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STATISTICAL PROPERTIES OF THE INTERBEAT INTERVAL CASCADE IN HUMAN HEARTS

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Statistical properties of interbeat intervals cascade in human hearts are evaluated by considering the joint probability distribution $P(\Delta x_2, \tau_2; \Delta x_1, \tau_1)$ for two interbeat increments Δx_1 and Δx_2 of different time scales τ_1 and τ_2. We present evidence that the conditional probability distribution $P(\Delta x_2, \tau_2 | \Delta x_1, \tau_1)$ may be described by a Chapman–Kolmogorov equation. The corresponding Kramers–Moyal (KM) coefficients are evaluated. The analysis indicates that while the first and second KM coefficients take on well-defined and significant values, the higher-order coefficients in the KM expansion are small. As a result, the joint probability distributions of the increments in the interbeat intervals are described by a Fokker–Planck equation, with the first two KM coefficients acting as the drift and diffusion coefficients. The method provides a novel technique for distinguishing two classes of subjects, namely, healthy ones and those with congestive heart failure, in terms of the drift and diffusion coefficients which behave differently for two classes of the subjects.

Keywords: Heartbeat fluctuations; Kramers–Moyal expansion; Markov processes; Fokker–Planck equation.

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1. Introduction

Cardiac interbeat intervals normally fluctuate in a complex manner.[1–6] Recent studies reveal that under normal conditions, beat-to-beat fluctuations in the heart rate may display extended correlations of the type typically exhibited by dynamical

systems far from equilibrium. It has been argued,[2] for example, that the various stages of sleep may be characterized by long-range correlations of heart rates separated by a large number of beats. The interbeat fluctuations in the heart rates belong to a much broader class of many natural, as well as man-made, phenomena that are characterized by a degree of stochasticity. Turbulent flows, fluctuations in the stock market prices, seismic recordings, the internet traffic, and pressure fluctuations in packed-bed chemical reactors are examples of time-dependent stochastic phenomena, while the surface roughness of many materials[7,8] are examples of phenomena that are length scale-dependent.

The focus of the present paper is on the intriguing statistical properties of interbeat interval sequences, the analysis of which has attracted the attention of researchers from different disciplines.[9–15] Analysis of heartbeat fluctuations focused initially on short-time oscillations associated with breathing, blood pressure and neuroautonomic control.[16,17] Studies of longer heartbeat records, however, revealed $1/f$-like behavior.[18,19] Recent analysis of very long time series indicates that under healthy conditions, interbeat intervals may exhibit power-law anticorrelations,[20] follow universal scaling in their distributions,[21] and are characterized by a broad multifractal spectrum.[22] Such scaling features change with the disease and advanced age.[23] The possible existence of scale-invariant properties in the seemingly noisy heartbeat fluctuations may be attributed to highly complex, nonlinear mechanisms of physiological control,[24] as it is known that circadian rhythms are associated with periodic changes in key physiological processes.[25–33] In Fig. 1 samples of interbeats fluctuations of healthy subjects and those with congestive heart failure (CHF) are shown.

Recently, Friedrich and Peinke were able[34] to derive a Fokker–Planck (FP) equation for describing the evolution of the probability distribution function of stochastic properties of turbulent free jets, in terms of the relevant length scale. They pointed out that the conditional probability density of the *increments* of a stochastic field (for example, the increments in the velocity field in turbulent flow) satisfies the Chapman–Kolmogorov (CK) equation, even though the velocity field itself contains long-range, nondecaying correlations. As is well-known, satisfying the CK equation is a necessary condition for any fluctuating data to be a Markovian process over the relevant length (or time) scales.[35] Hence, one has a way of analyzing stochastic phenomena in terms of the corresponding FP and CK equations.

In this paper the method proposed by Friedrich and Peinke is used to compute the Kramers–Moyal (KM) coefficients for the *increments* of interbeat intervals fluctuatations, $\Delta x(\tau) = x(t+\tau) - x(t)$. Here, Δx is the interbeat increments which, for all the samples, is defined as, $\Delta x \equiv \Delta x/\sigma_\tau$, where σ_τ is the standard deviations of the increments in the interbeats data. It is shown that the first and second KM coefficients representing, respectively, the drift and diffusion coefficients in the FP equation, have well-defined values, while the third- and fourth-order KM coefficients are small. Therefore, a FP evolution equation[35] is developed for the probability

