Detecting deterministic dynamics of cardiac rhythm

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Abstract **Under the acceptable hypothesis that cardiac rhythm is an approximately deterministic process with a small scale noise component, an available way is provided to construct a model that can reflect its prominent dynamics of the deterministic component. When applied to the analysis of 19 heart rate data sets, three main findings are stated. The obtained model can reflect prominent dynamics of the deterministic component of cardiac rhythm; Cardiac chaos is stated in a reliable way; Dynamical noise plays an important role to the generation of complex cardiac rhythm.**

Keywords: cardiac rhythm, nonlinear dynamics, Bayesian estimation.

It has been proposed that the heart rate variability may display complex nonlinear dynamics, including deterministic chaos[1—5]. Furthermore, it may be more reasonable that cardiac dynamics is neither chaotic nor stochastic, but rather both. In such a system, the unpredictability of the output will be due to the uncertainty generated by the deterministic component, and to the stochastic inputs[6,7].

The primary goal of this study is the desire to obtain a model that can reflect the prominent dynamics of the deterministic component for heart rate variability under such an assumption. That is, the model should not only fit data and make a good short-term prediction, but should also have dynamical behavior similar to that of the observed variable [8—12]. If we can obtain such a model, the dynamics of the model will then present a reliable detection of deterministic dynamics for the heart rate variability. To satisfy this stringent criterion, some available methods with partial solutions have been provided[8—11].

Since dynamical noise is a major source of variability in the feedback system and the reliability of the resulting model as a long-term predictor is highly dependent on the amount of measurement and dynamical noises present, some questions remain concerning the significance of the models obtained by such methods directly in the analysis of cardiac dynamics[4,8]. It has been also stated that the new directions for such methods, including elimination of the influences of measurement and dynamical noises, may be proved useful for modeling in the presence of noise and full detection of deterministic dynamics[8,13].

To obtain our primary goal for modeling heart rate variability, the cluster-weighted filtering (CWF) method is proposed to model the deterministic component of the approximately dynamical system from complex and noisy time series. In order to approach the complexity of original attractor, the normalized Gaussian network is used as function approximator[9]. By putting the problem of nonlinear noise reduction into a Bayesian framework[14,15], we introduce an appropriate way of combining model estimation with noise reduction procedures. It enables us to determine the correct amount of noise reduction from the data itself and thereby avoiding over-fitting and over-filtering[16,17].

With the applications of CWF to the analysis of heartbeat intervals[18], we investigate the free-run dynamics of the models to see if they exhibit linear and nonlinear features consistent with those of original time series. This involved comparing the time delay plots of the free-run behavior derived from the models with that of originals. We estimates the dynamical and measurement noise levels to confirm that CWF neither changes the underlying deterministic structure nor introduces spurious deterministic structure into the data. In order to test whether the deterministic component of cardiac dynamics is sensible to initial conditions, we estimate the largest Lyapunov exponents from the filtered time series and free-run behavior of the models. We also use surrogate data analysis to confirm the hypothesis that the heart rate variability is not consistent with a linear Gaussian process.

1 Method of cluster-weighted filtering

Let $\{x_i\}_{i=1}^{N}$ be the observed time series of an approximately dynamical system.

$$x_i = y_i + \varepsilon_i, \tag{1}$$

$$y_i = f(\boldsymbol{y}_i) + e_i, \tag{2}$$

where $\boldsymbol{y}_i = (y_{i-1}, y_{i-2}, \cdots, y_{i-d})$. f denotes system dynamics with unknown parameters that need to be estimated, e a stochastic element in the dynamics and ε acts as measurement noise.

Our goal is thus to estimate y and f from x. In order to find the dependencies of y on $\boldsymbol{y}$ and $\boldsymbol{y}$ on x based on the joint density $p(x, y, \boldsymbol{y})$ (for simplicity, $\boldsymbol{y}$ and x are defined as input and output of an approximately dynamical system under consideration respectively), we expend the joint density $p(x, y, \boldsymbol{y})$ into M clusters c_m, $m = 1, \ldots, M$, each of which contains the product of four terms [9].

$$p(x, y, \boldsymbol{y}) = \sum_{m=1}^{M} p(x|\, y, \boldsymbol{y}, c_m) \cdot p(y|\boldsymbol{y}, c_m) \cdot p(\boldsymbol{y}|c_m) \cdot p(c_m), \tag{3}$$

where $p(c_m)$ is the weight of a cluster, and $p(\boldsymbol{y}|c_m)$ the domain of influence in the input space of the cluster. $p(y|\boldsymbol{y}, c_m)$ denotes the dependence of y on $\boldsymbol{y}$ and c_m, the remaining item expresses the output distribution of the cluster.

