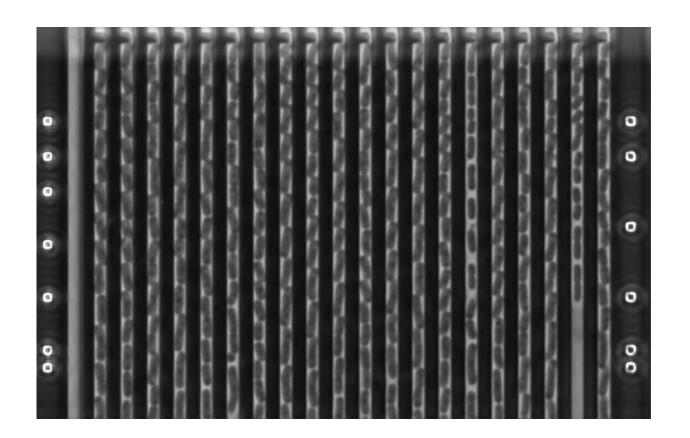


New ultrafast method for determining antibiotic resistance

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Klebsiella pneumoniae growing in the microfluidic chip imaged in phase contrast. The bacteria are 0.003mm long and divide every 30 min. Credit: Özden Baltekina, et al

Researchers at Uppsala University have developed a new method for very rapidly determining whether infection-causing bacteria are resistant



or susceptible to antibiotics. The findings have now been published in the U.S. journal *Proceedings of the National Academy of Sciences* (*PNAS*).

Antibiotic resistance is a growing medical problem that threatens human health globally. One important contributory factor in the development of resistance is the incorrect use of <u>antibiotics</u> for treatment. Researchers therefore seek reliable methods to quickly and easily identify bacterial resistance patterns, known as antibiotic susceptibility testing (AST), and provide early treatment, i.e. right from the doctor's appointment. This has been inhibited by the current time-consuming <u>antibiotic resistance</u> tests. Now, researchers at Uppsala have, for the first time, developed an antibiotic resistance test that is fast enough to inform antibiotic choice in the doctor's office. The test is primarily intended for <u>urinary tract</u> <u>infections</u>—a condition that, globally, affects approximately 100 million women a year and accounts for 25 per cent of antibiotic use in Sweden.

"We've developed a new <u>method</u> that allows determination of bacterial resistance patterns in urinary tract infections in 10 to 30 minutes. By comparison, the resistance determination currently in use requires one to two days. The rapid test is based on a new plastic microfluidic chip where the bacteria are trapped and methods for analysing bacterial growth at single-cell level," says PhD student Özden Baltekin, who performed most of the experimental work.

The "fASTest" method is based on sensitive optical and analytical techniques developed to study the behaviour of individual bacteria. Monitoring whether individual bacteria grow in the presence of antibiotics (i.e. are resistant) reveals their <u>resistance</u> or susceptibility within a few minutes.

"It's great that the research methods we developed to address fundamental questions in molecular biology are useful for such a



tremendously important medical application," says Johan Elf, one of the researchers behind the study.

The detection method is now being developed by an Uppsala company, Astrego Diagnostics AB, into a user-friendly product. The company expects to have an automated <u>test</u> for urinary tract infections within a few years.

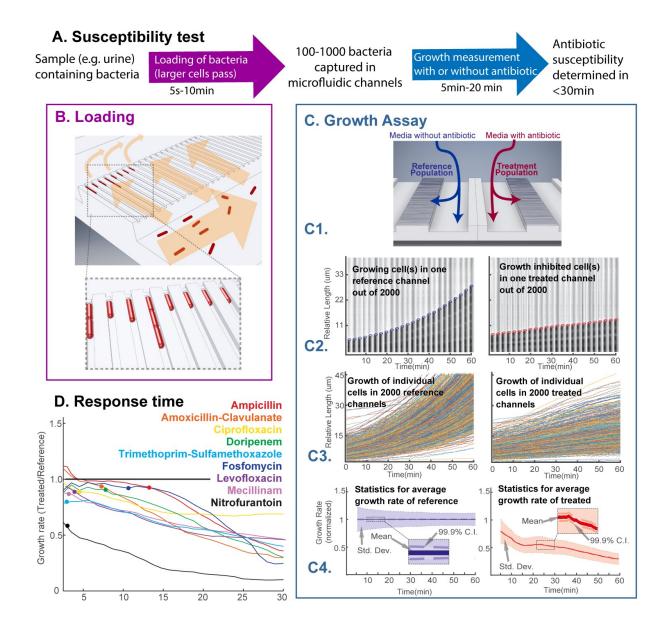




Figure 1 A. Overall workflow for fast AST B. Individual cells are sucked into the cell channels where they get stuck at the 300 nm constriction at the end(inset) C1. One row of 2000 cell channels are treated with an antibiotic and the other row is used as a reference. C2. Growth in one individual cell channel without antibiotic (left) and one with antibiotic (right) monitored over time (x-axis) as observed with phase contrast microscopy. C3. Length extension over time as determined for cells in 1600 individual cell channels without antibiotic (left) and with antibiotic (right). C4 Average growth rates for the bacteria in C3 together with 99.9% SEM and population standard deviation D. The average growth rate and 99.9% SEM for susceptible bacteria exposed to one of of nine different antibiotics (colors), normalized to the growth rate in the non-treated reference channels. Only data from one typical references channel is displayed(gray). dots indicate when the growth rate has dropped below untreated reference with 99.9% probability. Credit: Johan Elf

"The hope is that, in future, the method could be used in hospitals and health centres to quickly provide correct treatment and reduce unnecessary use of antibiotics," says Dan Andersson, one of the researchers behind the study.

"We believe the method is usable for other types of <u>infection</u>, such as blood infections where prompt, correct choice of antibiotic is critical to the patient."

More information: Özden Baltekina, et al., Antibiotic susceptibility testing in less than 30 min using direct single-cell imaging, *PNAS*, <u>DOI:</u> <u>10.1073/pnas.1708558114</u>, <u>www.pnas.org/content/early/201</u>... <u>8/07/1708558114.full</u>

Provided by Uppsala University



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