



Agostino Guarino

Tutor: Mario di Bernardo

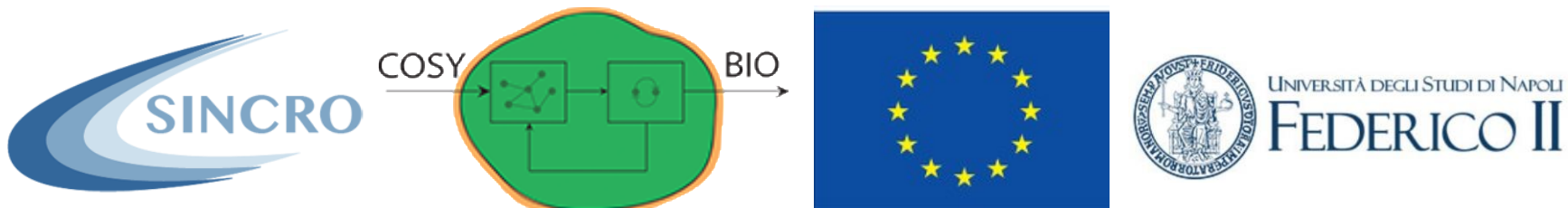
XXXIII Cycle - I year presentation

Analysis and Control of Bacterial
Populations in Synthetic Biology



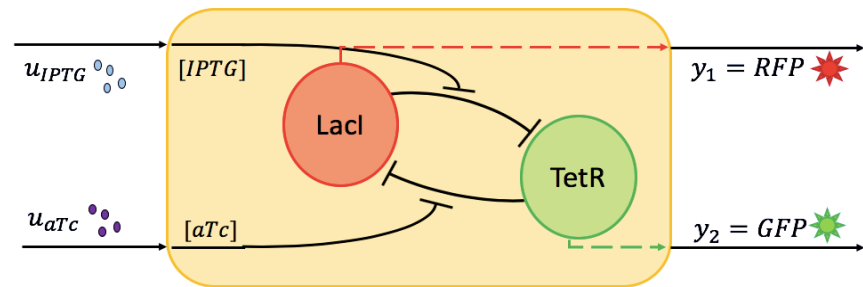
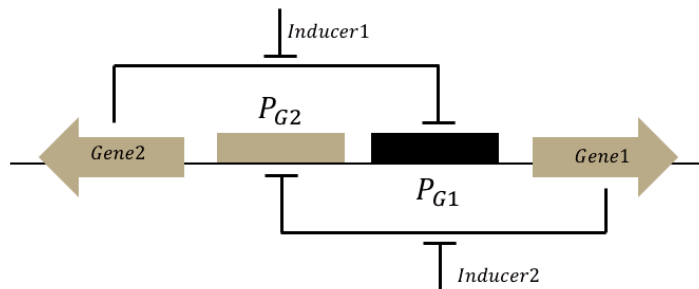
Background

- Received the Master Degree cum laude in Ingegneria dell'Automazione at Università degli Studi di Napoli Federico II on 02/10/17.
- Master Thesis about Control of Cryogenic Systems at CERN.
- Fellowship type: Borsa su Progetto Europeo COSYBIO.
- Part of:
 - SINCRO group
 - COSYBIO European Project

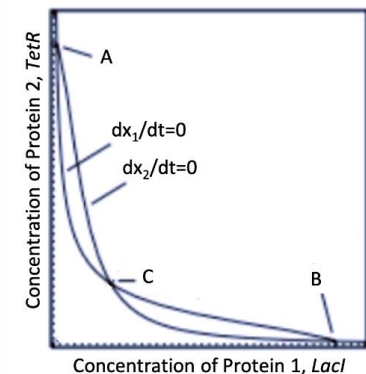


Problem 1/2: Genetic Toggle Switch

- Synthetic Biology is a new emerging field that is born from the union of several branches of science to research in the biological field.
- The Genetic Toggle Switch [1] is a genetic network composed by two mutually repressive genes.



