Modelling Heart Rate Variability

P. Laguna* and L. Sörnmo†

1 Introduction

The study of heart rate variability (HRV) has become increasingly popular because information on the state of the autonomic nervous system can be noninvasively inferred by the use of relatively basic signal processing techniques [4]. Despite the seeming simplicity of deriving the series of RR intervals from the ECG signal and defining a related measure of dispersion, it is essential to make sure that the heart rate variability is accurately characterized. Several definitions of signals for representing the heart rhythm have been suggested which characterize variability either in terms of successive RR intervals or instantaneous heart rate. In particular, spectral analysis of heart rhythm signals has received considerable attention since oscillations embedded in the rhythm, for example due to respiratory sinus arrhythmia or the blood pressure control system, can be quantified from their corresponding peaks in the power spectrum. Such oscillations are characterized by low frequency components which typically are located in the interval below 0.5 Hz.

The starting point of HRV analysis is the series of successive time instants, $t_0, t_1, \ldots, t_K$, produced by a QRS detector applied on the ECG signal, commonly transformed into a series of RR intervals $d_{IT}(k)$,

$$d_{IT}(k) = t_k - t_{k-1}, \quad k = 1, \ldots, K, \tag{1}$$

as illustrated by Figure 1; the subscript "IT" is used since the definition in (1) is also referred to as the *interval tachogram*.

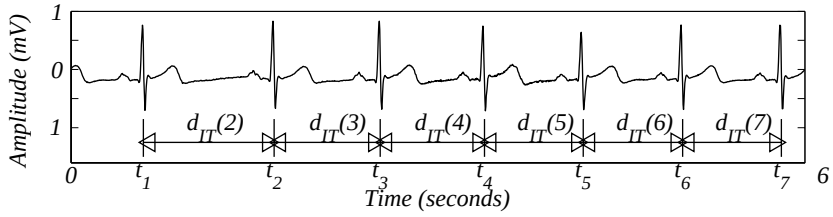

Figure 1: The definition of RR intervals used for the study of heart rate variability.

Clinical studies of heart rate variability have commonly been synonymous to the use of simple time domain measures such as the standard deviation of the RR intervals. Although a variety of heart rhythm representations may be used, the interval tachogram $d_{IT}(k)$, as defined in (1), is the preferred starting point for the design of such measures.

A straightforward way to quantify HRV is thus to calculate the standard deviation of the available NN intervals,

$$\text{SDNN} = \sqrt{\frac{1}{K-1}\sum_{k=1}^{K}(d_{IT}(k) - \bar{m}_d)^2}, \tag{2}$$

where $\bar{m}_d$ denotes the mean length of the K different NN intervals. For long-term recordings, SDNN only provides a very rough characterization of HRV since the mean heart rate will change considerably from

*P. Laguna is with the Communications Technology Group (GTC), Aragón Institute for Engineering Research (I3A), Universidad de Zaragoza, María de Luna, 3, 50018 Zaragoza, Spain. e-mail: laguna@unizar.es

†L. Sörnmo is with the Signal Processing Group, Department of Electroscience, Lund University, Box 118, SE-221 00 Lund, Sweden. e-mail: Leif.Sornmo@es.lth.se

the active parts of the day to the night during sleep. In Holter recordings, both SDNN and other variants reflect long-term variations in heart rate. Therefore, additional dispersion measures have been suggested which reflect short-term variations by exploiting the difference between successive NN intervals, that is, $d_{IT}(k) - d_{IT}(k-1)$. The effect of the difference operation is to accentuate the high-frequency content of the series of NN intervals. This measure is commonly referred to as the root mean square of successive differences ("rMSSD"). These type of measures integrate the rich information present at the HRV and then other representations that do not loose information seems to be potentially preferable.

2 Heart Rhythm Representations

The purpose of a heart rhythm representation is to produce a signal which accurately reflects variations in heart rhythm, and which lends itself to different types of analysis. The heart rhythm can be represented in terms of either *interval* or *rate*. The latter entity is thus defined by the inverse of the RR intervals. Other representations have, however, also been put forward which take their starting point in the series of time instants of the QRS events rather than in the series of successive RR intervals (the distinction between these two types of series is important from a conceptual viewpoint although the difference as such is small since the latter series is easily derived from the former). The proposed representations, in addition to interval tachogram are:

- Inverse interval tachogram $d_{IIT}(k)$

$$d_{IIT}(k) = \frac{1}{t_k - t_{k-1}}, \quad k = 1, \ldots, K, \tag{3}$$

- Interval function

$$d^u_{IF}(t) = \sum_{k=1}^{K} (t_k - t_{k-1})\, \delta(t - t_k) = \sum_{k=1}^{K} d_{IF}(t)\delta(t - t_k), \tag{4}$$

