Lorena Postiglione

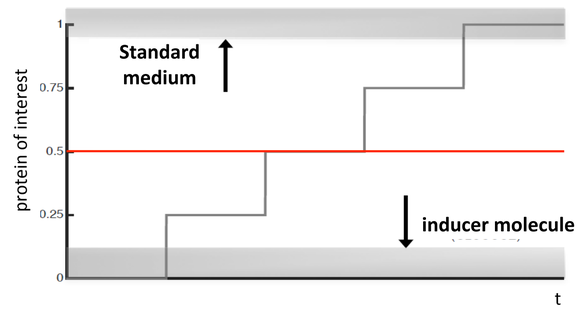
Tutor: Diego di Bernardo

XXIX Cycle - II year presentation

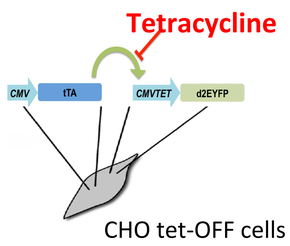
Microfluidics-based Automatic Control of gene expression in mammalian cells

Control of gene expression from inducible promoters

In **System and Synthetic Biology lab** at Telethon Institute of genetics and Medicine, we exploit **Control Engineering** to regulate the dynamics of gene expression in mammalian cells by using a negative feedback control strategy.
Our results show for the first time that it is possible to apply Control Engineering Theory to regulate at will protein expression in a mammalian cell line, and open new possibilities for the quantitative study of cellular dynamics.



Control in mammalian cells: cellular model

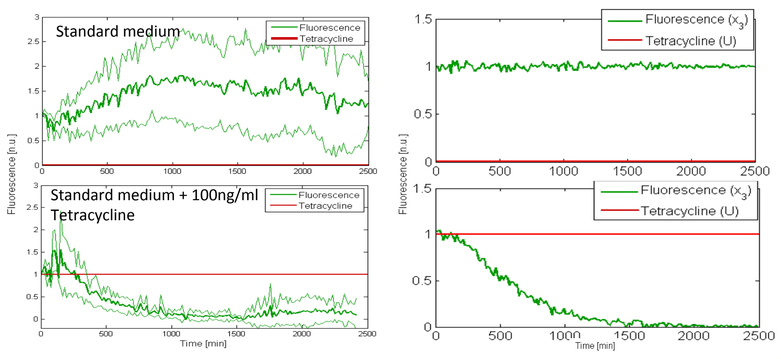


CHO tet-OFF cells

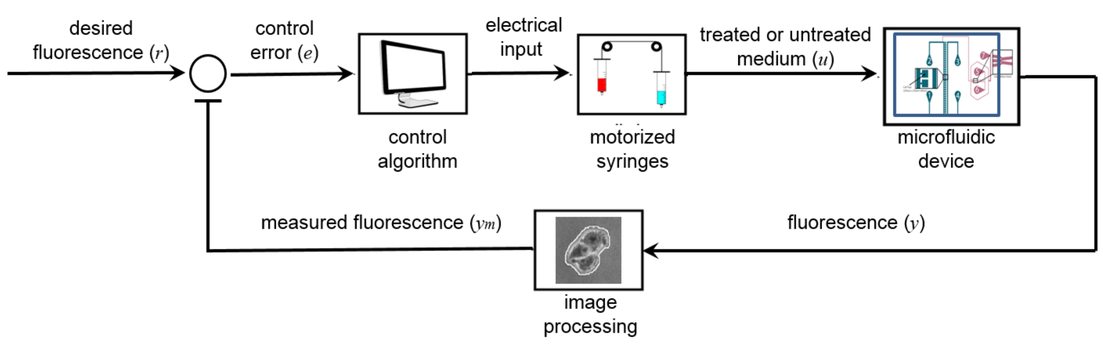
$$\frac{dx_1}{dt} = v_1\alpha_1 + v_1\alpha_2 U - d_1 x_1 \quad \textit{d2EYFP mRNA}$$

$$\frac{dx_2}{dt} = v_2 x_1 - (d_3 + K_f)x_2 \quad \textit{unfolded d2EYFP protein}$$

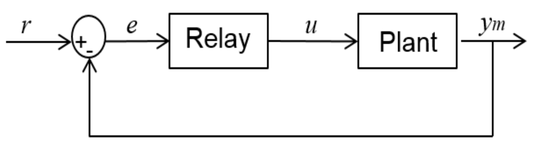
$$\frac{dx_3}{dt} = K_f x_2 - d_3 x_3 \quad \textit{folded d2EYFP protein}$$