Generally, $p(\boldsymbol{y}|c_m)$ is taken to be Gaussian with a mean μ_m and covariance matrix C_m. The dynamical noise e and measurement noise ε are also taken to be Gaussian with variances σ_{me}^2 and $\sigma_{m\varepsilon}^2$ associated with cluster C_m respectively. Here the mean value of y is replaced by the output of local model $f_m(\boldsymbol{y}, \beta_m)$,

$$f_m(\boldsymbol{y}, \beta_m) = \sum_{i=1}^{I} \beta_{mi} f_{mi}(\boldsymbol{y}). \tag{4}$$

An iterative algorithm, the expectation-maximization (EM) algorithm search of the maximization of the model likelihood given a data set and initial conditions, is used for modeling and filtering [9,19].

In the E-step, we assume the current cluster parameters to be correct and evaluate the posterior probabilities that relate each cluster to each data point. These posteriors can be interpreted as the probability that particular data are generated by a particular cluster.

$$p(c_m \mid x, y, \boldsymbol{y}) = \frac{p(x, y, \boldsymbol{y} \mid c_m) p(c_m)}{\sum_{m=1}^{M} p(x, y, \boldsymbol{y} \mid c_m) p(c_m)}. \tag{5}$$

In the M-step, we assume the current data distribution to be correct and find the cluster parameters that maximize the likelihood of the data. The new estimate for the unconditioned cluster probabilities is

$$p(c_m) \approx \frac{1}{N} \sum_{i=1}^{N} p(c_m \mid x_i, y_i, \boldsymbol{y}_i). \tag{6}$$

Given $p(c_m)$, we define a cluster-weighted expectation of function $\theta(x, y, \boldsymbol{y})$

$$\langle \theta(x, y, \boldsymbol{y}) \rangle_m \approx \frac{\sum_{i=1}^{N} \theta(x_i, y_i, \boldsymbol{y}_i) p(c_m \mid x_i, y_i, \boldsymbol{y}_i)}{\sum_{i=1}^{N} p(c_m \mid x_i, y_i, \boldsymbol{y}_i)}. \tag{7}$$

The cluster-weighted expectation is used to update μ_m, C_m, σ_{me}^2 and $\sigma_{m\varepsilon}^2$ discussed above[14]. An expression to update $\beta_m = [\beta_{m1}, \beta_{m2}, \ldots, \beta_{mI}]$ for each cluster c_m can be obtained by maximizing the log-likelihood function. $\log \prod_{i=1}^{N} p(x_i, y_i, \boldsymbol{y}_i)$.

$$\beta_m = B_m^{-1} A_m, \tag{8}$$

where $[B_m]_{ij} = \langle f_{mi}(\boldsymbol{y}) f_{mi}(\boldsymbol{y}) \rangle_m$, $[A_m]_i = \langle y f_{mi}(\boldsymbol{y}) \rangle_m$.

In this note, Metropolis-Hastings algorithm is used for updating time series $\{y_i\}_{i=1}^{N}$ [14]. For simplicity we chose $\alpha(y_i^{\text{new}}, y_i)$ as the criterion to accept or reject y_i^{new} as a new sample of y_i:

$$\alpha\left(y_i^{\text{new}}, y_i\right) = \min\left\{ \frac{p\left(y_i^{\text{new}} \middle| \{y_j\}_{j\neq i}, x, \{\beta_m, \sigma_{m\varepsilon}^2, \sigma_{me}^2\}_{m=1}^{M}\right)}{p\left(y_i \middle| \{y_j\}_{j\neq i}, x, \{\beta_m, \sigma_{m\varepsilon}^2, \sigma_{me}^2\}_{m=1}^{M}\right)}, 1 \right\}, \tag{9}$$

