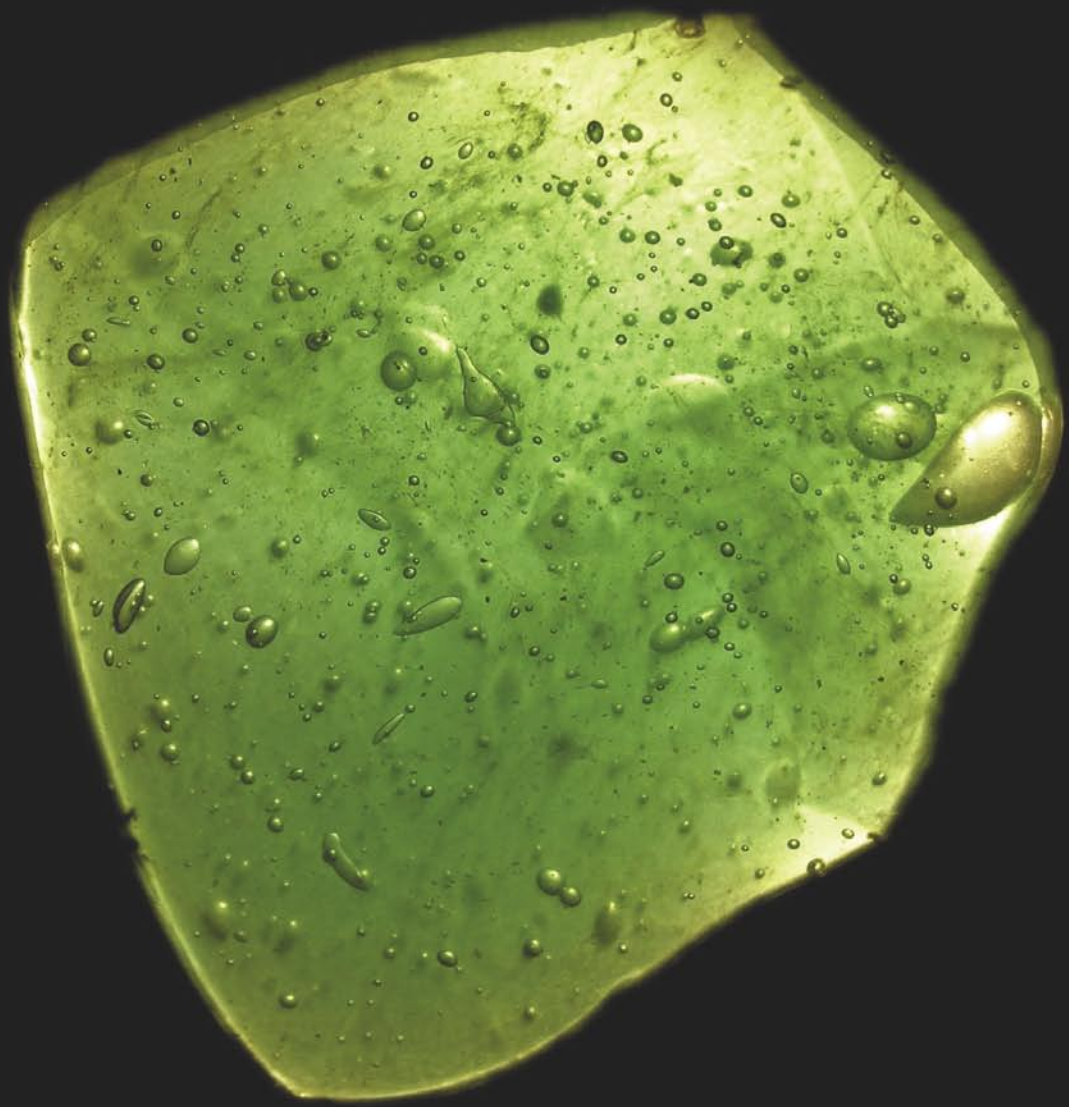
Sending slime



packing

RESEARCHER FINDS KEY TO BIOFILM BREAKUP

David Davies has discovered and is synthesizing a molecule that could help put one of the most virulent "terrorist cells" in all of nature out of business.

Biofilms are complex aggregations of bacteria marked by the excretion of a protective and adhesive matrix, which is why these bacterial colonies are commonly referred to as slime.

Davies, an associate professor of biology at Binghamton University, has isolated a compound that will cause biofilm colonies to disperse, thus leaving individual bacteria up to 1,000 times more susceptible to disinfectants, antibiotics and immune functions, will likely mean a sea change in health care, manufacturing, shipping and pharmaceutics over the coming years. It will most certainly drive worldwide biofilm research in new directions.

"I CONSIDER THIS THE HOLY GRAIL OF RESEARCH IN BIOFILMS. IT'S A NEW PARADIGM IN THE WAY WE LOOK AT HOW BACTERIA REGULATE THEIR BEHAVIOR."

— David Davies

The small molecule Davies is working with appears to be one of the few known examples anywhere in nature of a communication signal that remains effective across species, family and phyla. In fact, though the evidence isn't yet in on that, Davies predicts the compound may also prove to have communicative effect even across bacterial kingdoms.

"I consider this the Holy Grail of research in biofilms," he said. "It's a new paradigm in the way we look at how bacteria regulate their behavior."

Davies' prominence in his field was already secured when he showed in the

late 1990s that bacteria "talk to one another" through cell-to-cell communication and that such signaling is key to biofilm formation. Davies discovered the molecular medium of that communication in *Pseudomonas aeruginosa,* a biofilm-forming microorganism that is arguably the most common organism on the planet.

Since that time, building on Davies' work, others in the field have characterized two other molecular signals, or autoinducers, that are key to various phases of bacterial development cycles either within a particular bacterial species or across species.

