Establishing performance bounds of synthetically engineered gene circuits

Supervisor: Andreas Hilfinger https://hilfinger.group

Background: Regulating gene expression lies at the heart of all life. Modern molecular biology tools allow us to build synthetic biological circuits to control the expression of specific genes in organisms. Such synthetic circuits have the potential not only to revolutionize healthcare but also to support the production of renewable biofuels [1].

Unfortunately, gene regulatory circuits are not as robust or as easy to understand as electric control circuits due to non-linear and stochastic interactions combined with the fact that a lot of interactions remain uncharacterized. Our work focuses on understanding general performance trade-offs in gene regulatory systems. In particular, we are interested in the necessary requirements to achieve robust average levels in the face of noisy environment within biological cells.

Project description: In this project you will study a particular type of feedback motif called anti-thetic integral control, see Fig. 1. In particular, you will analyze its stochastic noise properties. Your numerical simulations will supplement our approximate analytical approaches to characterize the modular properties of feedback control in biological cells.

Requirements: Strong mathematical modelling skills and programming experience (preferred in C++ but any language will do). Prior training in stochastic processes is advantageous but not required.

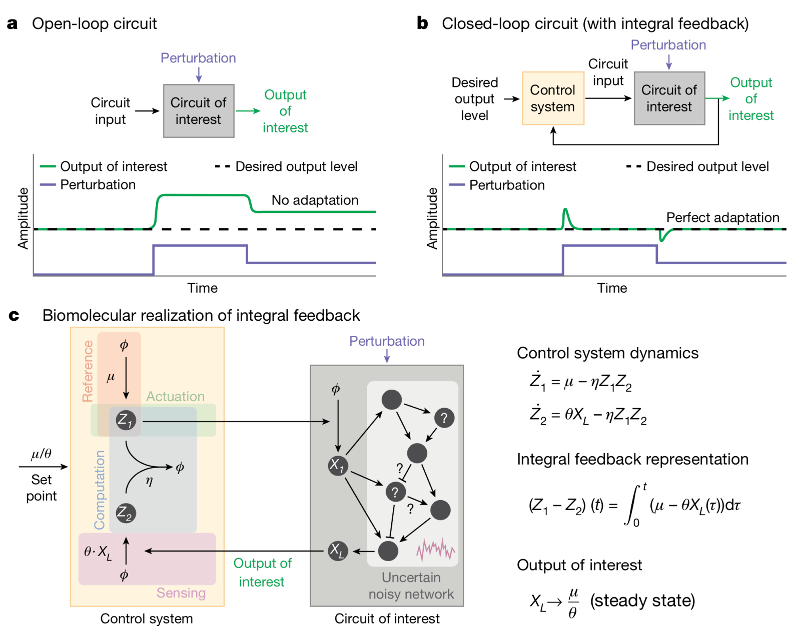

Figure 1 Schematic diagram of integral feedback enabling robust perfect adaptation. Taken from [2].

[1] El Karoui, Meriem, Monica Hoyos-Flight, and Liz Fletcher. "Future trends in synthetic biology—a report." *Frontiers in bioengineering and biotechnology* 7 (2019): 175. doi.org/10.3389/fbioe.2019.00175

[2] Aoki, Stephanie K., et al. "A universal biomolecular integral feedback controller for robust perfect adaptation." *Nature* 570.7762 (2019): 533-537. doi.org/10.1038/s41586-019-1321-1