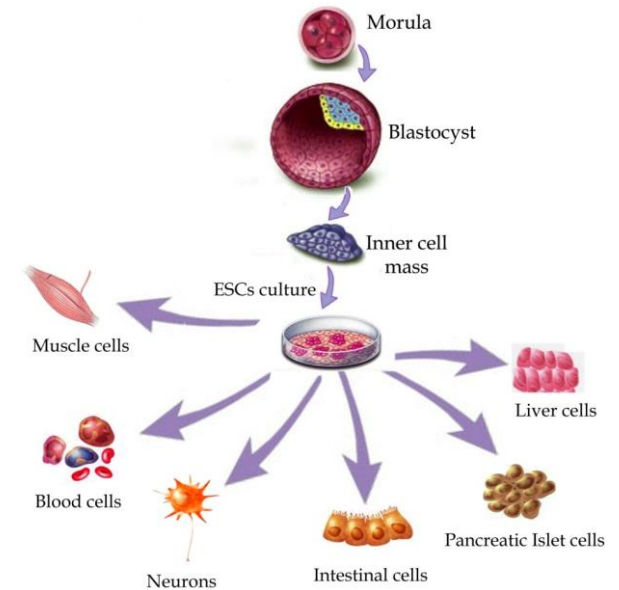
- It behaves as a bi-stable system; external inducers drives the system near an equilibrium (stable or unstable) point.



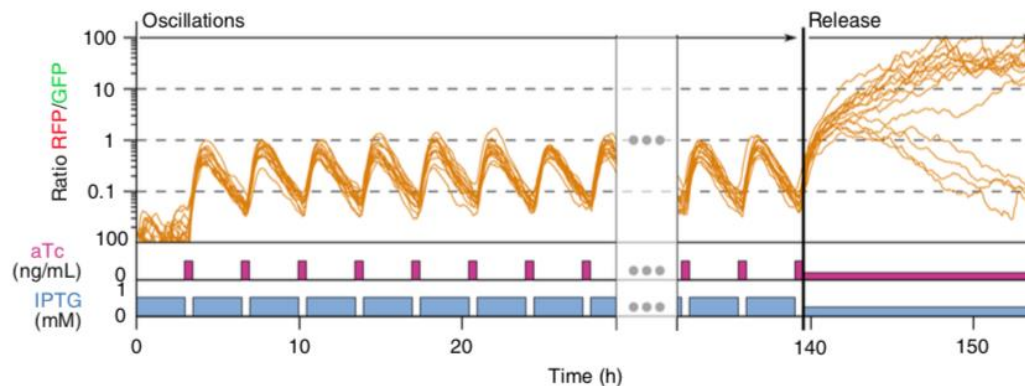
[1] T. S. Gardner, C. R. Cantor, and J. J. Collins, "Construction of a genetic toggle switch in Escherichia coli," Nature, vol. 403, no. 6767, p. 339, 2000.

