Nonlinear analysis of human physical activity patterns in health and disease

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The reliable and objective assessment of chronic disease state has been and still is a very significant challenge in clinical medicine. An essential feature of human behavior related to the health status, the functional capacity, and the quality of life is the physical activity during daily life. A common way to assess physical activity is to measure the quantity of body movement. Since human activity is controlled by various factors both extrinsic and intrinsic to the body, quantitative parameters only provide a partial assessment and do not allow for a clear distinction between normal and abnormal activity. In this paper, we propose a methodology for the analysis of human activity pattern based on the definition of different physical activity time series with the appropriate analysis methods. The temporal pattern of postures, movements, and transitions between postures was quantified using fractal analysis and symbolic dynamics statistics. The derived nonlinear metrics were able to discriminate patterns of daily activity generated from healthy and chronic pain states.

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I. INTRODUCTION

Daily life physical activity is an important feature of human behavior and its measurement is important for a variety of medical disciplines including behavioral science, psychology, and physiology. Physical activity has many dimensions that can be characterized and quantified. The frequency, the intensity, the duration, and the patterns (i.e., temporal distribution) of various activities can be measured. The assessment of physical activity has evolved from self-reported methods, such as diaries and questionnaires to objective measurements using sophisticated miniaturized accelerometers and gyroscopes or a combination thereof [1,2]. These devices allow for long-term (i.e., days or weeks), detailed, and continuous measurement of the body movements in subjects living their normal life.

The ability to perform physical activities is a common indicator to assess the functional condition in medicine. In chronic pain patients behavioral modifications occur frequently as a result of physical disability, psychological changes, or both. The reliable measurement of physical activity is therefore important for diagnostic purposes as well as for the assessment of the efficacy of treatment. The information provided by changes in quantitative physical activity parameters such as time spent in different postures or activities, and gait parameters (stride length, walking distance, speed) has obvious intuitive relevance that was confirmed by clinical trials in patients with various disorders including chronic pain [3], cardiovascular diseases [4,5], obesity [6,7], and children's hyperactivity [8,9]. Similarly, abnormal patterns of physical activity characterized by very active periods followed by very long periods of inactivity have been shown to occur in chronic fatigue syndrome [10].

As our understanding of human physical activity is improving, the quantitative approach where activities and patterns can be assessed intuitively (visually) by numbers and graphs, is showing limitations. New paradigms involving nonlinear analysis of less straightforward parameters appear promising [11]. Trials on various biological signals [12] have paved the way for studies looking at the frequency and the temporal organization of activity parameters such as posture changes or walking episodes in patients suffering from chronic pain. Advanced mathematical tools applied to long-term physical activity time series resulted in new metrics and outcome parameters suggesting the presence of predictable correlations between the intensity of pain and features of physical activity [11]. The aim of our study was to define a methodology for the analysis of human activity pattern based on the definition of different physical activity time series with the appropriate analysis methods.

To evaluate the dynamics of human activity the temporal pattern of postures, movements, and transitions between postures was quantified using fractal analysis and symbolic dynamics in both chronic pain patients and a healthy control group.

This paper is organized in separate sections to describe the physical activity monitoring system and the measurement protocol (Sec. II), to define the different physical activity time series (Sec. III), to present mathematical tools and to quantify the dynamics of temporal activity patterns (Sec. IV), to present results (Sec. V), and to discuss the findings (Sec. VI).

II. DATA RECORDING

The daily motor function was recorded using an ambulatory system based on three inertial sensors (each composed on two accelerometers and one gyroscope) fixed on the chest, the thigh, and the shank. Given this particular sensor configuration and the use of appropriate software [13] it is possible to detect and analyze a number of physical activity parameters including the sitting, standing, and lying posture, transition between postures, walking activity, and dynamic

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gait variables. The monitoring system and the posture analysis algorithms were validated in chronic pain patients treated by spinal cord stimulation (SCS). By considering 61 hours of data obtained from 21 patients before and after SCS, the sensitivity and specificity in detecting lying, sitting, standing, and walking were superior to 95% [13]. The system was designed to record physical activity in the normal life environment over prolonged periods of time.

In this study, body posture and movements were recorded in 15 patients (7 female, 8 males, age=66±14) suffering from chronic intractable pain caused by spinal stenosis, peripheral artery disease, or polyneuropathy and in 15 age-matched healthy subjects (8 females, 7 males). Ethical committee approval and detailed written and oral informed consent was obtained in each patient or healthy subject. Measurements were performed under free-living conditions in order to capture the actual daily life behavior. Signals from inertial sensors were recorded at a sampling rate of 40 Hz during five consecutive days and eight hours each day. In the chronic pain group pain intensity was assessed on a 10 cm visual analogue scale (VAS).

III. DEFINITION OF PHYSICAL ACTIVITY PATTERNS

Humans participate on a daily basis in a large number of distinct activities ranging from planned events (work, recreation) to unforeseen random events and spontaneous activity which is biologically determined as part of a feedback system that homeostatically controls body weight [8,9]. Factors such as chronic disorders including chronic pain, fatigue, or depression can modify the usual course of daily living either because of disease related impairment, constraints to carry out specific tasks, or both.

Notwithstanding the complexity of factors controlling human activity, all daily life activities are spent in one or more basic body postures (sitting, standing, lying) as well as walking. Since physical activity is both very variable and influenced by a myriad of physiological and pathological causes, quantitative parameters only provide a partial assessment and do not allow for a distinction between normal and abnormal activity.

