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Chapter 8

Current State and Perspective in the Models Applicable to Oenology

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Additional information is available at the end of the chapter

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Abstract

Modeling, simulation, and control of the alcoholic fermentation of grape juice into wine are still not a totally resolved problem. A model that makes it possible to predict alcoholic fermentation development would be a valuable instrument to its technical and economical implications. Considering the field of bioprocess used in food production at the industrial scale, the chapter will be centered on models applicable to oenology. On the first part, the chapter proposes the different approaches that have been taken: "knowledge-based" models, non-physiological mathematical descriptions, behavior prediction models, and empirical models. The second part will deal with a nonlinear model for white wine alcoholic fermentation process which, besides the detailed kinetic model, involves equations corresponding to the physiological phases of yeast cells, the inhibitory effect of ethanol, heat transfer equations, and the dependence of kinetic parameters on temperature.

Keywords: modeling, simulation, advanced control of technological process

1. Introduction

If the twentieth century belonged to electronics and computer science, the twenty-first century would belong to biology and biotechnologies [1]. *Bioprocesses* are the foundation of life and especially of human health. Therefore, on an international scale, there are studies being conducted in order to find ways of improving the food safety quality.

A new science was born at the turn of two centuries of technical and scientific revolution: *bioinformatics*. The methods and the concepts of computer science began to hold the interest of many biologists, especially to the molecular biology specialists [2]. These methods are essential for various problems such as the analysis of evolutionary processes, the complex molecular structures shaping, and the simulating of some biological aspects. Researchers are currently

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overwhelmed by the enormous data quantity that comes from the multiple projects belonging to genomics, transcriptomics, proteomics, and metabolomics. The necessity of using computerized methods in manipulating and assembling these extremely complex high-level data is obvious. But the great challenge lies not only in the genetic sequencing and cartography but especially in understanding what do transcriptomics, proteomics, and metabolomics mean, when associated with certain life conditions and with a certain hereditary program at a given time. The identification of the structure and function of the proteins that were biosynthesized by the organisms, the complex mechanisms that allow the development of life, is therefore required. In order to achieve this, theoretical informatics—through some of its domains, which have reached a certain level of maturity, formal languages, data structures, and artificial intelligence—offer viable theoretical models.

At the same time, the beginning of our century is righteously marked by *biology*, determined and largely conditioned by the revolution within the biological sciences [1]. Therefore, modern biology begins to determine the main directions of some interdisciplinary developments, constantly calling on the discoveries of chemistry, physics, mathematics, and engineering. A new, promising branch of science was born at a specific meeting point: *bioengineering*. Bioengineering especially has developed in connection with biotransformation processes (biosynthesis-biodegradation), in order to obtain antibiotics, enzymes, vitamins, amino acids, organic acids, bicarbonates, biopolymers, as a result of the cooperation among microbiologist, biochemist, chemical, food industry and mechanical engineer, operator and computer scientist, in a domain which is called *Microbial Engineering* and *Biochemical Engineering* [3]. Food safety and its quality is a primary field in European and global policy and legislation of the twenty-first century because it concerns the required conditions for a healthy population. The key issues for improving the biochemical and micro-biochemical safety and the quality of food reside in knowing, understanding, and leading the *bioprocess* used in food production as well as possible [4]. The volume of bioprocesses in the technical development and implementation of the processes of obtaining new food products and a significant number of non-food items based on microbiological processes and enzyme technology have grown significantly in the last years.

It is very difficult to monitor, design, and control a bioprocess [5]. For example, in the last years, an impressive number of kinetic models were developed only for fermentation processes and the various phenomena that influence fermentation kinetics were taken into account. That is why these models needed the estimation of a large number of sizes, which are often very hard to identify [6–8]. A series of artificial intelligence-based control and optimization models and techniques were also developed (fuzzy and neuro-fuzzy techniques) [9–12]. These models allowed a more realistic definition of some model sizes, which carry a high degree of uncertainty.

The mathematical model of a biotechnological process is generally represented using differential equation systems, which are obtained by writing, for each component, the mass and energy balance equations. In these equations, the components or the concentrations of the components involved in the reactions that take place in the bioreactor appear. The dynamics of the temporal variation of each component is expressed by two types of phenomena. First, there are chemical and biochemical reactions that transform some components into some

others. Second, there is the mass transfer, caused by the liquid or gas interchanges between the reactor and the environment or with other reactors. In this context, the mathematical model of a bioprocess is a mathematical description of two types of phenomena, in which chemical and biochemical reactions generate the *kinetics* of the bioprocess, while the mass transfer phenomena define the *transport dynamics*.

Another important aspect in connection to the control of the bioprocesses is the lack of transducers and on-line biosensors, specific to biochemical and micro-biochemical sizes, that characterize these kinds of processes [13, 14]. Attempts of obtaining these biosensors are made [11, 15, 16], but the research is far from being finished.

At the same time, the general model of a bioprocessor can provide a series of structural properties which might be useful for the resolution of some identification, state estimation (state observers development), or bioprocesses leading problems. The need for the state observers is imposed by the absence of reliable and cheap biosensors, capable of making on-line measurements of the biochemical and biological variables, used in implementing some convenient methods of monitoring and leading biotechnological processes [1]. The acquisition of biomass, sublayer, and the metabolism products are made through lab analysis; this method makes the leading of the bioreactors difficult (as for the direct adjustment of these sizes). The lab analysis requires taking a sample from the contents of the bioreactor, and this represents a higher risk of contaminating the culture. Also, lab models for determining the number of microorganisms, the concentration of the sublayer, as well as the concentrations of metabolism products are quite imprecise, thus generating uncertainties in appreciating the evolution of the abovementioned sizes. These problems are strongly amplified in the industrial environment, especially because of the lack of adequate equipment and sufficient staff in order to realize quality measurements in the lab. Normally, under these conditions, there are maximum three-four reliable analyses during the unfolding of a biotechnological process.

The estimation of sizes of the biotechnological process is considered to be a way of avoiding the various drawbacks connected to the acquisition of data from the bioreactors. The *state estimator* (also known as software sensor or observer in specialized works) is an algorithm used for determining some measurements of the process, which are not measurable in real time, based on other accessible measurements as related to their acquisition.

An essential problem, specific to industrial scale food industry bioprocesses, is the fact that the technological background results are very variable [1]. In many cases, the variability of raw materials used in the industrial processes leads to a non-reproducibility of the charges. Taking into consideration these aspects, the use of the technical operator's experience for leading the process is recommended, and it is possible by systems based on *system expert* type of knowledge.

Also, heat transfer aspects led to the development of models and automatic control techniques regarding the optimization of the thermal regime of the bioprocessors [17].

All these research and achievements are proper to the examined bioprocesses and usually have a low degree of reproducibility. A generalization has not been achieved at the moment; it is very difficult to achieve and this can only be made to a certain extent.

Another aspect is the improvement of the technological performances concerning the energy consumption. As a result, optimizing the energy consumption through the introduction of advanced leading systems leads to a conservation of fossil fuels. It can be affirmed that, indirectly, a bio-economy is being advocated for. In *Bio-economy versus biodiversity*, Hall [18] says "The bio-economy agenda is especially attractive to fossil fuel companies who want to be seen pursuing an exit- from-oil strategy; and to biotechnology companies desperately in need of a Trojan horse to provide safe passage for risky and unpopular new technologies."

After a brief introduction regarding the modeling of bioprocesses, on the first part, the chapter proposes the different approaches that have been taken: "knowledge-based" models, non-physiological mathematical descriptions, behavior prediction models, and empirical models. The second part will deal with a nonlinear model for white wine alcoholic fermentation process which, besides the detailed kinetic model, involves equations corresponding to the physiological phases of yeast cells, the inhibitory effect of ethanol, heat transfer equations, and the dependence of kinetic parameters on temperature.

2. Current stage in fermentation processes modeling

2.1. The biotechnological processes modeling

A *biotechnological process* implies a development (growth) of a microorganism population (culture medium), *biomass*, in a bioreactor (vessel) by the consumption of some nutrients (carbon, nitrogen, oxygen, vitamins, etc.) that represent the *substrate*, if the physical and chemical conditions (temperature, pH, aeration, etc.) are favorable. Customarily, the microorganisms' growth takes place in a liquid medium (aqua). It is obvious that in a bioreactor many biochemical and biological reactions take place simultaneously. Each elementary reaction is, usually, catalyzed by a protein (enzyme) and can form a specific *product* or a *metabolite*. The aim of such a culture can be

- biomass producing (bacteria, yeasts, etc.);

- producing a principal component (amino acid, medicines, marsh gas, etc.);

- biological decontamination (biological consumption of the pollutant substrates by the biomass).

