Cover Story

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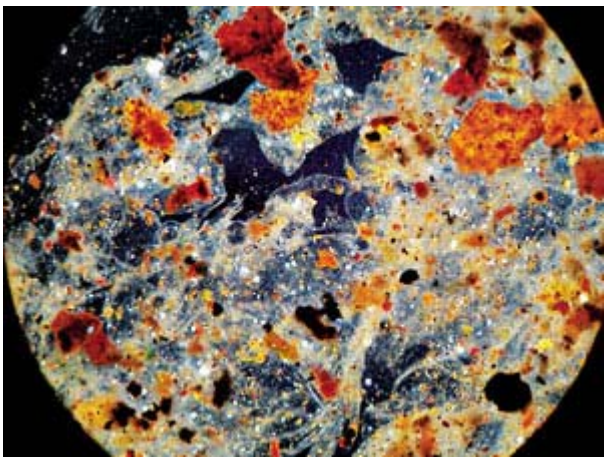
Battling Biofilms

It took decades before researchers believed that bacteria were sophisticated enough to organize into slimy biofilms

Sarah Everts

From Louis Pasteur onward, microbiologists have mostly studied bugs in suspension, not realizing that microbes are far happier in close quarters, living in slimy, carbohydrate-based scaffolds called biofilms or protected in the light organ of a squid or the root of a plant.



Marlin Vangsness/University Of Dayton Research Institute

Fuel Fare A bacterial biofilm at the bottom of a jet fuel storage tank can clog filters, corrode tank coatings, and degrade aviation fuel.

Until the 1990s, microbiologists weren't prepared to accept the fact that bacteria live social lives, chatting through quorum sensing and living in biofilms, says Staffan Kjelleberg, a microbiologist at the University of New South Wales. "Studying microbes in suspension is also far simpler than studying them in a biofilm."

And so in the 1970s when researchers discovered that individual microbes were using chemical signals to coordinate luminescence, microbiologists "vehemently" did not pay attention, says Kenneth H. Nealson of the University of Southern California, who discovered quorum sensing as a postdoc at Harvard University with J. Woodland Hastings. "Reviewers would write things like, 'We can't find anything wrong with this paper but it can't be true.'"

During that same decade, advances in electron microscopy sparked another voice of dissent against the notion of a solitary bacterial existence. J. William Costerton, then a microbiologist at the University of Calgary and now at the University of Southern California, also happened to be an avid mountain climber. On a trip to the Canadian Rockies, he sampled water from mountain streams that was so clean—fewer than eight bugs per mL—that "you could wash glassware in it.

"But the rocks were slippery and clearly covered in a slimy film. When we looked at the films, using electron microscopy, we saw bacteria clinging to them," Costerton recalls. At the time, he was also a consultant for Alberta's oil industry, whose pipes were being clogged by what appeared to be bacterial films. Costerton's own son had cystic fibrosis, which is exacerbated by films of bacteria in the lung. "I argued that bacteria don't know where they are, in a stream or a lung; it makes no difference to them. It was live bacteria living in these films that were causing the problem. So if they were alive in these films, maybe that's how they liked to live," Costerton says. "For years, other microbiologists pooh-poohed this idea. They said, 'These are dead cells. The important ones are planktonic (floating cells).'"


Montana State University
Stewart


University of Southern California
Costerton


University of Southern California
Nealson

"The development of sophisticated microscopy revealed structure and function far more complex than we had ever supposed," says Philip S. Stewart, director of the Center for Biofilm Engineering at Montana State University. "We used to think biofilms were just amorphous slime stuck to a surface. Now we talk architecture, communication, cooperation. These features suggest a multicellular lifestyle."

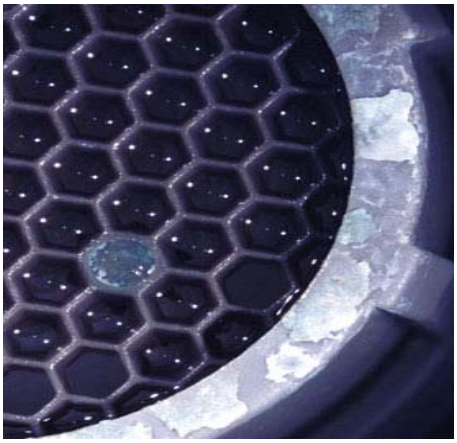
The microbiology community finally came around after researchers in other fields were noticing biofilms too. "At first, I felt like a missionary, going to many different meetings in many different fields and presenting my biofilm research," Costerton says. "The first people to show interest in biofilms were engineers concerned with pipe corrosion, which can occur through metal-fixing bacterial films. The first medical researchers to pay attention were the urologists whose patients with catheters had persistent infections."

According to the National Institutes of Health, biofilms account for at least 80% of microbial infections in the body. Treatment is another thing: By some estimates, healing a biofilm infection on a catheter can cost upward of $25,000.

If biofilms are bacteria's natural habitat, researchers are bound and determined to block their formation. "There's a very practical drive. We want to heal human chronic infections on medical implants. We've even found evidence for biofilms in the open wounds of diabetics and in bed sores. They need to be prevented," Stewart says.

Blocking quorum sensing is just one strategy to thwart biofilms. But what should researchers specifically target when a variety of species coexist in a biofilm? Researchers estimate that in dental plaque, hundreds of different species of bacteria live together. Dozens of species populate the lungs of cystic fibrosis patients. Initially, when a quorum of bacteria colonize a surface, the genes turned on by their chitchat produce the proteins that construct the slimy polysaccharide, DNA, and protein matrix. So many bacterial species make for a very complex matrix, since each microbe is expelling its own mix of biofilm-forming polymers.

"People are trying to figure out the biosynthetic pathways that govern matrix production. This could lay the foundation for interruption," Stewart says. "But each kind of bacteria makes several polymers, and the pathways are diverse. If you have



Center for Biofilm Engineering/Montana State University

Shower Film Bacterial biofilm on a shower head.

a biofilm of several pathogens, then it can be difficult to find one inhibitor that's going to stop everyone's biosynthesis," Stewart says. "However, one common feature of these matrix polymers is acetylation or pyruvylation. These modifications seem to change the physical chemistry of whether the matrix is sticky or not." So instead of blocking synthesis, researchers are trying to block these modifications.

Researchers are also looking for enzymes that would degrade the matrices. And they are trying to change the chemistry of surfaces that tend to be scaffolds for biofilms, putting inhibitors for the proteins that link to surfaces on medical devices, for instance. "If we can prevent attachment, there's not a problem to treat," Stewart says.

Graham Hatfull, Anil Ojha, and Tom Harper/University of Pittsburgh

Lung Biofilms of the bacteria that cause tuberculosis.

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