In addition to the measurement of quantitative aspects, a complete assessment of physical activity requires the measurement and analysis of the intricate pattern of postures, movements, and transitions between postures.

The sequence, the timing, the time spent in a posture, and any combination thereof can be used to define *physical activity time series* that can be analyzed with appropriate mathematical tools to provide information which might be either characteristic of normal physical activity or specific of one or more disorders.

A. Sequence of posture allocation (pattern 1)

By gathering posture parameters over the measurement time (five consecutive days, eight hours per day) we consider the sequence of posture allocation quantified from low to high intensity activity, i.e., lying=1, sitting=2, standing=3, and walking=4 (Fig. 1). Each sample of the generated time series corresponds to the *type* of the underlying posture or activity and discards information about *duration*, therefore the length of the time series is related to the number of postural changes during the monitoring time.

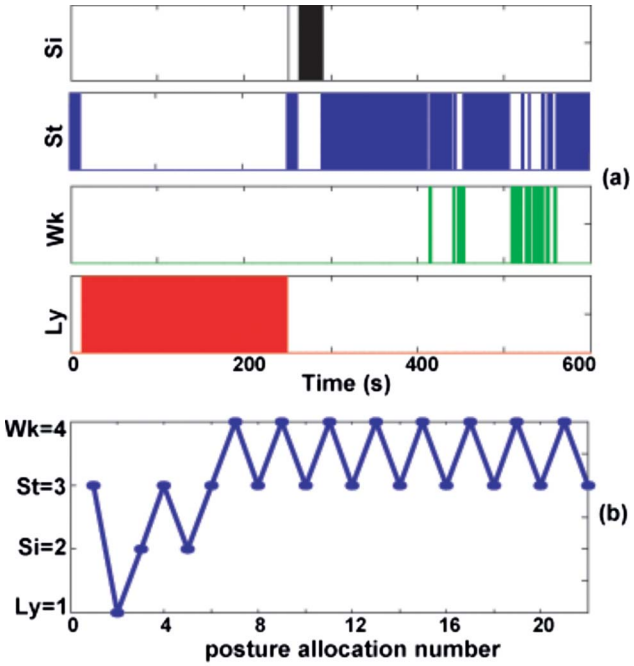

FIG. 1. (Color online) Illustrative example of posture allocation time series (pattern 1). (a) Assessment of postures (sitting-Si, standing-St, lying-Ly) and walking activity (Wk) from body-fixed kinematical sensors. (b) Posture allocation time series obtained from (a). Each sample of the time series carry information about the type of underlying posture or activity, discarding information about the duration.

B. Duration of walking periods (pattern 2)

Many authors consider walking to be the quintessential activity and it is often suggested the measurement of the walking is an adequate representation of a person's overall activity level [14,15]. As almost every task in daily routine activities implies the action of walking, we expect the sequence of walking episodes characterized by their duration to provide reliable information about the temporal organization of physical activity in real life conditions.

C. Time of activity-rest transitions as point process (event series) (pattern 3)

A variety of human actions are initiated by activity-to-rest or rest-to-activity postural transitions. Quantifying the timing of human actions in daily life could be of great importance to understand human behavior in relation with chronic diseases such as chronic pain, chronic fatigue syndrome, and neurodegenerative disorders such as Alzheimer's disease.

We have defined *activity* as standing or walking and rest as sitting or lying postures. The statistical behavior of an activity-rest daily pattern can be studied replacing the complex wave form by *point events* corresponding to the time of

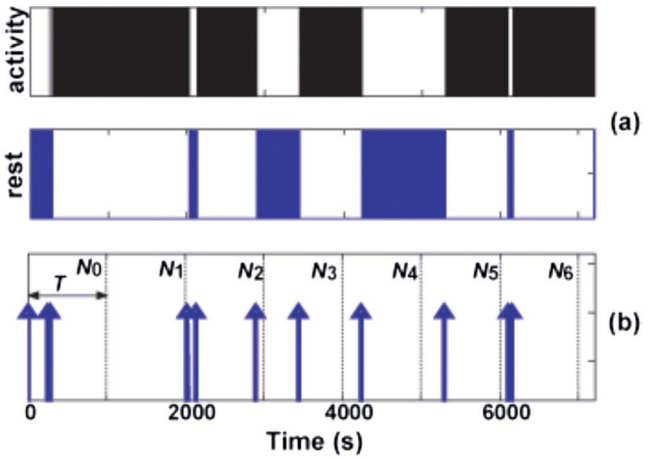

FIG. 2. (Color online) Typical representation of activity-rest or rest-activity postural transitions as a stochastic point process (pattern 3). (a) Activity-rest allocation during the monitoring time. (b) The event series corresponding to the occurrence time of activity-rest or rest-activity postural transitions (point process). The sequence of counts $\{N_i\}$ is a discrete-time, non-negative, integer value stochastic process formed from the point process by recording the number of events in successive counting windows of duration T.

transitions between postures. Mathematically, the sequence of activity-rest transitions can be viewed as a realization of a *stochastic point process* specified by the set of occurrence time $\{t_i\}$ of transitions.

The features of the defined point process can be studied in terms of the sequence of numbers of events (counts) $\{N_i\}$. Figure 2 illustrates how the sequence is obtained. The time axis is divided into equally spaced contiguous time windows, each of a duration of T seconds, and the number of events in the ith window is counted and denoted as N_i. This sequence $\{N_i\}$ forms a discrete-time random counting process of non-negative integers. An attractive feature of this representation is that it preserves the correspondence between the discrete-time axis of the counting process $\{N_i\}$ and the absolute real axis of the underlying point process.