$$p\left(y_i \middle| \{y_j\}_{j\neq i}, x, \{\beta_m, \sigma_{m\varepsilon}^2, \sigma_{me}^2\}_{m=1}^{M}\right) = \exp\left(\sum_{m=1}^{M} \left(p(c_m | x_i, y_i, \boldsymbol{y}_i) \left(\frac{-(y_i - x_i)^2}{\sigma_{m\varepsilon}^2} + \frac{-[y_i - f_m(\boldsymbol{y}_i, \beta_m)]^2}{\sigma_{me}^2} \right) + \sum_{j=i+1}^{i+d} p(c_m \mid x_j, y_j, \boldsymbol{y}_j) \frac{-[y_j - f_m(\boldsymbol{y}_j, \beta_m)]^2}{\sigma_{me}^2} \right) \right), \tag{10}$$

where $\boldsymbol{y}_i^{\text{new}} = (y_{i-1}, \cdots, y_i^{\text{new}}, \cdots, y_{i-d})$. For the fast convergence of the algorithm, the candidate sample y_i^{new} can be obtained based on taking the derivative of the total log-likelihood function with respect to the data point (terms associated with measurement noise are ignored so that the algorithm will proceed[14]).

Finally, the model estimation and the noise reduction process by cluster-weighted filtering can be summarized: (ⅰ) Initialization (choose $1/M$ as the initial cluster probabilities. Pick randomly M points from data set as the cluster input means); (ii) evaluation of the probability of the data $p(x, y, \boldsymbol{y}|c_m)$; (iii) calculation of the posterior probability of the clusters $p(c_m|x, y, \boldsymbol{y})$; (iv) update of the cluster weights $p(c_m)$, the cluster-weighted exceptions for input means μ_m and covariance matrix C_m, the maximum log-likelihood model parameters β_m, dynamical noise variance σ_{me}^2 and measurement noise variance $\sigma_{m\varepsilon}^2$; (v) update of $\{y\}_{i=1}^{N}$ based on M-H algorithm; (vi) return to (ii) until the total data likelihood does not increase any more.

2 Experimental materials

19 mixed breed male dogs (15—24 kg in weight, 2—4 years old by dentition) free of heartworms were conditioned for chronic study. Each dog was prepared surgically with an anteroseptal myocardial infarction or was shamed operated. Heart rate variability was studied before infarction. After the last heart rate variability test, each dog was identified as being at either high or low risk for the development of ventricular fibrillation during a submaximal exercise and transient myocardial ischemia test.

The procedure describing the surgically created myocardial infarction was presented in detail elsewhere[18]. During surgical plane anesthesia, the heart was exposed and the fatty tissue was dissected from the vessel approximately 2 cm from the origin surrounding the circumflex branch of the left coronary artery. A loose fitting (diameter 3.0—3.5 mm) Doppler flow probe (20 MHz, Hartley) and, immediately distally, a pneumatic vascular occluder were implanted. To produce the myocardial infarction, the anterior intraventricular branch of the left coronary artery immediately proximal to the first major diagonal artery perforator was critically stenosed for 20 min and then permanently ligated. A catheter was planted in the descending aorta for the later direct measurement of arterial pressures.

30 d after myocardial infarction, the dogs were studied consecutively and characterized for developing ventricular fibrillation during an exercise and myocardial ischemia test on a motor-driven treadmill. Briefly, each dog was exercised submaximally for 12—15 min while the work load was increased progressively every 3 min. (4.8 km/h at 0% grade and 6.4 km/h at grades of 0%, 4%, 8%, 12%) until heart rate reached a target range of 215—225 beats/min. At that time, the left circumflex artery was pneumatically occluded for 2 min; the treadmill was stopped after the 1st min of occlusion, while ischemia was maintained for an additional minute. The 2 min period myocardial ischemia was verified by a zero flow trace signal from circumflex artery Doppler flow probe. During the 2-minute of exercises a myocardial ischemia, 8 dogs (S_MI group) are susceptible to a sudden death because of developing ventricular fibrillation. 11 dogs that did not develop ventricular fibrillation were considered to be at low risk and were defined to have resistance to a sudden death (R_MI group).

