Autocorrelations of *R-R* distributions as a measure of heart variability

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We introduce an algorithm for on-line measurement of instant changes of heart dynamics. It measures the variability of *R-R* segments in electrocardiagrams. The method is based on measuring the autocorrelations of the distributions of the system's dynamical variable. The algorithm has been tested on a sample of cardiac conditions. [S1063-651X(97)09608-6]

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One of the main problems in the physics of complex systems is to how to define tools that measure (or at least point to) the type of dynamics characterizing the system. Often the problem is even more basic: how to define a variable that can diagnose the type of dynamics of the system. The potential applications of such a measure are enormous. It can be applied to any complex system in any branch of science and technology (see [1] and references therein). Since it has been shown that the dynamics of the heart changes with the overall heart condition [2–6], on-line diagnostics of heart dynamics could be used in assessing patients' conditions and as a source of guidance in medical treatment. The proposed analysis of instantaneous dynamics of the heart may be used later to assess the patterns of temporal changes in heart rate variability. Those temporal patterns in turn can be checked later for their prognostic value in long-term medical prognoses.

In the past 20 years, it has become recognized that heartrate variability (HRV) reflects neurohormonal influences and the ability of the heart to respond to external inputs and that this variable therefore provides one of the most valuable markers of cardiovascular mortality. The phenomenon of HRV refers to the existence of different lengths in consecutive *R-R* intervals (cardiac cycles) during normal sinus rhythm. Decreased HRV shortly after myocardial infarction was found to be associated with higher mortality [7,8]. It was also shown that decreases in HRV precede serious arrhythmia (ventricular tachycardia) in patients with coronary artery disease [9]. An analysis of HRV enables the detection of subclinical autonomic neuropathy, which is associated with high mortality in diabetic subjects [10]. There is also a wide range of cardiovascular diseases (e.g., congestive heart failure, hypertension, and heart transplantation) for which HRV may be used as a potential prognostic marker or as a tool in assessing therapeutical interventions. In clinical practice, there are two main methods used to evaluate the HRV: the time domain and the frequency domain method [11,12]. Time domain indices, routinely obtained from 24-h electrocardiagram (ECG) recordings, are relatively easy to obtain, allowing the calculation of short- and long-term variability of *R-R* intervals. The frequency domain method, which is usually derived from 5–10 min segments of an ECG, provides information about the amount of overall variance in heart rate resulting from periodic oscillations of heart rate at various frequencies. These frequencies are influenced by the autonomic nervous system and other neurohormonal factors. There is a strong correlation between specific indices derived from time and frequency domain analyses. There are also various nonlinear methods available for evaluating HRV [13], and these are potentially useful in the assessment of risk of sudden cardiac death. At present, however, these methods are not ready for application in clinical and physiological studies. Despite the proven clinical pathophysiological values of both time and frequency domain measures, these methods have shortcomings in many situations. It has been reported that long after myocardial infarction, indices of HRV cannot identify patients who develop life-threatening ventricular arrhythmias [14,15]. Spectral analysis, which is often used to assess the sympathetic and vagal input, does not adequately reflect autonomic changes during exercise (possibly due to non-neural mechanisms that affect the HRV during maximal effort) [16]. Hence there is clearly a need to develop a more accurate method of analyzing HRV, one that is more sensitive in detecting patients who are prone to sudden cardiac death due to electrical imbalance. There is also a need to obtain a quick (on-line) analysis of HRV, which can be applied in intensive care units to assess rapid changes of HRV. Such a measure would reflect subclinical changes in a patient's status and thereby improve diagnostic and therapeutical procedures. It may be that nonlinear dynamic measures of HRV will fulfill our expectations.

The analysis of a 24-h Holter recording is somewhat problematic because of the stability of the measured signal. It is common in medical analyses to average the results over the entire measured signal. An analysis based on averaging, however, may be inadequate and thus inappropriate for the

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data obtained in a Holter recording because the stability of the signal depends a great deal on the patient's emotional and physical condition at each moment. It may be adequate, though, to analyze possibly short recordings of an ECG [17]. We present yet another efficient algorithm for analyzing that type of data, one that provides information about momentary changes in the distribution of heart rate.

