

A Statistical Model of the Sleep-Wake Dynamics of the Cardiac Rhythm

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Abstract

The beat-to-beat heart rate varies considerably over the course of 24 hours. The Computers in Cardiology Challenge of 2002 was based on understanding and modelling the dynamics of the source of this variation. The diverse range of entries for simulating the RR tachogram emphasises the level of ambiguity that exists when attempting to model the cardiovascular system over long time scales. In 2002, a model that combined both deterministic and stochastic descriptions of the data generating process was developed to reproduce both short term variations and long range correlations in RR intervals. In this paper these ideas are extended and new observations of sleep-wake transitions observed during sleep are incorporated. The new model more faithfully represents some of the key empirical characteristics that have been observed in actual recordings of healthy human subjects from the Physionet database. These characteristics include the distribution of RR intervals during wake and sleep periods. In particular the model emulates the existence of a scale-free power law distribution during wakefulness and the exponential distribution (with a characteristic time scale) of sleep-wake activity during prolonged sleep. Concurrence with real data is demonstrated using detrended fluctuation analysis and multiscale entropy. In order to increase the model's utility for assessing biomedical signal processing methods applied to the RR interval time series, a label for each beat is available as either normal, ectopic or artifactual. Furthermore, a state label (wake or sleep) is available.

1. Introduction

The cardiac rhythm fluctuates throughout the day, responding to different demands on the body and varying levels of physical and mental activity. The ability of the heart to adapt to internal and external perturbations may provide useful information about its state of health. In particular, the loss of adaptability resulting from ageing or the onset of disease may, in some cases, be detected from long

recordings of cardiac inter-beat time intervals derived from the electrocardiogram [1].

Quantifying the self-similarity of such cardiac signals provides a means of distinguishing between health and disease and monitoring the effect of ageing [2, 3]. One approach for measuring the self-similarity of a signal is to calculate its power-spectral density, $S(f)$, and estimate the power-law scaling exponent, β , that satisfies $S(f) \sim f^{-\beta}$. This exponent, β , may be viewed as a measure of the roughness of the time series, with smoother self-similar time series having larger values of β . For cardiac signals, a $1/f$ -like noise ($\beta = 1$) is found [4]. This value is midway between the complete randomness of white noise ($\beta = 0$) and the much smoother Brownian motion ($\beta = 2$) [5].

During sleep the human body is less exposed to physical activity and variations in the heartrate mainly result from neuronal activity. For this reason, it is advantageous to investigate the statistical properties of cardiac activity during sleep and during sleep-wake transitions. The scaling exponents have been found to vary between wake and sleep and also during different sleep stages [1, 6].

2. Methods

In this section, a method is described for producing realistic RR interval tachograms spanning twenty-four hours. These tachograms incorporate both sleep and wake activity. A dynamical model is used to govern the switching between states of sleep and wake [7]. Data simulated from a white noise process is transformed to produce segments of RR tachogram with pre-specified temporal and spectral properties [8].

2.1. Sleep-wake dynamics

Lo *et al.* [7] analysed the distribution of time durations spent in periods of sleep and wake for 39 full-night sleep records of 20 healthy subjects. These included 11 females and 9 males aged between 23 and 57 with an average sleep duration of 7.0 hours. The cumulative distribution of durations, given by $P(t) = \int_t^\infty p(t')dt'$, was employed to

demonstrate the difference between periods of sleep and wake. The periods of time spent in a wake state followed a power-law distribution,

$$P(t) \sim t^{-a} \quad (1)$$

where, for the twenty subjects, a had a mean value of 1.3 and a standard deviation of 0.4. In contrast, the periods of time spent in a sleep state greater than 5 minutes followed an exponential distribution,

$$P(t) \sim \exp(-t/\tau), \quad (2)$$

with a characteristic time scale τ . For the twenty subjects investigated, τ had an average of 20 minutes and a standard deviation of 5 minutes.

A simple model of sleep-wake dynamics uses a latent variable, $x(t)$, to define wake states when x is positive and sleep states when x is negative and satisfies $-\Delta \leq x \leq 0$. The latent variable $x(t)$ is assumed to follow a random walk, which corresponds to the noisy behaviour generated by interactions between competing sleep-active and wake-promoting neurons. To ensure a bias towards sleep, once x moves into the wake state, there is a restoring force to attract it back to the sleep state. The sleep-wake transitions during nocturnal sleep usually demonstrate two features: (i) during short wake periods there is a strong probability of falling asleep and (ii) as the period of wake state is prolonged, the probability of falling asleep is reduced. The model imposes a restoring force that weakens as x moves away from the critical transition value of $x = 0$. These observations about nocturnal sleep may be represented by a random walk in a logarithmic potential, $V(x) = b \ln x$, with an associated force $f(x) = -dV(x)/dx = -b/x$, where the bias b gives the magnitude of the restoring force. The model may be written as $x(t+1) = x(t) + \delta x(t)$ with

$$\delta x(t) = \begin{cases} \varepsilon(t), & \text{if } -\Delta \leq x(t) \leq 0 \text{ (sleep),} \\ -\frac{b}{x} + \varepsilon(t), & \text{if } x(t) > 0 \text{ (wake),} \end{cases} \quad (3)$$

where $\varepsilon(t)$ is an uncorrelated normally distributed random variable with zero mean and unit standard deviation. As the distribution of durations spent in the wake state follow the return times of a random walk in a logarithmic potential and therefore provide a power-law distribution for large times with cumulative distribution given by $a = 1/2 + b$. In contrast, the distribution of periods spent in the sleep state is the same as that of return times of a random walk in a space with a reflecting boundary. For large times, the cumulative distribution is exponential with characteristic time τ satisfying $\tau \sim \Delta^2$.

