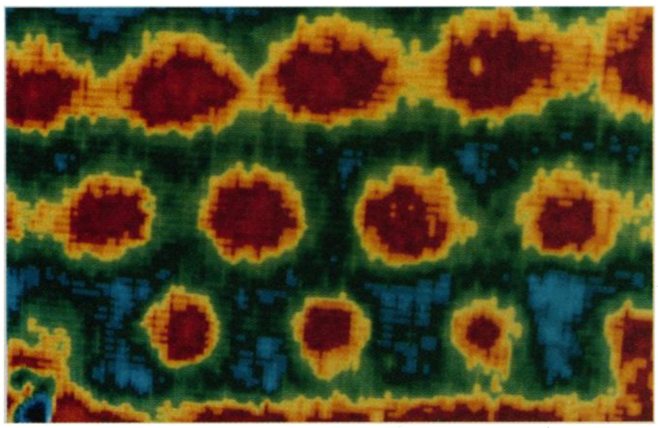
Did Turing Discover How the Leopard Got Its Spots?

Understanding the way a simple chemical system produces patterns may offer insights into animal development

NEARLY 40 YEARS AGO, THE mathematician Alan Turing proposed an intriguing explanation for how spots, stripes, and other patterns might develop on the coats of animals. Turing, who is better known as the father of modern computing science, suggested that biological development might be directed by the concentrations in cells of certain chemicals called morphogens: In an embryonic zebra, for instance, wherever the morphogen concentration was above a given level, the cells in that area might produce black hairs, while at lower levels of morphogen the cells would produce white hairs. In what became one of the most influential papers in theoretical biology, Turing suggested a mechanism by which stable patterns in the concentrations of these morphogens could arise spontaneously—and that, he said, could explain the development not only of spots and stripes but also of other biological features.



Patrick De Kepper *et al.*, University of Bordeaux

Seeing spots. *A computer-enhanced image of an experimental Turing structure.*

Turing's ideas, although they influenced the thinking of developmental biologists, have lacked an essential dimension: direct experimental proof. Until recently little has been known about stable patterns of morphogens in the developing embryo, and, until recently, no chemist had even been able to produce the so-called Turing structures—static patterns of differing concentrations of chemicals—in the laboratory.

All this began to change recently when a team of chemists announced that they had shown that Turing structures can be created experimentally. Last summer, researchers from the University of Bordeaux, led by Patrick De Kepper, reported in *Physical Review Letters* that they had produced a stable pattern of dots in a chemical reactor. From its appearance, the pattern seemed to be a Turing structure, but without understanding how or why the pattern arose, the scientists couldn't be sure. Now, on page 650 of this issue of *Science*, Irving Epstein of Brandeis University in Waltham, Massachusetts, and Istvan Lengyel of Brandeis and Kossuth Lajos University in Debrecen, Hungary, offer a theoretical explanation for how the Bordeaux group's pattern formed and show that it was indeed a Turing structure. This theoretical understanding, Epstein says, should not only make it possible to design other chemical systems that produce Turing structures, but also offer some insights into how morphogens may create patterns in living creatures.

Turing's original work depended on abstract systems of chemical reactions that were unlike any known physical systems. In particular, as other scientists expanded on Turing's work, the mathematical analysis made it clear that creating static concentration patterns in a reacting chemical system would demand a special condition: One of the reacting chemicals, called an inhibitor, would have to diffuse through the system much more rapidly than a second, the activator.

This proved difficult to do in chemical systems, notes John Tyson, a chemist at Virginia Polytechnic Institute and State University in Blacksburg. In aqueous solutions, all molecules diffuse at about the same rate, so although researchers tried various tricks to slow down the diffusion of the activator, nothing seemed to work. "The chemists had just about given up hope of discovering a simple example [of a Turing structure]," Tyson says.

The Bordeaux group was not quite ready to give up, however. They fed several different chemicals into a gel and allowed the chemicals to diffuse through the gel; as the chemicals reacted with one another, the scientists could follow the changing concentrations of the reactants by observing the color of the gel, which varied from yellow to blue depending on the concentrations of two of the chemicals. After several hours, a pattern of yellow dots on a blue background appeared in the reactor.

Lengyel and Epstein have now shown that the key to the success of this experiment is how the reacting chemicals diffuse through the gel. The inhibitor molecules, in this case ClO_2^- ions, do not interact with the gel, Epstein says, but instead move unimpeded through the liquid that permeates the gel. On the other hand, the activator molecules (iodine ions) "interact chemically with the gel, forming short-lived or long-lived complexes, and this slows them down," he says. To test this, he and Lengyel measured how quickly the ClO_2^- and I^- ions moved down columns of the gel used by the Bordeaux group and found that indeed the ClO_2^- came through much faster.

Working on this assumption, Lengyel and Epstein calculated mathematically how the concentration of ClO_2^- and I^- ions would vary inside a chemical reactor of the type described by the Bordeaux group, and found that their model predicted just what the French scientists had found: a static pattern of dots containing high concentrations of I^-.

Interest in the study of Turing structures is bound to pick up now, Tyson says, because "we finally have a nice, clean example of Turing structures in chemistry with a nice, clean theory to go along with it." But that doesn't mean that the puzzle of how the leopard got its spots has been solved. "We're still woefully ignorant of the mechanisms of biological pattern formation," he says. Once developmental biologists determine the molecular signals that control development, then it will be possible to study how these molecules distribute themselves throughout a developing organism and to look for Turing structures in the complicated biochemistry of the body. But that problem is not likely to be solved any time soon, Tyson says. It took 40 years to prove that Turing structures actually do exist in some simple chemical systems, and it might take another 40 to prove or disprove their existence in a complex system like the leopard. ■ ROBERT POOL

ADDITIONAL READING

V. Castets *et al.*, "Experimental evidence of a sustained standing Turing-type nonequilibrium chemical pattern," *Phys. Rev. Lett.* **64**, 2953 (1990).

J. D. Murray, "How the leopard gets its spots," *Scientific American* **258**, No. 3, 80 (1988).