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„Autonomic cardiovascular control - Data analysis and modeling“

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Autonomic cardiovascular control - Data analysis and modeling

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Introduction

Allegorically, the human heart may be compared with the engine of a car, enabling movement and functionality, both due to an inherent oscillator. However, in contrast to the completely regular action of a perfectly working car engine, the healthy heart's performance is irregular. The intervals between heartbeats widely fluctuate and the diagnostic value of cardiovascular dynamics and its complex variability via data analysis and modelling techniques are an important challenge for physicians, as well as for mathematicians, biologists, and physicists. Therefore, we consider that the time has come to establish a new field of interdisciplinary cardiovascular research to gain deeper insight into pathophysiology and treatment options through a collaborative approach [1].

Spontaneous fluctuations of cardiovascular signals such as heart rate and blood pressure had already been described more than 100 years ago. However, the physiological interpretation of these variabilities is still an interesting and exciting research area. The fluctuations of heart rate and blood pressure represent not only oscillations around a fixed value; they are the expression of several influences such as respiration and different self-regulating rhythms. The analysis of heart rate variability (HRV) has become a powerful tool for the assessment of autonomic control. HRV measurements have proven to be independent predictors of sudden cardiac death after acute myocardial infarction, chronic heart failure, or dilated cardiomyopathy [2]. Moreover, it has been shown that short-term HRV analysis already yields a prognostic value in risk stratification independent of that of clinical and functional variables. How-ever, the underlying regulatory mechanisms are still poorly understood.

Methods

Standard HRV analysis methods include time and frequency domain parameters, often being referred to as linear methods. Time domain parameters are based on classic statistical methods derived from the beat-to-beat intervals as well as the differences between them. Mean heart rate is the simplest parameter, but the standard deviation over the whole time series (sdNN) is the most prominent HRV measure for estimating overall HRV. Frequency domain HRV parameters enable a distinct division into spectrum components of the heart rate dynamics. There are mainly two different techniques for spectral analysis: methods based on fast Fourier transform (FFT) and parametric auto-regressive model estimations of wavelet approaches. Heart rate and blood pressure variability reflect the complex interactions of many different control loops of the cardiovascular system. In relation to the complexity of the sinus node activity modulation system, a predominantly nonlinear behaviour has to be assumed. Thus, the detailed description and classification of dynamical changes using time and frequency measures often is not sufficient.

Data driven modeling analysis

From the electrocardiogram, the times of the heart beats were determined using appropriate algorithms. Intervals between successive heart beats $\{B_i\}$ were calculated. The maximum blood pressure value in each beat-to-beat interval was extracted, which led to the time series of systolic blood pressure $\{S_i\}$. The values of the respiration signal were determined at the times of the heart beats ($\{R_i\}$ respiration on a beat-to-beat basis). Artifacts caused by, e.g., premature beats were removed in $\{B_i\}$ by means of an adaptive filter. The following model equations were nonparametrically fitted to the data:

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

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

<B> and <S> are the mean values of the analyzed time series $\{B_i\}$ and $\{S_i\}$. p and q denote the orders of the two autoregressive processes which were determined minimizing a cross validation criterion. f_j, g_j, h_j, k_j, l_j, and m_j are transformations of the predictors. $\{\varepsilon_i\}$ and $\{\mu_i\}$ are realizations of white noise processes. The nonlinear models were estimated for different parts of the time series to reduce trends and exclude nonstationarities [3]. Additivity was checked using a special statistical test. Using the Kolmogorov-Smirnov test, it was checked whether the residues are normally distributed with the same mean and variance. Analysis of the autocorrelation function from lag 1 to 10 is supposed to indicate whether the residues may be considered as realizations of independent random variables. The improvement of the nonlinear approach is also checked by means of an approximated F test and the investigation of the coefficient of determination R^2.