The model parameters, b and Δ may change during the night to reflect the circadian rhythm. Both b and Δ , were varied to reproduce the recorded signals and the best estimates suggested that Δ decreases from 7.9 ± 0.2 in the

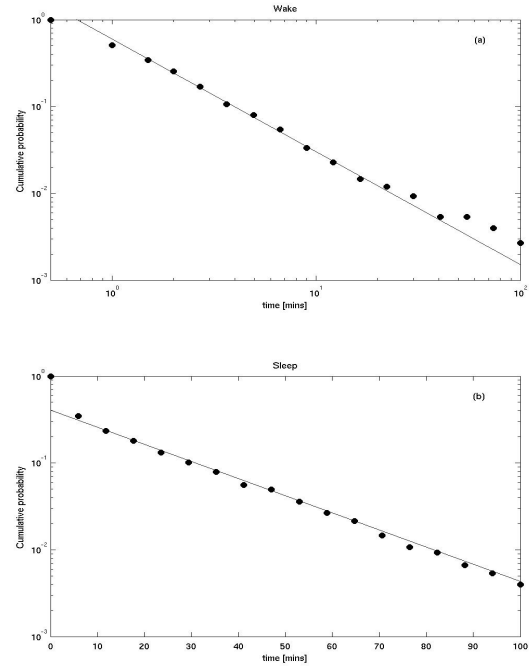


Figure 1. Cumulative distribution functions arising from the dynamics of the sleep-wake model for time duration spent in (a) the wake state (log-log) and (b) the sleep state (log-linear), showing power-law and exponential behaviour respectively.

first hours of sleep to $\Delta = 5.5 \pm 0.2$ for the final hours of sleep. The bias b was found to remain approximately constant during the night with $b = 0.8 \pm 0.1$ [7].

2.2. Sleep-wake scaling

The self-similar structure of cardiac interbeat intervals gives rise to an approximate $1/f$ spectrum, also known as pink noise [4]. In the biomedical literature, this scaling is often quantified using a technique known as detrended fluctuation analysis (DFA) [3]. For a review and comparison of techniques, see [9]. Results from investigations of scaling of during both sleep and wake periods are used to specify suitable scaling coefficients [1]. These results, calculated from 18 healthy subjects (13 females and 5 males with ages between 22 and 71) in the Physionet Normal Sinus Rhythm database [10] gave an average β of 1.10, standard deviation of 0.14, for wake and an average β of 0.70, standard deviation of 0.20, for sleep.

2.3. Simulation

A realisation of a noise process with a particular scaling exponent, β , may be obtained by (i) computing the discrete Fourier transform (DFT) of a normally distributed white noise with N points, (ii) filtering the resulting Fourier coefficients, X_k , using $X'_k = (k/N)^{-\beta/2} X_k$, and (iii) taking the inverse DFT of the filtered Fourier coefficients, X'_k . The new time series were transformed to have means of μ_s and μ_w during sleep and wake where μ_s is normally distributed with mean 1.0 and standard deviation 0.1 and μ_w/μ_s is uniformly distributed on $[0.75, 0.85]$. The standard deviations were taken as 5% of the mean values.

3. Comparing real and artificial data

Apart from visual inspection and the reproduction of the dynamics of sleep-wake distribution times, it is also important to evaluate how well the model reproduces empirical heart rate variability statistics. Two common statistics which describe the variability of the RR interval time series over a range of scales are *Detrended Fluctuation Analysis* (DFA) [11], and *Multi-scale Entropy* (MSE) [12].

As a representative sample of real RR interval dynamics, the normal sinus rhythm RR interval database [10] which consists of 54 long-term ECG recordings of subjects in normal sinus rhythm (30 men, aged 28.5 to 76, and 24 women, aged 58 to 73) was chosen. Artificial data were generated using 100 random seeds of the described model, each approximately 24 hours in length. Only the sleep periods of both the real and artificial RR intervals were employed to analyse the sleep-wake dynamics.

Figure 3 presents a comparison of the DFA scaling for real and model-generated RR intervals. Note that the DFA scaling exponent, α is related to the power-spectral exponent through $\beta = 2\alpha - 1$. The model-based RR interval time series has a DFA scaling of $\alpha = 1.05$ with a standard deviation of 0.05 over the 100 realisations. The real data exhibits a similar DFA scaling of $\alpha = 1.00$ with a standard deviation of 0.06 over the 54 records. The real data displays more variability at small values of n , possibly reflecting that the model does not produce enough inter-subject differences for small values of n . Both real and artificial populations provide results that are similar to the value of $\alpha = 1$ reported in the literature [11].