A few days after myocardial infarction, 30 min ECG samples at rest were obtained. All recordings were collected in the late morning or early afternoon without the use of sedation or physical restraint and before feeding. After a 10—20 min daily transition period in the laboratory, ECG data were obtained while the dog was quiet and lying down but not sleeping on a padded examination table. Specific care was taken to eliminate extraneous noise, unfamiliar personnel and other environmental distractions. Data were not recorded when rectal temperature was >39℃ or the dog was judged to be behaviorally upset. A transthoracic modified lead I surface ECG was obtained with the use of self-adhesive pads, amplified and filtered at a low frequency (5 Hz) and digitized at 400 Hz. All digitally encoded files were analyzed with a commercially available program (Corazonix). Aberrant ECG complexes such as premature ventricular beats, electrical noise, or other aberrant ECG signals and their adjacent RR intervals were rejected by software.

3 Results and discussions

From the results in ref. [7], when applying parsimonious Volterra series model method directly to the analysis of heart beat intervals, we find that the largest Lyapunov exponents are negative for most (89%) subjects as shown in table. 1 (Lyap_kor). These results suggest that cardiac chaos is not prevalent in heart. In spite of the fact that this method had been successfully tested by artificial data sets[7], it does not eliminate the influences of noise essentially. So the conclusion that the deterministic component of cardiac dynamics is chaotic or not obtained by such methods is suspicious. In order to approach the complexity of original attractor and eliminate the influences of noise in modeling the deterministic component of cardiac dynamics, we introduce the method of CWF. The parsimonious Volterra series models, which are used as local models for cluster-weighted filtering, are fitted to the time series using a search space that included linear, bilinear, and trilinear terms of up to 3th order. Despite the large search space (1 constant, 4 linear, 10 bilinear, 20 trilinear terms), only six significant terms are included in the local models. By searching the space of the candidate terms, the one that gives the greatest reduction in the MSE is selected. By repeating this greatest reduction in MSE at each step, a parsimonious model can be constructed. Empirically, six to eight embedding data points, which are chosen randomly from the training set, are used as the cluster input means initially. We discuss the power of CWF as follows.

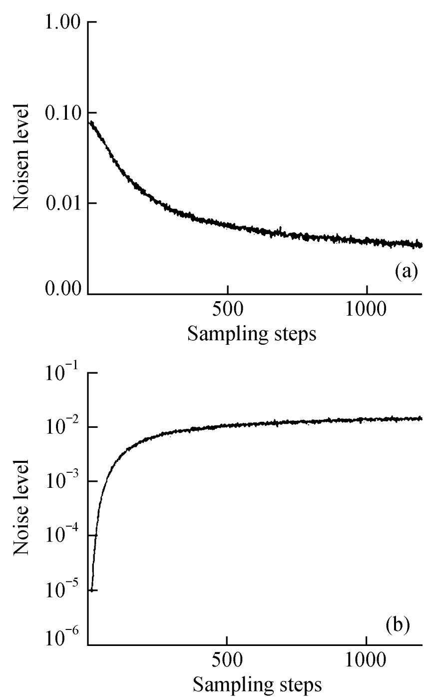

Fig. 1. 1200 samples of dynamical noise variance (a) and measurement noise variance (b).

First, cluster-weighted filtering yields a property of automatic noise level estimation. For example, we apply CWF to 1000 points observed from a stochastically driven Henon map (the variances of dynamical and measurement noises are 0.004 and 0.01 in delay coordinates respectively[14]). Fig.1 shows 1200 samples of dynamical and measurement noise variances. One can find that both dynamical and measurement noise variances do converge approximately to the correct values after 400 iterations. To some extent, CWF not only eliminates influences of noises but also avoids the tendency to over-clean the data in the process of filtering.

Second, fig. 2 shows delay plots of original (a, d) and filtered (b, e) time series of heart beat intervals of two subjects respectively. One can see that the attractors between the original and the filtered are very similar. Additionally, table 1 shows values of estimated relative dynamical (Amp_dyn) and measurement noise amplitudes (Amp_mea) for all time series of heart beat intervals, each of which is not larger than 3.5% of the original signal amplitudes. It implies that CWF does neither change the underlying dynamics nor introduce spurious dynamics for the heart beat intervals[20].

Third, fig. 2 (c), (f) also shows delay plots of the free runs of the model obtained by CWF. That is, the model is iterated 500 times without any corrections from the data. Attractors similar to that of originals are also obtained. For both subjects, free runs show complex deterministic structures. Results can tell us that the deterministic components of cardiac dynamics can be primarily described by only a few of local nonlinear dynamical models. Comparison between the originals and the model dynamics also discovers that dynamical noise plays an important role in the generation of complex cardiac rhythm.

