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Tutor: Diego di Bernardo

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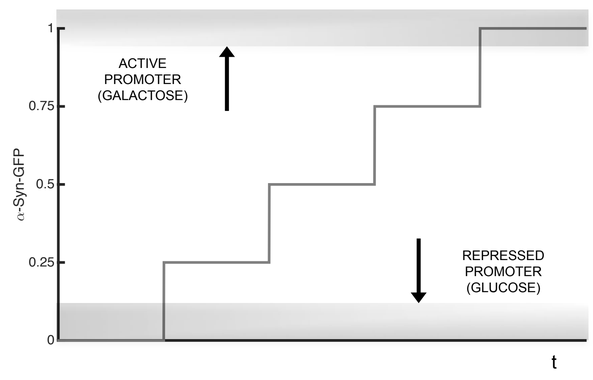
XXIX Cycle - II year presentation

Identification and Control of Gene Expression in Yeast

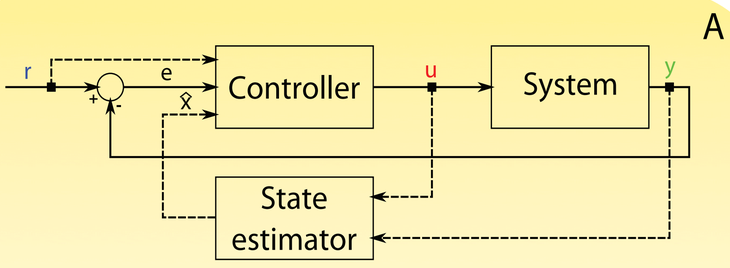
SYNTHETIC BIOLOGY aims at building novel biological ‘circuits’, synthetic networks, which can alter cell behavior by performing specific desirable tasks. Additionally it can be used to build simplified models of complex biological pathways in order to better understand their working mechanisms.

REAL-TIME AUTOMATIC REGULATION OF GENE EXPRESSION is a key technology for synthetic biology enabling, for example, synthetic circuit's components to operate in an optimal range. Additionally it can be used to attain a quantitative understanding of the dynamical behavior of a protein.



IDEA: to use *control engineering* to regulate gene expression in yeast.

A



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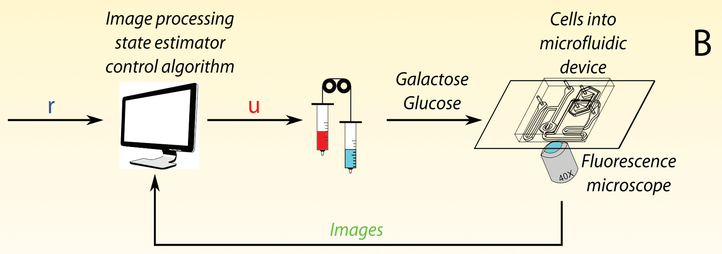
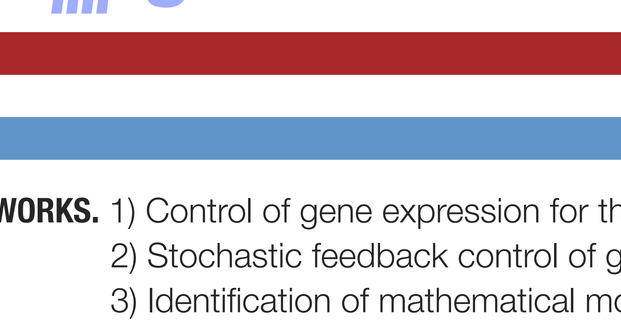


EXPERIMENTAL PLATFORM



EXPERIMENTAL TEST-BED for the assessment of control strategies: GAL1 promoter in *Saccharomyces cerevisiae.*

FEEDBACK CONTROL

- Proportional-Integral Control

$$u(t) = K_p e(t) + K_i \int_0^t e(\tau) d\tau$$

- Zero Average Dynamics Control (model-based)

$$\mathbb{E}_T\left[s\left(x(t)\right)\right] = \frac{1}{T}\int_{kT}^{(k+1)\,T} s\left(x(t)\right)\,dt = 0$$

