EUROPHYSICS LETTERS 15 April 2003

Europhys. Lett., **62** (2), pp. 147–153 (2003)

Modeling transient correlations in heartbeat dynamics during sleep

J. W. KANTELHARDT[1], S. HAVLIN[2] and P. CH. IVANOV[1,3]

[1] *Center for Polymer Studies and Department of Physics, Boston University Boston, MA 02215, USA*

[2] *Gonda-Goldschmied-Center and Department of Physics, Bar-Ilan University Ramat-Gan 52900, Israel*

[3] *Beth Israel Deaconess Medical Center, Harvard Medical School Boston, MA 02215, USA*

(received 19 August 2002; accepted in final form 16 February 2003)

PACS. 02.50.Ey – Stochastic processes.
PACS. 05.40.-a – Fluctuation phenomena, random processes, noise, and Brownian motion.
PACS. 87.19.Hh – Cardiac dynamics.

Abstract. – We propose a model to generate stochastic signals with transient correlations, *i.e.* correlations of different strength and different typical duration within finite segments of the signal. The exponents and crossovers characterizing the correlations in the signal and in its variance can be tuned independently and allow us to generate model time series which are in agreement with data of heartbeat dynamics observed during wake and during different sleep stages. We also propose a model dynamics that reproduces the changes in the heartbeat fluctuations during the entire night, including transitions between different sleep stages.

In recent years, $1/f$ noise and long-range correlations have been reported in many physical and biological systems [1], ranging from weather and climate records [2] to certain parts of DNA sequences [3,4]. In many cases, the scaling behaviour in the correlations is characterized by a power law with a fractal exponent [1]. In physiology, long-range power law correlations have been found in heartbeat dynamics [5,6], neuron spike trains [7], and gait time series [8]. Often the length of the examined records has been 50000–100000 data points, *e.g.*, when heartbeat recordings of 24 h duration were analyzed. The reason for analyzing such long records was to obtain good statistics for the fluctuation and correlation properties. However, physiological data does not remain stationary and homogeneous over long periods of time [9]. Since nonstationarities and trends in the data can lead to a spurious detection of long-range correlations if conventional methods such as autocorrelation, power spectrum, or Hurst analysis are used, special methods have been developed to determine the correlation behaviour in the presence of trends. Among these is the detrended fluctuation analysis (DFA) method [3, 10, 11], which has become a widely used technique for quantifying correlations and scaling in noisy and nonstationary time series. Using such detrending methods, long-range power law scaling has been reported, *e.g.*, for heartbeat time series up to scales of more than 10000 heartbeats [6].

While detrending methods [3, 10, 11] can accurately quantify correlations in signals with trends, they cannot reveal transient correlations, *e.g.*, when applied to long series comprised of segments with different local correlations. Recent studies have attempted to characterize and

