University of Southern California

Annenberg Files

A showcase of Annenberg student work

annenberg.usc.edu

Story Files

That Lawn Between Your Teeth

Outside Bill Costerton's cavernous office on the USC Dentistry School's fourth floor, a cartoon shows a bacterium sitting in a psychiatrist's office.

"I just feel like something's missing," the bug says to its bacterium shrink. "I'm thinking of joining a biofilm."

The cartoon bacterium could find a few biofilms to join at the school where the high, piercing whine of a dentist's drill rings through the hallway. Despite popular belief, the sugar from too many lollipops didn't cause the decay the drill bit is obliterating. The invisible culprits are actually the lawns of bacteria that fed on the sweets along with the unfortunate patient.

Costerton invented the word biofilms, meaning communities of bacteria. USC recruited him from the University of Montana a few years ago to direct a new Center for Biofilms—a center uniting engineers, molecular biologists, physicists, doctors and material scientists. He has devoted his life to studying bacteria—the microscopic bugs as much a part of this earth as the air we breathe.

Louis Pasteur first brought bacteria to notoriety in the mid-1800s when he saw under his microscope "great tangled dancing masses of tiny rod-like things, some of them alone, some drifting along like strings of boats." He noticed the lightning-quick multiplication of these "wee beasties," and he also discovered that they were infectious. When he stuck a chicken with a clean sliver of wood dipped into the liquid mixture of anthrax-causing bacteria, the hen died a day later.

One fateful day about 70 years later, Scottish biologist Alexander Fleming found a mysterious ring on one of his forgotten Petri dishes where no bacteria or mold grew. He isolated the substance—penicillin--and found that it could kill free-floating, "planktonic" bacteria.
Modern medicine was thus born.

The power of free-floating bacteria to make animals, including humans, sick is a cornerstone of today's treatments for infections. An infection in the body can, in many cases, be killed with the right dose of antibiotics. Until Costerton came along, the basics of microbiology had remained unchanged since Pasteur and Fleming made their discoveries. For reasons unknown, antibiotics are almost useless against a biofilm.

"The universal approach was so flawed that we missed the organism," Costerton says. "It's like studying botany for 150 years, and only seeing the seeds."

This was a simple case of not seeing the bacteria as they really live—as members of a community. A biofilm is a group of bacteria that colonizes a surface. It starts with a single bacterium that happens by a nice piece of real estate, like your tooth, and decides to stick. The bacterium excretes sticky glue, made of sugars and starches, which serves as a landing pad for others to join.

Once a large group congregates, complex features of biofilms begin to emerge. The bacteria leave room for nutrient rivers to flow between them. Some bacteria assemble into large mushroom plumes that billow with the ebb and flow of the rivers, allowing the bugs to sense their environment. The bacteria differentiate. Some are the powerhouses and some are the waste removers. Biofilms have all of the characteristics of tissues or organs, or even animals. A complex, multicellular organism emerges from a mass of undifferentiated precursors.

Biofilms are organisms unto themselves.

This paradigm shift from free-floating single bugs to stationary communities of bacteria that Costerton and his colleagues created has reverberated throughout medicine, biology and industry.

"These kinds of studies spawned a new perspective," Rita R. Colwell, former director of the National Science Foundation, told a group of microbiologists at a recent conference. "Instead of trying to eradicate microorganisms, we should attempt to manipulate and engineer their behavior."

Costerton's perspective on bacteria incorporates bits and pieces from all sorts of different places. One of his graduate students said Costerton is "the great facilitator" on campus. Costerton is also multilingual. "He speaks engineering, math, physics, microbiology, medical, dental, and even botany," another student said. "I've seen him leave a meeting with doctors where he was talking about the 'minimum inhibitory concentration' of antibiotics, walk into a room of physics professors and immediately shift his language to things like 'fluid dynamics.'" Just like a biofilm, he transfers information through complex infrastructures.

As he begins talking, Costerton sketches little pictures on post-it notes and sticks them onto my notebook. He draws a detailed picture of a river with rocks in it while he tells me about his early career. After he received his PhD from the University of Western Ontario, he became a photographer, of sorts. He took pictures of bacteria with a high-powered microscope in Marmot Creek in Alberta, Canada. To Costerton's surprise, most of the bacteria he photographed were living in large groups. His observation was published in American Scientific in 1978 and immediately embraced by the scientific community.

To find out how prevalent these biofilms truly are, to figure out if the group of bacteria he saw in Marmot Creek was a fluke or the normal state of affairs for bacteria in the wild, Costerton's next step was clear. "I put on my hiking boots."

Costerton's long walk led him from the slimy rocks of the Athabasca River in Alberta to the beaks of breeder hens on a farm in the Midwestern United States. He has examined industrial water pipelines, oil refineries and bovine tongues, and he has found biofilms on them all.

After his journey spent isolating and studying bacteria in the wild, Costerton estimates that about 99.9 percent of all bacteria exist in a complex community.