Synchronization analysis analysis

In most studies the heart beat time series as well as the respiration time series were investigated in a univariate manner. We are, however, also interested in the synchronization between them [4]. In the synchrogram method

the momentary phase of the breathing signal RES_i is reconstructed by calculating

$$\phi(t_i) = 2\pi(t_i - t_k)/(t_{k+1} - t_k) + 2\pi k \quad \text{with} \quad t_k \le t_i < t_{k+1}$$

t_k is the beginning of the *k*th respiratory cycle characterized by the *k*th local minima in the original signal. t_i is the time of the *i*th heartbeat. To obtain the synchrogram, the relative cyclic phase

$$\psi_m(t_i) = (\phi(t_i) \bmod 2\pi m)/2\pi$$

is plotted versus the times t_i of the heartbeats. In this contribution we used m=2, that means that all heart beats within two successive respiratory cycles are plotted. Phase synchronization in synchrograms is characterized by parallel horizontal lines.

Symbolic coupling traces

First, the time series are transformed into two symbol sequences s_t^{BBI} and s_t^{SBP} via the transformation rule:

$$s_t^z = \begin{cases} 1, & z(t) \le z(t+\theta) \\ 0, & z(t) > z(t+\theta) \end{cases}$$

Next, we construct series of words w_t^{BBI} and w_t^{SBP} following the scheme in Fig. 1. Afterwards, the bivariate delay-time probability matrix $p_{ij}(\tau)$ is estimated (e.g. τ=0 in Fig. 1). The quantification of the complete probability densitiy by means of Shannon-entropy does not reveal the correct lags clearly. The reason for this is, that too much information about mixed forms of symmetric and diametric structures are involved. This leads to a blur, hiding the correct lags. Therefore, the SCT parameters is only based on the diagonal elements of $p_{ij}(\tau)$:

$$\Delta T(\tau) = \sum_{i=j} p_{ij}(\tau) - \sum_{\substack{i=1,\ldots,d \\ j=d+1-i}} p_{ij}(\tau)$$

Apart from the SCT parameter, cross correlation function R, mutual information I, and cross recurrence base on order patterns were calculated for comparison. The significance limits of the parameter are calculated for 100 surrogates produced by random shuffeling. Coupling is assumed if the parameter value of the original time series lies out of the interval which is bounded by these limits [5].

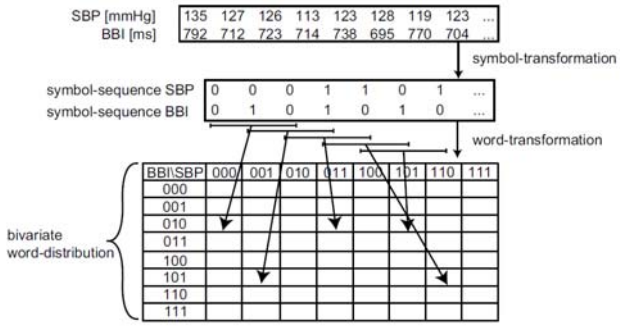

Fig. 1: Scheme for calculating the bivariate word distribution. Starting from SPB and BBI (upper panel), a two-dimensional symbol sequence (middle panels) is calculated by a symbol transformation (θ=1 and l=3) which leads then to the bivariate word distribution.

Results

After having briefly introduced some methods of cardiovascular physics this section of the paper will give an overview of selected clinical applications, which be presented in more details in [6].

Preeclampsia, a serious, pregnancy-specific disorder characterized by proteinuria and hypertension after the 20th week of gestation, is still the leading cause for maternal and neonatal morbidity and mortality and occurs in 3–5% of all pregnancies. Therefore, we investigated 58 consecutive patients with uterine perfusion disturbance and 44 parallel recruited normal pregnancies.

Cardio surgical patients are a high risk group in clinical praxis. For this reason, the intensive care and the postsurgical monitoring are one of the most important research subjects in biomedical engineering. We could show that patients experiencing postoperative atrial fibrillation obviously suffer from an impaired baroreflex sensitivity before surgery already. These findings may be used to guide prophylactic antiarrhythmic therapy.

A function of deep sleep is physical recreation with very low consumption of energy, and therefore an ergonometric optimization is favoured. If during sleep the cardiorespiratory synchronization is lost then this might indicate a lowered physical recreation. Using our nonparametric data-driven modeling approach we were able to show that both regular breathing and dominant coupling functions are necessary but not sufficient to obtain cardiorespiratory synchronization.

Conclusions

We could demonstrate in this tutorial that our data analyses and modeling methods lead to significant improvements in different medical fields. Patients as well as the whole society would benefit from a rapid use of these potentials in clinical practice.

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