Because the microbial mechanism of growth that involves alive organisms is very complex, a detailed modeling is not possible or is very complicated. Usually, the bioreactor assumes a perfect stirred and is described by a number of macro-scope variables, such as biomass, substrate, product, oxygen concentrations, pH, temperature, etc. Function of the fermentation type could also be defined by another concentration.

The mathematical model of a bioreactor depends on its operating mode. In this way, in practice, for these types of bioreactors three operating modes could be defined:

- *Batch mode*—A batch bioreactor is a reactor with a cyclical operating, without feed, and exit flows. The entire quantity of substrate and nutrients, with a small quantity of

biomass, is introduced in the bioreactor at the beginning of the fermentation. During the fermentation, the bioreactor will not be fed with any substrate and the process will be completed after the substrate has been sufficiently consumed. The result is that the entire quantity of biomass is collected, from which then the desire product will be extracted. The possibilities of process control in this case are very limited and could be resumed with some physical variables: temperature, pH, energetically consumption, length of fermentation, and so on.

- *Fed-batch mode*—The fed-batch bioreactors type or with semi-continuous operating is a reactor with cyclical working, with a continuous or intermittent feeding and without an exit. In the vessel, both a small quantity of substrate and a biomass are initially introduced. Then, during the fermentation process, and in the function of the microorganisms' necessities, the reactor will be fed with a controlled flow of substrate. Therefore, the possibilities of process control of this kind of bioreactors are more diverse than that of the batch type. Aside from the physical variables, the biological variables: substrate concentration, biomass concentration, and so on, can also be controlled.

- *Continuous mode*—This mode is more efficient from the economical point of view and the bioreactors are stirred, with continuous operation, eventually with separation and recycling, as well as the gas-liquid bioreactors, used especially in the industry for obtaining a great volume of biomass (i.e., unicellular proteins) or for the biological treatment of residual water. In such a reactor, the biomass is evacuated with a flow equal with that of the substrate feeding.

The mathematical model of a biotechnological process is formed by an equation system in which the components or the concentrations of components implied in reactions that take place in bioreactor appear, equations which are obtained by writing, for each component, the mass and energetic balances. The dynamic or variation in time of the quantity of each component is expressed by two phenomena. Primarily, there are chemical, biochemical, and biological reactions which transform certain components in others. Secondarily, mass transfer due to the liquid and gas interchanges between the reactor and the environment or with other bioreactors exists. Within this context, the mathematical model of a bioprocess represents a mathematical description of two types of phenomena, where the chemical, biochemical, and biological reactions cause the bioprocess *kinetics* while the mass transfer phenomena define the *dynamics of transport*.

If the process is passed off in a reactor with perfect stirring, which means a reactor in which the culture medium composition is supposed to be homogeneous, the dynamics of the two types of phenomena can be represented by a unitary description, by differential equations system which involve the reaction components concentrations, as well the pH, temperature, and so on, variables which can be organized like a state vector. There are also bioreactors without perfect stirred and in which a set of concentration gradients, temperature, pressure, and so on, appear. Such types of bioreactors are tubular, bioreactors with fix layers, and so on. These reactors are described by mathematical models which contain partial derivate equations, where, in the excepted the temporal variables, at least a spatial variable will appear.

The modeling of a biotechnological system can be done progressive. It begins with the information that could be easily obtained, namely the reaction of the components involved in the bioprocess, the reactions which take place in the bioreactor and the liquid or/and gas interconnections of the system, elements which define the *reaction schema* and the *system architecture*. With these information, the *general structure of the model* is settled out. The general model of the bioprocess can wise up a set of structural properties useful for solving some issues concerning the state estimation or the control of the bioprocesses.

2.2. The reaction kinetics modeling

2.2.1. The kinetic of microorganisms growing

The kinetic of microorganisms' growth (**Figure 1**) is necessary from the point of view of knowing the process phases (**Table 1**), the duration of these phases, the factors which influence them in order to choose then the type of vessel, and the process control mode for the bioreactor.

2.2.2. The types of kinetic models

The phenomena that take place in a bioreactor are complex and coupled. The complexity is given by the heterogenic medium three phases (solid, liquid, and gas), in which the biosynthesis process takes place; the three phases medium is in a dynamic evolution and has a nonlinear character. The processes are coupled among them, an operational variable (the feed flow with substrate, the pressure, the temperature, the stirred, etc.) or the way in which the oxygen reaches at the microorganisms, are important both individually and for the whole microorganisms, for the biomass process control [19].

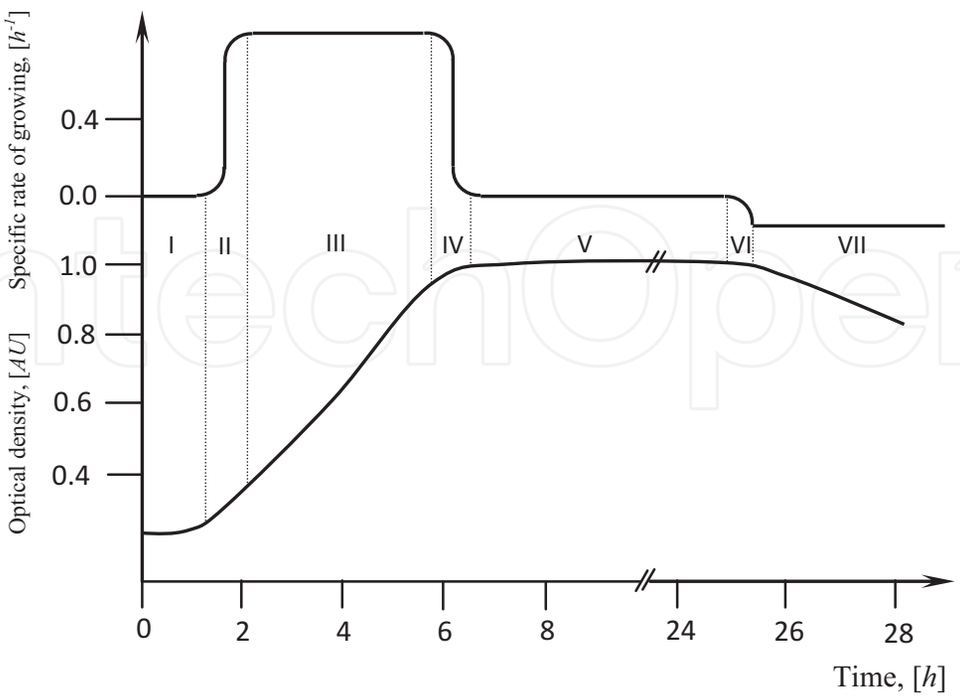


Figure 1. The microorganisms number evolution versus time.

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Phase	Characterization	Observations
I. Latent (adaptation)	The regeneration processes of the hyphes or the germination of the spores, the function of the inoculums type take place.	Generally, this phase has a reduced practical importance. For this reason, in order to eliminate this phase, more generation of cells are cultivated on the respective medium aiming to accustom the cells with it.
II. Beginning of growth	The volume of the cells grows fast.	
III. Exponential growth	The specific growth rate μ is constant and the biomass growth is exponential.	This phase presents a practical importance when we have the obtaining of biomass in view. The metabolical activity from the exponential phase is in fact the primary metabolite; it corresponds with trot phase.
IV. Deceleration growing	The specific growth rate μ comes down.	It appears when the feed with an essential nutrient becomes insufficient or an element necessary for growth has been run out or intermediary substances have been accumulated in the medium.
V. Stationary	The microbial cells reach a maximum concentration, the proportion between alive and death cells number remains constant. The quantity of limiting nutrient influences this quantity of biomass, named total production.	The secondary metabolism is typical for the stationary phase; it corresponds to idiophase.
VI. Decay	The cells die, the autolysis takes place, and the quantity of biomass comes down.	At one point, it is possible that an easy growth of biomass takes place, due to the alive cells' consumption of the nutrients. The nutrients have been delivered by the lysated cells. For a valorous culture, the decline phase must be eliminated.

Table 1. The microbial population growing phases (adapted from [19]).

In **Figure 2**, the main phenomena are presented, the interactions and variables which influence the kinetic behavior of the population cells. The two systems, the biological system (represented by the microbial population) and the physical and chemical system (external medium), are in close correlation; the cells consume nutrients and transform the substrate in reaction products. The cells generate heat which warms the medium, and the medium temperature influences the cell behavior.