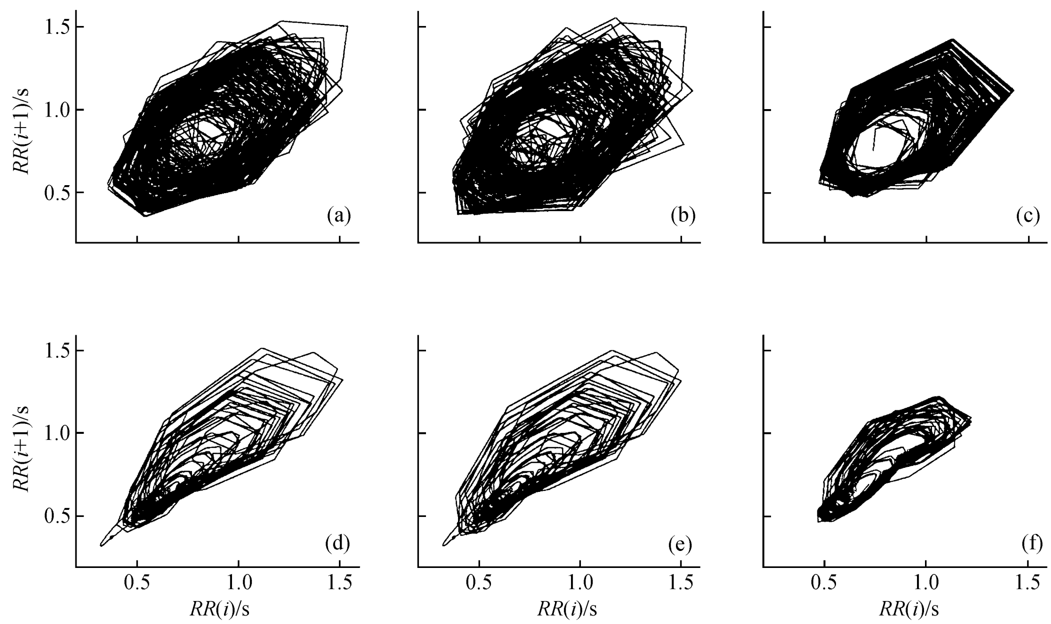

Fig. 2. Delay plots of the time series of RR intervals from two subjects (No. 732v2, No. 683v2). (a) and (d) Original heartbeat intervals; (b) and (e) filtered time series by CMF; (c) and (f) free runs from models.

It is of considerable interest to study whether the heartbeat series are chaotic. However, presence of dynamical and measurement noise can often lead to false positive or negative identifications of chaos when traditional methods of nonlinear dynamics analysis are used. Discussions listed above suggest that the models obtained by CWF can reflect prominent dynamics of the deterministic component of an approximately dynamical system, and CWF does neither change the underlying dynamics nor introduce spurious dynamics. So the characteristic exponents of the deterministic components of cardiac dynamics can be estimated reliably from filtered time series. By evaluating the Jacobians over all the filtered time series of heartbeat intervals, we estimate the largest Lyapunov exponent by the algorithm based on QR decomposition[7]. The numerical results are shown in table 1. Let us first consider the largest Lyapunov exponents derived from filtered time series of RR intervals (Lyap_fil). 17 of 19 time series show positive values. When considering that for free run behavior of the models, again we find 16 of 19 time series show positive values. The remainders show negative values but very near to zero. It implies that the deterministic components of cardiac dynamics for most subjects under studying are sensible to initial conditions. What should be noted is that there are not apparent differences between R_MI group and S_MI group in the values of the largest Lyapunov exponents.

