independent two-tailed *t*-test to compare between the ACL deficient and the healthy control knees. The level of significance was set at 0.05.

## Results

Our results revealed that the healthy control knee exhibited significantly larger LyE values when compared to the ACL deficient knee ($P = 0.026$) (Fig. 2). The statistical power of our study was found to be 71.1% [9]. To establish a basis for comparison, we calculated the LyE for a known chaotic (the Lorenz attractor), a purely random and a purely periodic (the sine wave) data set (Fig. 2). Positive values were obtained for both chaotic and random data (Fig. 2). The LyE for the chaotic data was smaller than the random. The periodic data had LyE that was 0. If we compare these results to the results from our data, we can see that our LyE values are closer to the chaotic.

## Discussion

The purpose of this study was to investigate if alterations exist in stride-to-stride variability after ACL rupture in the ACL deficient knee when compared to a healthy control knee utilizing the nonlinear measure of LyE. The LyE allows for a close examination of stride-to-stride variability, which can provide with useful information concerning the neuromuscular mechanisms that produce human gait. Specifically, the LyE provides an estimate of the sensitivity to initial conditions with larger values indicating increased variability and increased sensitivity. This measure has been used to investigate the neuromuscular mechanisms involved in the development of sitting postural control [21] and in the degradation of performance due to aging [7].

In addition, using LyE it has been found that the ACL deficient knee exhibits differences in stride-to-stride variability when compared to the contralateral intact knee [46]. Specifically, it has been shown that the ACL deficient knee is more sensitive to initial conditions as compared to the intact contralateral knee [46]. However, there is biomechanical evidence that after an ACL rupture, adaptations occur not only in the ACL deficient knee but also in the intact contralateral knee when compared to uninjured controls [4, 17, 48]. Thus, it will be incorrect to establish the intact contralateral as the healthy standard. Comparisons with actual healthy controls are needed to clearly identify true clinically important differences. Based on the above it was not a surprise that in the present study we found that the ACL deficient knee exhibited smaller LyE values and it is therefore less variable and less sensitive to initial conditions than a healthy control knee.

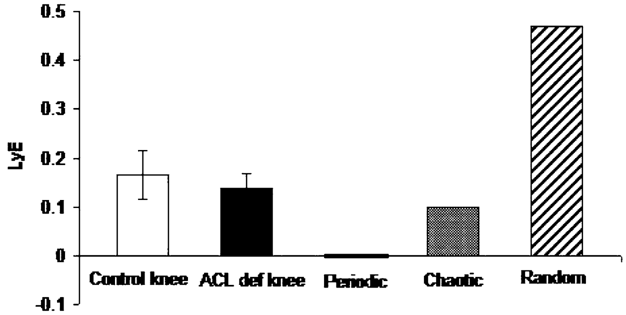

**Fig. 2** *Bar graph* indicating group mean values and standard deviations for the Lyapunov Exponents (*LyE*) from the knee angle data and from known data sets (Appendix 1)

This finding may be due to altered muscular activity in the ACL deficient individuals to compensate for the loss of ligament. The ACL plays an important role in knee stability because of its mechanical properties and the mechanoreceptors that exist in it [26, 44]. For instance it has been shown, using both animal and human subjects, that activation of the ACL mechanoreceptors induces hamstring contraction resisting anterior tibial translation (ACL-hamstring reflex) [15, 18, 47]. It has been proposed that 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 muscle patterns and postural synergies [10, 13, 49]. For instance, Courtney et al. showed that ACL deficient patients exhibit altered somatosensory evoked potentials and also different gastrocnemius and hamstrings activity during treadmill walking [10]. 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. These altered properties could be the reason for the decreased LyE values found in the present study for the ACL deficient knee when compared to a healthy control knee.

These decreased values apart from signifying decreased sensitivity to initial conditions and decreased variability, they also suggest decreased complexity. Specifically, a close examination of the LyE values from the known data sets (Fig. 2) reveals that the periodic data has the smaller LyE values while the noisy random data the largest. We can then claim that ACL deficiency resulted in a tendency toward greater periodicity and rigidity and decreased complexity. Thus, our findings are in agreement with the “loss of complexity hypothesis” [20, 41]. Therefore, the decreased variability that was found in the ACL deficient knee is a nondesirable phenomenon since it may represent decreases in system flexibility and narrowed functional responsiveness. Using an example from cardiology, decreased complexity of heart rate variability was found to precede the spontaneous onset of atrial fibrillation [43]. In addition, decreases in cardiovascular complexity have been associated with aging and it has been concluded that complexity may be a useful physiological marker for system's health [20, 29]. Therefore, decreases in gait complexity as a result of neuromuscular changes caused by the ACL deficiency, may result in a lower extremity more susceptible to injury. If the lower extremity is less complex and more rigid, it is less capable to respond to different perturbations and to adapt to the changing environment. This may in turn increase susceptibility to injury and future pathology, such as the increased amount of osteoarthritic changes and meniscal tears that was found in the ACL deficient knee [28, 37, 38]. However, the hypothesis and the clinical significance of the decreased stride-to-stride variability found in ACL deficiency must be evaluated in longitudinal studies where alterations in variability will be correlated to clinical and radiological changes.

