Research internship

Optimal design of parallelized light signals for optically-controlled gene networks in single cells

1. Context

With the exponential decrease of DNA synthesis costs, and the development of standardized cloning methods and of liquid handling robots, the automation of biological experiments will have a decisive impact on tomorrow's research, notably in health and biotechnology domains. Actually, it has already started and "cloud biology" companies offer to "access a fully automated cell and molecular biology laboratory, all from the comfort of web browsers" (Transcriptic). We will therefore enter an era in which novel experiments can be specified entirely on the computer as control algorithm that give instructions to the experimental platform.

2. Problem and Goals

In collaboration with Calin Guet at IST Austria, we have recently constructed a computer controlled experimental platform in which hundreds of single bacterial cells, growing in a microfluidic device (mother machine), can be observed (by microscopy) and stimulated (through an optically inducible gene expression system) at the same time. Importantly, the observations are automatically processed and the computer can make real-time decisions on how to continue stimulating each individual cell. This allows us to perform experiments that could provide much more information about the functioning of biochemical processes at the level of single cells than conventional experiments. However, given that this experimental platform is the first of its kind, it is unclear what experiments would be the most useful and how the resulting data should be analyzed. The goal of this project is to develop and

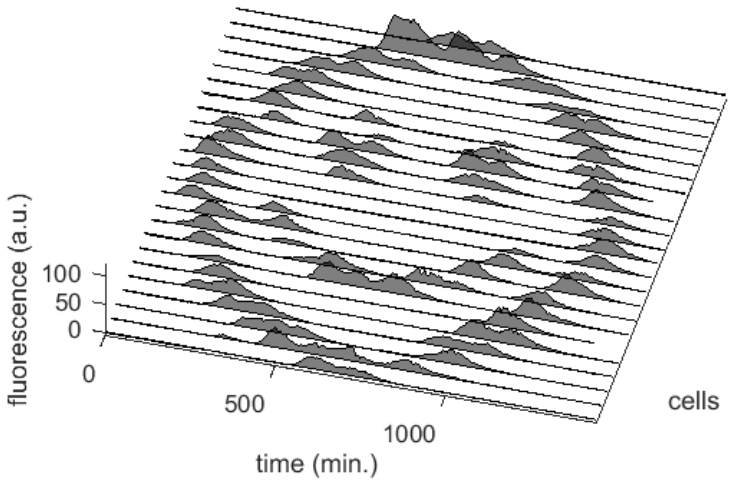

Figure 1: Optogenetic control of gene expression. Expression of a reporter protein is induced in single cells such that the fluorescence of the cells follows designable output profiles over time.

implement mathematical methods that can be used for the design of experiments that provide the maximal amount of information about the underlying gene expression dynamics. Our long-term goal is to develop press button tools for the biology lab of the future that can be used to automatically characterize and model gene networks with minimal experimental effort.

3. Supervision, location and contact details

The work will be supervised by Jakob Ruess and Gregory Batt at Institut Pasteur (Paris) in the newly created Inria/Pasteur InBio group. The project is at the core of the long-term research goals of the group and, if successful, could potentially serve as the basis of a PhD-project in which the methods are developed further and applied in our wet lab.

Web: https://research.pasteur.fr/en/team/experimental-and-computational-methods-for-modeling-cellular-processes/

Contact: jakob.ruess@inria.fr, gregory.batt@inria.fr

4. References

[1] Olson et al. (2014), *Characterizing bacterial gene circuit dynamics with optically programmed gene expression signals,* Nature Methods 11, 449-455, doi:10.1038/nmeth.2884.

[2] Ruess et al. (2015), *Iterative experiment design guides the characterization of a light-inducible gene expression circuit,* PNAS 112, 8148-8153, doi: 10.1073/pnas.1423947112.

[3] Milias-Argeitis et al. (2016), *Automated optogenetic feedback control for precise and robust regulation of gene expression and cell growth,* Nature Communications 7, 12546, doi:10.1038/ncomms12546.