Regulation of *trp* operon in *E. coli*

The mechanism of the *trp* operon repression in *Escherichia coli* seems to be well-known, and therefore, it serves as a paradigm of gene regulation in prokaryotes. However, it turned out that theoretical models of the *trp* operon repression were incomplete and based on incorrect assumptions. I have proposed a new model of TrpR interactions with Trp and *trp* operator. The *trp* operon repression has an additional, previously unrecognized, step in the regulation pathway that is the Trp binding to/unbinding from the repressor-operator complex. This unknown up to date step is necessary for proper regulation of the *trp* operon. The proposed model is based on raw experimental data that was not analyzed or interpreted. I have performed detailed analysis of kinetic and equilibrium parameters of the model. The mathematical modeling and analysis of reaction rate constants and equilibrium constants show that the regulation of the *trp* operon is effective. Consumption of Trp, by the cell, causes considerable initiation of the transcription only in the case of very low Trp concentration. This is caused by many repressor binding sites within the operator region. In the case of abrupt decrease in the intracellular Trp level, the probability density function of transcription initiation time is narrow. The release of Trp molecules is a key factor in the *trp* operon repression because it destabilizes the repressor-operator complex.

Induction of gene expression may cause a binary or graded time-evolution of gene products. In the case of binary response, the time-dependent probability distribution for gene product numbers among cells are bimodal when level of gene products increases. Graded response, however, reveals single-peaked probability distributions. I have derived an analytical expression for the time-dependent probability distribution for gene product numbers in a cell population. The analysis of the obtained probability distributions have revealed that observed, in experiments and numerical simulations, time-dependent heterogeneity of cells in a population can be easily interpreted. The mode of the response depends solely on the ratio, $r$, of the gene activation rate constant to the rate constant of the gene product degradation. If $r \ll 1$, the response is binary. Otherwise ($r > 1$), the graded response pattern is present. Moreover, the intermediate response is present for a narrow range of values of the parameter $r$ (from 0.1 to 1).