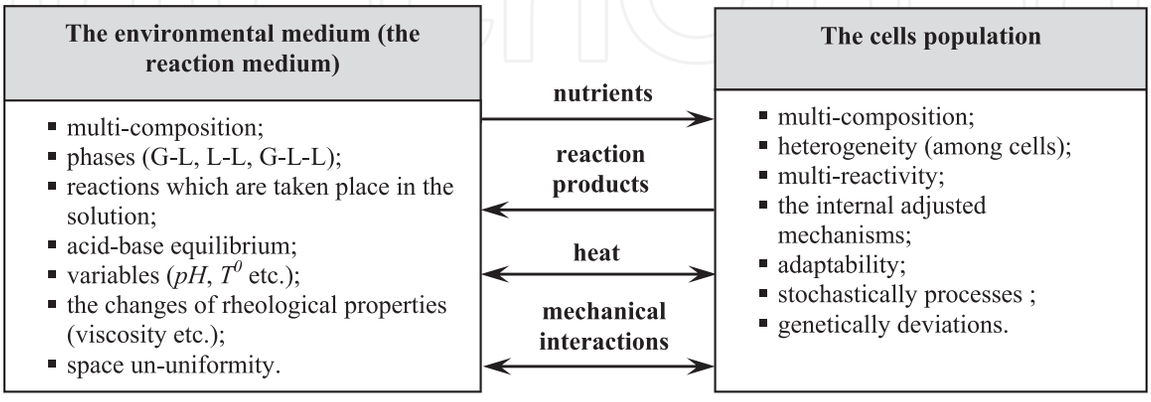


Figure 2. The main phenomena, interactions, and variables which influence the kinetic of the microbial populations.

The mechanical interactions are due to the hydrostatic pressure and to the flow effects of the medium on the cells and also to the medium viscosity changes, caused by the cells accumulation and/or by the cellular metabolites.

The medium is a multi-composition system that must contain the necessary nutrients for the growth of the microorganisms (carbon, nitrogen sources, mineral salts, vitamins, growing factors, oxygen, etc.) and in which different products of cellular metabolism (primary and secondary metabolites) are accumulated while the cells grow on.

In solution reactions that could modify the structure of the final products (i.e., the penicillin hydrolyses) could take place.

Often, the cells consume or produce components that could influence the medium acidity and the interrelation between cell needful and acid-base equilibrium determinates the medium pH, which, in turn, influences the cells' activity and the transport processes.

During the cellular reactions, the medium temperature, pH, ionic strength, and rheological properties can change in time.

A complex model of a bioreactor is multi-phases; it consists of a medium with solid particles among which liquid and gas particles (at the surface being the microbial culture) are dispersed or from a liquid medium in which gas bulls are dispersed. An example of three phases model, with two physical phases, gassy and liquid phases and a biotical one—the microorganisms culture, is presented in **Figure 3**, model which could be considered a model of a fermentation process.

Because of the great volume of bioreactors, of the higher viscosity and of the non-Newtonian nature of medium, in most cases, the technological conditions from vessel can vary from point to point.

Every individual of microbial population is a complex component of the system, frequently non-homogeneous, even at the level of a single cell. Many independent biochemical reactions take

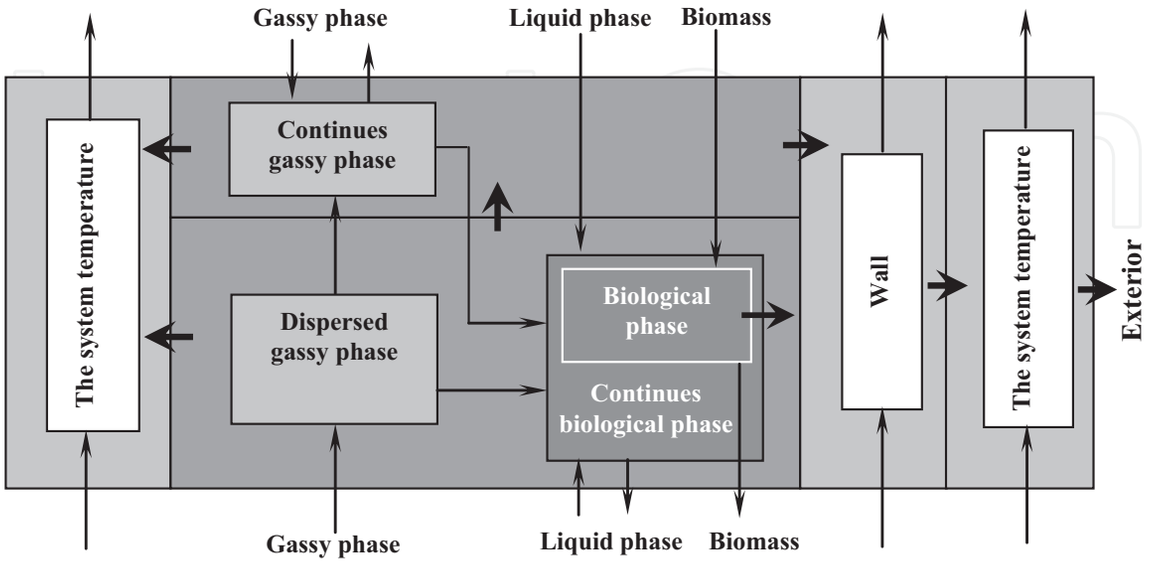


Figure 3. A bioreactor model with three-structured phases.

place simultaneously in every cell, which involves an internal complex control; this control allows the cell to adapt its activity and even to the biochemical type reaction in function of the external medium.

The dissimilarity among the cells is given by the variation in time and space of the cells' age (some cells are just born while others are dying or dividing); the cells with different ages are often characterized by various types of activities and metabolical functions.

In the cultivation for longer period, many spontaneous mutations of some individuals of cells population may appear.

Analyzing all these aspects, it becomes obvious that, in practice, a kinetic model that may include all the phenomena and interactions of the system cannot be formulated, a first simplification concerning the medium being necessary. It is considered that even a single component of medium, which is in quite great quantities, can influence the microbial growth of the medium. Sometimes, it could be necessary to include other components of medium such as the products with inhibitory role, which are accumulated in medium, in order to obtain a suitable description of the kinetics of the cells population.

2.2.3. The unstructured kinetics models

2.2.3.1. Models based on Monod equation

From the kinetics point of view, in order to construct a model it is necessary to study the rates and mechanisms of the physical, biochemical, and microbiological processes, in which microorganisms are involved (growing, cellular cycle, the components produced by reaction, the medium effects, and the biological interactions).

The *specific growth rate*, μ, represents the variation in time of the microbial cells concentration in synthesis medium:

$$\frac{1}{X} \cdot \frac{dX}{dt} = \mu \tag{1}$$

or in integrating form:

$$X = X_0 \cdot e^{\mu \cdot t} \tag{2}$$

where X represents the microbial cells concentration in biosynthesis medium [mol/m^3];

X_0 is the steady-state operation point of microbial concentration [mol/m^3];

t is the development time [s];

μ is the specific growth rate in exponential phase, [s^{-1}];

The specific growth rate depends, among other elements, on the limiting substrate concentration (i.e., the glucose concentration), S, taking place after the following equation:

$$\mu = \frac{\mu_{\max} \cdot S}{K_S + S} \tag{3}$$

with the name Monod equation where S is the limiting substrate concentration (glucose concentration); $\mu_{\max}$ is the maximum specific growth rate, achieving when $S>>K_s$ and the concentration of all the nutrients is unchanged; K_s is a constant which has a concentration dimension and represents the value of limited nutrient concentration at which $\mu = \frac{1}{2} \cdot \mu_{\max}$.

The values of the two variables depend on the microorganism, on the work conditions (pH and temperature), and on the substrate complexity. The typical curves of biomass evolution and substrate consumption in time are presented in **Figure 4**, for a batch fermentation system. The value of substrate concentration S was pointed out for which $\mu = \frac{1}{2} \cdot \mu_{\max}$.

K_s can be considered a measure of the microorganisms affinity against substrate:

- a small value of K_s indicates a great affinity, the microorganisms can grow in conditions of very small substrate concentrations (small dilution at continuous processes);

- a great K_s indicates a small affinity for the substrate, the microorganisms growth takes place slowly, even if the substrate concentrations are great.

The specific forming rate of the metabolism product:

$$q_p = \frac{r_p}{X} \tag{4}$$

where

$$r_p = k_1 \cdot X + k_2 \cdot r_x \tag{5}$$

is the forming rate of metabolism product $\left[mol/\left(m^3 \cdot s\right)\right]$; X is the biomass concentration; r_x is the growing rate of cellular mass $\left[mol/\left(m^3 \cdot s\right)\right]$; k_1 is the proportionality factor between the forming rate of product and biomass concentration $[mol\,product/(mol\,biomass \cdot s)]$; k_2 is the proportionality factor between the forming rate of the product and the growing rate of the cellular mass $[mol\,product/mol\,biomass]$.

