PROJECT 41

LINEAR MODEL FOR THE SYNTHESIS OF PROTEIN

1. INTRODUCTION TO THE PROBLEM

The profound complexity that characterizes living organisms and the innumerable relationships existing between their different components, make it impossible to describe the system in its entirety and require the highlighting of specific sub-phenomena, with the introduction of drastically simplified models with respect to reality, to understand the individual aspects that contribute to making natural phenomena complex.

In this paper, the focus is on a linear model for the synthesis of proteins. It is a fundamental process in which various actors intervene, including enzymes and messenger ribonucleic acid.
The biochemical activity of all cells depends almost exclusively on the action of enzymes which, with their catalytic properties and their ability to regulate intracellular reactions, maintain the control and coordination of all metabolic processes.
The enzymatic patrimony is contained in the genes of each cell, but no cell simultaneously transcribes all its genes. Furthermore, the number of enzymes varies according to need to avoid waste and disordered functioning. Due to this great variability, the cell has developed some systems for regulating enzymatic activity aimed at solving the problem of having enzymes ready when needed without wasting too much material and energy to synthesize them all.
Control mechanisms can:

- to vary the synthesis and therefore the quantity of enzymatic or non-enzymatic proteins produced, i.e. their cellular concentration;
- modify the activity of an enzymatic protein already present in the cell.

In the first case, ie the regulation of protein synthesis, all the metabolic steps that lead from the gene to the protein, transcription, post-transcription, translation, are control points. In the model presented in this report, reference is made in particular to the translation phase, as the concentration of messenger RNA (mRNA), i.e. a linear sequence of nucleotides that transfer information for the synthesis of the ribosome proteins.
In the second case, without touching the relative quantities of enzymes it is possible, by increasing the activity of some or decreasing that of others, to adapt the different enzymatic reactions to environmental changes. This type of control is much faster than that relating to enzymatic synthesis and allows the metabolic flow of each cell to be regulated instant by instant.

The enzymatic activity, in fact, depends on various factors, including the pH level, the temperature, the concentration of the enzyme and the concentration of the substrate. In particular, as regards the control of concentrations, retroactive inhibition, or retroinhibition, called feedback, plays a leading role. Feedback is the process by which the final product of a metabolic sequence inhibits the action of the enzyme that triggered the sequence itself. In this way, the cells stop the production of the

final compound when it is already present in sufficient concentration and resume it when its concentration is too low.

The deduction of appropriate mathematical models for the study of biological phenomena leads to the identification of their essential properties and their operating mechanisms. This allows us to understand how a given biological situation is reached and how to predict future developments.

2. DESCRIPTION OF THE MATHEMATICAL MODEL

The linear model for protein synthesis consists of two first-order linear differential equations.
The main actors involved in these relationships are the concentrations of the enzyme and the protein, respectively, **n(t)** and **y(t)**. The concentration of messenger ribonucleic acid (mRNA) is indicated with **u(t)**. The model is based on some simplifying assumptions that help to make the system resolution and the interpretation of the results more understandable. In particular, the assumptions made are the following:
- the speed of protein synthesis is directly proportional to the concentration of the enzyme;
- the synthesized protein is removed from the reaction (by decomposition or transport) at a rate proportional to the concentration;
- enzyme production is supposedly regulated by a negative feedback control. More precisely, it is assumed that an increase in the concentration of protein present leads to a decrease in the synthesis rate of the enzyme.
The assumptions made can be translated into mathematical terms as follows:

$$\frac{dn}{dt} = a_1[u - k(y - y_r)] - a_2 n$$

$$\frac{dy}{dt} = a_2 n - a_3 y$$

where $u(t)$ is a given function and a_1, a_2, a_3 and k are positive constants, and y_r represents a control threshold. Probably, these parameters are the carriers of the information of the various factors that affect enzymatic activity and protein synthesis.

When $y > y_r$ the speed of concentration synthesis dn/dt decreases, while if $y < y_r$ this speed increases.

For initial given values $n(0) = n_0$, $y(0) = y_0$, this model represents the process evolution. Solve the system of ODE using appropriate numerical methods.

In applications it is particularly interesting to examine the asymptotic behavior of the solution, representative of the steady state condition of protein synthesis. Being a linear model, this behavior is indicated by the eigenvalues of the matrix of the coefficients of the differential system, i.e. of the matrix:

$$A = \begin{bmatrix} -a_2 & -ka_1 \\ a_2 & -a_3 \end{bmatrix}$$

with characteristic polynomial:

$$P(z) = z^2 + (a_2 + a_3)z + ka_1a_2 + a_2a_3$$

In particular, when the eigenvalues have a negative real part, the model is stable, in the sense that the solution tends asymptotically to the stationary value. It can be shown (using the Routh-Hurwitz criterion) that the system is stable when:

$$ka_1a_2 + a_2a_3 > 0$$

That is:

$$k > -a_3/a_1$$

In figure 1, left, the behavior of the solutions of the model is shown, corresponding to the function represented $u(t) = 1$ *and* parameters $a_1 = 0.8$, $a_2 = 0.3$, $a_3 = 0.05$, $k = 0.5$, $y_r = 2$.

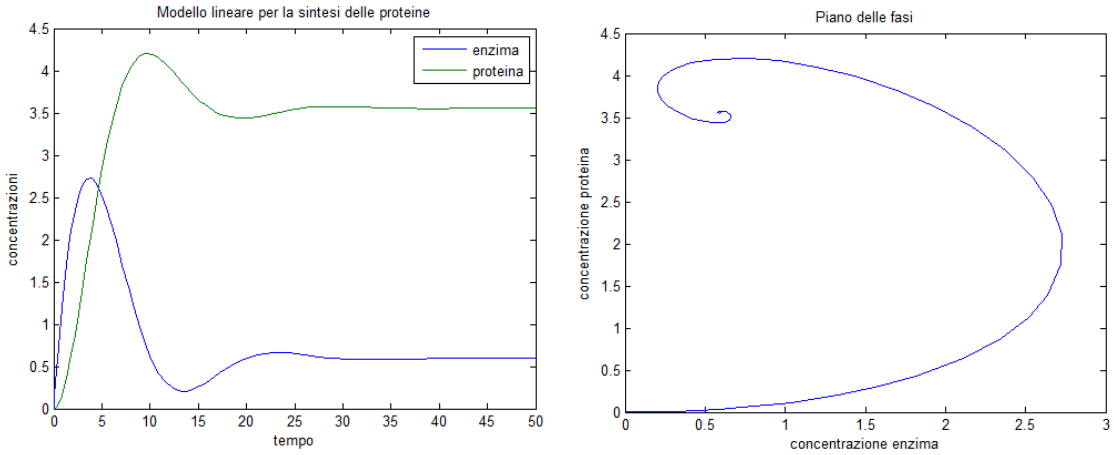

Fig. 1 **Trend in concentrations as a function of time (left), Phase trend (right)**

The eigenvalues of the coefficient matrix, in this specific case, are:

$$\lambda = -0.175 \pm 0.323\, i$$

The fact that these values are complex justifies the oscillatory behavior of the solution, as shown on the phase plane in Figure 1, on the right.