UNI BASEL

BIOZENTRUM
Universität Basel
The Center for
Molecular Life Sciences

Master thesis / internship (2021-2022): quantitative biology of bacterial metabolism.

When studying the behavior of bacteria in the laboratory, cells are almost always grown at high or saturating concentrations of their nutrients, not only because this allows fast growth, but also because it allows sufficiently large cell numbers to measure using bulk assays. However, it is believed that, out in the real world, bacteria often have to deal with trace amounts of nutrients at very low concentrations. Thus, the ability of different microbes to colonize ecological niches and compete with others will crucially depend on how much and fast they can grow on low concentrations of nutrients.

While the total growth of bacterial cultures typically increases simply linearly with the amount of available nutrient, their growth rate as a function of nutrient concentration is thought to follow a hyperbolic function known as the *Monod curve*. This predicts that growth-rate stays close to its maximum value over a wide range of concentrations, decreasing abruptly when concentrations fall below a particular given low concentration. Although this hyperbolic relationship between nutrient concentration and growth-rate is universally assumed to hold across bacteria and nutrients, and has important implications from systems biology to biotechnological applications, only very little experimental data is available to support that growth-rates indeed exhibit this dependence on nutrient concentration. This is mostly due to technical challenges: the growth rate decreases markedly only for concentrations of nutrients which are so low that total growth is too small to accurately measure bacterial growth with standard methods.

Our lab has developed a microfluidic system that allows us to measure growth, division and gene expression of single cells in a dynamically changing environment [1]; we have recently extended this setup in order to monitor bacteria growing in a continuous flow of media, which opens the door to precisely measuring growth at very low concentration of nutrients. We have already obtained a proof of principle by successfully measuring growth-rate as a function of glucose concentration using an *E. coli* lab strain (down to 0.3 mg/L of glucose). The student will use this integrated setup to measure single-cell growth-rates as a function of nutrient concentration for several nutrients and/or several bacterial strains and species. Importantly, because we quantitatively track single cells, we will not just obtain an average growth rate, but the entire distribution of growth rates. Results obtained from these experiments will allow us to either support or challenge existing models of bacterial physiology. Mechanistic hypotheses derived from these observations could be tested in follow-up experiments using fluorescent reporters in order to quantify the activity of relevant transcription factors.

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, (s)he will learn to process the data with our automated image analysis pipeline, and will help implement data analysis procedures aimed to quantitatively characterize the dependence of growth rate on nutrient concentration. Depending on the student's abilities and interest, the work can be extended to include more sophisticated computational modeling. Moreover, competitive funding is available for motivated students desiring to continue with a PhD after the internship (in particular through the Biozentrum's "Fellowships for Excellence").

The van Nimwegen Lab [2] 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 Google Scholar [3]. The computational and experimental sections of our group work together to combine cutting edge statistical and computational tools with quantitative experiments.

Contact: thomas.julou@normalesup.org, erik.vannimwegen@unibas.ch

[1] Kaiser M*, Jug F*, Julou T*, *et al*. (2018) *Nat Commun* 9, 212.
[2] http://www.biozentrum.unibas.ch/nimwegen/
[3] http://scholar.google.ch/citations?user=N24KB1wAAAAJ