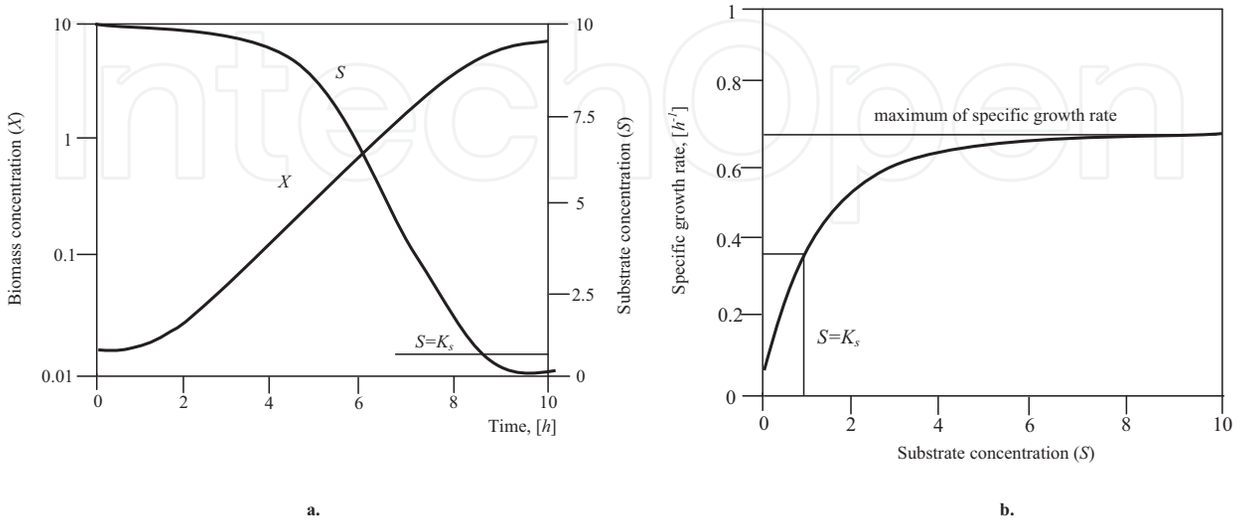


Figure 4. The evolution of biomass and substrate consume versus time, for a fermentation in batch system (a); for the same batch system-specific growth rate μ as a function of limiting substrate concentration, S (b).

Introducing Eq. (5) in Eq. (4), the specific rate of metabolism product can be determined:

$$q_p = k_1 + k_2 \cdot \mu \tag{6}$$

where $\mu = r_x/X$.

The forming rate of the product doesn't depend on the biomass X but on the growing rate of the cellular mass r_x at the obtained primary metabolites (ethanol, acetic acid, gluconic acid, butyric alcohol, acetone, etc.). Therefore, k_1= 0 and Eq. (5) become

$$r_p = k_2 \cdot r_x \tag{7}$$

In case of obtaining secondary metabolites, r_p depends only by biomass X:

$$r_p = k_1 \cdot X \tag{8}$$

If the development of microorganisms is limited by the concentration of a biosynthesis medium component, the microorganisms quantity that is formed is proportionally with the used quantity of substrate. Therefore, the *efficiency coefficient for biomass producing* can be defined:

$$Y'_{xs} = \frac{dX}{dS} = \frac{mols\ of\ biomass\ produced}{mols\ of\ substrate\ consumed\ for\ biomass\ producing} \tag{9}$$

and the *efficiency coefficient for metabolite producing*:

$$Y'_{ps} = \frac{dP}{dS} = \frac{mols\ of\ metabolism\ produced}{mols\ of\ substrate\ consumed\ for\ metabolism\ producing} \tag{10}$$

In *aerobic* conditions, at the biomass forming, the rate consume of substrate is

$$-r_s = \frac{r_x}{Y'_{xs}} + \frac{r_p}{Y'_{ps}} + m_s \cdot X \tag{11}$$

where m_s is a forming coefficient $[mol\,substrate/(mol\,biomass \cdot s)]$, specific for microorganism.

With the growth in the *anaerobic* conditions, the energy necessary to cell is obtained by the substrate transformation in reaction products; therefore, the metabolism products forming is a consequence of biomass growing:

$$-r_s = \frac{r_x}{Y'_{xs}} + m_s \cdot X \tag{12}$$

For *S>0*, the forming rate of metabolites in anaerobe conditions is

$$r_p = \frac{Y'_{ps}}{Y'_{xs}} \cdot r_s + m_p \cdot X \tag{13}$$

where m_p is a coefficient that describes the product forming during the growth $[mol\,substrate/(mol\,biomass \cdot s)]$. This coefficient can be determined from m_s on the basis that the

reaction of the stoichiometric coefficients substrate consumed formed product. From Eqs. (5) and (3), the k_1 and k_2 coefficients could be obtained in anaerobic conditions.

The total efficiencies of biomass and metabolic products are used in practice.

During the *aerobic* processes, considering Eqs. (5) and (11), the result is

$$Y_{xs} = \frac{r_x}{-r_s} = \frac{r_x}{\frac{r_x}{Y'_{xs}} + \frac{r_p}{Y'_{ps}} + m_s \cdot X} = \frac{\mu \cdot X}{\frac{\mu \cdot X}{Y'_{xs}} + m_s \cdot X} = \frac{\mu}{\frac{\mu}{Y'_{xs}} + \frac{k_1 + k_2 \cdot \mu}{Y'_{ps}} + m_s} \tag{14}$$

At the specific growth very high rates, Y_{xs}=Y'_{xs}

$$Y_{ps} = \frac{r_p}{-r_s} = \frac{r_p}{\frac{r_x}{Y'_{xs}} + \frac{r_p}{Y'_{ps}} + m_s \cdot X} = \frac{k_1 \cdot X + k_2 \cdot r_x}{\frac{\mu \cdot X}{Y'_{xs}} + m_s \cdot X} = \frac{k_1 + k_2 \cdot \mu}{\frac{\mu}{Y'_{xs}} + \frac{k_1 + k_2 \cdot \mu}{Y'_{ps}} + m_s} \tag{15}$$

For the *anaerobic* processes:

$$Y_{xs} = \frac{r_x}{-r_s} = \frac{r_x}{\frac{r_x}{Y'_{xs}} + m_s \cdot X} = \frac{Y'_{xs}}{1 + \frac{m_s}{\mu} \cdot Y'_{xs}} \tag{16}$$

$$Y_{ps} = \frac{r_p}{-r_s} = \frac{\frac{Y'_{ps}}{Y'_{xs}} \cdot r_x + m_p \cdot X}{\frac{r_x}{Y'_{xs}} + m_s \cdot X} = \frac{Y'_{ps} + \frac{m_p}{\mu} \cdot Y'_{xs}}{1 + \frac{m_s}{\mu} \cdot Y'_{xs}} \tag{17}$$

There is a simplified modality to express the efficiencies with the following equations:

$$Y_{xs} = \frac{X - X_0}{S_0 - S} \quad \text{and} \quad Y_{ps} = \frac{P - P_0}{S_0 - S} \tag{18}$$

2.2.4. Alternative variants of models are based on Monod equation.

It is expected that the specific growth rate of biomass, expressed by Monod equation, does not match for all the fermentation processes. Many authors have tried to improve the Monod model and some examples will be presented in the subsequent part.

2.2.4.1. Teissier model

$$\mu = \mu_{\max} \cdot \left(1 - e^{-\frac{S}{K_S}}\right) \tag{19}$$

A disadvantage of the Monod and Teissier models is that these models do not take into consideration the inhibitory factor of the substrate when it is in excess. Andrews model abolishes this disadvantage by adding S^2/K_i at the denominator of biomass specific growth rate expression.

2.2.4.2. Andrews model

Therefore, a great quantity of substrate inhibits the cells' growth (i.e., glucose in quantities of >800 mol/m^3) and the following equation can be used:

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$$\mu = \frac{\mu_{\max} \cdot S}{K_s + S + \frac{S^2}{K_i}} \tag{20}$$

where K_i is the inhibitory factor and $\mu_0 = \mu_{\max}\left(1 + \sqrt{\frac{K_S}{K_i}}\right)$.

Contois model, which takes into consideration the inhibitory effect of the biomass on the specific growth rate, is often used [1].