D. Symbolic sequence from comparison of successive rest-activity-rest periods (pattern 4)

Another way to characterize the sequence of successive activity-rest periods is to use a context dependent *symbolic description*. A coding procedure suitable to assess the dynamics of daily activity in relation with chronic diseases such as lower limbs or low back chronic pain, chronic fatigue syndrome, cardiovascular disease, etc., is to compare the duration of each activity period (a_j) with the rest periods just before (r_{j-1}) and after it (r_{j+1}). In this way, the original daily activity-rest sequence can be represented as a *symbolic sequence*, $S=S_1,\ldots,S_k$ $(k=1,M-1)$ as follows:

$$\text{if } a_j \geqslant \varepsilon r_{j-1} \quad \text{then } S_k = 1,$$

$$\text{else } S_k = 0,$$

$$\text{if } a_j \geqslant \varepsilon r_{j+1} \quad \text{then } S_{k+1} = 1,$$

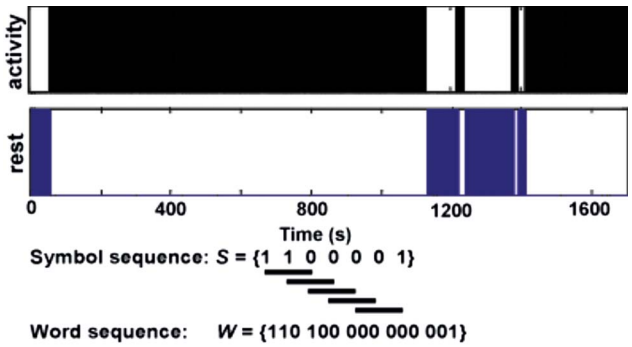

FIG. 3. (Color online) Symbolic representation of activity-rest allocation (pattern 4). The mapping procedure is based on Eq. (1) ($\varepsilon=4$) and three-step template.

$$\text{else } S_{k+1} = 0, \tag{1}$$

where r_{j-1}, a_j, r_{j+1}, $j=1,M$ is the succession of rest-activity-rest periods and ε is an arbitrary constant.

After symbolization, the next step in identification of temporal patterns is the construction of *word sequence* W, from the symbol series S by collecting groups of symbols together in temporal order. This sequencing process typically involves definition of a finite-length template (for example, three-step template) that can be moved along the symbol series one step at a time, each step revealing a new sequence (word). Figure 3 illustrates this process for an activity-rest time series that has been initially converted into a binary symbol series based on Eq. (1). If we look for the occurrence of symbol sequences consisting of three consecutive symbols, there will be eight (2^3) possible distinct words which can be observed.

IV. STRUCTURAL NONLINEAR ANALYSIS METHODS

A. Fractal analysis

The dynamics of a stochastic series can be explored through its correlation properties, or in other words, the time ordering of the series. *Fractal analysis* is an appropriate method to characterize complex time series by focusing on the time-evolutionary properties of the data series and on their correlation structure. Fractal structures are characterized by a complex pattern of correlations appearing following multiple time scales. In such a process, the value at a particular time is related not just to the immediately preceding values, but also to fluctuations in the remote past. Fractal time series are also characterized by *self-similarity (scale invariance)*, signifying that the statistical properties of segments within the series are similar, whatever the time scale of observation. In mathematical terms a time series $y(t)$ is self-similar if $y(t) \equiv a^{\alpha} y(t/a)$, where $\equiv$ means that the statistical properties of both sides of the equation are identical, a is the change in scale and α is the self-similarity parameter (scaling exponent).

In the context of stochastic point processes, a fractal data set exhibits clusters of events in time. Self-similar clusters have smaller clusters within larger clusters of clusters (burst of events interspersed with quiescent periods at many differ-

ent time scales). To quantify the characteristics of the temporal correlations in the physical activity time series we use the *cumulative distribution function* (CDF), *detrended fluctuation analysis* (DFA), and *Fano factor analysis* (FFA) methods.

1. Cumulative distribution of durations

The distribution of duration of activities and postures is a useful measure for studying the underlying dynamics and the fractal properties of long-term recorded activity. In this study we used the cumulative distribution $P(d)$, which is defined as [16]

$$P(d) \equiv \int_d^\infty p(r)dr, \tag{2}$$

where $p(r)$ is the probability density function of durations between r and $r+dr$.

Finding a power-law behavior for the distribution of duration (e.g., activity, rest, walking), $P(d) \propto d^{-\alpha}$, suggests a scale invariant dynamics, typical for fractal-like phenomena. The exponential behavior $P(d) \propto e^{-d/\tau}$ for the distribution of duration suggests a dynamical process with a characteristic time scale, τ.

2. Detrended fluctuation analysis

The DFA method can quantify the temporal organization of the fluctuations in a given nonstationary time series by a single scaling exponent α—the self-similarity parameter that represents the long-range power-law correlation properties of the signal. The scaling exponent α is obtained by computing the root-mean-square fluctuation $F(n)$ of an integrated and detrended time series at different observation windows of size n and plotting $F(n)$ against n on a log-log scale. Fractal signals are characterized by a power-law relation between the average magnitudes of the fluctuations $F(n)$ and the number of points n, $F(n) \sim n^{\alpha}$. The slope of the regression line relating $\log_2(F(n))$ to $\log_2(f(n))$ determines the scaling exponent α. The time series of fractal signals can therefore be indexed by the deviation of α from 0.5 to 1. For a value of $\alpha=0.5$ the signal is random; increasing values of α $(0.5 < \alpha \leqslant 1)$ indicate rising power-law scaling behavior of the signal and the presence of long-range (fractal-like) correlations. The scaling range allowing for a correct assessment of the power-law behavior is $5 \leqslant n \leqslant L/10$, where L is the length of the time series [17].

