Perspective

Spiral Waves in Chemistry and Biology

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CHEMISTS HAVE DEVOTED CONSIDERABLE EFFORT TO designing and building molecular systems that mimic and, possibly, provide insights into many aspects of biological structure and function. For example, molecules that selectively bind and transport ions or serve as "artificial enzymes" have been synthesized and studied. At a higher level of organization, chemical reactions have been heralded as vehicles for understanding temporal and spatial organization in living systems. In this issue of *Science* a major step is taken toward realization of this promise by Lechleiter *et al.* (*1*), who describe observations of propagating spiral waves of calcium in *Xenopus laevis* oocytes.

A striking example of spatiotemporal pattern formation in chemical systems occurs in the Belousov-Zhabotinskii (BZ) reaction, the bromination of malonic acid by bromate ion in the presence of a ferrous phenanthroline (ferroin) catalyst (*2*). An initially homogeneous red solution of reaction mixture can spontaneously develop a pattern of concentric blue rings, known as target patterns, that propagate outward from a set of centers. If the rings are sheared, mechanically or as a result of concentration gradients, they evolve to propagating spirals (*3*) (Fig. 1A). When waves come in contact, they annihilate; the blue curves disappear and the neighboring medium returns to the red state.

Chemists and mathematicians have developed an understanding of this process in terms of the behavior of an excitable medium. (Other examples of excitable media include cardiac and neural tissues.) In such a medium, small perturbations of the homogeneous stationary state are rapidly damped out, but disturbances larger than a critical size cause the medium to undergo a large excursion in the concentrations of reactive species before returning to its initial state. If such a medium contains a pacemaker nucleus, a small region capable of generating periodic supercritical perturbations, then, as a result of diffusion, targetlike patterns of chemical reactivity will develop (*4*). If these circles are broken, the loose ends wrap into rotating spirals.

Target patterns and spiral waves have been observed not only in the BZ reaction, but also in other chemical systems and, as seen in Fig. 1B, in the aggregation of the cellular slime mold *Dictyostelium discoideum* (*5*). Recent investigations with high-resolution imaging techniques (*6*) have revealed details about traveling wave patterns and the size and concentration profile of the pacemaker nuclei in the BZ system. Both experiments and theoretical considerations (*7*) suggest that the velocity of chemical waves should depend upon their curvature. Also crucial to wave propagation is the dispersion relation, which relates the wave speed to the wavelength (distance between successive loops of the pattern). The effects of curvature and dispersion are modeled with remarkable accuracy by a simple cellular automaton model (*8*), in which the medium is represented by a lattice of cells. Each cell can be in any of a finite set of states corresponding to various degrees of excitation or refractoriness and recovery. The key element of the model is a set of rules that specify how a cell changes its state according to its current state and that of its neighbors.

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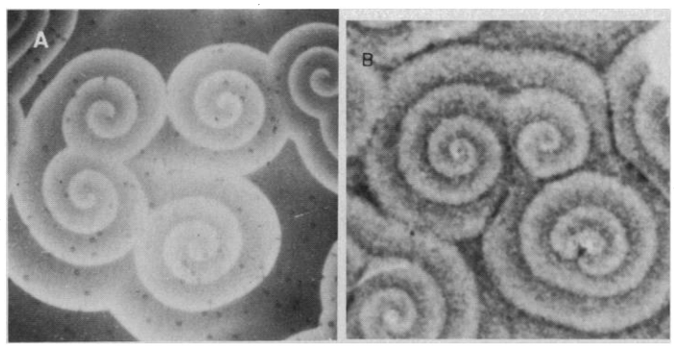

Fig. 1. Spiral waves in (**A**) the BZ reaction and (**B**) the aggregating slime mold *Dictyostelium discoideum*. [Courtesy of A. T. Winfree for (A) and P. N. Devreotes for (B)]

The results of Lechleiter *et al.* correspond well to the behavior of the chemical system. By using the Ca^{2+} indicator fluo-3, they are able to obtain confocal images of a single optical slice close to the plasma membrane of the oocyte. They observe both target and spiral patterns of propagating calcium release, which annihilate on collision. They measure the critical radius of a pacemaker nucleus to be about 10 μm, compared with ~30 μm for the BZ reaction (*6*). The wavelength of the oocyte patterns is smaller than that in the BZ system by a similar factor, perhaps suggesting a simple scaling relationship. Use of a cellular automaton model to fit their data enables the authors to estimate the refractory time of an individual Ca^{2+}-store at about 5 s.

Studies of chemical oscillators have elucidated, at a molecular level, the mechanisms of several complex reactions. Oscillatory behavior provides more information for constructing and testing mechanisms than do more classical kinetics methods based on monotonic dynamics. Lechleiter *et al.* are able to obtain insights on the mechanisms of their system as well. Two pathways had been proposed for the positive feedback that gives rise to the excitability of the oocyte cytoplasm. The first involves direct Ca^{2+}-induced calcium release (CICR). The alternative hypothesis focuses on activation of phospholipase C, which causes variation in levels of inositol 1,4,5-triphosphate, which in turn releases stores of intracellular calcium. By using their data to estimate the diffusion coefficient of the excitable signal, the authors obtain evidence favoring CICR as the mechanism of wave propagation.

There is no doubt that spatiotemporal patterns like those obtained in *Xenopus laevis* carry information in many other biological systems. Many biochemical processes are regulated by the concentration of free calcium in a cell. The availability of Ca^{2+}-sensitive dyes can now be combined with advances in image acquisition and analysis to allow us to study these phenomena in unprecedented detail. It should now be possible to apply the insights gained from traveling waves in excitable chemical systems to biological phenomena.

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