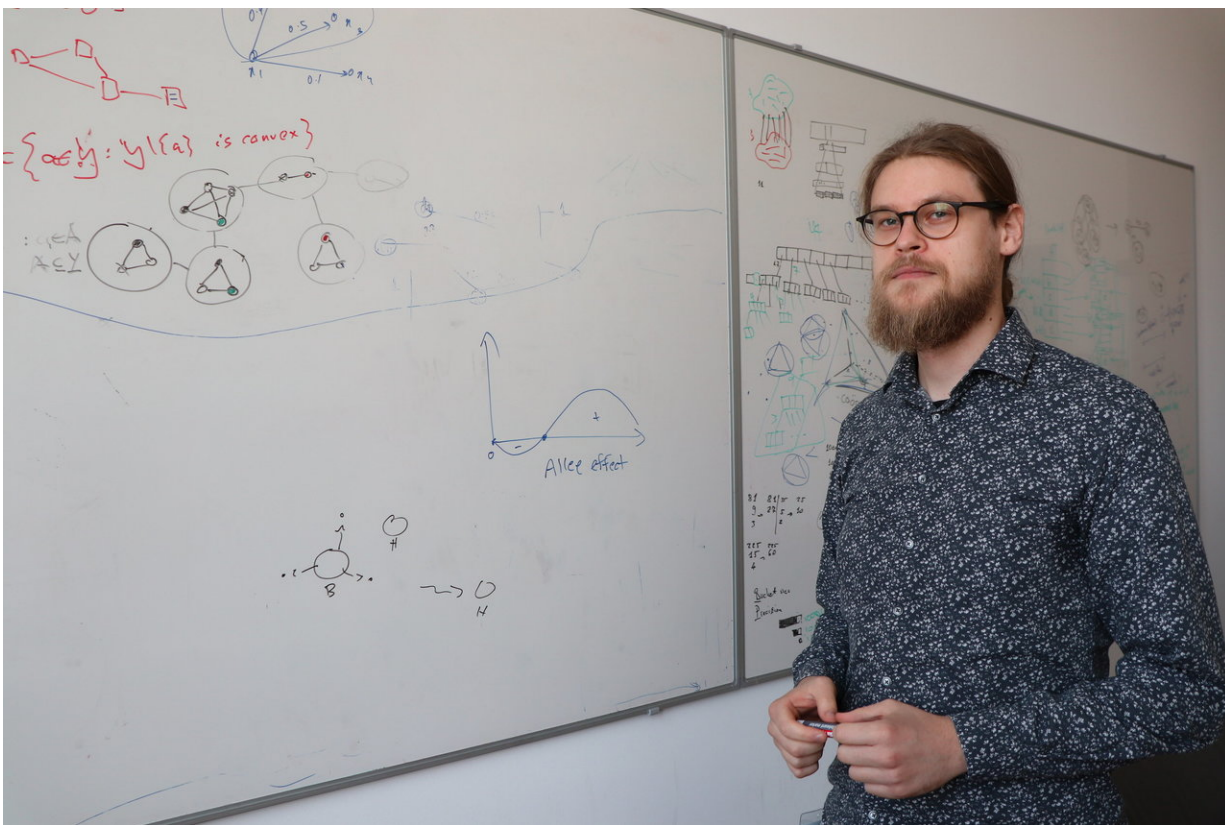


Mathematical model explains why some bacteria cause illness even in small doses

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Joel Rybicki is an ISTplus postdoctoral fellow in the group of Dan Alistarh
Credit: IST Austria/Sophie Fessler

Just a few *Shigella* bacteria are enough to make anyone develop gastroenteritis, while illness from cholera requires ingestion of thousands

to millions of *Vibrio cholerae* bacteria. Why does the disease-causing dosage differ so much between bacteria?

Based on observational data, biologists have previously proposed that this difference could be due to how [bacteria](#) attack their hosts. For example, while the *Shigella* bacteria act locally by directly injecting proteins into host cells, [cholera bacteria](#) attack from a distance by secreting cholera toxin. Joel Rybicki, postdoc at the Institute of Science and Technology Austria (IST Austria), and his colleagues Eva Kisdi and Jani Anttila at the University of Helsinki, built a mathematical model of bacterial infections. Their results support the hypothesis that the scale of pathogenetic mechanisms is the reason why different bacteria have different infective doses. They predict that the mechanism also influences how quickly an [infection](#) spreads in the host. Their study is published today in *PNAS*.

Rybicki and colleagues built a [mathematical model](#) that reflects bacterial infections. Compared with real-life bacteria, this "theoretical" [bacterium](#) allows the researchers to change a single aspect, in this case, the mechanism of pathogenesis, while keeping all other aspects the same—a feat that would be difficult, if not impossible, to accomplish experimentally. In their model, the researchers can adjust the distance at which the bacterium acts to attack the host and evade the immune system. When the bacterium releases a toxin that acts locally, only few bacteria are needed to start an infection. When the bacterium releases a toxin that acts over a long distance, a large number of bacteria are needed to get an infection going. Their model gives a theoretical basis for the phenomenon linking infective dose and the scale of the pathogenic [mechanism](#).

The models show that there is a threshold for infective doses. Rybicki explains: "Bacteria that attack a host using spreading toxins have a problem. When there is only one bacterium, the toxin it produces

spreads away, leaving it defenseless, and the immune system can attack the bacterium. So the bacterium needs a little help from its friends. Only when there are enough other bacteria around releasing toxins are they all protected from the immune system. For bacteria with locally acting toxin, the threshold is lower. The [toxin](#) doesn't spread away, so even a few bacteria acting together are protected from immune attack."

Simulations of what happens during local and distant infections showed that when distantly acting bacteria have taken hold and started an infection, the infection spreads quickly. Locally acting bacteria start an infection at a lower threshold, but the infection spreads more slowly at higher doses. "This could be an explanation for why these different mechanisms of pathogenesis evolved in the first place," Rybicki says.

More information: Joel Rybicki et al., "Model of bacterial toxin-dependent pathogenesis explains infective dose," *PNAS* (2018).

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