One important advantage of DFA over conventional methods (e.g., spectral analysis) is that it permits the detection of intrinsic self-similarity embedded in a seemingly nonstationary time series, and also avoids the spurious detection of apparent self-similarity, which may be an artifact of extrinsic trends. This method has been successfully applied to a wide range of simulated and physiologic time series in recent years [18–20].

3. Fano factor analysis

Fano factor (F_f) is a useful statistical measure to test whether the fluctuations of activity-rest or rest-activity transitions counts $\{N_i\}$ illustrated in Fig. 2 occur randomly or are of a time-scale invariant (fractal) nature. The Fano factor $F_f(T)$ is defined as the event-number variance divided by the event-number mean, which is a function of the counting time T (in seconds) as follows:

$$F_f(T) = \frac{\langle N_i^2(T)\rangle - \langle N_i(T)\rangle^2}{\langle N_i(T)\rangle}, \tag{3}$$

where $\langle\ \rangle$ denotes the expectation value and $N_i(T)$ is the number of transitions in the ith window of length T [21,22].

The Fano factor curve is constructed by plotting $F_f(T)$ as a function of the window size T on a log-log scale. For a data block of length $T_{\max}$, T is progressively increased from a minimum of 2 s to a maximum of $T_{\max}/10$ so that at least ten nonoverlapping windows are used for each measure of $F_f(T)$. For a random Poisson process $F_f(T)$ is approximately 1.0 for all window sizes [22,23]. For a periodic process $F_f(T)$ approaches zero as the window size increases due to decreasing variance. For a *fractal-rate stochastic point process* (the fractal character lies in the dependencies among the interevent intervals) $F_f(T)$ assumes a power-law form for large T as follows:

$$F_f(T) = 1 + \left(\frac{T}{T_0}\right)^{\alpha_F}, \quad 0 < \alpha_F < 1, \tag{4}$$

where T_0 is the fractal onset time, and marks the lower limit for significant scaling behavior in the F_f. The power-law relationship appears as a straight line on the log-log scale with a positive slope α_F. The parameter α_F is defined as the fractal scaling exponent of the point process. The correlation coefficient is used to test for linearity on the log-log scale, and linear regression is used to calculate α_F.

The value of F_f indicates the degree of event clustering $(F_f \gg 1)$ or anticlustering $(F_f < 1)$ in a point process relative to the standard homogeneous Poisson process for which $F_f(T) \cong 1$ or all T. Whether or not a power-law relationship in the F_f curve reflects a fractal rate process (characterized by clusters of events at many time scales) is tested by constructing *surrogate data* sets in which the interevent intervals (duration of activity and rest periods) are randomly shuffled. Specifically, we randomly shuffled the activity and the rest periods separately then constructed the surrogate time series by altering the shuffled activity and rest periods. This creates a randomized data set with activity and rest periods (duration) identical to the original time series but with randomized activity-rest and rest-activity transition times. The lack of fractal behavior in the F_f curve of the shuffled data suggests that the power-law features are related to the ordering of activity and rest periods in the original data.

Ugo Fano first used this method for characterizing statistically the fluctuation in the number of ions generated by fast charged particles [24]. In physiological systems, Fano factor analysis has been used to demonstrate the fractal characteristics of heart rate variability, and the firing patterns of sympathetic, auditory, and visual neurons [22,23,25,26].

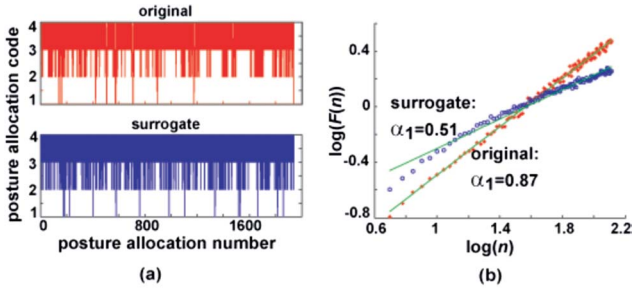

FIG. 4. (Color online) Illustrative example of DFA analysis of posture allocation time series. (a) Original time series obtained from five consecutive days recording and surrogate time series generated from a first order Markov model with the same transition probability between states (postures) as original series. (b) DFA scaling exponent for original and surrogate data.

B. Symbolic dynamics statistics

The temporal structure of the symbolic sequences defined in Fig. 3 is revealed by the probability of each possible symbol sequence obtained by counting the number of times each word occurs (n_{w_k}) and dividing by the total number of observed words (N_w): $P_{w_k}=n_{w_k}/N_w$.

Another useful measure is the *transition probability matrix* (T) between different words with elements $T_{w_iw_j}$ defined as $T_{w_iw_j}=N_{w_iw_j}/N$, where $N_{w_iw_j}$ is the number of transitions from word w_i to word w_j and N is the total number of transitions during the monitoring time.

C. Statistical analysis

In order to study the sensitivity of each method to differentiate chronic pain behavior from healthy control, we have calculated the parameters that quantify the temporal dynamics of the physical activity pattern (scaling exponents, symbolic dynamics statistics) for each subject as well as the means and the standard deviations in both healthy control and chronic pain groups. Differences between the two groups were assessed using the two-sided Mann-Whitney test.