Problem 2/2: Control of Genetic Toggle Switch

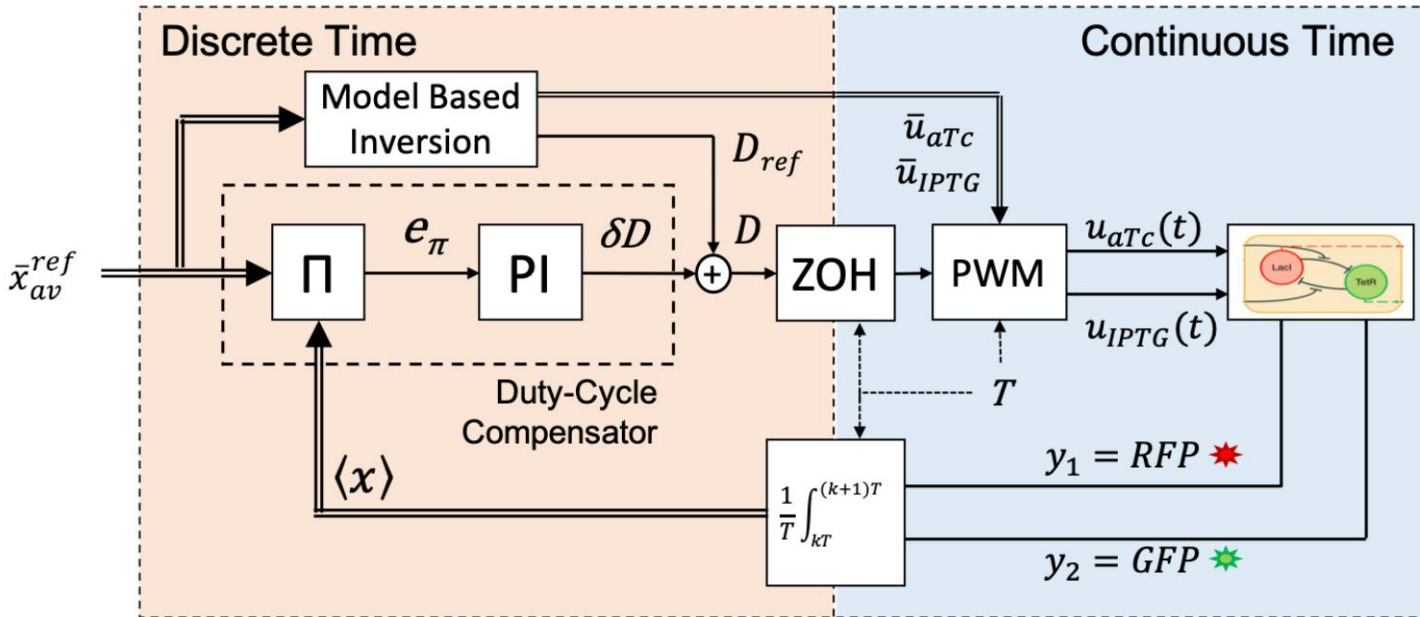
- Controlling the Toggle Switch over the unstable equilibrium plays a key role in fate decision of stem cells.



- Periodic Mutually Exclusive Pulse Wave Inputs have been shown to be useful to keep the Toggle Switch in a given region [2].



