Chapter 2

Methods for evoked HR and BP

Phasic changes in heart rate (HR) and blood pressure (BP) are often measured in psychophysiology; particularly evoked HR has been studied for a long time (e.g. Chase, Graham, & Graham, 1968; Lacey & Lacey, 1970; Obrist, 1976; Wölk, Velden, Zimmerman, & Krug, 1989; Otten, Gaillard, & Wientjes, 1995; Van der Veen, Mulder, Hoekzema, & Mulder, 1996). In most studies the phasic changes are presented on a time axis, so that changes can be seen during a number of successive seconds. For this purpose, the irregularly occurring HR and BP values had to be converted into equidistantly sampled signals. This chapter focuses on methods to perform this conversion. One method, which uses low-pass filtering for the conversion of HR-data was presented by Rompelman, Coenen, & Kitney (1977) and De Boer, Karemater, & Strackee (1985), and will presently be extended and used for the conversion of BP as well. The method is based on a model for the generation of heart beats, the Integral Pulse Frequency Modulation (IPFM) model, a model which has been used now for about twenty years, and has proven to be useful (Hyndman & Molin, 1975; Rompelman, 1985).

A number of different representations of HR are possible. Mostly a method of linear interpolation is used, where first the interval between two R-waves in the ECG is measured; these IBIs (interbeat intervals) are converted to HR in beats-per-minute (bpm), which are then interpolated to values per second or per half-second (e.g. Gatchel & Lang, 1973; Coles & Duncan-Johnson, 1975; Graham, 1978; Simons, Öhman, & Lang, 1979; Klorman & Ryan, 1980; Somsen, van der Molen, Boomsma & Orlebeke, 1985; Elbert, Tafil-Klawe, Rau, & Lutzenberger, 1991). Chase et al. (1968) first interpolated the IBIs to obtain one value per second, and then converted the values to HR. The following other methods have been applied. Connor & Lang (1969) used a cardiocentimeter curve, which was sampled every 160 ms; for each second in the trial of interest, the median value of the six samples in that second was used. Obrist, Wood, & Perez-Reyes (1965) and Furedy, Randall, Fitzovich, & Shulhan (1989) presented IBI-values on a second-by-second time scale. Finally, some authors did not use a time scale to present their data, but presented the IBI- or HR-values in successive cardiac
cycles (Lacey & Lacey, 1970; Simons, Rockstroh, Elbert, Fiorito, Lutzenberger, & Birbaumer, 1987).

In contrast to most of these methods used in the literature, the presently introduced filtering method is based on a theoretical model. The method was presented for heart rate by Rompelman et al. (1977), and is extended for blood pressure. In the following section, an extensive description of the filtering method is given, followed by a description of the interpolation method. The subsequent section presents the implementation of each of the methods, as well as an overview of the way the methods are compared. This is followed by the comparison of the results obtained with each of the methods, and the last section discusses the advantages and disadvantages of each of the methods, and gives recommendations regarding their use.

2.1 Presentation of two methods

2.1.1 Filtering method

The filtering method is based on theoretical assumptions arising from the Integral Pulse Frequency Modulation (IPFM) model. This model explains how heart beats are generated.

IPFM model and heart rate The IPFM model was first used as a model for the generation of heart beats by Hyndman & Mohn (1975). Figure 2.1 gives a schematic representation of the model. It is based on the assumption that heart beats are generated in the following way. The effective autonomic input to the heart, i.e. the sum of effective vagal and sympathetic activity, is represented in the model by the modulating signal $M$. The pacemaker membrane of the heart is represented in the model by an integrator and a comparator. The autonomic activity $M$ is integrated by the integrator. The integrated signal $Y$ represents the membrane potential. When this potential reaches a certain threshold value, an action potential occurs and the heart contracts. This physiological process is represented by the comparator, which compares the accumulated modulating input ($Y$) with a fixed threshold $R$. When the value of $Y$ reaches the threshold value, a pulse is generated, and the integrator is reset. Depending upon the value of $M$, the speed at which the threshold is reached varies, which results in varying pulse interval lengths. The pulses form the output event-series, representing the succession of cardiac events (R-waves). The event-series is a frequency modulated signal; fixed events occur at irregular intervals, depending on the amplitude of the input signal. In effect, the larger the amplitude of the modulating signal, the more pulses will be generated, and the higher the heart rate.

