Universität Basel

Research Project

Measuring single-cell pharmacodynamics with deep learning

Third-party funded project

Project title Measuring single-cell pharmacodynamics with deep learning
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The pharmacodynamics of antibiotics are currently almost exclusively defined at the population level.ăHowever, recent studies have highlighted that microbial pathogens diversify into different physiologicalăstates within their hosts, and that the action of antibiotics can vary dramatically with the physiologicalăstate of single cells. Thus, a comprehensive approach to quantifying pharmacodynamics at the single-cellălevel, across bacterial strains and growth conditions, will likely have a profound impact on theădevelopment of novel antimicrobial therapies.
Recently developed microfluidic setups, when used in combination with time-lapse microscopy, allowălong-term monitoring of growth and gene expression in single bacterial cells exposed to preciselyăcontrolled environments. However, the throughput of such methods is currently highly constrained by theăimage analysis, which still requires manual curation.
We here propose to harness recent progress in deep learning image analysis methods to develop a fullyăautomated image analysis tool for time-lapse microfluidic data. As a proof-of-principle, we will use ourătool in combination with downstream Bayesian probabilistic methods to infer detailed single-cellăpharmacodynamics of several antibiotics from measurements of growth inhibition and killing of individualăbacteria exposed to antibiotics with different growth conditions and treatment protocols.

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