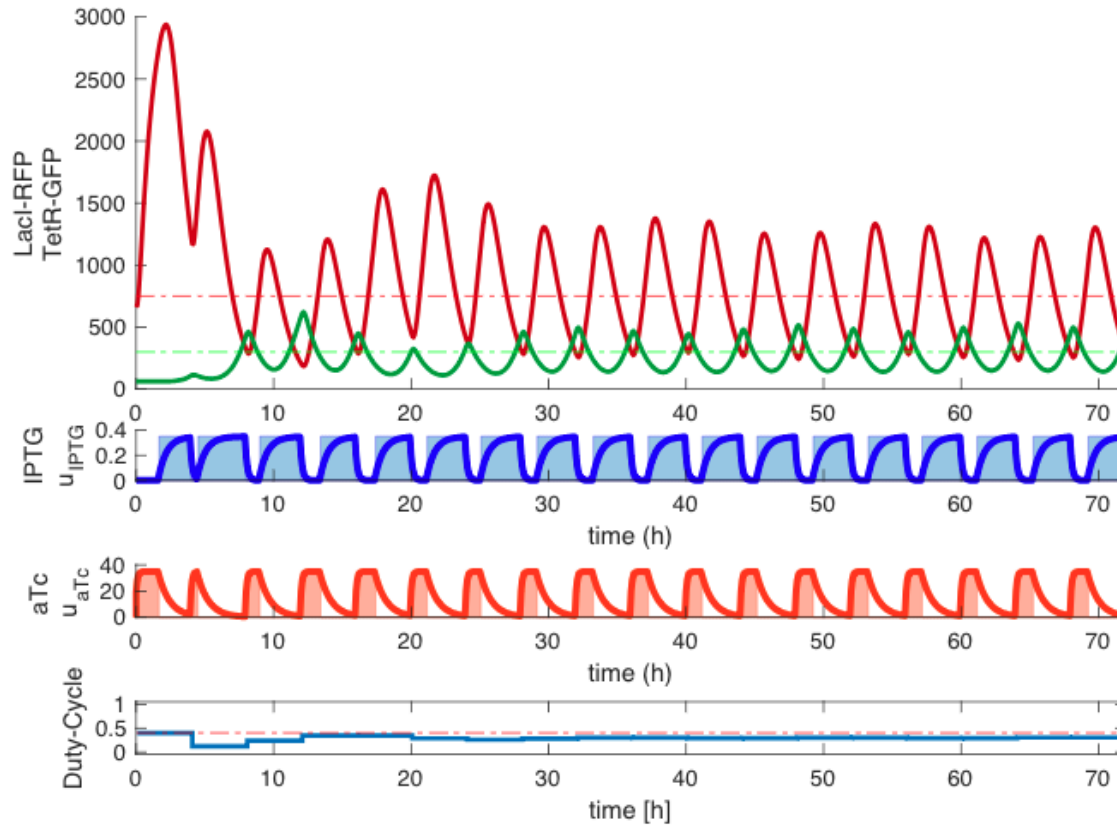
Results 1/3: PIPWM Strategy



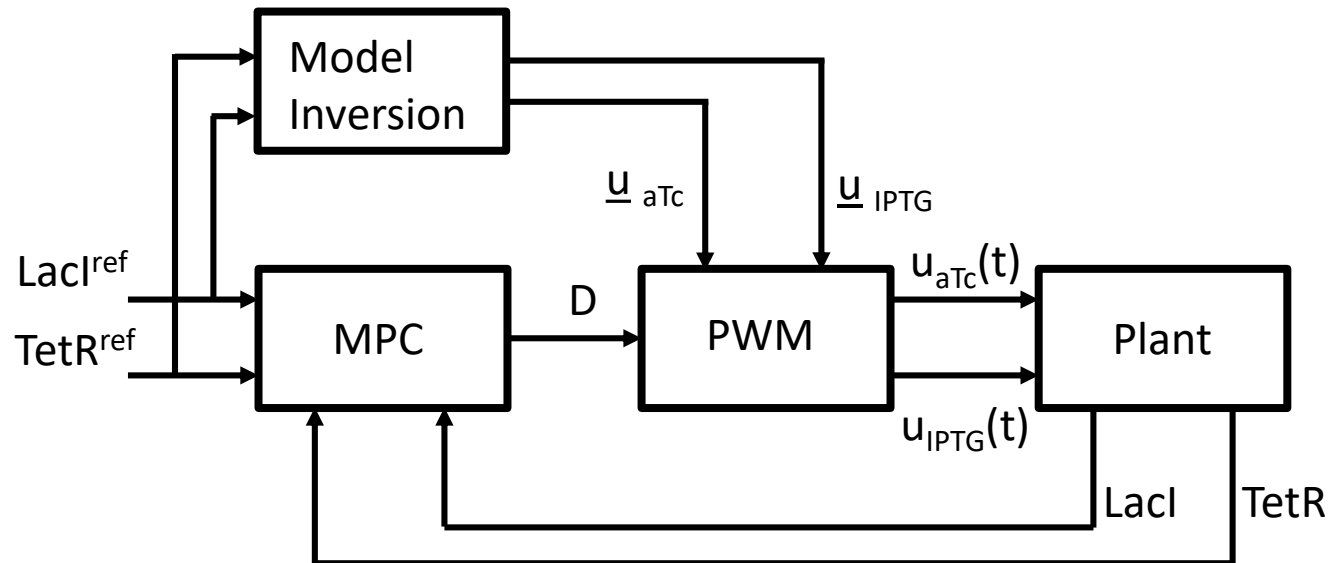
- A Feed Forward Model Based Inversion action evaluates the amplitudes and the duty cycle of the Pulse Wave Inputs.
- A Feed Back Loop corrects the duty cycle to compensate the effects of diffusion

