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„Model-Based Aanalysis of Cardiovascular Variability Insleep Medicine“

N. Wessel, M. Riedl
Interdisciplinary Center for Dynamics of Complex Systems, University of Potsdam, Germany
E-Mail: wessel@agnld.uni-potsdam.de

J. Kurths
Department of Physics, Humboldt-Universität zu Berlin, Germany

Potsdam Institute for Climate Impact Research, Germany

T. Penzel
Centre for Sleep Medicine, Charité, Berlin, Germany

A. Suhrbier, G. Bretthauer, H. Malberg
Institute for Applied Computer Science, Forschungszentrum Karlsruhe GmbH, KIT Karlsruhe Institute of Technology, Germany

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MODEL-BASED ANALYSIS OF CARDIOVASCULAR VARIABILITY IN SLEEP MEDICINE

N. Wessel[1,2], M. Riedl[1], J. Kurths[2,3], T. Penzel[4], A. Suhrbier[5], G. Bretthauer[5], H. Malberg[5]

[1]Interdisciplinary Center for Dynamics of Complex Systems, University of Potsdam, Germany
[2]Department of Physics, Humboldt-Universität zu Berlin, Germany
[3]Potsdam Institute for Climate Impact Research, Germany
[4]Centre for Sleep Medicine, Charité, Berlin, Germany
[5]Institute for Applied Computer Science, Forschungszentrum Karlsruhe GmbH, KIT Karlsruhe Institute of Technology, Germany
E-Mail: wessel@agnld.uni-potsdam.de

Introduction

The cardiovascular system often shows complicated temporal, spatial, and spatiotemporal behaviour, which reflects the complex interactions of many different inherent control loops. Modelling provides insights into the mechanisms of the cardiovascular regulation. Linear modelling approaches [1] resulted in the successful detection of dysfunctions of cardiovascular regulation. But various non-linear phenomena, for example synchronisation in the cardiorespiratory coordination as well as threshold effects, saturations or amplitude-frequency-coupling in the HRV, have been observed in this system and therefore to be regarded in the modelling process. In the last years non-linear models have proved to be very efficient and necessary to explain such phenomena of HRV and BPV, for instance in sleep medicine [2-4].

We propose in this paper a non-linear additive autoregressive model with exogenous influences (NAARX), which is characterized by nonlinear transformations of the predictor values [5]. We study whether this model is suitable to describe the complex dynamics of the heart rate (HR) as well as the systolic blood pressure (BP) and whether the fitted models allow a detection of pathological changes in sleep disorders.

Data

To study the influence of obstructive sleep apnoea syndrome (OSAS) on cardiovascular regulation, three OSAS patients with hypertension as well as three patients without hypertension (age 44±6 years) were analyzed. Additionally, three healthy persons (age 30±8 years) were considered for comparison. For each subject, an electrocardiogram (ECG, sampling rate 1000Hz), the continuous blood pressure (via finger cuff of Portapres device mod. 2, BMI-TNO, Amsterdam, The Netherlands; sampling rate 200Hz), and the respiration curve (by means of a thorax strap, sampling rate 10Hz) were recorded. The persons were awake with a relaxed respiration in supine position. From the ECG, the times of the heart beats were determined using appropriate algorithms [6]. Intervals between successive heart beats ({Bi} - Beat-to-beat-intervals) were calculated. The maximum blood pressure value in each beat-to-beat interval was extracted, which leads to the time series of systolic blood pressure corresponding to the intervals ({Si} – Systolic blood pressure). The values of the respiration signal ($\{R_i\}$) were determined at the times of the heart beats. Artefacts caused by e.g. premature beats (beats not initialized by the sinus-atrial node) were substituted in $\{B_i\}$ by means of an adaptive filter [7] (see http://tocsy.agnld.uni-potsdam.de) in order to prevent that phenomena not originating from the autonomous heart rate regulation influence the analysis. A sample time series is shown in Fig. 1.

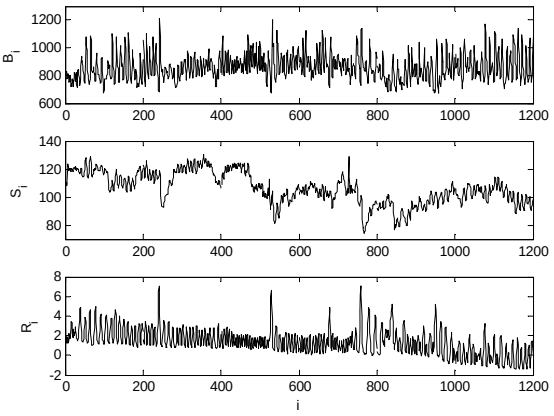

Figure 1: Extracted time-series of beat-to-beat interval $\{B_i\}$, systolic blood pressure $\{S_i\}$ on beat-to-beat basis and respiratory movement $\{R_i\}$ on beat-to-beat basis for a normotensive OSAS patient.

