UNIVERSITY OF ASTON IN BIRMINGHAM

ANALYSIS OF SUBSTRATE LIMITED FERMENTATION IN A DISPERSED PLUG-FLOW REACTOR

by

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SUMMARY.

A tubular reactor, in which there is a dispersed plug-flow and in which a single cell fermentation occurs is critically analyzed using a lumped approximation technique. Estimates of the bounds of Fermentation Number where multiple solutions can occur and the necessary and sufficient conditions for stability to small perturbations are presented.

Analysis has been made of fermentation processes involving both gaseous and non-gaseous limiting substrates and operated under sterile and non-sterile feed conditions: non-inhibitory and inhibitory kinetic have been examined in all cases. The results are presented both analytically and graphically, and they are compared with those obtained using a marching Runge-Kutta method.

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C O N T E N T S.

CONTENTS (contd)

CONTENTS (contd).

Page No.

FIGURES.

CONTENTS (contd)

PREFACE

The work of the The Tower Fermentation Group at the University of Aston in Birmingham is jointly supervised by Dr. E.L. Smith (Department of Chemical Engineering) and Dr. R.N. Greenshields (Department of Biological Sciences). The overall objective of the Group is to study the design, operation and control of tower fermenters and to explore their use in selected fermentation processes. As explained in Chapter 2, the tower fermenters developed at Aston are simple tubular reactors which when used for aerobic fermentations are operated as bubble columns.

At present, four members of the Group are examining the feasibility of using tower fermenters for the following processes:

1. the continuous production of alcohol from sugar solutions using flocculent yeasts,
2. the treatment of effluents containing simple sugars and polysaccharides using filamentous fungi, and
3. the production of secondary metabolites, in particular acetic acid using bacteria.

Because of interest in the use and production of fungi, two other members of the Group are studying factors that control the growth and aggregation of filamentous micro-organisms.

In the past, preliminary work with the processes described above was undertaken : research into the effects of tower design and operating conditions on gas hold-up, liquid-phase mixing and gas-liquid mass-transfer was also carried out. A summary of much of this work has been given by FIDGETT (8), whose research and that of the author was prompted by the need to develop mathematical models of tower fermentation systems so that experimental results could be correlated with design and operating parameters and future research could be well planned and executed.

Fidgett was the first member of the Group to carry out research on the mathematical modelling of tower fermentation processes, and this thesis describes work which complements that of Fidgett. Whereas Fidgett used stage-wise models to describe mixing in tower fermenters, the author has directed his attention to the axially dispersed plug-flow model in order to take advantage of the results of SHAYEGAN SALEK (27). (Shayagan Salek, a former member of the Group, obtained experimental values for the liquid phase Peclet or Bodenstein Number in tower systems).

Kinetic models used to describe fermentation processes are still at the development stage, and so relatively simple models must still be used in order to gain insight into what is happening in real processes. The dispersed plug-flow model has been applied previously by CHEN (69) in a study of processes involving exponential growth of micro-organisms and by other researchers (33,70) in studies of processes involving Monod kinetic models. Consequently, it seemed to the author that the next logical step in the mathematical analysis of general fermentation processes was to consider inhibitory effects. In order to take advantage of developments that have already occurred in the analysis of continuous flow stirred tank fermenters (31,32), the author chose as his objective the analysis of nutrient-inhibited fermentation processes.

The thesis is divided into six chapters, the first including a general description of fermentation processes. This description highlights the complexity of microbiological systems and includes features which cannot be readily included in mathematical models at present. A classification of kinetic models devised by TSUCHIYA, FREDRIGKSON and ARIS (6) is also given in this chapter. This has been included because the author is of the opinion that it provides excellent insight into the nature of kinetic models. The final section describes the kinetic model

used in the research.

In the second chapter attention is focussed on tower fermenters. A description of mixing in gas-sparged tubular reactors is given, and alternative models of liquid-phase mixing are outlined. The mixing model used in the author's research, that is to say the axially dispersed plug-flow model, is also included.

The dimensionless equations describing the behaviour of a dispersed plug-flow reactor in which a nutrient-inhibited fermentation occurs are introduced in the third chapter. A physical explanation for all dimensionless parameters appearing in the equationsis also given. Steady-state equations, used in the fifth chapter, are presented at the end of chapter three.

In chapter four advantage is taken of the lumped approximation technique described by HLAVACEK and HOFMANN (67) to obtain equations which can be treated analytically. Modified dimensionless groups are also defined : these make it possible to disregard the extent of mixing and to present results in a concise manner since the Bodenstein Number is not used explicitly. Steady-state solutions for the following situations are then given:

1. non-inhibitory fermentation processes
   (a) sterile feed conditions
   (b) non-sterile feed conditions
2. inhibitory fermentation processes
   (a) sterile feed conditions

All positive roots of the equations have been calculated and the bounds of multiplicity domains determined. These results are then used to analyse system stability using the First Method of Liapunov, and various stable and unstable situations are explained by comparing expressions for the rate of wash-out of micro-organisms and for the rate of microbial

growth. In a final section, graphs summarising the steady-state results are presented : all parameters that influence system behaviour are included in the plots.

Steady-state solutions have also been obtained numerically using a "shooting" method : the method and results are introduced in the fifth chapter. Graphs are used to compare the results obtained by the lumped approximation method with those found by the exact method. At low values of the Bodenstein Number agreement is excellent : at high values there are some interesting differences which deserve further study.

In chapter six ideas for future work are given.

The work summarised in this thesis represents the first step in a systematic analysis of fermentation processes taking place in tubular devices. The results obtained to date will open the way for the use of more powerful methods of analysis and will make it possible to study more complex kinetic models. These latter models will include those describing product-inhibited fermentations and processes involving more than one rate-limiting nutrient or product.

I - MATHEMATICAL MODELLING OF FERMENTATION PROCESSES.

1.1) INTRODUCTION.

Before starting this chapter it is necessary to stress that practical fermentation processes are so complicated that kinetic models have to be much simplified. The insight gained even from the most elementary model is not to be despised, although it would be the height of folly to expect such a model to explain exactly the behaviour of real systems. Since no kinetic model is ever the perfect expression of a real fermentation process, the simplifying assumptions on which it is based must be clearly stated and understood and tested experimentally.

The microbial mass in a culture can exist in two geometrical states [1] - either freely suspended or adhering to surfaces in the container. Freely suspended micro-organisms can occur either as single cells or in multi-cellular groups called flocs. Also, any surface in contact with a microbial suspension may become biologically active due to adhesion of micro-organisms which sometimes form continuous layers of microbial mass called films. Very little is known about the flocculation and adhesion processes: a more detailed discussion of flocculation is presented in the paper by ATKINSON and DAOUD [2] and of adhesion in the paper by ATKINSON and FOWLER [3]. In this work the flocculation and adhesion processes will be neglected and a single cell fermentation will be analyzed. This does not mean that these processes are considered unimportant, but simply that the author does not intend to consider them in this thesis.

Unicellular micro-organisms occur in all sorts of different shapes and sizes, depending on the species and on the way they have been grown. But for our purpose, it is possible to disregard these variations and consider a generalized unicellular micro-organism. It will be supposed that this micro-organism can

grow in a medium containing a carbon source (e.g. glucose), a nitrogen source (e.g. ammonium ions), a sulphur source (e.g. sulphate ions) and small amounts of other nutrients. This typical micro-organism should be regarded as an abstraction in much the same way as the average man.

The number of chemical reactions involved in microbial growth processes is unknown but it is probably of the order of a thousand. Of these a few may occur spontaneously but the vast majority have to be catalyzed by specific enzymes. These reactions can be classified into two groups - catabolic reactions and anabolic reactions. The catabolic reactions, also called degradative reactions, degrade the carbon substrate, usually after the introduction of inorganic phosphate, to smaller molecules which can then be utilized as building blocks for the synthesis of new cell material. In the course of these reactions energy in the form of ATP is produced for utilization in the subsequent energy-requiring reactions. The anabolic reactions, also called biosynthetic reactions, convert the basic small molecules into macromolecules using ATP as the source of energy.

According to species, micro-organisms are able to live either in the presence or in the absence of oxygen. Some are intolerant to one or other of these conditions and are classified as strict aerobes or anaerobes: but many micro-organisms can tolerate both conditions and are referred to as facultative anaerobes.

The consititution of a micro-organism is determined to a considerable extent by the medium in which it is growing. A rich medium tends to cause the cells to grow more rapidly than does a poor medium. Sometimes, one substrate (e.g. glucose) is preferred to another (e.g. galactose), and organisms will grow in the presence of both, using only one until it is exhausted and then, after a short lag, the other. Following such a switch, the generation time may

change, and cells of different size and composition may be produced.

Temperature also affects the growth of a culture but probably has less effect on composition than does the nature of the growth medium. Many species grow best between 30° and 37°C, but, although some tolerate much higher or lower temperatures, only a few are truly thermophilic or cryophilic in the sense of growing better at high or low temperatures.

Some micro-organisms have the genetic ability, under adverse conditions, to undergo physiological and morphological changes called sporulation. The most characteristic property of spores is extreme resistance to environmental hazards such as heat, desiccation, organic solvents and starvation conditions. Sporulation may occur at the end of the growth process when nutrients becomes exhausted or at low frequencies during the growth.

When a spore suspension is introduced to favourable environmental conditions, the spore will, after adequate activation followed by germination, undergo a period of intense biosynthetic activity which ends at the time of cell division called outgrowth. During this period the micro-organism is rebuilt and normal growth resumed.

Mutations occur spontaneously in a culture and there is no way of preventing their occurrence. Some mutants may be able to grow better in the environment prevailing in the culture than non-mutants. Such mutants tend to disseminate through the whole population as growth progresses. Mutations can be specially troublesome in continuous culture.

In a growth culture dead micro-organisms make no contribution to the growth of the population. A micro-organism may die as a result of adverse environmental factors such as high temperature or high concentration of a toxic chemical, or due to the

occurrence of non-viable mutation. Before an experimental determination of the amount of dead cells is started it is necessary to devise a method to distinguish between dead and dormant cells.

In this section are summarized all the important aspects of the growth of microbial populations. In this work we do not intend to present a universal analysis which includes all these aspects. The aim of this section is to give the reader some idea of the limitation of our analysis.

The literature of microbial growth is vast, but the books by DEAN and HINSHELWOOD [4] and MANDELSTAM and MACQUILLEN [5] provide excellent insight into the nature and structure of microbial growth processes and are good starting points for those with a chemical engineering background.

1.2) CLASSIFICATION OF FERMENTATION KINETIC MODELS.

In this section we follow closely TSUCHIYA, FREDERICKSON and ARIS [6]. They proposed a complete classification of kinetic models for growth of microbial populations.

The mathematical approach to the study of microbial populations has generally been based either on the use of population density (number of cells per unit of volume) or biomass concentration (mass of cells per unit of volume). Kinetic models based on the first approach are referred to as "segregated kinetic models", since life is considered to be segregated into structural units which are called "cells". On the other hand, kinetic models based on biomass concentration are referred to as "non-segregated kinetic models"*

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*The name "non-segregated kinetic model" was introduced by FREDRICKSON, MEGEE III and TSUCHIYA [7].

since the population mass is considered to be distributed uniformly throughout the culture.

Another basis for classification of mathematical approaches is provided by the observation that the cells may be assumed to be "structured" or "unstructured". A segregated kinetic model is referred to as a "structured segregated kinetic model" if properties for distinguishing one cell from another are specified: such properties might be age, size, mass or chemical composition of the cells. A non-segregated kinetic model may also be said to be "structured", if the composition of the population varies with the conditions of growth.

Finally, it is possible to classify the mathematical approaches as either "stochastic" (probabilistic) or "deterministic". In fact, a real fermentation process is always segregated and structured, and its growth and reproduction should be treated stochastically. However, the biological knowledge and mathematical tools necessary for formulation and study of this general model do not exist, and a less general approach gives useful results. In this work only "deterministic, unstructured, non-segregated kinetic models" will be considered: these models have been reviewed in FIDGETT'S thesis [8].

1.3) DETERMINISTIC,UNSTRUCTURED,NON-SEGREGATED KINETIC MODELS.

The most widely used deterministic, unstructured non-segregated kinetic model is the MONOD model*[9] which is a modification of the M'KENDRICK and PAI model [10]. M'KENDRICK and PAI assumed that the growth rate is proportional to biomass concentration,** i.e.,

$$R_g = \mu m \qquad (1.3.1)$$

*MONOD attached much less significance to his model than subsequent researchers.

**The use of biomass concentration was recommended by MONOD:M'KENDRICK and PAI used population balance.

only if an "unlimited supply of nutrient" is available. When substrate for growth has been consumed, they postulated that the specific growth rate is a linear function of concentration of this substrate, i.e.

$$\mu = \alpha s \tag{1.3.2}$$

so

$$R_g = \alpha s m \tag{1.3.3}$$

M'KENDRICK and PAI assumed also that the rate of consumption of a given substrate is proportional to the rate of growth, so

$$R_c = - \frac{R_g}{Y} \tag{1.3.4}$$

MONOD [9] recognized that the specific growth rate could have a maximum value and proposed the following relationship

$$\mu = \frac{\mu_{max}\, s}{K_s + s} \tag{1.3.5}$$

which is similar to the BRIGGS-HALDANE [11] relationship for enzyme kinetics*.

It is easy to show that for $s >> K_s$ we obtain

$$\mu \simeq \mu_{max} \tag{1.3.6}$$

and for $s << K_s$ we get

$$\mu \simeq \frac{\mu_{max}\, s}{K_s} . \tag{1.3.7}$$

K_s is a constant having the same dimensions as those of the substrate concentration and is known as the MICHAELIS constant**. If

$$\mu = \frac{\mu_{max}}{2} \tag{1.3.8}$$

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*This is known to physical chemists as LANGMUIR-HINSHELWOOD, to chemical engineers as HOUGEN-WATSON and to biochemists as MICHAELIS-MENTEN.

**Sometimes known as the saturation constant.

we obtain

$$s = K_s. \qquad (1.3.9)$$

Thus, numerically, K_s equals the concentration of substrate at which the specific growth-rate is equal to one-half the maximum specific growth-rate.

Most investigators have found that the MONOD relationship provides a reasonable fit for experimental data. However, as pointed out by POWELL [12], this relationship cannot be valid for those substrates which limit growth at low concentrations and are inhibitory to the organisms at higher concentrations.

One plausible mechanism for substrate inhibition would be a reduction in the activity of an enzyme by complexing with excess substrate. The most widely used kinetic model for this situation is the one proposed by HALDANE [13] in 1930 for the inhibition of enzymes at high substrate concentrations. This model may be expressed as

$$\mu = \frac{\mu^* s}{K_s + s + s^2/K_i}. \qquad (1.3.9)$$

Although there is no theoretical basis for the use of this kinetic model for micro-organism growth, some researchers [14] [15] [16] have concluded that this equation provided the best fit for their data. Recently, EDWARDS [17] tested five inhibitory kinetic models with eight sets of experimental data and found that the above model was the best choice.

The maximum specific rate attainable may be obtained by setting the first derivative equal to zero to obtain:

$$s_m = \sqrt{K_s K_i} \qquad (1.3.10)$$

The maximum specific growth rate is then

$$\mu_{max} = \frac{\mu^*}{1 + 2\sqrt{\frac{K_s}{K_i}}} \qquad (1.3.11)$$

If $K_i >> K_s$ we get

$$\mu^* = \mu_{max}$$

and equation (1.3.11) becomes

$$\mu = \frac{\mu_{max}\, s}{K_s + s}. \qquad (1.3.12)$$

Consequently, the Monod model is only a special case of this kinetic model. A more detailed treatment of the properties of this model is given by DIXON and WEBB [18].