Hyndman & Mohn (1975) showed that the event-series can be demodulated by low-pass filtering, and they called the output of this procedure a 'low-pass
2.1 Presentation of two methods

Figure 2.1: Schematic representation of the IPFM model (top) and its input and output signals (bottom). \( M(t) \) represents the effective autonomic input to the heart, which is integrated. When the output \( Y(t) \) of the integrator exceeds the threshold value \( R \), a pulse is generated. The series of pulses is represented by \( E(t) \). (After Rompelman, 1985.)

Filtered cardiac event series (LPFES)’. Rompelman (1985) made a comparison of the event-series generated by the IPFM and the LPFES obtained by filtering the event-series. He computed the power spectrum of both signals, and concluded that there were, theoretically and practically, no differences between the signals, although this did depend to some extent on the type of filter used to obtain the LPFES. The filter should approach an ideal filter as much as possible to obtain the best result. The cut-off frequency of the ideal filter should be half the mean HR. This shows that \( M \), representing the effective autonomic activity, can be quite reliably reproduced by low-pass filtering of the event-series, provided that an (almost) ideal filter is used.

This crucial conclusion implies that when low-pass filtering is applied to a series of cardiac events, a representation of the underlying autonomic activity is derived. This is exactly what is intended by computing phasic changes in HR (and BP), and therefore the filtering method appears to be a theoretically justified and correct method.
Blood pressure  The procedure just described for heart rate is not directly applicable to blood pressure. Consider, for instance, the event-series. In experimental data, this series most likely consists of R-wave occurrence times derived from the raw ECG signal. When scanning the signal in time, it is clear that this signal is essentially binary in nature: either something happens (an event occurs), or nothing happens (the time between the events). The event series is a signal which represents discrete events.

The raw BP signal, however, is clearly a continuously varying signal; it changes from the minimum, diastolic value, to the maximum, systolic value, and then slowly back to the minimum. The BP signal cannot be used directly, since separate representations are desired for systolic and diastolic BP. First these values have to be derived from the raw BP-signal. Then, they have to be related to the heart beats in which they occurred.

By considering the origin of the pulsatile waveform in terms of an extension of the IPFM model, a correct way can be derived for the representation of BP (Mulder, 1988). Consider the effective autonomic activity M, which results in the R-wave event series. In the extended IPFM model, a pulsatile pressure signal is generated along with the event-series. This pressure signal induces fluctuations in baroreceptor activity, depending on both the current BP-level and the characteristics of pulsatile pressure signal. The baroreceptor activity affects the autonomic activity M, which affects the timing of the next heart beat, and thus the pressure signal, etc.

This shows that the series of systolic and diastolic BP values measured from the raw signal can be viewed as representing a sample from a continuous theoretical systolic or diastolic BP signal. Since each heart beat (event) is accompanied by a systolic and diastolic BP-value, and the time between the occurrence of the R-wave and the respective values of diastolic and systolic BP is fairly constant, the samples may be taken at the R-wave times. The BP-values are assumed to be valid in the heart beat interval in which they occur, and are assigned to the R-wave time following it in time. An R-wave time is thus accompanied by three values; the IBI which is the length of the interval between the current and the previous R-wave, and the systolic and diastolic BP values which occurred in that interval.

Analogous to the HR event-series, the BP event-series can be low-pass filtered in order to obtain the underlying modulating signal. The difference with HR is that now there is amplitude modulation in addition to frequency modulation, which has to be taken into account. This is done by considering the BP-value to be valid in the entire interval in which it occurred. So, instead of a pulse representing a very short event, as is the case with R-waves, the BP value is seen as an ongoing event, which does not change until the next heart beat occurs with its own BP value (Mulder, 1988).
2.1 Presentation of two methods

Summary of the filter method  The filtering method is a logical consequence of the IPFM model; in the literature it has been shown that the information content of the LPFES is similar to the information hidden in the cardiac event series. Low pass filtering of the event-series, resulting in an LPFES, will therefore be a suitable method for representing the irregularly occurring heart beats in a continuous representation. Since the occurrence of BP can be viewed as an extension of the IPFM model, the BP-values can be low-pass filtered as well.