It seems therefore that nonlinear measures such as the LyE could be very helpful for the evaluation of the effects of ACL rupture and the subsequent therapeutical interventions on gait properties. The significance of LyE as a tool for evaluation and diagnosis has already been recognized in other medical domains, such as neurology, where it has been used for the development of an epileptic seizure warning algorithm [8].

A possible limitation of the study is that our subjects walked on a motorized treadmill instead of overground. Actually, the collection of a large number of continuous data required for the calculation of stride-to-stride variability enforces the walking measurements to be collected on a motorized treadmill. We also selected to use a motorized treadmill because we wanted to ensure that the speed remains constant for each condition. It has been shown that walking overground does not warrant a constant speed for a long period of time (such as in the case with multiple strides) due to intermittency [36, 52]. It has also been found that speed can affect variability during walking [14, 19, 27, 53]. Therefore, in the present study it was imperative to use a motorized treadmill to eliminate any confounding effects of the walking speed. In addition, even though it has been demonstrated that treadmill walking affects variability measures, it has been shown that kinematic measurements from familiarized treadmill walking do not differ markedly from overground walking [32, 43].

Another possible limitation is that both males and females were included in the study groups. It has been shown that there are gender differences concerning the biomechanics of lower extremities during walking [25, 30]. On the other hand, it is currently unknown if gender differences exist regarding stride-to-stride variability. However, in an attempt to overcome this shortcoming, we included the same number of female and male subjects in the ACL deficient and control group.

In conclusion, we used nonlinear methods to examine stride-to-stride variability in the ACL deficient knee during walking. Our results showed that the ACL deficient knee was less variable and less sensitive to initial conditions when compared with a healthy control. These changes are probably not desirable because they result in decreases in the system's complexity, indicating narrowed functional responsiveness. This may be related to the increased pathology developed in the ACL deficient knees. Nonetheless the present methods showed great promise for being used as biomedical diagnostic tools to examine the impact of injury and pathology on human gait.

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## Appendix 1

The behavior of a continuously changing system over time can be periodic, random or chaotic.

Periodic systems are organized. They are repeatable and predictable (Fig. 3).

Random systems, on the other hand, contain no order. They are unpredictable and their behavior is never repeated (Fig. 4).

Chaotic systems have characteristics of both. They seem to be random and unpredictable but they contain order and are deterministic in nature. They are very flexible and can operate under various conditions (Fig. 5).

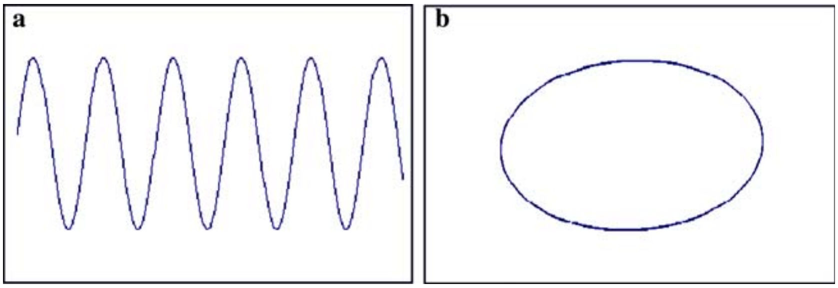

**Fig. 3** Graphic representation of a periodic system [sin(1/10)] (**a**) and the corresponding phase plane plot (**b**), where the time series data is plotted versus the first derivative

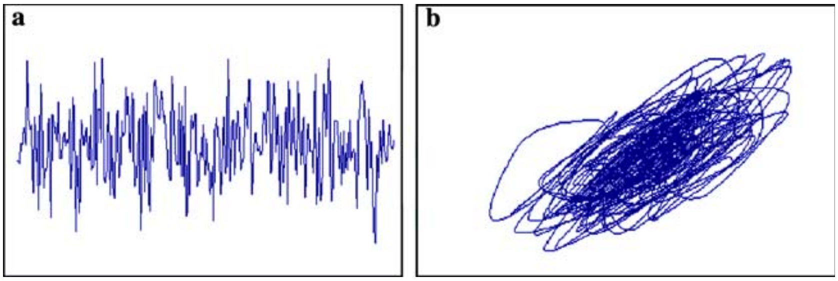

**Fig. 4** Graphic representation of a random system (Gaussian noise centered on 0 and a standard deviation of 1.0) (**a**) and the corresponding phase plane plot (**b**)

