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Noise Effects on the Complex Patterns of Abnormal Heartbeats

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Patients at high risk for sudden death often exhibit complex heart rhythms in which abnormal heartbeats are interspersed with normal heartbeats. We analyze such a complex rhythm in a single patient over a 12-hour period and show that the rhythm can be described by a theoretical model consisting of two interacting oscillators with stochastic elements. By varying the magnitude of the noise, we show that for an intermediate level of noise, the model gives best agreement with key statistical features of the dynamics.

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Individuals with frequent abnormal heartbeats (Fig. 1) may be at high risk for sudden cardiac death [1]. Such abnormal heart rhythms often have a random appearance. Attempts have been made to analyze these rhythms by inspecting short data strips [2–3] and matching them beat by beat to various models [4–7]. Other approaches [7–9] characterize statistical properties in longer records of up to several hours. However, the mechanisms underlying these abnormal rhythms and their changes over long periods of time remain elusive. Here we show that a theoretical model consisting of two coupled oscillators [3–6] describes the observed patterns of abnormal heartbeats in one clinical case provided we introduce noise to the model.

We consider a continuous 12-hour segment of the ambulatory electrocardiographic record of an individual with heart failure and frequent abnormal heartbeats (Fig. 1). The normal sinus heartbeats, S-beats, arise from activity in the sinus node, the normal pacemaker of the heart. The time intervals between the normal beats appear to be periodic in this short tracing, but they do fluctuate during the 12-hour period. The abnormal ventricular beats, V-beats, arise in the lower chambers of the heart, the ventricles. Although the timing between the V-beats appears to be irregular, the histogram of the time intervals between consecutive V-beats, consists of equidistant peaks implying that the interventricular time intervals are multiples of a fixed number (Fig. 1). This result is consistent with the possibility that the heart rhythm arises from a competition between two oscillators: the normal sinus oscillator, and an abnormal ventricular oscillator with periods $T_S$ and $T_V$, respectively. Such rhythms are called parasystolic.

After each S-beat or V-beat, there is a time period, called the refractory time $\theta$, during which all other heartbeats are blocked. Thus, all V-beats must occur at least a time $\theta$ after an S-beat. Because in our case $\theta/T_S \geq 1/2$, such a V-beat will block the following S-beat [1].

![Figure 1: Upper panel: Electrocardiogram over 6.6 s of a patient with heart failure. Sinus (S) and ventricular (V) beats differ in morphology. S-beats are separated by an interval $T_S$. The time interval between the S-beats with an intervening V-beat is approximately $2T_S$ implying that an S-beat has been blocked (downward white arrow). The interventricular time interval $T_V$, determined from the histogram in the lower panel, is also indicated and is consistent with a blocked V-beat (upward white arrow). Lower panel: The histogram of the time intervals between consecutive abnormal V-beats for the 12-hour record from which the segment in the upper panel was extracted ($\approx 80,000$ beats with $\approx 5000$ V-beats). The time interval between the peaks is $1.67s$ ($\approx 3T_S$). The inset is an enlargement of the peak at $5s$. The sampling rate of the underlying electrocardiographic time series is $128\, \text{Hz}$. To describe the parasystole mechanism we introduce the phase $\phi_i$ of the $i$th ventricular beat in the sinus cycle, i.e., the time interval between the $i$th ventricular beat and the previous sinus beat normalized by $T_S$. Successive values of $\phi_i$ are determined by iterating the difference

\[\phi_{i+1} = \phi_i + \frac{T_V}{T_S}, \quad \phi_i \in [0, 1)\]
equation:

\[ \phi_{i+1} = (\phi_i + T_V/T_S) \mod 1, \quad (1) \]

where a ventricular beat is expressed if \( \phi_{i+1} > \theta/T_S \).
For a fixed irrational ratio \( T_V/T_S \) (incommensurate periods), the phase of the V-oscillator with respect to the S-oscillator will, for sufficiently long times, be equally distributed in the interval \([0,1)\). Interestingly, the sequence of the number of intervening S-beats between consecutive V-beats, called the NIB sequence, consists of only three different values (NIB-triplet). The values in these NIB-triplets change with \( T_V/T_S \) and \( \theta/T_S \) \([1]\). Examples are shown in Fig. 2a.

