Optimal phenotypic switching model for bacterial populations under fluctuating environmental conditions

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Abstract – Optimal phenotypic switching model for bacterial populations under fluctuating environmental conditions

In a fluctuating environment, cell populations need to adapt to survive. There are several ways to achieve it, but in general cells take benefit from biological noise to switch to alternative phenotypes, leading to improved fitness in the new environment. This is a known phenomenon that gives rise to phenotypically heterogeneous populations, but the dynamics of the adaptation are still unclear.

Understanding those dynamics is key if one wants to control gene expression in bio-processes in general, but the literature on ways to reproduce population behaviours quantitatively *in silico* is still nascent; and if a few models are available, they have not been validated based on experimental data.

Therefore, in this work, an existing model was applied and improved to better fit experimental data obtained based on the use of high-throughput, automated, flow cytometry. In particular, a simple model derived from the general model developed by Thattai and Van Oudenaarden was applied to data representing populations of *E. coli* growing under continuous cultivation conditions. The fluctuating environment for the population was based on a constant feed of glucose, but varying amounts of arabinose in the medium.

The existing model used basal stochastic switching to drive the population diversification. It was found insufficient to reproduce the observed data, and several possible new contributions to the model were therefore devised. Each one was considered independently of the others, thanks to a succession of models, each taking into account a different set of contributions, and fitted as well as possible to the data.

Eventually, it was found that several of those contributions could indeed improve the model for this particular case. Moreover, this work also sheds new lights on two important points that are likely applicable in most systems with heterogeneous cell populations: the growth rates of the different phenotypes need to be considered in details if the population is to be modelled correctly, and representing the switching mechanism adequately is likely often easier and more exact by simulating single cells with a stochastic behaviour, rather than using differential equations.

Data

Model