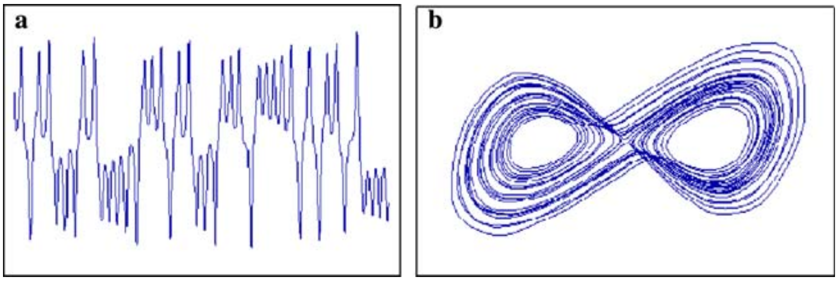

**Fig. 5** Graphic representation of a chaotic system (the Lorentz attractor) (**a**) and the corresponding phase plane plot (**b**)

## Appendix 2

To properly reconstruct a state space, it is essential to quantify an appropriate time delay and embedding dimension for the investigated data set.

To reconstruct the state space, a state vector was created from the data set. This vector was composed of mutually exclusive information about the dynamics of the system (Eq. 1).

$$\mathbf{y}(t) = [x(t),\ x(t - T_1),\ x(t - T_2), \ldots], \tag{1}$$

where $\mathbf{y}(t)$ is the reconstructed state vector, $x(t)$ is the original data and $x(t - T_i)$ is time delay copies of $x(t)$. The time delay ($T_i$) for creating the state vector is determined by estimating when information about the state of the dynamic system at $x(t)$ was different from the information contained in its time-delayed copy. If the time delay is too small then no additional information about the dynamics of the system will be contained in the state vector. Conversely, if the time delay is too large then information about the dynamics of the system may be lost and can result in random information. Selection of the appropriate time delay is performed by using an average mutual information algorithm 1 (Eq. 2).

$$I_{x(t),x(t+T)} = \sum P(x(t)),x(t+T))\log_2\left[\frac{P(x(t),x(t+T))}{P(x(t))P(x(t+T))}\right], \tag{2}$$

where $T$ is the time delay, $x(t)$ is the original data, $x(t + T)$ is the time delay data, $P(x(t), x(t + T))$ is the joint probability for measurement of $x(t)$ and $x(t + T)$, $P(x(t))$ is the probability for measurement of $x(t)$, $P(x(t + T))$ is the probability for measurement of $x(t + T)$. The probabilities are constructed from the frequency of $x(t)$ occurring in the time series. Average mutual information is iteratively calculated for various time delays and the selected time delay is at the first local minimum of the iterative process. This selection is based on previous investigations that have determined that the time delay at the first local minimum contains sufficient information about the dynamics of the system to reconstruct the state vector.

It is additionally necessary to determine the number of embedding dimensions to unfold the dynamics of the system in an appropriate state space. An inappropriate number of embedding dimensions may result in a projection of the dynamics of the system that has orbital crossings in the state space that are due to false neighbors and not the actual dynamics of the system. To unfold the state space we systematically inspect $x(t)$ and its neighbors in various dimensions (e.g. dimension = 1, 2, 3,…). The appropriate embedding dimension occurs when neighbors of the $x(t)$ stop being unprojected by the addition of further dimensions of the state vector (Eq. 3).

$$\mathbf{y}(t) = [x(t),\ x(t+T),\ x(t+2T), \ldots x(t+(d_E-1)T)], \tag{3}$$

where $d_E$ is number of embedding dimensions, $\mathbf{y}(t)$ is the $d_E$-dimensional state vector, $x(t)$ is the original data, and $T$ is the time delay. A global false nearest neighbors algorithm with the time delay determined from the local minimum of the average mutual information is used to determine the number of necessary embedding dimensions to reconstruct the step time interval data series. The calculated embedding dimension indicates the number of governing equations that were necessary to appropriately reconstruct the dynamics of the system. The Tools for Dynamics (Applied Chaos LLC, Randle Inc., San Diego, CA, USA) software was used to calculate the embedding dimension for our data sets, and it was found to five.

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