Claustrophobic cells slow their own growth, forming beautiful patterns of concentric circles

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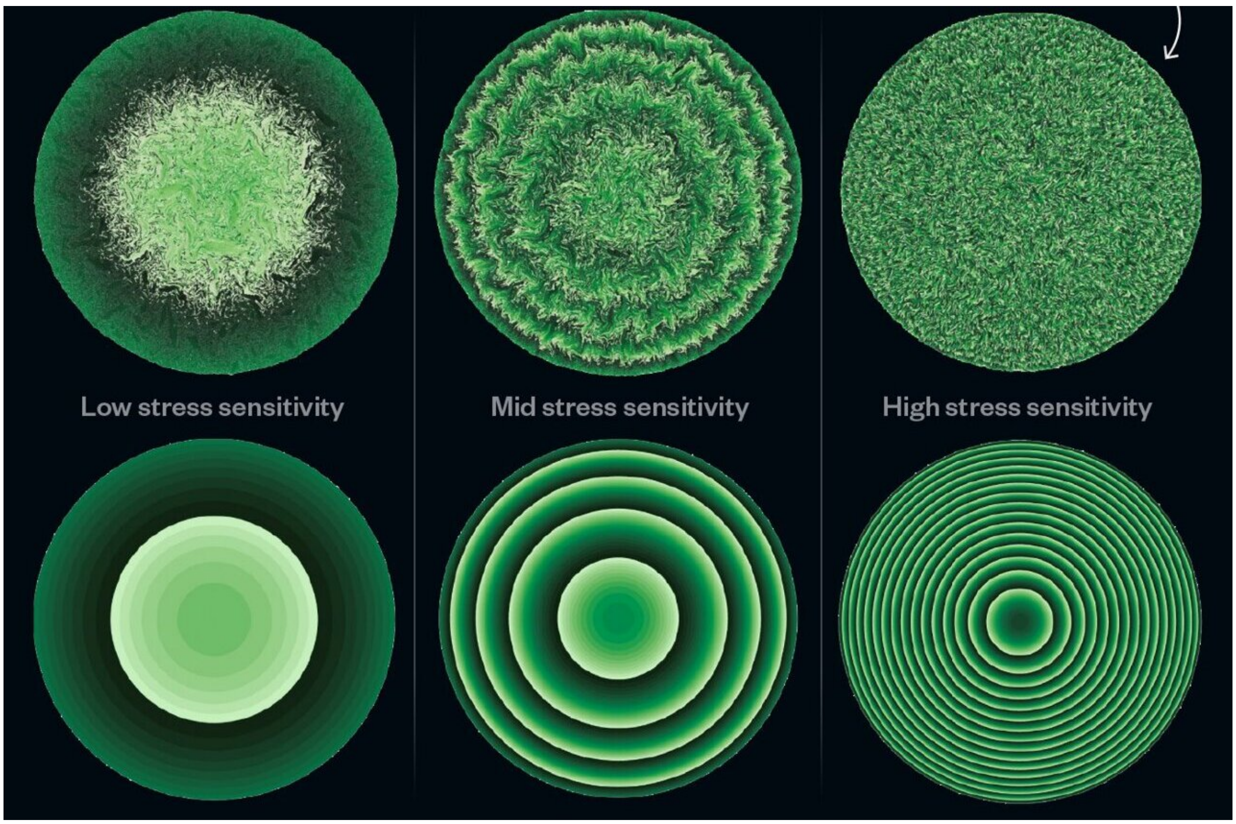


An infographic explaining the new findings about cell proliferation. Credit: Lucy Reading-Ikkanda/Simons Foundation

Like so many organisms on the planet, when cells experience mosh-pitlevel crowding, they may just become stressed. Yet unlike most other life forms, cells subject to physical stress from crowding by neighbors can find some relief by dramatically slowing their own growth—and in doing so form an eye-catching pattern of concentric circles as a spectacular consequence.

This process, discovered through simulations and modeling of dividing bacterial colonies, is described in a new study published in *Physical Review Letters*. The findings could suggest new ways to slow the growth of harmful microorganisms in infections or manufacturing, says study lead author Scott Weady, a research fellow at the Flatiron Institute's Center for Computational Biology in New York City.

"I was definitely surprised to see that cells under this kind of mechanical stress can mitigate growth in that way," Weady says. "It's interesting that they form these concentric circles where each ring shows how much they've been stifled by their neighbors, ultimately impacting how large they can grow. It's a robust pattern that comes from a very simple rule, and it's just something that no one had really thought to measure before."