The above kinetic models are the most widely used ones [19]-[21], and all the other models are modifications of them [22]-[23].

It is well known that deterministic, unstructured, non-segregated kinetic models (at least the known models) cannot explain unbalanced growth processes, i.e., situations where structural properties change with conditions of growth. These situations are expected to be explained by structured kinetic models, but such models as pointed out by FREDERICKSON [25], are not suitable for use in dispersed plug-flow models of reactors. Consequently, we will neglect them in this thesis. Those interested in such models should keep the papers of FREDERICKSON, TSUCHIYA and co-workers under close surveillance.

1.4) SUMMARY.

In this chapter we have reviewed the points which are essential to the development of the research. In the first section we described all the important aspects of the growth of microbial populations: this was necessary to call attention to the complexity

of growth processes. In the following section we looked at ways of classifying kinetic models, and based on this classification we chose the class of kinetic models most suitable for use with the dispersed plug-flow model. In the last section we introduced the most widely used deterministic, unstructured, non-segregated kinetic model, which will constitute the centre of the analysis.

II - MATHEMATICAL MODELLING OF A TUBULAR REACTOR USED AS A FERMENTER.

2.1) INTRODUCTION.

The aim of this chapter is to review the mathematical models which can be used in the analysis of tubular devices. As it is interest in the use of the tower fermenter which has motivated the research it seems appropriate to begin this chapter with a few comments about it.

The tower fermenter is a piece of industrial equipment specially devised for fermentation processes often involving flocculent micro-organisms. It can be described as a tubular reactor, the top of which opens out into a large settling zone. FIGURE (2.1.1) shows diagrammatically a tower fermenter.

For the purpose of design and mathematical analysis it is convenient to separate the tubular zone (reaction zone) from the settling zone (separation zone). If we consider the tubular section only the tower fermenter may be considered as a tubular reactor.

As the kinetic models of flocculent microbial process are still not sufficiently developed to be used in mathematical analysis of growth processes, they will not be considered in this work. Our intention is to apply the single-cell fermentation kinetics presented in the previous chapter to the analysis of a tubular reactor as a fermenter. The reader has to accept this work as a first step opening the way to more sophisticated mathematical analysis.

2.2) MIXING IN A TUBULAR REACTOR USED FOR AN AEROBIC PROCESS.

Mixing in a tubular reactor in which an aerobic fermentation process is occurring is achieved by injecting air. This produces swarms of air bubbles which travel up through the equipment.

According to MORRIS, GREENSHIELD and SMITH [26] the air

F I G U R E (2.2.1)

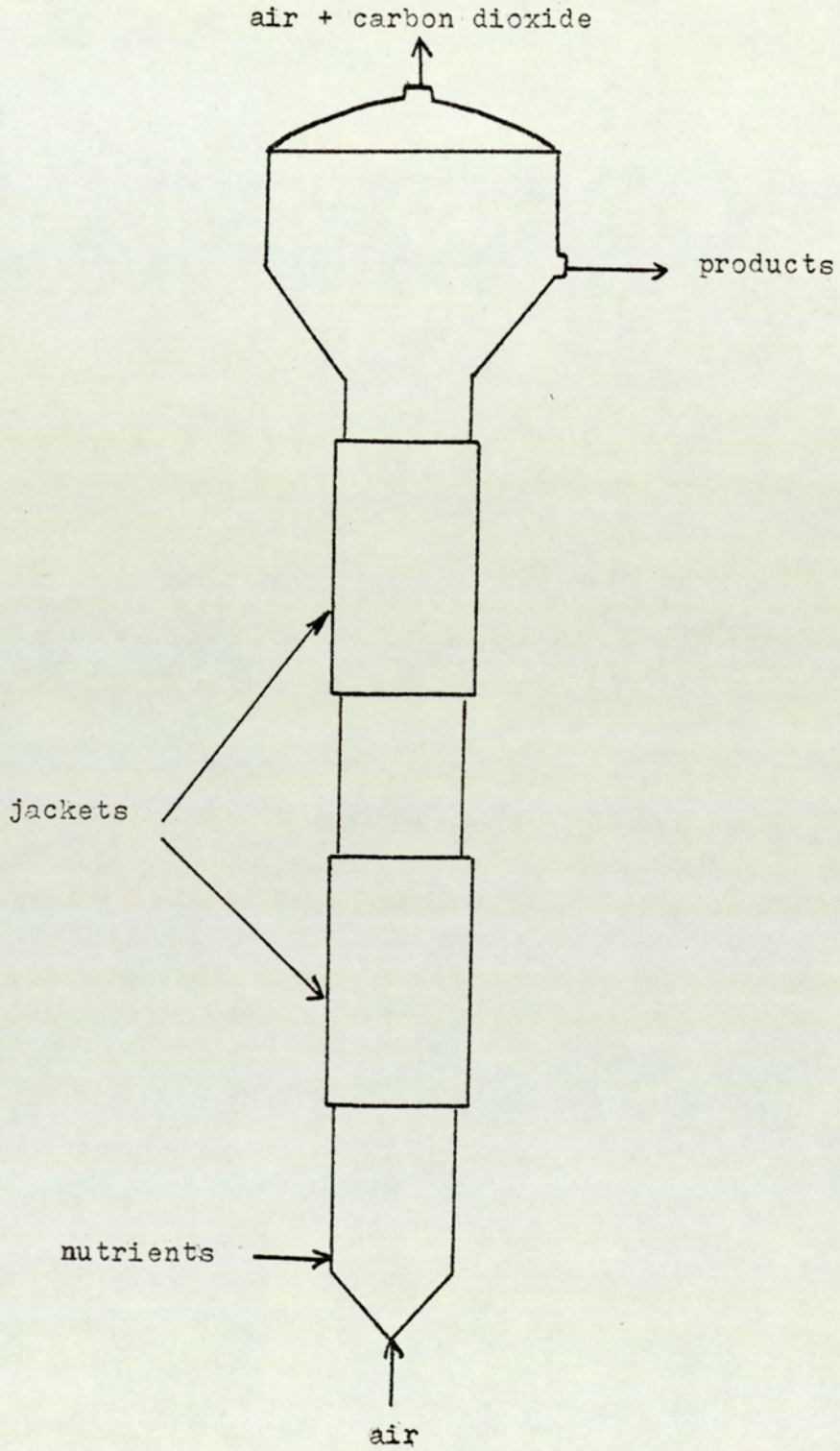


Diagram of a tower fermenter

flow may be characterized by three general patterns:

1. bubbly flow with low backmixing;
2. bubbly flow with high backmixing; and
3. slug flow.

The first pattern occurs at low superficial gas velocities (~ 1 cm/sec), the second at higher velocities (~ 3 cm/sec) and the last one at still higher values (> 5 cm/sec). We will restrict our analysis to the first two patterns since the difference is due only to the intensity of mixing. Three important parameters are influenced by the superficial gas velocity - the gas hold-up, the volumetric mass transfer coefficient and a mixing parameter which depends on the mathematical model we use to analyse the process. It has been shown that the liquid flow rate has an insignificant effect on these parameters [27].

Since we are considering single cell fermentation processes we may neglect the influence of flocs on the mixing patterns and consider the mixing behaviour as similar to that in bubble column reactors.

There are several ways of expressing the quality of the mixing process which occurs within a tubular reactor. One extreme possibility is that of perfect mixing: this can be defined as a state in which the composition of the culture is the same at all points in the tube. The other extreme possibility is plug-flow: this can be defined as the state in which the culture moves without any axial mixing with a flat velocity profile. All the other states of mixing lie between these two extremes and are called **non ideal mixing.**

2.3) MATHEMATICAL MODEL FOR A TUBULAR REACTOR USED FOR AN AEROBIC PROCESS.

In order to model the behaviour of a tubular reactor in which an aerobic fermentation process is occurring we have at our disposal several approaches. For ideal situations, as mentioned in

the last section, the well mixed and the plug-flow models are suitable. Since the pioneer work of MONOD [28] and NOVICK and SZILARD [29], who formulated the basic theory of the use of the well mixed reactor as a fermenter, the well mixed approach has been widely studied. A detailed study of non-inhibitory fermentation processes (MONOD model) under sterile feed conditions for a non-gaseous limiting substrate using the LIAPUNOV theorem can be found in the work of RAMKRISHNA [30]. The same type of analysis for inhibitory fermentation processes has been carried out by YANO and KOGA [31], and ANDREWS [32] and for the case with wall growth by CHI, HOWELL and PAULOWSKY [33]. A similar problem involving substrate-inhibited enzyme reactions has been analyzed by MACGRATH and YANG [34], O'NEILL [35], and O'NEILL,LILLY and ROWE [36]. The plug flow approach is rarely considered [37],[38].

For mixing patterns between these two extremes we have three options:

1. stagewise models,
2. dispersed plug-flow models and
3. more sophisticated models.

The last option involves any combination one can imagine of well mixed and plug-flow models. Those interested in the applications of the third option to non-inhibitory fermentation processes should read FAN, TSAI and ERICKSON [39]

2.4) STAGEWISE MODELS.

The mixing cell model and back-flow cell model are the best known examples of stagewise models. Their basic unit is the stirred cell. The mixing cell model consists of a series of stirred cells: the culture and the air are fed to the first cell from which they flow through the other cells in succession. The back-flow cell model is very similar to the mixing cell model, the difference being the recirculating flow between neighbouring cells which contributes

to the mixing. In both models the total volume between the inlet and the outlet of the tube is equally divided between the cells. The mixing parameter common to both models is the number of cells, N, which is determined by the analysis of the mixing process: in the case of back-flow cell model the recirculating flow between neighbouring cells is an additional mixing parameter.

The use of the above models in the analysis of tubular reactor has the following advantages from a mathematical view point:

1. the transient behaviour is represented by a set of non-linear first order ordinary differential equations, and
2. the steady-state is represented by a set of non-linear algebraic equations.

Applications of these models to non-inhibitory fermentation processes can be found in the paper by FAN, ERICKSON, SHAH and TSAI [40]. Some research involving use of the back-flow cell model in fermentation is being carried out at Aston University [41]. In this thesis we will ignore such models.

2.5) DISPERSED PLUG-FLOW MODELS.

In a tubular reactor we have deviations from the two ideal cases described in Section (2.2) due to two factors:

1. non-flat velocity profile, and
2. low intensity mixing processes.

Usually these two factors are superimposed. In order to overcome the difficulties that arise we have to use the dispersed plug-flow model [42]. This model is the most widely used model for describing the non-ideal mixing behaviour of tubular devices [43]-[47].

Mathematically this model is much more complicated than the stagewise model, but the mathematical tools necessary to analyse

it have developed fast in the last ten years. The unsteady-state behaviour of a dispersed plug-flow reactor is described by a set of parabolic partial differential equations and the steady-state is represented by a set of second order ordinary differential equations. The most widely used set of boundary conditions was independently determined by LANGMUIR [48] and DANCKWERTS [49]; this aspect of the problem has been widely studied by several other researchers [50]-[54]. The numerical methods which can be used in the exact analysis of the steady-state have been presented in a sequence of papers by KUBICEK and HLAVACEK [55]-[63]. Stability analysis of the exact problem can be found elsewhere [64]-[66]. Approximate methods are described in the paper of HLAVACEK and HOFMANN [67] and COHEN and POORE [68]: use is made of a lumped approximation method in Chapter IV.

Since the dispersed plug-flow model is the most extensively studied mathematical model we have chosen it as the basis for our studies.

2.6) SUMMARY.

In this section we have described in a very simple way the mixing behaviour of the equipment which constitutes the centre of our interest - the tower fermenter. Following that description we have summarized the mathematical models at our disposal, explaining the reason for choosing the dispersed plug-flow model.

III - BALANCE EQUATIONS.

3.1) INTRODUCTION.

The dispersed plug-flow model is the most widely used model in the analysis of tubular reactors. It has been used by CHEN [69] in a study of processes involving exponential growth of micro-organisms and by CHEN, FAN and ERICKSON [70] in an analysis of fermentation reactions described by a modified MONOD model, in which endogenous metabolism is considered. FREDRICKSON, MEGEE and TSUCHIYA [7] in their analysis of mathematical models for fermentation processes presented the general equations which govern the tubular reactor but they only considered non-gaseous substrates.

The aim of this chapter is to present the balance equations together with appropriate boundary and initial conditions describing the behaviour of a dispersed plug-flow reactor in which a growth-limited fermentation occurs. In the development of the equations we will avoid detailed consideration of the gas-phase by assuming that the concentration of a gaseous limiting substrate at the gas/culture interface is constant and independent of the concentrate of this substrate in the gas-phase. In order to simplify the equations, the air hold-up is assumed to be constant and uniform. To eliminate the air hold-up from the equations we define the volumetric mass transfer coefficient relative to culture volume. Finally, we assume that the dispersion coefficients for the limiting nutrient and for the biomass are the same.

3.2) CONSERVATION EQUATIONS.

In this work a vertical tubular reactor in which turbulent flow occurs and in which a nutrient-inhibited fermentation process takes place will be analyzed. In such a reactor the air or other gas is introduced through holes or

nozzles in a perforated plate or pipe, while the nutrients or the culture itself are introduced either from the bottom concurrently or from the top countercurrently. The fermentation process, in which the raw material is converted into desirable products, occurs along the length of the tube.

For mathematical simplicity, the reactor is assumed to be operating under isothermal conditions, with constant air hold-up, and with axial dispersion superimposed on a flat profile. Under these circumstances, when radial dispersion can be neglected in comparison with axial dispersion, the material balance equations for a gaseous limiting nutrient are (see Appendix A)

$$\frac{\partial m}{\partial t} + V \frac{\partial m}{\partial \ell} = D \frac{\partial^2 m}{\partial \ell^2} + \frac{\mu^* \, s \, m}{K_s + s + s^2/K_i} \qquad (3.2.1)$$

$$\frac{\partial s}{\partial t} + V \frac{\partial s}{\partial \ell} = D \frac{\partial^2 s}{\partial \ell^2} + K_L \, a(s^*-s) - \frac{1}{Y} \frac{\mu^* \, s \, m}{K_s+s+s^2/K_i} \qquad (3.2.2)$$

where the symbols have their usual significance (see Nomenclature).

3.3) BOUNDARY AND INITIAL CONDITIONS.

Following the pioneer work of LANGMUIR [48] and DANCKWERTS [49] the consensus is that appropriate boundary conditions for this mathematical model are

$$\ell = 0;\ t > 0 \Longrightarrow \begin{cases} V(m-m_o) = D \dfrac{\partial m}{\partial \ell} \\ \\ V(s-s_o) = D \dfrac{\partial m}{\partial \ell} \end{cases} \qquad (3.3.1)$$

$$\ell = L;\ t > 0 \Longrightarrow \begin{cases} \dfrac{\partial m}{\partial \ell} = 0 \\ \dfrac{\partial s}{\partial \ell} = 0 \end{cases} \qquad (3.3.2)$$

In order that this mathematical problem becomes a completely defined problem, we must specify in addition initial conditions. The appropriate initial conditions appear to be

$$t = 0;\ \ell \in (0,L) \Rightarrow \begin{cases} m = m_i \\ s = s_i \end{cases} \qquad (3.3.3)$$

where $(0,L)$ is the open set $0 < x < L$.

3.4) DIMENSIONLESS MATHEMATICAL PROBLEM.