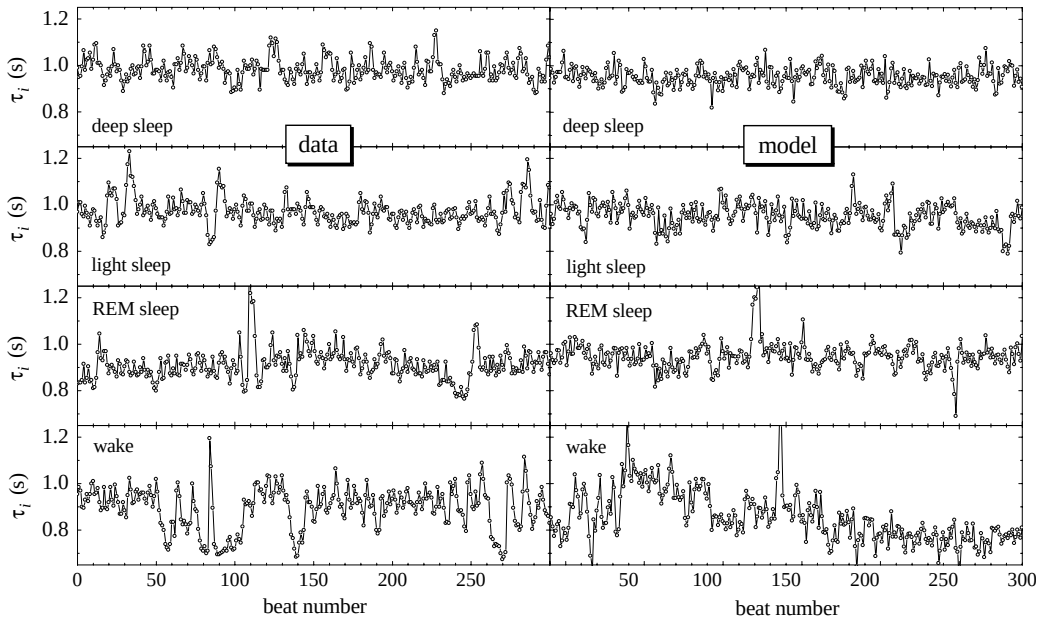

Fig. 1 – On the left: representative recordings of 300 time intervals between successive heartbeats for a healthy subject during deep sleep, light sleep, REM sleep, and an intermediate wake state (from top to bottom). On the right: corresponding series simulated by the proposed model.

quantify the correlation properties by segmentation of the data series before analysis —*e.g.*, long heartbeat series have been split into segments corresponding to sleep hours (night time) and wake hours (day time) [12], and further into segments corresponding to different sleep stages [13,14] or segments corresponding to periods of rest and exercise [15]. These studies have reported very different correlation behaviour for segments associated with different physiologic functions, suggesting that long heartbeat time series do *not* exhibit homogeneous fractal scaling behaviour. Rather, these series are heterogeneous, composed of segments characterized by different linear and nonlinear properties [14]. We call such features *transient*, since they change gradually or abruptly in accordance with physiologic function, reflecting dynamic changes in the underlying mechanism of heartbeat regulation. Thus, the scaling behaviour is often the result of a complex superposition of patches with different local scaling behaviour [11] and exhibits crossovers. Further, even for homogeneous segments where there is no change in physiologic function, one can often observe a crossover in the scaling behaviour suggesting a change in the type of correlations from small to large time scale regimes.

Here we propose a model based on a stochastic process with two parameters which generates complex fluctuating signals with transient correlations. It accounts for the correlation properties observed in the nonstationary physiologic time series. Specifically, we consider human heart rate dynamics during sleep —a representative of complex multicomponent physiological processes with transient correlations.

Healthy sleep consists of cycles of approximately 1-2 hours duration. Each cycle is characterized by a sequence of sleep stages usually starting with light sleep, followed by deep sleep, and rapid eye movement (REM) sleep [16]. It is known that certain changes in physiological processes are associated with circadian rhythms (alternation of wake and sleep states) and with different sleep stages. Differences in cardiac dynamics corresponding to these stages are