2.1.2 Linear interpolation method

The linear interpolation method will be explained by using a numerical example, derived from Graham (1978). Take a period of two seconds, in which exactly three heart beats are represented. The first IBI has a duration of 900 ms, the second 300, and the third 800. The second time period is furthermore divided into two sample intervals, of one second each. Graham (1978) proposed how a HR-value can be obtained for each of the sample intervals; the average HR is to be computed for each of the sample intervals. When numbering the sample intervals with index \( j \), and the IBIs with index \( i \), the HR value for each of the sample intervals can be computed according to the following formula:

\[
HR_j = \sum_i \frac{60}{IBI_i} \cdot \frac{t_i}{t_j}
\]

where \( 60/IBI_i \) represents the computation of a HR-value from the IBI-value, and \( t_i/t_j \) gives the weighting factors for each of the HR-values in the sample interval. Effectively, a linear interpolation is performed on the HR-values present in the sample interval. Velden & Wölk (1987) presented the same formula, with \( 60/IBI_i \) written as \( HR_i \) (see also Velden & Graham, 1988).

When using the values of the above example, the mean heart rate in the first sample interval (\( j = 1 \)) becomes

\[
HR_1 = \frac{60}{0.9} \cdot \frac{0.9}{1} + \frac{60}{0.3} \cdot \frac{0.1}{1} = 80 \text{ bpm}
\]

Note that the first HR-value takes up 90 % of the sample interval (\( t_i/t_j = 0.9/1 = 0.9 \)); the second HR-value fills the remaining 10 % (0.1/1). The HR-value in the second sample interval is \( (60/0.3) \cdot (0.2/1) + (60/0.8) \cdot (0.8/1) = 100 \text{ bpm} \).

Although this method appears to be simple, there is a problem with using HR and IBI-values in this way. The use of \( 60/IBI_i \) for \( HR_i \) implies that momentary HR can be derived from the IBI-value at a given point. However, this is only an approximation, and not mathematically correct, since HR is, by definition, the number of heart beats in a certain period of time. We can use the example above to illustrate that the use of IBIs or HR-values is different; in the example, three heart beats were represented in two seconds time. The average IBI is
(0.9 + 0.3 + 0.8)/3 = 0.67 s, which gives an average HR of 60/0.67 = 90 bpm. When first the interval times are converted to HR with the 60/IBI formula, the average HR-value becomes (66.67 + 200 + 75)/3 = 113.9 bpm. It was Graham (1978) herself, who illustrated this difference, but nonetheless she used both the HR and IBI measures in the same formula. Only when the average HR in a certain time period is calculated, there is no difference between counting the number of heart beats and divide this number by the length of the time period (e.g. 3/(2/60) = 90 bpm), and taking the average of all the IBIs and transform this to bpm by doing 60/IBI (e.g. 60/((0.9 + 0.3 + 0.8)/3) = 90 bpm.

Blood pressure For the conversion of blood pressure data, Velden & Wölk (1990) proposed a similar, but slightly different procedure. The difference is in the timing: In the procedure for HR, the IBI represents the time between two heart beats, e.g. the time between two R-peaks in the ECG. However, the time-unit for a BP value is defined by Velden & Wölk as extending from midway between the occurrence of the previous and the current BP-value, until midway between the occurrence of the current and the next BP-value. The BP values are measured directly from the analog blood pressure signal; the maxima in the signal are the systolic BP-values, and the minima the diastolic. These 'BP-intervals' are then interpolated in the same way as the HR values in the formula above:

\[
BP_j = \sum_i \frac{t_iBP_i}{t_j}
\]

where \(BP_j\) is the mean BP-value in sample interval \(j\), \(t_i\) is the time that 'BP-interval' \(BP_i\) extends in sample interval \(j\), and \(t_j\) is the duration of the sample interval.

Summary of the linear interpolation method The linear interpolation method is frequently used to obtain an equidistantly sampled representation of HR, even though this method lacks a firm theoretical background. However, since it is easy to use it may be practical, provided that the results are the same as those obtained with the filtering method.

2.2 Comparing the two methods

Two methods were introduced for the conversion of irregularly sampled raw HR and BP data into equidistantly sampled representations, which can be used to compute evoked HR and BP responses. This section gives an overview of the comparison made between the two methods.
Description of the experimental data  In most cases, phasic changes in HR and BP are studied in task situations where a number of trials are averaged. For the purpose of comparing the conversion procedures, experimental data were used from one subject who performed a task in an S1-S2 paradigm. The S1 was an auditory warning signal, and consisted of the spoken letter ’Q’. S2 was a visual stimulus, consisting of two small squares presented on a screen which was placed in front of the subject. The time between S1 and S2 was six seconds. The subject had to push a button as fast as possible after the presentation of S2. Forty trials were presented, with an intertrial (S1-S1) interval varying between 12 and 16 seconds. A trial consisted of the time segment from one second before the presentation of S1 until four seconds after S2.

