

SCIENCE IN PICTURES

# Chaos and Fractals in Human Physiology

*Chaos in bodily functioning signals health. Periodic behavior can foreshadow disease*

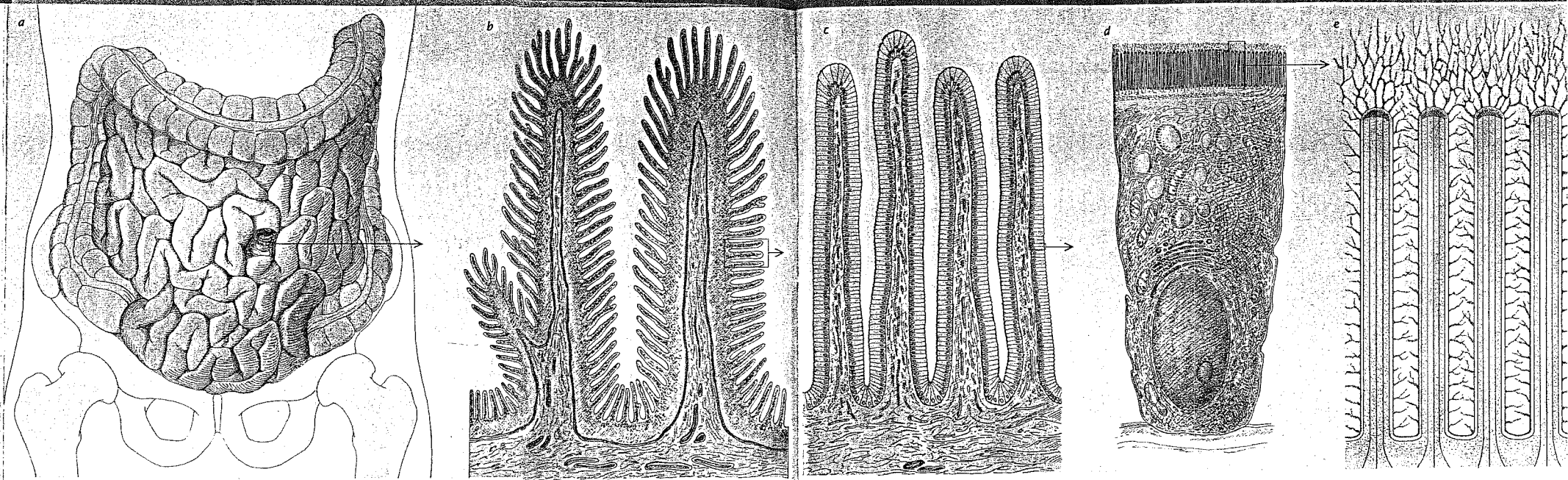
by Ary L. Goldberger, David R. Rigney and Bruce J. West

A medical student monitoring the rhythms of a heart notices that the tempo sometimes changes dramatically from minute to minute and hour to hour. A clinician maneuvering a bronchoscope into a lung observes that the trachea branches into smaller and smaller airways. The student senses that the interval between heartbeats varies chaotically. Perhaps the clinician recognizes that the network of airways resembles a fractal. Physiologists and physicians have only recently begun to quantify such possibilities of chaotic dynamics and fractal architectures. Their investigations are challenging long-held principles of medicine and are revealing possible forewarnings of disease.

The conventional wisdom in medicine holds that

disease and aging arise from stress on an otherwise orderly and machinelike system—that the stress decreases order by provoking erratic responses or by upsetting the body's normal periodic rhythms. In

*AIRWAYS OF THE LUNG (left) shaped by evolution and embryonic development resemble fractals generated by computer (below). The bronchi and bronchioles of the lung (here a rubber cast) form a "tree" that has multiple generations of branchings. The small-scale branching of the airways looks like branching at larger scales. When physiologists quantified observations of the branching pattern, they discovered that the lung tree has fractal geometry.*



the past five years or so we and our colleagues have discovered that the heart and other physiological systems may behave most erratically when they are young and healthy. Counterintuitively, increasingly regular behavior sometimes accompanies aging and disease.

Irregularity and unpredictability, then, are important features of health. On the other hand, decreased variability and accentuated periodicities are associated with disease. Motivated by these ideas, we and other physiologists have looked for periodic behavior that might indicate developing sickness (especially diseases of the heart). In addition, we have begun to analyze the flexibility and strength of irregular fractal structures and the adaptability and robustness of systems that exhibit apparently chaotic behavior.

