ON A MECHANISM OF CARDIAC ELECTRICAL STABILITY

The Fractal Hypothesis

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ABSTRACT Electrical activation of the ventricles via the His-Purkinje system is represented on the body surface by a waveform with a broad range of frequency components. We speculate that this process is mediated by current flow through a fractal-like conduction network and therefore that the broadband spectrum of the depolarization waveform should be scaled as a power-law distribution. The prediction is confirmed by Fourier analysis of electrocardiographic data from healthy men. This observation suggests a new dynamical link between nonlinear (fractal) structure and nonlinear function in a stable physiologic system.

INTRODUCTION

Normally, myocardial cells in the ventricles are depolarized by the spread of current through a branching network of specialized conduction fibers, the His-Purkinje system (Fig. 1) (1). Depolarization of the muscle cells of the left and right ventricles is represented in the electrocardiogram by a waveform referred to as the QRS complex. Fourier analysis of the normal QRS complex reveals a broadband spectrum with a long tail corresponding to the presence of low-amplitude relatively high-frequency components (>100 Hz) in the waveform (Fig. 2) (2–4). This type of frequency scaling is reminiscent of $1/f$-like distributions in which the power spectral density is inversely related to frequency. The term $1/f$-like applies to spectra of the form $1/f^{\beta}$ where β is a positive exponent (5). When β is close to one, the distribution is $1/f$.

The general form of the frequency distribution of the normal QRS complex appears to be independent of both the spatial position of the recording electrodes and the precise shape of the waveform (2–4). Furthermore, this broadband spectrum contrasts with the frequency profile associated with certain life-threatening cardiac pathologies (6–7), which are found to suppress the high-frequency components of the spectrum.

Therefore a central problem relates to understanding the mechanisms responsible for the genesis of this physiological waveform and its attendant power-law spectrum. We hypothesize that the fractal-like nature of the His-Purkinje network serves as the structural substrate for the broadband type of spectrum associated with normal ventricular depolarization. The term fractal defines a ubiquitous class of geometric shapes, traditionally thought to be merely irregular, whose subunits replicate the structure of the larger unit in accord with the principle of self-similarity (5). While the anatomic dimensions of the multiple generations of the ventricular conduction system have not been quantitatively analyzed, the general appearance of the system is that of a highly complex, fractal network that demonstrates self-similar structure over progressively smaller scales. The repetitive bifurcations of the human conduction system are schematized in Fig. 1. As shown, the main bundle of His divides into left and right bundle branches, which, in turn, subdivide into smaller branches. These bifurcations then repeat over multiple generations down to the microscopic level of the most distal Purkinje fibers (1). Other examples of physiologic fractals with a self-similar branching pattern include the bronchial network and the vascular tree and are catalogued by Mandelbrot (5), who introduced the term fractal into the scientific lexicon.

HYPOTHESIS

The fractal His-Purkinje network is a labyrinth of conduction paths of unequal length. A single pulse incident on a branching site will activate a new pulse along each conduction branch, thus yielding two pulses for one. Each of those pulses will propagate along its respective path until a new

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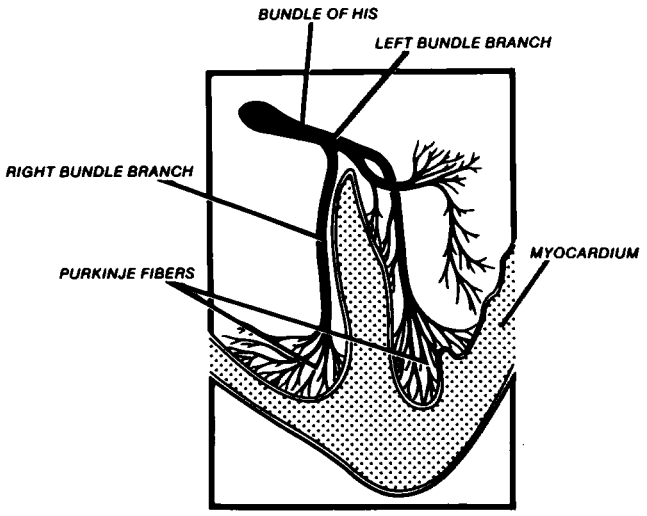

FIGURE 1 The ventricular condition system appears to be a fractal-like structure demonstrating repetitive branching on progressively smaller scale.

