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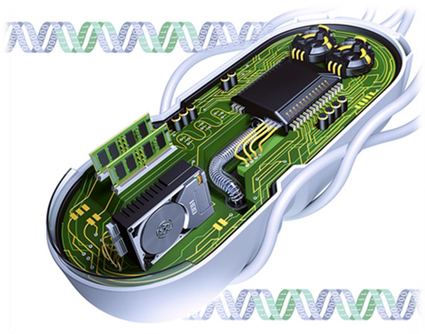
Tutor: Mario di Bernardo

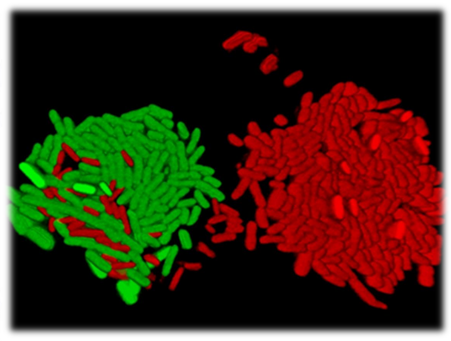
XXXIII Cycle - II year presentation

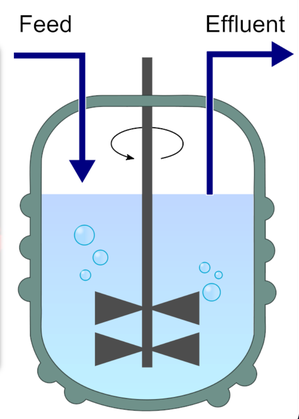
Analysis and Control of Bacterial Populations in Synthetic Biology

Key Research Questions

- Is it possible to steer the behaviour of **living cells** via *external feedback control* algorithms?
- How to design these feedback control strategies?
- Applications of microbial populations are fundamental in research in Biology, Engineering and Medicine, as well as in the production of pharmaceuticals and chemical molecules.
- Is it possible to design ad hoc *host environments* for multicellular control experiments?

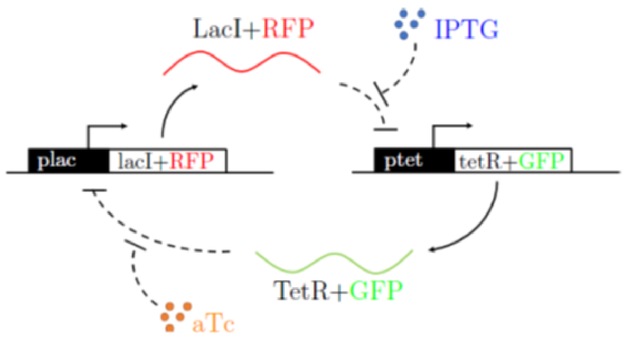






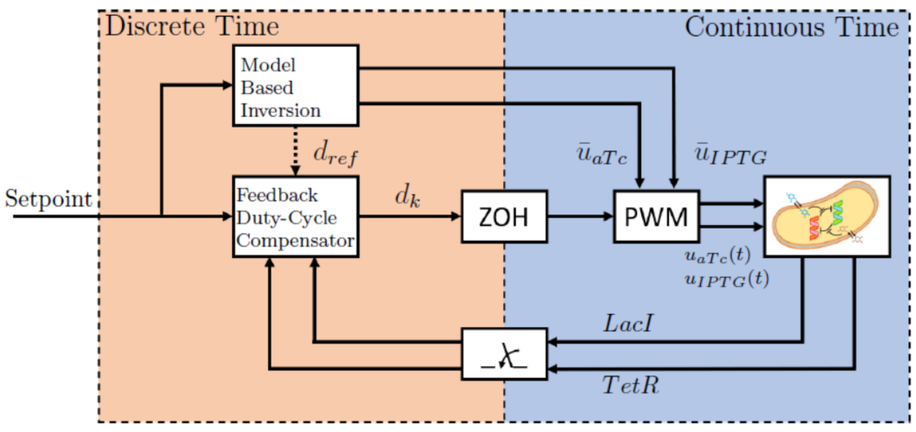
A testbed example

The Genetic Toggle Switch (GTS) is a Gene Regulatory Network (GRN) that shows the typical bi-stable dynamics and regulates fundamental processes in cells life (eg. stem cell fate decision, differentiation). The GRN is composed by two mutually repressive genes, whose expression can be regulated by external inducers. The GTS can be modelled by a 6th order non-linear non-smooth MIMO ODE system.



