Master project offered in the van Nimwegen group, Biozentrum, Basel

Bacterial Isolates Adaptation Strategies (BACILAS)

Our laboratory:

Using theoretical and experimental approaches, our group study the function and evolution of regulatory networks that cells use to control the expression of their genes.

The proposed project:

When it comes to adapt to an environmental change, bacteria display different strategies. First, they can sense environmental cues and couple them to gene regulatory factors to change which genes are expressed (e.g the lac operon regulation [1]). Second, recent results suggest that bacteria can even anticipate future certain environment changes when they experience them frequently [2]. Finally, bacteria can use a third strategy called "bet-hedging" [3]. Due to the inherent stochasticity of gene expression genetically identical cells can display different phenotypes (phenotypic heterogeneity), such that a fraction of the population is pre-adapted to sudden environmental changes. It has been shown experimentally that these 3 strategies are responsible for shorter adaptation time and/or survival in adverse conditions.

These strategies depend on the genetic background and involve phenotypic heterogeneity. In spite of this, they are mostly studied using laboratory strains of E. coli (reduced genome diversity), at the population level, where only the mean behaviour of the population is measured. Instead, we seek to quantitatively understand how a given genetic background enables a given bacterial strain to adapt to an environmental change using the before mentionned strategies, by the means of single-cell techniques.

How can we study bacterial phenotypic adaptation? In experimental conditions bacterial growth is characterized by how bacterial culture optical density (OD) changes over time. When a liquid bacterial culture is diluted from one medium to a new one, the OD versus time graph presents the following phases: a lag phase during which OD is constant, an exponential growth phase during which OD increases exponentially and a the stationary phase during which OD reaches a plateau. The duration of the lag phase is set by the capacity of single cells to resume growth and division after being switched from one environment to the new one. Therefore, we are looking for a motivated student to study how single bacteria resume growth during lag phases, in a collection of genetically diverse wild E. coli strains. This will be done using classical microbiology tools, as well as single-cell microfluidics tools that were developed in our lab [4,5].

Work proposed. First, the student will measure lag phase durations in our collection of E. coli strains, in flask. This will be performed in 96 well plates, using our experimental setup which consists of an incubator and a spectrophotometer connected with a robot. These lags will then be studied at the single cell level, using time-lapse microscopy and a new generation of "Mother Machine" microfluidic devices in order to study single cell growth dynamics upon sudden environmental changes (see figure). Depending on the student's abilities and interest, the work can be extended to include mass spectroscopy (proteomics) measurement of bacterial cell content, before, during, and after the lag phase [6].

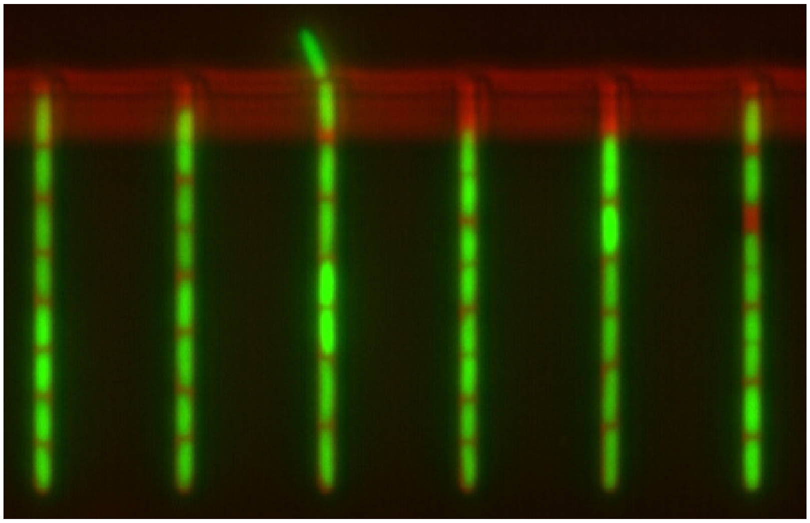

Figure: Mother machine experiments enable to track single bacteria and measure their lags in fluctuating environments.

We offer. The student will joined a dynamic research group which adresses fundamental questions related to the function and evolution of regulatory networks, experimentally and theoritically. He will be closely mentored and taught how to plan and perform the mentionned experiments, as well as analyzing the results, using the R programming language and our image analysis pipeline.

Applicant profile. Bachelor degree in Physics/Engineering or quantitative Biology. With possibly experience in molecular biology and/or microbiology techniques. A minimum of experience with programming is mandatory. The applicant should be highly motivated, eager to learn new techniques and also capable of working independently. The primary language of the laboratory is English.

Application. Please send us your CV, a transcript of records, together with a brief personal statement (maximum half a page), explaining your motivation to apply for this internship. Depending on the master student curriculum, the internship can begin upon request and last from 6 to 18 months.

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References:

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