Manipulating way bacteria 'talk' could have practical applications

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By manipulating the way bacteria "talk" to each other, researchers at Texas A&M University have achieved an unprecedented degree of control over the formation and dispersal of biofilms – a finding with potentially significant health and industrial applications, particularly to bioreactor technology.

Working with *E. coli* bacteria, Professor Thomas K. Wood and Associate Professor Arul Jayaraman of the university's Artie McFerrin Department of Chemical Engineering have employed specific signals sent and received between bacteria to trigger the dispersal of biofilm. Their findings appear online in the Jan. 3 edition of Nature Communications.

The finding is a significant one, Wood said, because biofilms are notoriously difficult to break apart. A community of bacteria living together, a biofilm is a protective and adhesive slime that exhibits increased resistance to outside threats such as antibiotics. The film can grow on a variety of living and nonliving surfaces, including submerged rocks, food, teeth (as plaque) and biomedical implants such as knee and hip replacements.

While biofilm can pose serious health risks, its use in industrial applications such as in bioreactors is offering hope for an alternative-fuels future, Wood said. Genetically tweaked and grown in these reactors, biofilm can be used to produce a variety of chemicals such as propanol and butanol. And because the bacteria within biofilm feed on glucose, bioreactors using biofilms have the potential to help transform

the economy. These reactors also benefit from the robust nature of biofilm, a trait that makes the film ideal for use, Wood said.

"We want to eventually make with bacteria all the things we currently make in chemical refineries," Wood said. "Towards this goal, the reactor of the future is a biofilm reactor. The main reason is if someone who is operating the reactor, for example, coughs, it doesn't go crazy. If the pH level drops, the biofilm will remain robust and the cells won't die whereas if cells were growing independently (not in a biofilm), and there was a change inside the reactor, you could lose all the cells and the products they are producing."

But before this technology can be realistically implemented, scientists and engineers need to be able to control a number of variables associated with the film, such as how much of the film grows in the reactor, how long it must remain in the reactor and in what proportions different biofilms coexist within the reactor.

That's where Wood and Jayaraman's research comes into play.

"Never before has a group discovered proteins that make biofilms disperse and then used them in a synthetic circuit," Wood said. "We took advantage of the fact that cells talk to each other. We took another bacterium's signal and had *E. coli* make it because it doesn't normally make it. We also inserted the receiving mechanism in *E. coli*. And we were responsible for putting an 'on-off switch' within the bacteria because we wanted this signal broadcast continuously."

By genetically inserting a foreign chemical signal from another bacterium – Pseudomonas aeruginosa – into *E. coli*, the research team was able to force one group of *E. coli* to continuously emit this chemical signal. The group then inserted this group of bacteria into an environment where a biofilm was present. That existing biofilm was also

genetically modified to receive the chemical signal. Once the signal was received, Wood explains, the bacteria within the biofilm responded by breaking apart and leaving the environment, effectively dispersing the biofilm.

"We developed novel miniature models of biofilm reactors where we can exquisitely control which bacterial species is colonizing, for what duration, and to which signals it is exposed to during growth," Jayaraman explained. "Apart from enabling us to control the reactors, this also allows us to investigate several experimental conditions in a high-throughput manner, which is essential for optimizing bioprocesses."

This unprecedented degree of control over biofilm, Wood said, is key to advancing bioreactor technology because it enables scientists to work with bacteria, growing them at greater densities and in specific proportions. For example, by controlling the formation and dispersal of biofilms, scientists would be able to switch the production of a bioreactor from one chemical to another with limited downtime, in effect creating a seamless manufacturing refinery that continuously pumps out in-demand chemicals. And that's exactly where the team's research is leading.

"In the next application, we want to maintain a consortia – a mix of different bacteria – where one group makes the first part of some important chemical and the other group makes the second part that is needed," Wood said. "Also, both groups could make two things that are needed at the same time and you don't want to separate. We want to create complex groupings of bacteria to create complex chemicals. To do this, the bacteria groups need to be in the right proportions, and no one had yet approached this. This can be done now with what we've discovered."

What's more is that these technologies are also applicable to drug

discovery, drug delivery and pharmaceutical applications, as they can be used to mimic the human body environment, Jayaraman noted. For example, any ingested drug needs to pass through the microbial consortia that exists inside of a person before acting on its target, he explained. Using this model, researchers can now better assess the effect of this consortia on the fate and clearance of the drug molecule, he said.

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