V. RESULTS

A. Pattern 1—DFA

The sequence of posture allocation in Fig. 1 was analyzed using the DFA method. Figure 4(a) (top) shows a typical example of postures and activities sequences from five consecutive daily recordings in one subject (starting at about the same time in the morning). An intrinsic property of this original time series is the order of the data points. As the quantitative nature of the temporal organization of these time series is intuitively unremarkable, we applied the DFA method to detect potential long-range correlations. The validity of the results is verified by considering *surrogate sequences* with known statistical properties [27]. The most straightforward way in this case is to build a first order Markov process having the same transition probabilities as the original sequence but with data points in a shuffled order [Fig. 4(a) bottom]. As illustrated in Fig. 4(b), the fluctuations in the original time series exhibit long-range correlations ($\alpha_1=0.87$), whereas the surrogate data behave as uncorrelated white noise ($\alpha_1=0.51$).

B. Pattern 2—CDF, DFA

The pattern emerging from the analysis of the duration of walking episodes can display very different statistical properties, ranging from exponential [Figs. 5(a) and 5(b)] to scale-free power-law distribution [Figs. 5(c) and 5(d)]. This suggests that for a given clinical outcome the appropriate analysis may involve different methods.

The power-law form of CDF indicates that there are a large number of short episodes, a smaller number of medium, and a few long episodes. If the power-law form extends over at least two orders in time then (i) such data cannot be meaningfully characterized by mean and variance, though (ii) a proper assessment is provided by the slope of power-law CDF and the self-similar correlations in the fluctuations of the data, and (iii) the respective patterns may result from sequences of indoor vs outdoor walking, since continuous walking during hundreds of seconds is more likely to occur outdoors.

Figure 6(a) (top) shows an example of time series obtained from the duration of walking episodes recorded during five consecutive days. DFA analysis [Fig. 6(b)] reveals the presence of long-range correlations in the fluctuations of walking episodes ($\alpha_2=0.91$) suggesting that under normal conditions, the walking episodes have a duration that is organized rather than random. This hypothesis is confirmed by the analysis of surrogate data (obtained by randomly shuffling the samples of the original time series, Fig. 6(a) (bottom) that show no long-range correlations ($\alpha_2=0.53$).

C. Pattern 3—FFA

An illustrative example of the FFA method for original and surrogate data is shown in Fig. 7. The Fano factor curve for the original event series of time of activity-rest transitions deviates from those of surrogate data. The slope of the power law in the Fano factor curve for the original data is $\alpha_F=0.54$. The monotonic power-law increase indicates the presence of fluctuations on many time scales, with the exponent α_F identified as an estimate of the fractal exponent of the point process describing the original "pattern 3." However, a plot of the $F_f(T)$ curve alone cannot reveal whether this large Fano factor arises from the distribution of the interevent intervals, or from their ordering. This issue is resolved by plotting the Fano factor for the shuffled intervals. As illustrated, the power-law relationship in the Fano factor curve has been eliminated by randomly shuffling the activity-rest intervals ($\alpha_F=0.09$).

D. Pattern 4—Symbolic dynamics statistics

Figure 8 illustrates the word frequency distribution in a chronic pain patient. The mapping from daily activity-rest allocation to symbols is based on relation (1) with $\varepsilon=4$. The picture emerging from this analysis is that the probability of words related to successive "long activity, short rest," that is,

