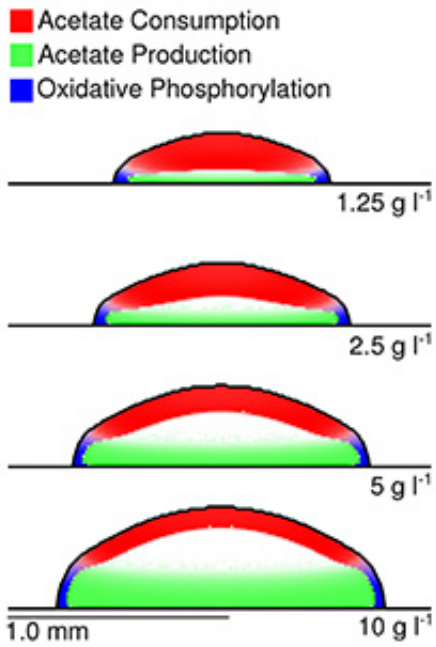
From the depths of a microscopic world, spontaneous cooperation

May 6 2015, by Claudia Lutz



Maybe it's not such a dog-eat-dog world after all. A clever combination of two different types of computer simulations enabled a group of Illinois researchers to uncover an unexpectedly cooperative group dynamic: the spontaneous emergence of resource sharing among individuals in a community. Who were the members of this friendly, digitally represented collective? *Escherichia coli*, rod-shaped bacteria found in the digestive systems of humans and many other animals.

The finding, initially predicted by mathematical models and then confirmed through empirical testing, was reported recently in *BMC Systems Biology*. William and Janet Lycan Professor of Chemistry Zan Luthey-Schulten, graduate student John Cole, and colleagues have worked for several years on computer simulations of bacterial growth. Cole was initially intrigued by the possibility of modifying the lab's Lattice Microbe software, which models how molecules such as sugars or proteins diffuse and react, with another type of computer simulation, which tracks how individual cells metabolize those molecules.

"We thought, can we marry these two approaches?" said Cole. "Let's put a whole bunch of cells in a shared environment and simulate the glucose and oxygen concentrations outside." Cole merged the two models, eventually developing an entirely new simulation code, in order to predict how bacteria within colonies access and metabolize resources as the colony expands.

Bacteria such as *E. coli* adapt their metabolism—what they use as fuel and how they break it down—according to what resources they have available. Just like human muscle cells, bacteria prefer to burn glucose in the presence of oxygen, but can also release some of the energy stored in glucose through a form of metabolism that does not require oxygen. Similar to lactic acid production in a tired sprinter's muscles, this metabolic pathway produces a chemical byproduct, acetate, that still contains some unharvested chemical energy.

Luthey-Schulten is a faculty member at the Carl R. Woese Institute for Genomic Biology (IGB). In the Luthey-Schulten lab's work, colony growth was simulated in 3D, which allowed Cole and others to model what would happen as the colony grew larger, making it harder for oxygen to penetrate to inside layers, or for glucose from the growth substrate to reach the top.

Allowing these resource disparities to emerge in the model revealed something unexpected and novel, yet intuitive. The model predicted that the bacteria would spontaneously begin to cooperate to make the most of their resources.

In the simulated colonies, cells at the bottom, lacking oxygen, would break down glucose into acetate. Cells at the top would take up that acetate and use their access to oxygen to complete its breakdown, extracting the remaining available energy from the original glucose substrate. Cells in the outermost ring, with access to both glucose and oxygen, exhibited the most growth and reproduction.

"As soon as I saw it, I thought, it makes perfect sense," said Cole. "It has to be going on at some level, and I'm sure it's testable."

To test the model's predictions, Luthey-Schulten, Cole and colleagues ventured into empirical work: they grew and monitored bacterial colonies in the lab, in conditions that matched those they had simulated. With microscopy support from Miyandi Sivaguru, assistant director of the IGB Core Facilities, they used a genetically engineered fluorescent dye to visually track bacterial cells that used acetate as a fuel source. The fluorescent label could be seen in the upper layers of cells in the middle of the colony, just as the simulation predicted.

One striking feature of both the simulated and real colonies in the study is that cooperative task specialization was able to quickly emerge among genetically identical or near-identical cells. The authors hope that the model can be adapted to reveal new insights into the behavior of other groups of cells, including cancer-causing tumors.

More information: doi: 10.1186/s12918-015-0155-1