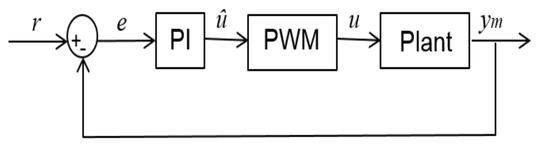
Implementation of control scheme



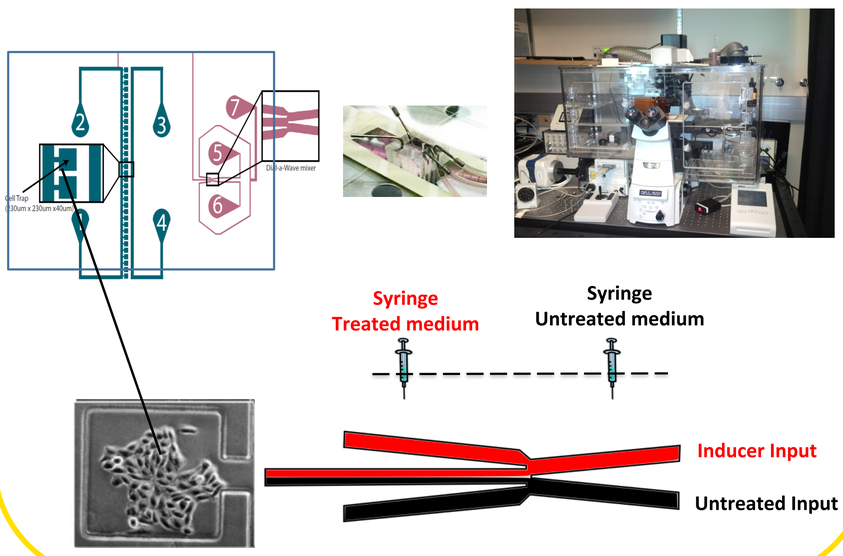
Relay Control with Hysteresis



Proportional-Integral controller with Pulse Width Modulator



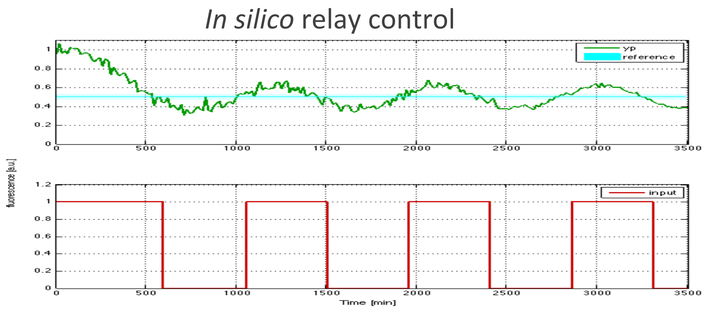
Experimental Platform



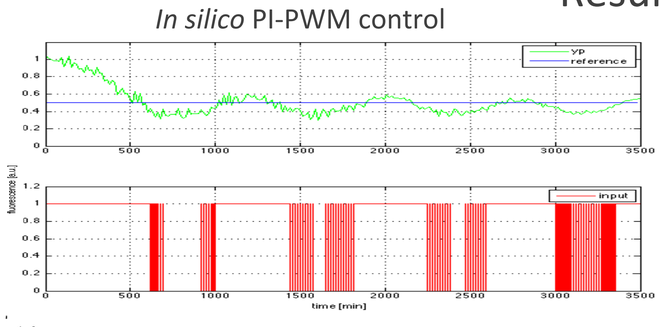
Automatic Control of Gene Expression in Mammalian Cells.
(Fracassi C**, Postiglione L**, Fiore G, di Bernardo D**)**
ACS synthetic biology, 2015