Figure 4 presents the results for MSE analysis, showing the average sample entropy for both real and artificial data sets. The scale factor gives the number of points averaged to form each element of the coarse-grained time series. Note that both populations have approximately similar values and variances at high scale factors, where any variability over short time scales has been averaged out by the coarse-graining. In contrast, the sample entropy is underestimated by the artificial RR intervals at the low scale

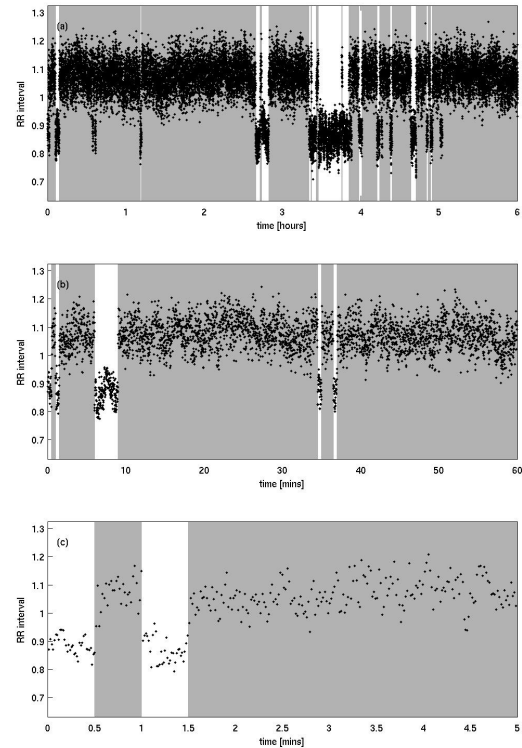


Figure 2. Sleep-wake tachogram simulation showing: (a) first 6 hours, (b) first hour and (c) first 5 minutes. The shaded/white regions indicate periods of sleep/wake respectively.

factors. Note that a scale factor of one corresponds to the standard measure of sample entropy calculated using the raw time series. The level of inter-subject variability is similar for both populations over all scale factors.

The high values of sample entropy at low scale factors for the artificial RR intervals may reflect a lack of structure caused by changes in sympathovagal activity and details of different sleep stages. Furthermore, the model presented here does not incorporate circadian variability.

4. Conclusion

A realistic RR interval generator has been described which preserves both the temporal and spectral properties of RR intervals during periods of sleep and wakefulness. The sleep-wake dynamics were encoded using a binary description of sleep and wake periods. A method of filtering the Fourier coefficients was used to simulate data with specific scaling properties that reflect the values observed in real RR intervals. The mean, variance and length of

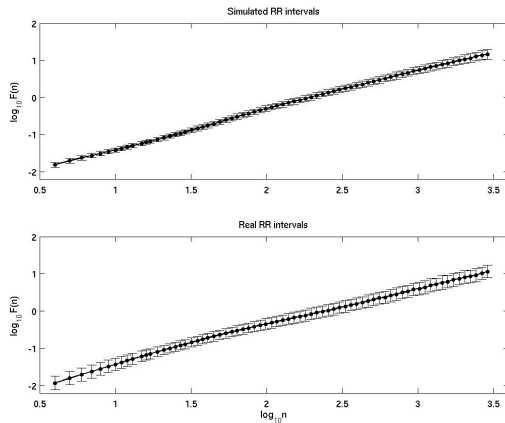


Figure 3. Comparison of DFA scaling for 100 artificial and 54 real RR tachograms. Error bars show one standard deviation above and below the mean.

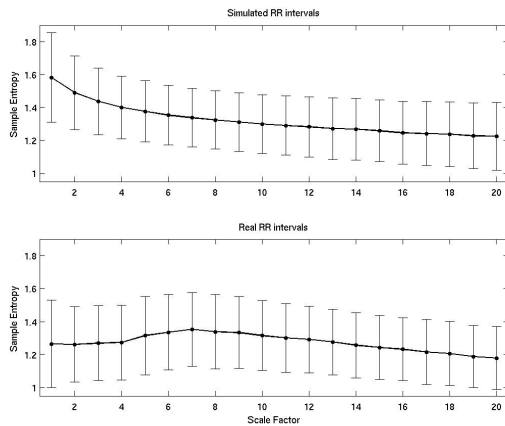


Figure 4. Comparison of mean sample entropy for 100 artificial and 54 real RR tachograms. Error bars show one standard deviation above and below the mean.

each segment mimics empirically observed distributions, including the significant differences observed between periods of sleep and periods of wakefulness. The model's output therefore includes both RR intervals and a binary level of consciousness.

The increasing convergence of the fields of cardiovascular and sleep medicine means that such a model may help researchers develop more robust signal processing algorithms to identify cardiovascular problems both within sleep and during wakefulness. Further developments of the model could include the introduction of RSA and Mayer waves (see [13]), circadian variability and sleep staging such that the parasympathetic balance (as observed in the LF/HF ratio) varies through sleep stage changes in a manner consistent with physiology.

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