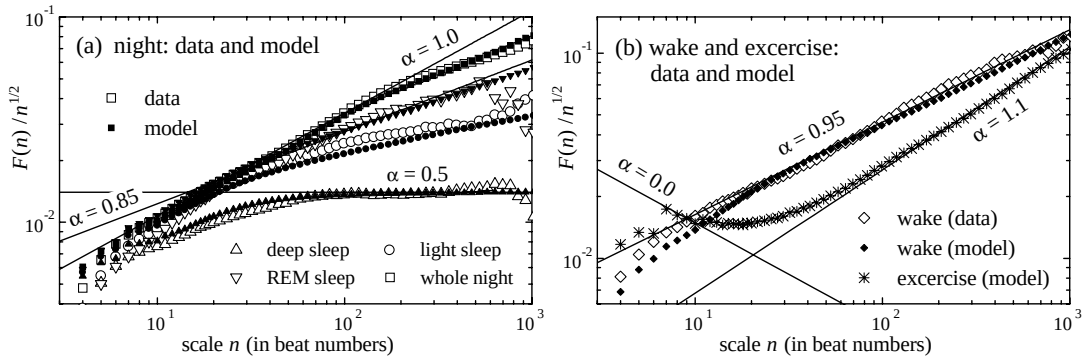

Fig. 2 – Average results of detrended fluctuation analysis (DFA) of 18 heartbeat time series (≈ 30000 beats each) from 10 healthy subjects (open symbols) compared with results for model series (filled symbols). The rescaled DFA fluctuation functions $F(n)/\sqrt{n}$ of the heartbeat interval series τ_i are shown in (a) for deep sleep, light sleep, REM sleep, and the whole night, and in (b) for wake states and for exercise. Since $F(n) \sim n^\alpha$, on log-log plot of $F(n)/\sqrt{n}$ *vs.* time scale n, long-range correlations are indicated by a positive slope with a scaling exponent $\alpha > 0.5$. The straight lines indicate the approximate power law scaling behaviour $F(n) \sim n^\alpha$ observed for large scales n (except for the $\alpha = 0$ line indicating the intermediate behaviour during exercise [15]). The model series we generate consist of 500000 beats each.

reflected in the average and standard deviation of the heartbeat intervals [17]. Figure 1 shows representative recordings of the time intervals τ_i between successive heartbeats (registered by the R-peaks in the ECG) for a healthy subject during deep sleep, light sleep, REM sleep, and an intermediate wake state. Data show that the average duration of the interbeat intervals is slightly longer during deep sleep and light sleep and that the signal is more homogeneous in deep sleep compared with light sleep, REM sleep, and wake where it exhibits more irregular fluctuations.

Recent studies have specifically focused on the correlation properties of heartbeat fluctuations and found that the correlations change in time in accordance with the sleep stages. During deep sleep the time series of heartbeat intervals τ_i are nearly uncorrelated above the breathing cycle period [13]. For light sleep only short-range correlations in the τ_i are observed, suggesting a more random regulation of the heartbeat at large scales [13]. In contrast, long-range correlations corresponding to a power law decay of the correlation function and characterized by a DFA scaling exponent $\alpha \approx 0.85$ are present in the REM phase [13]. They are reminiscent of the wake phase characterized by long-range correlations with $\alpha \approx 1.0$ for healthy subjects [12]. Even larger values of $\alpha \approx 1.1$ have recently been observed during exercise [15]. Figure 2 shows, for the different sleep stages, the average DFA fluctuation function $F(n)$ for 18 heartbeat recordings from 10 healthy subjects in our data base [13, 14].

Further, positive long-range correlations in the heartbeat magnitude series have been recently observed [14, 18]. The magnitude series is defined by the absolute values $|\delta\tau_i|$ of the heartbeat increments, $\delta\tau_i \equiv \tau_i - \tau_{i-1}$, and it is also sometimes referred to as the volatility [18, 19]. These correlations in the magnitude are strong during REM sleep, weaker during light sleep, and nearly vanish during deep sleep. Since positive correlations in the magnitude series have been related to the nonlinear properties of the original time series [18], these findings suggest that the nonlinear properties of the heartbeat dynamics are more pronounced during REM sleep [14]. In fig. 3(a) we show the DFA function $F_{\rm mag}(n)$ for the magnitude series averaged over the 18 heartbeat recordings in our data base.