The uniform distribution of the phases of the V-beats allows us to derive the fraction of V-beats. Call \( n_V \), the number of V-beats observed on the electrocardiogram in a time interval \( T \), and \( N \) the total number of S-beats and V-beats during the same time interval. The total number of observed and blocked V-beats in \( T \) is \( T_V/T_S \) and the total number of observed beats is \( N = T/T_S \). The fraction of observed V-beats, i.e. those which occur outside of the refractory period is \( (T_S - \theta)/T_S \). It follows that \( n_V = (T_S - \theta)/T_S \times T/T_V \), and consequently

\[ n_V/N = (T_S - \theta)/T_V. \quad (2) \]

Perturbation of the timing of the V-beats by Gaussian noise does not affect this distribution, because the uniform distribution of the phases of the V-beats remains unchanged.

To illustrate the properties of the unperturbed model, we iterate Eq. (1) using typical parameter values for the patient under consideration. Histograms showing the NIB values for three sets of parameters are shown in Fig. 3a.

We now compare the results of Eq. (1) with the clinical data. Since the value of \( T_S \) fluctuates during the record, we combine the data from different times of the day during which \( T_S \) falls in a fixed 10 ms range. Fig. 3b shows the histograms of NIB values for three different values of \( T_S \). For \( T_S = 0.61 \) s \( (T_V/T_S < 3) \) and \( T_S = 0.51 \) s \( (T_V/T_S > 3) \), we find the same NIB-triplets as in the deterministic model (Fig. 3a). However, additional peaks in the data (Fig. 3b) contradict the “rule” of only three NIB-values in the purely deterministic model. Furthermore, for \( T_S = 0.55 \) s \( (T_V/T_S \approx 3) \), fewer beats with NIB=2 are present in the data, and new NIB-values appear largely corresponding to the sequence 5, 8, 11 . . . = 3n - 1, where \( n \geq 2 \) is an integer \([2]\).

There are also significant discrepancies between the predicted fraction of V-beats from Eq. (2) and the observed values. Fig. 4a shows that, for \( T_V/T_S \approx 3 \), the model of Eq. (2) predicts many more V-beats than are found.

\[ \phi_{i+1} = \left( \phi_i + \frac{T_V}{T_S} + \frac{f(\phi_i, T_S, T_V)}{T_S} + \frac{\eta}{T_S} \right) \mod 1, \quad (3) \]

where \( \eta \) is a Gaussian random variable distributed around 0, and \( f(\phi_i, T_S, T_V) \) gives the change of \( T_V \) due to the coupling of the S-beats to the V-beats \([3]\). Each of the 2 or 3 S-beats that may appear between consecutive (expressed or blocked) V-beats iteratively changes the position of the next V-beat depending on the timing of the S-beats as shown in Fig. 4a. These changes add up to \( f(\phi_i, T_S, T_V) \) \([3]\).

FIG. 2. Generation of NIB-triplets for \( \theta/T_S = 0.5 \) and two different values of \( T_V/T_S \). The boxes are the S-beats including their refractory times. An empty box is a blocked beat, and a dashed box an expressed beat. The expressed V-beats are symbolized by black bars, the blocked ones by empty bars. The S-beat after each expressed abnormal beat is blocked since \( \theta/T_S \geq 0.5 \). (a) Deterministic model without coupling. In the upper panel, the ratio of the periods \( T_V/T_S \approx 3 \). The phase of the V-beat with respect to the S-beats is therefore changing slowly, and the NIB is 2 for several periods until the V-beat falls into the refractory time of the S-beats and is blocked for several periods. For \( T_V/T_S \approx 3.3 \) the NIB-triplet 2,6,9 is generated. (b) Model with coupling and noise. Coupling shifts the V-beats into the refractory time for \( T_V/T_S \approx 3 \). For \( T_V/T_S \approx 3.3 \) the coupling has minimal effects. The addition of noise (arrows) changes the NIB-sequences by moving some V-beats into or out of the refractory time. For \( T_V/T_S \approx 3 \), this combines two consecutive appearances of NIB=2 into NIB=5 (8,11, . . . ). For \( T_V/T_S = 3.3 \), combinations of NIB=2 with one of the other two values, 6 or 9, generates NIB=9 or 12.

