

Sequence-oriented Modelling of Gene Expression

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ABSTRACT

Transcript levels and protein levels differ significantly from one protein product to another, due to the complex regulatory processes involved in gene expression control. Many of these control mechanisms may be ultimately based on the characteristics of the coding and regulatory sequences.

At the example of bacterial protein synthesis, an attempt is made to deduce a mathematical connection between nucleotide sequence and some of the key dynamics observed during gene expression. The transcription kinetics derived distinguish a dependency on parameters related to initiation, elongation, and termination of transcript polymerization. The model representing mRNA degradation considers various steps of both endonuclease and exonuclease activities. In addition to the impact of substrate and effector concentrations, ribosomal protein synthesis takes into account the sterical interaction among translating ribosomes in the context of codon usage. At the same time, the structural properties of mRNA and their influence on translation efficiency and on message stability are further reflected.

The model as a whole provides a possibility to study the nonlinear interdependencies among the various levels of gene expression regulation. Further applications of this model span the improvement of recombinant protein production and the optimum design of metabolic pathways by modulating the enzyme expression levels.