MATHEMATICAL MODELING OF NUCLEOTIDE BIOSYNTHESIS IN *Escherichia coli*

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Motivation and Aim: The development of the ***in silico cell***, a bioinformatics resource for modeling, simulation and analysis of intracellular processes, is vital for systems biology. In this regard, the modeling of pyrimidine and purine nucleotide metabolism in *E. coli* cells is of not only purely scientific but also practical significance. In addition to the fact that nucleotides are components of DNA and RNA, ATP and GTP are involved in nearly all cell processes as phosphate and energy sources. Formulas on the base of various nucleotides are widely used in medicine and sports. Their industrial production, in particular, by transgenic producers, is still expensive. Mathematical modeling of processes and analysis of model behavior against altered genetic background provide an approach to the solution of pertinent fundamental and applied problems.
Methods and Algorithms: The construction of elementary models invoked the mass-action law, Michaelis–Menten equation, King–Altman method, and generalized Hill functions [1]. Metabolic system models were constructed as systems of ordinary differential equations describing global rates of variations in low-molecular-weight compound concentrations consumed or produced in the system to be modeled. The global rates were calculated from the law of summation of local rates described in the elementary models. Numerical calculations and model analysis were performed with STEP+ software [2].
Results: On the base of earlier results [3, 4], we developed mathematical models describing instantaneous rates of 47 elementary reactions in the nucleotide biosynthesis pathways. These elementary models were assembled into models of metabolic networks of pyrimidine (PyB) and purine biosynthesis (PuB). It was shown that the model operates either in the steady-state mode or in the continuous self-oscillation mode with a short period. Only steady-state modes were detected in the PuB model. The PyB model contains parameters substantially affecting the yields of target products: UTP, CTP, dCTP, and TTP.
Conclusion: Analysis of the operation mode of mathematical models of pyrimidine and purine nucleotide biosynthesis in *E. coli* cells shows that continuous short-period oscillations of substrate/product concentrations can arise in the range of physiological values of model parameters corresponding to the log phase of cell growth in the PyB model but not in PuB. The biological significance of the theoretically predicted qualitative differences in model behavior is discussed.
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