Single cell studies of the action of antibiotics

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Brief description: Microbiology has traditionally focused on studies at the population level, which look at the average behavior of cells. However, in recent years, the availability of tools to study individual cells, has allowed a new understanding of the existence and significance of cellular heterogeneity. Importantly, even cells from isogenic populations, growing in the same conditions, can exhibit phenotypic variation.
We will use as a model organism the Gram positive bacteria *Staphylococcus aureus*, an extremely versatile pathogen capable of causing from minor infections to life threatening ones. We want to determine if different cells from isogenic populations of *S. aureus* strains have an heterogeneous response to the presence of antibiotics due to (i) biochemical and morphologic differences arising from cells being at different stages of the cell cycle (ii) stochastic fluctuations in the expression of genes required for the stress response of *S. aureus* to the presence of cell wall active antibiotics.

In this master project we aim to determine if there is a dependence of the killing action of antibiotics on the cell cycle stage.

Variations in susceptibility/tolerance to antibiotics over the bacterial cell cycle can be due to variations of the internal biochemical parameters, or to variations in the morphology of the cells which can affect, for example, the access of antibiotics to their targets and/or the susceptibility of the targets to the antibiotics. We will use dyes which specifically label dead cells to determine if there are stages of the cell cycle during which the cell is either more tolerant or more susceptible to death by the action of different classes of antibiotics (namely antibiotics that inhibit either cell wall synthesis or DNA replication).