UC San Diego
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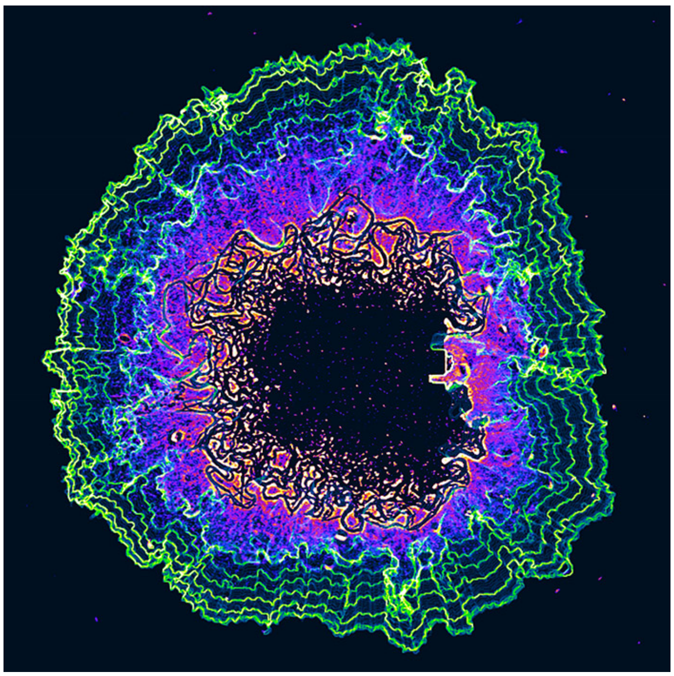
Resolving Social Conflict Is Key to Survival of Bacterial Communities



UC San Diego biologists imaged oscillations (displayed as colored contour lines) from a growing biofilm at center. Credit: Suel lab, UC San Diego

Far from being selfish organisms whose sole purpose is to maximize their own reproduction, bacteria in large communities work for the greater good by resolving a social conflict among individuals to enhance the survival of their entire community.

It turns out that, much like human societies, bacterial communities benefit when they can balance opposing needs within the group.

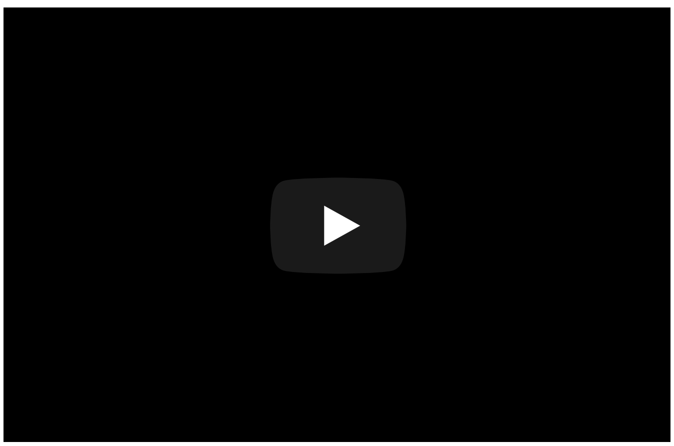
The discovery of this unusual behavior among bacteria in large communities, detailed in a paper in the July 22 advance online publication of *Nature,* comes not from any inherent altruism among the bacteria. Instead, it "emerges" spontaneously from the community in which the bacteria grow.

"It's an example of what we call 'emergent phenomena'," explained Gürol Süel, an associate professor of molecular biology at UC San Diego who headed the research effort. "Emergent phenomena are processes that you cannot observe or understand if you are studying individuals. You can only understand the process if you look at the collective."

Süel and his colleagues observed this unusual phenomenon while carefully measuring the growth of a microbial community called a "biofilm." Such communities of bacteria and other microorganisms form thin structures on surfaces—such as the tartar that develops on teeth—that are highly resistant to chemicals and antibiotics.

The UC San Diego biologists discovered that when the biofilm community reached a certain size, it suddenly began to oscillate in its growth. By complementing their experiments with mathematical modeling, the researchers discovered that these oscillations resolved a social conflict between individual cells that were cooperating, but also had to compete for food. The reason these biofilms are so hardy is that individuals within the community manage to resolve this internal conflict through coordinating their activities in space and time.

“Scientists have been trying for the longest time to figure out how to kill these biofilms,” said Süel. “We also were puzzled by the resilience of these biofilms until we realized that the ability to resolve conflicts that naturally arise within the bacterial communities may play an important role.”



