

Project Proposal

Data-driven and learning-based control approaches for cybergenetics

Project Description (*max 500 words*)

The problem of devising controllers to tame the dynamics of synthetic biological systems is becoming a crucial part of Systems and Synthetic Biology, giving rise to the emerging field of cybergenetics. In the external control paradigm, the control algorithm is implemented on a PC (or microcontroller) and the control input is delivered to the cells via some external actuators. Typically, in the literature, model based approaches are used to synthesize a controller. However, some key challenges of this approach include: (i) the lack of a precise knowledge of the model of the system under control; (ii) the intrinsic stochasticity of the processes considered; (iii) the presence of noise in the measurements. This project aims at overcoming these challenges by exploring a data-driven/learning approach to external cellular control. The idea is to develop novel control techniques that do not necessarily require the identification of a mathematical model. The techniques will be benchmarked against state-of-the-art approaches both in-silico, via realistic simulators and, in-vivo. As such, the project will include both a methodological component (including control methodology development, synthesis of key performance indicators, study of stability and robustness properties) and an experimental, hands-on, component on the systems under control.

Supervisor(s), Lab/Group details, other additional info.

Mario di Bernardo (DIETI)
Diego di Bernardo (DICMAPI/TIGEM)
Giovanni Russo (UNISA)
Lucia Marucci (Bristol)

Funding (*how the reagents, equipments, conference and travels will be supported*)

Funding available to MdiB and TIGEM via industrial collaborations and other funding sources

References

1. Iacopo Ruolo et al. "Control engineering meets synthetic biology: Foundations and applications". In: *Current Opinion in Systems Biology* 28 (2021), p. 100397.
2. Domitilla Del Vecchio et al. "Future systems and control research in synthetic biology". In: *Annual Reviews in Control* 45 (2018), pp. 5–17.
3. Davide Fiore et al. "Analysis and control of genetic toggle switches subject to periodic multi-input stimulation". In: *IEEE control systems letters* 3.2 (2018), pp. 278–283.
4. Gianfranco Fiore et al. "In vivo real-time control of gene expression: a comparative analysis of feedback control strategies in yeast". In: *ACS synthetic biology* 5.2 (2016), pp. 154–162.
5. Agostino Guarino et al. "Balancing cell populations endowed with a synthetic toggle switch via adaptive pulsatile feedback control". In: *ACS synthetic biology* 9.4 (2020), pp. 793–803.

6. M. Khammash, M. Di Bernardo, and D. Di Bernardo. “Cybergenetics: Theory and Methods for Genetic Control System”. In: 2019 IEEE 58th Conference on Decision and Control (CDC). 2019, pp. 916–926.
7. Jean-Baptiste Lugagne et al. “Balancing a genetic toggle switch by real-time feedback control and periodic forcing”. In: Nature communications 8.1 (2017), pp. 1–8.