# Flexible and multiplexed microfluidic cultivation platform for monitoring bacteria under drug exposure

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Microfluidics-based technologies represent a valuable tool in the studies of microbial cells. Such downscaled systems offer precise cell manipulation, great control over the cell cultivation conditions and multimodal analysis with a single-cell resolution. The possibility of monitoring and studying bacterial cells under well-controlled exposure to antibiotic compounds could provide a rapid resistance profile of the studied bacteria and valuable information about bacterial subpopulations, such as cells with antibiotic persistence or hetero-resistance. Thereby, microfluidic devices hold great potential to provide clinicians with vital strategies to combat difficult-to-treat and reoccurring infections.

Here, we present a straightforward microfluidic system for a rapid determination of antibiotic susceptibility based on the evaluation of changes in bacterial metabolism under antibiotic exposure. The system contains four arrays with more than a hundred bacterial growth chambers made in air-tight thermoplastic polymer, cyclic olefin copolymer (COC). Each of the growth chambers contains a growth medium, oxygen-sensing nanoprobes and different concentrations of the antibiotics embedded in a gel matrix. Growing bacteria are consuming oxygen, what is observed as an increase in the luminescence of the oxygen-sensing nanoprobes. Therefore, we can correlate observed changes in metabolic activity with morphological changes during antibiotic exposure (Figure 1A).

The system was characterised and successfully tested using *Escherichia coli* strains (ATCC 25922, ATCC 35218 and a clinical sample), providing the resistance profiles within 2.5 hours of incubation. A simple change in the gel matrix and growth medium enabled us to use the system to obtain resistance profiles of gram-positive bacterial strains, such as *Mycobacterium smegmatis* (ATCC 19420) in approximately 15 hours of incubation. Further, we demonstrate the possibility of using the developed platform to study mixed bacterial cultures with different antibiotic resistances and to study bacterial cells under antibiotic exposure in an artificial urine medium. An image of a selected growth chamber is presented in Figure 1B.

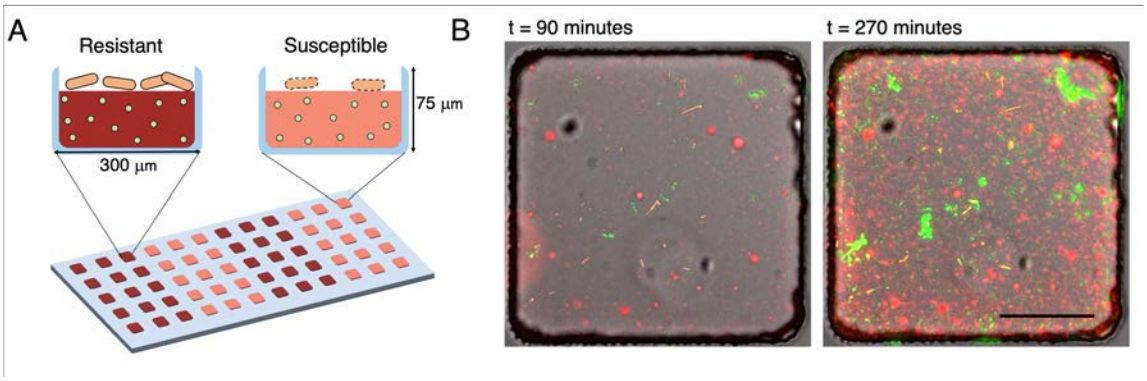


*Figure 1. A: Scheme of the system. B: A growth chamber containing different* E. coli *strains in co-culture. One strain is resistant to ampicillin (green-sfGFP), while the other is susceptible (orange-mKate2). The chamber also contains oxygen-sensing particles (red); bacteria are consuming oxygen and the luminescence signal of the particles increases. Scale bar: 100 µm*