Obituary

Arthur T. Winfree (1942–2002)

High above the roiling waves on the NaPali Coast of Kauai Island, Hawaii, Art Winfree is kneeling down and photographing the lichens inscribed on the rocks along the Kalalau trail. He had passed the same way several years before and had documented the spiral patterns of lichen growth. These seemed similar to the spiral waves of activity that were now well known in certain types of chemical reactions and in the electrical rhythms of the heart. Could the lichens be growing with the same geometries, though on an infinitely slower timescale? Art Winfree's pioneering studies of the topological features of biological oscillations defined whole new areas of research. He died on 5 November 2002, struck down by an aggressive glioblastoma that had invaded his brain.

Winfree's scientific path was already set by the time he attended high school in Stanford, Connecticut. He figured out ways to blow huge soap bubbles, and for this feat he was one of the Westinghouse Science Talent Search finalists in 1961. He went on to study engineering physics at Cornell University, and then embarked on graduate studies of circadian rhythms — the roughly 24-hour oscillations of physiology and behaviour that most organisms display — at Princeton University.

Before completing his doctorate, Winfree was recruited to a faculty position in the Department of Theoretical Biology at the University of Chicago. There, he launched two different experimental efforts — to reset the circadian rhythms of fruitflies using short light flashes, and to describe the patterns of an oscillating chemical reaction, the Belousov–Zhabotinsky (BZ) reaction. Although these appear to be in completely different scientific domains, Winfree demonstrated theoretical links that led to testable predictions. To understand the connection, first think of a rotating disc, for example an old-fashioned long-playing record. At the very centre of the disc lies a fixed point that does not move at all. Winfree recognized that, in any mathematical equation describing a biological or chemical oscillator, there must also be a fixed point that does not lead to oscillation.

But how could this fixed point be observed experimentally? Well, there are lots of ways. For instance, if stimuli are delivered to the oscillator at different phases of the cycle, and the magnitude of resetting of the oscillator cycle is plotted

Scientist who shaped studies of biological and chemical oscillations

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as a function of the timing of the stimuli, the graph will have different topological properties for small and large stimuli. Winfree demonstrated these features in studies of the circadian rhythms of fruitflies in the 1970s, using light pulses as the stimuli. Much later, Charles Czeisler and colleagues at Harvard Medical School showed that similar phenomena could be observed after perturbing the human sleep–wake cycle with light pulses.

For chemical reactions, if the fixed point could be trapped in a thin layer of a solution, spiral waves of chemical activity would be observed. In a landmark 1972 paper, Winfree rediscovered spiral waves in the BZ reaction (an earlier report of such waves by Anatol Zhabotinsky and Albert Zaikin was not well known outside the Soviet Union). Winfree's lectures on this work were enlivened by his distribution of the BZ reaction on filter papers to his audience.

At the same time that Winfree's studies were under way in Chicago, scientists in the former Soviet Union were expanding on a conjecture (by Norbert Wiener and Arturo Rosenblueth) that spiral waves might underlie fibrillation — a fatal heart rhythm. Recognizing the importance of this work, Winfree arranged for and edited a translation of a 1984 monograph by Vladimir Zykov that summarized the contributions of the Soviet school.

Winfree extended this work by showing how a stimulus delivered to the heart would lead to the initiation of fibrillation. But to analyse the geometry of wave propagation in the pumping chambers of the heart, it would be necessary to consider waves in three dimensions. Winfree introduced the concept of scroll waves to describe the three-dimensional rotating waves that, in cross-section, appear as a spiral. He now teamed up with Steven Strogatz and, in a beautiful series of papers in the 1980s, they classified the ways that scroll waves could be twisted, linked and knotted in three dimensions.

In contrast to the current scientific environment, which encourages large research grants and large teams, most of Winfree's work was done alone or in collaboration with one or two students or colleagues, and with comparatively small sums of money used in imaginative ways. This approach is evident in one of his last major studies, carried out at the University of Arizona, his academic home after 1989. The work involved the visualization of scroll rings in three-dimensional chemical reactions, and for this purpose Winfree built a three-dimensional optical tomograph that was cobbled together from miscellaneous bits of equipment.

Winfree was also generous with his ideas. His masterpiece *The Geometry of Biological Time* (first published in 1980), for instance, is a gold-mine of suggestions for new scientific directions, and a second edition (2001) identifies almost 200 research questions. Sending a manuscript to Winfree before publication would lead to a meticulous set of annotations, in green felt-tip pen, pointing out areas for further digging. He was scrupulous about crediting his colleagues, and his papers and books (which also include *The Timing of Biological Clocks*, 1986, and *When Time Breaks Down*, 1987) are notable for their comprehensive nature, containing hundreds of references.

From the growth of lichens on rocks, to the delicate patterns of chemical waves, to fatal cardiac arrhythmias, Art Winfree delighted in finding unexpected connections between geometry and dynamics. As researchers develop new ways to visualize the patterns of excitation in chemical systems and heart tissue, Winfree's predictions about the initiation, geometry and stability of spiral waves and scroll waves are being tested and are yielding new insights. His many friends, colleagues and members of his family rejoice in his contributions, and mourn the passing of this wise and gentle man.

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