Fractal Mechanisms
in the Electrophysiology of the Heart

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The mathematical concept of fractals provides insights into complex anatomic branching structures that lack a characteristic (single) length scale, and certain complex physiologic processes, such as heart rate regulation, that lack a single time scale. Heart rate control is perturbed by alterations in neuro-autonomic function in a number of important clinical syndromes, including sudden cardiac death, congestive failure, cocaine intoxication, fetal distress, space sickness and physiologic aging. These conditions are associated with a loss of the normal fractal complexity of interbeat interval dynamics. Such changes, which may not be detectable using conventional statistics, can be quantified using new methods derived from "chaos theory."

What Is a Fractal?
The term fractal, coined by the mathematician B. Mandelbrot [1], is currently used in three related contexts: geometric, temporal (dynamical), and statistical. In the most general terms, fractals are defined by a property called self-similarity [1-3]. Fractal objects are composed of subunits that resemble the larger scale shape. These subunits in turn are composed of yet smaller units that also look similar to the larger ones, and so on. Fractals, therefore, do not have a single length scale, but rather have structure on multiple scales of length (Fig. 1).

The term fractal also relates to the fact that these irregular structures may have a noninteger (fractional) dimension. For example, the branching tracheobronchial tree, a fractal-like structure, has a dimension between 2 and 3, since it converts a volume of gas in the trachea ($D = 3$) into something approaching a surface area ($D = 2$) in the alveoli.

The notion of self-similarity has also been extended into temporal and statistical domains. A temporal fractal
1. The self-similar branchings of the His-Purkinje system constitute a fractal-like network.

is a process that does not have a characteristic scale of time, analogous to a fractal structure that lacks a characteristic scale of length. Instead, fractal processes have self-similar fluctuations on multiple scales of time. This property is reflected by a type of broadband frequency spectrum, i.e., one having multiple frequencies. The concept of temporal fractals is closely related to that of “chaos.” Finally, the fractal concept has been applied in a statistical context. One example is the irregular structure of the mammalian lung, where there is a self-similar distribution of scale sizes across multiple generations of branchings [4, 5].

The Heart’s Fractal-like Anatomy
A number of cardiac structures have a self-similar or fractal-like appearance [6-8]. Examples of this nonlinear architecture include the coronary arterial and venous trees, the chordae tendinae, certain muscle bundles, and the His-Purkinje network (Fig.1). The latter provides an efficient way of distributing the depolarization stimulus to the ventricles. Recently, there has been interest in modeling the electrogensis of the QRS complex using a fractal-like conduction system, as well as for studying alterations in the frequency content of the normal QRS due to changes in His-Purkinje geometry or in myocardial conduction [6, 9, 10]. Abbott and colleagues [8, 9] have shown that slow conduction in myocardial cells activated by such a fractal network can lead to “late potentials” or to selective attenuation of higher frequency content of the QRS simulating changes seen in ischemic coronary syndromes.

Controversy surrounding the fractal hypothesis of QRS electrogensis centers on two questions [11-12]:
1. Is the His-Purkinje system really a fractal?
2. Does its macroscopic structure actually relate in any way to the frequency content of the QRS complex?

Idealized (computer-generated) fractals have infinite scales of length and literally have no smallest scale. Physiologic fractals are obviously bounded at both the upper and lower ends. However, the definition of a fractal does not require infinite scales of length [3]. Furthermore, it is also apparent that physiological fractals are not identical on different scales of magnification. However, structures such as the tracheo-bronchial tree and the His-Purkinje system do maintain a similarity of dichotomous branching for which the term “fractal-like” is mathematically appropriate [1-8]. Interconnections between branches of the His-Purkinje system, which makes the system more than a simple branching structure, also do not undermine the fractal-like nature of the geometry.

Spectral analysis of normal QRS complexes reveals a broadband frequency

2. Activation of a three-dimensional network of myocardial “cells” by a self-similar conduction system (see Fig. 1) in a computer model generates realistic QRS complexes (left panel), with a broadband frequency spectrum (middle panel) comparable to that obtained from actual ECG data in healthy men (right panel). Computer model QRS and spectrum are from [9] and [10]; clinical data from [6].
spectrum (Fig. 2). While most of the frequency content of the QRS is comprised of frequencies below 20-30 Hz, there is a small but important contribution of higher frequencies, which go up to several hundreds Hz. Furthermore, spectral analysis has indicated an inverse power-law distribution to the frequency components of the normal QRS. That is, a graph of log QRS frequency versus log power makes a good fit to a straight-line plot with a negative slope [6, 7].

A theoretical argument has been made that this broadband spectrum with its inverse power-law distribution is consistent with depolarization of the myocardium via an irregular, self-similar branching network [5]. Therefore, according to this fractal theory, the frequency content of the QRS complex is importantly related to the macroscopic structure of the His-Purkinje system, and not exclusively to the microscopic nature of the Purkinje-myocardial cell interactions and local wavefront propagation. Support for this counterintuitive notion has come from computer modeling studies in which a self-similar branching network has been used to depolarize a three-dimensional network of cells [9, 10]. Such experiments reveal that with nine or ten generations of conduction system branchings, one can generate QRS complexes that are essentially indistinguishable from those seen clinically. Furthermore, the simulated QRS complexes have a broadband frequency spectrum comparable to that observed physiologically (Fig. 2). Such models also confirm that changes in the geometry of the branching conduction system may alter the frequency content of the QRS complexes, independent of any changes in myocardial conduction. This macroscopic fractal model of QRS electrogenesis, based on myocardial activation via an irregular conduction network, is not inconsistent with microscopic observations on the nature of the Purkinje-subendocardial muscle cell interface [13].

