



The Control Theory and Systems Biology group (<http://www.bsse.ethz.ch/ctsb>) of the Department of Biosystems Science and Engineering (D-BSSE), ETH Zürich in Basel, is seeking for a

MSc student

for **the theoretical development of in-vivo control methods for synthetic biology** as part of a master thesis.

Biomolecular control theory is a subfield of synthetic biology whose goal is to design in-vivo regulation circuits in order to ensure certain objectives for the controlled network. Perfect adaptation (i.e. constant reference tracking and/or constant disturbance rejection) will be the control objective considered in this work. Potential applications include the optimization of the production of molecules such as drug precursors, biofuels, flavors, fragrance, colorants, etc. in bioreactors. Many adaptation motifs have been proposed and observed [1], some of them relying on the well-known concept of integral action or incoherent feedforward motifs. It has also been recently theoretically shown that a new motif implementing an integral action can be considered as a potential in-vivo controller [2]. These controllers have the advantage of being implementable in terms of chemical reactions, a property that we will call here “bio-realizability”. However, it is actually still unclear what classes of systems are bio-realizable. This problem has been partially solved for few classes of linear systems in [3]. Unfortunately, the scope of this framework seems limited as the family of systems that can be represented in this way seems small.

The first part of this project will be devoted to the explicit characterization of (linear) bio-realizable systems using the method described in [3]. The objective of the second part is to extend these ideas in order to cover a more general class of systems. The validation of these ideas will be done both theoretically and numerically, and will be possibly illustrated using realistic control applications.

The prospective student should have prior experience in dynamical systems and control theory. Prior knowledge on systems biology would be an advantage, but is not necessary. The student should be able to work independently but proper support will be provided.

Note: candidates living in Zürich are also highly encouraged to apply. Presence in Basel may only be necessary for one or two days per week.

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References :

[1] W. Ma, A. Trusina, H. El-Samad, W. A. Lim, and C. Tang. Defining network topologies that can achieve biochemical adaptation. *Cell*

[2] C. Briat, A. Gupta, and M. Khammash. A new motif for robust perfect adaptation in noisy biomolecular networks

[3] K. Oishi and E. Klavins. Biomolecular implementation of linear I/O systems. *IET Systems Biology*