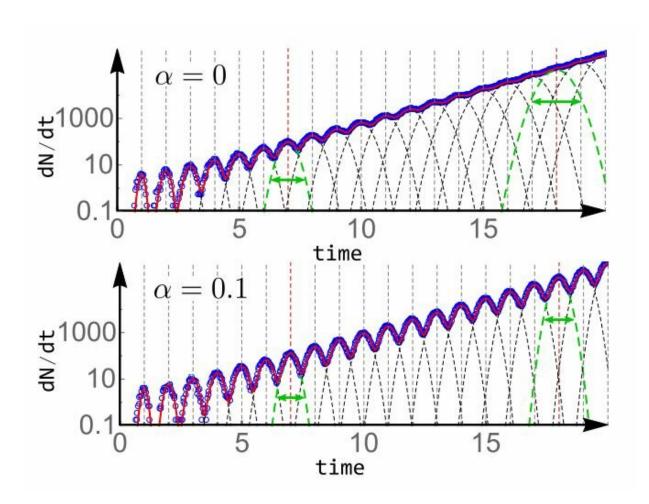


## Bacterial population growth rate linked to how individual cells control their size

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Log-scale plot of the expected value of the rate of change of the number of cells in a population starting with a single cell, calculated analytically (red solid curve) and compared with simulation (blue circles). The rate of change of the number of cells can be written as the sum of the division rates (parabolic dashed lines) of all generations. (Top) In the absence of cell size control,  $\alpha = 0$ , the distribution of division times of higher generations get wider and start to overlap, damping



out the oscillations in the growth rate. (Bottom) In the presence of even a small cell size control,  $\alpha = 0.1$ , the distribution of successive division times quickly approach a steady state distribution with a finite variance leading to the persistence of oscillations in the growth of the population. The distribution of timing of the 7th and 18th generations are highlighted in both cases for comparison. Credit: arxiv.org/pdf/1809.10217.pdf

When family weddings all seem to coincide with one another, the phenomenon happens for a reason. An individual and their first cousins tend to be of a similar age, so their weddings usually happen in a similar time frame. But weddings for extended family members, say second and third cousins, tend to be more spread out. This is because the time between one generation to the next varies, meaning that families become more spread out from generation to generation.

A new study by University of Pennsylvania post-doc Farshid Jafarpour from the Department of Physics & Astronomy, who works in the lab of Andrea Liu, reveals that variations in generation times don't accumulate over multiple generations in single-celled organisms, like <u>bacteria</u>. He proposes a new theory, published in *Physical Review Letters*, that describes how factors that regulate the size of individual cells influence the growth rate of an entire population.

Unlike animals and plants, bacteria increase the size of their population simply by growing in size and then splitting in half to make two new bacterial cells. By studying bacteria when they are dividing on a regular basis, known as the exponential growth phase, Jafarpour was able to develop a model that mathematically describes this fundamental phase of population growth. "If you want to study the physics of bacterial growth, you really want to remove all the other parts that are not part of the growth phase," he says.



Jafarpour used a combination of math equations, computer simulations, and data from biology experiments that tracked the growth of individual bacteria cells. He was surprised to find that the model predicts that bacteria oscillate between slower and faster bursts of growth, in "synchronized bursts of divisions," instead of the population growing at a constant rate. These population-level oscillations in growth now provides a new, mathematical way for biologists to think about and to study population dynamics.

Previously, biologists knew that the generation time in bacteria populations was directly related to the size of individual cells. If a bacterium grows for too long, for example, its daughter cells are larger, and they must divide earlier to compensate for their size difference. This process, known as cell-size regulation, also cancels out some of the variability in the generation time, which keeps the division times in sync with one another for a much longer period of time than previously expected. It's this individual metric of cell size regulation that also seems to be causing the oscillations in growth rates seen in Jafarpour's model.

"The variability in <u>generation</u> times has two different sources: the variability in growth and the variability in division," Jafarpour explains. "The interesting result is that cell-size regulation is completely cancelling out the variability in division, so the only thing that's left is the variability in the growth of the individual <u>cells</u>. And, because that's smaller, the oscillations last a lot longer than you would expect."

This new model can now be used by biologists to obtain information on the <u>variability</u> of individual growth rates, which are difficult to measure in the lab but are extremely important for studying bacterial evolution. And while this model would need some modifications before it could be used to study other species, Jafarpour believes that helping biologists gain a better understanding of the physics that underlie <u>population</u> growth in bacteria is just one of many ways that physics can support the



work done by biologists.

"Biology has become more focused on figuring out the molecular basis of mechanisms since the 1950s with the discovery of the structure of DNA, but now we are reaching a level where we have to go back and do more quantitative studies. Physicists have a long tradition of working with real-world systems, knowing how to apply a lot of the quantitative methods developed in mathematics and also understanding what variables are relevant and what variables aren't," Jafarpour says.

**More information:** Farshid Jafarpour, Cell Size Regulation Induces Sustained Oscillations in the Population Growth Rate, *Physical Review Letters* (2019). DOI: 10.1103/PhysRevLett.122.118101, arxiv.org/pdf/1809.10217.pdf

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