The subject whose data were used was a twenty-year old, right handed male. Only one subject was used because in experiments where the effects of manipulations on the patterns of the phasic changes in HR and BP are studied, these single-subject averages from each condition are used for peak detection. The ECG was measured from precordial leads, and continuous BP was measured from the middle finger of the left hand with a Finapres device (TNO prototype 4). The ECG and the analog BP-signal were sampled at 100 Hz. The R-waves from the ECG were detected with a special purpose program (time resolution 10 ms). The systolic and diastolic BP-values were detected and assigned to the R-wave occurrence times with CARSPAN (Mulder, van Dellen, van der Meulen, & Opheikens, 1988).

The dataset consisted of 607 R-wave occurrence times, i.e. 606 IBIs, in 556 seconds. The average IBI was 917 ms, the HR was 65.4 bpm, or 1.09 Hz. The average SBP was 126.9 mmHg, and the average DBP was 68.8 mmHg.

Filtering method  Before the filtering can take place, the input data file has to be preprocessed; the time-series containing the R-wave occurrence times is converted into an equidistantly sampled file, sampled at 100 Hz, where all samples have the value zero (representing the fact that no signal is available between the events), except when an R-wave occurs (one sample with a fixed value). This representation is, in fact, an equidistantly sampled version of the event-series obtained with the IPFM model. The BP-values, which are values assigned to R-wave occurrence times, have to be transformed as well. The BP-values are considered as a sampled time series, where the sample values do not change until new information is available, i.e. until the next R-wave has occurred. For spectral analysis applications, this has been shown to be a correct method (see Mulder, 1988, p.55). IBI-values can be treated in the same way as BP-values; for the comparison, IBI was computed as well.

For practical reasons (accuracy of the filter algorithms) the filtering takes place in two runs. In the first run, the low-pass filter has a cut-off frequency of 5 Hz, and the second filtering run is performed with a low pass filter with cut-off frequency of 0.5 Hz. Between the filtering steps, the sample frequency is
reduced from 100 to 10 Hz. The filter cut-off frequency of 0.5 Hz was chosen because this is about half the mean HR. The ideal low-pass filter to obtain the LPFES from the event series should have a cut-off frequency of about half the sample frequency of that event series. Since the event series is sampled at the HR, the ideal cut-off frequency is about half the mean HR (Hyndman & Mohn, 1975; Rompelman et al., 1977). The mean heart rate in the experimental data used in this comparison was 65.4 bpm, or 1.09 Hz. After the filtering steps, the resulting file contains values for HR (in Hz), IBI (in ms), and SBP and DBP (in mmHg), sampled equidistantly with a rate of 10 Hz.

**Linear interpolation method** The program which performs the linear interpolation method was adapted from an implementation by Otten (see Otten et al., 1995). A number of adaptations were made to meet our demands:

First, Velden & Wölk (1987) propose to use sample intervals of 500 ms, in order to keep distortion of the 'real' autonomic activity at a minimum. However, when measuring phasic changes in HR and BP in an S1-S2 interval with six seconds between S1 and S2, we consider a time resolution of 500 ms too crude. Particularly when examining latency differences, we feel that sample intervals of 100 ms would be more appropriate. Elbert et al. (1991) also used 100 ms intervals.

Second, unlike Velden & Wölk (1990), we did not use separate timing for HR, SBP and DBP, but assigned the BP-values to the R-wave occurrence times; the BP values are considered to be valid in the R-wave interval in which they occur. Velden & Wölk (1990) state that they use their definition for the timing of the BP-value 'for the sake of simplicity', but also 'because we have no model assumptions to define this time interval' (Velden & Wölk, 1990, p. 100). We have two arguments against their definition. Our first argument is that the definition of Velden & Wölk does not make the computations easier; it requires that the timing of both systolic and diastolic peaks should be tracked, and the 'BP-intervals' should be derived for SBP and DBP-values separately. Furthermore, these have to be combined with yet another time track of the HR-values if BP and HR are to be compared. A second argument is that if Velden & Wölk (1990) did not have model assumptions about defining the interval, then why did they first reject the procedure followed by Weipert, Shapiro, & Suter (1987), who attributed SBP and DBP values to the cardiac cycle in which they occurred, as we propose to do. By using this method, Weipert et al. could use the timing information of the heart beats for BP as well. This simplifies the computation of the linear interpolation, since the weighting factors derived to compute HR can also be used for SBP and DBP.

