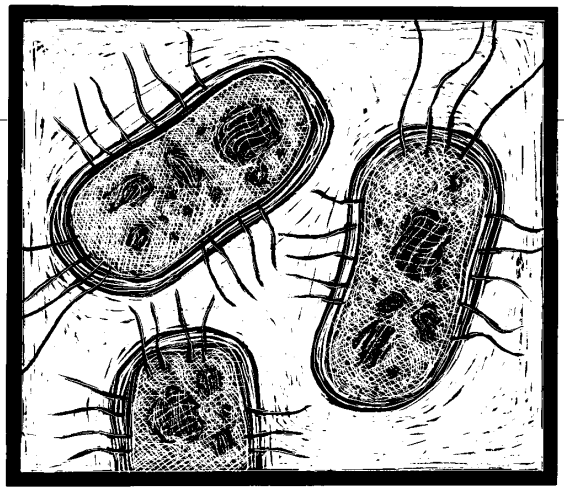
Battling biofilms

By George O'Toole, Ph.D.



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We encounter biofilms every day—that slimy build-up in your sink drain, the green stuff on the walls of your fish tank, and the slippery coating on rocks in a streambed are all communities, or biofilms, of microorganisms attached to surfaces. Most bacteria spend the majority of their lives attached to a surface, but, until recently, microbiologists were interested in studying bacteria only in their planktonic cell form—that is, swimming freely in liquid environments.

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Evident: One of the earliest reports concerning biofilms is a 1933 paper by Arthur Henrici, who stated, "It is quite evident that for the most part water bacteria are not free-floating organisms, but grow upon submerged surfaces." The actual word "biofilm" wasn't coined until 1978; William Costerton, who is now the director of the National Science Foundation-funded Center for Biofilm Engineering at Montana State University, came up with the term. His early studies on environmental and medical biofilms quickly caught the interest of the scientific community. His center developed new technologies for studying biofilms, including flow cells, which are small chambers that allow the continuous feeding and observation of a live biofilm, and microprobes, which permit detailed measurements within biofilms. In addition, confocal scanning laser microscopes, which produce crisp images of biofilms magnified up to 1,000 times, now provide detailed images of live biofilm communities.

We now know that biofilms are aggregates of microbes with a distinct architecture. They are like tiny cities where bacterial cells, each only one or two micrometers long, form towers that can be hundreds of micrometers high. The "streets" between the towers are really fluid-filled channels that bring in nutrients, oxygen, and other necessities that keep the microbial metropolis thriving.

Flagella: Different microbes have their own ways of forming biofilms. *Pseudomonas aeruginosa*, the organism that causes infections in the lungs of cystic fibrosis patients, uses propeller-like flagella to move to a surface, and then hair-like pili to move across the surface and attach to other *Pseudomonas* to form clusters of cells. *Staphylococci*, another major group of biofilm-forming organisms, are completely nonmotile, yet still form the characteristic towers and channels. It's thought that sticky extracellular sugars may hold these structures together.

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In the last decade, numerous biofilm-related problems have driven researchers to explore the molecular basis of biofilm-building. Biofilms cost industry billions of dollars a year. They clog pipelines, sour oil, and foul ships' bottoms. In medical settings, biofilms form on the surfaces of catheter lines, contact lenses, pacemakers, artificial hips, and other surgical implants. The Centers for Disease Control estimates that more than 65% of hospital-acquired infections are due to biofilms. Biofilm-based infections often lead to extended hospital stays—an average of three days longer—and place a big economic burden on the health-care system as doctors struggle to fight them.

The problem is that biofilm-grown bacteria are incredibly resistant to antimicrobial agents. Microbes in a biofilm can be up to 1,000 times more resistant to antibiotics than the same strain growing planktonically. Consequently, biofilm-based infections cannot be treated using standard antibiotic therapies. Often, the only treatment recourse is to remove the contaminated implant, causing additional trauma to the patient. While no one is sure just why biofilms are so resistant to biocides, scientists have speculated that the clustering of bacteria may protect some organisms at the center of each group. It's also possible that biofilm bacteria may develop new properties—slower metabolism, antibiotic-degrading enzymes, the ability to pump drugs out, or the altered expression of biofilm-specific genes—that allow them to resist antimicrobial agents in a special way.

Strategies: Until recently, the search for new antibiotics has focused on fighting infections in microbes' planktonic forms, so it is not surprising that most antimicrobial compounds are ineffective against biofilm infections. We need new strategies to identify therapies that will target the biofilm lifestyle. Work from our lab and others has led to two novel approaches to developing antibiofilm compounds. First, large-scale and easy-to-manipulate systems to study biofilm formation will allow us to test drug libraries for new compounds effective against biofilm-grown microbes. Second, since we have identified some of the genes and regulatory systems required to make a biofilm, we can focus on designing compounds that will target and specifically disrupt this process. Fortunately, biofilm research has attracted the attention of pharmaceutical companies, and they may be interested in developing new drugs to fight biofilm infections.

I'm optimistic that a concerted effort will lead to better understanding of biofilms and improved ability to control the formation of these complex and troublesome microbial communities. ■