It is advantageous to render the equations (3.2.1) and (3.2.2) together with conditions (3.3.1)-(3.3.3) dimensionless by introducing the following set of dimensionless variables:

$$u = \frac{m - m_o}{YK_s} \qquad (3.4.1)$$

$$v = \frac{s_o - s}{K_s} \qquad (3.4.2)$$

$$x = \frac{Vt}{L} \qquad (3.4.3)$$

and

$$y = \frac{L-\ell}{L} \qquad (3.4.4)$$

When these dimensionless variables are inserted in equations (3.2.1) and (3.2.2) and in conditions (3.3.1)-(3.3.3) we get

$$\frac{\partial u}{\partial x} = \frac{1}{Bo}\frac{\partial^2 u}{\partial y^2} + \frac{\partial u}{\partial y} + Fe\,\frac{(u_o+u)(v_o-v)}{1+(v_o-v)+In(v_o-v)^2} \qquad (3.4.5)$$

$$\frac{\partial v}{\partial x} = \frac{1}{Bo}\frac{\partial^2 v}{\partial y^2} + \frac{\partial v}{\partial y} + Ma(v^*-v) + Fe\,\frac{(u_o+u)(v_o-v)}{1+(v_o-v)+In(v_o-v)^2} \qquad (3.4.6)$$

together with conditions

$$y = 0\ ;\ x > 0 \qquad \frac{\partial u}{\partial y} = \frac{\partial v}{\partial y} = 0 \qquad (3.4.7)$$

$$y = 1\ ;\ x > 0 \qquad u + \frac{1}{Bo}\frac{\partial u}{\partial y} = v + \frac{1}{Bo}\frac{\partial v}{\partial y} = 0 \qquad (3.4.8)$$

$$x = 0\ ;\ y \in (0,1) \qquad u = u_i\ ;\ v = v_i. \qquad (3.4.9)$$

It becomes evident that there are nine parameters. The first

$$Bo = \frac{LV}{D} \tag{3.4.10}$$

is the BODENSTEIN NUMBER: it defines the intensity of the mixing process that occurs within the reactor. The second parameter

$$Fe = \frac{\mu^* L}{V} \tag{3.4.11}$$

which we will call the FERMENTATION NUMBER, is the ratio between the characteristic time of the reactor[+], L/V, and the characteristic time of the fermentation process, $1/\mu^*$. The third parameter

$$Ma = \frac{K_L\, a\, L}{V} \tag{3.4.12}$$

is the MASS TRANSFER NUMBER. It is the ratio between the characteristic time of the reactor, L/V, and the characteristic time of the mass transfer process. If we compare the interpretation of Ma and Fe we perceive that they are similar. The parameter

$$In = \frac{K_s}{K_i} \tag{3.4.13}$$

is the INHIBITION NUMBER*. Its domain is

$$0 \leq In < 1 \tag{3.4.14}$$

as $K_s < K_i$. The nutrient inhibition increases as In increases.

The parameters u_o and v_o must not be confused with the values of the variables u and v at the inlet. Their definitions are

---

[+]The characteristic time of the reactor is sometimes called the residence time. Biochemical engineers know the inverse of the characteristic time of the reactor as the dilution rate.

*The inverse of the Inhibition Number is known to Biochemists as The Relative Inhibition Constant [18].

$$u_o = \frac{m_o}{YK_s} \qquad (3.4.15)$$

and

$$\dot{v_o} = \frac{s_o}{K_s} . \qquad (3.4.16)$$

Finally u_i, v_i and v^* are, respectively, the initial value of u, the initial value of v and the value of v at the gas/culture interface.

3.5) STEADY STATE CONSERVATION EQUATIONS.

The steady state equations are obtained by setting the time derivative equal to zero

$$\frac{1}{Bo}\frac{d^2u_s}{dy^2} + \frac{du_s}{dy} + Fe\,\frac{(u_o+u_s)(v_o-v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} = 0 \qquad (3.5.1)$$

$$\frac{1}{Bo}\frac{d^2v_s}{dy^2} + \frac{dv_s}{dy} + Ma(v^*-v) + Fe\,\frac{(u_o+u_s)(v_o+v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} = 0 \qquad (3.5.2)$$

together with conditions

$$y = 0 \Longrightarrow \begin{cases} \frac{du_s}{dy} = 0 \\ \frac{dv_s}{dy} = 0 \end{cases} \qquad (3.5.3)$$

$$y = 1 \Longrightarrow \begin{cases} u_s + \frac{1}{Bo}\frac{du_s}{dy} = 0 \\ v_s + \frac{1}{Bo}\frac{dv_s}{dy} = 0 \end{cases} \qquad (3.5.4)$$

where the subscript s refers to the steady state.

For a non-gaseous substrate (Ma = 0) it is possible to reduce the boundary problem (3.5.1)-(3.5.4) to a homogeneous problem. Introducing the variable

$$w_s = u_s - v_s \tag{3.5.5}$$

we obtain

$$\frac{1}{Bo}\frac{d^2w_s}{dy^2} + \frac{dw_s}{dy} = 0 \tag{3.5.6}$$

$$y = 0 \Rightarrow \frac{dw_s}{dy} = 0 \tag{3.5.7}$$

$$y = 1 \Rightarrow w_s + \frac{1}{Bo}\frac{dw_s}{dy} = 0 \tag{3.5.8}$$

The only possible solution of the problem (3.5.6)-(3.5.8) is the fermentation invariant

$$w_s = 0 \tag{3.5.9}$$

or

$$u_s = v_s \tag{3.5.10}$$

Consequently, for a non-gaseous substrate equations (3.5.1)-(3.5.4) become

$$\frac{1}{Bo}\frac{d^2u_s}{dy^2} + \frac{du_s}{dy} + Fe\,\frac{(u_o+u_s)(v_o-u_s)}{1+(v_o-u_s)+In(v_o-u_s)^2} = 0 \tag{3.5.11}$$

$$y = 0 \Rightarrow \frac{du_s}{dy} = 0 \tag{3.5.12}$$

$$y = 1 \Rightarrow u_s + \frac{1}{Bo}\frac{du_s}{dy} = 0. \tag{3.5.13}$$

3.6) SUMMARY.

In this chapter we have presented the balance equations together with appropriate boundary and initial conditions which constitute the model of dispersed plug-flow reactor in which a nutrient-inhibited fermentation process occurs. Suitable dimensionless variables and parameters were introduced into the equations in order to obtain a dimensionless mathematical problem. Finally, suitable steady-state equations for gaseous and non-gaseous limiting substrate have been obtained.

Mathematically, the problem to be studied for

unsteady-state conditions is a system of non-linear parabolic partial differential equations and for the steady-state conditions a system of non-linear second order ordinary differential equations. For a non-gaseous limiting substrate under steady-state conditions the system of ordinary differential equations can be reduced to only one equation subjected to appropriate boundary conditions.

The equations presented in this chapter will be extensively used in the following chapter.

4.1) INTRODUCTION.

In this chapter the problem formulated in the last chapter will be analyzed qualitatively. In order to do this an analytical but approximate method described by HLAVACEK and HOFMANN [67] will be used. This method which reduces the system of non-linear parabolic partial differential equations to a system of first order non-linear ordinary differential equations enables us to obtain "first approximation" estimates of the bounds of the multiplicity domains. These estimates are not exact in the sense that we never known whether they will lie above or below the exact values: but very often, especially in the analysis of fermentation processes, the coefficients in the governing equations are not known precisely enough to justify an exact approach. Finally, it is worth remembering that an exact analysis without the use of "first approximation" estimates is an excellent method of wasting computer time. From the above considerations it is evident that a qualitative investigation is an important step in the overall analysis.

Before starting the analysis it is necessary to point out that the method chosen enables us to take advantage of Liapunov's First Method to draw a number of useful conslusions.

To finish this section we should like to point out that the method used in this chapter was first given by FRANK-KAMENETSKII [71]. The application to general parabolic partial differential equations with a non-linear source term is shown in the paper by HLAVACEK and KUBICEK [55].

4.2) LUMPED APPROACH.

In this section we will follow closely HLAVACEK and HOFMANN [67]. The simplest linear form of equation (4.3.5) or (4.3.6) occurs for Ma and Fe equal to zero. It is

$$\frac{\partial \phi}{\partial x} = \frac{1}{Bo} \frac{\partial^2 \phi}{\partial y^2} + \frac{\partial \phi}{\partial y} \qquad (4.2.1)$$

together with the boundary conditions

$$y = 0 \qquad \frac{\partial \phi}{\partial y} = 0 \tag{4.2.2}$$

$$y = 1 \qquad \phi + \frac{1}{Bo} \frac{\partial \phi}{\partial y} = 0 \tag{4.2.3}$$

and the initial condition

$$x = 0 \; ; \; y \in (0,1) \qquad \phi = \phi_i \tag{4.2.4}$$

The solution of this problem is [67]

$$\phi = \sum_{m=1}^{\infty} F(\lambda_n, Bo, y, \phi_i) \exp\left[- \left(\frac{\lambda_n^2}{Bo} + \frac{Bo}{4} \right) x \right] \tag{4.2.5}$$

where

$$\tan \lambda_n = \frac{\lambda_n \, Bo}{\lambda_n^2 - \frac{Bo^2}{4}} \, . \tag{4.2.6}$$

After a short initial period the first term corresponding to the lowest eigenvalue, λ_1, will dominate the series; consequently

$$\phi \simeq F(\lambda_1, Bo, y, \phi_i) \exp \left[- \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) x \right] . \tag{4.2.7}$$

Differentiation of equation (4.2.7) with respect to x leads to

$$\frac{\partial \phi}{\partial x} \simeq - \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) \phi \tag{4.2.8}$$

and a comparison of equation (4.2.8) and (4.2.1) yields

$$\frac{1}{Bo} \frac{\partial^2 \phi}{\partial y^2} + \frac{\partial \phi}{\partial y} \simeq - \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) \phi \, . \tag{4.2.9}$$

Introducing (4.2.9) into the system of equations (4.3.5)-(4.3.6) results in

$$\frac{du}{dx} = - \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) u + Fe \; \frac{(u_o+u)(v_o-v)}{1+(v_o-v)+In(v_o-v)^2} \tag{4.2.10}$$

$$\frac{dv}{dx} = - \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) v + Ma(v^*-v) + Fe \; \frac{(u_o+u)(v_o-v)}{1+(v_o-v)+In(v_o-v)^2} \tag{4.2.11}$$

together with the initial condition

$$x = 0 \Longrightarrow u = u_i \; ; \; v = v_i \, . \tag{4.2.12}$$

The above derivation, as pointed out by ARIS [72], is notable for its complete abandonment of rigour.

Since

$$\lim_{Bo \to 0} \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4} \right) = 1 \qquad (4.2.13)$$

the lumped approach provides a mathematical relationship between the stirred tank reactor and the tubular reactor.

The steady state equations are obtained by setting the time derivative equal to zero, so

$$u_s = Fe^* \frac{(u_o+u_s)(v_o-v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} \qquad (4.2.14)$$

$$v_s = Fe^* \frac{(u_o+u_s)(v_o-v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} + Ma^*(v^*-v_s) \qquad (4.2.15)$$

where

$$Fe^* = \frac{Fe}{\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}} \qquad (4.2.16)$$

and

$$Ma^* = \frac{Ma}{\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}} \qquad (4.2.17)$$

are the Modified Fermentation Number and the Modified Mass Transfer Number, respectively. It is easy to show that

$$\lim_{Bo \to 0} \frac{Fe}{Fe^*} = \lim_{Bo \to 0} \frac{Ma}{Ma^*} = \lim_{Bo \to 0} \psi = 1 \qquad (4.2.18)$$

Table (4.1.1) was obtained using the values of λ_1 calculated by HLAVACEK and HOFMANN [67]. It shows that

$$Fe \geq Fe^* \qquad (4.2.19)$$

and

$$Ma \geq Ma^* \qquad (4.2.20)$$

and that the ratio Fe/Fe* or Ma/Ma* increases as Bo increases. If the characteristic time of the fermentation process, $1/\mu^*$, and the characteristic time of the mass transfer process, $1/K_La$, are considered to be independent of the mixing process, one must

TABLE (4.4.1)

Bo	$\psi = \frac{Fe}{Fe^*} = \frac{Ma}{Ma^*}$
0.01	1.0025
0.05	1.0080
0.10	1.0166
1.00	1.1720
2.00	1.3534
3.00	1.5433
5.00	1.9430
10.00	3.0219
50.00	12.669

Modifying factors for several values of Bo.

conclude that the characteristic time of the chemical reactor increases as Bo increases.

4.3) CALCULATION OF THE STEADY-STATE SOLUTIONS.

Let us consider the steady-state equations (4.2.14) and (4.2.15). A simple relationship between the dimensionless microbial concentration and the dimensionless substrate concentration is obtained by subtracting equation (4.2.14) from equation (4.2.15): this leads to

$$v_s = \frac{u_s + Ma^* v^*}{1+Ma^*} \tag{4.3.1}$$

This relation is not valid for unsteady-state conditions. Combining equation (4.3.1) and equation (4.2.14) it is possible to obtain a single equation for the dimensionless microbial concentration which can be written as

$$u_s = Fe^* \frac{(u_o+u_s)[v_o(Ma^*+1)-Ma^* v^*-u_s]}{(Ma^*+1)+[v_o(Ma^*+1)-Ma^* v^*-u_s]+\frac{In}{Ma^*+1}[v_o(Ma^*+1)-Ma^* v^*-u_s]^2} \tag{4.3.2}$$

It is advantageous to start the calculation of the steady-state by considering non-inhibitory fermentation processes under sterile feed conditions. Under these circumstances $u_o = 0$ and $In = 0$ and equation (4.3.2) becomes

$$u_s = Fe^* \frac{u_s[v_o(Ma^*+1)-Ma^* v^*-u_s]}{(Ma^*+1)+[v_o(Ma^*+1)-Ma^* v^*-u_s]} \tag{4.3.3}$$

It is easy to see that

$$u_{s_1} = 0 \tag{4.3.4}$$

is a possible steady-state. The other possible steady-state is

$$u_{s_2} = [v_o(Ma^*+1)-Ma^* v^*] - \frac{Ma^*+1}{Fe^*-1} \tag{4.3.5}$$

Since u_s can never fall below zero, we have

$$Fe^* > \frac{(v_o+1)(Ma^*+1)-Ma^* v^*}{v_o(Ma^*+1) - Ma^* v^*} . \tag{4.3.6}$$

Consequently, in the domain

$$0 < Fe^* \leqslant \frac{(v_o+1)(Ma^*+1)-Ma^*v^*}{v_o(Ma^*+1) - Ma^*v^*} \qquad (4.3.7)$$

the sterile steady-state is the only possible steady-state. On the other hand, in the domain

$$\frac{(v_o+1)(Ma^*+1)-Ma^*v^*}{v_o(Ma^*+1) - Ma^*v^*} < Fe^* < \infty \qquad (4.3.8)$$

both the sterile and the non sterile steady-states are possible.

For non-inhibitory fermentation processes under non-sterile feed conditions equation (4.3.2) becomes

$$u_s = Fe^* \frac{(u_o+u_s)[v_o(Ma^*+1)-Ma^*v^*-u_s]}{(Ma^*+1)+ [v_o(Ma^*+1)-Ma^*v^*-u_s]} . \qquad (4.3.9)$$

Firstly, we will study the existence and uniqueness of solutions in the domain

$$0 \leqslant u_s \leqslant v_o(Ma^*+1) - Ma^*v^*. \qquad (4.3.10)$$

A strong uniqueness condition independent of Fe^* is obtained by writing the above equation as

$$Fe^* = \frac{u_s\{(Ma^*+1)+[v_o(Ma^*+1)-Ma^*v^*-u_s]\}}{(u_o+u_s)[v_o(Ma^*+1)-Ma^*v^* - u_s]} . \qquad (4.3.11)$$

The right-hand side of equation (4.3.11) varies from zero, as $u_s \to 0$, to infinity, as $u_s \to v_o(Ma^*+1)-Ma^*v^*$; this ensures the existence of solutions in the domain (4.3.10) for all values of Fe^*. If the right-hand side of equation (4.3.11) is monotomically increasing in that domain there is only one value of u_s for which the left-hand side is equal to Fe^*. Consequently a necessary and sufficient condition for uniqueness is [73]

$$\frac{d}{du_s}\left\{\frac{u_s\{(Ma^*+1)+[v_o(Ma^*+1)-Ma^*v^*-u_s]\}}{(u_o+u_s)[v_o(Ma^*+1)-Ma^*v^*- u_s]}\right\} \geqslant 0 \qquad (4.3.12)$$

An algebraic manipulation shows that condition (4.3.12) is satisfied when

$$u_o^2(1+Ma^*)[v_o(1+Ma^*)-Ma^*v^*] > 0. \qquad (4.3.13)$$

Since $u_o > 0$, $1+Ma^* > 0$ and

$$v_o(1+Ma^*) - Ma^*v^* > 0 \qquad (4.3.14)$$

we conclude that the uniqueness condition is satisfied for all possible values of u_o, v_o, v^* and Ma^*. Consequently, equation (4.3.11) has only one solution in the domain (4.3.10).