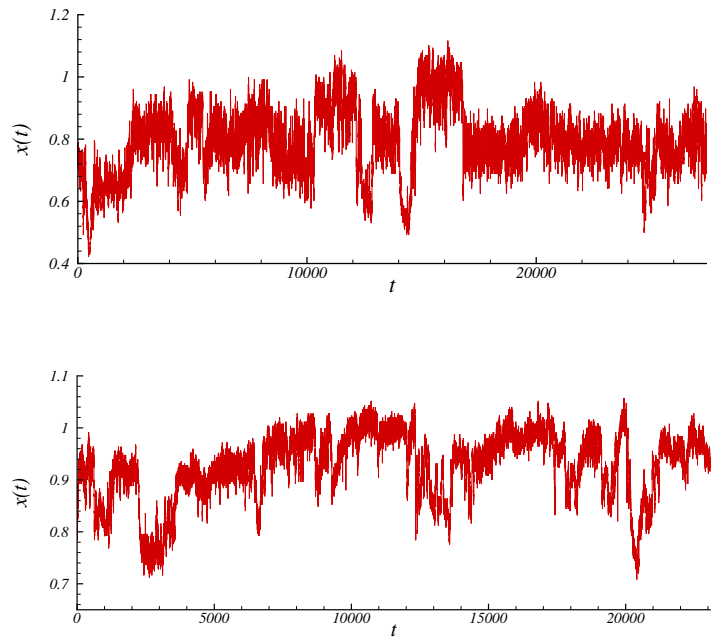

Fig. 1. Time series of interbeat intervals $x(t)$ versus interval number t for a typical person with congestive heart failure (bottom) and a healthy subject (top).

density function (PDF) $P(\Delta x, \tau)$ which, in turn, is used to gain information on changing the shape of PDF as a function of the time scale τ[36] (see also Ref. 37 for another interesting and carefully analyzed example of the application of CK equation to stochastic phenomena).

The plan of this paper is as follows. In Sec. 2 we describe the Friedrich–Peinke method in terms of a KM expansion and the FP equation. We then apply the method in Sec. 3 to the analysis of the increments in the interbeat fluctuations.

2. The Kramers–Moyal Expansion and Fokker–Planck Equation

A complete characterization of the statistical properties of the interbeat fluctuation requires evaluation of the joint PDFs, $P_N(\Delta x_1, \tau_1, \ldots, \Delta x_N, \tau_N)$, for an arbitrary N, the number of data points. If the phenomenon is a Markov process, an important simplification arises in that, the N-point joint PDF P_N is generated by the product of the conditional probabilities $P(\Delta x_{i+1}, \tau_{i+1}|\Delta x_i, \tau_i)$, for $i = 1, \ldots, N-1$. Thus, as the first step of analyzing a stochastic time series, we check whether the increments in the data follow a Markov chain. As mentioned above, a necessary condition for a stochastic phenomenon to be a Markov process is that the CK equation,[34]

$$P(\Delta x_2, \tau_2|\Delta x_1, \tau_1) = \int d(\Delta x_3) P(\Delta x_2, \tau_2|\Delta x_3, \tau_3)\ P(\Delta x_3, \tau_3|\Delta x_1, \tau_1)\,, \qquad (1)$$

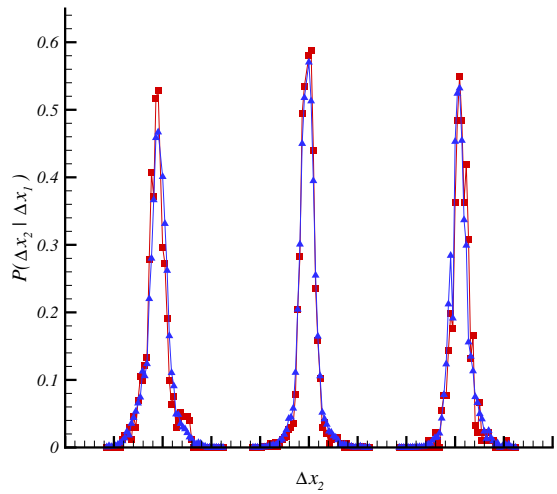

Fig. 2. Test of Chapman–Kolmogorov equation for $\Delta x_1 = -0.42$, $\Delta x_1 = 0$ and $\Delta x_1 = 0.42$. The solid and open symbols represent, respectively, the directly-evaluated PDF and the one obtained from Eq. (1). The PDFs are shifted in the horizontal directions for clarity. Values of Δx are measured in units of the standard deviation of the increments. The time scales τ_1, τ_2 and τ_3 are 10, 30, and 20, respectively.

should hold for any value of τ_3, in the interval $\tau_2 < \tau_3 < \tau_1$.[35] Therefore, we check the validity of the CK equation for describing the data using many values of the Δx_1 triplets, by comparing the directly-evaluated conditional probability distributions $P(\Delta x_2, \tau_2 | \Delta x_1, \tau_1)$ with those calculated according to the right-hand side of Eq. (1). In Fig. 2, the directly-computed PDF is compared with the one obtained from Eq. (1). Allowing for a statistical error of the order of the square root of the number of events in each bin, we find that the PDFs are statistically identical.

