Beat-to-beat blood-pressure fluctuations and heart-rate variability in man: physiological relationships, analysis techniques and a simple model

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Summary

Both blood pressure (BP) and heart rate (HR) in resting subjects show spontaneous fluctuations around their mean values. These fluctuations are partly coupled to respiratory activity (period of approximately 4 s), partly to the so-called 10-second waves, of which the origin is not well understood, and partly to slower rhythms. We studied the relationship between the BP- and HR-fluctuations, in order to gain insight in properties of the cardiovascular regulatory system. Spectral analysis techniques were developed and used to separate the different kinds of variability in the HR- and BP-recordings. We developed a mathematical beat-to-beat model which explains in a physiologically plausible way the respiratory heart-rate fluctuations and the 10-s rhythm in heart rate and blood pressure.

This thesis consists of eight chapters, a postscript (chapter 9) and two appendices. Most of the text was adapted from previously published papers (see section 1.6).

In Chapter 1 the aims of the investigation are stated and some relevant information is given about the cardiovascular system, about the signal-properties of blood pressure (BP) and heart rate (HR) and about the concept "BP and HR variability". A survey of the literature on the application of spectral analysis methods to BP and HR variability is given.

Chapter 2 gives a comprehensive description of several methods that are used to represent the series of heart beats as a signal that can be treated by signal-analysis techniques. Its main question is: which heart-rate variability signal is to be preferred in the study of HRV? We argue that such a HRV signal should be related to a physiologically acceptable model for the genesis of heart beats. We chose the Integral Pulse Frequency Modulation (IPFM) model for this purpose and hence the Instantaneous Heart Rate (IHR) signal appears to be the most attractive signal for the time-domain description of HRV. The IHR signal has between two beats the value of the inverse interval between these beats. In contrast, the standard (delayed) heart rate signal has always the value of the inverse previous interval. In addition we show that the shape of the IHR signal is less affected by trigger errors or extrasystoles than the standard DHR signal.
In Chapter 3 we compare different spectral analysis techniques that are used to calculate a spectrum of heart-rate variability data. The focus is on the two principal ones: the interval spectrum, i.e. the spectrum of the interval series, and the spectrum of counts, which is related to the representation of the event series as a series of spikes (delta-functions). Both autospectra are estimated for experimental heart-rate data and are shown to produce similar results. This similarity is proven analytically and it is shown that for small variations in interval length the ratio of these spectra is $P_I(f)/P_C(f) = \frac{(\sin(f \bar{T})}{(f \bar{T})^2}$ with $P_I$ and $P_C$ the Interval Spectrum and the Spectrum of Counts, respectively, $f$ the frequency and $\bar{T}$ the mean interval length. It is concluded that both autospectra are equivalent for the considered heart-rate data but that, when relating the heart-rate signal to other signals (e.g. respiration, blood pressure) by means of cross spectra, the technique to be used depends on the characteristics of the second signal.

Chapter 4 deals with the relation between the spectra of the input-signal and of the output-signal of the IPFM model (see Chapter 2). The Spectrum of Counts is analytically known for the event-series belonging to a sinusoidal input signal (Bayly, 1968). An approximation to the Interval Spectrum of this series is presented. Using data from a simulated IPFM model, it is shown that, for an input signal consisting of the sum of two sinusoids, terms at sum and difference frequencies appear in the Interval Spectrum but not in the Spectrum of Counts. However, the Spectrum of Counts is contaminated by sidebands of the mean repetition frequency. It is concluded that in general the spectral properties of the input signal can not be recovered fully from the Interval Spectrum, nor from the Spectrum of Counts, the more so as physiological series of events will seldom be generated by an ideal IPFM-model.

Chapter 5 describes a simple mathematical beat-to-beat model of the cardiovascular system, consisting of a set of three difference equations. The equations are based on the following physiological considerations: 1) The length of the RR-interval is dependent on the systolic pressure (baroreflex). 2) The pulse pressure is dependent on the length of the preceding interval (due to the restitution properties of the myocardium and to Starling's law). 3) During diastole the pressure decay can be described by a Windkessel-equation. Cross-correlation techniques are used to test the validity of the model. It is shown that blood-pressure
data from hypertensive patients which showed respiratory sinus arrhythmia agreed well with equations 1) and 3), and that data from a patient with atrial fibrillation agreed with equations 2) and 3).

Chapter 6 describes a method to study blood-pressure and heart-rate variability by spectral analysis methods. Power spectra of RR-intervals, systolic, mean, diastolic and pulse pressures are presented, and also cross-spectra (coherence spectra and phase spectra) of RR-intervals against the various pressure variables. The spectra are discussed in physiological terms. Interval values as well as systolic, mean and pulse pressures show variations linked to respiration and to the so-called 10-second-rhythm. The diastolic pressure values are scarcely influenced by respiration in the normal respiratory range (0.20-0.35 Hz), but do show 10-second variability.

Relationships between pressure and interval variability become manifest in cross-spectra, which indicate that the 10-second variability in systolic pressure leads the interval variation by two to three beats; however, no such lag is found between the respiration-linked variations in systolic pressure and intervals. The technique presented provides a critical test for models of the fast regulation of the cardiovascular system.

Chapter 7 presents a tentative interpretation of the phase spectra of RR-intervals against pressure variables (Ch.6) by means of the beat-to-beat model of Ch.5. The model, when applied to interval and blood-pressure data from resting subjects, explains the lack of respiratory variability in the diastolic pressure values. The baroreflex equation seems to describe the data only in the region of respiratory frequencies. The shape of the phase spectrum of systolic pressures against intervals is modelled by difference equations, but no physiological interpretation of these equations seems possible.

Chapter 8 consists of the general discussion of the preceding chapters and of the summary of the conclusions. A method is suggested to obtain a value of the baroreflex sensitivity coefficient (the gain of the baroreflex loop) from the spontaneous pressure and heart-rate fluctuations, using spectral analysis techniques.
In a postscript (Chapter 9) an extended version of the beat-to-beat model of the cardiovascular system is given (cf. Chapter 5). This model consists of the following mechanisms: (1) control of heart rate and peripheral resistance by the baroreflex, (2) Windkessel properties of the systemic arterial tree, (3) contractile properties of the myocardium (Starling's law and restitution) and (4) mechanical effects of respiration on blood pressure. Power and cross-spectra of simulated data from this model agree quantitatively with spectra of actual data from resting subjects. In the model the 10-s rhythm in heart rate and blood pressure appears as a resonance phenomenon, due to the delay in the sympathetic control loop of the baroreflex. Respiratory sinus arrhythmia (RSA) is secondary to the respiratory blood-pressure waves; the latter are transformed into RSA by the baroreflex. The simulated response of the model to an imposed increase of blood pressure is found to correspond with the pressure and heart-rate response in patients following administration of a pressure-increasing drug (e.g., phenylephrine).

Appendix A contains the text of a paper by Dr.J. Penaz, describing an instrument for the continuous non-invasive measurement of blood pressure by the principle of the "unloaded vascular wall". Part of the blood-pressure data analysed in this thesis were obtained with the Fin.A.Pres-instrument, developed by Ir.K.H.Wesseling and coworkers following the principles described in the paper of Penaz.

Appendix B contains the text of a paper in which the advantage of the use of spectral analysis techniques for the description of heart-rate and blood-pressure variability is discussed. As an application of these techniques it is shown that a large difference in distribution of variability over the frequencies exists between day-time and night-time pressure and heart-rate recordings. A tentative explanation of this finding is given. In this paper we present an explanation of the spectral analysis techniques in non-mathematical terms.