bifurcation site is encountered; then the process repeats. In this way a single pulse entering the His-Purkinje network with N branches will generate N pulses, all of approximately the same amplitude. The net voltage, $V(t)$ measured at the myocardium will consist of a superposition of these individual pulses, $v(t - t_j)$, each with a slightly different arrival time t_j, i.e.,

$$V(t) = \sum_{j=1}^{N} v(t - t_j). \tag{1}$$

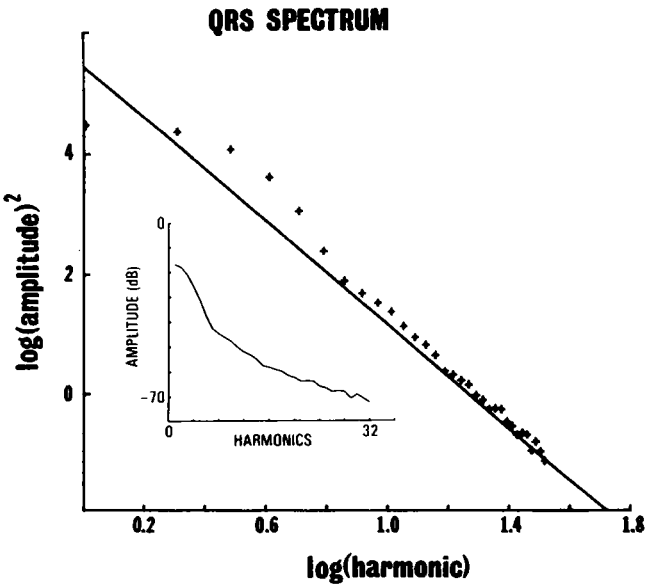

FIGURE 2 The power spectrum (*inset*) of normal ventricular depolarization (QRS) waveform (mean data of 21 healthy men) shows a broadband distribution with a long, high-frequency tail. Power-law scaling is demonstrated by replotting the same data on a log-log graph. The straight line is the linear regression to a power-law power spectrum. Fundamental frequency = 7.81 Hz. $y = -4.3x + 5.41$; $r = -0.99$; $P < 0.001$

We assume that the conduction of the individual pulse after emerging from the His-Purkinje network does not modify the statistics of $v(t - t_j)$.

The conduction velocities (s_j) along each branch $j = 1, 2, \ldots N$ may each differ one from the other owing to differences in the diameter of each branch and other factors (8). Such conduction velocity variability can be taken into account by rescaling the branch dimensions from their physical length, l_j, to their effective length, $l'_j = (l_j s_j)/(s_{max})$, where s_{max} is the maximal attainable velocity in any of the branches. The arrival time of each pulse at the myocardium, therefore, will be determined solely by the rescaled length of the conduction path traveled by that pulse.

We assume that the autocorrelation function of these activation pulses (action potentials) in a system comprised of a single branching site is a monotonically decreasing function that can be characterized by a one-parameter fit using an exponential function. This parameter is the time scale over which these pulses are correlated, and is determined by the increased distance (d) traveled by one of the pulses. Thus, the rate at which the pulses decorrelate is $\gamma_c = (S_{max})/(d)$, where d is the difference between the two effective path lengths. For a system with a large number of pulses the autocorrelation function, C_τ, is given by the average of the single-pulse autocorrelation function over the distribution of decorrelation rates, $P(\gamma_c)$, referenced to the shortest effective path length

$$C_\tau = \int_0^{\gamma_{max}} e^{-|\tau|\gamma_c} P(\gamma_c)\, d\gamma_c, \tag{2}$$

and γ_{max} is determined by the shortest separation distance between paths.

We do not specify the detailed form of the distribution of decorrelation rates, but instead construct an argument that is intended to capture the underlying effect of the fractal conduction system without such detailed knowledge. Consider a distribution density $P(\gamma_c)$ having finite central moments; in particular a finite mean decorrelation rate $\bar{\gamma}$. We now assume that the scaling nature of the conduction system gives rise to a new average decorrelation rate, $\lambda\bar{\gamma}$, which is longer than the original, i.e., λ is a parameter greater than unity. Thus the distribution is shifted as follows

$$P\left(\frac{\gamma_c}{\bar{\gamma}}\right) d\gamma_c \rightarrow P\left(\frac{\gamma_c}{\lambda\bar{\gamma}}\right) \frac{d\gamma_c}{\lambda\bar{\gamma}}, \tag{3}$$

