A Tiny Pinch from a 'Z-Ring' Helps Bacteria Cells Divide

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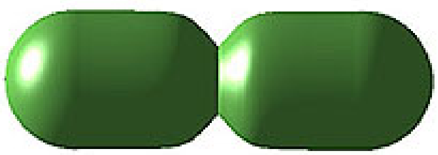

This computer-generated image depicts a rod-shaped microbe in the midst of dividing. A little-understood structure called a Z-ring pinches the midsection during the division process. Image by Ganhui Lan

In process that is shrouded in mystery, rod-shaped bacteria reproduce by splitting themselves in two. By applying advanced mathematics to laboratory data, a team led by Johns Hopkins researchers has solved a small but important part of this reproductive puzzle.

The findings apply to highly common rod-shaped bacteria such as E. coli, found in the human digestive tract. When these single-celled microbes set out to multiply, a signal from an unknown source causes a little-understood structure called a Z-ring to tighten like a rubber band around each bacterium’s midsection.

The Z-ring pinches the rod-like body into two microbial sausages that finally split apart. To shed light on this process, the Johns Hopkins-led team developed a mathematical tool that computed the mechanical force exerted by the Z-ring when it helps these cells split.

The calculation will aid scientists who are trying to learn more about how these microbes live and reproduce. The work also may hasten the development of a new type of antibiotic that could disable the Z-ring to keep harmful bacteria in check.

The bacteria research was reported in the Oct. 9 edition of *Proceedings of the National Academy of Sciences*. The work was led by Sean X. Sun, an assistant professor of mechanical engineering in Johns Hopkins' Whiting School of Engineering.

"This type of bacteria is commonly found in the human body," said Sun, a co-author of the journal article. "Understanding how organisms like this work can help us find new ways to treat bacterial illnesses, develop medications or do any type of bioengineering involving bacteria. If you want to target certain cellular activities, you need to know how single-celled creatures like this operate."

Sun's team brought a fresh perspective to the study of cell activity. While traditional biologists try to identify and learn the function of tiny of bits of genetic material within cells, Sun studies how such proteins work together to form "molecular machines" that carry out tasks inside the cells. "Biologists are just beginning to understand that mechanical processes at the cellular level are also important," he said. "I'm bringing the tools of mechanical engineering to bear on biological mysteries."

Toward this goal, Sun's team's sought to measure how much mechanical force the Z-ring applies to rod-shaped bacteria during cell division. The researchers knew that each rod-shaped bacterium possesses, around the inside of its midsection, a belt made of a filamentous protein called FtsZ. Most of the time, this ring is inactive. But when a bacterium cell is healthy and has sufficient food, it seeks to reproduce by dividing in two. When it is time for this to occur, the Z-ring receives a signal and begins to contract. This pinching continues until the rod breaks apart to form two daughter cells.

Sun's team gathered data from microbiology labs that are studying cell division and then translated these observations into mathematical equations. The researchers used the equations to create computer simulations of the cell division process, models that yielded a prediction of the Z-ring force: 8 piconewtons. A piconewton is one-trillionth of a newton. One newton is approximately the amount of force needed to lift a baseball in Earth's gravity.

"The surprise was that the amount of force generated by the Z-ring was so small," Sun said. "Most researchers believed a lot more force would be required during the cell division process."

This information could be used, Sun said, by drug developers seeking a way to disable the Z-ring so that harmful bacteria can no longer reproduce. The research has wider implications as well. "Our mathematical equations could also be used to help understand how plant and animal cells divide, including human cells," Sun said. "Human cells have an actin ring that behaves the same way as a Z-ring. It contracts during division. The mathematical formulas developed in this study could also be used in research concerning the division of human cells. The more we know about this process, the better we can affect the process through drugs or genetic manipulation."

Source: Johns Hopkins University

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