The Healthy Heartbeat Is a Temporal Fractal

As noted, the fractal concept can be extended from geometry to dynamics. In this latter context, one can describe certain complex processes that do not have a characteristic scale of time. The regulation of the heart rate may be one such fractal process [6-8]. This notion has proven controversial, in part because it runs counter to the conventional dictum that the normal heartbeat is highly regular ("regular sinus rhythm"). Palpation of the pulse and observation of the electrocardiogram in a healthy individual gives the appearance of metronomic regularity. However, actual
measurements of interbeat interval fluctuations reveal quite a different impression (Fig. 3).

Normal subjects, even those at rest, show a high degree of heart rate variability, which is not subjectively perceptible. Furthermore, these fluctuations are not simply those associated with respiration. In fact, spectral analysis of heart rate data from healthy subjects shows a broadband spectrum with a so-called $1/f$-like distribution (Fig. 4). Note that the term $1/f$-like is synonymous with the inverse power-law type of scaling defined above.

Another controversial aspect of the concept of the fractal heartbeat relates to its mechanism. The interbeat interval fluctuations of the healthy heart may be due, in part, to intrinsic variability of autonomic control ("chaos") [8]. This hypothesis apparently conflicts with the theory of homeostasis enunciated by Walter B. Cannon [14] and others, which states that apparently erratic fluctuations of variables such as heart rate are due primarily to external influences, and that the normal condition of the cardiovascular system, and of other physiologic systems, is that of a steady state. A number of lines of evidence support the countervailing theory that deterministic chaos, not homeostasis, is the "wisdom of the body" [15]. The broadband spectrum of the healthy heartbeat is consistent with, but not diagnostic of, deterministic chaos. Additional tests for chaos include the measurement of a finite correlation dimension and of a positive Lyapunov exponent. Measurement of these nonlinear metrics from biologic data sets is fraught with potential problems, which have been discussed in detail elsewhere [16]. However, preliminary attempts to perform such measurements from heart rate data have been consistent with the hypothesis that these fluctuations do in fact represent deterministic chaos [17-19]. Finally, phase space portraits (delay maps) of interbeat interval time series are also consistent with those of so-called strange (chaotic) attractors (Fig. 5).

The mechanism for such physiologic chaos of the heartbeat, if it exists, is not certain. However, it is clear that heart rate fluctuations are primarily due to autonomic nervous system control and, therefore, any chaos of the heartbeat must reflect chaos in nervous system dynamics. There is evidence for this kind of deterministic chaos even in the nervous systems of more simple organisms [19].

### Chaos and Disease

A corollary of the classical notion of homeostasis relating health to constancy is that disease and other perturbations are likely to cause a loss of regularity. The chaos hypothesis advanced above predicts just the opposite, namely, a variety of disease states that alter autonomic function may lead to a loss of physiologic complexity and, therefore, to greater, not less regularity [8]. Support for this notion comes from the comparison of heart rate time series from patients with a variety of different clinical syndromes, including those at high risk of sudden death and those with heart failure, whose sinus rhythm dynamics are typically less complex than those seen normally (Fig. 6) [20]. Similar changes are found in experimental animals with severe cocaine toxicity [21]. The term "complexity" is used here to include the fractal type of variability described above. It should be emphasized that quantifying losses of this type of nonlinear complexity cannot be accomplished by use of traditional statistics such as variance. An illustration of this principle comes from comparing two signals, one a large amplitude sine wave and the other a lower amplitude, highly erratic signal. Clearly, the sine wave is less complex despite its greater variance. This observation is of more than theoretical import, since there has been a flurry of interest in recent years in the analysis of heart rate variability using conventional statistics.

Aging is also associated with a loss of physiologic complexity [22, 23]. We have recently observed a reduction in both the approximate dimension and approximate

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5. Heart rate time series from a healthy subject has complex variability. Two-dimensional phase space plot reveals a complex trajectory suggestive of a so-called strange attractor. Delay map plots heart rate in beats per minute (bpm) at a given time against the heart rate after a fixed delay (in this case, 4 seconds), and then tracks the evolution of this heart rate vector after an arbitrary time (also 4 seconds in this case). Data in this example and Fig. 6 were filtered with singular value decomposition.
6. Normal sinus rhythm in healthy subjects (left) shows complex variability with a broad spectrum and a phase space plot consistent with a strange (chaotic) attractor. Patients with heart disease may show altered dynamics, sometimes with oscillatory sinus rhythm heart rate dynamics (middle) or an overall loss of sinus variability (right). With the oscillatory pattern, the spectrum shows a sharp peak, and the phase space plot shows a more periodic attractor, with trajectories rotating about a central hub. With the flat pattern, the spectrum shows an overall loss of power, and the phase space plot is more reminiscent of a fixed-point attractor. (Adapted from [8].)
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Dr. Goldberger and his colleagues were among the first to apply concepts from nonlinear dynamics, chaos theory and fractals to sudden cardiac death and bedside cardiology. Dr. Goldberger is the author of more than 90 scientific papers and two textbooks on electrocardiography. In 1988, he was the recipient of the S. Robert Stone Award for excellence in teaching at Harvard Medical School and Beth Israel Hospital. Address for correspondence: Beth Israel Hospital, 330 Brookline Ave, Boston, MA 02215.

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