Chaos and fractals are subjects associated with the discipline of nonlinear dynamics: the study of systems that respond disproportionately to stimuli. The theory of nonlinear dynamics provides insights into the phenomenon of epidemics, the kinetics of certain chemical reactions and the

changes in the weather. Under some circumstances deterministic nonlinear systems—those that have only a few simple elements—behave erratically, a state called chaos. The deterministic chaos of nonlinear dynamics is not the same as chaos in the dictionary sense of complete disorganization or randomness. Nonlinear chaos refers to a constrained kind of randomness, which, remarkably, may be associated with fractal geometry.

Fractal structures are often the remnants of chaotic nonlinear dynamics. Wherever a chaotic process has shaped an environment (the seashore, the atmosphere, a geologic fault), fractals are likely to be left behind (coastlines, clouds, rock formations). Yet at first the mathematics of fractals developed independently of nonlinear dynamics, and even today the connections between the disciplines are not fully established.

A fractal, as first conceived by Benoit B. Mandelbrot of the IBM T. J. Watson Research Center, consists of geometric fragments of varying size and orientation but similar shape. Certain neurons, for instance, have a fractal-like structure. If one examines such neurons through a

low-power microscope lens, one can discern asymmetric branches, called dendrites, connected to the cell bodies. At slightly higher magnification, one observes smaller branches on the larger ones. At even higher magnification, one sees another level of detail: branches on branches on branches. Although at some level the branching of a neuron stops, idealized fractals have infinite detail.

Perhaps it is even more remarkable that the details of a fractal at a certain scale are similar (though not necessarily identical) to those of the structure seen at larger or smaller scales. If one saw two photographs of the dendrites at two different magnifications (without any other reference), one would have difficulty in deciding which photograph corresponded to which magnification. All fractals have this internal, look-alike property called self-similarity.

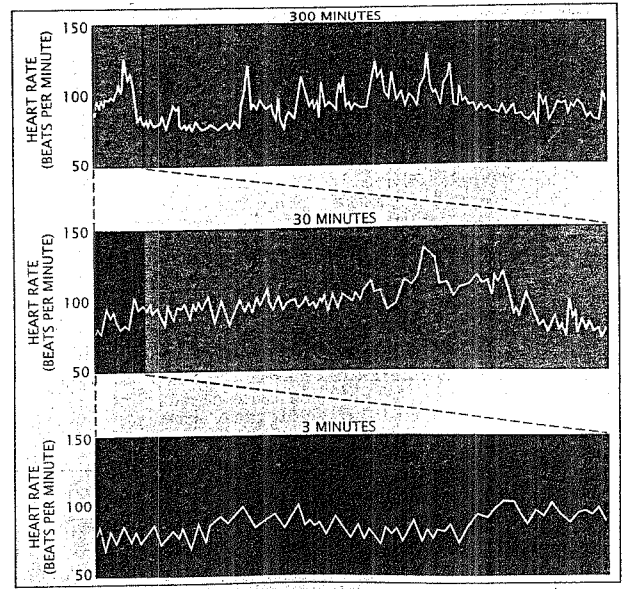
Because a fractal is composed of similar structures of ever finer detail, its length is not well defined. If one attempts to measure the length of a fractal with a given ruler, some details will always be finer than the ruler can possibly measure. As the resolution of the measuring instrument increases, therefore, the length of a fractal grows.

Because length is not a meaningful concept for fractals, mathematicians calculate the "dimension" of a fractal to quantify how it fills space. The familiar concept of dimension applies to the objects of classical, or Euclidean, geometry.