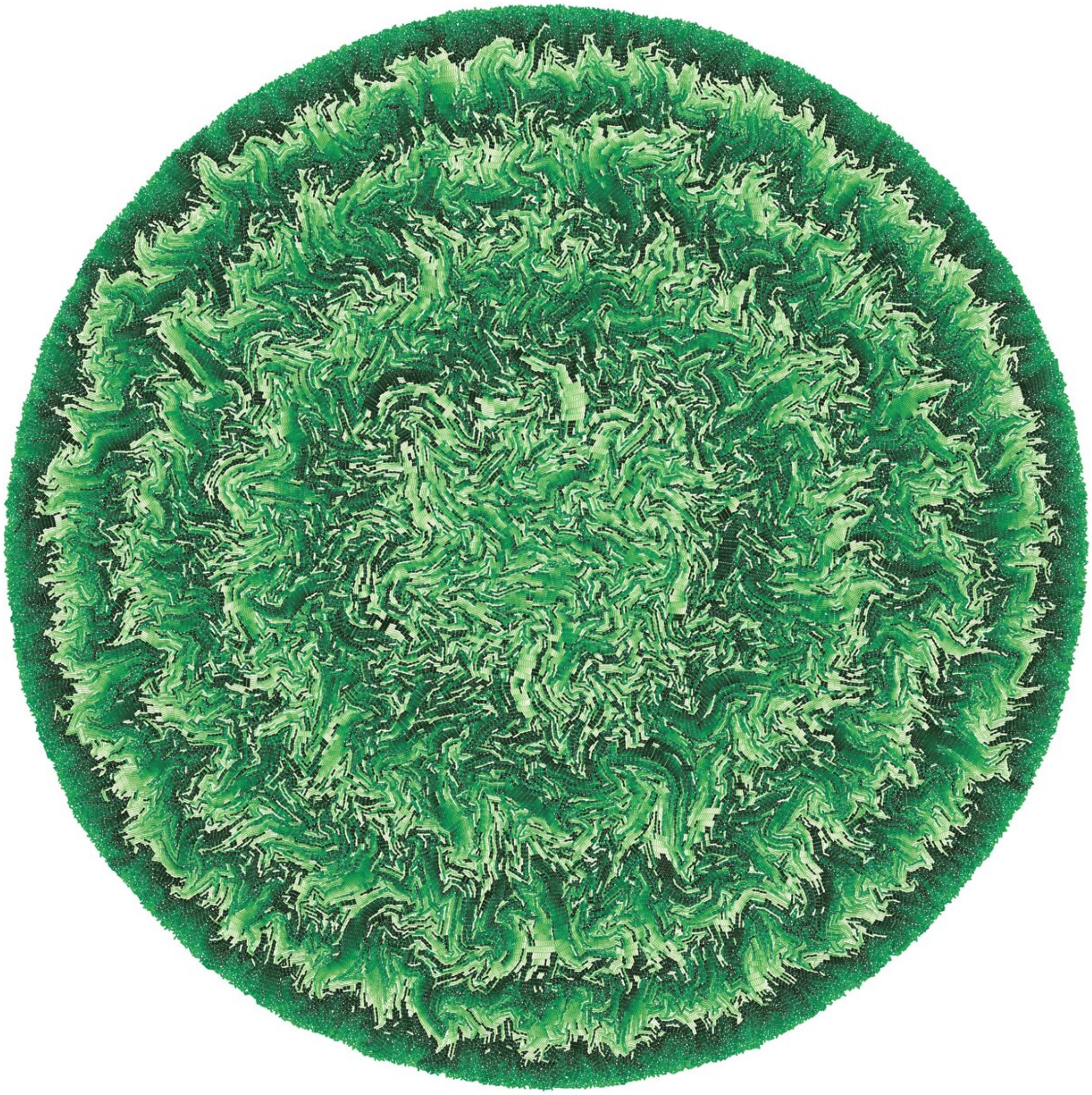
Weady co-authored the study with fellow Flatiron Institute researchers Bryce Palmer, Adam Lamson, Reza Farhadifar and Michael Shelley, as well as Taeyoon Kim of Purdue University.

A deep dive into dividing cells

Weady's group is interested in biophysical modeling—or, as he puts it, how small-scale rules govern large-scale behaviors. In this case, his team wanted to investigate cell proliferation, the process by which cells divide to make more copies of themselves.

The group began with an exploratory approach, examining simulations of growing bacterial colonies. In the beginning, they were looking at more general measures like cell size regulation, but then started noticing a pattern.

Typically, the cell proliferation process is exponential: A cell splits in two, and those offspring split in two, and so forth, to keep growing at an increasing rate. In their simulations, however, the team noticed that cells weren't dividing as you'd expect—in fact, their proliferation rate significantly slowed as their environment became more crowded.



Particle simulations capture the cycles in which bacterial cells grow and then divide. Credit: Weady et. al (2024); Lucy Reading-Ikkanda/Simons Foundation

"You start with a single cell, which feels little or no stress. Then it divides, and those cells divide, and the cells closer to the center get more and more stressed because there's more pushing on them, and that causes them to slow their growth," Weady says. "And so, as you move toward the edge of the circle, you get these bands of nonuniform stress sensitivity that manifest as concentric circles."

This initial work is based on particle simulations, which illustrate how the proliferation process plays out in a relatively small number of cells. Based on this data, the team then developed what's called a continuum model, which estimates how the process could work in extremely large numbers of cells.

"With particle simulations, you're looking at something discrete—in this case bacteria that you're tracking over time," says Weady. "But the continuum model operates differently, by assuming that the number of particles is very large, so that you can represent it as a continuous material. This helps us better investigate the process on a larger scale and understand how robust it is."

Excitingly, the team found that their continuum model matched up very well with what they saw in the particle simulations, suggesting that their hunch was true: Cells backed into a corner will slow their own growth, creating an arresting pattern in the process.

Getting a grip on cell growth

Cell proliferation is valuable to study because it's such a fundamental process, but also because when the proliferating cells are harmful (think: a bacterial infection), they can cause detrimental effects.

"It's important to figure out how the process is naturally regulated, as well as how to control it," says Weady. "Our model identifies environmental factors that can enhance a cell's response to mechanical stress, and promoting these factors could slow down exponential growth."

The model developed in this study could also serve as a basis to investigate other cellular behaviors.

"I think the model is a useful tool for people who want to look at perturbations to the way cells respond, whether through stress, nutrient access or something else," Weady says. "It's very clear how to ask those questions with a model like this, so I find that exciting as far as what it will enable more broadly."

More information: Scott Weady et al, Mechanics and Morphology of Proliferating Cell Collectives with Self-Inhibiting Growth, *Physical Review Letters* (2024). DOI: 10.1103/PhysRevLett.133.158402. On *arXiv*: DOI: 10.48550/arxiv.2405.10158

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