For an inhibitory fermentation process under sterile feed conditions equation (4.3.2) becomes

$$u_s = \frac{Fe^*u_s[v_o(Ma^*+1)-Ma^*v^*-u_s]}{(Ma^*+1)+[v_o(Ma^*+1)-Ma^*v^*-u_s] + \frac{In}{Ma^*+1}[v_o(Ma^*+1)-Ma^*v^*-u_s]^2} \qquad (4.3.15)$$

This equation admits only one solution in the domain

$$0 < Fe^* < 2|\sqrt{In}| + 1; \qquad (4.3.16)$$

this solution is the sterile solution

$$u_{s_1} = 0. \qquad (4.3.17)$$

For

$$Fe^* = 2|\sqrt{In}| + 1 \qquad (4.3.18)$$

there are two solutions:

$$u_{s_1} = 0 \qquad (4.3.19)$$

and

$$u_{s_2} = v_o(Ma^*+1)-Ma^*v^* - \frac{(Ma^*+1)}{|\sqrt{In}|}. \qquad (4.3.20)$$

In the domain

$$2|\sqrt{In}|+1 < Fe^* < \frac{(1+Ma^*)+[v_o(Ma^*+1)-Ma^*v^*] + \frac{In}{Ma^*+1}[v_o(Ma^*+1)-Ma^*v^*]^2}{[v_o(Ma^*+1)-Ma^*v^*]} \qquad (4.3.21)$$

three solutions are admissible:

$$u_{s_1} = 0 \qquad (4.3.22)$$

$$u_{s_2} = [v_o(Ma^*+1)-Ma^*v^*]-(Ma^*+1)\left\{\frac{(Fe^*-1)+|\sqrt{(Fe^*-1)^2-4In}|}{2In}\right\} \qquad (4.3.23)$$

$$u_{s_3} = [v_o(Ma^*+1)-Ma^*v^*]-(Ma+1)\left\{\frac{Fe^*-1)-|\sqrt{(Fe^*-1)^2-4In}|}{2In}\right\} \qquad (4.3.24)$$

Finally, in the domain

$$\frac{(1+Ma^*)+[v_o(Ma^*+1)-Ma^*v^*] + \frac{In}{Ma^*+1}[v_o(Ma^*+1)-Ma^*v^*]^2}{[v_o(Ma^*+1)-Ma^*v^*]} < Fe^* < \infty \qquad (4.3.25)$$

both

$$u_{s_1} = 0 \qquad (4.3.26)$$

and

$$u_{s_2} = [v_o(Ma^*+1)-Ma^*v^*] - (Ma^*+1)\left\{\frac{(Fe^*-1)-\sqrt{(Fe^*-1)^2-4In}}{2In}\right\} \qquad (4.3.27)$$

are possible solutions.

For inhibitory fermentation processes under non-sterile feed conditions the algebraic manipulation becomes cumbersome and, consequently, the old-fashioned graphical method of analysis will be used. The stability analysis for a non-gaseous limiting substrate may be found in section (4.5).

4.4) STABILITY ANALYSIS.

It was shown by LIAPUNOV [74] that the stability of a steady-state could be studied by considering the linear approximation of the equation describing small departures from the steady-state. This mathematical tool is described in APPENDIX B.

Let us start the analysis of the steady-state by considering a non-inhibitory fermentation process under sterile feed conditions. As we have shown in the last section the possible steady-states are

$$u_{s_1} = 0 \qquad (4.3.4)$$

for

$$0 < Fe^* < \infty \,, \qquad (4.4.1)$$

and

$$u_{s_2} = [v_o(Ma^*+1)-Ma^*v^*] - \frac{Ma^*+1}{Fe^*-1} \qquad (4.3.5)$$

for

$$\frac{(v_o+1)(Ma^*+1)-Ma^*v^*}{v_o(Ma^*+1)-Ma^*v^*} < Fe^* < \infty \qquad (4.3.8)$$

The corresponding dimensionless limiting substrate concentrations are

$$v_{s_1} = \frac{Ma^*v^*}{1+Ma^*} \qquad (4.4.2)$$

and

$$v_{s_2} = v_o - \frac{1}{Fe^*-1} \,. \qquad (4.4.3)$$

For the sterile steady-state we have, as shown in Appendix B

$$\underset{\sim}{A} = \begin{bmatrix} -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) + Fe\,\frac{(v_o-v_s)}{1+(v_o-v_s)} & 0 \\ Fe\,\frac{(v_o-v_s)}{1+(v_o-v_s)} & -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right)-Ma \end{bmatrix} \qquad (4.4.4)$$

or after introducing equation (4.4.2)

$$\underset{\sim}{A} = \begin{bmatrix} -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) + Fe\,\frac{[v_o(Ma^*+1)-Ma^*v^*]}{(1+Ma^*)+[v_o(Ma^*+1)-Ma^*v^*]} & 0 \\ Fe\,\frac{[v_o(Ma^*+1)-Ma^*v^*]}{(1+Ma^*)+[v_o(Ma^*+1)-Ma^*v^*]} & -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right)-Ma \end{bmatrix} \qquad (4.4.5)$$

and consequently

$$tr\underset{\sim}{A} = -2\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right)-Ma + Fe\,\frac{[v_o(1+Ma^*)-Ma^*v^*]}{(1+Ma^*)+[v_o(1+Ma^*)-Ma^*v^*]} \qquad (4.4.6)$$

and

$$det\underset{\sim}{A} = -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}+Ma\right)\left[Fe\,\frac{[v_o(1+Ma^*)-Ma^*v^*]}{(1+Ma^*)+[v_o(1+Ma^*)-Ma^*v^*]} - \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right)\right] \qquad (4.4.7)$$

So, the sterile steady-state will be asymptotically stable, i.e.,

$$tr\underset{\sim}{A} < 0 \qquad (B-9)$$

and

$$det\underset{\sim}{A} > 0 \qquad (B.10)$$

if

$$0 < Fe^* < \frac{(1+Ma^*)+[v_o(1+Ma^*)-Ma^*v^*]}{[v_o(1+Ma^*)-Ma^*v^*]} \,, \qquad (4.4.8)$$

and unstable, if

$$\frac{(1+Ma^*)+[v_o(1+Ma^*)-Ma^*v^*]}{[v_o(1+Ma^*)-Ma^*v^*]} \leq Fe^* < \infty. \qquad (4.4.9)$$

For the non-sterile steady-state we have

$$\underset{\sim}{A} = \begin{bmatrix} -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) + Fe\,\frac{(v_o - v_s)}{1+(v_o-v_s)} & -Fe\,\frac{u_s}{[1+(v_o-v_s)]^2} \\ Fe\,\frac{(v_o-v_s)}{1+(v_o-v_s)} & -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) - Ma - Fe\,\frac{u_s}{[1+(v_o-v_s)]^2} \end{bmatrix} \qquad (4.4.10)$$

or

$$\underset{\sim}{A} = \begin{bmatrix} 0 & \cdots \\ \left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) & \cdots \end{bmatrix}$$

$$\begin{bmatrix} \cdots\ Fe\,\dfrac{\{[v_o(1+Ma^*)-Ma^*v^*](Fe^*-1)-(1+Ma^*)\}(Fe^*-1)}{(Fe^*)^2} \\ \cdots -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) - Ma + Fe\,\dfrac{\{[v_o(1+Ma^*)-Ma^*v^*](Fe^*-1)-(1+Ma^*)\}(Fe^*-1)}{(Fe^*)^2} \end{bmatrix} \qquad (4.4.11)$$

From (4.4.11)

$$tr\underset{\sim}{A} = -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right) - Ma + Fe\,\frac{\{[v_o(1+Ma^*)-Ma^*v^*](Fe^*-1)-(1+Ma^*)\}(Fe^*-1)}{(Fe^*)^2} \qquad (4.4.12)$$

and

$$\det\underset{\sim}{A} = -\left(\frac{\lambda_1^2}{Bo} + \frac{Bo}{4}\right)\frac{Fe\{[v_o(1+Ma^*)-Ma^*v^*](Fe^*-1)-(1+Ma^*)](Fe^*-1)}{(Fe^*)^2} \qquad (4.4.13)$$

consequently the condition

$$tr\underset{\sim}{A} < 0 \qquad (B-9)$$

and

$$\det\underset{\sim}{A} > 0 \qquad (B-10)$$

imply that

$$\frac{(v_o+1)(Ma^*+1)-Ma^*v^*}{v_o(Ma^*+1)-Ma^*v^*} < Fe^* < \infty \qquad (4.4.14)$$

Thus, we see that the sterile steady-state is stable in the domain (4.4.8) and the non-sterile steady-state in the domain (4.4.9), in which the sterile steady-state is unstable.

For an inhibitory fermentation process under sterile feed conditions we have

$$\underset{\sim}{A} = \left[\begin{array}{ll} -\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right) - Fe\,\frac{(v_o-v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} & \cdots \\ Fe\,\frac{(v_o-v_s)}{1+(v_o-v_s)+In(v_o-v_s)^2} & \cdots \end{array}\right.$$

$$\left.\begin{array}{ll} \cdots -Fe\,\frac{u_s\{1-In(v_o-v_s)^2\}}{[1+(v_o-v_s)+In(v_o-v_s)^2]^2} & \\ \cdots \quad -\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right) - Ma - Fe\,\frac{u_s[1-In(v_o-v_s)^2]}{[1+(v_o-v_s)+In(v_o-v_s)^2]^2} & \end{array}\right]. \qquad (4.4.15)$$

Considering the sterile steady-state we have

$$u_{s_1} = 0 \qquad (4.3.22)$$

and

$$v_{s_1} = \frac{Ma^*v^*}{1+Ma^*}\ ; \qquad (4.4.16)$$

so

$$A = \left[\begin{array}{ll} -\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right) + Fe\,\frac{[v_o(Ma^*+1)-Ma^*v^*]}{1+[v_o(Ma^*+1)-Ma^*v^*]+} & \\ Fe\,\frac{[v_o(Ma^*+1)-Ma^*v^*]}{1+[v_o(Ma^*+1)-Ma^*v^*]+\frac{In}{1+Ma^*}[v_o(Ma^*+1)-Ma^*v^*]^2} & \end{array}\right.$$

$$\left.\begin{array}{ll} \frac{In}{1+Ma^*}[v_o(Ma^*+1)-Ma^*v^*]^2 & 0 \\ \cdots & -\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right) - Ma \end{array}\right] \qquad (4.4.17)$$

Consequently

$$tr\underset{\sim}{A} = -2\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right) - Ma + Fe\,\frac{[v_o(Ma^*+1)-Ma^*v^*]}{1+[v_o(Ma^*+1)-Ma^*v^*]+\frac{In}{Ma^*+1}[v_o(1+Ma^*)-Ma^*v^*]^2} \qquad (4.4.18)$$

and

$$det\underset{\sim}{A} = -\left[\left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right)+Ma\right]\left[Fe\,\frac{[v_o(1+Ma)-Ma^*v^*]}{1+[v_o(1+Ma^*)-Ma^*v^*]+\frac{In}{1+Ma^*}[v_o(1+Ma^*)-Ma^*v^*]^2} - \right.$$

$$\left. - \left(\frac{\lambda_1^2}{Bo}+\frac{Bo}{4}\right)\right] \qquad (4.4.19)$$

consequently, the sterile steady-state will be asymptotically stable if

$$0 < Fe^* < \frac{1+[v_o(1+Ma^*)-Ma^*v^*] + \frac{In}{1+Ma^*}[v_o(1+Ma^*)-Ma^*v^*]^2}{[v_o(1+Ma^*)-Ma^*v^*]} \qquad (4.4.20)$$

For

$$u_{s_2} = [v_o(1+Ma^*)-v^*Ma^*]-(1+Ma^*)\left\{\frac{(Fe^*-1)+|\sqrt{(Fe^*-1)^2-4In}|}{2In}\right\} \qquad (4.3.23)$$

and

$$u_{s_3} = [v_o(1+Ma^*)-Ma^*v^*]-(1+Ma^*)\left\{\frac{(Fe^*-1)-|\sqrt{(Fe^*-1)^2-4In}|}{2In}\right\} \qquad (4.3.24)$$

which implies that

$$v_{s_2} = v_o - \frac{(Fe^*-1)+|\sqrt{(Fe^*-1)^2-4In}|}{2In} \qquad (4.4.21)$$

and

$$v_{s_3} = v_o - \frac{(Fe^*-1)-|\sqrt{(Fe^*-1)^2-4In}|}{2In} \qquad (4.4.22)$$

After introducing (4.4.21) or (4.4.22) into (4.4.15) we get

$$\underset{\sim}{A} = \begin{bmatrix} 0 & \cdots \\ -\left(\frac{\lambda_1}{Bo}^2+\frac{Bo}{4}\right) & \cdots \end{bmatrix}$$

$$\begin{bmatrix} \cdots -\left(\frac{\lambda_1}{Bo}^2+\frac{Bo}{4}\right)\frac{[2-(Fe^*-1)(v_o-v_s)]u_s}{Fe^*(v_o-v_s)^2} \\ \cdots -\left(\frac{\lambda_1}{Bo}^2+\frac{Bo}{4}\right)-Ma^*-\left(\frac{\lambda_1}{Bo}^2+\frac{Bo}{4}\right)\frac{[2-(Fe^*-1)(v_o-v_s)]u_s}{Fe^*(v_o-v_s)^2} \end{bmatrix} \qquad (4.4.23)$$

The conditions

$$\det\underset{\sim}{A} > 0 \qquad (B\text{-}10)$$

and

$$\mathrm{tr}\underset{\sim}{A} < 0 \qquad (B\text{-}9)$$

implies that

$$2 > (Fe^*-1)(v_o-v_s) \qquad (4.4.24)$$

or after assuming Fe* > 1

$$u_s > v_o(1+Ma^*) - Ma^*v^* - \frac{(1+Ma^*)}{|\sqrt{In}|} \qquad (4.4.25)$$

But

$$u_{s_{bif}} = v_o(1+Ma^*) - Ma^*v^* - \frac{(1+Ma^*)}{|\sqrt{In}|} \qquad (4.4.26)$$

is the bifurcation point where the two non-sterile steady-states are generatad. This corresponds to the condition

$$(Fe^*-1)^2 - 4In = 0. \qquad (4.4.27)$$

And so the solution

$$u_{s_2} = [v_o(1+Ma^*) - Ma^*v^*] - (1+Ma^*)\left[\frac{(Fe^*-1)+\sqrt{(Fe^*-1)^2-4In}}{2In}\right] \qquad (4.4.28)$$

does not satisfy the above inequality and consequently, this steady-state is unstable. The solution

$$u_{s_3} = [v_o(1+Ma^*) - Ma^*v^*] - (1+Ma^*)\left[\frac{(Fe^*-1)-\sqrt{(Fe^*-1)^2-4In}}{2In}\right] \qquad (4.4.29)$$

obeys the inequality for all values and so it is stable.