Contois model

$$\mu = \mu_{\max} \frac{S}{S + K_S X} \tag{21}$$

Because of the greater concentration of biomass, the biotical phase can be a substantial part from the total volume of the bioreactor and thus it is difficult to assimilate the substances by the biomass. Anyway, it is heavy to imagine in which mode the cells' concentration can inhibit its own growth and, probably, the ability of Contois kinetics to be in concordance with the experimental data is explained by the toxic effect of some metabolic products.

Another model that takes into consideration the inhibitory effect of the biomass on the specific growth rate is *Luong model*:

$$\mu = \frac{\mu_{\max} \cdot S}{K_s + S} \cdot \left(1 - \frac{S}{S_{\max}}\right) \tag{22}$$

where K_i is the inhibitory constant and $S_{\max}$ is the substrate concentration at which the microorganisms are in a stationary growth phase.

A similar variant of the specific growth rate of Monod biomass in which the substrate S appears at power n (empirical) is *Moser model*:

$$\mu = \frac{\mu_{\max} \cdot S^n}{K_S + S^n} \tag{23}$$

On the case of bioreactors with two substrates (S_1 and S_2), the models with Eqs. (3) and (19)–(23) are combined. For example:

Monod-Monod model

$$\mu = \mu_{\max} \cdot \frac{S_1}{K_1 + S_1} \cdot \frac{S_2}{K_2 + S_2} \tag{24}$$

Monod-Andrews model

$$\mu = \mu_{\max} \cdot \frac{S_1}{K_1 + S_1} \cdot \frac{S_2}{K_2 + S_2 + \frac{S_2^2}{K_i}} \tag{25}$$

When a metabolic product inhibits the growth, the specific growth rate has the following expression:

Jarusalimsky model

$$\mu = \mu_{\max} \cdot \frac{S}{K_s + S} \cdot \frac{K_p}{K_p + P} \tag{26}$$

Levenspield model

$$\mu = \mu_{\max} \cdot \frac{S}{K_s + S} \cdot \left(1 - \frac{P}{P_{\max}}\right) \tag{27}$$

where K_p represents the concentration of the metabolic product P at which $\mu = \frac{1}{2} \cdot \mu_{\max}$ and $P_{\max}$ is the maximum concentration of the metabolic product with inhibitory action.

The variables of the biotechnological process can also be described in function of the variables that represent the control variables of the bioreactor (temperature, pH, etc.). The control algorithms of pH and temperature are often complex because of frequent changes of their optimal values, during the bioprocess period [1].

The influence of the temperature on the maximum specific growth rate of biomass is important: decreasing or increasing with one grade the temperature of the optimal value caused the beginning of the proteins' denaturing process, which is undesirable process. At the smaller temperatures then that at which the denaturing of the proteins appears, the maximum specific growth rate of biomass can be modeled using the Arrhenius equation:

$$\mu_{\max} = A \cdot e^{-\frac{Ea}{R \cdot T^0}} \tag{28}$$

where Ea is activation energy [kJ/mol]; A—pre-exponential factor; R—universal gas constant and T^0 is temperature [K].

Considering that the proteins were denaturized at a temperature of a chemical reversible reaction having the free energy ΔG_d [kJ/mol] and that the denaturized proteins are inactive, Roels [20] has proposed a mathematical equation for the maximum specific growth rate of biomass, equation which is relatively alike with Hougen-Watson equation for catalyses activity in heterogeneous chemical reactions:

$$\mu_{\max} = \frac{A \cdot e^{-\frac{Ea}{R \cdot T^0}}}{1 + B \cdot e^{-\frac{\Delta G_d}{R \cdot T^0}}} \tag{29}$$

where B is a constant.

Topiwala and Sinclair model (for temperature)

$$\mu_{\max} = \begin{cases} a_1 \cdot e^{-\frac{Ea_1}{RT^0}} - a_2 \cdot e^{-\frac{Ea_2}{RT^0}} - b, & if\ T_1^0 \le T^0 \le T_2^0 \\ 0 \qquad\qquad , if\ T^0 < T_1^0\ or\ T^0 > T_2^0 \end{cases} \tag{30}$$

where Ea_1 and Ea_2 are activation energies;

$R$is universal gas constant;

a_1, a_2, and $b$are constants.

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Eq. (30) shows that the specific growth rate of biomass is continually growing until a maximum $T^0{}_2$, value, at which the microorganisms enter in idiophase and then in autolysis.

The pH influence on the cellular activity is determined by the enzymes sensibility at the pH changes. Enzymes are active only in a particular interval of pH and therefore the enzymes total activity of cells is a complex function by medium pH.

Rozzi model (for pH)

$$\mu_{\max} = a \cdot pH^2 + b \cdot pH + c \tag{31}$$

For complex dependences $\mu = f\left(S_1, \ldots, S_{ms}, P_1, \ldots, P_{mp}, X, pH, T^0, \ldots\right)$, the multiplicative principle is often used:

$$\mu = \mu_{\max} \cdot f_1(pH) \cdot f_2(T) \cdot f_3(X) \cdot \prod_{j=1}^{ms} \varphi_j\left(S_j\right) \cdot \prod_{j=1}^{mp} \psi_j\left(P_j\right) \tag{32}$$

where $f_1(.)$, $f_2(.)$, $\varphi_j(.)$, j=1,…, ms and $\Psi_j(.)$, j=1,…,mp are penalization functions.

In **Table 2**, the most used mathematical models in biotechnological processes simulation, models used in process and optimal control of fermentative industrial processes are presented.

Nr. crt.	$\frac{dX}{dt}$	$\frac{dP}{dt}$	$\frac{dS}{dt}$	Model
1.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Monod**
Inhibitory effect of the substrate				
2.	$\mu_{\max} \cdot \left(\frac{S^n}{K_s+S^n}\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S^n}{K_{sp}+S^n}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Moser**
3.	$\mu_{\max} \cdot \left(1 - \exp\left(-\frac{S}{K_s}\right)\right) \cdot X$	$q_{p\max} \cdot \left(1 - \exp\left(-\frac{S}{K_{sp}}\right)\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Teissier**
Inhibitory effect of the substrate and of one of the metabolism products				
4.	$\mu_{\max} \cdot \left(\frac{S}{1+\frac{K_s}{S}+\frac{S}{K_{Xi}}}\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{1+\frac{K_{sp}}{S}+\frac{S}{K_{Pi}}}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Andrews and Noack**
5.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \exp\left(-\frac{S}{K_{Si}}\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \exp\left(-\frac{S}{K_{Pi}}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Aiba**
6.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \left(1 - \frac{S}{S_{\max}}\right) \cdot n_x$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \left(1 - \frac{S}{S_{\max}}\right) \cdot n_x$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Loung**
7.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \left(1 - \frac{P}{P_{\max}}\right) \cdot n_x$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \left(1 - \frac{P}{P_{\max}}\right) \cdot n_x$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Levenspiel**
8.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \exp\left(-K_p \cdot P\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \exp\left(-K_{pp} \cdot P\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Aiba**
9.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \left(\frac{K_{Pi}}{K_{Pi}+P}\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \left(\frac{K_{ppi}}{K_{ppi}+P}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Jerusalimsky**
10.	$\mu_{\max} \cdot \left(1 - \frac{P}{P_{\max}}\right) \cdot X$	$q_{p\max} \cdot \left(1 - \frac{P}{P_{\max}}\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Ghose and Tyagi**
11.	$\mu_{\max} \cdot \left(\frac{S}{K_s+S}\right) \cdot \left(1 - K_p \cdot P\right) \cdot X$	$q_{p\max} \cdot \left(\frac{S}{K_{sp}+S}\right) \cdot \left(1 - K_{pp} \cdot P\right) \cdot X$	$-\left(\frac{1}{Y_{xs}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{ps}} \cdot \frac{dP}{dt}\right)$	**Hinshelwood**

Table 2. The empirical models most used in fermentation industrial processes simulation.

2.2.5. A batch bioreactor modeling

A batch bioreactor is a closed system that is fed at the beginning of the process with sterile medium (with S_0 initial concentration) and pure culture of the microorganisms with X_0 initial concentration. The microorganisms will grow up by multiplication, and eventually they will produce metabolisms products by substrate consummation. Inside the bioreactor, the conditions for multiplication will be established: pH, temperature, oxygen feeding (at aerobic processes), and stirring (at processes with liquid substrate).

Suppose that the growth rate of the biomass depends only by the cells' mass, the mass balance equations could be written for

biomass: $\frac{dX}{dt} = r_x$;

substrate: $\frac{dS}{dt} = r_s$;

metabolism product: $\frac{dP}{dt} = r_p$.

One of the simplest models that respect the previous equation is those of Malthus model:

$$r_x = \mu \cdot X \tag{33}$$

where μ is constant; the equation corresponds to exponential growing phase.