Onset of Biofilm Growth Oscillations

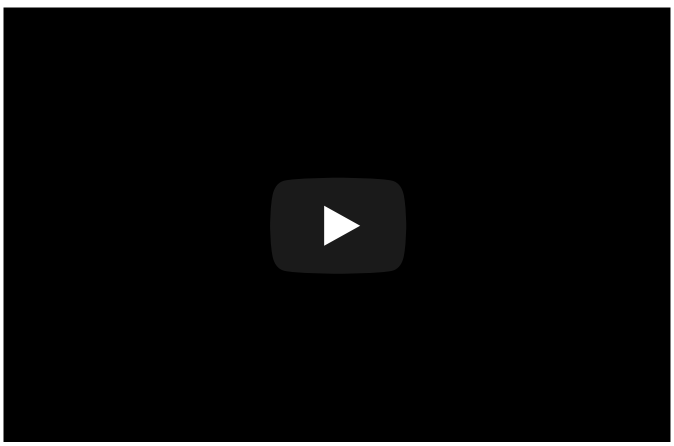
The conflict is essentially this: Bacteria at the outer edges of the biofilm are the most vulnerable within their community to chemical and antibiotic attacks. At the same time, they also provide protection to the interior cells. But the bacteria at the outer edge are the closest to nutrients necessary for growth. So if they grow unchecked, they can consume all the food and starve the sheltered interior cells.

But that doesn’t happen, because the biofilm develops an ingenious solution to this problem that the scientists call “metabolic codependence.” Essentially, the interior cells produce a metabolite necessary for the growth of the bacteria on the outside. This provides the inner cells with the ability to periodically put the brakes on the growth of outer cells, which otherwise would consume all the food and starve the cells they are protecting from attack. By periodically preventing the growth on the periphery, inner cells ensure that they have sufficient access to nutrients. By keeping the protected inner cells alive, the biofilm has a much higher chance of surviving antibiotic treatment.

This strategy allows bacteria with conflicting needs to take turns, like drivers approaching an intersection from different directions. In many ways, the internal social conflict within bacterial communities is not unlike the conflicts that opposing groups of individuals must find ways to resolve in order to maintain successful nations or communities.

“Here we have simple bacteria that are genetically identical,” added Süel, “and yet in the process of forming a community, they develop distinct areas, like a medieval castle with protective walls manned by soldiers that can provide protection for peasant families to ensure survival of their clan. The fact that you’re starting a community where individuals will find themselves either manning the walls or being tucked away inside the castle, gives rise to this emergent phenomenon where you have a division of labor. The bacteria are not ‘aware’ of this division of labor, none of the bacteria are doing anything consciously. It’s something that just emerges out of the complexity of a system with social interactions.”

Süel and his colleagues, who work in an emerging discipline of biology that employs mathematics and physics called “quantitative biology,” focused on developing new methods to measure and mathematically model biological systems.



Oscillatory Growth of Biofilm

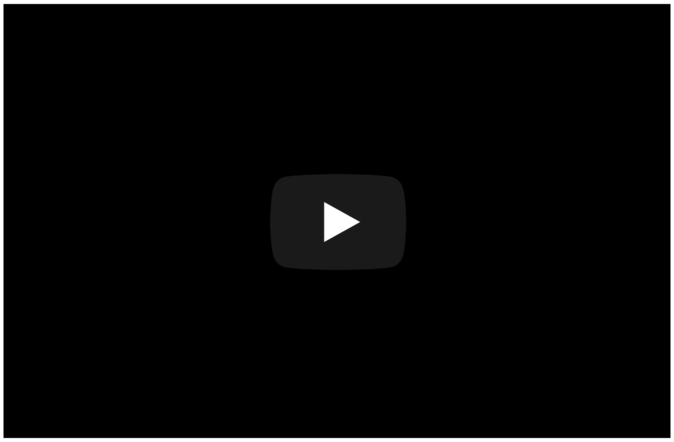
“We developed new techniques to precisely measure biofilm growth, and then quantitatively perturbed the system,” said Süel. “And what we found was that the metabolic pathway in question may have been selected for this process by evolution because it involves a small molecule, ammonium, which can diffuse, that is, can get in and out of the cell quickly and can be shared among bacteria.”

The discovery that bacteria essentially signal one another with this ammonium metabolite also allows them to chemically communicate with one another over very long distances.

Because the discovery offers a new way to control the growth of biofilms by eliminating the co-dependence of the interior and exterior bacteria, making them selfish rather than altruistic, UC San Diego has submitted a patent application to license the discovery.

“This is a new way to also think about attacking disease-causing biofilms, which are responsible for two-thirds of infections in hospital clinics and are a thousand times more resistant to antibiotics than the same bacterial cell might be outside the biofilm,” Süel explained. “We allow the peripheral cells to become selfish or independent and then they kill the protected interior cells for us.”

Beyond the obvious medical and industrial applications, bacterial communities may also offer some other lessons for modern society.



"The social conflict we studied is directly applicable to conflicts that arise in human societies," added Süel. "We all face the social dilemma where supporting others, even our competitors, may ultimately make our society stronger. We may be able to learn more about how to resolve our own social conflicts by studying bacterial societies."

Other members of the research team were Jintao Liu, Arthur Prindle, Jacqueline Humphries, Dong-yeon Lee and San Ly from UC San Diego, Marcal Gabalda-Sagarra and Jordi Garcia-Ojalvo from the University of Popeu Fabra in Spain, and Munehiro Asally from the University of Warwick in the United Kingdom.

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