- Inverse interval function

$$d^u_{IIF}(t) = \sum_{k=1}^{K} \left(\frac{1}{t_k - t_{k-1}} \right) \delta(t - t_k) = \sum_{k=1}^{K} d_{IIF}(t)\delta(t - t_k), \tag{5}$$

- Event series

$$d^u_E(t) = \sum_{k=0}^{K} \delta(t - t_k). \tag{6}$$

The performance requirement of a heart rhythm representation should be that it "well reflects variations in heart rhythm", however this is, unfortunately, not easily expressed in exact terms and will depend on the underlying physiology that generates the HRV. Then, models that account for the physiological behavior will lead to mathematical modelling of HRV, giving not only a representation of the autonomic nervous influence on the heart rate, but also providing a tool which helps in indicating which of the HRV representations exhibiting the better performance in term of modelling the underlying physiology. One such model is the integral pulse frequency modulation (IPFM) model which has gained wide popularity in the field of HRV analysis.

3 The integral pulse frequency modulation (IPFM) model

The integral pulse frequency modulation (IPFM) model is a model for the generation of an event series, such as the series of heart beat occurrences, and assumes the existence of a continuous-time input signal which possesses a particular physiological interpretation[7, 8, 9, 10, 11, 1]. Figure 2 presents a block

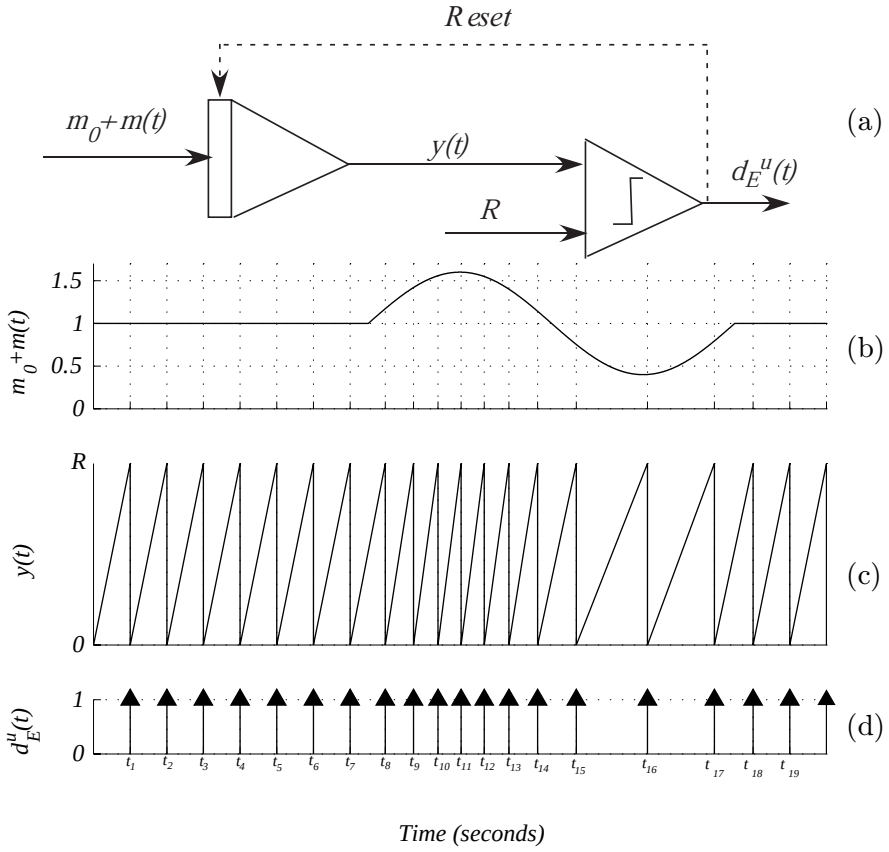

Figure 2: (a) The integral pulse frequency modulation model, (b) the input signal $m(t)$ which modulates the variations in interval length, (c) the output of the integrator assuming a threshold level at R, and (d) the resulting event series at times $t_0, t_1, \ldots$.