The dispersion autoinducer Davies is now investigating has shown itself to be effective in dispersing biofilms containing *Pseudomonas aeruginosa, Streptococcus mutans* (strep), *Escherichia coli* (E. coli) and *Staphylococcus aureus* (staph) whether those bacteria exist in a pure or mixed-culture biofilm.

"We've also tested it on undefined mixed cultures that we just got from the air and the water in the lab, and it worked on that, too," he said.

The dispersion-inducing molecule provokes genetic and physiological changes in the biofilm bacteria, causing them to disperse and return to a planktonic state. In lay terms, Davies has discovered at the very least how to tell four of the most problematic organisms around to pack up and get out of Dodge. And in so doing, the bacteria become easier to kill than the average mosquito.

"There have been a lot of people working on finding a dispersion autoinducer, and it's been a very tricky thing to nail down," Davies said of his most recent breakthrough.

"But we now have a way of isolating and purifying the compound, and we should soon be able to synthesize it so we can make it in higher concentrations."

JUST LIKE SUPER VILLAINS UNABLE TO CONTROL THEIR NEFARIOUS URGES, BIOFILMS ARE MORE OFTEN THAN NOT UP TO NO GOOD FROM A HUMAN PERSPECTIVE.

Ask any bacteria. There is strength — not to mention mischief and worse — to be found in community. And Davies' discovery of the naturally occurring molecule that signals them to forsake the security of a biofilm and disperse is decidedly bad news for them. That's because, although when traveling alone in planktonic form they are of small consequence and generally easy to manage even with antibacterial hand soaps, when they form biofilms, bacteria seem to gain super powers.

And just like super villains unable to control their nefarious urges, biofilms are more often than not up to no good from a human perspective. Biofilms develop almost anywhere that water and solids, or solids and gases, meet, which means they are virtually everywhere. They are formed when individual microorganisms embed themselves in a gelatinous structure of their own making, so in human terms the characteristic "slime" of biofilms, which comprises organic polymers that can grow to several centimeters thick and cover large areas, spells all kinds of big trouble.

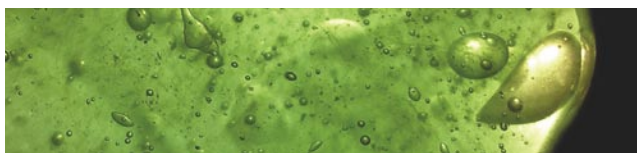
Biofilms, for instance, fog your contacts, help to rot your teeth and cause or complicate outcomes in a host of diseases from ear infections and ulcers to colitis and cystic fibrosis. They are a leading cause of hospital infections and non-healing wounds, and were even at the root last summer of corrosion that forced the replacement of 16 miles of the Alaska pipeline. As a result of that incident, 400,000 barrels a day of production from the largest oil field in the United States was suspended. The indefinite shutdown, at a cost equal to 8 percent of U.S. petroleum output, led to immediate increases in the price of crude oil, and drove up fuel oil and gasoline prices.

The annual worldwide costs of biofilm infection and remediation are in the high billions of dollars, even according to the most modest estimates, and they are costs borne by industries and consumers alike.

Name a manufacturing process and biofilms are probably a serious and costly issue. They have even been discovered in pipes at factories producing prepadine, the anti-bacterial, iodine-based solution that doctors swab on patients to "prep" them for surgery.

Biofilms' resilience and unusual resistance to remediation stem from a combination of mechanisms, including such things as restricted transport of antibiotics through the biofilm, reduced metabolic activity of biofilm bacteria and such physiological resistance mechanisms as the use of membrane pumps to remove antibiotics from inside the cell, Davies said.

But even in nature, biofilms will disperse when environmental conditions become adverse. If sources of nutrition run low or waste products build up, bacteria within a biofilm community "save" themselves by breaking free of the bad situation, turning on some genes and turning off others, and returning to a planktonic state.



IN HUMAN TERMS THE CHARACTERISTIC "SLIME" OF BIOFILMS…SPELLS ALL KINDS OF BIG TROUBLE.

By homing in on the regulatory device that he thinks leads to their natural dispersion, Davies not only seems to have found the key to inducing biofilm dispersion at will, but might also have solved one of the older mysteries in microbiology.

Biofilms will not grow in a flask — no matter how many bacteria you put there. They require a flowing system — water, tears, saliva, a pipeline, etc. — and nutrients. But against all intuition and previous thinking, turning up the flow in a pipe or stream doesn't shear off or break up biofilms. It only produces more robust biofilms. And Davies now thinks he knows why.

"I think this dispersion molecule is just something naturally produced with growth. And the idea is that the flowing liquid will wash out the dispersion-inducer molecule, so the faster the flow rate, the less the inducer molecule builds up in the biofilm, and the biofilm gets bigger and bigger and bigger," he says.

"So, in fact, if you have a batch system, like in a flask, the inducer molecule can't get washed away. Instead it builds up so much that you can't grow any biofilm at all."

Davies feels certain his discovery will dramatically change the way infections are treated.

"I think people will start inducing dispersion to disaggregate biofilms and, then, treat them concurrently, and with significantly greater efficacy, with antibiotics."

He envisions his discovery first making its way to market as a topical treatment for cuts, lacerations and minor burns, perhaps even as an additive in adhesive bandages.

But his major interest, and something he hopes to turn his attention toward in earnest in the coming year, is the area of non-healing wounds. Davies watched his diabetic great-aunt lose both of her feet to amputation after bacterial biofilm infections set in.

"If we can treat those kinds of wounds and clear up the infection, they will heal. We know that from wound debridement studies," he said. "I really think we can make a difference with these people, and if that was the only thing we did, it would be worth everything we're doing."■