



Master thesis / internship: cross-induction dynamics in a simple genetic circuit

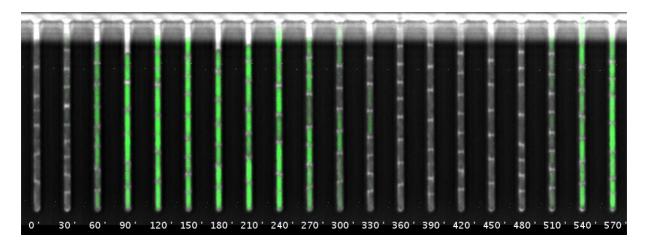
The behaviour of cells is driven by molecular processes that are intrinsically stochastic. Consequently, even genetically identical cells can exhibit different behaviours in a homogeneous environment. This stochastic variability in phenotypes underlies many important processes such as persistence to antibiotics and sporulation in bacteria, and theoretical considerations suggest that stochasticity is particularly significant when cells face changing environments. With the advent of microscopy and microfluidics, studying bacteria populations with single-cell resolution has become a powerful approach to study the stochasticity of cellular processes.

Our lab uses a combination of experimental and theoretical approaches to study growth and gene expression at the single-cell level in bacteria, with a strong focus on the interplay between gene expression noise and gene regulation. We have recently developed a microfluidic system that allows us to measure growth, division and gene expression of single cells in a dynamically changing environment [1]. This led us to discover that, while the *lac* operon is designed to sense the presence of lactose, it has actually been selected to function in a regime where the majority of bacteria are waiting for the next stochastic burst of expression before reacting to lactose [2]. Moreover, preliminary results indicated that cells which respond to lactose early on are inducing the response of their neighbours too. While cross-feeding between bacteria has been described repeatedly, this constitutes to our knowledge the first case of cross-induction. In this internship, the focus will be to characterize cross-induction dynamics for the *lac* operon, and to identify its molecular basis – Which molecules are mediating the signal? How are they sensed by neighbouring cells?

The student will be in charge of running the experiments in which bacteria carrying fluorescent reporters are grown inside a microfluidic device and followed using time-lapse microscopy, he/she will learn to process their data with our image analysis pipeline, and will help implement quantitative data analysis procedures aimed to characterize cross-induction dynamics. Depending on the student's abilities and interest, the work can be extended to include computational. Moreover, competitive funding is available for motivated students desiring to start a PhD after the internship (in particular Biozentrum's "Fellowships for Excellence").

The <u>van Nimwegen Lab</u> [3] at Basel University's Biozentrum is an international and multidisciplinary team with extensive expertise in the study of transcription regulation and cell-to-cell variability. A list of our group's publications can be found on <u>Google Scholar</u> [4]. Our computational and experimental groups work together to combine cutting edge statistical and computational tools with quantitative experiments.

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- [1] Kaiser M*, Jug F*, Julou T*, et al. (2018) Nat Commun 9, 212.
- [2] preprint available at https://www.biorxiv.org/content/10.1101/2020.01.04.894766v2
- [3] http://www.biozentrum.unibas.ch/research/groups-platforms/overview/unit/nimwegen/
- [4] http://scholar.google.ch/citations?user=N24KB1wAAAAJ