Researchers create artificial cell cortex, a system to study how cells divide

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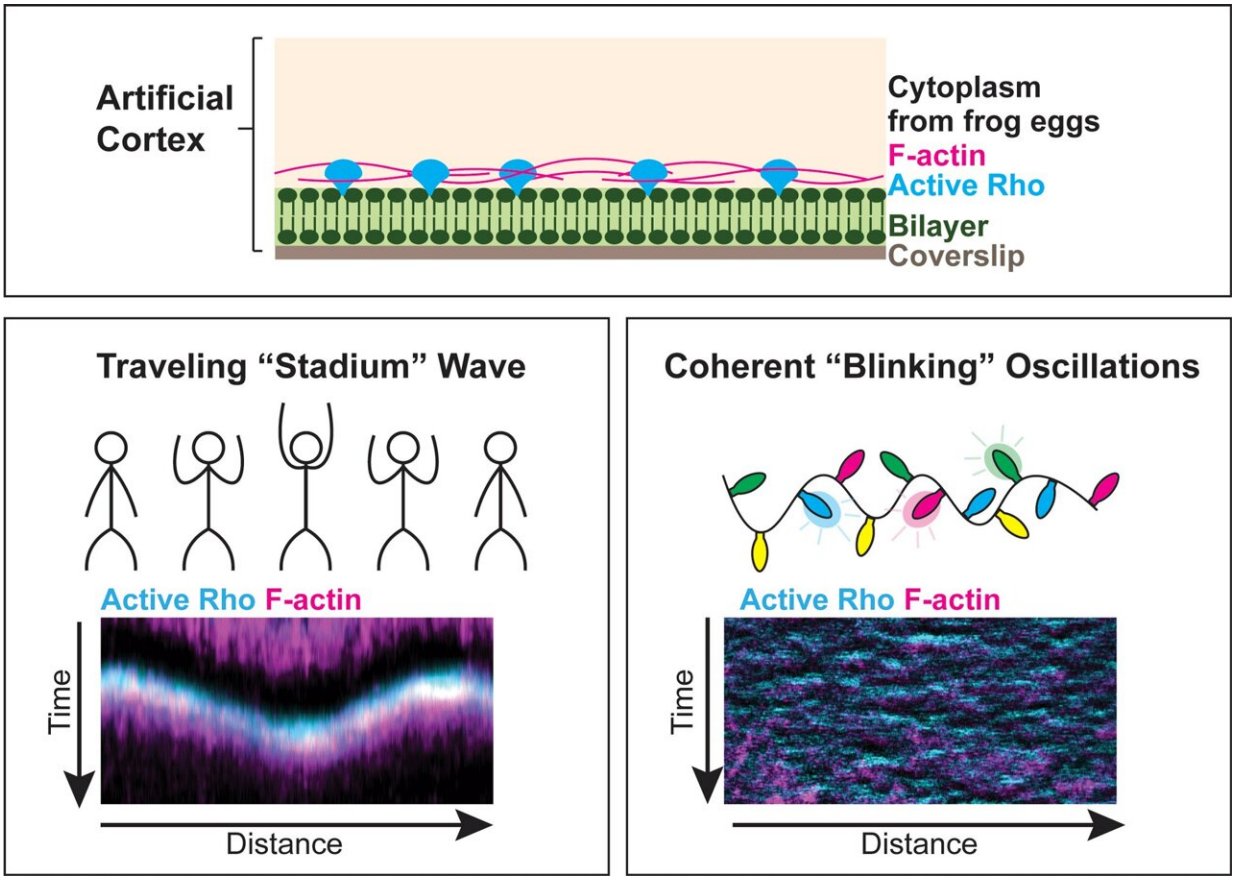

As a cell prepares to divide, its cell cortex proteins begin to move. First, its cortical proteins form an excitable wave, like spectators performing "the wave" at a football stadium. Second, cortical proteins organize into coherent oscillations, which behave like blinking holiday lights, associating and dissociating with the membrane at regular intervals. Credit: Jennifer Landino, A. Miller lab

Animal cells are bound by a structure called a cell cortex—and this structure, researchers say, is a bit like a tent.

A tent is constructed of a shell with a zippered opening that controls what can go into and out of the tent. This shell is held up by a system of poles. Similarly, an animal cell cortex is composed of a cell membrane that controls what enters the cell.

The cortex also contains proteins, which help the cell keep its shape. One of these key proteins, called actin, is a polymer with a linear structure—like a tent pole. But unlike a tent, a cell's cortical proteins aren't stationary. They move along the cell membrane, freely assembling and moving apart over time, in a process called "cortical excitability."

When these proteins begin to form wave patterns, it's a sign that the cell is preparing to divide. But studying this process within the cell membrane is difficult. Now, University of Michigan researchers have developed an approach to study these wave patterns outside of a cell by developing a cell-free artificial cortex.

In doing this, they showed that these cortical proteins can self-organize in two patterns. First, the proteins form an excitable wave, like spectators performing "the wave" in a stadium. Second, the proteins then organize into coherent oscillations, which behave like blinking holiday lights. Their study, which examines the proteins Rho and F-actin in frog egg extract, is published in the journal *Current Biology*.

"Almost a hundred years ago, people studying the cell cortex predicted that it was self-organized, that the patterns and shapes of these proteins were self-determined by the protein's properties, and the membrane's properties. But you can't really separate the cortex from the rest of the cell, because then everything just falls apart," said lead author Jennifer Landino, a postdoctoral researcher in the U-M Department of Molecular,

Cellular and Developmental Biology.

"It's very exciting that we now have a tool to study how these patterns work outside of cells. At the same time, it also confirms this long-standing hypothesis that the cortex is self-organizing, and that these patterns just arise from the properties of the molecules involved."

Landino says developing an artificial cortex to study these proteins is necessary because while biologists have tools they can use to manipulate proteins, they have fewer tools to manipulate lipids, the fats that compose the cell membrane. These tools rely on manipulating proteins that regulate membrane composition. In the artificial cortex, researchers can directly change the membrane by mixing different lipids, an approach that is not possible in cells.

Landino uses commercially available lipids to assemble the artificial cortex. She adds these to a flat well, which creates a surface layer that will be closest to the microscope. The researchers use an inverted microscope, which means that the magnification component is underneath the sample being studied. On top of that, she adds a layer of cytoplasm taken from frog eggs that contains all the protein components normally found in the cytoplasm. The moment the cytoplasm is laid over the artificial membrane, the proteins within the cytoplasm begin to self-assemble—just as they would in a natural animal cell, Landino said.

"When a cell divides, it pinches in the middle and splits in two. We also see these wave patterns form in cells, and we see that they're associated with cell division," Landino said. "We think that's the function of the waves, to prepare the cell cortex to undergo a dramatic change in shape, but it's really hard to test in cells. So we're hoping to use this artificial system to both understand how these wave patterns form, and also what their function might be."

Ann Miller, associate professor of molecular, cellular and developmental biology, is senior author of the paper. The research, which was funded by the National Science Foundation, is part of a collaborative effort between the Miller lab and Anthony Vecchiarelli, assistant professor of molecular, cellular and developmental biology, as well as collaborators at the University of Wisconsin and the University of Edinburgh.

"These findings represent a powerful, novel synthetic platform for cell-free studies of the mechanisms that regulate cortical patterning," Miller said. "The system that Dr. Landino has developed opens new possibilities for deepening our understanding of how self-organized cortical patterns drive essential cell processes like cell division."

More information: Jennifer Landino et al, Rho and F-actin self-organize within an artificial cell cortex, *Current Biology* (2021). DOI: 10.1016/j.cub.2021.10.021

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