One way to gain insight into the dynamics of the system is to study the changes in the distributions of a given variable associated with the measured signal. The *dynamics* of the change in distributions may help determine whether the system is stable or unstable and identify the system's basic properties. A number of such measures have been developed recently [1]. These methods, however, are not very effective with respect to short data series. As mentioned earlier, the analysis of long time series in biological systems (such as the heart) is usually meaningless because of the lack of stability in the signal.

Furthermore, in medical applications on-line assessment of a patient's condition is especially important because it can provide information necessary for the fast delivery of appropriate treatment. The majority of the methods that have been used recently to assess changes in a system's dynamics, however, are too slow and thus are not applicable for on-line medical use.

We present here a measure that essentially checks the autocorrelation of the distribution of a global property of the system. The proposed measure detects changes in the width of the distribution and the distribution's stability as a function of time. The algorithm is easy to interpret. It checks the overlap of the probability distributions in different time windows. The advantage of this algorithm is its applicability to on-line assessment of heart dynamics. As shown below, this method is effective in tracking the momentary changes in heart dynamics. There are three essential steps in this method of analyzing ECG recordings.

(i) The signal to be analyzed is divided into a sequence of time periods (windows), which are moved by τ with respect to each other. The length of this sequence needs to be sufficiently long to obtain acceptable statistics and small enough to produce a stable signal. In the example presented below, the value of τ $(=4)$ was chosen on a trial and error basis. It is important, however, that the value of τ is small enough to detect momentary changes in the distributions rather than the global ones (which reflect unstable conditions of the system).

(ii) A probability distribution is calculated for a given property of the system (in our case, *R-R* segments in an ECG).

(ii) The autocorrelation is calculated according to the equation

$$A(\tau)=\sum_{i=1}^{h} p_i(t)p_i(t+\tau), \tag{1}$$

where h is the number of cells in histogram and $p_i(t)$ is the ith cell in a histogram of the probability distribution of the window starting at time t.

In essence, the algorithm calculates the overlap of the histogram of the *R-R* variability for two consecutive windows. The measure $A(\tau)\in[0,1]$. $A(\tau)$ will tend toward zero if the probability distributions are very wide (for example, white noise) or if they do not overlap in two given windows. Those two cases define a signal that is unstable or stochastic. On the other hand, if the distributions in both windows have peaks at approximately the same value of $A(\tau)\to 1$, $A(\tau)=1$, and if the distributions from different windows are δ-like, then they overlap perfectly. In other words, the $A(\tau)$ measures the stability and predictability of a system's dynamics at a given time.

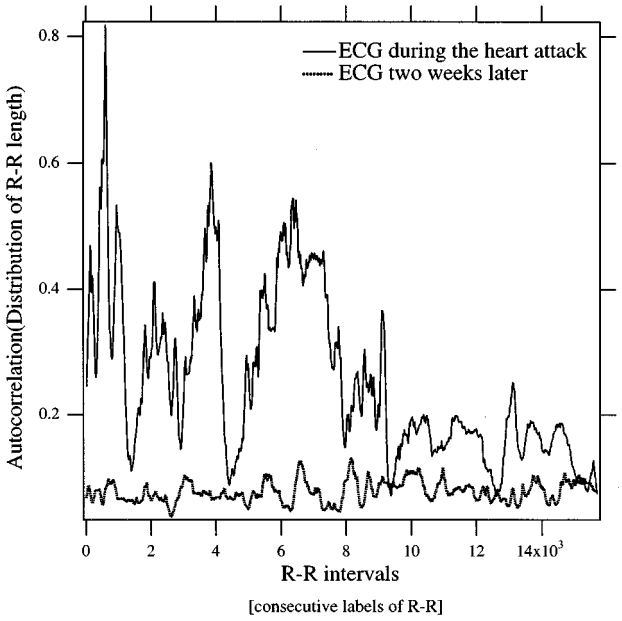

FIG. 1. Autocorrelation of probability distributions of *R-R* intervals (in units of one). The ECG was obtained during the patient's heart attack and two weeks later.

The method was used to discriminate among patients with different degree of heart problems. The method analyzed the variability of the *R-R* segments in patients immediately after experiencing a heart attack (upon admission to the hospital) and again when the patients prepared to leave the hospital in a stabilized condition (on average, two weeks after the heart attack).