Thirdly, Velden & Wölk (1987) mentioned that the interpolated values should be plotted in the middle of the sample interval. Their way of defining the time interval in which a BP-value is valid shows this, too. However, in sampling a
continuous signal we prefer to consider a sample value to be valid until the next value comes along; this implies that the values are plotted at the beginning of the sample interval. When using sample intervals as short as 100 ms, the difference is only marginal (0.05 seconds).

Finally, in the method of Graham (1978) and Velden & Wölk (1987) values for HR are used, as well as IBIs. Although HR is the measure which is most often used to represent the phasic changes, it is much easier to use IBI-values for the computations, because the input datafile does not contain HR-values, but only R-wave occurrence times and IBIs. Instead of first converted every single IBI to HR, the conversion from IBI to HR can performed as the last step in the procedure.

Data converted with both the filtering and the linear interpolation method are shown in Figure 2.2.

![Figure 2.2](image)

Figure 2.2: Representation of the HR, IBI, SBP, and DBP values before (original) and after conversion with the filtering method and with the linear interpolation method. Twenty-six seconds of data are shown.

**Comparison** The experimental data were converted to equidistantly sampled time-series with a sample frequency of 10 Hz. The converted time-series contained 550 seconds of data, i.e. 5500 sample values. The data were compared in two ways. First, averaged data were compared. From the time-series, 39 trials of data were extracted and averaged. Each trial consisted of 11 seconds, i.e. 110
sample values. The averages from the time-series converted with the filtering method were then compared with the averages obtained from the interpolated data. Linear regression was used to investigate the proportion of explained variance when one average was used to predict the other.

Secondly, the 'raw' time-series after conversion were compared. This was done by decomposing the data with spectral analysis (Fast Fourier Transform), in which all 5500 samples values were used. The power density spectra of HR, IBI, SBP, and DBP were compared first. Subsequently, three transfer functions were computed between the time-series: the squared coherence, transfer amplitude (gain), and the phase relation were computed. The time series were smoothed, using a window of five points. The spectral computations were performed with the program Statistica (StatSoft Inc., 1996). All spectral measures were considered in the frequency range below 0.5 Hz (i.e. lower than about half the mean HR). This frequency range was subdivided in five successive frequency bands of 0.1 Hz each. From these bands, the average values for the transfer functions are given; these values are obtained by averaging across the frequency points in the bands.

2.3 Results

Averaged data Figure 2.3 presents the averages of the 39 trials of HR, SBP, and DBP data, converted with both the filtering and the linear interpolation method. The figure shows that the results obtained with the filtering method look smoother than the results obtained with the linear interpolation method. This is obviously due to the difference between averaging a number of smooth, filtered signals and averaging a number of square wave signals; in order to obtain the same level of smoothness in the interpolated data, a very large number of trials should be included in the average. Furthermore, minor differences can be seen in the amplitude of some of the peaks in the patterns. These differences, however, are so small, that they certainly will not affect the statistical results of the peaks detected in the HR and BP patterns, such as used for example in the next chapter. Linear regression of the averaged data, where data obtained with one method is used to explain the data obtained with the other method, shows the \( \beta \)s are between 0.975 and 0.992.

Although these results are promising, a closer look has to be taken to the differences between the methods.

Power density spectra Figure 2.4 shows the power density spectra from the HR, IBI, SBP and DBP data. For this analysis, the raw converted data were used, i.e. 550 seconds of equidistantly sampled data. The figure shows that for IBI, SBP, and DBP, the spectra match almost perfectly. For HR, the filtered data had more power in the higher frequencies (above 0.3 Hz). This is caused by the use of IBI-converted-to-HR in the linear interpolation method. The differences
can be shown by expressing the variability in the high frequency bands as a proportion of the total spectral power. Between 0.3 and 0.4 Hz, the filtered data contained 7.2% of the total power, and the interpolated data only 3.8%. Between 0.4 and 0.5 Hz, these percentages were 5.3 and 1.9, respectively.