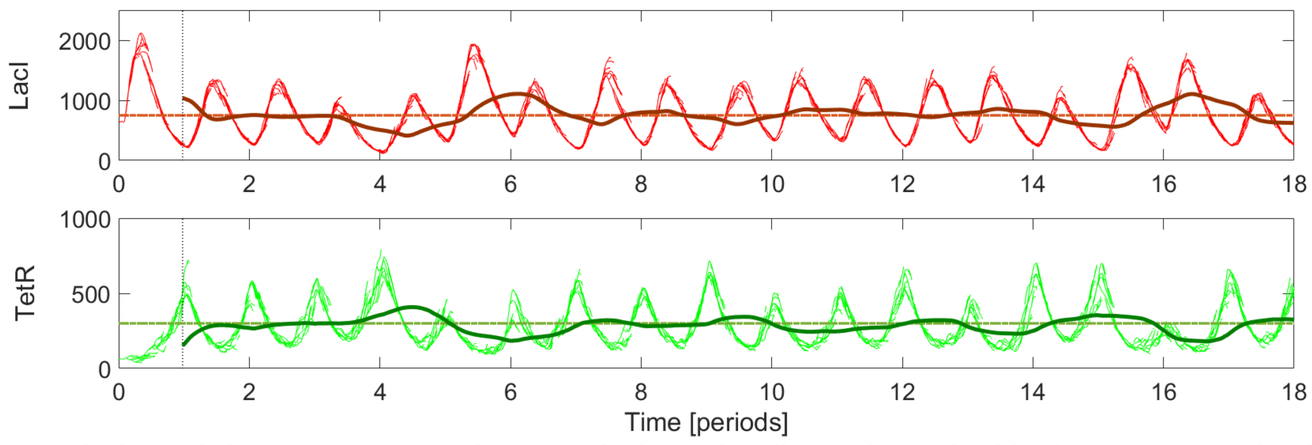
➢ **Control Goal:** *<u>Balance the GTS about its unstable equilibrium</u>*

Our control approach



Block Diagram of the external control strategy: Nonlinear Feedforward + Feedback loop to modulate PWM inputs

In silico control experiments

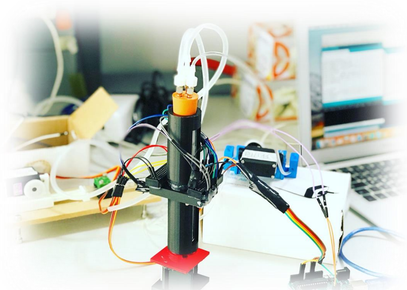


Evolution of the two output of a population of cells endowed with the GTS. Dashed lines are the setpoints, light lines are the evolution of the single cell, dark lines the average evolution evaluated with a moving window.

<u>Theoretical investigation involves</u>: Bifurcations, Non Linear Control, Time-Average Models, Filtering Properties, Approximation of Equilibria, Non Linear Projector, Model Predictive Control, Genetic Algorithm, Gillespie Simulation Algorithm, Agent-Based simulations.

The Turbidostat

We designed and assembled from scratch a *modular*, *versatile*, and *open-source* bioreactor to host *in-vivo* experiments. The machine controls the concentration of bacteria in a vessel and it is based on a control loop closed over a measure of turbidity of the solution.



Contacts and Acknowledgements

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more info & publications available here

Future developments

- Design a new type of bioreactor for multicellular *in vivo* control experiments that guarantees the survival of both the species (controllers and targets) involved.