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Regulation of E.coli respiration: molecular genetic network reconstruction and mathematical modeling



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Short Abstract: By using the GeneNet technology, we reconstructed the molecular genetic network of the regulation of E. coli cell respiration. The mathematical models describing the influence of oxygen concentration in the environment on the regulation of E.coli respiratory system and main catabolic pathways functioning were constructed.

Long Abstract:

Regulation of E.coli respiration: molecular genetic network reconstruction and mathematical modeling

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Molecular genetic network controlling cell respiratory processes in pro- and eukaryotes plays a crucial role in a life cycle of living cells. At present time experimental data on the structure functional organization of this system are rapidly collected. The thorough analysis of such data and understanding of the system behavior under various conditions have become key problems in computational systems biology.

In the present work the computer annotation, systematization and analysis of experimental data on molecular genetic mechanisms of E.coli cell respiration were carried out. The gene network of the regulation of E.coli respiration was reconstructed on basis of GeneNet technology [1]. The gene network consists of 22 operons, 27 mRNA, 111 proteins, 64 different metabolites and others small molecules, and 313 interrelations between components. The information has been extracted from 241 scientific papers (<http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/viewer/index.shtml>). The mathematical models describing the influence of oxygen concentration in the environment on the regulation of E.coli respiratory system functioning (nuoA-N, ndh, cydAB, cyoABCDE operons; NADH dehydrogenases I and II and terminal cytochrome oxidases bd and bo types) were constructed in terms of generalized Hill functions. The results of calculation of steady-state and dynamic parameters deduced from the models were in agreement with experimental data [2]. For completeness of the system the generalized models of the basic catabolic pathways of E.coli: (i) the tricarboxylic acid cycle; (ii) acetyl-CoA formation (pyruvate formate-lyase and pyruvate dehydrogenase complex functioning); (iii) acetate and ethanol formation were also constructed. The verification of the model structures and values of its parameters was carried out. The numerical analysis of dynamics of the respiration regulation system in E.coli both in wild type and in $\Delta arcA$ and Δfnr cells (mutant strains with knockout *arcA* and

fnr genes, which code global regulators of aerobic and microaerobic respiration in E.coli) depending on oxygen concentration in the environment was carried out. The predicted oxygen consumption rates in various strains were in agreement with the experimental data [3].

The developed models can be applied to determination of key links of the molecular genetic network, analysis of the effect of mutations on its operation, and study of mechanisms of transition between respiration modes. The proposed methodology allows us to reduce the model dimension keeping the complex effects and description adequacy. It can be applied to construction of the minimal models of the molecular genetic systems controlling different functions of prokaryotic cells depending on various environment characteristics. These models are very perspective and helpful to solve the biotechnological processes optimization problems.

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References

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