Methods

We describe the HRV and the BPV by discrete models to take pulsatile character of heart rate and blood pressure on the short time scale into account. In the model of heart rate (see Eq. 1), the so called baroreflex is considered by the influence of the previous systolic blood pressure values. Another important source of HRV is the respiration, but it is not clear yet, whether this cardiorespiratory coordination takes place directly via coupling of the breath control centre and the nervous control of the heart rate or indirectly via the baroreflex of respiratory induced blood pressure variations. Therefore, the model of heart rate (see Eq. 1) contains additionally previous values of the respiration movement, in order to consider both possible cases. As the functional relationship of the different cardiovascular values is not clear, we

use a non-parametric approach. This will ensure the highest possible flexibility of the model. Further assumptions made in our model are additivity of the influencing parameters and white noise as random disturbances. Additivity means that the individual predictors do not interact with each other. Hence, one-dimensional functions can be analyzed instead of multi-dimensional ones, leading to the following model equations:

$$B_i = <\{B_i\}> + \sum_{j=1}^{p}\left(f_j(B_{i-j}) + g_j(S_{i-j}) + h_j(R_{i-j})\right) + \varepsilon_i \qquad (1)$$

$$S_i = <\{S_i\}> + \sum_{j=1}^{q}\left(k_j(B_{i-j}) + l_j(S_{i-j}) + m_j(R_{i-j})\right) + \eta_i \qquad (2)$$

$<\{B_i\}>$ and $<\{S_i\}>$ are the mean values of the considered part of $\{B_i\}$ and $\{S_i\}$. i ranges from p+1 and q+1 to N (length of the time series). p and q denote the orders of the autoregressive process. f_j, g_j, h_j, k_j, l_j and m_j are transformations of the considered predictors. $\{\varepsilon_i\}$ and $\{\eta_i\}$ are realizations of white noise.

Results and Conclusions

The estimated functions take a non-linear shape and are clearly distinguishable from a straight line. The mean value of p and q is two, in the group of healthy or normotensive subjects and three for hypertensive OSAS patients respectively. In order to show the diagnostic relevance of our approach, the fitted NAARX model (Eqs. 1 and 2) are compared inside the different groups of subjects and among them. Therefore, the non-linear model of order two is recalculated for each subject in order to get comparable results. For these fits, g_1 and g_2, the transformations of the first and second predecessor value of blood pressure in Eq. 1, are drawn in Fig. 2. The examples in Fig. 2 reveal that pronounced group-specific properties exist. The slope of the transformation g_1 is remarkably smaller in the normotensive OSAS patients than in the healthy persons, which corresponds to decreased influence of the systolic blood pressure on the beat-to-beat interval. The changed monotony of this transformation in the group of hypertensive OSAS patients characterises the pathological regulation of the blood pressure. The comparison of transformation (see Fig. 2) indicates that the slope of g_1 nearly zero seems to be linked to the risk for hypertension evoked by the OSAS. To validate this guess, more cases must be studied. The non-linear shapes of the estimated transformations in the fitted NAARX model (e.g. sharp bends of the transformations) point to different regimes in the cardiovascular regulation. The parameterisation of these forms with piecewise linear functions leads to threshold autoregressive models which are able to generate non-linear phenomena, e.g. amplitude-frequency coupling or synchronization, in combination with external excitation. These phenomena are also found in signals of heart rate and respiratory movement during sleep. Therefore we are able to describe the complex cardiovascular regulation in sleep, e.g. synchronization between respiration and heart rate or the resetting of the baroreflex, the influence of the blood pressure on the heart rate. Finally, looking at the results of the nonlinearity and additivity tests [5] demonstrates the superiority of our nonlinear data-driven modelling approach over linear ones. Moreover, the fact that we are able to discriminate different patient groups may enable an application for clinical OSAS risk stratification.

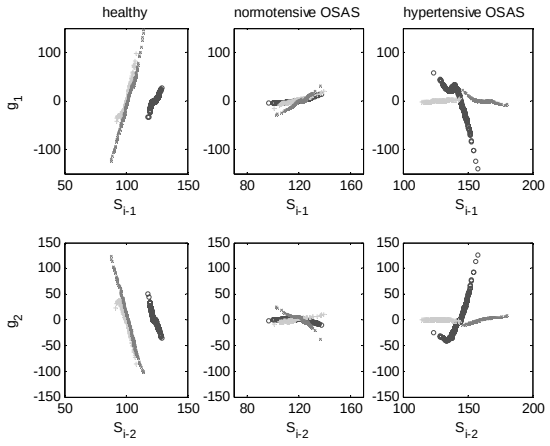

Figure 2: Transformation of the NAARX models (Eq. 1 and 2) of order 2 fitted to the time series $\{B_i\}$. The columns summarize the transformations of the predictor S_{i-1} and S_{i-2} for the subjects of group. The different persons in the group are given the symbols '+' (light), 'x', and 'o' (dark).

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