and we assume that this lengthened average rate occurs with relative frequency (probability) p. Now if the conduction system is fractal this scaling must occur again so that the scaled mean decorrelation rate is again scaled and the new mean is $\lambda^2\bar{\gamma}$ with total probability p^2. This process is repeated continually for a fractal structure resulting in the series

$$\mathbf{P}(z) = (1 - p)\left[P(z) + \frac{p}{\lambda} P(z/\lambda) + \frac{p^2}{\lambda^2} P(z/\lambda^2) + \ldots\right] \tag{4}$$

for the new distribution of decorrelation rates $\mathbf{P}(z)$ and $z = \gamma_c/\bar{\gamma}$. In the present physiologic context each term in the series corresponds to a longer and longer mean decorrelation rate. This lengthening of the mean decorrelation rate is a consequence of superimposing finer and finer scales onto the spatial structure of the conduction system. The resulting finely detailed branching structure decorrelates the pulses over successively shorter time intervals, thereby increasing their mean decorrelation rate.

The series (Eq. 4) can be more compactly written as the functional equation

$$\mathbf{P}(z) = \frac{p}{\lambda}\mathbf{P}(z/\lambda) + (1 - p)\,P(z) \tag{5}$$

from which it is clear that $\mathbf{P}(z) \rightarrow P(z)$ as $p \rightarrow 0$. Montroll and Shlesinger (9,10) first derived an equation analogous to Eq. 5 in an economic context, but their basic ideas apply here as well. In fact, for $p \neq 0$, but still small, $p = 0.01$ say, throughout most of the range of z the behavior of the new distribution is given by that of the old one since the coefficient of $P(z)$ in Eq. 5 is 0.99. It is not until z becomes large, where since $\lim_{z\rightarrow\infty} P(z) = 0$, that the effect of the first term in Eq. 5 becomes important. Thus we assume that $P(z)$ decreases more rapidly with increasing z than does $\mathbf{P}(z)$.

In the asymptotic region where the contribution of $P(z)$ can be neglected we write Eq. 5 as

$$\mathbf{P}_{asy}(z) = \frac{p}{\lambda}\mathbf{P}_{asy}(z/\lambda). \tag{6}$$

The assumed solution to this functional equation is

$$\mathbf{P}_{asy}(z) = \frac{A}{z^{\mu}}, \tag{7}$$

which when substituted into Eq. 5 yields the constraint

$$\mu = 1 + \frac{\ln(1/p)}{\ln\lambda} \tag{8}$$

with A given by a constant. This equation establishes the relation between the power-law index μ and the scaling parameters p and λ. Therefore, we see that the distribution function makes a transition from $P(\gamma_c/\bar{\gamma})$ to a power-law $(1/\gamma_c^{\mu})$ in the region of large decorrelation rates. The resulting autocorrelation function of the measured signal is

$$C_\tau = \int_0^{\gamma_{max}} e^{-i\tau\gamma_c}\mathbf{P}(\gamma_c)\,d\gamma_c. \tag{9}$$

The power spectrum of the measured signal is given by the Fourier transform of Eq. 9

$$S(\omega) = \int_{-\infty}^{\infty} e^{-i\omega\tau}\,d\tau\,C_\tau \tag{10}$$

so that in terms of the distribution of decorrelation rates we have, by inserting Eq. 9 into Eq. 10 and integrating over time τ,

$$S(\omega) = 2\int_0^{\gamma_{max}} \frac{\gamma_c d\gamma_c \mathbf{P}(\gamma_c)}{\omega^2 + \gamma_c^2}. \tag{11}$$

Using the asymptotic form of $P(\gamma_c)$ given by Eq. 7 we can evaluate the integral in Eq. 11 to obtain the asymptotic spectrum

$$S_{asy}(\omega) = \frac{B_\mu}{\omega^{\mu}} \tag{12}$$

and B_μ is a constant dependent on γ_{max}. The exponent in the power spectrum $1/f^{\beta}$ is then

$$\beta = \mu = 1 + \frac{\ln(1/p)}{\ln\lambda}, \tag{13}$$

which can be arbitrarily large. Note that this result is independent of the original form of $P(\gamma_c)$ given only that it has a finite first moment, but the spectrum does depend strongly on the logarithmic ratio of the parameters p and λ, which characterize the fractal system. This argument suggests that the passage of a stimulus through a fractal conduction network to its multiple distal interfaces with the myocardium should result in a voltage-time pulse with a power spectral density that is a power-law.