We propose that the pattern of V-beats in the data may be understood by assuming that the timings of the V-beats are not strictly periodic as in Eq. (1), but that they are described by a stochastic difference equation \([3]\):

\[ \phi_{i+1} = \left( \phi_i + \frac{T_V}{T_S} + \frac{f(\phi_i, T_S, T_V)}{T_S} + \frac{\eta}{T_S} \right) \mod 1, \quad (3) \]
Further, the model reproduces the asymmetrical form of the count for NIB=2 is 2465 in (a), 677 in (b), and 686 in (c). (a) Simulation of the deterministic model with constant white noise with a standard deviation of the standard deviation of the noise. The histogram of the NIB-values is computed from all sequences of the record that have the same mean. The histogram of the NIB-values are included in the simulation. The model now reproduces this behavior. (b) The coupling between the two oscillators. The change ΔT\text{V} of the period of the V-oscillator as a function of the ratio of the time t\text{VS} between the last V-beat and an S-beat, and T\text{V}. The coupling shortens the intrinsic T\text{V}0 to the apparent T\text{V}.

In order to reproduce Fig. 4a we have chosen a coupling that leads, for T\text{V}/T\text{S} ≈ 3, to a fixed point in Eq. (3), such that the V-beats always fall in the refractory period of the S-beat and thus are always blocked. However, the noise term leads to a dispersion of the phases of the V-oscillator such that some of the V-beats are expressed. Thus, both the coupling and the stochastic term interact to generate the dynamics. The effects of the coupling and the noise for T\text{V}/T\text{S} ≠ 3 are represented schematically in Fig. 3b. Fig. 3b shows how the distributions of the NIB-values change when both coupling and noise are included in the simulation. The model now reproduces quantitatively the data. For T\text{S} ≈ 0.55 s (T\text{V}/T\text{S} ≈ 3) the number of the V-beats is reduced by the coupling, and the NIB-sequence 2, 5, 8, . . . is generated by the noise. As a consequence of the random noise moving the V-beats randomly in and out of the refractory time, the blocking mechanism gives rise to a discrete Poisson process leading to an approximately exponential fall-off of the peak heights of the occurrences of the NIB values 2, 5, 8, . . . . Finally, the model gives an accurate estimate of the fraction of V-beats as a function of T\text{S} shown in Fig. 3b.

In order to estimate the magnitude of the noise, we calculate the cross-correlation between the numbers of occurrences of each NIB value in the model and the clinical data. Fig. 3c shows the correlation as a function of the standard deviation σ of the noise. The correlation function has a maximum at σ ≈ 0.07 s. This value of σ also best reproduces the broadness of the peaks in the distribution of the interventricular time intervals (Fig. 3d). Further, the model reproduces the asymmetrical form of

FIG. 3. Histograms of the number of intervening beats (NIB) on a logarithmic scale for T\text{S} = 0.51 s, 0.55 s, and 0.61 s, from top to bottom. For T\text{V} = 1.67 s, the corresponding ratios of the periods are T\text{V}/T\text{S} = 3.27, 3.03, and 2.73. In the middle panel the count for NIB=2 is 2465 in (a), 677 in (b), and 686 in (c). (a) Simulation of the deterministic model with constant T\text{S}, T\text{V} = 1.67 s. The average S-beat interval T\text{S} varies from 0.47 s to 0.64 s based on the dataset we study. For each histogram, the number of S-beats corresponds to the number of S-beats in the data with the same average T\text{S}. (b) NIB-histogram for the data. The value for T\text{S} at each V-beat is the average S-beat interval in a window of 20 beats centered at the V-beat. All V-beats in this window are replaced by the corresponding blocked S-beats which are placed in the middle of the two neighboring S-beats. The histogram of the NIB-values is computed from all sequences of the record that have the same mean T\text{S}. For T\text{S} = 0.55 s (T\text{V}/T\text{S}=3.03), we find NIB-values 2, 5, 8, 11, . . . , 3n − 1 that do not appear in the deterministic model. (c) Simulation with coupling (Fig. 3b) and noise. Instead of a constant T\text{S}, we use the S-beat intervals of the data, and we add to T\text{V} Gaussian white noise with a standard deviation σ = 0.07 s. Note that the intrinsic period T\text{V}0 = 1.76 s is larger than the apparent period T\text{V} ≈ 1.67 s because of the coupling.