4.5) PHYSICAL INTERPRETATION OF STABILITY FOR A NON-GASEOUS LIMITING SUBSTRATE.

In this section a physical explanation of stability of a fermentation process involving a non-gaseous limiting substrate is obtained by using the old-fashioned graphical method.

Let us consider the non-inhibitory fermentation process under sterile feed conditions. The steady state equation can be written as

$$\frac{u_s}{Fe^*} = \frac{u_s(v_o-u_s)}{1+(v_o-u_s)} \qquad (4.5.1)$$

The left hand side of the above equation can be interpreted as the rate of microbial wash-out and the right hand side as the rate of microbial growth. The rate of microbial wash-out is a linear function of u_s with angular coefficient $1/Fe^*$. For a given

experiment the angular coefficient increases when the culture flow rate increases. In FIGURE (4.5.1) we plot both rates as a function of u_s.

Let us examine the physical meaning of FIGURE (4.5.1). The intersections of the curve OAB and the straight lines OQ or OR are the possible steady-states. The straight line OQ represents the case

$$0 < Fe^* \leq \frac{1+v_o}{v_o} \tag{4.5.2}$$

and the straight line OR represents the case

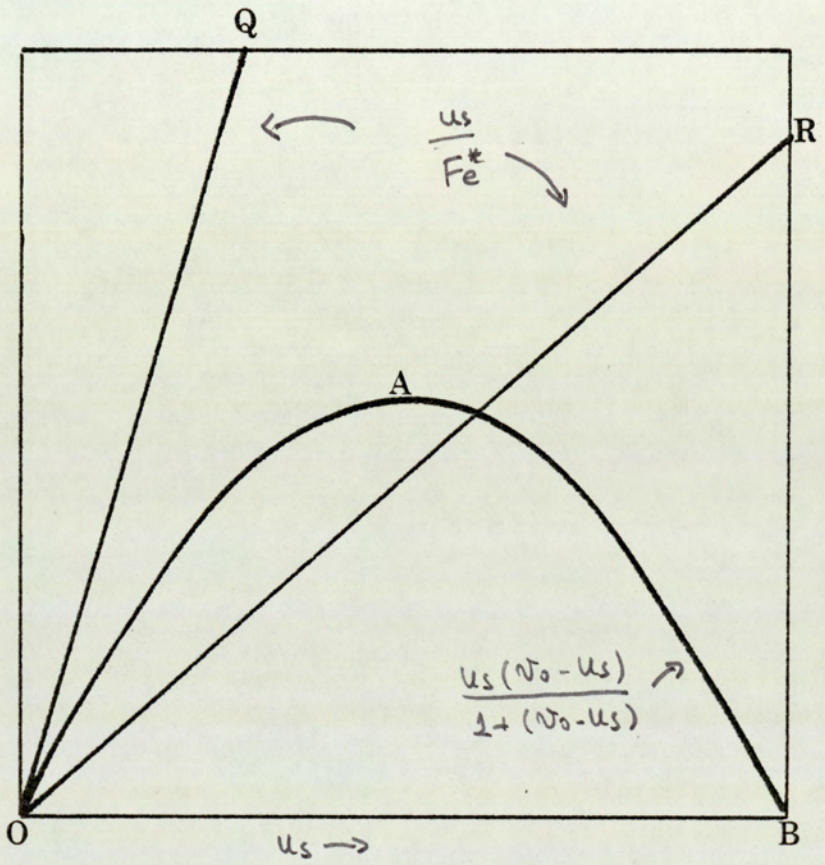
$$Fe^* > \frac{1+v_o}{v_o} \tag{4.5.3}$$

In the first case we have only one intersection at OAB. Consider a small positive variation of u_s while all the other parameters remain constant we perceive the rate of microbial wash-out becomes bigger than the rate of microbial growth. This brings the microbial concentration back to the steady-state, so the steady-state is stable.

In the second case the straight line intersects the curve OAB in two points. Consider the sterile steady-state; we perceive that for a small positive variation of u_s the rate of microbial growth becomes bigger than the rate of microbial wash-out. This brings the microbial concentration away from the steady-state, so it is unstable. For the non-sterile steady-state a small increase of microbial concentration makes the rate of wash-out bigger than the rate of microbial growth. This brings the microbial concentration back to the steady-state. On the other hand, a small decrease of microbial concentration makes the rate of microbial growth bigger than the rate of microbial wash-out, so the non-sterile steady-state is stable to both types of perturbations.

The above analysis gives a physical interpretation for the results we obtained in the previous section for non-inhibitory

F I G U R E (4.5.1)



Graphical analysis of a non-inhibitory fermentation process under sterile feed conditions.

fermentation processes under sterile feed conditions.

For non-inhibitory fermentation processes under non-sterile feed conditions we have

$$\frac{u_s}{Fe^*} = \frac{(u_o+u_s)(v_o-u_s)}{1+(v_o-u_s)} \qquad (4.5.4)$$

The above relationship is plotted in FIGURE (4.5.2). As we can see there is only one steady-state for all possible values of Fe*. This steady-state is stable.

For inhibitory fermentation processes under sterile feed conditions we have

$$\frac{u_s}{Fe^*} = \frac{u_s(v_o-u_s)}{1+(v_o-u_s)+In(v_o-u_s)^2} \qquad (4.5.5)$$

As we can see in FIGURE (4.5.3) there are four possible situations. The first one, represented by the straight line OQ corresponds to

$$0 < Fe^* < 2\sqrt{In} + 1 \qquad (4.5.6)$$

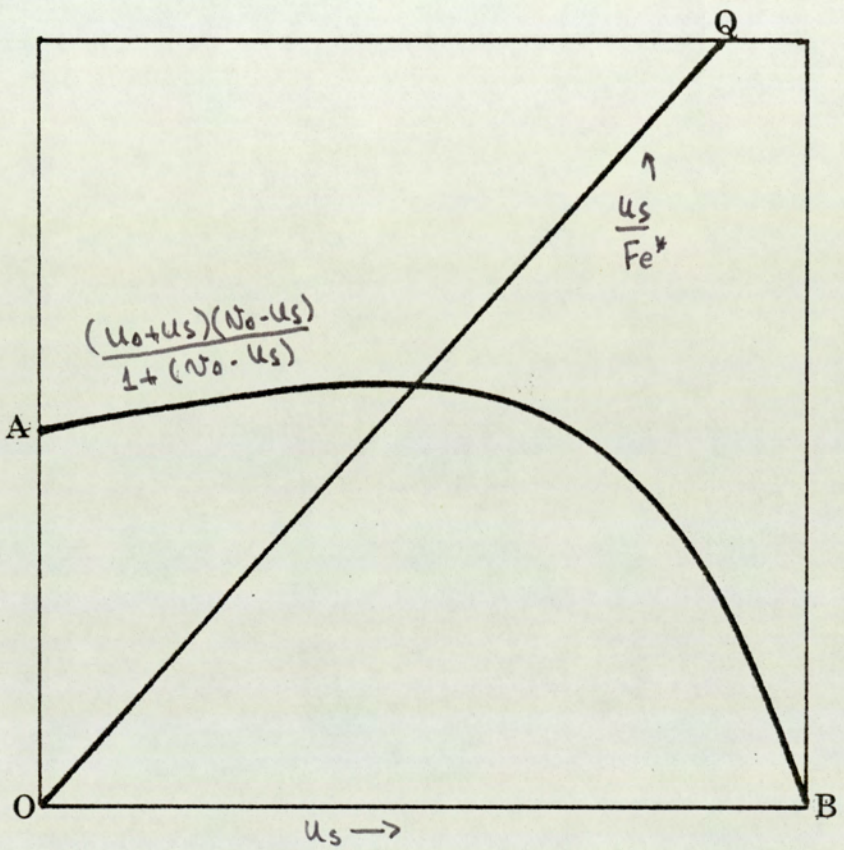
In these circumstances there is only one steady-state the sterile steady-state. The graph shows that it is stable.

The second case which corresponds to

$$Fe^* = 2\sqrt{In} + 1 \qquad (4.5.7)$$

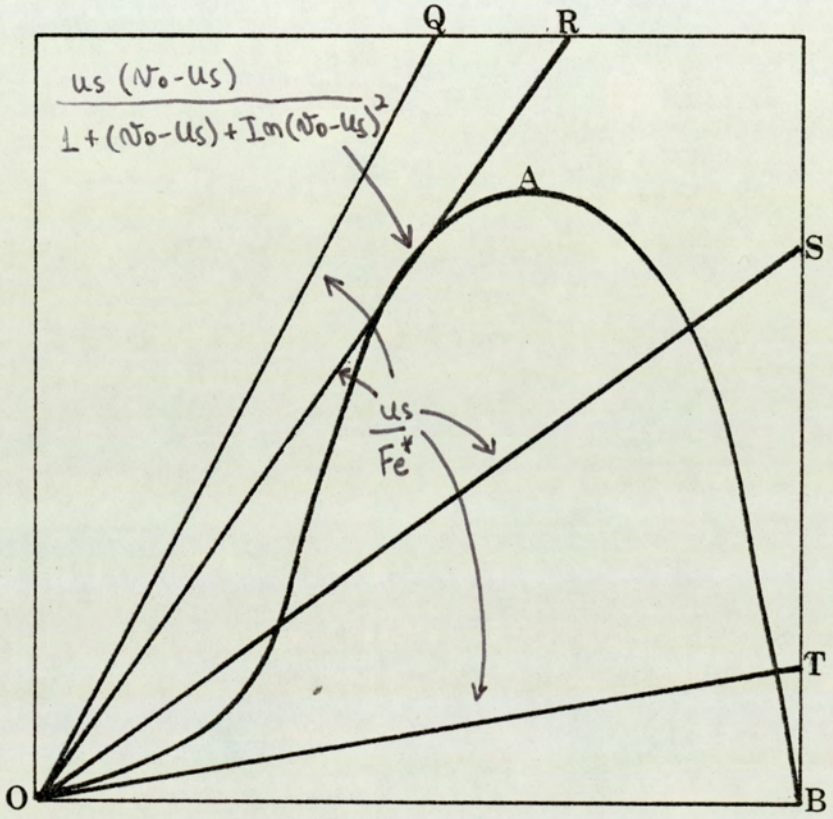
is represented by the line OR. The sterile steady-state is still stable: but the non-sterile steady-state is stable only to positive perturbations and not to negative perturbations and so must be considered unstable. The third case is represented by the line OS. This case admits three steady-states as shown in the graph - one sterile and two non-sterile steady-states. The sterile steady-state is still stable, the middle steady-state is unstable and the other is stable. The middle steady-state may be described as a "growth point" because it represents the minimum initial microbial concentration to avoid wash-out. This case corresponds to the domain

F I G U R E (4.5.2)



Graphical analysis of a non-inhibitory fermentation process under non-sterile feed conditions.

F I G U R E (4.5.3)



Graphical analysis of a inhibitory fermentation process under sterile feed conditions.

$$2\sqrt{In} + 1 < Fe^* < \frac{1 + v_o + In.v_o^2}{v_o} \qquad (4.5.8)$$

Finally we have the case represented by the line OT. In this situation the sterile steady-state becomes unstable and the non-sterile steady-state becomes stable.

4.6) GRAPHICAL ANALYSIS.

The aim of this section is to plot graphically the results obtained in the last three sections in order to facilitate interpretation. To simplify the analysis the dimensionless parameters

$$V_o = \frac{v_o(1+Ma^*)-Ma^*v^*}{1+Ma^*} \qquad (4.6.1)$$

and

$$U_o = \frac{u_o}{1+Ma^*} \qquad (4.6.2)$$

and the dimensionless variable

$$U_s = \frac{u_s}{1 + Ma^*} \qquad (4.6.3)$$

are defined. These symbols were chosen because $V_o = v_o$, $U_o = u_o$ and $U_s = u_s$ when $Ma^* = 0$: this set of equations describes the case of a non-gaseous limiting substrate. - Introducing (4.6.1)-(4.6.3) into (4.3.2) we obtain

$$U_s = Fe^* \frac{(U_o+U_s)(V_o-U_s)}{1 + (V_o-U_s)+I\,(V_o-U_s)^2} \qquad (4.6.4)$$

Before starting the graphical analysis it is useful to give a physical interpretation of the parameters U_o and V_o. U_o is closely related to u_o; $U_o = 0$ corresponds to sterile feed conditions; and $U_o = 0$ to non-sterile feed conditions. The interpretation of V_o is more difficult: this parameter can never be equal to zero because this implies that the limiting substrate is not even fed into the reactor. So

1. for a non gaseous limiting substrate ($Ma^*=0$)

$$V_o = v_o \qquad (4.6.5)$$

2. for a gaseous limiting substrate under saturated feed conditions ($Ma^* \neq 0$)

$$V_o = u_o^* \tag{4.6.6}$$

where

$$v_o = v_o^* = \frac{s^*}{K_s} \tag{4.6.7}$$

3. for a gaseous limiting substrate with no limiting substrate in the feed ($v_o = 0$)

$$V_o = \frac{Ma^* v^*}{1 + Ma^*} \tag{4.6.8}$$

In the interpretation of the graphs it is useful to consider the particular situations listed above. Formulae used in preparing the graphs are tabulated in APPENDIX C.

As in the algebraic analysis we start by considering non-inhibitory fermentation processes under sterile feed conditions. In FIGURE (4.6.1) U_s/V_o is plotted versus Fe^*, the unstable steady-state being represented by a dotted line. In this graph we see that the sterile steady-state ($U_s = 0$) is stable in the domain