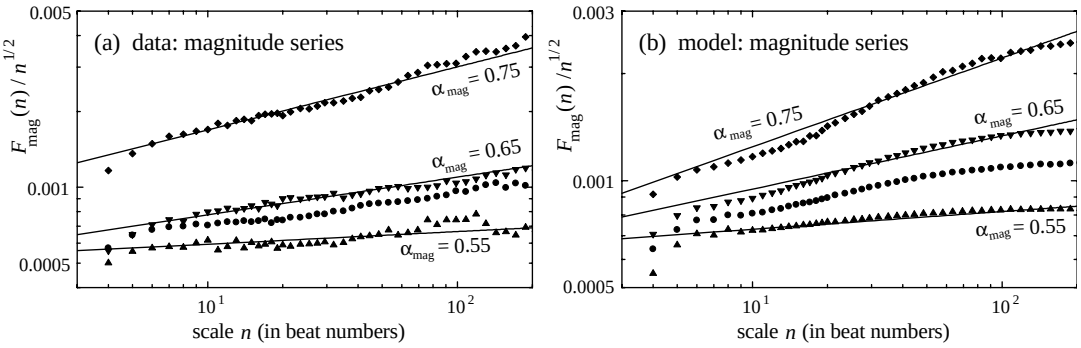

Fig. 3 – Rescaled DFA fluctuation functions $F_{\rm mag}(n)/\sqrt{n}$ for the magnitude series of absolute heartbeat increments $|\delta\tau_i|$ from (a) real data (same records as considered in fig. 2) and (b) model series. The straight lines indicate the approximate power law scaling behaviour $F_{\rm mag}(n) \sim n^{\alpha_{\rm mag}}$ observed for large scales n [20]. The symbols are the same as in fig. 2.

To model the complex transient changes in the correlation properties of the heart rate signal we introduce a process consisting of two series of random variables. We begin with a series of independently and identically distributed (i.i.d.) real numbers x_i, $i = 1, \ldots, N$, taken from an exponential distribution,

$$P(|x_i|) = \exp[-|x_i|], \tag{1}$$

and with random sign. The second series of random variables consists of i.i.d. integers k_i, $i = 1, \ldots, N$, following a power law distribution [21],

$$P(k_i) \sim k_i^{-\gamma}, \quad \text{for } k_i \geq 6. \tag{2}$$

The exponent γ determines the strength of the correlations in the model time series and relates to the DFA correlations exponent α. Using the series k_i, variance correlations are introduced into the series x_i, and we obtain a new series y_i, $i = 1, \ldots, N$,

$$y_i = x_i \sqrt{1 + b\langle y_{i-1}^2 \rangle_{k_i}}, \tag{3}$$

where $\langle y_{i-1}^2 \rangle_{k_i}$ designates the average of the previous values $y_{i-k_i}^2, y_{i-k_i+1}^2, \ldots, y_{i-1}^2$ with $y_j = 0$ for $j = i - k_i, \ldots, 0$ for initialization. Based on the two series of random variables y_i and k_i, we construct our model series τ_i, $i = 1, \ldots, N$,

$$\tau_i = \mu + 0.03 \sin\big(2\pi t_i/3.6\big) + 0.025 \sum_{j=1}^{i} y_j \Theta\big(k_j + j - i\big), \tag{4}$$

where $\Theta(m) = 1$ for $m > 0$ and $\Theta(m) = 0$ for $m \leq 0$, $t_i = \sum_{j=i-(i \bmod 4)-1}^{i-1} \tau_j$ for $i \geq 5$ and $t_i = 0$ for initialization ($i < 5$) is the time of the oscillation period, and all time variables and constants are in unit of seconds [22]. The values of the two parameters in our model, γ and b, are presented in table I for the different sleep stages, wake state, and exercise.

The first term μ in eq. (4) is constant and describes the mean interbeat interval τ_i, which varies for different sleep stages [17]. We choose the values of μ (as presented in table I) according to the averages determined from the 18 heartbeat recordings in our data base. The second term in eq. (4) accounts for the effect of breathing on the heartbeat. The breathing

TABLE I – *Parameters and data used to model the heartbeat during different sleep and wake states. The model uses two parameters: the correlation parameter γ in eq.* (2) *and the nonlinearity parameter b in eq.* (3)*. The mean interbeat interval μ in eq.* (4) *has been determined from the data. The other columns characterize the sleep stage dynamics during the night and are chosen according to experimental results* [23]*: the fraction f (percentage time) spent in a given sleep stage throughout the night, and the type of the distribution of sleep stage durations.*