Finally, the widespread surrogate data method is used to test the nonlinearity for heartbeat intervals[21,22]. In this study, the amplitude-adjusted Fourier transform

(AAFT) algorithm is used to generate surrogate data [21], and the short-term predictability calculated by Sugihara-May method acts as a statistic test [23,24]. The significance can be measured by S:

Table 1 Calculated characters of heart rate variability for each subject

Subject	Lyap_kor	Lyap_fil	Lyap_pre	Amp_dyn	Amp_mea	S_SM	S_CWF
732v2	0.21	1.26	1.43	0.0232	0.0126	2.96	19.73
679v2	− 0.34	0.49	0.60	0.0241	0.0172	1.88	16.92
665v2	−0.11	0.21	0.21	0.0104	0.0106	1.73	18.26
687v2	−0.07	0.07	0.36	0.0208	0.0024	4.34	12.78
717v2	−0.02	0.14	0.06	0.0064	0.0074	8.62	8.25
701v2	−0.26	-0.07	−0.08	0.0125	0.0047	4.24	9.52
682v2	−0.45	0.11	0.10	0.0107	0.0277	−3.35	8.82
673v2	−0.05	0.02	−0.02	0.0034	0.0042	3.52	5.75
671v2	−0.62	0.07	0.10	0.0302	0.0197	−2.97	10.43
669v2	−0.14	0.11	0.10	0.0066	0.0077	3.18	5.93
683v2	0.59	0.08	0.11	0.0157	0.0093	1.66	7.83
729v4	−0.23	0.14	0.16	0.0195	0.0121	3.34	15.07
724v4	−0.19	0.07	0.07	0.0144	0.0077	1.32	12.39
675v4	−0.12	0.07	0.11	0.0028	0.0041	2.13	7.42
725v4	−0.08	1.43	1.41	0.0186	0.0057	2.24	28.26
670v4	−0.19	0.08	0.16	0.0350	0.0078	1.18	2.96
706v4	−0.25	0.37	0.45	0.0144	0.0062	0.31	6.48
713v4	−0.16	0.13	0.21	0.0346	0.0188	−0.67	21.34
667v4	−0.11	−0.04	−0.01	0.0077	0.0022	1.71	5.92

$$S=\frac{\left(\langle M_{\text{surr}}\rangle - M_{\text{org}}\right)}{\sigma}, \tag{11}$$

where $\langle M_{\text{surr}}\rangle$ and σ are the mean value and standard deviation of the predicative error associated with 20 surrogate data sets, M_{org} is the predicative error of original time series.

Results are shown in table 1 (S_SM). Only for 47% of the subjects ($S>1.96$) can we reject the null hypothesis ($P<0.05$) that the data arise from a linear Gaussian process. By such a method, no obvious evidences of nonlinearity in cardiac rhythms are found. Similar results were also obtained by Lefebvre[24]. He concluded that the evidence of deterministic chaos in cardiac rhythms is not strong or persistent, and this relatively small effect was believed to be a consequence of many rapidly changing physiological inputs (can be viewed as dynamics noises) to the sinus node. Fortunately, CWF shows power in modeling deterministic components of such systems from complex and noisy time series. When the one step predicative errors of filtered time series of RR intervals and 20 surrogate data sets are obtained by CWF, we test nonlinearity reliably for all the subjects under studying. The values of significance are obtained in table 1 (S_CWF). For each subject, we can reject the null hypothesis ($P<$ 0.05).

4 Conclusions

An acceptable hypothesis is that cardiac rhythm is a complex deterministic process with a small scale noise (high dimensional) components. On the largest scales, cardiac rhythm behaves as a nonlinear deterministic system with finite degrees of freedom. At the smaller scales the system is likely to be dominated by noise (deterministic high dimensional motion or true noise source)[4,6,25,26]. This is in agreement with the physiology of the system. The heart rate is determined by the activity in the autonomic nerves that supplies the sinus. The activity in these fibres is not only determined by feedback from the baroreceptors in the cardiovascular system, but also influenced by inputs from many other systems, including hormonal systems, and higher centers such as the cerebral cortex[4,6]. Because of its intrinsic complex mechanism, although many researchers have studied cardiac rhythm in a variety of ways in an attempt to determine whether it is deterministic chaos or stochastic noise, the conclusions have been mixed, sometimes contradictory[4,6,24—27]. In this note, a powerful method has been presented for modeling deterministic component of such an approximately dynamical system from complex and noisy heartbeat intervals. After the reliability of the proposed method is both supplied from the point view of analysis and tested by artificial data, we applied it to the analysis of 19 heart rate data sets. The main findings are listed. The obtained models can reflect prominent dynamics of the deterministic component of cardiac rhythms; cardiac chaos is stated in a reliable way; Dynamical noise plays an important role to the generation of complex cardiac rhythm.

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