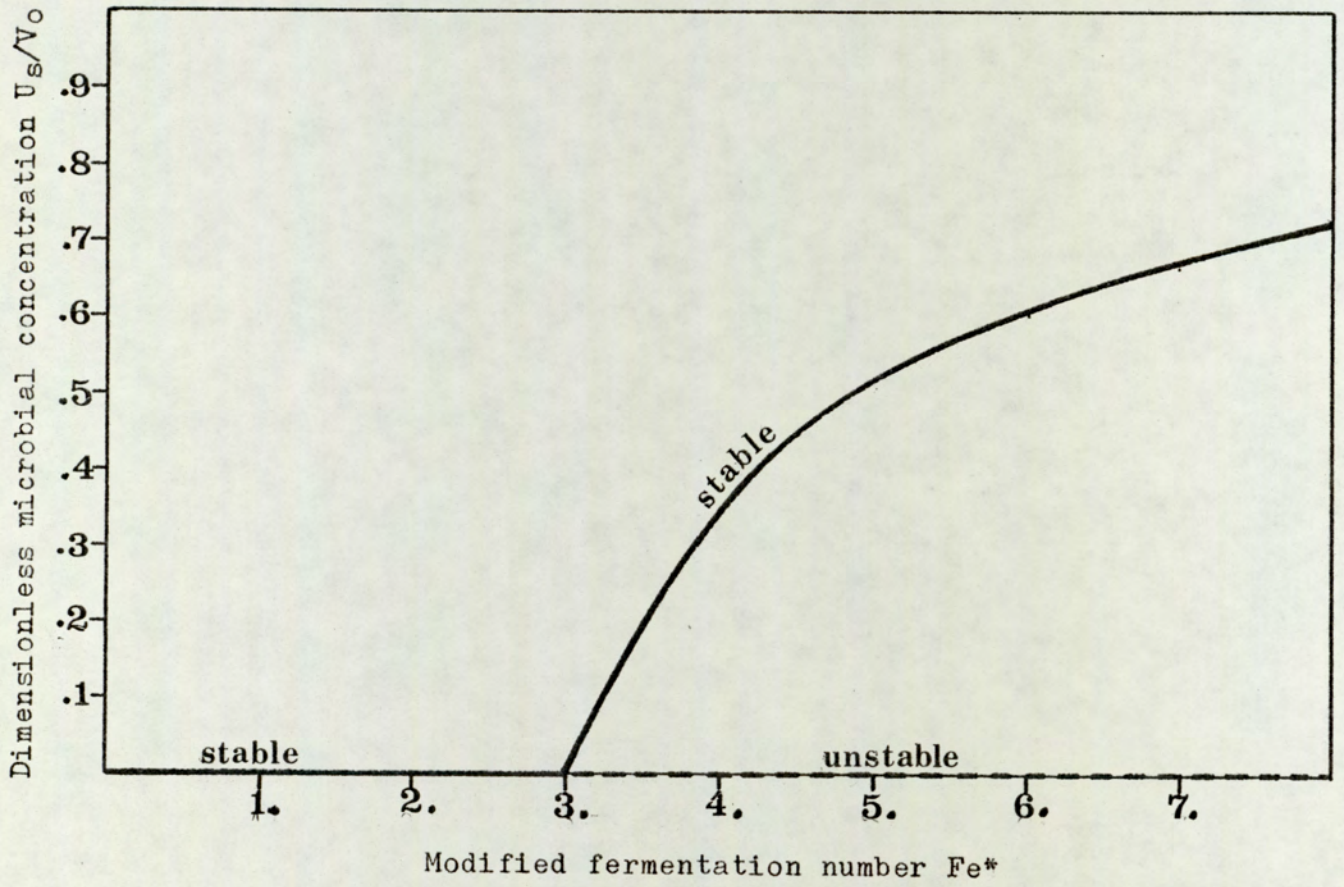
$$0 < Fe^* \leq \frac{1+V_o}{V_o} \tag{4.6.9}$$

and unstable in the domain

$$\frac{1+V_o}{V_o} < Fe^* < \infty \tag{4.6.10}$$

The non-sterile steady-state ($U_s > 0$) does not exist in the domain where the sterile steady-state is stable because in this region U_s/V_o is negative and thus has no physical meaning. But the non-sterile steady-state is stable in the domain where the sterile steady-state is unstable. Put in another way, in the domain

F I G U R E (4.6.1)



Non-inhibitory fermentation process under sterile feed conditions.
Stability for the case where $V_o = 0.5$.

$$0 < Fe^* \leq \frac{1+V_o}{V_o} \qquad (4.6.11)$$

the phenomena known by biochemical engineers as wash-out occurs: and so in practice for the reactor to work at all the condition

$$Fe^* > \frac{1+V_o}{V_o} \qquad (4.6.12)$$

must be obeyed. FIGURE (4.6.2) shows the non-sterile steady-state for several values of V_o. In FIGURE (4.6.3) we have plotted U_s/V_o versus Fe for a non gaseous limiting substrate to show the influence of Bo.

FIGURE (4.6.4) shows the only possible solution for a non-inhibitory fermentation process under non-sterile feed conditions. This solution is stable for all values of Fe*. FIGURE (4.6.5) shows the influence of U_o on the solution. It is easy to perceive that it approaches asymptotically the situation shown in FIGURE (4.6.1) as $U_o \to 0$. For high values of U_o the curve goes rapidly to the vicinity of $U_s/V_o = 1.0$. FIGURE (4.6.6) shows U_s/V_o plotted against Fe for several values of Bo.

For inhibitory fermentation processes under sterile feed conditions the situation illustrated in FIGURE (4.6.7) is obtained. In the domain

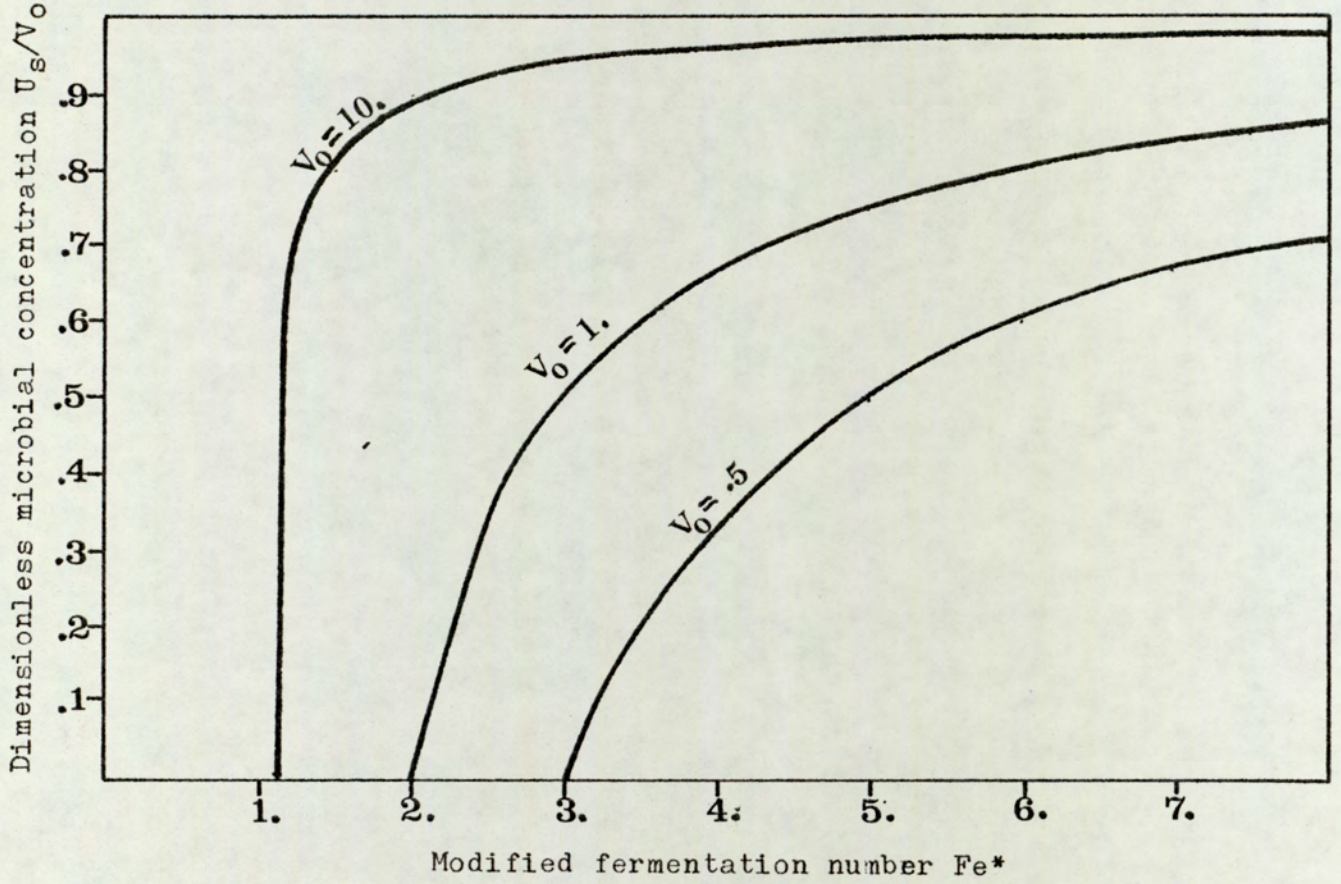
$$0 < Fe^* \leq 2|\sqrt{In}| + 1 \qquad (4.6.13)$$

only the sterile steady-state is stable: this corresponds to the so-called wash-out condition. In the domain

$$\frac{1+V_o+In\ V_o^2}{V_o} < Fe^* < \infty \qquad (4.6.14)$$

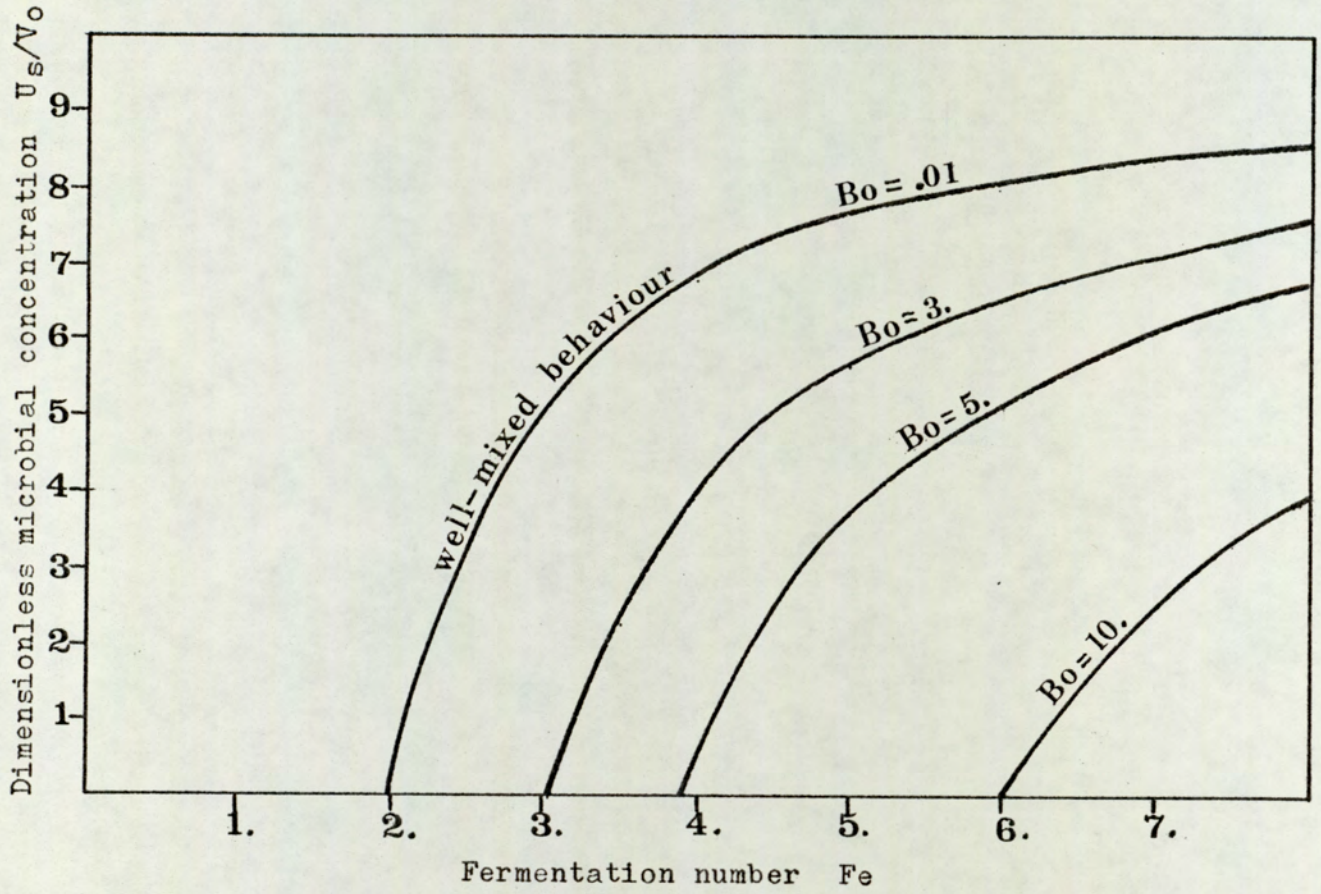
there are two solutions: the sterile steady-state which is unstable (dotted line) and a non-sterile steady-state which is stable. Finally in the domain

F I G U R E (4.6.2)



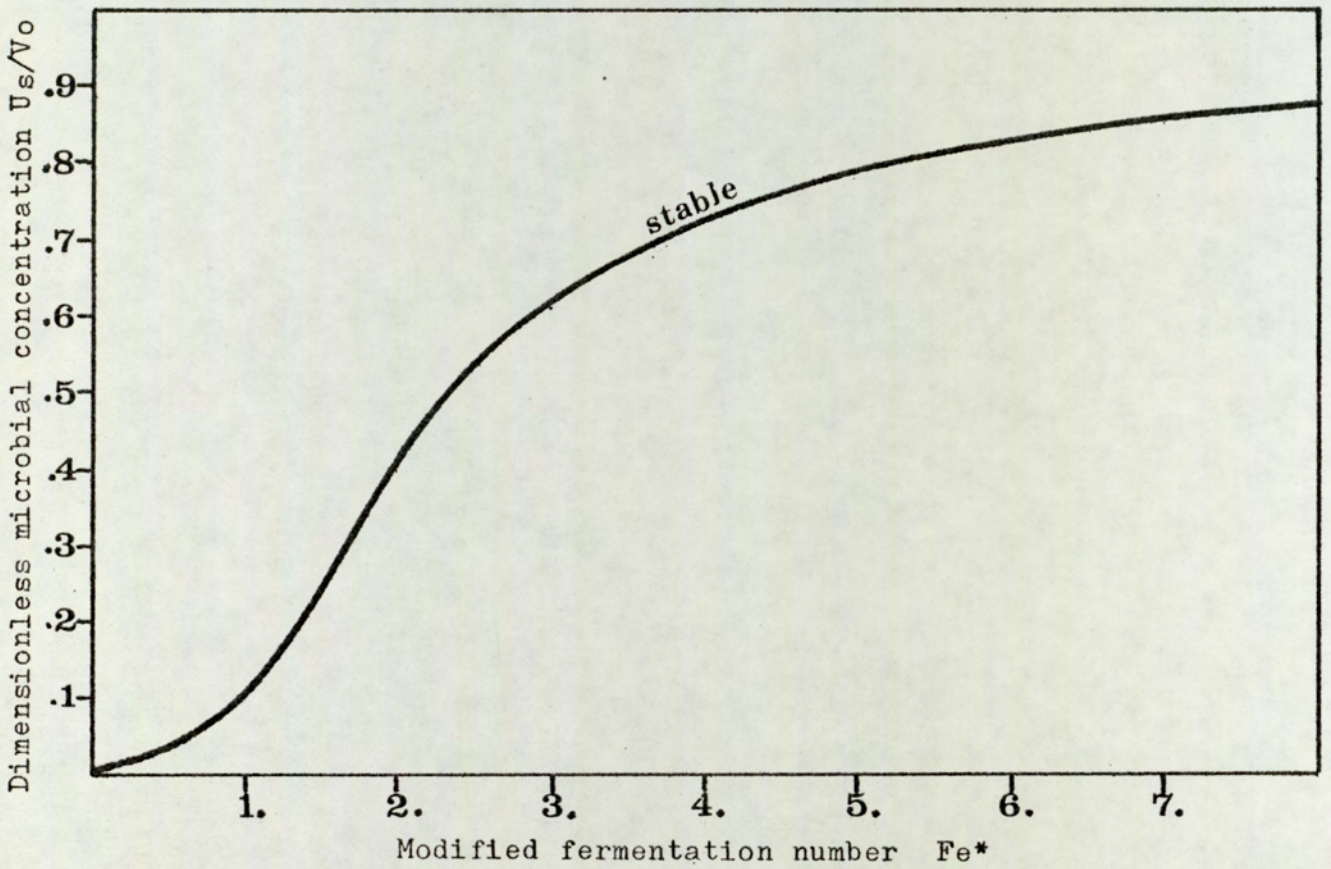
Non-inhibitory fermentation process under sterile feed conditions.
Effect of V_o on the non-sterile steady-state.