	γ	b	μ (s)	f	Type
Deep sleep	5.0	0.3	0.95	0.15	exponential
Light sleep	2.7	0.45	0.95	0.55	exponential
REM sleep	2.4	0.55	0.90	0.20	exponential
Wake states	2.1	0.75	0.85	0.10	power law
Exercise	1.8	0.75	0.7		

activity modulates the duration of the interbeat intervals, which also become synchronized with the breathing rhythm [24]. Thus, the modeled fluctuations are not completely random at short time scales, but are rather periodic with a period equal to the breathing interval. The amplitude of these breathing oscillations (prefactor value 0.03 s) and the breathing period (3.6 s) were chosen in order to obtain agreement with the heartbeat recordings. The synchronization between heartbeats and breathing [24] is modeled by the sum defining t_i in eq. (4). By using modulus 4 in the definition of t_i, we reset the phase of the breathing cycle to zero after each 4 heartbeats, so that the time t_i is defined from up to 4 preceding intervals τ_i. Modulus 4 is used, since there are about 4 heartbeats per breathing cycle. This rule introduces a rather strong synchronization, which could be weakened by increasing the number of preceding intervals τ_i taken into account.

The third term in eq. (4) is stochastic and accounts for the fluctuations in the heartbeat intervals by employing the i.i.d. stochastic process x_i. We choose x_i from an exponential distribution, eq. (1), because heartbeat increments were found to follow an exponential distribution [25,26]. We note that the effect of the distribution of the random variable x_i on the correlation properties of the generated series is negligible —a Gaussian or uniform distribution will lead to equivalent results. In order to model correlated series corresponding to the heartbeat dynamics during REM sleep, wake state, and exercise, we use the random variables x_j not only for the modeling of one interval τ_i, but for k_j successive intervals τ_i, where $j = i - k_j + 1, \ldots, i$. We first set $b = 0$, leading to $y_j = x_j$ in place of eq. (3). If $k_j > 1$, the value of x_j affects k_j successive values τ_i in eq. (4), because $\Theta(k_j + j - i) = 1$ for k_j successive values of i, and thus generates correlations in the τ_i series. Hence the form of the distribution $P(k_j)$ (eq. (2)) determines the choice of the integers k_j and thus accounts for the correlations in the τ_i series. We assume a power law distribution in eq. (2), since an automatic segmentation of heartbeat time series data was shown to lead to a power law distribution of segment lengths [27].

We analyze our model time series generated by eq. (4) (with the parameters given in table I) using the DFA method and compare the results with data (fig. 2). The curves correspond to the different sleep stages, wake state, and exercise. It can be seen that the modeled scaling behaviour is in agreement with the data. The correlation exponents α can be tuned with the parameter γ characterizing the decay in the distribution $P(k_i)$ (eq. (2)). We note that the correlations do not persist beyond several thousand heartbeats if $\gamma > 2$. Since the sleep stages and wake periods are usually of short duration, the transient correlations generated by our model are sufficient to mimic the data.

For $b = 0$, our model based on eqs. (1)-(4) does not include any nonlinearities or variance correlations, and the analysis of the corresponding magnitude series simply shows uncorrelated

behaviour ($\alpha_{\rm mag} = 0.5$) not consistent with data (see fig. 3(a)). Thus, we include in eq. (3) the term involving the square root, which causes correlations in the variance when $b > 0$. The term is similar to an autoregressive conditional heteroscedasticity (ARCH) process, that is often used to describe systems characterized by correlations in the variance [19, 28]. In order to generate long-range correlations in the variance, we propose a generalized ARCH process by replacing the square of the previous value, y_{i-1}^2, by the average of the previous k_i values in eq. (3). Figure 3(b) shows our results of the DFA analysis for the magnitude series corresponding to the different sleep stages and wake in our model in close agreement with the results obtained from data. We note that the use of the generalized ARCH process does not affect the regular correlations in the time series τ_i. Thus, the correlations in the magnitude series $|\delta\tau_i|$ can be tuned independent of the correlations in the original series τ_i by changing the parameters b and γ, respectively. This feature of our model makes it suitable for modeling of a broad range of physiological time series.