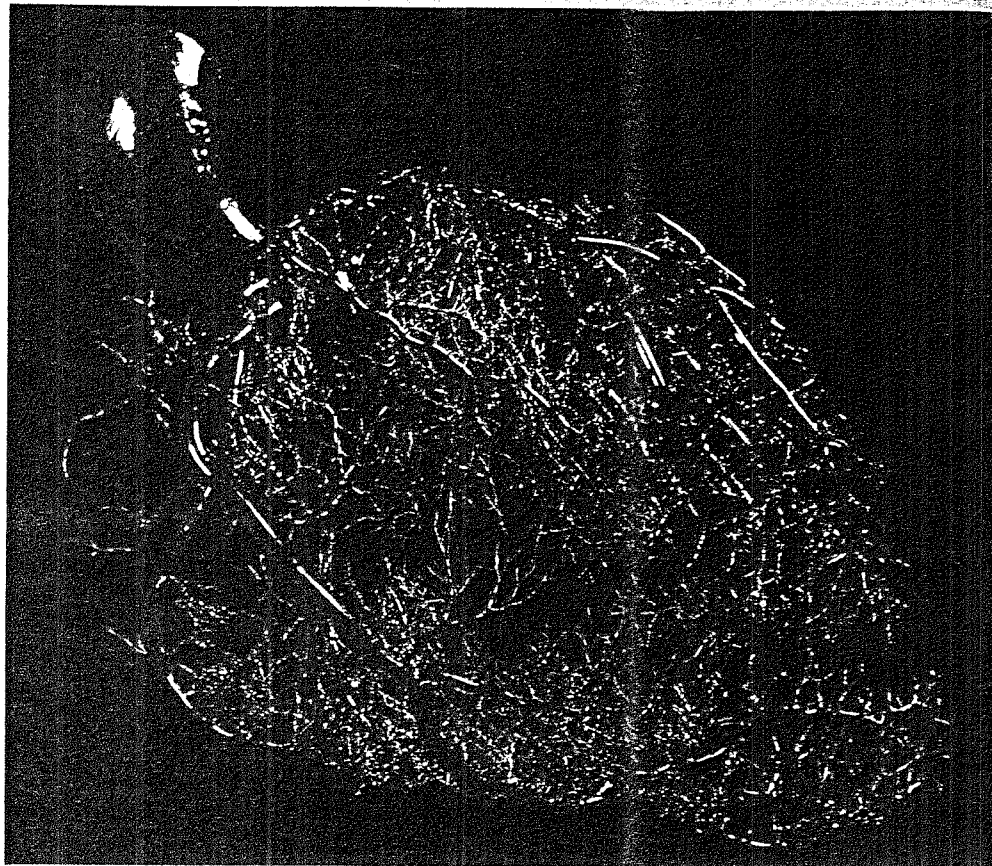
Lines have a dimension of one, circles have two dimensions and spheres have three. But fractals have noninteger (fractional) dimensions. Whereas a smooth Euclidean line precisely fills a one-dimensional space, a fractal line spills over into a two-dimensional space. A fractal line—a coastline, for example—therefore has a dimension between one and two. Likewise a fractal surface—a mountain, for instance—has a dimension between two and three. The greater the dimension of a fractal, the greater the chance that a given region of space contains a piece of that fractal.

In the human body fractal-like structures abound in networks of blood vessels, nerves and ducts. The most carefully studied fractal in the body is the system of tubes that transport gas to and from the lungs. In 1962 Ewald R. Weibel and Domingo M. Gomez and later Otto G. Raabe and his co-workers made detailed measurements of the lengths and diameters of tubes in this irregular network of airways. Recently two of us (West and Goldberger) in collaboration with Valmik Bhargava and Thomas R. Nelson of the University of California at San Diego reanalyzed these measurements from the lung casts of humans and several other mammalian species. We found, despite subtle interspecies differences, the type of scaling predicted for the dimensions of a fractal.

SELF-SIMILARITY of a system implies that features of a structure or a process look alike at different scales of length or time. When the structures of the small intestine are observed at several different magnifications (drawings above), the resemblance between the larger and smaller details suggests self-similarity. When the heart rate of a healthy individual is recorded for three, 30 and 300 minutes (curves below), the quick, erratic fluctuations seem to vary in a similar manner to the slower fluctuations.