diagram of the IPFM model and shows the signals occurring at various steps of the model. The input signal is integrated until a threshold, R, is reached at which an event is generated at time t_k; the integrator is then reset to zero and the procedure is repeated, and so on. The threshold R defines the mean interval length between successive events. The input signal, being positive-valued, is the sum of two quantities: a DC level, m_0, and a modulating signal, $m(t)$, whose DC component is equal to zero and whose amplitude is bounded such that $|m(t)| < m_0$ to ensure that the input signal always remains positive. Assuming that the IPFM model is valid, our objective is to design a method which can retrieve information on $m(t)$ from the observed series of event times t_k,

$$d_E(t) = \sum_{k=0}^{K} \delta(t - t_k). \tag{7}$$

In physiological terms, the output signal of the integrator in Figure 2 can be viewed as the charging of the membrane potential of a sino-atrial pacemaker cell [2]. The potential increases until a certain threshold is exceeded and then triggers off an action potential which, when combined with the effect of many other action potentials, initiates a new cardiac cycle. The input to the integrator consists of m_0, which defines the mean heart rate, and the modulating signal $m(t)$ which describes the variations in heart rate as modulated by the autonomic activity (that is, sympathetic and parasympathetic influences) on the sino-atrial node. In general, the signal $m(t)$ is band-limited such that spectral components above 0.4–0.5 Hz can be neglected during resting conditions. The assumption that $|m(t)| < m_0$ is included in order to account for the property that heart rate variability typically is small compared to the mean heart rate.

In mathematical terms, the series of event times is defined by the following equation which is crucial to the IPFM model,

$$\int_{t_{k-1}}^{t_k} (m_0 + m(\tau))d\tau = R, \quad k = 1, \ldots, K. \tag{8}$$

Variations in the modulating signal $m(t)$ determine the variations in interval length between two successive events at t_{k-1} and t_k. Without any modulation, that is, for $m(t) \equiv 0$, the resulting event series is perfectly regular and has a constant interval length equal to R/m_0; the corresponding unmodulated event repetition frequency F_0 is given by

$$F_0 = \frac{m_0}{R}.$$

The constant m_0 is typically set to one such that the threshold R defines the repetition frequency in units of Hertz, $F_0 = \frac{1}{R}$, and is then denoted by $R = \overline{T}_0$. Hence, the heart rate of the event series is equal to 60 beats per minute when $\overline{T}_0$ is chosen to one second.

Assuming that the initial beat occurs at $t_0 = 0$, the integral in (8) can alternatively be expressed as

$$\int_{0}^{t_k} (1 + m(\tau))d\tau = k\overline{T}_0, \quad k = 0, \ldots, K, \tag{9}$$

where k is an integer that indexes the k^{th} beat. Furthermore, instead of having the IPFM model defined for only those time instants t_k when the threshold $\overline{T}_0$ is exceeded, it can be generalized to a continuous-time function by introducing the following definition [1],

$$\int_{0}^{t} (1 + m(\tau))d\tau = \kappa(t)\overline{T}_0. \tag{10}$$

Here, integration up to a certain time t is proportional to a continuous-valued indexing function $\kappa(t)$ whose value at t_k is identical to the integer-valued beat index k, that is, $\kappa(t_k) = k$. This model generalization will later on allow us to develop a heart rhythm representation, the *heart timing* signal.

3.1 Heart timing representation

The heart timing signal is based on the IPFM model and aims explicitly at estimating the modulating signal $m(t)$ [1]. The heart timing $d^u_{HT}(t)$ is an unevenly sampled signal that is defined as the deviation of the event time t_k from the expected occurrence time related to the mean RR interval length $k\overline{T}_0$, that is,

$$d^u_{HT}(t) = \sum_{k=0}^{K} (k\overline{T}_0 - t_k)\delta(t - t_k) = \sum_{k=0}^{K} d_{HT}(t)\delta(t - t_k). \tag{11}$$

In order to see how this signal is related to the IPFM model, we rewrite the model equation in (9) for a particular time t_k such that

$$\int_{0}^{t_k} m(\tau)d\tau = k\overline{T}_0 - t_k = d_{HT}(t_k). \tag{12}$$

Hence, $d_{HT}(t_k)$ and $m(t)$ are linearly related to each other through the integration of $m(t)$ up to t_k. In order to compute the heart timing signal, an estimate of $\overline{T}_0$ is first required from the available data. This parameter is estimated by simply dividing the occurrence time of the last event with the number of events, that is,

$$\overline{T}_0 = \frac{t_K - t_0}{K} = \frac{t_K}{K}. \tag{13}$$

where it is assumed that $t_0 = 0$.