F I G U R E (4.6.3)



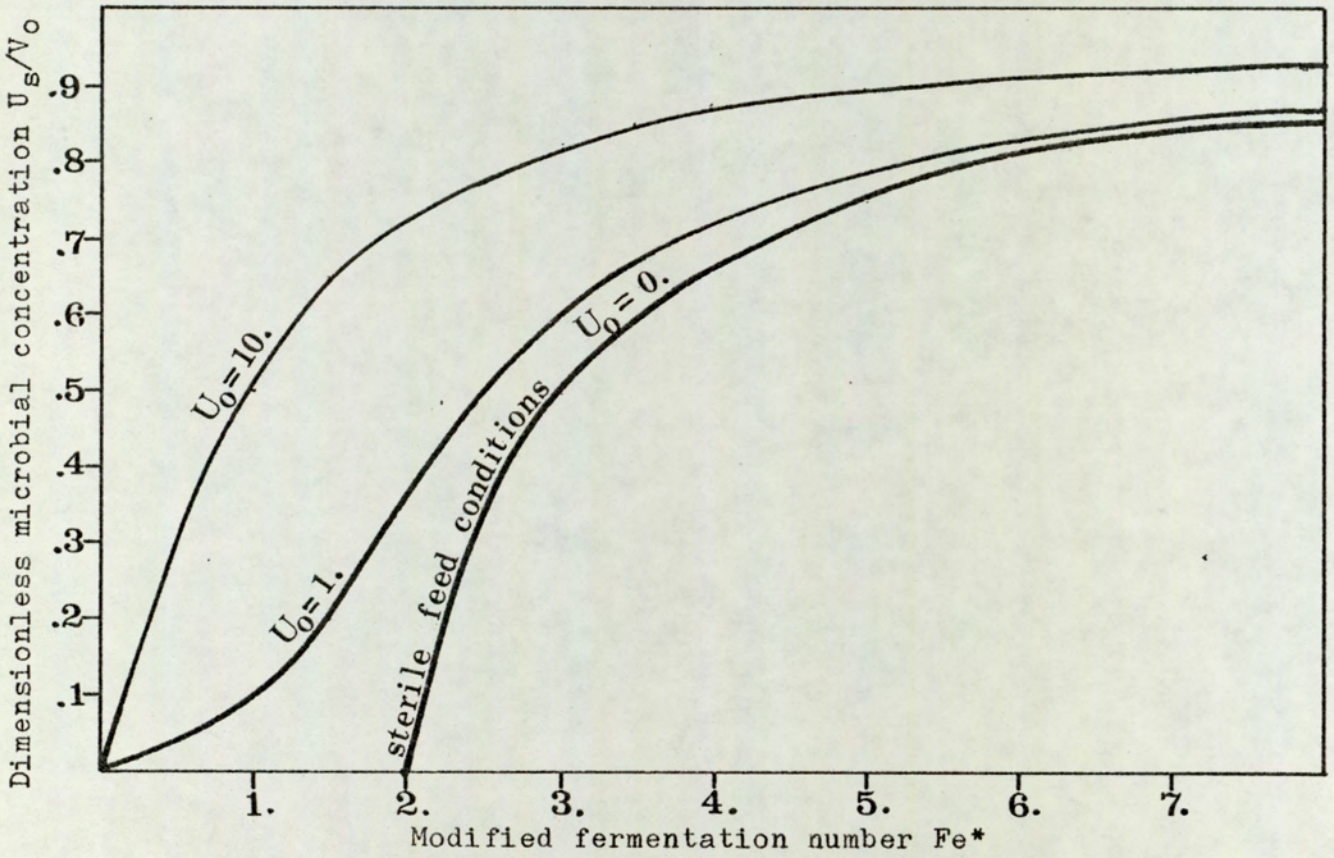
Non-inhibitory fermentation process under sterile feed conditions.
Effect of Bo for a non-gaseous limiting substrate.

F I G U R E (4.6.4)



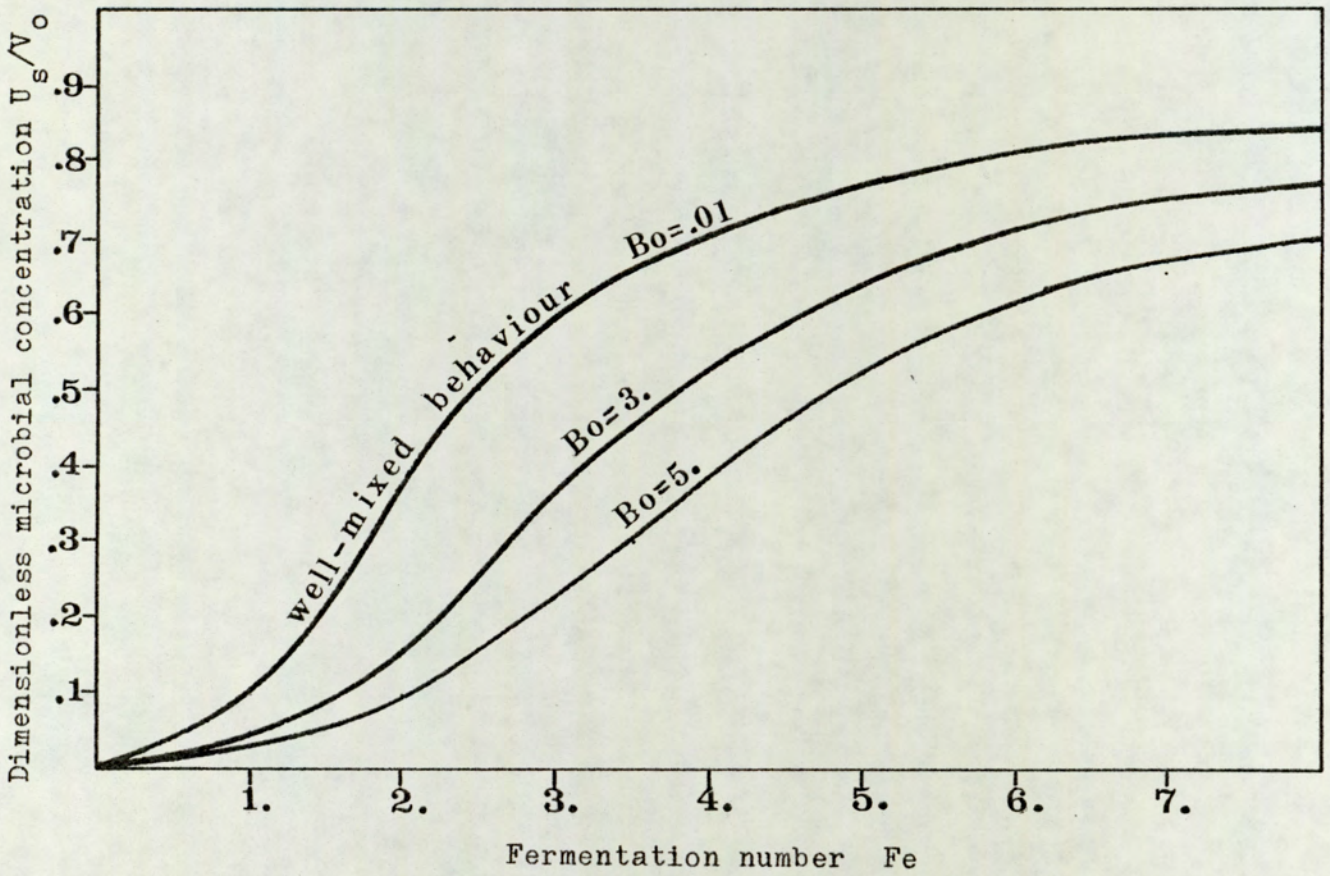
Non-inhibitory fermentation process under non-sterile feed conditions. Stability for the case where $U_o = 1.0$.

F I G U R E (4.6.5)



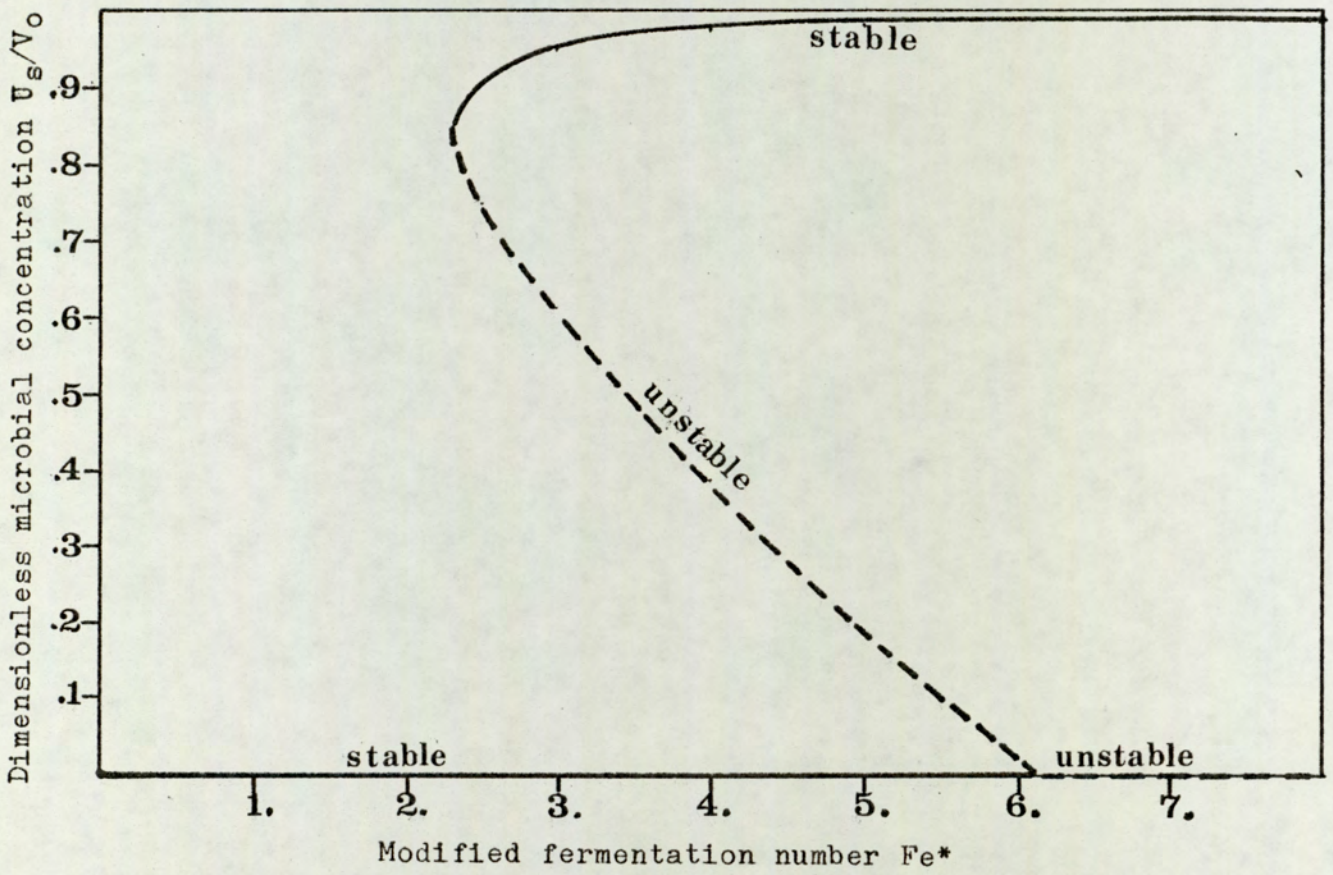
Non-inhibitory fermentation process under non-sterile feed conditions. Effect of U_o.

FIGURE (4.6.6)



Non-inhibitory fermentation process under non-sterile feed conditions. Effects of Bo for a non-gaseous limiting substrate.

F I G U R E (4.6.7)



Inhibitory fermentation process under sterile feed conditions.
Stability for the case where In = 0.5.

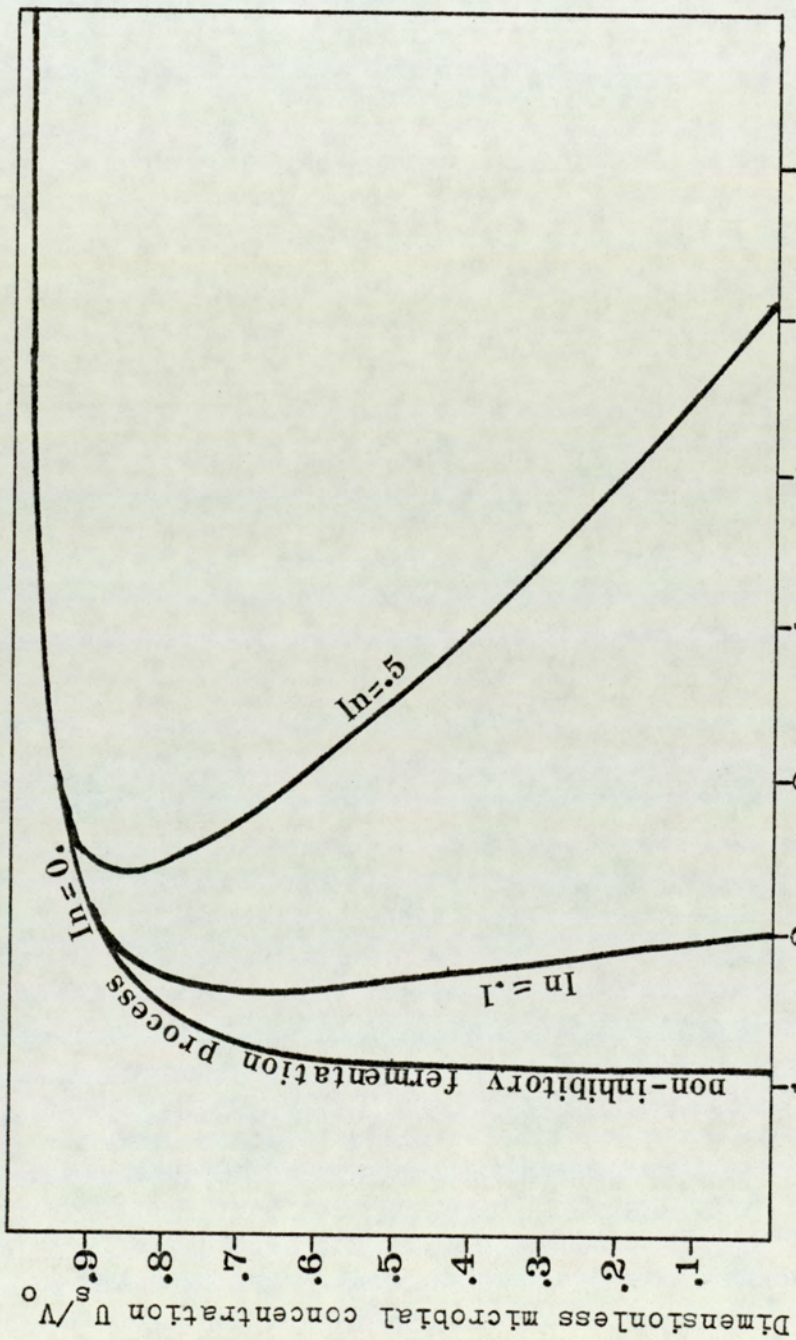
$$2|\sqrt{In}| + 1 \leq Fe^* \leq \frac{1+V_o+In\ V_o^2}{V_o} \qquad (4.6.15)$$

multiplicity occurs. In this domain we have three steady-states the sterile steady-state which is stable and two non-sterile steady-states one stable and the other unstable. FIGURE (4.6.8) shows the effect of In on the non-sterile steady-states. - FIGURE (4.6.9) illustrates the effect of Bo for a non-gaseous limiting substrate.

Finally, an inhibitory fermentation process under non-sterile feed conditions is considered. The stability analysis for this situation was done by means of the graphical method considered in FIGURE(4.6.13).FIGURE (4.6.10) shows the general shape of the curve to be expected, but it is not possible to obtain analytical estimates of the boundaries of the regions. The graph shows that for low values of Fe* there is only one solution, and this is also the case at high values of Fe*: these solutions are stable. For intermediate values of Fe* there is a region where multiplicity occurs. In this region three non-sterile steady-states occur, the intermediate steady-state being unstable (dotted line). FIGURE (4.6.11) shows the effects of U_o and FIGURE (4.6.12) the effect of Bo.

