Poster Title:

Microfluidic platform to visualize and quantify bacterial response to dynamic drug treatments

Authors:

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Abstract:

The heterogeneity of bacterial populations is considered an important factor in developing antibiotic resistance and persistence. Static assays, routinely used in clinics to identify potential resistance, do not sufficiently address this intercellular heterogeneity. Moreover, mimicking in vivo conditions, where bacterial cells are temporarily exposed to different antibiotic concentrations, is only possible using dynamic models. The available dynamic in vitro models, e.g., the state-of-the-art Hollow Fiber Infection Model (HFIM), require vast amounts of drugs and cells per experiment. Further, the drug effects on the cells are evaluated after invasive sampling and only represent a finite moment in time.

Inspired by the HFIM, we developed a microfluidic platform to investigate the effects of dynamic antibiotic treatments over time, with single-cell resolution and requiring only a fraction of volumes necessary for the HFIM. To bacterial cells are confined in a thin hydrogel layer. We expose bacterial cells to different temporal antibiotic gradient profiles using a pump ratio-based gradient generator and monitor the effects on bacterial cells using time-lapse microscopy for up to 24 hours. For the platform characterization, the quality control strains *E. coli* ATCC 25922 and *E. coli* ATCC 35218 used are exposed to single drugs and drug combinations (amoxicillin, clavulanic acid).

The obtained minimum inhibitory dose at constant amoxicillin supply on chip for *E. coli*ATCC 25922 is in the range accepted by clinical reference guidelines. Our results indicate that the growth behavior of the bacterial cells is dependent on the drug dosing profile. The growth behavior was investigated after exposing the bacterial cells to the same average concentrations of amoxicillin, but with different dosing profiles. We show that cells exposed to alternating antibiotic drug levels exhibit different growth behavior than cells exposed to the same drug amount, but at constant concentration. Finally, we have started to mimic the temporal gradient profile in a patient after oral administration of amoxicillin and clavulanic acid in our platform. We are currently focusing on the further comparison between constant and gradient drug dosing, the optimization of the developed platform for precise temporal antibiotic gradients and the extension of our study to clinically relevant pathogens.