The specific growth rate μ can be described by Monod model:

$$\mu = \frac{\mu_{\max} \cdot S}{K_s + S} \tag{34}$$

with the application of correction factors at the inhibitory process produce by the substrate or metabolism product.

With the forming rate of biomass r_x (33), the consuming rate of the substrate r_s and the forming rate of the metabolite r_p, which have been presented at the kinetics model, could be written by the following equations:

$$\text{biomass} : \frac{dX}{dt} = \mu \cdot X \tag{35}$$

$$\text{substrate} : \frac{dS}{dt} = -\frac{\mu \cdot X}{Y'_{xs}} - \frac{k_1 \cdot X + k_2 \cdot \mu \cdot X}{Y'_{ps}} - m_s \cdot X \tag{36}$$

$$\text{metabolism product} : \frac{dP}{dt} = k_1 \cdot X + k_2 \cdot \mu \cdot X \tag{37}$$

The biomass forming

It takes place in the *aerobic* conditions and in Eq. (36) the factor of metabolism products formed will not appear:

$$\frac{dS}{dt} = -\frac{\mu \cdot X}{Y'_{xs}} - m_s \cdot X \tag{38}$$

If the substrate is in excess (in exponential growing phase), this means $S>>K_s$ and the process issues with maximum growth rate of biomass, the model is more simple. The total efficiency equation of the biomass, at maximum growth rates and constant forming efficiency of the biomass, becomes

$$\frac{dS}{dt} = -\frac{\mu \cdot X}{Y'_{xs}} \tag{39}$$

From Eq. (18) results:

$$S = S_0 - \frac{X - X_0}{Y'_{xs}} \tag{40}$$

By combining the above equation with Eq. (35), the following could be obtained:

$$\mu_{\max} \cdot dt = \frac{K_S + S_0 - \frac{X-X_0}{Y'_{xs}}}{\left(S_0 - \frac{X-X_0}{Y'_{xs}}\right) \cdot X} \cdot dX \tag{41}$$

and by integrating it between $t=0$, $X=X_0$ and t and X the named Monod integrated equation will be obtained, by which the biomass variation against time can be determined:

$$\mu_{\max} \cdot t = \ln\left(\frac{X}{X_0}\right) + \frac{K_s}{S_0 + \frac{X_0}{Y'_{xs}}} \cdot \left[\ln\left(\frac{X}{X_0}\right) - \ln\left(\frac{S_0 - \frac{X-X_0}{Y'_{xs}}}{S_0}\right)\right] \tag{42}$$

2.2.5.1. The metabolism products forming

2.2.5.1.1. Aerobic processes

In order to model this type of the processes, Eqs. (35)–(37) will be used. If μ will be considered constant and if the total efficiencies of the biomass and product will be introduced, the variation of the substrate quantity will be given by Eq. (36) in which the Y'_{xs} efficiency has been introduced, which means Eq. (39):

$$\frac{dS}{dt} = -\frac{\mu \cdot X}{Y'_{xs}} \tag{43}$$

and the equation that expresses the reaction product quantity variation will be obtained from the total efficiency of the product equation, Y'_{ps}, and Eq. (43):

$$\frac{dP}{dt} = \frac{Y'_{ps}}{Y'_{xs}} \cdot \mu \cdot X \tag{44}$$

2.2.5.1.2. Anaerobic processes

The equations that characterize the cultivation model in the aerobiosis conditions of the microorganisms, where the products of the reaction (usually primary metabolites) are formed always, are the mass balance equations, as follows:

$$\text{biomass} : \frac{dX}{dt} = \mu \cdot X \tag{45}$$

$$\text{substrate} : \frac{dS}{dt} = -\frac{\mu \cdot X}{Y'_{xs}} - m_s \cdot X \tag{46}$$

$$\text{metabolism product} : \frac{dP}{dt} = \frac{Y'_{ps}}{Y'_{xs}} \cdot \mu \cdot X + m_p \cdot X \tag{47}$$

The biomass and metabolism production will be completed when the substrate will be wasted.

In case the specific growth rate remains constant, simplifications can be made. Keeping tabs of total biomass and metabolism products efficiencies, Eqs. (46) and (47) become

$$\frac{dS}{dt} = -\frac{\mu \cdot X}{Y_{xs}} \tag{48}$$

$$\frac{dP}{dt} = \frac{Y_{ps}}{Y_{xs}} \cdot \mu \cdot X \tag{49}$$

which are identical with the equations that describe the aerobic fermentation. Unfortunately, during the anaerobic fermentation the biomass growth rate is inhibited by the metabolism products and the model becomes more complex. An example is the inhibition of the biomass growth in an alcoholic fermentation by the concentration of formed ethanol:

$$\mu = \frac{\mu_{\max} \cdot S}{K_s + S} \cdot \left(1 - \frac{P}{P_{\max}}\right) \tag{50}$$

where $P_{\max}$ represents the maximum concentration of ethylic alcohol at which the biomass production is stopped.

2.2.5.1.3. Energetically model for the batch bioreactor

The balance energy for reaction medium and bioreactor's jacket can been written as

$$\frac{\Delta Hr \cdot \frac{dS}{dt}}{\rho \cdot c_p} - \frac{K_T \cdot A_T}{V \cdot \rho \cdot c_p}\left(T^0 - T^0_{ag}\right) = \frac{dT^0}{dt} \tag{51}$$

$$\frac{F_{ag}}{V_{ag}}\left(T^0_{agi} - T^0_{ag}\right) + \frac{K_T A_T}{V_{ag} \cdot \rho_{ag} \cdot c_{pag}}\left(T^0 - T^0_{ag}\right) = \frac{dT^0_{ag}}{dt} \tag{52}$$

where ΔH_r is the reaction heat of the fermentation [*J/mol of the produced alcohol*]; K_T is the heat transfer coefficient [W/m^2.K] ; A_T is the heat transfer area [m^2]; ρ, ρ_{ag} is the density of the mass of the reaction, respectively, of the cooling agent [kg/m^3]; c_p, c_{pag} is the heat capacity of the mass of the reaction, respectively, of the cooling agent [J/kg.K]; V, $V_{ag}$is the fermentation medium volume, volume of the jacket [m^3]; F_{ag} is the flow of the cooling agent [m^3/h]; T^0 and $T^0_{ag}$are the temperature of the fermentation medium and temperature of the cooling agent in the jacket [K].

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3. Study case—modeling of a white wine alcoholic fermentation process

Wine making is a complex ecological and biochemical process involving many interactions such as grape variety, microbiota, and several technological operations. The process' variables are often controlled empirically and traditionally. There are some factors that strongly affect the alcoholic fermentation. The most important ones are fermentation temperature, grape juice composition, anaerobic conditionsdue to CO_2 production, low media pH, sulfur dioxide concentration level, selected yeasts inoculation, and interaction with other microorganisms [21]. The models developed for these cases consequently have various domains of applications but none of them include the whole oenological aspects of the process. The majority of the models are of "knowledge-based" models type and they take into consideration a great number of phenomena that have an important effect on the kinetics of the process fermentation [22].

This part of the chapter proposes a complex nonlinear wine fermentation model based on previous researches by the author [23–25].

3.1. Experimental conditions

To evaluate the total fermentation yield losses under different operating conditions, four experiments were carried out and based on the data obtained within these experiments, a mathematical model was proposed. The strain and the culture medium, the equipment and the experimental conditions together with the measurements of the fermentation parameters were presented by Sipos and coworkers [23–25]. For the experiments, the *Saccharomyces cerevisiae* YEPD wine yeast was used, being seeded on a culture medium with the following composition: 5 g/L KH_2PO_4, 2 g/L $(NH_4)_2SO_4$, 0.4 g/L $(MgSO_4)\cdot 7H_2O$, 1 g/L yeast extract, 50 g/L glucose, and Mauzac must (sterilized through flash pasteurization). The sugar content of the grape must was supplemented with sucrose up to 180 g/L and 40 mL/h tiaminol was added. The SO_2 content reached 50 mg/L and the pH was adjusted at 3.8 mg/L H_3PO_4. Both the fermentation medium and the bioreactor were autoclaved for 20 min at 393 K. A New-Brunswick continuously stirred bioreactor equipped with *pH* and temperature sensors was used.

The following operating conditions were as follows: working volume, 8 L; temperature, 291 and 301 K; stirring speed, 150 rpm; pH, 3.8; influent glucose concentrations, 180 and 210 g/L; without aeration, the necessary oxygen was dissolved in must.