Results 1/3: PIPWM Strategy

PERFORMANCE:



Results 2/3: MPC Strategy



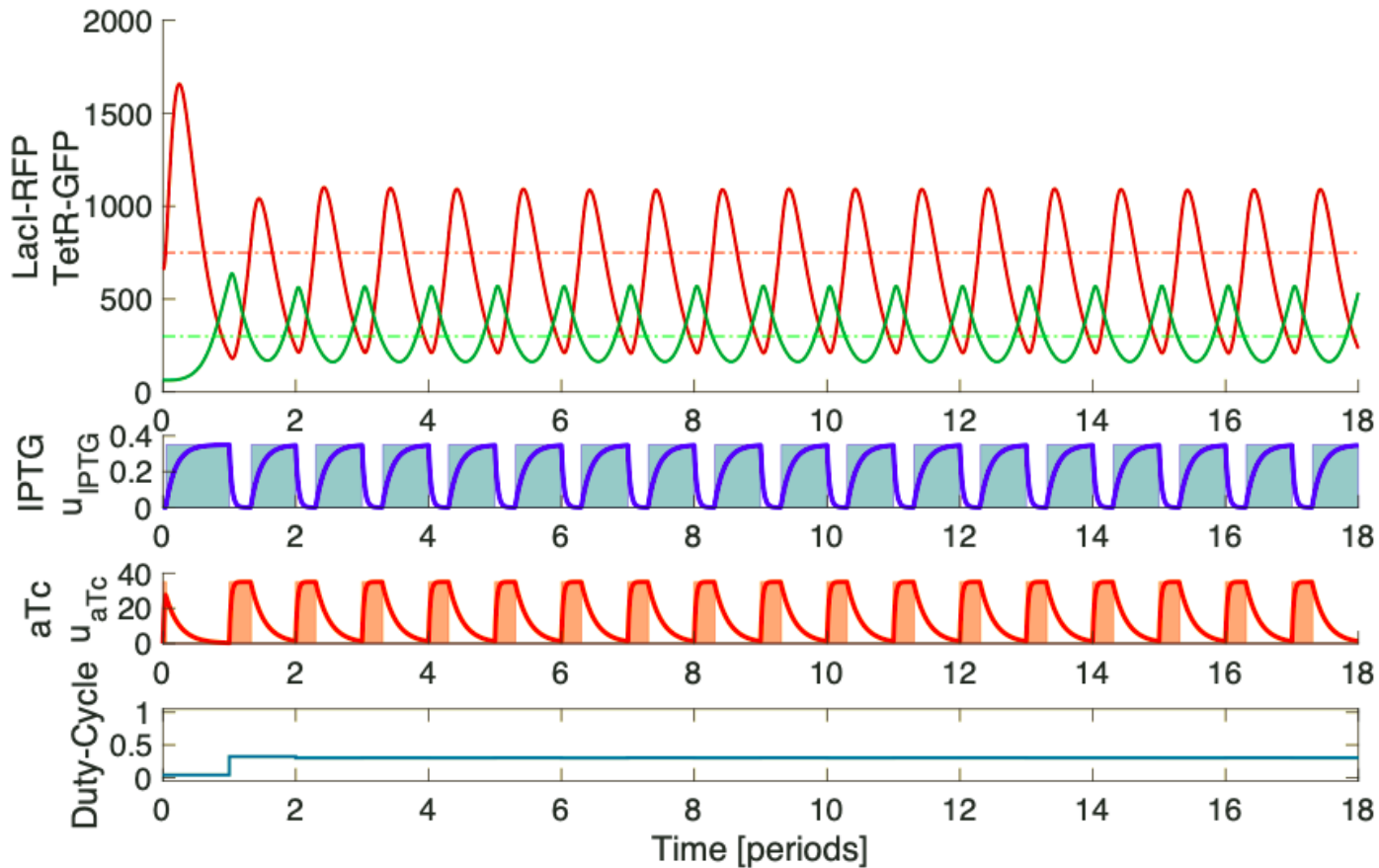
- Model Predictive Control is an optimization-based control algorithm that uses a model of the system to predicts its evolution.
- The optimization is carried out using Genetic Algorithms

Period: 4 hours.

