Towards a synthetic oscillating enzymatic network

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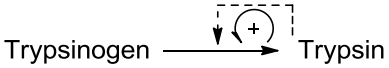
Key processes such as metabolism, signaling and gene expression in all living systems are regulated by complex enzymatic and genetic networks. These biological networks can display a wide variety of functions such as amplification or damping of signals, ultrasensitive switches, delay lines, oscillatory behavior with controllable frequency and amplitude and pattern formation.

Despite progress on understanding of biological systems, the design and implication of artificial enzymatic networks has been limited. Oscillators and clocks are the types of processes that are relatively well understood and would be a preferable target for engineering [1,2].

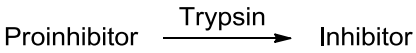
Thus, the aim of this work is to design and construct a modular oscillating enzymatic network.

The network consists of three main reactions:

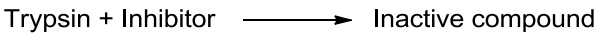
1. Autocatalytic generation of the active species (trypsin)



2. Trypsin catalyzed generation of an irreversible inhibitor from the "proinhibitor"



3. Inactivation of trypsin



The network shows a single oscillation of trypsin activity in the batch reactor and dump oscillations in the continuously stirred tank reactor (CSTR). Oscillations of trypsin activity in outlet of CSTR modulate activity of another enzyme in the case of system of two reactors. The experimental data were numerically simulated.

In this talk, we would like to discuss design of the enzymatic network and development of synthetic inhibitors for the negative feedback. We would also like to share our experience in assembly of a microfluidic version of a CSTR and monitoring of changes in enzymatic activity inside CSTR.

1. J. E. Ferrell, T. Y.-C. Tsai and Q. Yang, *Cell*, **144**, 874 (2011).

2. K. Montagne, R. Plasson, Y. Sakai, T. Fujii and Y. Rondelez, *Mol. Syst. Biol.*, **7**, 466 (2011).