3.2. The mathematical model

The mathematical model of the alcoholic fermentation process was determined on the basis of the approach of the zone modeling principle, taking into consideration the evolution of the viable biomass ($X_v(t)$). Based on the analysis of the phenomenological aspects of the alcoholic fermentation process, the evolution of $X_v(t)$ was divided into three parts (**Figure 5**) as follows:

- latent phase (1);
- growing phase (2);
- decay phase (3).

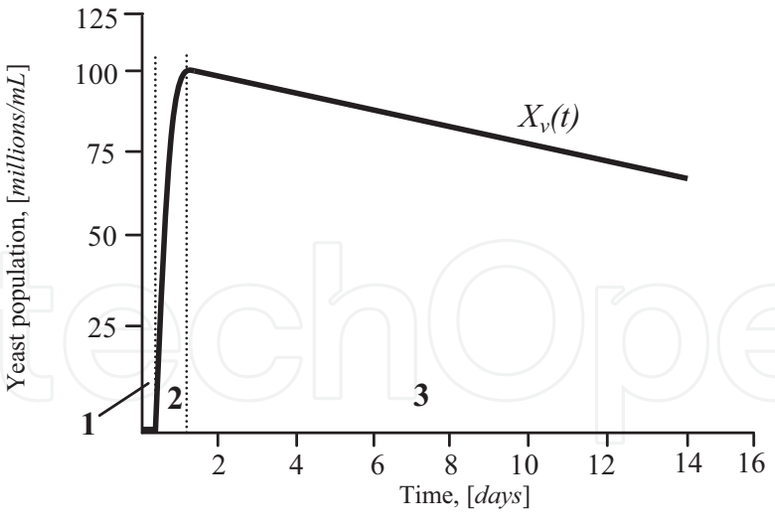


Figure 5. Evolution of the viable biomass concentration $X_v(t)$.

Table 3 presents the equations of the model. The parameters are adjusted through the nonlinear programming method, which compares the model predictions with experimental data and minimizes the errors.

Tables 4 and **5** present the list of the variables and parameters of the mathematical model.

Current phase	Model equations
Kinetic model	
Latent phase [23, 24]	$t_{lat} = \frac{a}{T^0} + b$
Exponential growing phase [1]	- biomass: $\frac{dX}{dt} = \mu_{\max} \cdot \left(\frac{S}{K_S+S}\right) \cdot e^{-K_p \cdot P} \cdot X$; $\mu_{\max} = A_1 \cdot e^{-\frac{E_{a1}}{R \cdot T^0}} - A_2 \cdot e^{-\frac{E_{a2}}{R \cdot T^0}}$ - alcohol: $\frac{dP}{dt} = q_{p\max} \cdot \left(\frac{S}{K_{SP}+S}\right) \cdot e^{-K_{pp} \cdot P} \cdot X$ - substrate: $\frac{dS}{dt} = -\left(\frac{1}{Y_{XS}} \cdot \frac{dX}{dt}\right) - \left(\frac{1}{Y_{PS}} \cdot \frac{dP}{dt}\right)$
Decay phase [23–26]	- biomass: $\frac{dX}{dt} = f \cdot X \cdot k$; $k = A \cdot e^{-\frac{Ea}{R \cdot T^0}}$ - alcohol: $P = P_0 + \eta \cdot (S_0 - S)$ - substrate: $\frac{dS}{dt} = -k \cdot S^{\alpha} \cdot P^{\beta}$
All phases	- carbon dioxide concentration: $\frac{dC_{CO_2}}{dt} = g \cdot C_{CO_2} \cdot k \cdot \frac{S}{K_{SP}+S} \cdot \ln\left(k \cdot \frac{S}{K_{SP}+S} \cdot t\right)$
Energetic model	
All phases [23, 26]	- for the bioreactor: $\frac{\Delta Hr \cdot \frac{dS}{dt}}{\rho \cdot c_p} - \frac{K_T \cdot A_T}{V \cdot \rho \cdot c_p}\left(T^0 - T^0_{ag}\right) = \frac{dT^0}{dt}$ - for the bioreactor's jacket: $\frac{F_{ag}}{V_{ag}}\left(T^0_{agi} - T^0_{ag}\right) + \frac{K_T A_T}{V_{ag} \cdot \rho_{ag} \cdot c_{pag}}\left(T^0 - T^0_{ag}\right) = \frac{dT^0_{ag}}{dt}$

Table 3. The model of the alcoholic fermentation process.

X	Biomass concentration		g/L
S	Substrate concentration		g/L
P	Alcohol concentration		g/L
k	Kinetic constant		1/h
A	Pre-exponential factor in Arrhenius' equation	148 (calculated using experimental data)	1/h
E_a	Activation energy	21,424 (calculated using experimental data)	J/mol
A_1	Pre-exponential factor in Arrhenius' equation	9.5×10^{8} [a]	1/h
E_{a1}	Activation energy	55,000[a]	J/mol
A_2	Pre-exponential factor in Arrhenius' equation	2.55×10^{33}	1/h
E_{a2}	Activation energy	220,000[a]	J/mol
R	Universal gas constant	8.31	J/mol·K
T^0	Temperature in bioreactor	291 and 301	K
K_s	Substrate limitation constant	0.2[a]	g/L
d	Pseudo-constant of the biomass	1.67 (calculated using experimental data)	
f	Pseudo-constant of the biomass	0.34	
α	Pseudo-order of the substrate	0.69[b]	
β	Pseudo-order of the alcohol	0.32[b]	
η	Efficiency in alcohol of fermentation reaction	48[b]	%
S_0	Steady-state operation point of substrate	180	g/L
P_0	Steady-state operation point of alcohol	0	g/L
t	Time		h
μ_{max}	Maximum specific growth rate		1/h
K_P	Alcohol limitation constant	0.14[c]	g/L
q_{pmax}	Maximum specific alcohol production rate	1.02[c]	g/g·cells·h
K_{SP}	Constant in the substrate term for ethanol production	1.68[c]	g/L
K_{PP}	Constant of fermentation inhibition by ethanol	0.07[d]	g/L
Y_{XS}	Ratio of cell produced per glucose consumed for growth	0.607[d]	g/g
Y_{PS}	Ratio of ethanol produced per glucose consumed for fermentation	0.435[c]	g/g

[a][6, 27, 28]
[b][26]
[c][29]
[d][16]

Table 4. Variables and parameters of the kinetic model.

K_T	Heat transfer coefficient	3.6×10^{5} [a]	J/ m^2·K·h
A_T	Heat transfer area	0.8[b]	m^2
F_{ag}	Flow of cooling agent	0.01[b]	m^3/h
V_{ag}	Volume of the jacket	0.2[b]	m^3
V	Volume of the mass of reaction	1[b]	m^3
T^0_{agi}	Temperature of cooling agent entering to the jacket	278[b]	K
ΔH_r	Reaction heat of fermentation	−98465[c]	J/mol
ρ	Density of the mass of reaction	1100[b]	kg/m^3
ρ_{ag}	Density of cooling agent	999.8[a]	kg/m^3
c_p	Heat capacity of mass of reaction	3391[b]	J/kg·K
c_{pag}	Heat capacity of cooling agent	4217[a]	J/kg·K
T^0_{ag}	Temperature of cooling agent in the jacket		K

[a][17]
[b]experimental data
[c][30]

Table 5. Parameters of the kinetic model.

3.3. Result and discussion regarding the mathematical model simulation

The nonlinear mathematical model of the batch fermentation process (**Table 3**) used in this work contains the following equations:

- an equation for the latent phase of fermentation that describes the dependence of the phase time of the process temperature;
- the model proposed by Aiba [1] for the growing phase with the three equations of biomass, alcohol production, and substrate consumption;
- the model presented by Bovée-Strehaiano [26] for the decay phase with two equations: one for the substrate consumption and the other for alcohol formation;
- an equation that describes the biomass behavior along the phase no. 3 (the model proposed by Sipos in [23–25]);
- an equation that describes the carbon dioxide concentration behavior along all the phases (the model proposed by Sipos);
- an energy balance model in which the rate of change of the medium's temperature (dT^0/dt) is a result of the balance between the rate of the heat generation due to fermentation and the rate of the heat transfer to the cooling medium inside the bioreactor jacket.

The model proposed by Aiba [1] includes the inhibitory effects of the fermentation product (alcohol). In the growing phase, the value of the maximum specific growth rate of the biomass

corresponds to the real one. The non-physiological model proposed by Bovée and Strehaiano [26] was chosen because it accurately describes the substrate consumption and the evolution of the alcohol concentration in the growing and decay phases. This model proposes the use of a semi-empirical model in which the velocity of sugar consumption is described by a chemical law that depends on substrate and product contents. The parameters of the model are adjusted by means of nonlinear programming methods, which compare model predictions with experimental data and minimize errors [23–25]. The Bovée and Strehaiano model is capable of predicting the fermented sugar (and thus thermal planning) within an error of 3.3% [25]. Thus, the model offers a good qualitative and quantitative description of the behavior of the alcoholic fermentation process.