Biofilms are up to a thousand times more resistant to antibiotics than their free-floating counterparts. Although the reasons for this aren't completely understood, researchers, including Costerton, believe the answer lies in the gunk around the bacteria.

Biofilms are composed of bacteria, but that's not all. The bacteria secrete a sugary, sticky slime, called the extracellular polymeric substance (EPS). The EPS forms the bulk of the biofilm, including the mushroom extensions and rivers' edges. These long sugar and carbohydrate molecules hold the bacteria together. This starchy-sweet paste also serves as a sticking pad for passers-by to land on and join the biofilm. When too many passers-by have joined and a critical limit has been reached, bacteria, through a mechanism called quorum-sensing, are able to detect the crowded conditions and launch some of their neighbors off into uncharted territory to establish a new biofilm colony elsewhere.

These colonies have since been found in places as fiery as volcanic hydrothermal vents and as icy as glaciers, in temperatures from 0-100 degrees Celsius, and with pH numbers, measuring acidity and alkalinity, ranging from 1 to 11.

One of the last uncharted territories was the human body. In 1983, Costerton found a biofilm on a patient's urine bag catheter that had been the culprit behind a series of urinary tract infections. This discovery was the first evidence that biofilms could live in humans. He and his colleagues speculated that maybe other infections were also caused by biofilms.

Although the scientific community was willing to acknowledge the fact that biofilms are the predominant form of bacteria in the natural environment, they were loath to accept that biofilms were in our bodies. So much of modern medicine was based on fighting infections with antibiotics (often quite successfully), that it seemed outrageous to suggest that our bodies could be harboring what Costerton calls "smoldering, indolent biofilm infections."

It turns out that these low-grade chronic biofilm infections can lurk in our bodies undetected for months, even years. When a weakened immune system lowers our defenses, the biofilm can grow to capacity and send its bacterial members out to new areas, like the bloodstream. This acute bacterial attack can cause the identical symptoms as a normal bacterial infection, and there was no way of knowing that there was an insidious biofilm causing it all. These free-floating biofilm cast-offs are susceptible to antibiotics while on their journey, and killing them often alleviates the patient's symptoms. The mother biofilm, however, would linger, safe from harm.

Costerton presented his data on the catheter biofilm, and his idea that maybe other infections could be based on 'indolent' biofilms, at a microbiology conference in 1978. He challenged the status-quo of treating infections with antibiotics, and there were strong objections from the audience. In particular, Harry Smith, an internationally recognized medical researcher, critically and publicly denounced Costerton's ideas. Smith went so far as to request extra time for the conference session so that he could more thoroughly debunk the idea that biofilms might be in the human body.

"He was witty, charming, and too good of a speaker," Costerton says with a grin. "He beat me. So I went out to prove it."

And he did. Costerton has since published more than 580 papers on biofilms, and many of them directly address biofilms in the human body. He has found biofilms on teeth in the form of plaque (which is why we are sitting in the dental school), inner ears (the cause of chronic ear infections in young children are biofilms), lungs (cystic fibrosis is thought to be caused by biofilms), and on almost every implanted medical device (knee replacements, heart stents, and pacemakers).

Debra Greene
Thomas Kelley
Allison Louie
Adriana Padilla
Haley Poland
Amanda Price
Jessica Roberts
Laura Sanders
Shirley Shin
Nick Street
Amy Tenowich
Lindsay Watts
Laura Weber
Rocio Zamora

To find a biofilm yourself, just run your tongue over your teeth. If you think that you feel a little fuzz, you're not alone. You are harboring entire communities of bacteria in each of those deep crevasses. Brushing, although beneficial, can't destroy them, and Listerine only kills the bugs on the surface. The majority of the biofilms persist happily, unperturbed, between your pearly whites.

The CDC now estimates that over 65 percent of infections are biofilms. The NIH estimate is even higher—they say 80 percent of all diseases in the developed world are caused by biofilms. Ten years after the infamous showdown at the microbiology conference, Costerton invited Harry Smith to give a seminar on bacteria at his department in Calgary. "He handed over the bouquet," Costerton says. "He even quelled skeptics in my own department."

The next wave of biofilm research is focused on how bacteria communicate to form a biofilm. There must be some way for a message, a molecular mechanism, to pass from one bacterium to another to tell each other what shape to take, what job to do, whether to stick or swim. If researchers can identify these signals and block them, they can prevent biofilm formation. The seven largest pharma companies are now working on these signal inhibitors (secretively, of course).

"I'm waiting for a big signal inhibitor any day now," says Costerton.

Despite what he says, Costerton is not the type to wait around for anything. His next project as the founding member of a new community, the Center for Biofilms, has kept him on the move almost continuously. Although he has been at USC only a few years, he has surrounded himself with talented, innovative researchers from diverse disciplines who all want to understand biofilms. Costerton makes people stick.

After we finish talking, I push open the large oak office door back out into the hallway. A dental student sees me and jokes, "Whoa! Watch out for that biofilm on the door."

Biofilms are everywhere, and now, thanks to Bill Costerton, everyone knows it.

Permalink