Results are presented in Figs. 1–3. Figures 1 and 2, respectively, show the autocorrelation of the probability distribution of data collected from two different patients immediately after their respective heart attacks and again two weeks later. As one can see, in both cases the measure shows a higher correlation between data points gathered immediately following a heart attack than two weeks later. The results thus confirm the frequent assertion [18] that the *R-R* variability in a healthy heart is greater than that in a pathological one. With respect to the first patient, the high autocorrelations of the signal observed immediately after the patient's heart attack are significantly reduced two weeks later, reaching a nominal value. For the second patient, improvement is not so obvious, but it is still detectable. This was reflected in the medical assessment of the patient's condition.

The difference of the mean value of $A(\tau)$ can reflect the fact that they had different heart conditions, each associated with the different heart's dynamics. Further studies on this feature of the data are planned.

It is also noteworthy that the variability in the proposed measure was greater for the first patient. This is primarily

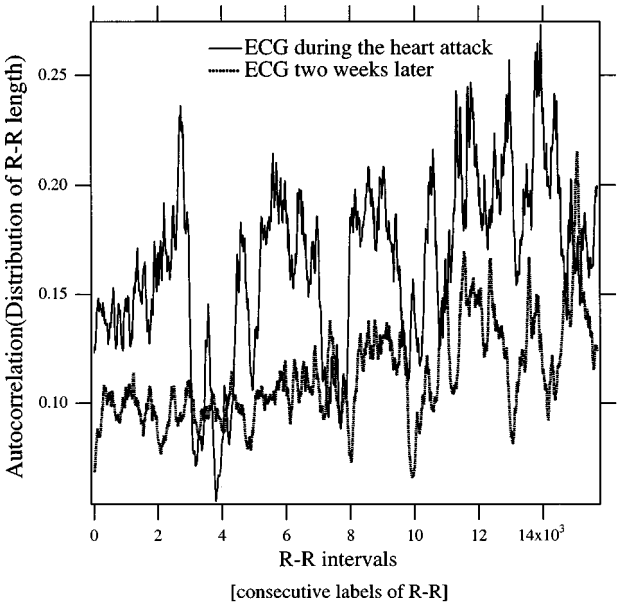

FIG. 2. Same as Fig. 1, but for a different patient.

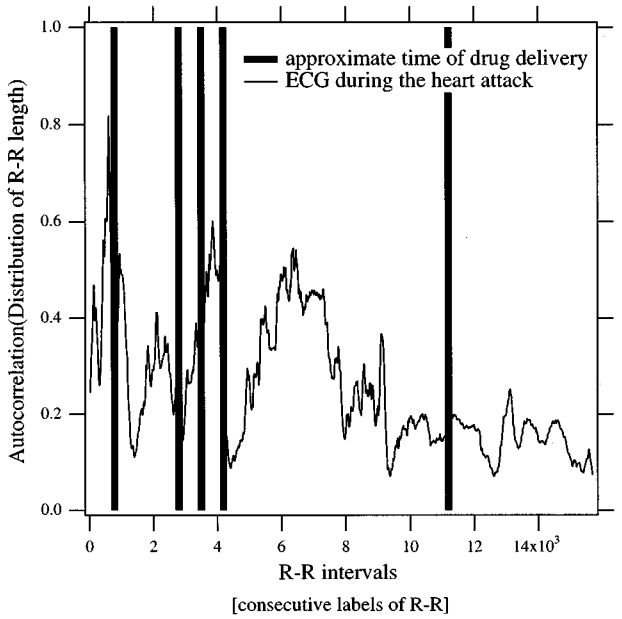

FIG. 3. Autocorrelation of probability distributions of *R-R* intervals (in units of one). The ECG of the patient undergoing heart attack. Shaded lines correspond to the approximate times of drug administration.

due to the fact that this patient underwent different treatments for his or her condition. As shown below, sharp peaks and valleys coincide very well with the time of the treatment.

The vertical lines in Fig. 3 show the timing of drug administration. The response time to the drug, represented by the shaded area, is approximately 2 min. During this period, there is an abrupt change in the value of the measure.

As stressed earlier, the primary advantage of the proposed algorithm is that it is sufficiently fast that it can be calculated in real time, making it applicable to the on-line assessment of patients' conditions and the impact of treatment for their conditions.

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