The rationale for using the heart timing signal becomes evident when the Fourier transform of its generalization to continuous time, $d_{HT}(t)$, is determined. To do this, we make use of the generalized IPFM model in (10) by which the heart timing signal can be expressed as,

$$d_{HT}(t) = \int_0^t m(\tau)d\tau = \int_{-\infty}^t m(\tau)d\tau. \tag{14}$$

Here, the integration interval has been extended to $-\infty$ due to the nonrestrictive assumption that $m(t)$ is a causal function, that is, it is equal to zero for $t < 0$. The Fourier transform of (14) is given by [3],

$$D_{HT}(\Omega) = \int_{-\infty}^{\infty} d_{HT}(t)e^{-\jmath\Omega t}dt = \frac{D_m(\Omega)}{j\Omega} + \pi D_m(0)\delta(\Omega) = \frac{D_m(\Omega)}{j\Omega}, \tag{15}$$

where $D_{HT}(\Omega)$ and $D_m(\Omega)$ denotes the Fourier transform of $d_{HT}(t)$ and $m(t)$, respectively, and $\Omega = 2\pi F$. The term $\pi D_m(0)\delta(\Omega)$ is identical to zero since $m(t)$ was earlier assumed to have a DC component equal to zero.

Consequently, the power spectrum $\hat{S}_m(\Omega)$ of $m(t)$ can be obtained by multiplying the spectrum of the heart timing signal $D_{HT}(\Omega)$, calculated from the event times $t_0, \ldots, t_K$ contained in the observation interval, with $j\Omega$,

$$\hat{S}_m(\Omega) = \frac{1}{(K+1)\overline{T}_0}|\hat{D}_m(\Omega)|^2 = \frac{1}{(K+1)\overline{T}_0}|\Omega\hat{D}_{HT}(\Omega)|^2. \tag{16}$$

The multiplicative factor $1/((K+1)\overline{T}_0)$ is included to account for number of event times. Once the spectrum of the heart timing signal in (11) has been computed, it is straightforward to estimate the spectrum of the modulating signal $m(t)$. The modulating signal $m(t)$ is assumed to be bandlimited to a maximum frequency lower than half the mean heart rate $1/(2\overline{T}_0)$. As a result, $d_{HT}(t)$ will also be bandlimited, being the integral of $m(t)$, and can therefore be fully recovered from the time instants t_k.

The agreement between $m(t)$ and the different heart rhythm representations are illustrated in Figure 3, assuming that $m(t)$ is sinusoidal. Figures 3(a)–(c) show the signals at different stages of the IPFM model, namely, the input signal, the output signal of the integrator, and the resulting event series. As expected, the heart timing signal $d_{HT}(t)$ is the preferred technique for recovering $m(t)$ although the inverse interval function $d_{IIF}(t)$ comes rather close. Another observation is that the representations which are inversely related to the interval length are better in estimating $m(t)$ than are those proportional to the interval length.

Finally, it may be appropriate to point out that although the heart timing signal exhibits a superior performance within the context of IPFM modeling than do the other representations, such model-based studies do not fully account for heart rate variability observed in humans. Hence, the improvement in performance for the heart timing signal remains to be demonstrated from a clinical point of view, and may eventually turn out to be embedded in the IPFM modeling error.

Further considerations will require the problem of estimating the spectrum from the unevenly sampled data, that can be address either by interpolation to evenly sampled plus usual spectral estimation techniques or by direct estimation from the unevenly sample data. The interested reader is referred to [6, 1]. Also artifact in QRS detection (false alarms and missed beat) cause disturbances in the contained spectrum that can be deal within the same framework of other physiological "artifact" call the ectopic beats originated at sites different from SA node and then not suitable for HRV analysis [5]

References

[1] Mateo J, Laguna P. (2000) *Improved heart rate variability signal analysis from the beat occurrence times according to the IPFM model.* IEEE Trans. on Biomedical Engineering, vol. 47, n. 8, pp. 985-996.

[2] Hyndman B. W, Mohn R. K. (1975) *A model of the cardiac pacemaker and its use in decoding the information content of cardiac intervals* Automedica, vol. 1, pp. 239-252.

[3] A. V. Oppenheim, A. S. Willsky, and S. H. Nawab, (1997) *Signals and Systems.* Prentice-Hall,

