BIOTECH USA '89

THE FRACTAL GEOMETRY OF THE HEART

SAN FRANCISCO, Calif.—Understanding the bases, and predicting the onset, of the cardiac arrhythmias called ventricular fibrillation are two major goals of cardiology. As participants at this year's Biotech USA, held here in October, learned, applying mathematical chaos theory to cardiac physiology is speeding progress toward both these goals.

Chaos theory, an aspect of nonlinear dynamics, is a branch of mathematics that investigates the behavior of constrained randomness. Since ventricular fibrillation—the principal cause of the annual 400,000 heart disease-related deaths in the U.S.—represents a change from a seemingly regular heartbeat to an extremely irregular one, it is not surprising that arrhythmogenesis is one of the first medical areas to which chaos theory is being applied. But, as clinical cardiologist Ary Goldberger (Harvard University, Cambridge, MA) reported, while the apparently regular beat of the normal heart describes a fractal geometry characteristic of nonlinear processes, the heartbeat of patients likely to suffer lethal fibrillation paradoxically follows a much more regular geometry.

Goldberger came to this conclusion by analyzing phase plots constructed from sinus rhythm recordings of two classes of patients—those with severe heart disease who later developed lethal arrhythmias and those with occasional benign arrhythmias. A phase plot represents a graph of heartbeat intervals at one time versus the heartbeat interval after a fixed time-delay. Such plots from the control group show a spider-like pattern with the points constrained around what chaos theoreticians call a strange attractor. The plots from those patients who went on to suffer lethal fibrillation, however, describe small circles characteristic of less chaotic dynamics. In fact, dynamical analysis of a fibrillating heartbeat reveals periodic oscillations. This periodicity, Goldberger speculated, reflects a cycling of the neural and chemical modulators of sinus rhythm. Under normal physiological conditions such cycling is avoided and the organism remains adaptable. Arrhythmogenesis, in this view, represents mode-locking of the control pathways. A little chaos, Goldberger suggests, is good for you.

IMAGE UNAVAILABLE FOR COPYRIGHT REASONS

Will the next generation of cardiac monitors display images like these? Applying a method from nonlinear dynamics, known as recurrence plots, to heartbeat recordings from an ischemic pig yields a patternless graph when the sinus rhythm is normal (left). Prior to the onset of a lethal arrhythmia a distinctive fiber-like pattern —corresponding to a loss in dimensional complexity (chaos)—appears (right).

COURTESY GOTTFRIED MAYER-KRESS, U.C. SANTA CRUZ

An important application of these studies is in the design of a new generation of cardiac monitors that perform complex dynamic analysis (instead of simply recording mean heart rate). Hearing Gottfried Mayer-Kress (University of California, Santa Cruz), one had the feeling such devices may be closer than previously thought.

Mayer-Kress has developed new mathematical tools with which to transform data from an observed time series—in this case, heartbeat intervals—into multidimensional vectors. These vectors can be manipulated further to allow direct visualization of brief recurrences (patterns) in arbitrary high-dimensional space. Performing such a recurrence analysis on data recorded by James Skinner (Baylor College of Medicine, Houston, TX) from ischemic pig-hearts prior to, and after the onset of, ventricular fibrillation, yielded quite dramatic results (see figure). A monitor that displayed recurrence plots of a patient every 10 or 20 minutes could become a welcome addition to cardiology units.

These pre-arrhythmic patterns, which Skinner has shown also correspond to minimal values in the chaotic correlation dimension (another method of nonlinear dynamics) of the heartbeat intervals, may be the abstract representations of the excitation rotors produced in the myocardium by electrically invoked fibrillation.

Raymond Ideker (Duke University Medical Center, Durham, NC) has developed methods to record the small signals generated by the intrinsic electrical activity of the heart in the presence of the much larger signals produced by electric shocks given to halt or induce arrhythmias. He was able to show that electrically evoked ventricular fibrillation is initiated by rotors of electrical activity that occur on the surface of the myocardium following delivery of two critically timed stimuli from bar electrodes placed at right angles to each other on the epicardial surface. The first stimulus induces an excitation wavefront that travels alongside the second electrode. When the wavefront reaches a critical distance, the second electrode produces its electrical gradient. This invariably gives rise to a rotating wave of electrical excitation in the center of the field defined by the two electrodes.

These results radically change the basic theory on which defibrillators have been designed, and should lead to the manufacture of smaller, longer-lasting, and more efficient implantable devices. **—Harvey Bialy**