How animals get their stripes and spots

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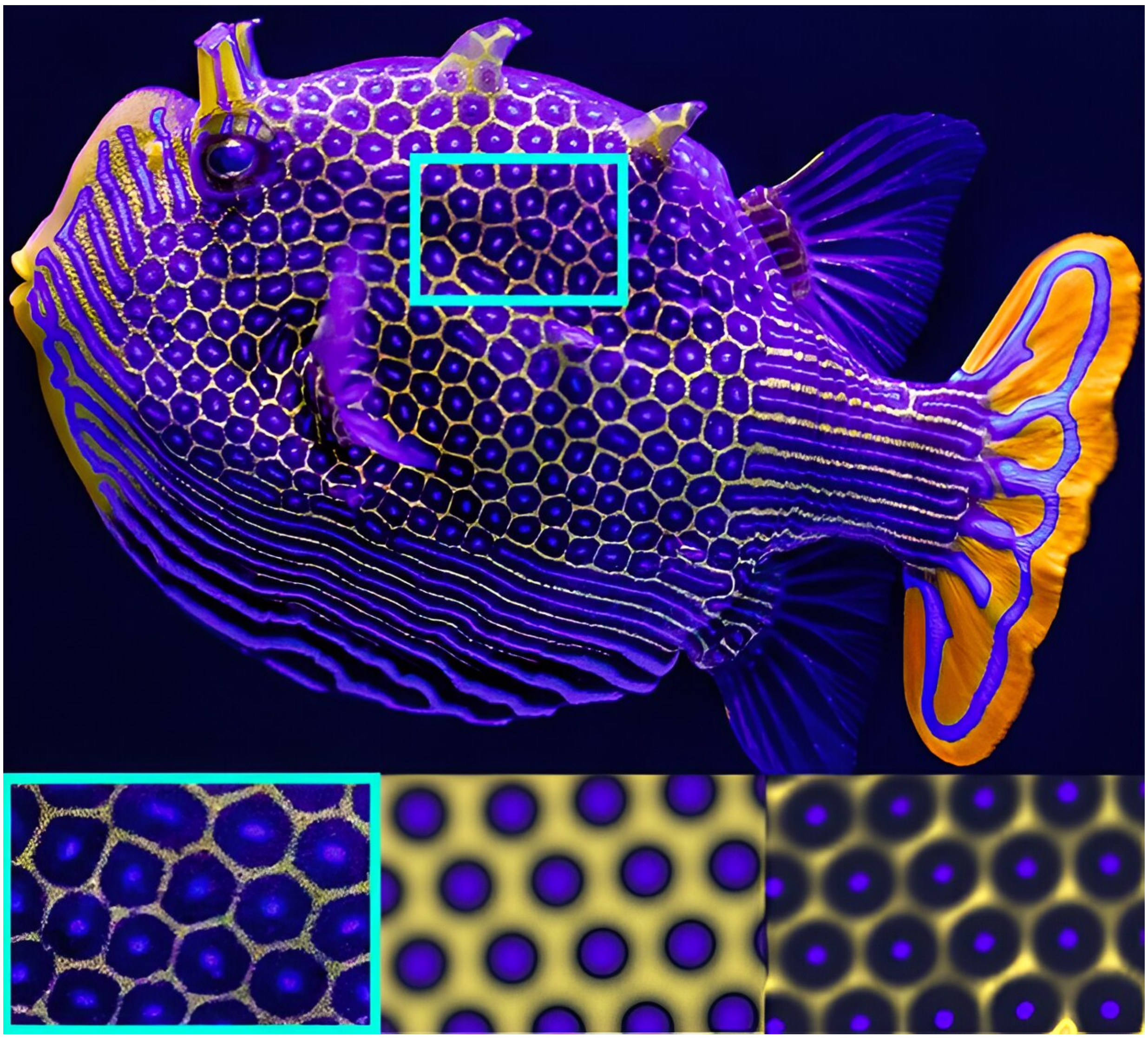

Top: A male Ornate Boxfish (Aracana ornata). Bottom left: A close-up picture of the fish's natural hexagonal pattern. Bottom center: Fish pattern simulation based on Turing's reaction-diffusion theory. Bottom right: Diffusiophoresis-enhanced reaction-diffusion simulation. Credit: The Birch Aquarium/ Scripps

Institution of Oceanography, Benjamin Alessio/University of Colorado Boulder

Nature has no shortage of patterns, from spots on leopards to stripes on zebras and hexagons on boxfish. But a full explanation for how these patterns form has remained elusive.