It is well-known that the CK equation yields an evolution equation for the distribution function $P(\Delta x, \tau)$ across the scales τ. The CK equation, when formulated in differential form, yields a master equation, which takes on the form of a FP equation:[35]

$$\frac{d}{d\tau} P(\Delta x, \tau) = \left[-\frac{\partial}{\partial \Delta x} D^{(1)}(\Delta x, \tau) + \frac{\partial^2}{\partial \Delta x^2} D^{(2)}(\Delta x, \tau) \right] P(\Delta x, \tau) \,. \tag{2}$$

The drift and diffusion coefficients, $D^{(1)}(\Delta x, \tau)$ and $D^{(2)}(\Delta x, \tau)$, are estimated directly from the data and the moments $M^{(k)}$ of the conditional probability distributions:

$$D^{(k)}(\Delta x, \tau) = \frac{1}{k!} \lim_{\Delta \tau \to 0} M^{(k)} \,, \tag{3}$$

$$M^{(k)} = \frac{1}{\Delta \tau} \int d\Delta x' (\Delta x' - \Delta \tau)^k P(\Delta x', \tau + \Delta \tau | \Delta x, \tau) \,. \tag{4}$$

The coefficients $D^{(k)}(\Delta x, \tau)$ are known as the Kramers–Moyal (KM) coefficients.

3. Application to Analyzing Human Heartbeat Data

As an application of the method, we analyzed both daytime (noon to 18:00 pm) and nighttime (midnight to 6:00 am) heartbeat time series of healthy subjects, and the daytime records of patients with CHF. Our database includes 10 healthy subjects (7 females and 3 males with ages between 20 and 50, and an average age of 34.3 years), and 12 subjects with CHF, with 3 females and 9 males with ages between 22 and 71, and an average age of 60.8 years). The resulting drift and diffusion coefficients, $D^{(1)}$ and $D^{(2)}$, are displayed in Figs. 3 and 4. It turns out that the drift coefficient

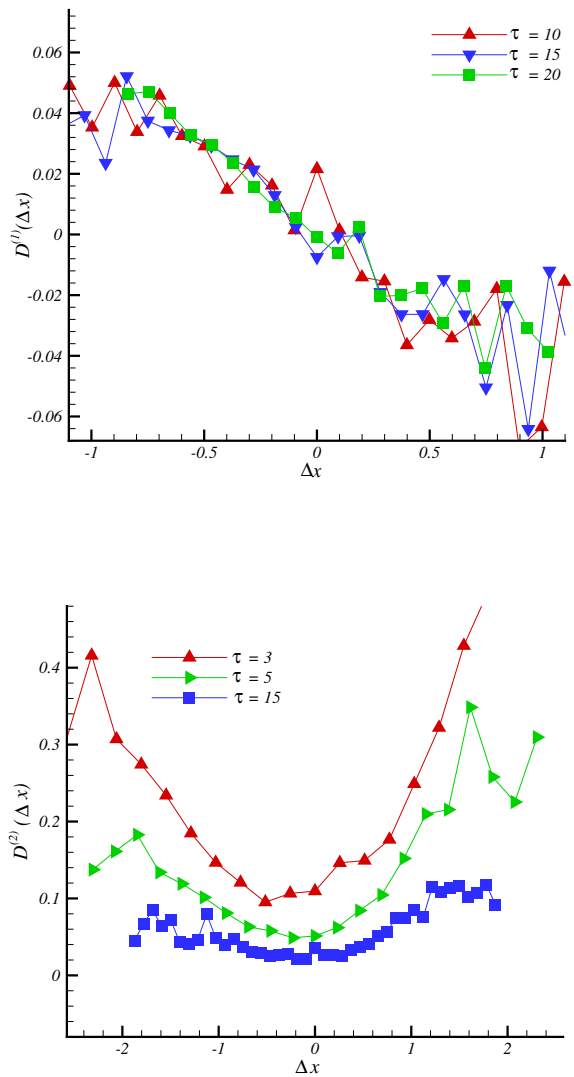

Fig. 3. The drift and diffusion coefficients $D^{(1)}(\Delta x)$ and $D^{(2)}(\Delta x)$, estimated from Eq. (5) for a healthy subject, follow linear and quadratic behavior, respectively.