In order to model heartbeat series not only for individual sleep stages but for the whole night, we utilize experimental results for the fraction f of total sleep time for each sleep stage and the corresponding distributions (see table I) [23]. The durations of the sleep stages follow an exponential distribution with the mean duration of approximately 600 seconds, while the intermediate wake states follow a power law distribution characterized by the scaling exponent $\delta = 2.1$ [29]. Using the values taken from [23], we have modeled heartbeat time series for entire nights. Since transitions between some sleep stages are associated with arousals [23] and impose stress on the body perhaps similar to exercise, we insert 30 beats of modeled exercise data at 50% of the sleep stage transitions. Figure 2(a) shows that the scaling behaviour of the modeled series for the whole night is in good agreement with data (square symbols). Thus, our model can describe the transient heartbeat dynamics associated with the sleep stages and wake states during the entire night.

Understanding the origins of nonlinear processes which exhibit scaling features characterized by long-range power law correlations remains a challenge. Previous work shows that physiologically motivated modeling approaches based on stochastic and feedback mechanisms can successfully account for key scaling features in physiological data observed over a wide range of time scales [26]. Here we show that stochastic concepts can be extended and utilized to account for *both* linear and nonlinear scaling features, as well as for the transient changes of these features in time and over different scaling regimes as observed in physiological data. In the context of heartrate regulation our modeling approach suggests that the volatility in heartbeat fluctuations is controlled by a long-memory process, and that transient patches of fluctuations with different magnitude are regulated by an inherent to the neuroautonomic system power law distribution. Such nonrandom transient changes in the volatility appear to reflect the nature of the sympathetic and parasympathetic interactions regulating the heartbeat fluctuations during different sleep stages, and our modeling approach provides a quantitative measure of this regulation through the parameters γ and b. Finally our study accounts for the synchronization between the breathing rhythm and the heartrate fluctuations in the presence of long memory.

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We thank the German Academic Exchange Service (DAAD), the Israel & USA Binational Foundation, and the NIH/National Center for Research Resources for financial support. The heartbeat recordings were obtained as part of the SIESTA project funded by the European Union grant no. Biomed-2-BMH4-CT97-2040 and were provided by T. PENZEL.

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[20] We note that we have used only single summation in the first step of the DFA here, in contrast to [14, 18], where double summation led to scaling exponents α_{mag} larger by one.

[21] Because k_i is an integer random variable, the distribution has to take the discrete form, $P(k_i) = P_{\mathrm{d}}(k_i) \equiv k_i^{1-\gamma} - (k_i+1)^{1-\gamma}$ for $k_i \geq 6$. For very small k_i the distribution is slightly modified, $P(k_i) = 0.8 P_{\mathrm{d}}(k_i)$ for $1 \leq k_i \leq 4$ and $P(5) = 0.2[P_{\mathrm{d}}(1) + P_{\mathrm{d}}(2) + P_{\mathrm{d}}(3) + P_{\mathrm{d}}(4)] + P_{\mathrm{d}}(5)$, to reduce the number of very short segments. This deviation from eq. (2) at low values of k_i takes into account the reduced randomness on small scales due to the breathing cycle.

[22] For the modeled heartbeat series during exercise, the two prefactors in eq. (4) have to be modified because breathing affects the heartbeat more strongly during exercise. We have used 0.1 for the prefactor of the second term and 0.0125 for the third term.

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[29] We note that ref. [23] reports the scaling behaviour of the cumulative distributions, while the scaling exponent δ of our distribution is always larger by one.