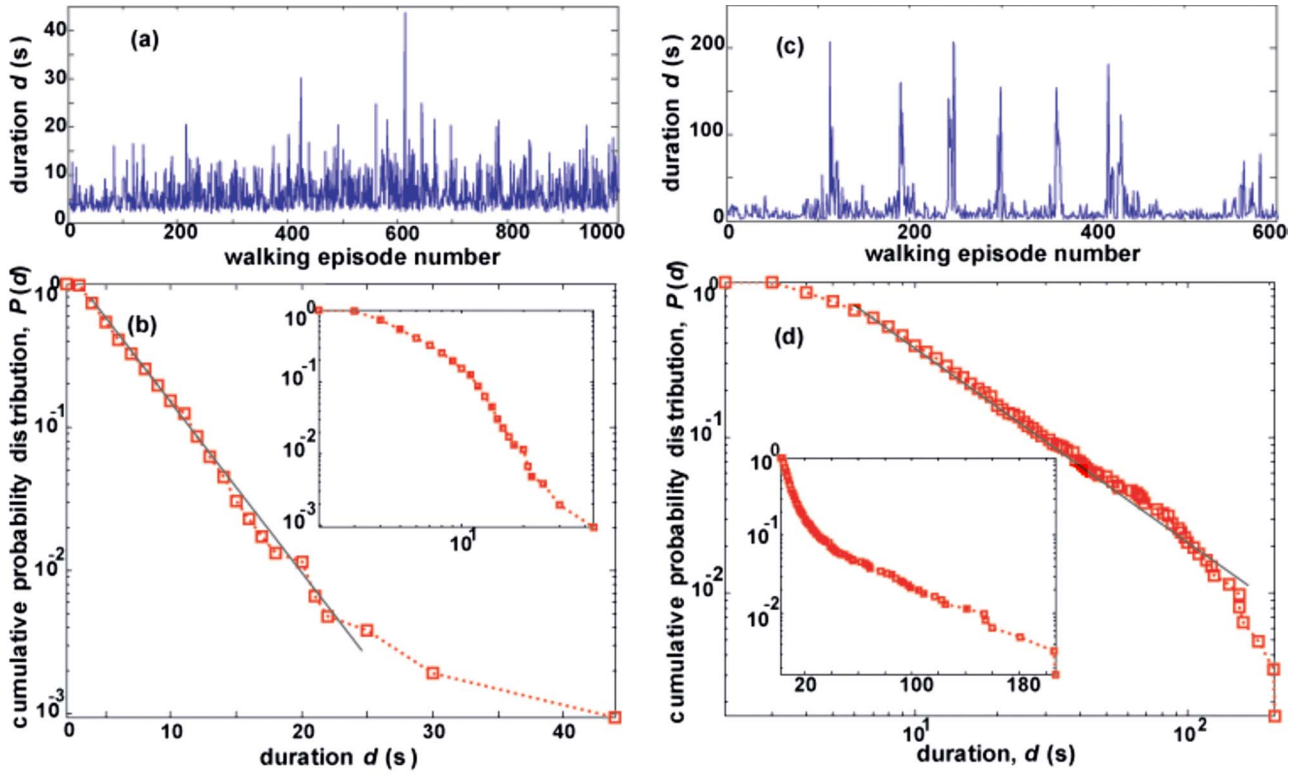

FIG. 5. (Color online) Cumulative probability distribution $P(d)$ of duration of walking episodes (pattern 2). [(a) and (c)] Illustrative example of two patterns recorded during five consecutive days in two subjects. (b) Semilogarithmic plot and double-logarithmic plot (inset) of $P(d)$ of the pattern represented in (a). (d) Double-logarithmic plot and semilogarithmic plot (inset) of $P(d)$ of the pattern represented in (c). For the pattern represented in (a) the distribution closely follows a straight line on the semilogarithmic plot indicating an exponential behavior while for the pattern represented in (c) the distribution follows a straight line on a double-logarithmic plot indicating a power-law behavior.

"111," "110," and "011" is lower than the probability of words related to successive "short activity, long rest" i.e., "000," "001," "010," "100," and "101."

E. Clinical significance

For the chronic pain group the average pain intensity and its standard deviation on a 10 cm VAS was 6 ± 2. The healthy control group was pain-free. In both groups, DFA showed fractal time structure in the daily posture allocation (pattern 1) though the average of the scaling exponent (α_1) was significantly smaller in chronic pain patients ($\alpha_1 = 0.756 \pm 0.090$) than in control ($\alpha_1 = 0.856 \pm 0.096$—Table I). It follows that in chronic pain patients, some aspects of daily life activity have lost the temporal organization that is found under normal healthy conditions.

Previous studies have suggested that factors such as pain, fear of pain, or depression can decrease the physical activity of chronic pain patients though it appears that this is not always the case [28]. It should be pointed out that until now,

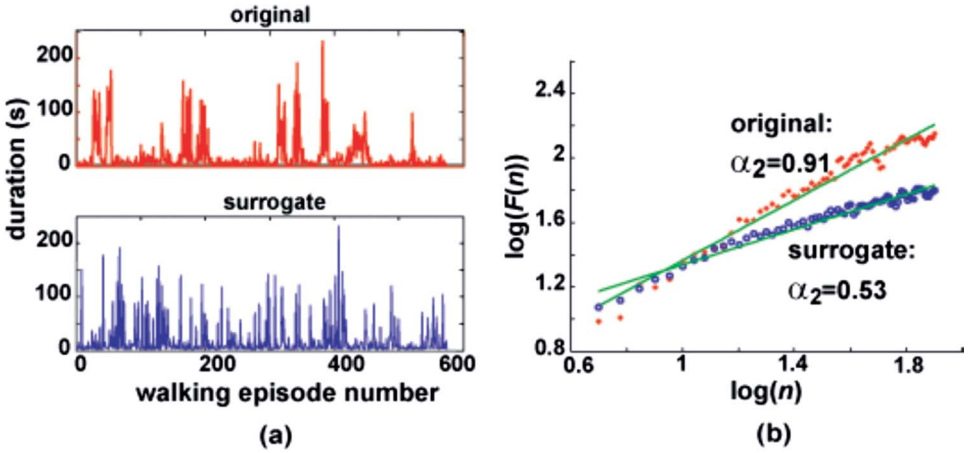

FIG. 6. (Color online) Illustrative example of DFA analysis of physical activity time series obtained from the duration of walking episodes. (a) Original time series obtained from five consecutive days recording and surrogate time series generated by randomly shuffling the original data. (b) DFA scaling exponent for original and surrogate data.

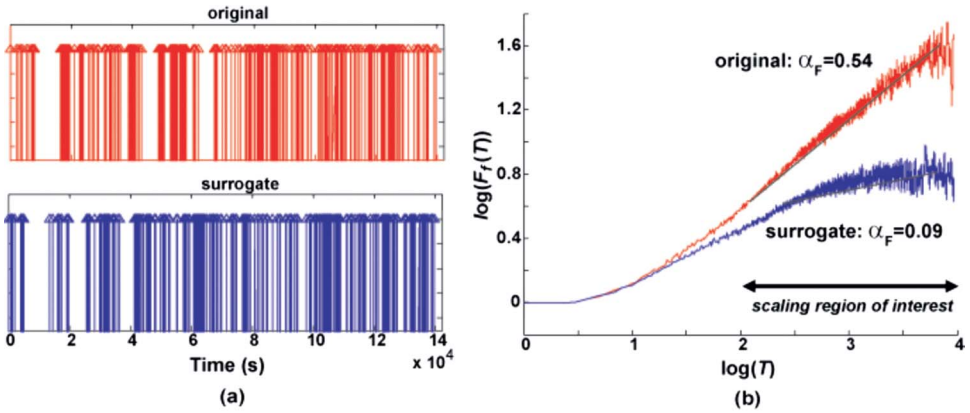

FIG. 7. (Color online) Illustrative example of Fano factor analysis. (a) Original and surrogate event series. (b) Double-logarithmic plot of the Fano factor function for a representative healthy subject and the surrogate data obtained by randomly shuffling the interevent intervals. The *scaling region of interest* is for $T > 100$ s where the original data and surrogate differ considerably.