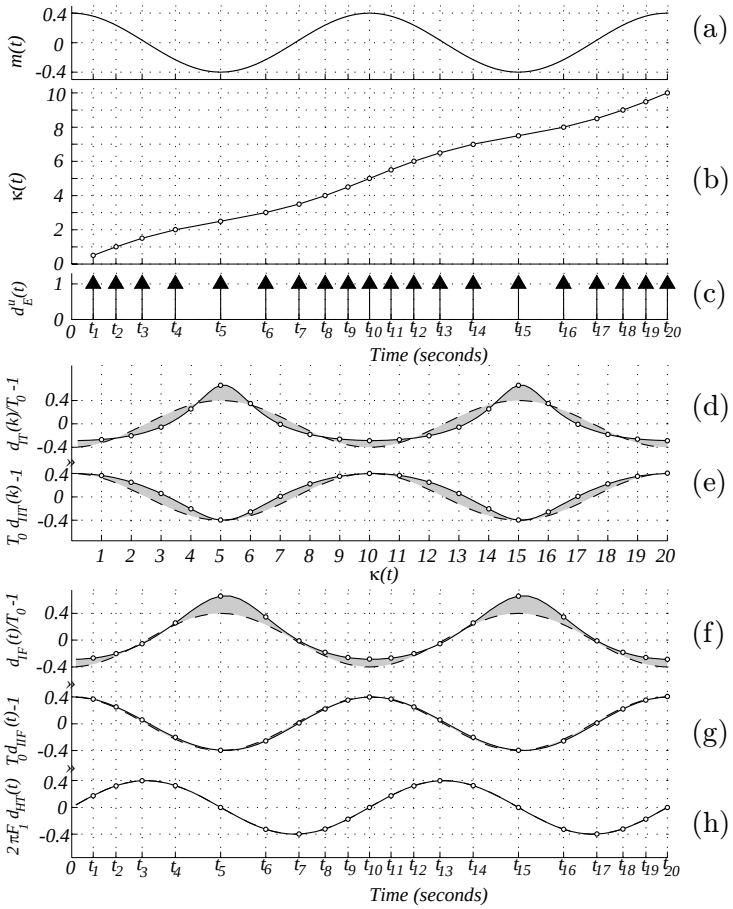

Figure 3: Different heart rhythm representations for an event series generated by the IPFM model using a modulating function $m(t)$=0.4 cos($2\pi F_1 t$) with F_1=0.1 Hz; the mean RR interval length is $\overline{T}_0$=1 second. (a) The modulating function $m(t)$, (b) the output of the integrator $\kappa(t)$, (c) the resulting event series, (d) the interval tachogram ($d_{IT}(k)/\overline{T}_0$-1), (e) the inverse interval tachogram ($\overline{T}_0 d_{IIT}(k)$-1), (f) the interval function ($d_{IF}(t)/\overline{T}_0$-1), (g) the inverse interval function ($\overline{T}_0 d_{IIF}(t)$-1), and (h) the heart timing signal $2\pi F_1 d_{HT}(t)$. The event times t_k are marked with circles and the intermediate values are obtained by interpolation [1]. The function $m(t)$ is superimposed for comparison (dashed line).

[4] (1996). *Task Force of The European Society of Cardiology and The North Americam Society for Pacing and Electrophysiology, Heart rate variability: Standards of measurement, physiological interpretation, and clinical use*, Circ., vol. 93, pp. 1043-1065.

[5] Mateo J. y Laguna P. (2003). *Analysis of Heart Rate Variability in the Presence of Ectopic Beats Using the Heart Timing Signal.* IEEE Trans. on Biomedical Engineering, vol. 50, n. 3, pp. 334-343.

[6] Laguna P., G. B. Moody and R.G. Mark (1998). *Power Spectra Density of Unevenly Sampled Data by Least-Square Analysis: Performance and Application to Heart Rate Signals.* IEEE Trans. on Biomedical Engineering Vol. 45, No. 6. June. pp. 698-715.

[7] Rompelman O., Coenen A. J. R. M., Kitney R. I., (1977) *Measurement of heart-rate variability: Part 1Comparative study of heart-rate variability analysis methods.* Med. Biol. Eng. & Comput., vol. 15, pp. 239-252.

[8] de Boer R. W., Karemaker J. M., and Strackee J., (1985) *Spectrum of a series of point event, generated by the integral pulse frequency modulation model* Med. Biol. Eng. & Comput., vol. 23, pp. 138-142.

[9] R. D. Berger, S. Akselrod, D. Gordon, and R. J. Cohen, (1986) *An efficient algorithm for spectral analysis of heart rate variability* IEEE Trans. Biomed. Eng., vol. 33, pp. 900-904.

[10] P . Castiglioni, (1995) *Evaluation of heart rhythm variability by heart or heart period: Differences, pitfalls and help from logarithms* Med. Biol. Eng. & Comput., vol. 33, pp. 323-330.

[11] B. J. TenVoorde, T. J. C. Faes, and O. Rompelman, (1994) *Spectra of data sampled at frequency modulated rates in application to cardiovascular signals: Part 1 Analytical derivation of the spectra* Med. Biol. Eng. & Comput., vol. 32, pp. 63-70.