Total Simulation Time: 72 hours 7

Results 2/3: MPC Strategy

PERFORMANCE:



Period: 4 hours.

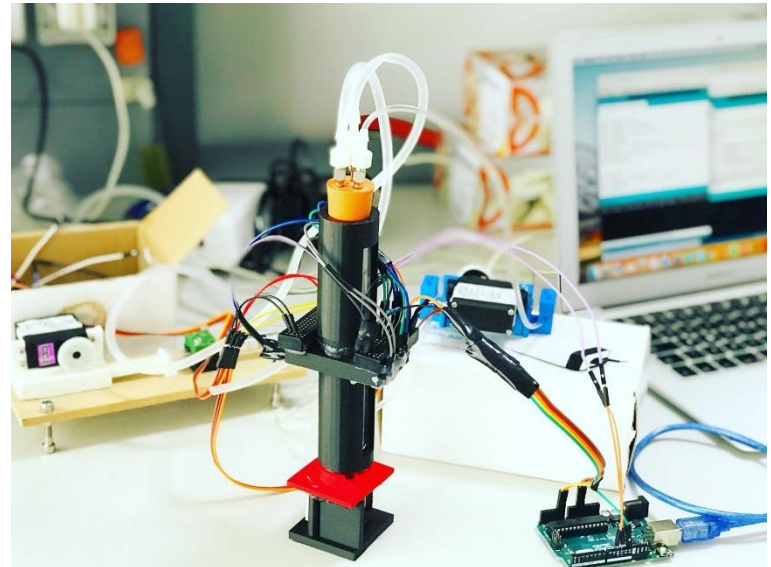
Total Simulation Time: 72 hours 8

Results 3/3

- Other Control Strategies have been proved not to be able to deal with the diffusion dynamics:
 - PI
 - Zero Average Dynamics Control (ZAD)
- Control Strategies have been validated via Stochastic Simulations with the Gillespie Algorithm.
- Currently designing in vivo experiments to test the proposed strategies.

Products

- Journal Paper:
 - D. Fiore, A. Guarino, M. di Bernardo *“Analysis and control of genetic toggle switches subject to periodic multi-input stimulation”*, IEEE Control System Letters 3 (2), 278-283, 2018.
- Submitted Conference Paper:
 - A. Guarino, D. Fiore, M. di Bernardo, *“In-silico Feedback Control of a MIMO Synthetic Toggle Switch via Pulse-Width Modulation”*, EUCA 17th European Control Conference (ECC’19).
- Prototype of Bioreactor:
 - Turbidostat
Host environment for in vivo experiments



Credits Recap

	Credits year 1							Credits year 2							Credits year 3							Total	Check		
	1	2	3	4	5	6	Summary	Estimated	1	2	3	4	5	6	Summary	Estimated	1	2	3	4	5			6	Summary
	bimonth	bimonth	bimonth	bimonth	bimonth	bimonth	Summary	Estimated	bimonth	bimonth	bimonth	bimonth	bimonth	bimonth	Summary	Estimated	bimonth	bimonth	bimonth	bimonth	bimonth	bimonth	Summary	Total	Check
Modules	0	0	6	3	0	1.9	10.9	0	5						0	5							0	10.9	30-70
Seminars	0	0	2.8	0.2	0	0.6	3.6	5							0	4							0	3.6	10-30
Research	10	10	1.2	6.8	10	7.5	45.5	5							0	51							0	39,5	80-140
	10	10	10	10	10	10	60	60	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	60	180

- Two modules have been attended during the first year but they have not been registered yet.
 - With those two modules, the Credits earned match the plan on the ITEE PhD website.

Thank you for your attention.

Questions?