physical activity has always been assessed either by questionnaires and other similar tools based on self-reporting, or by devices measuring quantitative parameters such as time spent in different postures, stride length, walking distance, or even speed. While it is largely recognized that self-reporting is unreliable, the interpretation of quantitative parameters is difficult because factors unrelated to the intensity of pain, whether physiological (age) or pathological (cardiorespiratory or orthopedic disorders, etc.) may have a profound influence on physical activity. The nonlinear analysis of physical activity patterns may significantly improve our ability to distinguish between pain and nonpain related behaviors though it has been shown that age as well as various medical disorders can change the organization of a number of biological signals.

In patients with chronic lower limb or low back pain, walking is often impaired and changes in walking patterns may therefore be very important. The analysis of the fluctuations of the correlations of the duration of walking episodes (pattern 2) showed that the scaling exponent is significantly smaller in the chronic pain group ($\alpha_2 = 0.734 \pm 0.100$ vs $\alpha_2 = 0.800 \pm 0.076$—Table I). In addition, the distribution of the walking episodes $P(d)$ was different. With healthy subjects (control group) a power-law scale-free distribution $P(d)$ was found in 11 out of 15 subjects. On the other hand, in only six out of 15 chronic pain patients did the distribution $P(d)$ show a power-law decay.

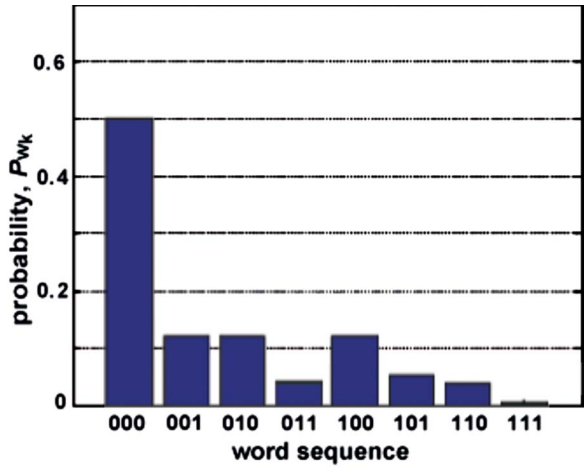

FIG. 8. (Color online) Word histogram illustrating the probability distribution of the word sequence in a chronic pain patient.

The Fano factor analysis revealed that under normal healthy conditions the timing of activity-to-rest transitions (pattern 3) follows a power-law distribution ($0 < \alpha_F \leqslant 1$) suggesting time clustering of activities at different time scales (ranging from ~2 min to 4 h). Statistical analysis (Table I) showed a significantly higher value of α_F for healthy controls ($\alpha_F = 0.350 \pm 0.085$) than for chronic pain patients ($\alpha_F = 0.178 \pm 0.100$), suggesting that activity-to-rest transitions are randomly spread over time with pain patients as opposed to organized in healthy people. Even though a large variety of factors can affect activities of daily life that are initiated by activity-to-rest transitions, the bursty feature that we observed seems to be robust. Although the significance, if any, of this finding is unclear and obviously requires specifically dedicated research it may relate to recent studies who suggest that the bursty nature of human behavior is a consequence of a decision-based queuing process where tasks are executed on the basis of their perceived priority. In this concept, most tasks are executed quickly whereas a few are delayed for a long period of time [29–31].

Figure 9 shows the mean value of the probability of words for the two groups, with an arbitrary value of ε ($\varepsilon = 4$) in relation (1). The words "000," "001" (short activity, long rest) are more frequent in the chronic pain group while "111," "110," "011" (long activity, short rest) are more frequent in the healthy control group. We believe this to be related to either pain or fatigue or both that intuitively are likely to be more frequent in pain patients than in healthy subjects.

Statistical analysis shows that the probability of words "111," "110," and "011" is significantly greater for the healthy control than for the chronic pain group (Table II). Moreover, the probability of transition from "111" to "111" is significantly greater in healthy controls (0.540 ± 0.08) than in chronic pain patients (0.400 ± 0.06).

The above results suggest that the parameters quantifying the temporal structure of physical activity pattern locate a significant difference between healthy control and chronic pain groups.

VI. DISCUSSION

The objective of this work is to help develop methods and computational models that capture as exhaustively as pos-

TABLE I. Fractal analysis: Estimated scaling exponents (mean ± std) in healthy control subjects and chronic pain patients.

Scaling exponents	Healthy subjects	Chronic pain patients (VAS=6±2)	p value (Mann-Whitney)
DFA-posture allocation (α_1)	0.856±0.096	0.756±0.09	$p=0.013$
DFA-walking episodes (α_2)	0.800±0.076	0.734±0.1	$p=0.039$
FFA-activity-rest transitions (α_F)	0.350±0.085	0.178±0.1	$p=0.0002$

sible all aspects (quantitative and dynamic) of the physical activity when measured under real daily life conditions. Physical activity is both very natural and extremely complex, and is controlled by a large number of often unrelated intrinsic (such as metabolic) and extrinsic (such as external constraints) factors. Although progresses have been achieved both in understanding and measuring various aspects of the physical activity, the current approach is still partial and unsatisfactory in many ways. Yet, the ability to perform unrestricted physical activity is a major determinant of the quality of life and is increasingly recognized as being a key feature for the assessment of a number of symptomatic treatments, in particular, the management of pain.