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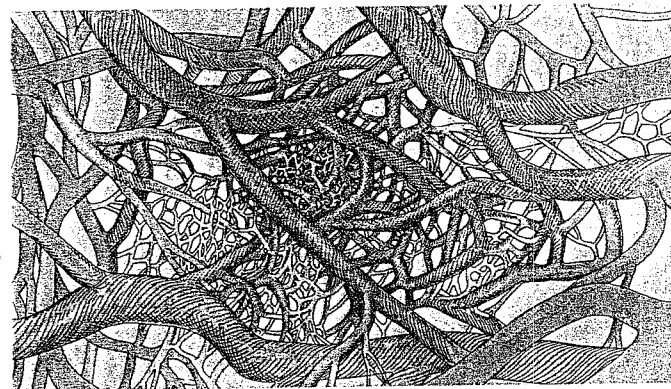
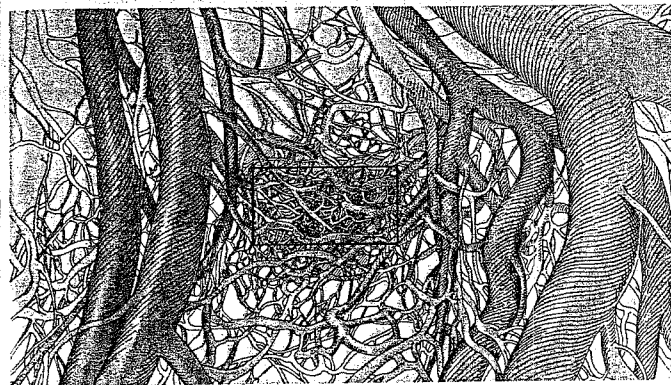
Many other organ systems also appear to be fractal, although their dimensions have not yet been quantified. Fractal-like structures play a vital role in the healthy mechanical and electrical dynamics of the heart. First, for example, a fractal-like network of coronary arteries and veins conveys blood to and from the heart muscles. Hans van Beek and James B. Bassingthwaite of the University of Washington recently used fractal geometry to explain anomalies in the blood-flow patterns to the healthy heart. Interruption of this arterial flow may cause a myocardial infarction (heart attack). Second, a fractal-like canopy of connective-tissue fibers within the heart—the chordae tendineae—tethers the mitral and tricuspid valves to the underlying muscles. If these tissues break, there can be severe regurgitation of blood from the

ventricles to the atria, followed by congestive heart failure. Last, fractal architecture is also evident in the branching pattern of certain cardiac muscles as well as in the His-Purkinje system, which conducts electrical signals from the atria to the cardiac muscles of the ventricles.

Although these fractal anatomies serve apparently disparate functions in different organ systems, several common anatomical and physiological themes emerge. Fractal branches or folds greatly amplify the surface area available for absorption (as in the intestine), distribution or collection (by the blood vessels, bile ducts and bronchial tubes) and information processing (by the nerves). Fractal structures, partly by virtue of their redundancy and irregularity, are robust and resistant to injury. The heart, for example, may continue to

pump with relatively minimal mechanical dysfunction despite extensive damage to the His-Purkinje system, which conducts cardiac electrical impulses.

Fractal structures in the human body arise from the slow dynamics of embryonic development and evolution. We have suggested that these processes—like others that produce fractal structures—exhibit deterministic chaos. Recent investigations in physiology have uncovered other examples of apparently chaotic dynamics on shorter, experimentally accessible time scales. In the early 1980's, when investigators began to apply chaos theory to physiological systems, they expected that chaos would be most apparent in diseased or aging systems. Indeed, intuition and medical tradition gave them good reason to think



**BLOOD VESSELS** of the heart exhibit fractal-like branching. The large vessels (cast at left) branch into smaller vessels (top drawing), which in turn branch into even smaller vessels (bottom drawing).

so. If one listens to the heart through a stethoscope or feels the pulse at the wrist, the rhythm of the heart seems to be regular. For an individual at rest the pulse strength and the interval between heartbeats seem roughly constant. For this reason cardiologists routinely describe the normal heart rate as regular sinus rhythm.

More careful analysis reveals that healthy individuals have heart rates that fluctuate considerably even at rest. In healthy, young adults the heart rate, which averages about 60 beats per minute, may change as much as 20 beats per minute every few heartbeats. In the course of a day the heart rate may vary from 40 to 180 beats per minute.

For at least five decades physicians have interpreted fluctuations in heart rate in terms of the principle of ho-

meostasis: physiological systems normally operate to reduce variability and to maintain a constancy of internal function. According to this theory, developed by Walter B. Cannon of Harvard Medical School, any physiological variable, including heart rate, should return to its "normal" steady state after it has been perturbed. The principle of homeostasis suggests that variations of the heart rate are merely transient responses to a fluctuating environment. One might reasonably postulate that during disease or aging the body is less able to maintain a constant heart rate at rest, so that the magnitude of the variations in heart rate is greater.

