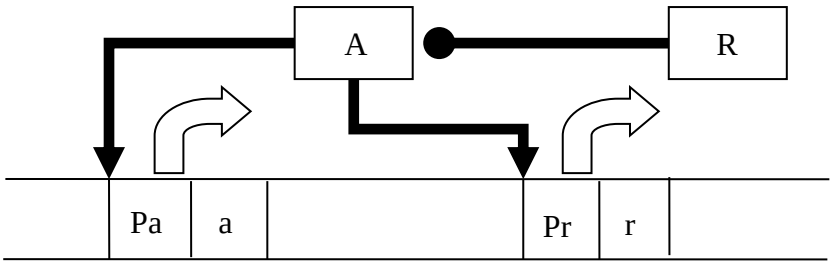
PROJECT 8 ODE

Transcript adjustment circuit with positive and negative feedback

The mechanism regulating the amount of protein produced during protein synthesis takes the name of transcription regulating circuit. In the DNA, upstream of the genes, there is a region called the promoter, which indicates the exact point where transcription must begin and end. The polymerized RNA binds downstream of the promoter and begins to create a copy of the gene that is called a transcript. This, inside the ribosomes, is then translated into a protein, the quantity of which is controlled by a transcription regulation module. This regulation can be of two types: direct, through activators and repressors, or indirect, through the use of inductors or inhibitors. Because all these molecules are present inside the cell, there will be genes that code for them, on which one can act for further regulation. In this case, a genetic circuit has been taken into consideration in which activator and repressor are linked together through a double feedback: a positive one to amplify the quantity and a negative one to keep the system stable. This will oscillate activator and repressor concentrations within the cell. From the biological scheme:



and from the chemical reactions that regulate the relationships between the various species present, it is possible to write a system of 4 differential equations that describe the trend over time of the concentrations of transcripts a and r and activator A and repressor R.

$$\begin{cases} \dfrac{da}{dt} = k_1 + \dfrac{k_2 A^n}{K_a^n + A^n} - k_8 a \\ \dfrac{dr}{dt} = k_1 + \dfrac{k_2 A^p}{K_r^p + A^p} - k_9 r \\ \dfrac{dA}{dt} = k_5 a - k_7 AR - k_{10} A \\ \dfrac{dR}{dt} = k_6 r - k_{11} R \end{cases}$$

Assuming that the dynamics of the transcripts are much faster than those of proteins, they can be considered to be in equilibrium and therefore the system is rewritten in only the two unknowns A and R:

$$\begin{cases} \dfrac{dA}{dt} = \alpha_a + \dfrac{\beta_a A^n}{K_a^n + A^n} - \delta AR - \lambda_a A \\ \dfrac{dR}{dt} = \alpha_r + \dfrac{\beta_r A^p}{K_r^p + A^p} - \lambda_r R \end{cases}$$

This is the system of 2 first order ODE equations that we want to solve, imposing both zero concentrations as initial conditions:

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alfa_a=0.00875;
alfa_r=0.025;
beta_a=7.5;
beta_r=2.5;
delta=4.10^(-8); lambda_a=10^(-4);
lambda_r=10^(-4);
Ka=0.2*2.5*10^4; % costanti di Michaelis Menten
Kr=0.14*2.5*10^4;
p=5
n=2
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having set the initial conditions to zero for both concentrations

$$\begin{cases} A(0) = 0 \\ R(0) = 0 \end{cases}$$

The simulation follows a time of 10^5 (the biological duration of the process is in the order of hours) and should behave as follows.

Initially, a very fast increase in the activator is observed because the positive feedback produces an amplification effect. Meanwhile A also begins with the synthesis of R, because it controls its promoter, so R also begins to increase, albeit slowly. Then, when the repressor concentration begins to become consistent, the negative feedback effect is seen, whereby R inhibits A that cannot catalyze the synthesis of itself and thus the activator concentration returns to decrease.