Turing Meets Synthetic Biology
Self-emerging patterns in an activator-inhibitor network.

ABSTRACT

We present a synthetic network that emulates an activator-inhibitor system. Our goal is to show that spatiotemporal structures can be generated by the behavior of a genetic regulatory network. We implement the model by means of several biobricks. We construct a self activating module and correspondingly an inhibitory one. Self-activation dynamics is given by the Las operon, while the inhibitory part is provided by the Lux operon. Quorum sensing and diffusion of AHL provide the reaction-diffusion mechanism responsible for the formation of Turing patterns. The importance of our work relies on the fact that we show that the action of the morphogens as originally proposed by Turing is equivalent to the effect of diffusion of chemicals interacting with the synthetic network, which accounts for the reactive part, a possibility implicit in Turing’s original work in the context of morphogenesis of biological patterns.

Reaction-Diffusion equations
Turing formally described his proposal with a set of partial differential equations where it is possible to represent the chemical interactions of the morphogens and the way they move over the space. This kind of dynamics are commonly called reaction-diffusion mechanisms, and the equations that describe them are known as Reaction-Diffusion equations:

\[ \frac{\partial c}{\partial t} = f(c) + D \nabla^2 c \]

\[ \frac{\partial A}{\partial t} = F(A, B) + D_A \nabla^2 A \]

\[ \frac{\partial B}{\partial t} = G(A, B) + D_B \nabla^2 B \]

The Activator-Inhibitor

In 1972 A. Gierer and H. Meinhardt published their work called “A theory of biological pattern formation” presenting a network based on the interaction of at least two morphogens acting as an activator and an inhibitor. The main qualitative dynamics of the morphogens is “short range activation, longer range inhibition and a conceptual distinction between effective concentrations of activator and inhibitor; on one hand, and the density of their sources on the other”.

\[ F(A, B) = \lambda_1 - k_1 A + \frac{k_2 D}{d} \frac{B}{\lambda_2} \]

\[ G(A, B) = K_2 A^2 - K_3 B \]

Spatial Model

Afterward, we described it as a system of ordinary differential equations the time change of the concentrations of PAI and AI based on the kinetic law equations, being “X” PAI and “Y” AI. With this system of differential equations describing the kinetic basis of the reaction and diffusion we proceeded to make a qualitative analysis of its behavior.

\[ \frac{dX}{dt} = k_1 X - k_2 X Y + k_3 Y \]

\[ \frac{dY}{dt} = k_4 X Y - k_5 Y \]

Initial instability damping by the sinusoidal initial condition of dynamical system simulation. The system evolution lead to a nonhomogenous state but an spatial gradient.

Experimental Work

During these months we accomplished the synthesis of II new biobricks (protein generators and inverters) which were added to the Registry, we have the 90% of advance of our system completed as follows.

We also have preliminary data confirming the proper functioning of the activator module, as show in the pictures.

Conclusions and further work

The preliminary results show that the activator system works. The inhibitor will be coupled by the end of the year. In order to test the experiments we planned to make the experiments to show if our biobricks is able to produce an spatiotemporal pattern, we will use a chemical gradient of IPTG and aTc. The modeling results have given us an insight of how the system will respond to particular chemical initial distributions. Besides we also need to complete the mode of this project with different perspectives, the use of stochastic approaches should allow us to introduce noise in the system and look how the emergence of biochemistry pattern could be affected.

We are not far to conclude if an activator-inhibitor mechanism implemented with biobricks could generate a spatiotemporal Turing like pattern.

Main references