A different picture develops when one carefully measures the normal beat-to-beat variations in heart rate and plots them throughout a day. This time-series

plot appears ragged, irregular and, at first glance, completely random. But a pattern emerges from the heart-rate data plotted over several different time scales. If one concentrates on a few hours of the time series, one finds more rapid fluctuations whose range and sequence look somewhat like the original, longer time-series plot. At even shorter time scales (minutes), one finds even more rapid fluctuations that again appear to be similar to the original plot. The beat-to-beat fluctuations on different time scales appear to be self-similar, just like the branches of a geometric fractal. This finding suggests that the mechanism that controls heart rate may be intrinsically chaotic. In other words, the heart rate may fluctuate considerably even in the absence of fluctuating external stimuli rather than relaxing to a homeostatic, steady state.

To investigate whether beat-to-beat heart-rate variations are indeed chaotic or periodic, one can compute the Fourier spectrum of the time-series plot for heart rate. The Fourier spectrum of any waveform (such as the time-series plot) reveals the presence of periodic components. If a time-series plot showed a heartbeat of exactly one beat per second, the spectrum would show a sharp spike at a frequency of one beat per second. On the other hand, the time-series plot of a chaotic heartbeat would generate a spectrum that showed either broad peaks or no well-defined peaks. Spectral analysis of normal heart-rate variability in fact shows a broad spectrum suggestive of chaos.

Another tool for analyzing the dynamics of a complex nonlinear system is a "phase space" representation. This technique tracks the values of independent variables that change with time. The number and type of independent variables depend on the system [see "Chaos," by James P. Crutchfield, J. Dooyne Farmer, Norman H. Packard and Robert S. Shaw; *SCIENTIFIC AMERICAN*, December, 1986]. For many complex systems all of the independent variables cannot be readily identified or measured. For such systems phase-space representations can be plotted using the method of delay maps. For the simplest delay map, each point on the graph corresponds to the value of some variable at a given time plotted against the value of that same variable after a fixed time delay. A series of these points at successive times outlines a curve, or trajectory, that describes the system's evolution.

To identify the type of system dynamics (chaotic or periodic), one determines the trajectories for many different initial conditions. Then one searches for an at-

tractor: a region of phase space that attracts trajectories. The simplest kind of attractor is the fixed point. It describes a system—such as a damped pendulum—that always evolves to a single state. In the phase space near a fixed-point attractor, all the trajectories converge to a single point.

The next most complicated attractor is the limit cycle. It corresponds to a system—such as an ideal, frictionless pendulum—that evolves to a periodic state. In the phase space near a limit cycle, the trajectories follow a regular path, for example, one that is circular or elliptical.

Other attractors are simply called "strange." They describe systems that are neither static nor periodic. In the phase space near a strange attractor, two trajectories that started under almost identical conditions will diverge over the short term and become very different over the long term. The system described by a strange attractor is chaotic.

We recently analyzed the phase-space representations for the normal heartbeat. What we found was more like a strange attractor than like the periodic attractor charac-

teristic of a truly regular process. This observation was another indication that the dynamics of the normal heartbeat may be chaotic.

The mechanism for chaos in the beat-to-beat variability of the healthy heart probably arises from the nervous system. The sinus node (the heart's natural pacemaker) receives signals from the involuntary (autonomic) portion of the nervous system. The autonomic nervous system in turn has two major branches: the parasympathetic and the sympathetic. Parasympathetic stimulation decreases the firing rate of sinus-node cells,