**Coherence**  The squared coherence is a measure for the linear relationship between changes in one signal and changes in the other signal, as a function of frequency. When the relation between the two signals is very strong, the coherence approaches 1.0, and when there is no relation, the coherence will be close to zero. The values of the coherence function are comparable to the proportion explained variance in a linear regression.

Figure 2.5 presents the squared coherence function for HR, IBI, SBP, and DBP, converted with both the filtering method and with the linear interpolation method. The top left of the figure shows the coherence between the HR signals. Note that the HR with the linear interpolation method is actually based on IBI, which is later converted to HR.

To derive a coherence measure in a particular frequency band, it is not correct to simply compute the mean coherence, due to the non-Gaussian distribution of the values. Therefore, a related measure is used, the weighted coherence (Porges, Bohrer, Cheung, Drasgow, McCabe, & Keren, 1980). The weighted coherence is
Figure 2.4: Power density spectra of HR, IBI, SBP, and DBP. The nine minutes of raw data were converted to equidistantly sampled time-series with either the filtering method (solid line) or the linear interpolation method (broken line).

derived with the following formula:

$$CW_{xy}(f_1, f_2) = \frac{\sum_{f_1}^{f_2} \text{Coh}_{xy}(f) \cdot P_{yy}(f)}{\sum_{f_1}^{f_2} P_{yy}(f)}$$

where $CW_{xy}(f_1, f_2)$ is the weighted coherence in the range between frequency $f_1$ and $f_2$, $\text{Coh}_{xy}(f)$ is the coherence between the signals $x$ and $y$ at frequency $f$, and $P_{yy}(f)$ is the power spectral density of signal $y$ at frequency $f$. Note that this measure takes into account the magnitude of the power spectral density in the frequency bands.

Across the entire frequency range, the weighted coherence for HR was 0.9993. In the frequency bands from 0 to 0.2 Hz, the weighted coherence was higher than 0.9998, between 0.2 and 0.3 Hz the coherence was 0.9959, between 0.3 and 0.4 Hz the weighted coherence was 0.9917, and between 0.4 to 0.5 Hz the coherence was 0.9833.

The top right drawing shows the coherence between the IBI signals. The weighted coherence in the entire frequency range was 0.9999; in the bands below 0.4 Hz the average coherence was above 0.9999, and between 0.4 and 0.5 Hz the weighted coherence was 0.9954.
2.3 Results

Figure 2.5: Squared coherence between HR, IBI, SBP, and DBP, converted with the filtering method and the interpolation method. Values can be reached between 0 and 1, with 1 representing a perfect linear relation.

The bottom left figure shows the coherence for SBP. The weighted coherence in the total range between 0 and 0.5 Hz was 0.9999; in the four frequency bands below 0.4 Hz the coherence was higher than 0.9999, and between 0.4 and 0.5 Hz the weighted coherence was 0.9927.

The bottom right drawing shows the coherence function for the DBP signals; the total weighted coherence was 0.9999; in the bands below 0.4 Hz the coherence was higher than 0.9999, and between 0.4 and 0.5 Hz the weighted coherence was 0.9944.

In summary, the coherence between the signals was very high; particularly in the frequency ranges lower than 0.4 Hz the linear relation between the signals was almost perfect. Above 0.4 Hz the coherence functions were less perfect. This was probably due to the small amount of spectral energy in those frequencies; when there is no variation in the signals, the variation can not be related. For instance, the power spectral density measures showed that less than 1 % of the total spectral power in SBP was represented by the highest frequency band (0.96 % for the filtered data, and 0.7 % for the interpolated data). However, the weighted coherence measures, which take the power spectral density into account, still showed values close to one.
Methods for evoked HR and BP

Gain (Modulus)

Figure 2.6: Transfer magnitude (gain) from HR, IBI, SBP, and DBP converted with the filtering method to the same data converted with the linear interpolation method. Gain of 1 indicates that amplitudes in one signal are equal to amplitudes in the other signal.

**Gain (modulus)** The transfer magnitude, or gain (modulus), is a measure for the relation between the fluctuations in one signal (considered the output signal) and in the other (considered as the input signal); it reflects the ratio of the changes in each of the signals. A gain of 1 indicates that a change of one unit (e.g. a HR-change of 1 bpm) in the input signal is accompanied by a change of exactly 1 unit in the output; a gain of 2 indicates that a change of 1 unit in the input signal is accompanied by a change of 2 units in the output signal.

