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CRITICISM

A Review of the Monograph by A.M. Bezborodov, N.A. Zagustina, and V.O. Popov *Fermentativnye protsessy v biotekhnologii* (Enzymatic Processes in Biotechnology) (Moscow: Nauka, 2008)

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The monograph summarizing the current state and future prospects of modern biotechnology is critically reviewed in this paper. Biotechnology as an interdisciplinary branch of science is in the process of active development, addressing global demands and challenges of a civilized society. The publication of a Russian monograph adequately reflecting the current state and problems of modern biotechnology is therefore a long-awaited and timely event. The authors of the monograph are outstanding experts in the field of biochemistry of microorganisms and biotechnology. There is no need to say that the book is very helpful for specialists in biotechnology, for researchers in related sciences, and as a guide for teachers, postdocs, postgraduates and students. An advantage of the monograph is the harmonious combination of extensive information on the fundamental aspects of biotechnology and critical analysis of advances in the practical applications of the new (pilot) biotechnological processes on the industrial scale. We do not lay a claim to in-depth analysis but confine ourselves to a brief enumeration of the sections and topics presented in the monograph.

The monograph comprises 12 chapters, conditionally grouped into three parts: "Microbiological Synthesis", "Extreme Forms of Microorganisms in Biotechnology", and "Enzymatic Reactions in Biotechnology".

The first chapter describes in detail three principles of regulation of the metabolic pathways in microorganisms, the basic mechanisms of allosteric regulation of enzyme activities, and the principles of regulation by the feedback mechanism. Using as examples the processes of the synthesis of vitamins, antibiotics, alkaloids, ethanol, amino acids, polysaccharides, polyhydroxybutyrate, carotenoids, and other practically important substances, the authors describe also different methods of regulation: enzyme induction and catabolic repression. Much attention is paid to the regulatory function of phosphates. Phosphorus is present in various vitally important compounds, including nucleic acids, ATP, pyro- and polyphosphates, etc. However, there is presently no clear understanding of the biochemical mechanisms of the negative effect of high concentrations of inorganic phosphorus in the medium.

The monograph describes the regulatory aspects of amino acid biosynthesis in bacteria and of the biosynthesis of glycogen and trehalose in yeasts as components of the general system of metabolic regulation in microorganisms.

Chapter 2, "Unconventional fermentation products", presents data on the peculiarities of the new biotechnological processes of obtaining the products currently applied in different fields of industries and biomedicine. These technologies are based on the methods using both intact microbial cells and the enzymes isolated from the latter as biochemical agents in fermentation processes. The production technologies for pyruvic acid (an intermediate product of organic synthesis, antioxidant), itaconic acid (ether copolymers, additives for lubricating oils), 5-aminolevulininc acid (pesticide, growth factor), mevalonic acid (growth factor, cosmetics), and polyglutamic acid (foodstuff, cosmetic and medicinal preparations) are described. This chapter also presents preliminary results of the experiments on the production of such exotic compounds as phenyl ethanol (aromatizer, simulator of the fragrance of rose blossoms), hyaluronic acid (cosmetics, medicine), and Indian blue from indole (fabric dyestuff), which potentially may become a base for competitive biotechnologies.

Chapter 7, "Metabolic engineering", describes a novel trend of biotechnology that has emerged at the interfaces between genetic engineering, biochemistry, chemistry, molecular biology, and related disciplines. In 1991, J. Baily gave a definition of the subject of metabolic engineering as a field comprising the processes of reconfiguration of metabolic pathways and improvement of cell systems through manipulations with enzymatic, transport, and regulatory cell functions, as well as the technologies of obtaining recombinant DNA. The authors of the monograph actually determine the algorithm of actions for beginners in this new, fascinat-

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ing field of biotechnology. For successful solution of the posed problems, it is necessary to have a complete view of the metabolic and genetic organization of a selected object. At present, the following trends of protein or metabolic engineering are considered the most promising for innovations and diversification in biotechnology: production of heterologous proteins and novel enzymes for technological processes, extension of the range of substrates used, and creation of conditions for the functioning of metabolic pathways for biosynthesis of new products. The relevant trends include also the genetic and metabolic engineering of xenobiotic destructors for refinement of the physiological and biochemical processes and for removal or reduction of the quantity of the by-products formed in the technological processes of microbial synthesis and for enhancement of the level of target products. The examples of the most prominent achievements of metabolic engineering are discussed.

The third part of the monograph describes the application of enzymes in various biotechnological processes. Chapter 9, "Enzymes as potential catalysts in the reactions of organic synthesis", presents a classification of the reactions performed by biocatalysts. The high competitiveness of enzyme-based processes is provided by their stereospecificity, i.e., the possibility of obtaining pure optical isomers. By now, the problem of regeneration of cofactors has been actually solved either by their recycling or by activation of other metabolic pathways, e.g., the application of the peroxidase bypass for regioselective oxidation of aromatic compounds. Enantio-selective processes are rather widely used already on an industrial scale. For example, when a specific lipase is used for the synthesis of the medicinal preparation Cardizeme (calcium antagonist reducing arterial pressure), it is possible to obtain a product with the enantiomer purity of more than 98%.

Chapter 10, "Chiral compounds as the substrates of enzymatic reactions", describes the enzymatic processes for production of highly purified enantiomers, which is often an obligatory condition for creation of various bioactive compounds (medicinal preparations, plant protection agents). Their action is often determined by the type of isomerism and the degree of enantiomeric homogeneity of the substance used. Numerous examples of chiral synthesis by bacterial and yeast cultures are considered, including enantio-selective hydrolysis of aryl- or alyl-cyclic and aliphatic compounds containing an epoxy group.

In the second part of the monograph, the block of four chapters (3–6) discloses the peculiarities of ecophysiology and the biotechnological potential of extreme forms of microorganisms, which produce stable enzymes for survival (extremozymes) and/or protective substances (extremolytes). In (hyper) thermophilic prokaryotes and eukaryotes, the spectrum of thermozymes used in various technological processes is particularly broad, in spite of intensive evaporation of the water phase and low biomass yield. Introduction of the genes encoding the target enzymes of thermophiles into the genome of mesophiles, therefore, has prospects of practical application. The same is true also for the enzymes of haloalkaliphiles, which require high salt concentrations or pH for growth, thus causing the corrosion of equipment. The enzymes of psychrophiles are of great interest for various technological processes, since they possess high specific activities and stereospecificity, so that biocatalytic reactions may be performed at low temperatures and hydration. In the ecological aspect, psychrophiles and their enzymes are vitally important for bioremediation of cold-climate territories polluted with petroleum products.

The list of extremolytes synthesized by (hyper) thermophiles and halophiles includes low- and high-molecular compounds of different classes: carbohydrates (trehalose, sucrose, glycogen, polysaccharides), amino acids (glutamate, ectoines), organic acids (α-ketoglutarate, citrate, isocitrate, polyhydroxybutyrate), and pigments (carotenoids, melanins).

Summing up the general impression from the book, we should mention its strictly logical structure, clear representation, and the high level of conceptualization provided by the references in the end of each part, summarizing tables, schemes, and figures. The uncorrected misprints may be considered a drawback of this excellent book. Introduction of a subject index and a summary in English would be of considerable assistance to readers. In spite of unavoidable minor shortcomings, the reviewed book as a whole is undoubtedly very informative and interesting for different generations of researchers working in various fields of quickly developing biotechnology.