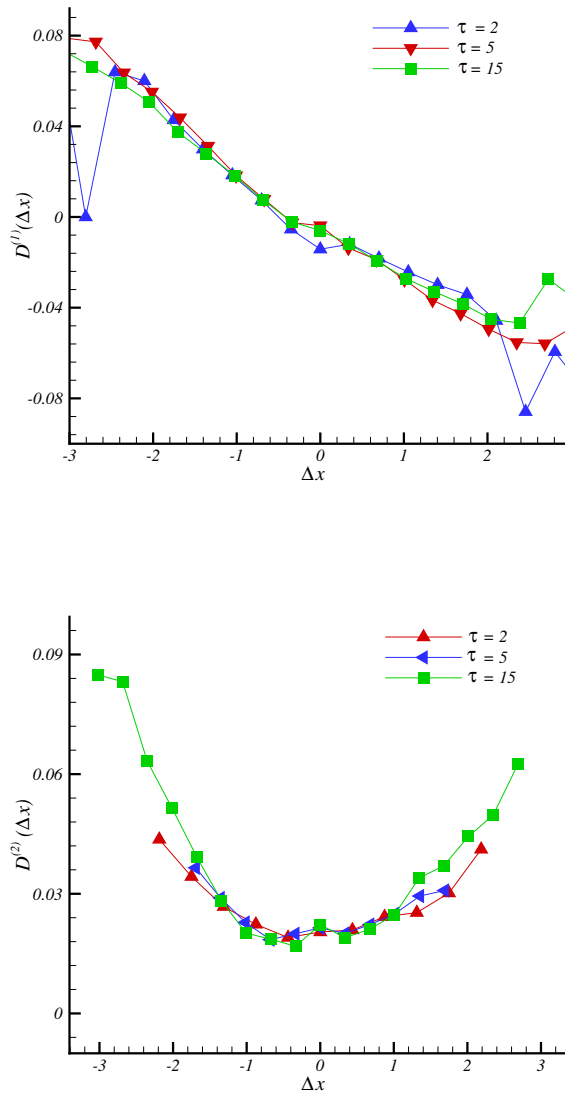

Fig. 4. The drift and diffusion coefficients $D^{(1)}(\Delta x)$ and $D^{(2)}(\Delta x)$ are estimated from the Eq. (6) for typical patients with congestive heart failure, and follow linear and quadratic behavior, respectively.

$D^{(1)}$ is a linear function of Δx, whereas the diffusivity $D^{(2)}$ is quadratic in Δx. Estimates of these coefficients are less accurate for large values of Δx and, thus, the uncertainties increase. Using the data set for the healthy subjects we find that,

$$\begin{aligned} D^{(1)}(\Delta x, \tau) &= -0.03\Delta x - 0.0046\,, \\ D^{(2)}(\Delta x, \tau) &= \left(0.01 + \frac{0.11}{\tau}\right)(\Delta x)^2 + \left(0.057 + \frac{0.287}{\tau}\right)\,, \end{aligned} \tag{5}$$

whereas for the patients with CHF we obtain,

$$D^{(1)}(\Delta x, \tau) = -0.013\Delta x - 0.0018\,,$$
$$D^{(2)}(\Delta x, \tau) = \left(0.005 + \frac{0.005}{\tau}\right)(\Delta x)^2 + \left(0.013 + \frac{0.066}{\tau}\right). \tag{6}$$

We also computed the *average* of the coefficients $D^{(1)}$ and $D^{(2)}$ for the entire set of the healthy subjects, as well as those with CHF. According to the Pawula's theorem,[34,37] the KM expansion is truncated after the second term, provided that the fourth-order coefficient $D^{(4)}(\Delta x, \tau)$ vanishes. For the data that we had analyzed the coefficient $D^{(4)}$ is about $1/10D^{(2)}$ for the healthy subjects, and about $1/20D^{(2)}$ for those with CHF.

Equations (5) and (6) state that the drift coefficients for the healthy subjects and those with CHF have the same order of magnitude, whereas the diffusion coefficients for given τ and Δx are different by about one order of magnitude. This points to a relatively simple way of distinguishing the two classes of the subjects. Moreover, the τ-dependence of the diffusion coefficient for the healthy subjects is stronger than that of those with CHF (in the sense that the numerical coefficients of the τ^{-1} are larger for the healthy subjects). These are shown in Figs. 3 and 4.