Figure 2.6 presents the transfer magnitude (gain) between the variables converted with each of the methods. It must be noted that the reliability of the gain-values depends upon the coherence between the two signals: the lower the coherence between the signals, the lower the reliability of the estimation of the transfer function. The gain function between the HR-signals shows a frequency dependent change; the higher the frequency of the changes in the signal, the lower the gain. Across the entire frequency range, the average gain was 0.8132 (with a standard deviation (sd) of 0.174). In the five successive bands the values were: 1.0122 (0.014) between 0 and 0.1 Hz, 0.9496 (0.024) between 0.1 and 0.2 Hz, 0.8541 (0.049) between 0.2 and 0.3 Hz, 0.7113 (0.059) between 0.3 and 0.4 Hz,
and 0.5502 (0.057) between 0.4 and 0.5 Hz. This frequency dependent gain is due to the difference between using HR and IBI-converted-to-HR; the changes in HR with higher frequencies are attenuated in the linear interpolation data relative to the filtered data. The ratio between the spectral densities of the filtered and the interpolated HR signals reflects the same information (for a discussion of this topic see also Mulder, 1988). When this ratio is multiplied with the gain values, the result is the value 1 for all frequencies; this shows that the decline of transfer is entirely due to the use of IBI-values in the linear interpolation method. This is expressed in the following formula:

\[
gain\text{-value at frequency } f \times \sqrt{\frac{\text{spectral density HR(filter) at } f}{\text{spectral density HR(interp.) at } f}} \approx 1
\]

Obviously, the IBI signals do not show this frequency dependent decline of the gain values. Here, in both the filtering and the interpolation method, the IBL-values were used. No conversion from IBI to HR has taken place. This gives a further indication that the frequency dependent gain-function for HR was the result of the conversion from IBI to HR. Across the entire frequency range the gain was close to one. The total average gain was 1.0176 (0.028). For the five successive bands the values were 1.0207 (0.003), 1.0127 (0.003), 1.0163 (0.009), 1.0135 (0.015), and 1.0219 (0.058), respectively.

For SBP the gain was close to one, but only in those frequency ranges where the coherence was high; above 0.4 Hz, the coherence declined, and thus the gain values were less reliable, and showed larger deviations from the ideal value. The average gain across entire frequency range the gain was 0.9599 (sd = 0.167), and in the five successive bands the values were 1.0199 (0.005), 1.0142 (0.009), 1.0252 (0.028), 0.9776 (0.051), and 0.8049 (0.263), respectively.

The values for DBP were close to one in the entire frequency range, although in the higher frequencies (above 0.4 Hz), where the coherence was quite low as well, the gain deviated from the ideal value. For the entire frequency range the average gain was 1.005 (0.057), and in the successive bands the gain was 1.0194 (0.004), 1.0144 (0.007), 1.0162 (0.021), 1.0037 (0.038), and 0.9652 (0.107), respectively.

The results of the gain between the signals show that all signals show good results below about 0.4 Hz. Above this frequency, the coherence starts to decline, which results in less reliable gain values. This is due to the low spectral power in the high frequency regions, which results in less reliable spectral estimates.

**Phase relation** The phase relation indicates the time lag between a change in one signal and a change in the other signal, as a function of frequency. When the phase shift is 0, both signals change at the same time, and in the same direction; a phase shift of \( \pi \) radians indicates that two signals have changes in the opposite direction.
Figure 2.7: Phase relations (in radians) between HR, IBI, SBP, and DBP converted with the filtering method and with the interpolation method. Phase of 0 indicates that both signals vary simultaneously.

Figure 2.7 shows the phase relations between the signals converted with each of the filtering and with the linear interpolation method. For HR the phase shift across the entire frequency range was close to zero, with an average of $-0.0845$ rad (and a standard deviation of 0.069); in the five successive frequency bands the shifts were $-0.0150$ (0.011), $-0.0464$ (0.018), $-0.0826$ (0.034), $-0.1324$ (0.059), and $-0.1534$ (0.071).

For IBI the phase shift also deviated very little from zero. Across the entire frequency range the average phase shift was $-0.0927$ (0.077) rad. The phase shifts in the five successive frequency bands were $-0.0168$ (0.010), $-0.0512$ (0.010), $-0.0832$ (0.013), $-0.1121$ (0.020), and $-0.2011$ (0.095), respectively.