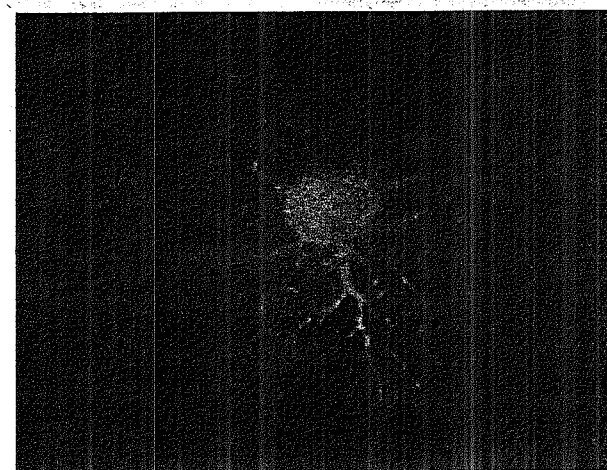
whereas sympathetic stimulation has the opposite effect. The influence of these two branches results in a constant tug-of-war on the pacemaker. The result of this continuous buffeting is fluctuations in the heart rate of healthy subjects. Recently investigators, including Richard J. Cohen and his colleagues at the Massachusetts Institute of Technology, have quantified the reduction in heartbeat variability that occurs after heart transplantation, a procedure in which the autonomic nerve fibers are cut.

Recent evidence from several laboratories suggests that chaos is a normal feature of other components of the nervous system. Gottfried Mayer-Kress of the Los Alamos National Laboratory, Paul E. Rapp of the Medical College of Pennsylvania and Agnes Babloyantz and Alain Destexhe of the Free University of Brussels have analyzed electroencephalograms of healthy individuals and have found evidence for chaos in the nervous system. Otto E. Rössler and his colleagues at the University of Tübingen in West Germany have also discovered indications of chaos in components of the nervous system that are responsible for hormone secretion. They have analyzed temporal changes in hormone levels in healthy human subjects and have found apparently chaotic fluctuations.

Other workers have recently simulated interactions among nerve cells to show how chaos might arise. Walter J. Freeman of the University of California at Berkeley has demonstrated that chaos can be generated in a model of the olfactory system. The model incorporates a feedback loop among the "neurons" and a delay in response times. Earlier, Leon Glass and Michael C. Mackey of McGill University had recognized the importance of time delays in producing chaos.

Why should the heart rate and other systems controlled by the nervous system exhibit chaotic dynamics? Such dynamics offer many functional advantages. Chaotic systems operate under a wide range of conditions and are therefore adaptable and flexible. This plasticity allows systems to cope with the exigencies of an unpredictable and changing environment.

Many pathologies exhibit increasingly periodic behavior and a loss of variability. Early indications that even the dying heart may behave periodically came from Fourier analysis of electrocardiographic waveforms during ventricular tachycardia or ventricular fibrillation, the very rapid cardiac rhythms that most commonly cause cardiac arrest. In the mid-1980's Raymond E. Ideker and his colleagues at the Duke University School of Medicine recorded the waveforms associated with ventricular fibrillation



NEURON exemplifies fractal structure. The cell body branches into dendrites, which in turn branch into finer fibers. This structure may be related to chaos in the nervous system.

from the innermost layers of the dog heart. They found that the fibrillatory activity inside the heart was a much more periodic process than previously thought.

In 1988 two of us (Goldberger and Rigney) did a retrospective study of the ambulatory electrocardiograms of people who had severe heart disease. We discovered that the pattern of heartbeats of those patients often became less variable than normal anywhere from minutes to months before sudden cardiac death. In some cases the overall beat-to-beat variability was reduced; in others highly periodic heart-rate oscillations appeared and then stopped abruptly.

Somewhat similarly, the nervous system may show the loss of variability and the appearance of pathological periodicities in disorders such as epilepsy, Parkinson's disease and manic depression. And whereas under normal conditions white-blood-cell counts in healthy subjects have been reported to fluctuate chaotically from day to day, in certain cases of leukemia the white-cell count oscillates periodically.