Figures 6–8 show the simulation results of the model presented in **Table 3** considering the following initial values: the initial substrate concentration was 210 g/L and the fermentation temperature was 301 K.

The equation of the latent phase is valid for a time interval [0, 100 h] and the model has been tested for a grape juice variety with an initial concentration of the substrate varying between 180 and 210 g/L, a fermentation temperature between 299 and 303 K and without aeration.

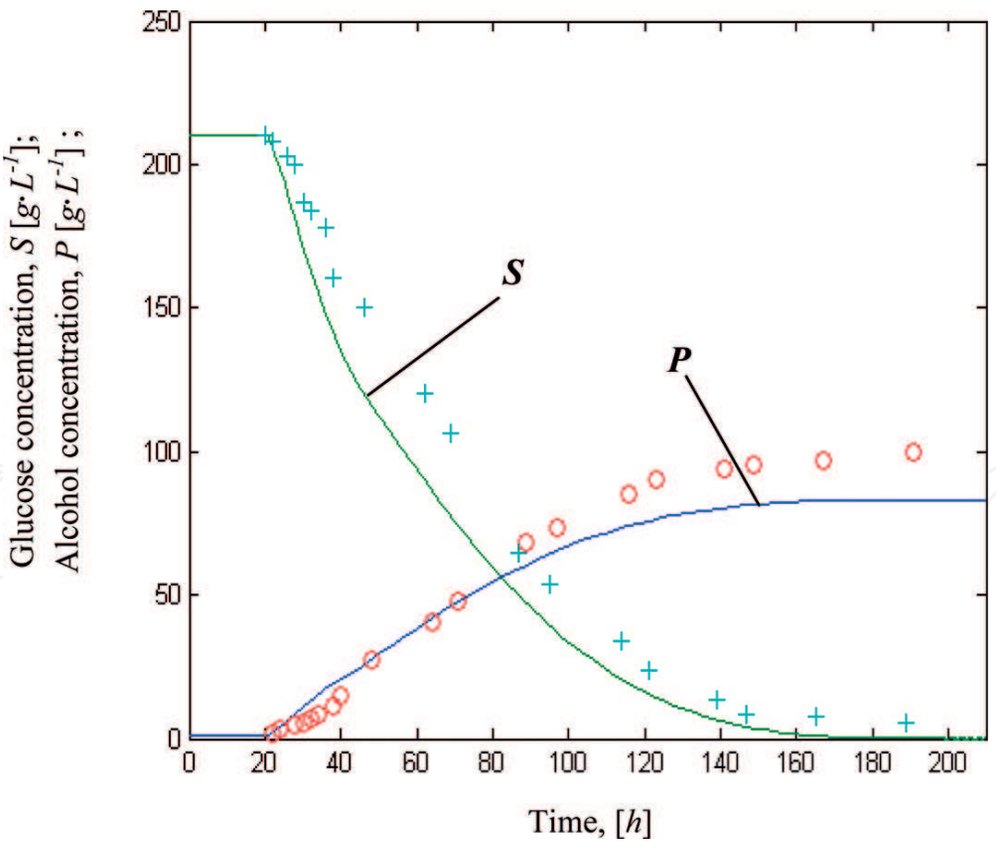


Figure 6. Evolution of glucose and alcohol concentrations; a comparison between experimental values (**o**—glucose and **+**—alcohol) and simulation results (continuous lines).

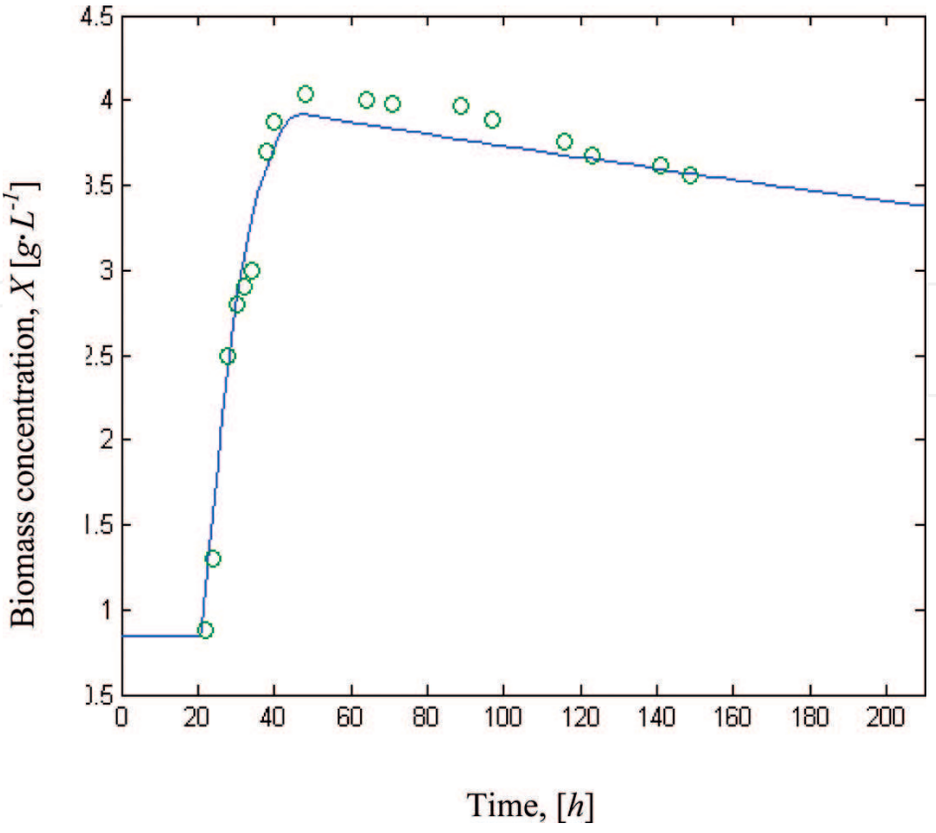


Figure 7. Comparison between the biomass simulation results (continuous line) and experimental data (o).

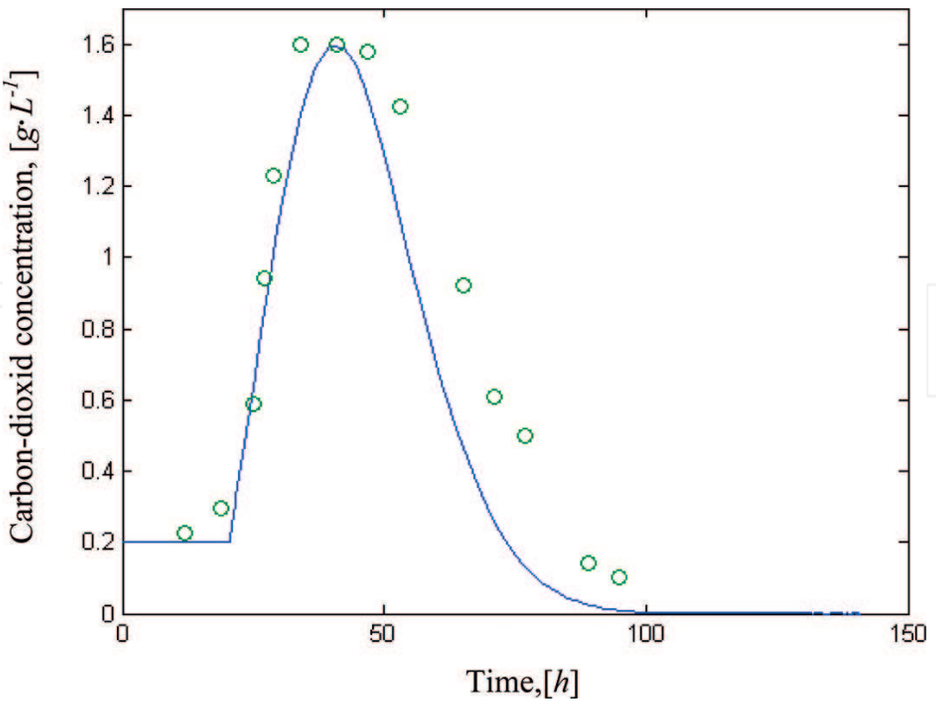


Figure 8. Comparison between the carbon dioxide concentration simulation results (continuous line) and experimental data (o).

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