The strong τ-dependence of the diffusion coefficient $D^{(2)}$ for the healthy subjects indicates that the nature of the PDF's increments Δx for given a τ, i.e. $P(\Delta x, \tau)$, is intermittent, and that its shape should change strongly with τ. However, for the subjects with CHF the PDF is not so sensitive to the change of the time scale τ, hence indicating that the increments' fluctuations for the subjects with CHF is *not* intermittent. These results are completely compatible with the recent discoveries that the interbeat fluctuations for healthy subjects and those with CHF have fractal and multifractal properties, respectively.[22]

4. Summary and Comparison with Other Methods

We have shown that the probability density of the interbeat interval *increments* satisfies a Fokker–Planck equation, which encodes the Markovian nature of the increments' fluctuations. We have been able to compute reliably the first two Kramers–Moyal coefficients for the stochastic processes Δx — the drift and diffusion coefficients in the FP representation — and, using the polynomial ansatz,[34] obtain simple expressions for them in terms of Δx and the time scale τ. We have shown that the drift and diffusion coefficients of the increments in the interbeat fluctuations of healthy subjects and patients with CHF have different behavior, when analyzed by the method that we used in this paper. Hence, they help one to distinguish the two groups of the subjects. Moreover, one can obtain the form of the path probability functional of the increments in the interbeat intervals in the time scale, which naturally encodes the scale dependence of the probability density. This, in turn, provides a clear physical picture of the intermittent nature of interbeat intervals fluctuations.

Let us emphasize that the previous analyses[1–6,20–23,26,27,30,31] of the type of data that we consider in this paper indicated that there may be long-range correlations in the data which might be characterized by self-affine fractal distributions, such as the fractional Brownian motion or other types of stochastic processes that give rise to such correlations. In that method one distinguishes healthy subjects from those with CHF in terms of the *type* of the correlations that might exist in the data. For example, if the data follow a fractional Brownian motion, then the corresponding Hurst exponent H is used to distinguish the two classes of the subjects, as $H < 0.5$ (> 0.5) indicates negative (positive) correlations in the data, while $H = 0.5$ indicates that the increments in the data follow Brownian motion. The method proposed in the present paper is different from such analyses in that, the *increments* in the data are analyzed in terms of Markov processes. Our analysis does indicate the existence of correlations in the increments which can be quite extended but, as is well-known in the theory of Markov processes, such correlations, though extended, eventually decay (the correlations in fractional Brownian motion do not). We distinguish the healthy subjects from those with CHF in terms of the *differences* between the drift and diffusion coefficients of the Fokker–Plank equation that we construct for the incremental data which, in our view, provides a clearer and more physical way of understanding the differences between the two groups of the subjects.

We should also mention the recent work of Lin[38] who argued that the daytime heart rate variability of healthy subjects may exhibit *discrete* scale-invariance (DSI). A stochastic process $x(t)$ possesses *continuous* scale-invariant symmetry if its distribution is preserved under a change of variables, $t \to \lambda t$ and $x \to x/\mu$, where λ and μ are *real* numbers, so that,

$$x(t) = \frac{1}{\mu} x(\lambda t)\,. \tag{7}$$

If Eq. (7) holds only for a countable (discrete) set of values of λ, $x(t)$ is said to possess DSI, which implies a power-law behavior for $x(t)$ that has a log-periodic correction of frequency $1/\log\lambda$, so that

$$x(t) = t^{\gamma} F(\log t/\log\lambda)\,, \tag{8}$$

with, $\gamma = \log\mu/\log\lambda$, and $F(x) = F(x+1)$ being a period scaling function. Generally speaking, one may write, $x(t) = c(t)t^{\zeta}$, with, $\zeta = \gamma + 2n\pi i/\log\lambda$, with $n = 1, 2, \ldots$ The existence of log-periodicity was first suggested by Novikov[39] in small-scale energy cascade of turbulent flows. Sornnette[40] and co-workers argued that log-periodicity may exists in the stock market crashes,[41] turbulence,[42] earthquakes,[43] and diffusion in disordered materials,[44] while Sahimi and Arbabi[45] provided numerical evidence that it may also exists in the fracture of materials near the macroscopic fracture point. The log-periodicity, if it exists in the heart rate variability (HRV), implies the existence of a cascade for the multifractal spectrum of HRV, previously reported by others.

As mentioned earlier, our approach is different from those of Lin and others in that, it attempts to construct a stochastic equation that governs the HRV data which can, (1) distinguish healthy subjects from those with CHF based on the differences between the drfit and diffusion coefficients of the Fokker–Planck equation that it constructs for the data, and (2) *predict* the stochastic variations of HRV over time scales that are of the order of the Markov time scale described above. Lin's method, on the other hand, neither provides a technique for distinguishing the HRV of healthy people from those with CHF, nor can it predict the future behavior of HRV based on some data at earlier times.

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