# THEORETICAL AND METHODOLOGICAL BASIS OF CONTINUOUS CULTURE OF MICROORGANISMS

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I. MÁLEK
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*CHAPTER*

# 1

# Introduction

I. MÁLEK

CHAPTER 1

# Introduction

## 1.1 The role of continuous processes and their study in the present development of science and production

I. MÁLEK

Rapid development has been taking place in world science in the last decades which is sometimes characterized as a new scientific revolution. This expression emphasizes the great changes in the position of science in human society which are reflected in the scope and growth of science itself. Science is increasingly becoming a decisive factor in the development of the productive forces and the living conditions of man are being changed rapidly and characteristically by the scientific achievements. The growing understanding of natural laws discloses with increasing effectiveness the means for improving the life of mankind.

This profound change in the effects of science manifests itself by a considerable and continuous increase of the number of scientific workers, of scientific institutions, of their technical possibilities and by a characteristic change in the topics of scientific work itself. To a much greater extent than in the recent past, possibilities are arising of proceeding from the simple description of phenomena, from "how" to the recognition of their essence and their causal connections "why" (BERNAL). This trend influences the structure of scientific work: the isolated, individual scientist becomes an anachronism. Especially in the natural sciences, teams of creative individuals of different specializations and methodical knowledge are arising, and teamwork leads to complex and purposeful studies of natural and social laws. This and the wide possibilities for the automation of analytical research considerably increase the productivity of scientific work.

This progress becomes manifest in the method and level of the conduct and control of production processes. Tendencies appear to overcome the descriptive empiricism which is the basis of the greater part of the complicated production processes in most fields of industrial and agricultural production, and to replace it by genuine scientific control based on a deep knowledge of the

causal interrelations and kinetics of the basic processes. This process is being accelerated by the new possibilities of mathematics and by new production techniques.

This change is apparent in chemical fermentation as well as in metallurgical production. This development will result in completely automated and scientifically controlled highly productive processes and has important consequences for the development of scientific research and production methods. The importance of studies and control of the kinetics of the single processes and their interrelation makes it necessary to work with better defined systems, whose course can be consciously influenced.

One of the approaches corresponding to this development and these requirements in research and production is the transition from discontinuous, closed, single-stage or cyclic processes to open and possibly fully continuous-flow processes. Provided thorough control of all conditions is ensured, these processes enable us to form steady states, which are fully characterized by the composition of the substrate which continuously enters the conversion reaction and by the coordination of the rate of their inflow and the conversion reaction. With increasing complexity of the system employed a more detailed knowledge of all the conditions and the total kinetics of the process becomes necessary.

Obviously such deeply investigated and completely understood continuous processes will have a considerably greater productivity, as a better utilization of the installed production equipment, better scientific control and complete development of the process is possible.

This general development of research and production methods must become manifest, wherever living systems and especially multiplying cells are used for studies of living processes or for the manufacture of important products. Another important factor enters here, i.e. the living system not only transforms the substances participating in the reaction, but synthesizes the substances of its organism from these, and multiplies. By this complex process the organism cultivated in a closed system necessarily changes the conditions of its environment. Only in an open continuous-flow system can the "steady state" be reached, provided we have sufficient knowledge of the necessary conditions and relations. Under these constant conditions the whole process can be fully and purposefully controlled. This fact gains importance with the increasing dynamics of multiplication and metabolism in the system under consideration and hence its importance for the cultivation of microorganisms. However, it also becomes manifest in the cultivation of isolated cells of higher organisms.

Microorganisms are employed in contemporary biological research to a considerable extent for the solution of metabolic, biochemical and genetic problems. They are relatively simple organisms, they multiply easily and therefore a whole series of generations can be obtained in a short period, sometimes

within a day. Hitherto, however, batch cultivation has been mainly used which was developed chiefly for the isolation and identification of the single types of microorganisms. These methods are less suitable when it is necessary to work under exactly defined conditions and biological material of constant properties is required. Here again only continuous-flow cultivation is the methodical solution.

Simultaneously, wide use is being made of the great metabolic capacity of microorganisms for the production of a series of substances valuable for mankind. The requirements for such microbial products, such as proteins, different products and metabolites, e.g. the classic fermentation products, antibiotics, amino acids, substances for biological insect control etc. have considerably increased. It is expected that the introduction of continuous processes for the production of these substances will considerably increase the intensity of their production. With the production of microbial mass there is a 5 to 10-fold utilization of the installed investments.

All these reasons emphasize the importance of the introduction of continuous processes for the cultivation of microorganisms and other isolated cells in research and fermentation industries.

It is a well known fact, recognized whenever continuous methods are being introduced, that the success of such a continuous process and the maximum utilization of the given possibilities can be ensured only by a far deeper knowledge of these processes than required for the discontinuous batch methods. In the latter case empirical knowledge with only a limited scientific basis is generally sufficient, whereas the continuous methods require fundamental knowledge of the process as well as of its total kinetics.

Continuous-flow cultivation is therefore the expression of a higher technical level and the basis of a characteristic transition from the empirical approach to genuine scientific control. The continuous processes combine these three basic characteristics of modern production: high productivity with regard to utilization of material and labour, the possibility of automation and the scientific approach, directed towards the fundamental understanding of the processes and thus to their full control.

The application of the continuous cultivation method not only concerns the introduction of the continuous process for a certain type of production, but it represents a basic change in the approach to the process, towards its knowledge and control; it means a change in the type of research and evaluation and even a change of thought and consideration of the individual questions and tasks. To summarize, it can be said that working with continuous processes requires a higher level of research, especially concerning the quality of work, than the single-batch processes. This, of course, means more and deeper biochemical and physiological research work than was required by the batch processes.