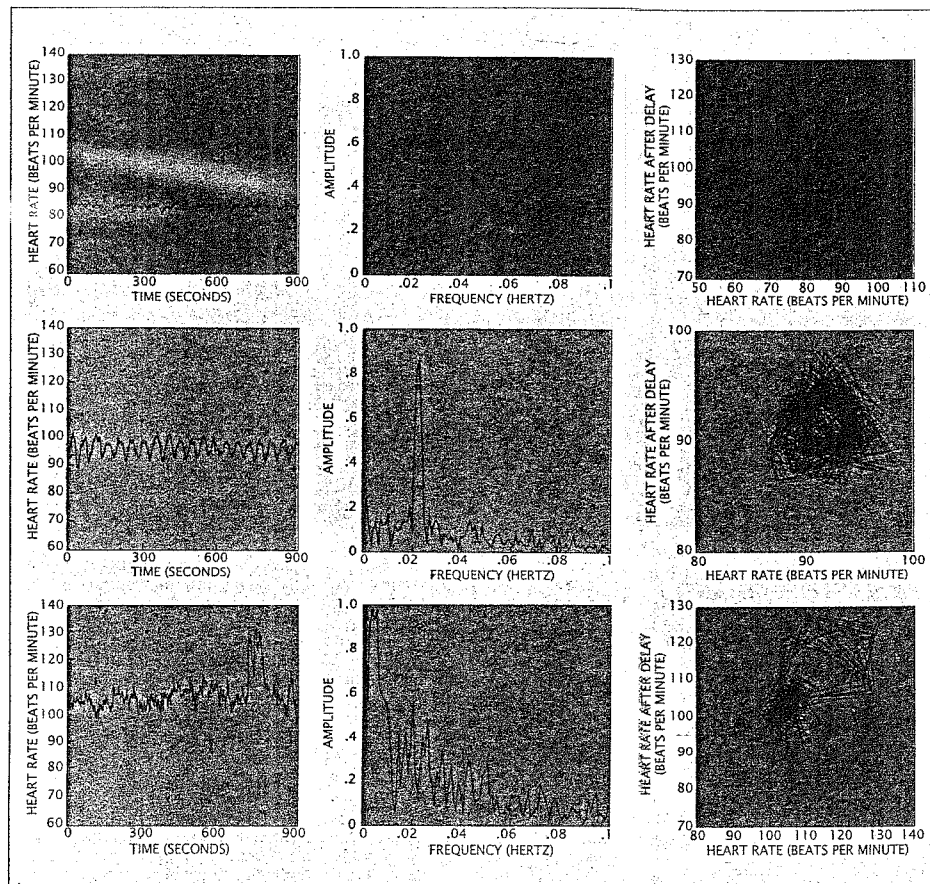
The periodic patterns in disease and the apparently chaotic behavior in health do not imply that all pathologies are associated with increased regularity. In some cardiac arrhythmias the pulse rate is so erratic that the individual may complain of "palpitations." Some of these events actually represent oscillations that seem irregular but are actually periodic when carefully analyzed. In other arrhythmias the heartbeat is in fact unpredictably erratic. None of these irregu-

lar pathologies, however, has been shown to represent nonlinear chaos—although the pulse may feel quite "chaotic" in the colloquial sense.

Physiology may prove to be one of the richest laboratories for the study of fractals and chaos as well as other types of nonlinear dynamics. Physiologists need to develop a better understanding of how developmental processes lead to the construction of fractal architectures and how dynamic processes in the body generate apparent chaos. In the near future, studies of fractals and chaos in physiology may provide more sensitive ways to characterize dysfunction resulting from aging, disease and drug toxicity.

#### FURTHER READING

- AN ESSAY ON THE IMPORTANCE OF BEING NONLINEAR. B. J. West in *Lecture Notes in Biomathematics* 62. Edited by S. Levine. Springer-Verlag, 1985.
- FRACTALS IN PHYSIOLOGY AND MEDICINE. Ary L. Goldberger and Bruce J. West in *Yale Journal of Biology and Medicine*, Vol. 60, pages 421-435; 1987.
- PHYSIOLOGY IN FRACTAL DIMENSIONS. Bruce J. West and Ary L. Goldberger in *American Scientist*, Vol. 75, No. 4, pages 354-365; July-August, 1987.
- NONLINEAR DYNAMICS IN SUDDEN CARDIAC DEATH SYNDROME: HEARTRATE OSCILLATIONS AND BIFURCATIONS. A. L. Goldberger, D. R. Rigney, J. Mietus, E. M. Antman and S. Greenwald in *Experientia*, Vol. 44, pages 983-987; 1988.



HEART RATE is shown as time-series plots (left), Fourier spectra (center) and phase-space plots (right). A heart rate 13 hours before cardiac arrest (top) is nearly constant as indicated by the flat spectrum and the phase-space trajectory suggestive of a point attractor. A

heart rate eight days before sudden cardiac death (middle) is quite periodic as shown by the spike and the trajectory suggestive of a noisy limit cycle. A healthy heart rate (bottom) appears erratic; it has a broad spectrum and a trajectory resembling a strange attractor.