Singularities

When Time Breaks Down. The Three-Dimensional Dynamics of Electrochemical Waves and Cardiac Arrhythmias. ARTHUR T. WINFREE. Princeton University Press, Princeton, NJ, 1987. xiv, 339 pp., illus. $60; paper, $19.95.

It is a pleasure to peer into the singular mind of Arthur Winfree, for the world of biological time wrapped around its own unexpected singularities has been better seen by Winfree than any other. *When Time Breaks Down*, his third book, continues and extends his topological view of rhythmic phenomena. The core of the book is an analysis of the vortices of rotating electrochemical activities in cardiac tissue that may underlie sudden death by fibrillation in apparently healthy hearts. But the interest extends beyond the spontaneous emergence of rotating reentrant waves in fibrillating hearts to rotating chemical reactions in petri dishes and even to cosmic strings.

The idea that cardiac fibrillation is due to a stably circulating reentrant wave of activity has long been familiar. The questions have been whether such rotors actually occur in unperforated tissue, whether such behavior stably persists, whether fibrillation is commonly due to such vortices of activity or to uncoordinated firing from a variety of isolated pacemakers, and how such vortices might be initiated in apparently normal hearts.

Winfree brings his topological perspective to these problems. Consider a typical biological rhythm, such as the circadian rhythm of eclosion in fruit flies. It is now well established, in part by Winfree's own work, that mild perturbations distort the phase of the rhythm slightly: each "old" phase is changed into a distinct "new" phase, and thus a full 2π cycle of old phase becomes a distorted but full 2π cycle of new phases. This phase transformation is called a type 1 resetting curve. The striking alternative, deduced and demonstrated by Winfree long ago, is a type 0 phase-resetting curve. Such curves result from strong perturbations. The critical feature is that the 2π cycle of old phases is changed into a subset of the possible 2π new phases. That is, under a strong stimulus, not all the 2π old phases occur as new phases.

Type 1 and type 0 resetting curves are topologically distinct. No smooth transformation takes one to the other. But more important, the existence of both types of curve in the response of a biological system as the stimulus perturbation increases implies a hidden catastrophe in which "time breaks down." More precisely, consider a two-dimensional plot, where the x-axis gives old phase, the y-axis gives stimulus intensity, and the interior of the xy-graph shows, at each point, the new phase resulting from that combination of old phase and perturbation strength. Since only a subset of phases occurs as new phases at strong stimulus perturbations and all phases occur as new phases for mild perturbations, a topological theorem asserts that somewhere within the two-dimensional plot a point or line *singularity* must occur, across which sudden jumps in phase are encountered. In the simplest case, the singularity is a point around which all phases occur infinitely close to one another. Throughout the book there are pictures of the color wheel color-coding 2π phases. Positions of the same new phases are connected zones called "isochromes." These end on a hueless, phaseless singularity, a point therefore where "phase," or local time, has no meaning, and time breaks down.

But this picture has no spatial dimension, nor does it include the promised vortices of electrochemical activity that might underlie cardiac arrhythmias. Winfree has begun here because the existence of such a singularity in simple phase-resetting curves itself appears to promise vortices rotating about a phaseless center point in excitable media such as cardiac tissue, or the now famous Belousov-Zhabotinsky reaction. Consider next a two-dimensional "tissue" of model cardiac cells, each if triggered passing through three states, "excited," "refractory," and "quiescent but excitable." Clearly, the entire tissue might be triggered to the excited states, hence fire and contract, simultaneously. Alternatively, if one edge were triggered rhythmically, waves of excitation would sweep across the tissue, followed by waves of refractory then quiescent states. But can one obtain a reentrant, self-sustaining, *rotating* wave of activity pivoting around a central point, and if so how? Here Winfree shows that the answer is yes and that such a wave may typically arise thanks to just the kind of type 1 and type 0 phase resetting seen above. In particular, if a spatially graded stimulus is applied to the tissue and is strong enough in some regions to cause type 0 resetting and less strong in other regions, the typical consequence is the formation of pairs of counterrotating vortices of activity that persist stably and "organize" the surrounding tissue. Thus we are led to admit that presumably even normal cardiac tissue might be triggered to misbehave and fibrillate by an unfortunately timed and distributed perturbation. Further, this appears to be no mere theory, for good evidence is adduced that fibrillation often consists of just such vortices of electrochemical activity.

But Winfree's singularities proliferate. Each vortex surrounds a phaseless point. If the excitable medium is three-dimensional rather than two-, then such vortices become more complex objects, and the phaseless point becomes a phaseless *line* about which the rhythmic reentrant activity circulates. The possible geometries of this phaseless line singularity are governed by some simple principles. Notably, in a connected medium, a singularity cannot "end" except on the boundaries, or by closing upon itself to form a ring. Consider the simplest case of a straight-line singularity in a three-dimensional medium. About it pivots a *scroll wave* of rotating activity, where each scroll surface is a surface of constant phase, or isochrome, and all 2π phases have their own scroll isochrome surfaces wound in order around the singularity, one inside the other. If the line singularity ends on a boundary at two points, say the actual surface of a three-dimensional medium in a petri plate with the Zhabotinsky reaction, then the counter-rotating spiral vortices are revealed as the two ends of the scroll seen "end on." But the singularities can be even more complex, for one line singularity can form a ring, through which is threaded another closed ring of singularities. Indeed, any organization of such rings looping through one another is possible. Furthermore, in passing around one phaseless ring on which all 2π phases abut, again a topological issue arises. For the phases can match up around the ring without a twist, or with a full positive or negative twist, or more generally with any integer number of positive or negative twists. Such twisted and intertwined rings of singularities then act as organizing centers controlling the temporal and spatial distribution of activities in the rest of the three-dimensional domain. Current questions concern the stability of such complex organizing centers, their capacities to transform into one another, and the varieties of initial conditions that lead to each such topologically distinct organizing center.

This is a beautiful book. It is intellectually elegant, visually elegant with its color plates showing isochrome resetting surfaces and scroll waves in three dimensions, and scientifically elegant in the insights it affords and the experiments it presages.

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