Now engineers at the University of Colorado Boulder have shown that the same physical process that helps remove dirt from laundry could play a role in how tropical fish get their colorful stripes and spots. Their findings were published Nov. 8 in the journal *Science Advances*.

"Many biological questions are fundamentally the same question: How do organisms develop complicated patterns and shapes when everything starts off from a spherical clump of cells," said Benjamin Alessio, the paper's first author and an undergraduate researcher in the Department of Chemical and Biological Engineering. "Our work uses a simple physical and chemical mechanism to explain a complicated biological phenomenon."

Biologists have previously shown that many animals evolved to have coat patterns to camouflage themselves or attract mates. While genes encode pattern information like the color of a leopard's spots, genetics alone do not explain where exactly the spots will develop, for example.

In 1952, before biologists discovered the double helix structure of DNA, Alan Turing, the mathematician who invented modern computing, proposed a bold theory of how animals got their patterns.

Turing hypothesized that as tissues develop, they produce chemical agents. These agents diffuse through tissue in a process similar to adding milk to coffee. Some of the agents react with each other, forming spots.

Others inhibit the spread and reaction of the agents, forming space between spots. Turing's theory suggested that instead of complex genetic processes, this simple reaction-diffusion model could be enough to explain the basics of biological pattern formation.

"Surely Turing's mechanism can produce patterns, but diffusion doesn't yield sharp patterns," said corresponding author Ankur Gupta, an assistant professor in the Department of Chemical and Biological Engineering. For instance, when milk diffuses in coffee, it flows in all directions with a fuzzy outline.

When Alessio visited the Birch Aquarium in San Diego, he was impressed by the sharpness of the boxfish's intricate pattern: It's made of a purple dot surrounded by a distinct hexagonal yellow outline with thick black spacing in between. Turing's theory alone would not be able to explain the sharp outlines of these hexagons, he thought. But the pattern reminded Alessio of computer simulations he had been conducting, where particles do form sharply defined stripes.

Alessio, a member of the Gupta research group, wondered if the process known as diffusiophoresis plays a role in nature's pattern formation.

Diffusiophoresis happens when a molecule moves through liquid in response to changes, such as differences in concentrations, and accelerates the movement of other types of molecules in the same environment. While it may seem like an obscure concept to non-scientists, it's actually how laundry gets clean.

One recent study showed that rinsing soap-soaked clothes in clean water removes the dirt faster than rinsing soap-soaked clothes in soapy water. This is because when soap diffuses out of the fabric into water with lower soap concentration, the movement of soap molecules draws out the dirt. When the clothes are put in soapy water, the lack of a difference in soap concentration causes the dirt to stay in place.

The movement of molecules during diffusiophoresis, as Gupta and Alessio observed in their simulations, always follows a clear trajectory and gives rise to patterns with sharp outlines.

To see if it may play a role in giving animals their vivid patterns, Gupta and Alessio ran a simulation of the purple and black hexagonal pattern seen on the ornate boxfish skin using only the Turing equations. The computer produced a picture of blurry purple dots with a faint black outline. Then the team modified the equations to incorporate diffusiophoresis. The result turned out to be much more similar to the bright and sharp bi-color hexagonal pattern seen on the fish.

The team's theory suggests that when chemical agents diffuse through tissue as Turing described, they also drag pigment-producing cells with them through diffusiophoresis— just like soap pulls dirt out of laundry. These pigment cells form spots and stripes with a much sharper outline.

Decades after Turing proposed his seminal theory, scientists have used the mechanism to explain many other patterns in biology, such as the arrangement of hair follicles in mice and the ridges in the roof of the mouth of mammals.

Gupta hopes their study, and more research underway by his research group, can also improve the understanding of pattern formation, inspiring scientists to develop innovative materials and even medicines.

"Our findings emphasize diffusiophoresis may have been underappreciated in the field of pattern formation. This work not only has the potential for applications in the fields of engineering and materials science but also opens up the opportunity to investigate the role of diffusiophoresis in biological processes, such as embryo formation and tumor formation," Gupta said.

More information: Benjamin Alessio et al, Diffusiophoresis-Enhanced Turing Patterns, *Science Advances* (2023). DOI: 10.1126/sciadv.adj2457. www.science.org/doi/10.1126/sciadv.adj2457

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