



**Digital *E. coli* swim randomly in a nutrient-free medium (green cells) or up a gradient of nutrient (red cells). Solid red and green lines indicate average position of each population. Courtesy of Thierry Emonet.**

The physical models might also prove valuable as talking devices when structural biologists collaborate with scientists who don't routinely think about structure, Olson says. And adding augmented reality to physical models may prove helpful in explaining complex concepts to students. In early tests, one thing is for sure, says Olson, "The students like it better."

## Bacteria with Byte

When a bacterium swims toward food, it follows a chaotic path, alternating between spinning randomly and driving forward, or 'tumbling' and 'running.' Computer scientists at the University of Chicago have now created a virtual colony of *E. coli* bacteria—complete with digital receptors, motors, and signaling pathways—that run and tumble just like real bacteria.

The simulation program, AgentCell, is the first to model a biochemical network at the molecular, single cell, and population levels simultaneously. By doing so, it might provide a framework for modeling other biological systems, including cancer and antibacterial resistance. AgentCell was introduced in the June 1 issue of *Bioinformatics*.

chemotaxis network, but you can use the program for any kind of network you want," says Thierry Emonet, PhD, a research scientist at the University of Chicago and lead author on the paper.

AgentCell uses agent-based simulation, a type of software developed to model social behavior, such as the stock market. An agent is a software object that makes completely autonomous decisions. In AgentCell, each single-celled bacterium decides to run or tumble based on input from the virtual environment and fluctuating intracellular signals. The program models the behavior of thousands of bacteria acting independently. Future versions will allow the bacteria to interact.

The researchers used bacterial chemotaxis as a test-bed for AgentCell because it is one of the best characterized systems in biology. An *E. coli* bacterium swims toward nutrients and away from poisons by alternating the rotation of its flagella: counterclockwise motion causes flagella to bundle into a tight propeller (running); clockwise motion causes the flagella to fly apart (tum-

bling). Chemical signals in the bacteria control the switch between run and tumble, but the mechanism is noisy: the frequency of switching is highly variable between two genetically identical cells in the same environment.

Using AgentCell, Emonet hopes to better understand how cells make decisions in the face of such variability. Chemotaxis is super-simple decision-making; a more complicated decision for a cell is whether or not to divide, Emonet says. When customized, AgentCell could be used to study how cell division goes awry in cancer.

Computer simulations can test competing theoretical models and guide future lab experiments. In the lab, it takes months to grow cells with a mutated protein. In the computer, it takes just a quick and elegant change of the code.

AgentCell will soon be available as open source code on the website: [www.agentcell.org](http://www.agentcell.org). "We'd love to have people grabbing the code and adding modules, adapting it to their own needs," Emonet says.

"Because of its modular architecture, the system readily integrates pre-existing simulators and algorithms with very little development overhead," says

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Tom Schmitz, a post-doctoral fellow at Harvard University. For example, you could easily swap in your own favorite model of intracellular signaling or of receptor binding into AgentCell, and then test it against data from the real world. >