The phase shift in SBP was close to zero for the frequencies below 0.4 Hz; above that frequency the low coherence made the values less reliable. For the entire frequency range the average phase shift was $-0.0550$ (0.233) rad, and for the five bands separately the values were $-0.0164$ (0.010), $-0.0515$ (0.014), $-0.0769$ (0.037), $-0.0968$ (0.060), and $-0.0889$ (0.374), respectively.

Finally, for DBP the phase shift was very close to zero; in the total frequency range the shift was $-0.082$ (0.072) rad. In the five successive frequency bands the values were $-0.0164$ (0.010), $-0.0484$ (0.008), $-0.0785$ (0.021), $-0.1152$ (0.041),
These phase shifts represent the time delay between the two signals considered. When these time differences are computed, all these phase relations appear to represent a fixed time difference of 50 ms between the two methods. This shows that when the values of the linear interpolation method would have been assigned to the time in the middle of the sample interval, as Velden & Wölk (1990) proposed, there would have been no difference. Thus, for example if a sample now is assigned to time point 1.35 seconds (i.e. considered valid until the next value appears at 1.45 s), it should have been represented at 1.40 seconds (although the value would still represent the time period between 1.35 and 1.45 s). This shows that the different representations of the values in the sample intervals do lead to shifts in the resulting patterns. With the small sample intervals as used here (100 ms, resulting in a delay of 50 ms), this is no problem. However, when larger sample intervals are used, e.g. the 500 ms as proposed by Velden & Wölk (1990), larger differences will occur.

In summary, the phase shifts are very small, and indicate a fixed time delay of 50 ms between the methods. This difference is entirely due to the representation of the sample values.

2.4 Discussion and conclusion

The linear interpolation method is the most often used method for converting irregularly occurring HR and BP values to an equidistantly sampled HR and BP signal. Although linear interpolation is easy to perform, it has the problem that it lacks a theoretical basis. This chapter uses a physiologically plausible model for the generation of heart beats. The work done with this IPFM model over the past years (see for instance Rompelman et al., 1977; Rompelman, 1985; Ten Voorde, 1992; Mulder, 1988) has shown that it is useful. Based upon properties of the IPFM model, low pass filtering of the cardiac event series was proposed as a method for representing the underlying continuous autonomic signal. By regarding the generation of BP signal as an extension of the IPFM model, it was shown that BP time series can be adequately derived in a similar way.

The comparisons made in the present study show that the results of the computationally complicated and time-consuming filtering on the one hand and the ‘simple’ linear interpolation method on the other are very similar. When multi-trial averages are made (see Figure 2.3), the methods show virtually identical results. The minor differences which occur are mostly due to the square wave representation in the linear interpolation method; many trials have to be averaged to smooth the edges of a square wave signal. The small differences between the results obtained with each of the conversion methods are, however, much smaller than the individual differences which occur in evoked heart rate and blood pressure patterns.
In addition to viewing the ultimate multi-trial average, a comparison of the 'raw' transformed data was made by using spectral analysis. Overall, the spectral characteristics of the signals were very similar, particularly when the frequencies below 0.4 Hz were considered; above this frequency, the reliability of the spectral estimates slightly decreases due to the relatively small power density in the signals. However, this should be no problem when the method is used in computing phasic changes in experimental settings such as in an S1-S2 paradigm. At first glance, the gain function between the HR signals shows that at higher frequencies the linear interpolation method gives an underestimation of the HR values. This is entirely due to the use of IBIs in the interpolation method, as was shown in the results section.

This comparison shows that the filtering method and the linear interpolation method both give a good representation of phasic changes in HR and BP. Both methods have advantages and disadvantages. A major advantage of the filtering method is that it is based on the solid theoretical IPFM model. Furthermore, the filtering method generates a continuous signal, which can easily be used for sampling or averaging procedures. However, as De Boer et al. (1985) pointed out, the LPFES is not easy to compute. The linear interpolation method has the great advantage that it is very easy to perform. A disadvantage is the lack of theoretical framework for its use; particularly the conversion of IBI values to instantaneous HR values is not correct.

The conclusion of this chapter is therefore that for practical reasons the linear interpolation method is preferred over the filtering method. Since the results are virtually the same when multi-trial averages are made, linear interpolation is a very good method. However, when using the interpolation procedure, one should keep in mind the theoretical justification of this method.