Results

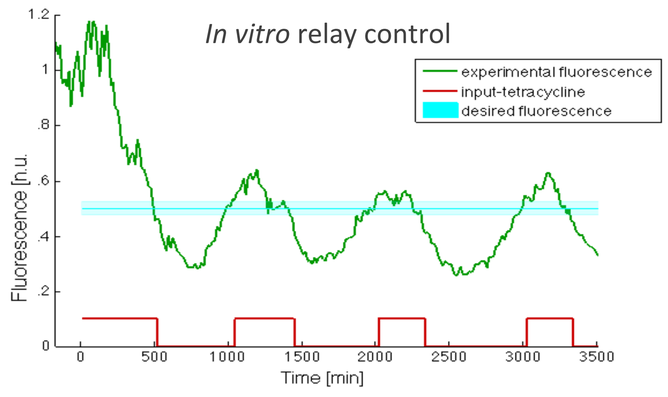
In silico relay control



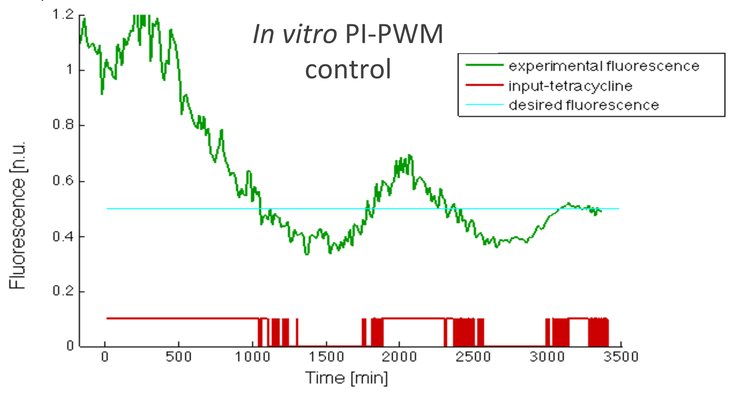
In silico PI-PWM control

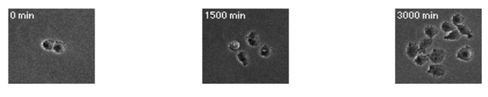


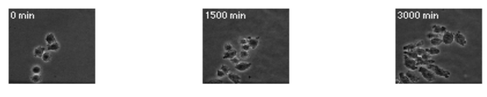
In vitro relay control



In vitro PI-PWM control



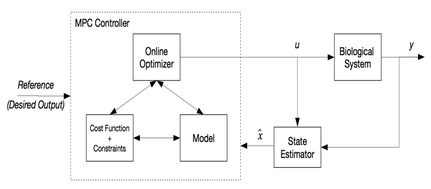


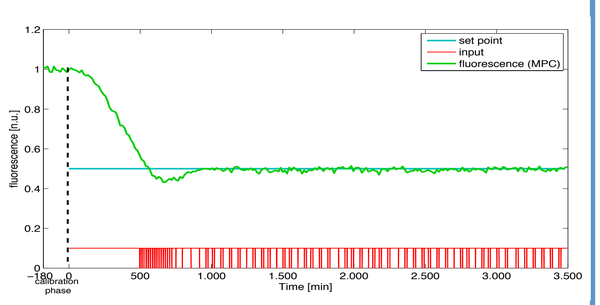


Internship in the Systems and Synthetic Biology Lab at the Telethon Institute of Genetics and Medicine. **Affiliation** to the Istituto Italiano di Tecnologia.

Future Works (I):

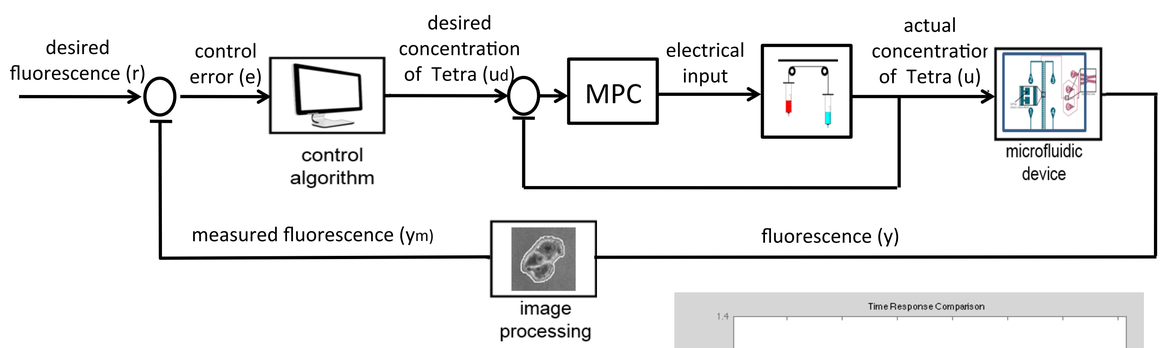
- Model Predictive Control





- Control of gene expression in **single cell**

Future Works (II): Improvement of control strategy



Syringes model

$$\frac{dx}{dt} = -0.2234x(t) + 0.0506u(t)$$
$$y(t) = 4.946x(t)$$

$$t_a \approx 22 \text{ min}$$