The advances in sensor technology have been associated with substantial improvements in the quality and the reliability of the data. Though better systems have allowed long-term recording of quantitative parameters (distances, speed) as well as postures (lying, sitting, standing, walking), the conventional analysis proved unable to reliably discriminate between physical activity in health and disease.

An approach to analyze human activity is proposed. Using nonlinear methods derived from statistical physics (fractal analysis, symbolic dynamics) the temporal organization of physical activity is assessed from time series (patterns) of defined events. The preliminary results that are presented suggest that healthy subjects and chronic pain patients can be discriminated reliably on the basis of specific patterns of their physical activity. Subtle though obvious clinical changes may therefore be quantified which may significantly improve the assessment of symptomatic treatments and perhaps even diagnostic accuracy.

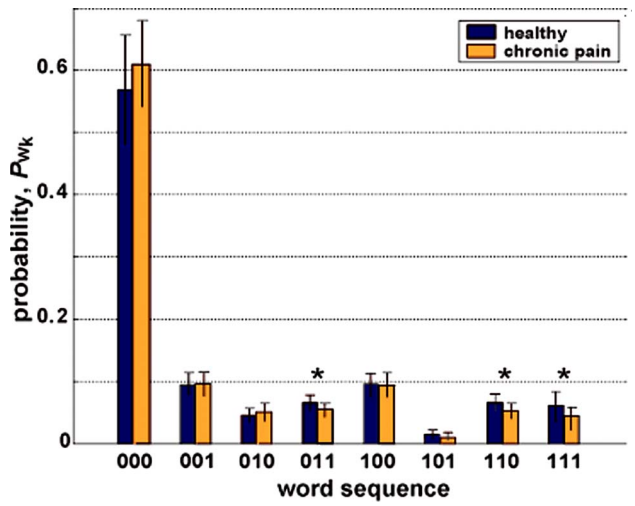

FIG. 9. (Color online) Word histogram illustrating the probability distribution (mean ± std) of the word sequence in healthy control and chronic pain groups.

Fractal analysis has shown that scale invariance appears to be as a general mechanism underlying many physiological functions [32,33]. While physical activity and energy consumption are directly linked by obvious mechanisms, their progressive decrease with age is less clear although a "biological control center" has been postulated [8,9]. Similarly, we have an intuitive understanding of why physical activity is reduced during a painful or incapacitating disease but the notion of a fundamental pattern in physical activity does not refer to common physiological knowledge. Yet, our findings suggest that physical activity in normal subjects has a fractal structure and that this organization is disrupted by chronic pain. The reason as to why there is a fractal pattern and what its clinical (or physiological) significance may be is unclear, and requires specifically dedicated research.

The number of data points needed for fractal analysis is crucial because finite size effects can occur with short time series. As the time series obtained from physical activity monitoring during one day are short (especially for chronic pain patients), we applied DFA and FFA on time series obtained by stitching together data from the five consecutive days. With this approach the resulting time series are characterized by four discontinuities corresponding to the transitions between the monitoring days (physical activity is not recorded from about 17 h p.m. to 9 h a.m., including the night). Discontinuities are frequent in "real" data and can arise from the nature of experimental recordings or from the fact that noisy and unreliable portions of continuous physiological recordings must be discarded prior to analysis. Several studies were dedicated to the analysis of this type of nonstationarity on the accuracy of estimated DFA scaling coefficients [34–36]. It was found that removing a segment

TABLE II. Symbol dynamics statistics: Probability of words (mean ± std) in healthy control subjects and chronic pain patients.

Probability of words	Healthy subjects	Chronic pain patients	p value
P_{111}	0.060±0.02	0.043±0.01	$p=0.02$
P_{110}	0.063±0.01	0.052±0.01	$p=0.008$
P_{011}	0.065±0.01	0.053±0.01	$p=0.009$

from a signal and stitching together the remaining parts does not affect the scaling behavior of positively correlated signals even when up to 50% of the points in these signals are removed.

In future studies we will investigate gap-filling techniques for physical activity time series given that long-term continuous monitoring in chronic disease states is often limited by technical or ethical considerations.

Symbolic dynamics appears to be a useful and flexible method to quantify context-dependent aspects of activity patterns. The definition of symbols [Eq. (1)], the word length, and the word statistics allow quantifying various aspects of daily posture and activities. In this study we applied the symbolic dynamics method to find out whether episodes of activity are followed by longer resting episodes in patients with presumably increased fatigue or pain or both. The findings indicate that the word frequency and the probability of transition between words are statistically different in pain patients compared to normal controls.

In a new book B. J. West [37] argues that the emerging fractal picture of physiology and behavior will replace standard ways of thinking about living systems and lead to innovations in diagnosis and treatment. Whether or not this dramatic change in our thinking will occur, there is a present need for better methodological tools for empirical studies and a wider understanding of the tools that already exists and what they can tell us about human behavior in health and disease.

Our study showed that the advanced analysis of the temporal pattern of human activity under real-life conditions can contribute to a deeper understanding of the behavioral consequence of chronic pain. Although the mechanisms involved are not completely elucidated, our observation is based on robust results and is not likely to be related to trivial extrinsic causes. As a similar pattern behavior has been described for other biological signals, it is reasonable to postulate the existence of a control system or mechanism that may or may not be organ or function specific.

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