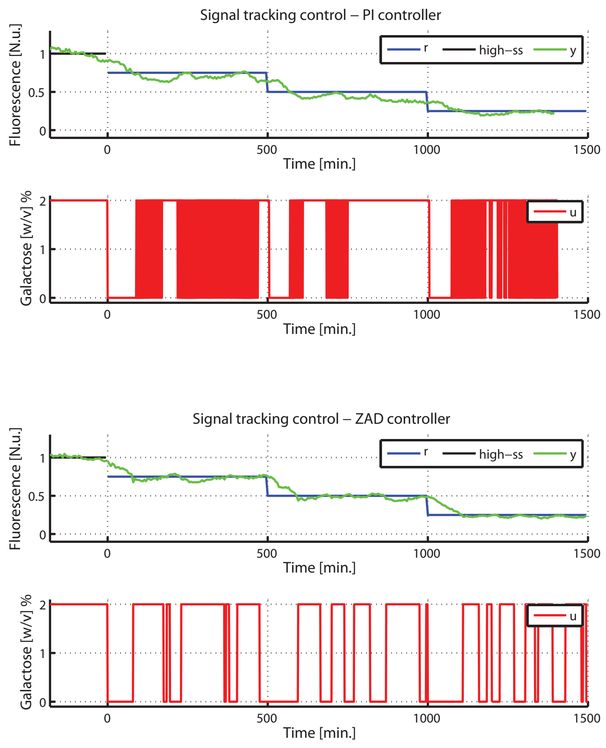
$$s\left(x(t)\right) = \left(x_2(t) - x_{2_{ref}}(t)\right) + \left(\dot{x}_2(t) - \dot{x}_{2_{ref}}(t)\right)$$

- Model Predictive Control (model-based)

*GAL1*p model

$$\dot{x}_1 = -d_1 x_1 + bu \quad \text{mRNA}$$

$$\dot{x}_2 = v_2 x_1 - d_2 x_2 \quad \text{GFP protein}$$



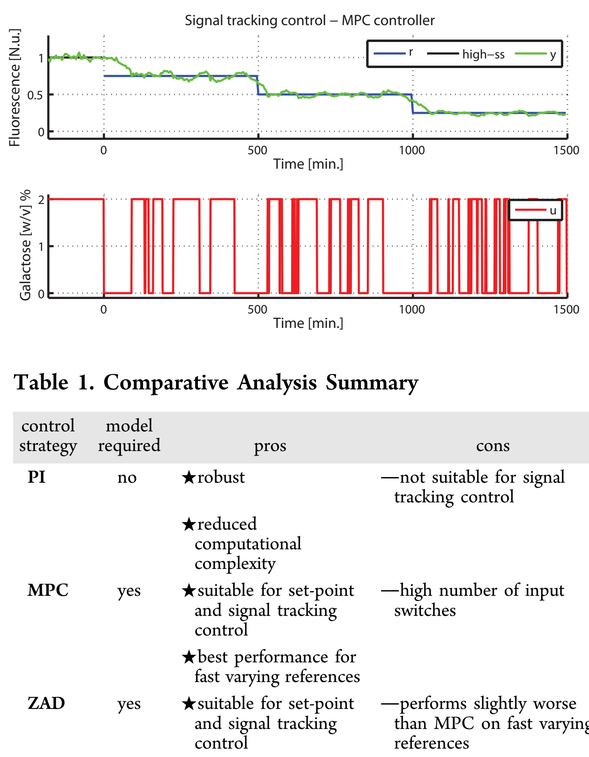


Table 1. Comparative Analysis Summary

control strategy	model required	pros	cons
PI	no	★robust	—not suitable for signal tracking control
		★reduced computational complexity	
MPC	yes	★suitable for set-point and signal tracking control	—high number of input switches
		★best performance for fast varying references	
ZAD	yes	★suitable for set-point and signal tracking control	—performs slightly worse than MPC on fast varying references
		★reduced number of input switches	

EXPERIMENTAL RESULTS

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

ISTITUTO ITALIANO DI TECNOLOGIA

FUTURE WORKS. 1) Control of gene expression for the study of neurodegenerative disorders (e.g. Parkinson’s disease).
2) Stochastic feedback control of gene expression at the single-cell level.
3) Identification of mathematical models to describe gene expression at single-cell level by means of linear mixed-effects modeling.
4) Stochastic simulator of biological ‘circuits’.