Toying with biological systems

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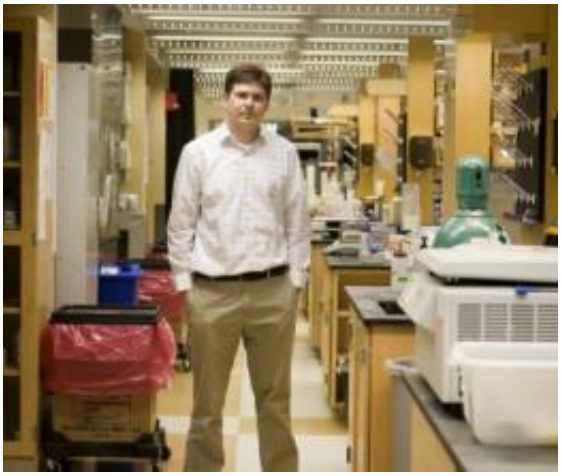

Biological engineer Chris Voigt. Photo: M. Scott Brauer

Bacteria don't normally take photographs. Nor do they attack tumor cells or produce chemicals. But with some help from biological engineer Chris Voigt, they can do all that and more.

Voigt, who joined MIT's faculty in July as an associate professor of biological engineering, likes to tinker with bacteria and other microbes to get them to perform myriad useful tasks that nature never intended — an approach known as synthetic biology.

For example, to develop their "bacterial camera," Voigt and his students inserted a light-detecting sensor from an alga into the bacterium E. coli, coupled with a gene that causes the bacterium to make a black pigment.

A sheet of these bacteria acts as the “film,” and when a stencil is laid over the film and light shone upon it, an image of the stencil forms on the sheet of bacteria.

Likewise, his tumor-targeting E. coli incorporate genes from other bacteria that detect low oxygen levels and high cell density, both conditions often found in tumors. Voigt, who had been on the faculty of the University of California at San Francisco before coming to MIT, then linked those genes with a cell circuit that triggers production of a protein called invasin that enables E. coli to invade mammalian cells.

Despite all Voigt has accomplished in synthetic biology, he got into the field almost by accident. As an undergraduate at the University of Michigan, he majored in chemical engineering, focusing mainly on theoretical studies of reaction mechanics and catalysis. But one day, he was in the chemistry building picking up an exam, and a professor who saw him standing near his door invited him in, thinking he was a student who had applied for a summer job. (That student never showed up.)

“I happened to be standing there, so we started talking,” Voigt recalls. “He was doing protein folding and because of the work that I had been doing on catalysis, I was able to converse with him on some of the theoretical underpinnings of protein folding, and that’s how I got the job. That’s how I got into biology, but I had never really taken any classes in it.”

In graduate school at the California Institute of Technology, he started to work on directed evolution of proteins — specifically, developing a computer program that would identify locations in a protein where mutations would produce a better protein. During a postdoctoral stint at the University of California at Berkeley, he became interested in synthetic biology, which was then just emerging as a new field, based on the idea that novel biological circuits could be assembled from a set of

standardized parts — in this case, genes.

At Berkeley, Voigt worked on extracting genetic circuits from a bacterium called B. subtilis and reconstituting them in E. coli, so they could be studied in isolation. Upon joining the faculty at UCSF, he started working on building simple circuits such as a sensor that would respond to a specific stimulus, which led to his bacterial camera.

Complex circuits

Voigt, who is co-directing MIT's new Synthetic Biology Center, is now working on building larger, highly interconnected systems that include sensors and circuits that can respond to sensors' input.

"Right now we're integrating components into an individual cell. One of the problems with that is getting all of the pieces to interact with each other," he says. Another challenge is preventing pieces that are not supposed to interact from doing so.

"If you want to create a system with 50 circuits that are all working together as part of a computation that the cell is running, then you need each one of those individual circuits to not interfere with all the others. So it becomes an exponentially challenging problem to build each additional new circuit and show that it doesn't interact with all the others," Voigt says.

Such complex circuits could form the basis of microbes that can regulate their own fermentation processes — for example, the yeast that ferment biomass into ethanol, Voigt says. Ethanol fermentation produces acetate, which is toxic to yeast, as a byproduct. Therefore, fermentation vats must be equipped with sensors that detect dangerous acetate levels and take corrective action, such as slowing down delivery of the microbes' food supply (glucose).

Using synthetic biology, it's possible that this monitoring process could be transferred into the cells themselves. Yeast cells would sense the elevated acetate levels and shut off their own glucose transporters until acetate levels go down again.

Voigt says he came to MIT in part because of its focus on biological engineering as a way to impact a variety of fields — not just medicine but also agriculture, energy, industrial chemistry, environmental cleanup and materials. To that end, the new Synthetic Biology Center has recruited researchers from a wide range of backgrounds.

"Our hope is that this place really brings together different people with the same objectives who can think innovatively about the types of systems we can design," Voigt says.

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