FIG. 4. (a) The fraction n\text{V}/N plotted against the ratio T\text{V}/T\text{S}. The theoretical curve given by Eq. (3), with θ as in Fig. 4a, is reproduced by the model without coupling, and remains unchanged when noise is added. The data deviate from this curve at the ratio T\text{V}/T\text{S} = 3, where we find less than half of the predicted V-beats. The model with coupling and noise reproduces this behavior. (b) The coupling between the two oscillators. The change ΔT\text{V} of the period of the V-oscillator as a function of the ratio of the time t\text{VS} between the last V-beat and an S-beat, and T\text{V}. The coupling shortens the intrinsic T\text{V}0 to the apparent T\text{V}.
the peaks in the histogram (inset of Fig. 1). In the simulation, the coupling splits the peaks into two subpeaks giving them an asymmetrical appearance (not shown).

In this work we analyzed the patterns of abnormal heartbeats in a 12 hour record from a single patient and proposed that the dynamics results from a combination of deterministic and stochastic mechanisms. Quantitative comparison between predictions of the model and the clinical data shows best agreement for an optimal level of noise in the model.

Our approach is in contrast to standard approaches [1] in which crude measures, such as the average numbers of abnormal heart beats per unit time, are used for clinical assessment. We believe that distinctive dynamics are associated with different mechanisms, and hence different therapeutic strategies. Thus, the detailed program assessment. We believe that distinctive dynamics are essential to better classify cardiac arrhythmias based on therapeutic strategies. Thus, the detailed program assessment. We believe that distinctive dynamics are essential to better classify cardiac arrhythmias based on the underlying mechanisms and resulting dynamics.

We thank R. Goldsmith for providing the data, and the German Academic Exchange Service (DAAD), NIH/NCRR (P41RR13622), NASA, and the Mathers Charitable Foundation for support.

![Cross-Correlation](image)

FIG. 5. The cross-correlation between data and model as a function of noise. We cross-correlate the histograms in Fig. 3b,c for all values of $T_3$ from 0.48-0.62 s in steps of 0.01s [18].

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[12] For the purely deterministic model, the NIB-sequences can be shown to follow three “rules” [2]: (i) there are at most three different values for the NIB, (ii) the sum of the two smaller ones is the largest NIB-value minus one, implying that (iii) one of the NIB-values must be odd. The $\theta/T_3$, $T_{V}/T_{S}$-parameter space can be completely partitioned into regions of these triplets [4]. The problem is related to the gaps and steps problem in number theory: G.A. Hedlund, Am. J. Math. 66, 605 (1944); N.B. Slater, Proc. Camb. Phil. Soc. 63, 1115 (1967).
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$$T_{Vn} = T_{Vn-1} + \Delta T_V \left( \frac{(n - \phi_i)T_3}{T_{Vn-1}} \right),$$

where $\Delta T_V(x)$ is given by Fig. 4, and $T_{V0} = 1.76$ s, the intrinsic period of the V-beats. In Eq. 4, we then have

$$f(\phi, T_3, T_V) = T_{Vn_{max}} - T_V.$$ The number $n_{max}$ of S-beats between consecutive V-beats, expressed or blocked, is the smallest integer number such that $(n_{max} - \phi)T_3 \leq T_{Vn_{max}}$. In our particular case, $n_{max}$ may be 3 or 4.
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$$\langle y_{ij} - \bar{y} \rangle \left( \sum_{i,j} (x_{ij} - \bar{x})^2 \right)^{-1/2},$$

where $x_{ij}$ and $y_{ij}$ are the components of the matrices in Fig. 3b and c.