METHODS AND RESULTS

The hypothesis was tested by analyzing electrocardiograms (bipolar lead $V_5 - V_2$) obtained with a microprocessor-based system (sample rate, 500 Hz) interfaced to a computer (4052A; Tektronix, Inc., Beaverton, OR). As previously described (4), the study group consisted of 21 healthy men (19–37 yr old). Two cardiac cycles per subject were acquired (without signal averaging) with the subjects at rest in the end expiratory phase of respiration. The QRS complex with the lower noise content, determined by visual inspection, was selected for spectral analysis. The QRS mode amplitudes for each waveform were derived by standard methods using a fast Fourier transform algorithm. Based on a sample window of 128 ms, the fundamental frequency was 7.81 Hz. The initial sample point in all cases was in the PR segment; the final sample point in the ST segment or the beginning of the T wave. The broadband spectrum of the normal QRS (7.81 to 249.92 Hz), obtained by averaging the square of the mode amplitudes from the 21 subjects, was noted to correlate highly ($r = -0.99$) with the predicted power-law form (Fig. 2). Power-law scaling was tested by performing a linear regression on the plot of the log $\overline{|\text{amplitude}|^2}$ vs. the log(harmonic), where the bar denotes an average over the 21 subjects.

DISCUSSION

The observation of a power-law spectrum for the ventricular depolarization complex complements previous findings suggesting the importance of broadband, $1/f$-like (11) spectra in physiologic systems. In particular, a $1/f$ spectrum characterizes action potential transmission along a single nerve axon in response to a Gaussian impulse train (12). Furthermore, $1/f$ scaling at a higher level of neural organization has been reported based on spectral analysis of interbeat interval variability in healthy subjects (13). The interbeat interval is the period between successive QRS complexes. Thus, power-law scaling, evidenced by

$1/f$-like distributions, appears to be a salient feature of physiological dynamics (6) from the level of the single neuron (12, 14) to the His-Purkinje-myocardial cell network (reflected by the QRS spectrum) as we have shown here, and to the complex level of neurocardiac integration (reflected by heart-rate variability).

The present investigation therefore supports a connection between nonlinear structure, represented by the fractal conduction system, and physiologic nonlinear function, manifest in the power-law spectrum of the ventricular depolarization waveform. Power scaling, although not commented on, is also apparent in the data of Golden et al. (3) obtained with a different lead configuration. This type of spectrum, associated with healthy electrophysiologic dynamics, contrasts with the narrow-band spectra of ventricular tachycardia and fibrillation (6, 7, 15, 16), life-threatening arrhythmias in which the normal hierarchical (fractal) sequence of ventricular depolarization no longer occurs.

The relatively narrow-band spectra seen with certain major cardiac pathologies may reflect disruption of the normal fractal depolarization mechanism. Furthermore, loss of broadband spectral stability may be a characteristic feature of other disease processes whose narrow-band spectra are reflected by strongly periodic behavior (17, 18). In our scaling argument we observe that if the scaling parameter λ is reduced by a factor ϵ, i.e., $\lambda \rightarrow \lambda/\epsilon$ and $\epsilon > 1$, then Eq. 5 becomes

$$\mathbf{P}(z) = \frac{\epsilon p}{\lambda} P(\epsilon z/\lambda) + (1 - p)\, P(z). \tag{14}$$

The scaling solution to Eq. 14 yields the exponent for the power spectral density

$$\mu_{new} = 1 + \frac{\ln (1/p)}{\ln \lambda - \ln \epsilon} \tag{15}$$

so that $\mu_{new} \geq \mu_{old}$, given by Eq. 13. Thus, the high-frequency contributions to the spectrum are inhibited resulting in a steeper spectral slope. The suppression of the high-frequency energy content of the waveform is a consequence of the disturbance of the fractal depolarization mechanism and subsequent loss of the shorter correlation times in the underlying conduction system. Based on this analysis, we would also predict a relative decrease in higher frequency components in various types of bundle branch blocks in which the fractal depolarization sequence is also disrupted, as well as in some patients with large, chronic myocardial infarction (see Fig. 1, reference 19).

We finally note that the power-law index β in Eq. 13 is related to the average fractal dimension associated with the variability in scale of the conduction system. The fractal dimension D is given by $\ln (1/p)/\ln \lambda$. It is not our intention here to determine the statistical properties of the fractal dimension, but rather to suggest its utility in characterizing certain structural properties of normal physiology.

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