4.7) SUMMARY.

In this chapter an analysis of the problem proposed in Chapter 3 is made by using a lumped approximation technique. First, steady-states are calculated for all situations except inhibitory fermentation processes under non-sterile feed conditions; and then the stability of these steady state is analyzed by using the Direct Liapunov Method. In order to analyse inhibitory fermentation processes under non-sterile feed conditions use is made of an elementary graphical method



F I G U R E (4.6.8)

Inhibitory fermentation process under sterile feed conditions.
Effect of In.

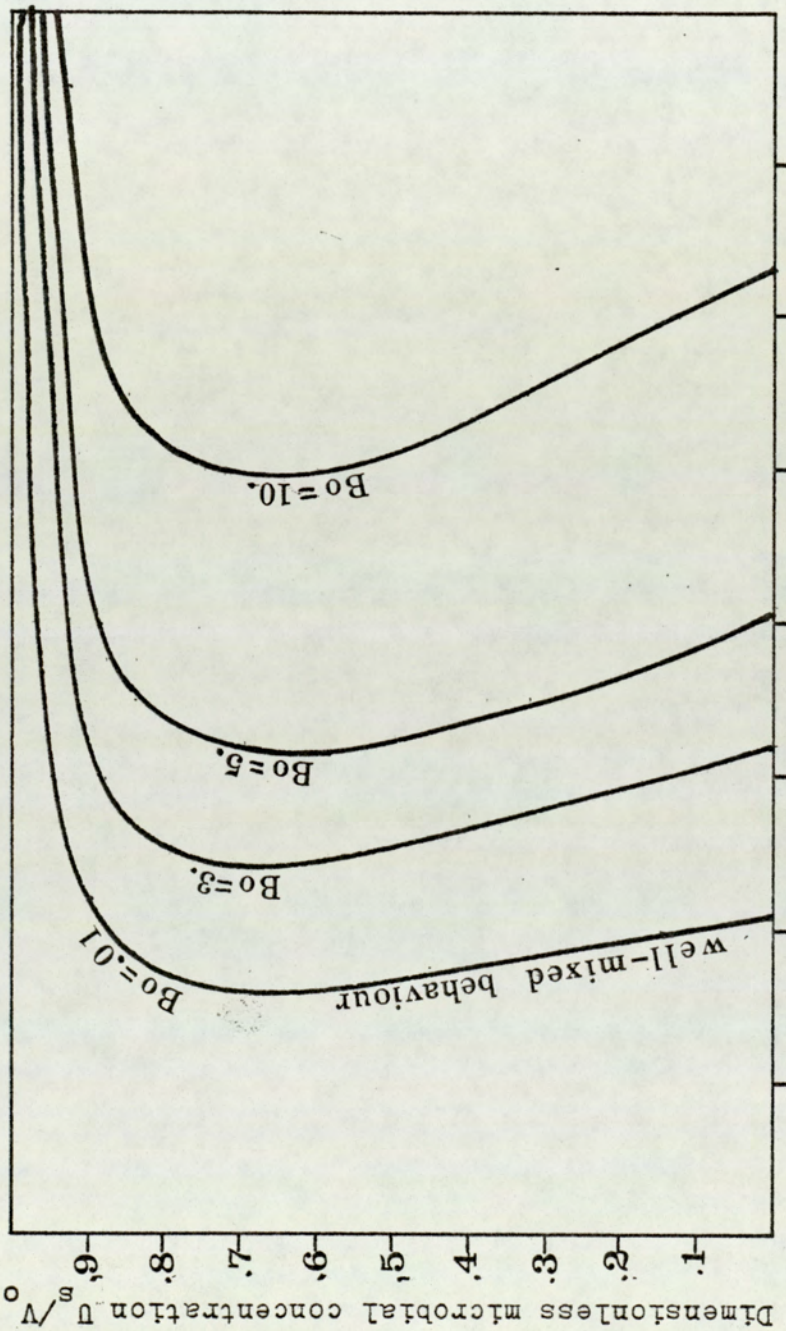
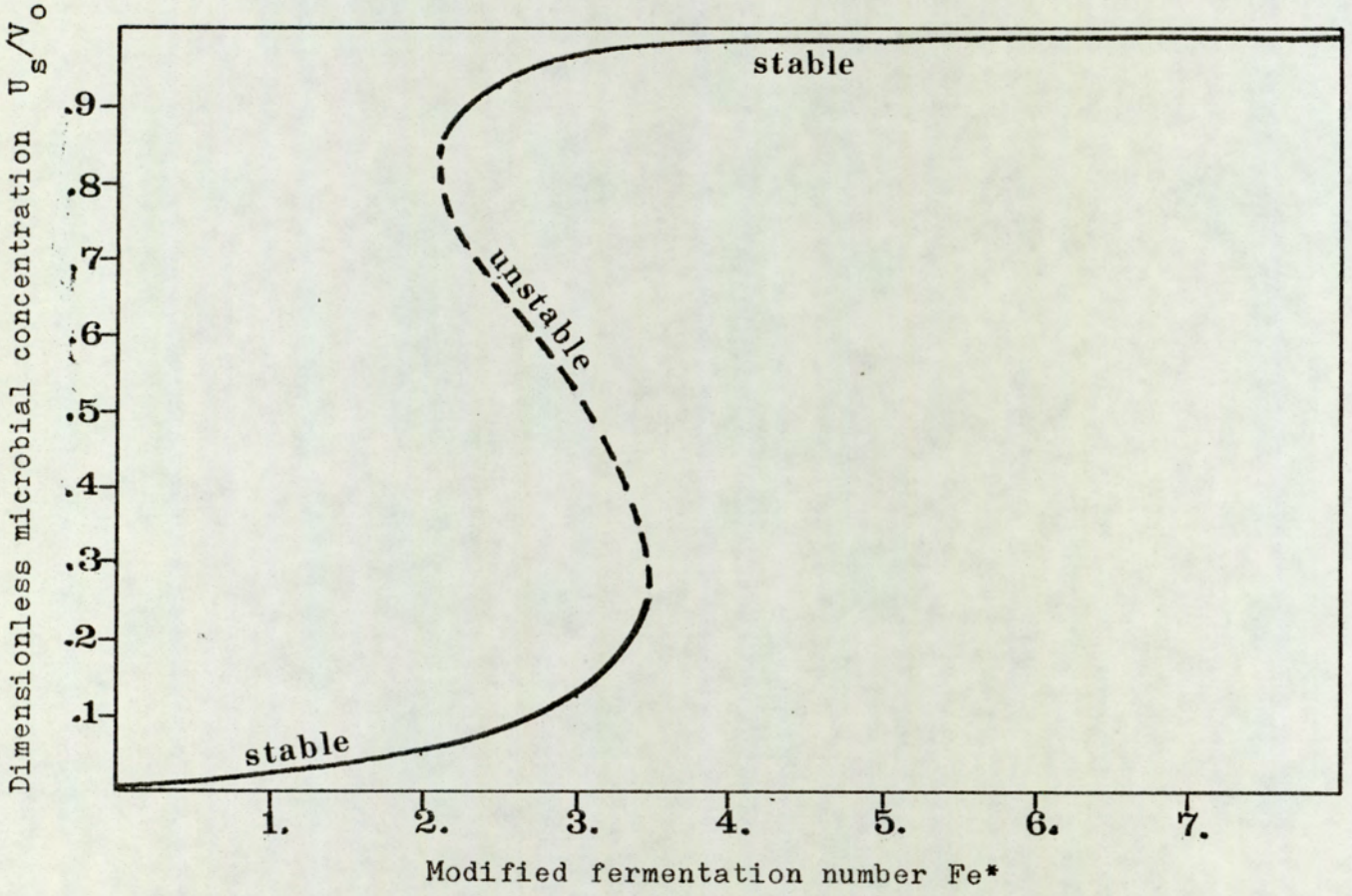


FIGURE (4.6.9)

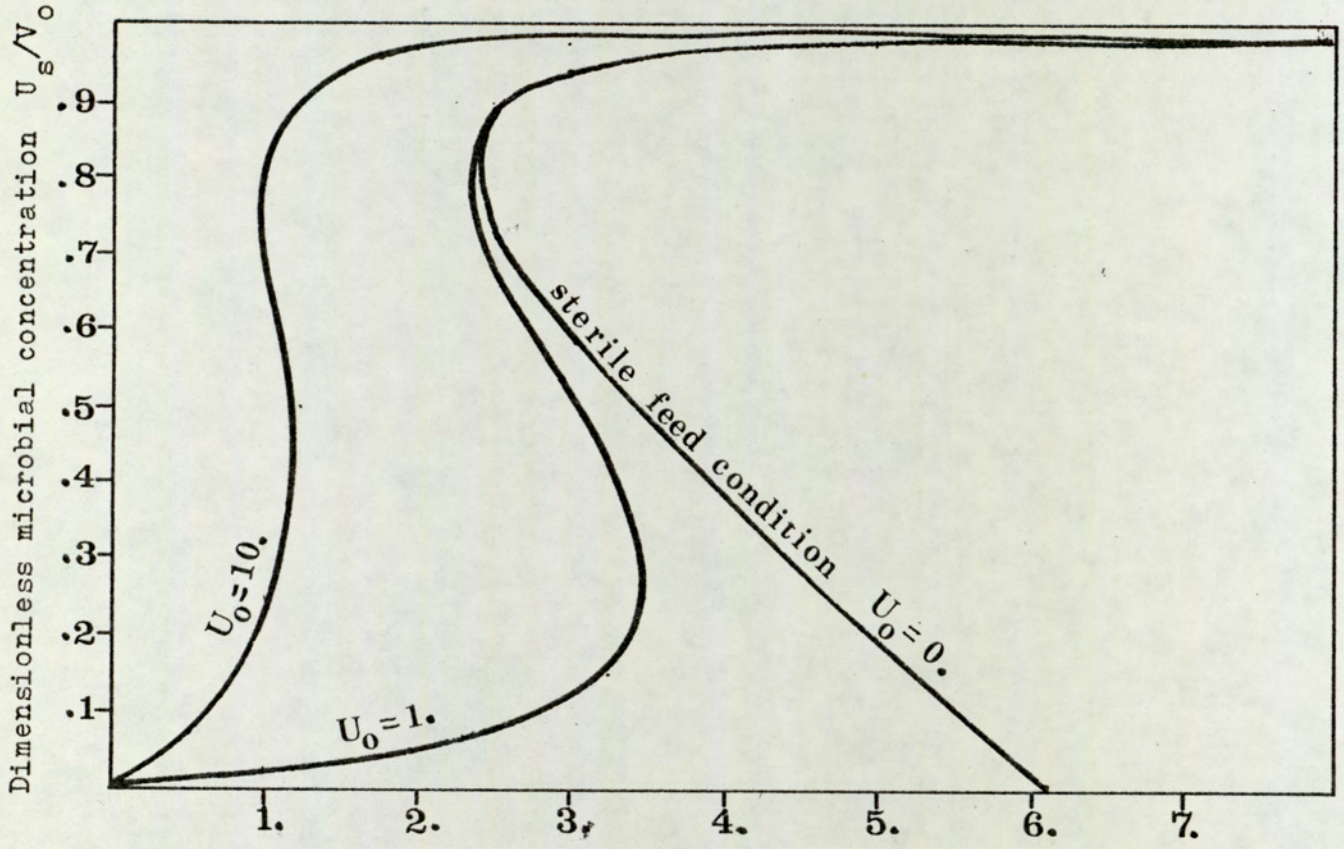
Inhibitory fermentation process under sterile feed conditions.
Effect of Bo for a non-gaseous limiting substrate.

F I G U R E (4.6.10)



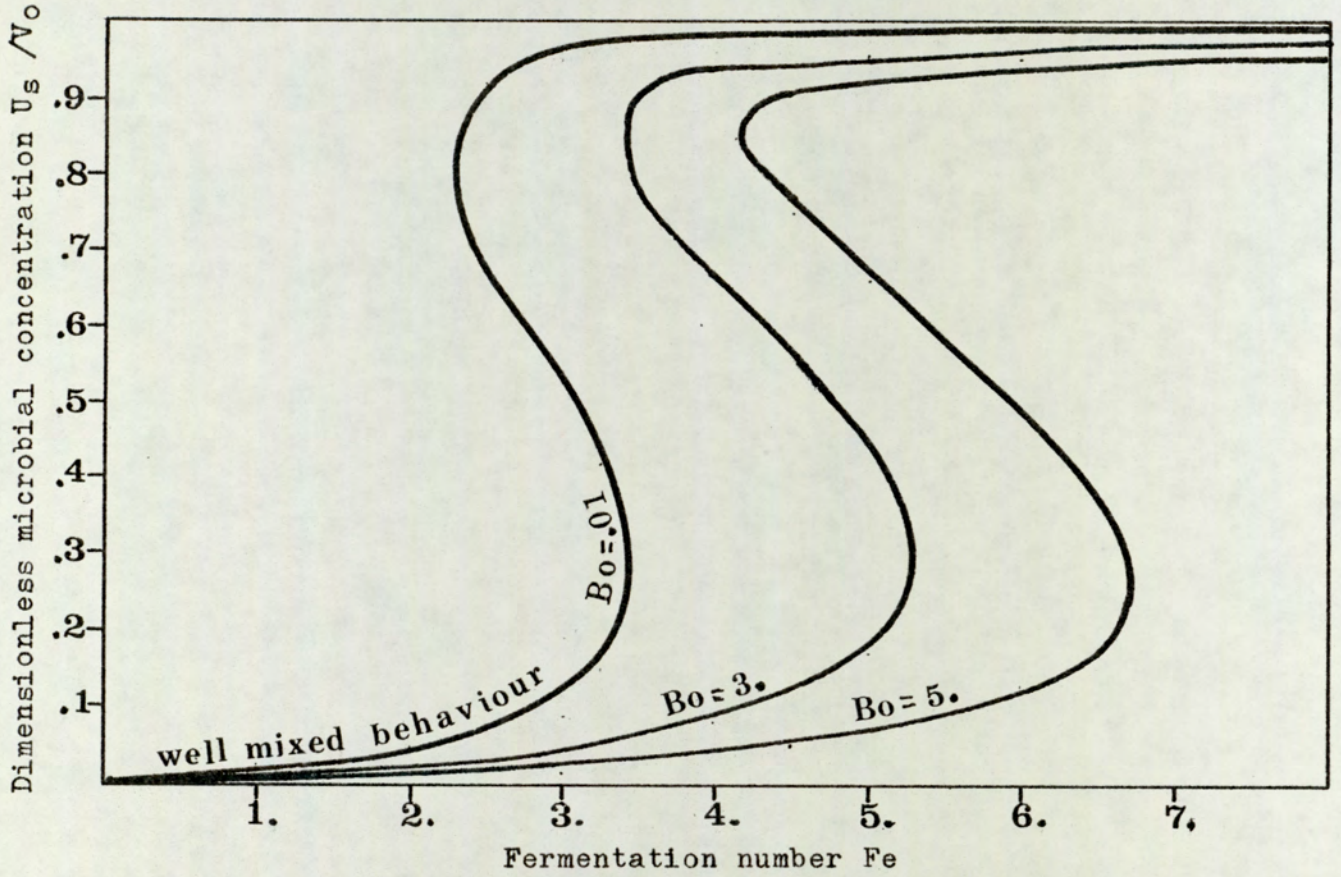
Inhibitory fermentation process under non-sterile feed conditions.
Stability for the case where U_o = 10.0.

F I G U R E (4.6.11)



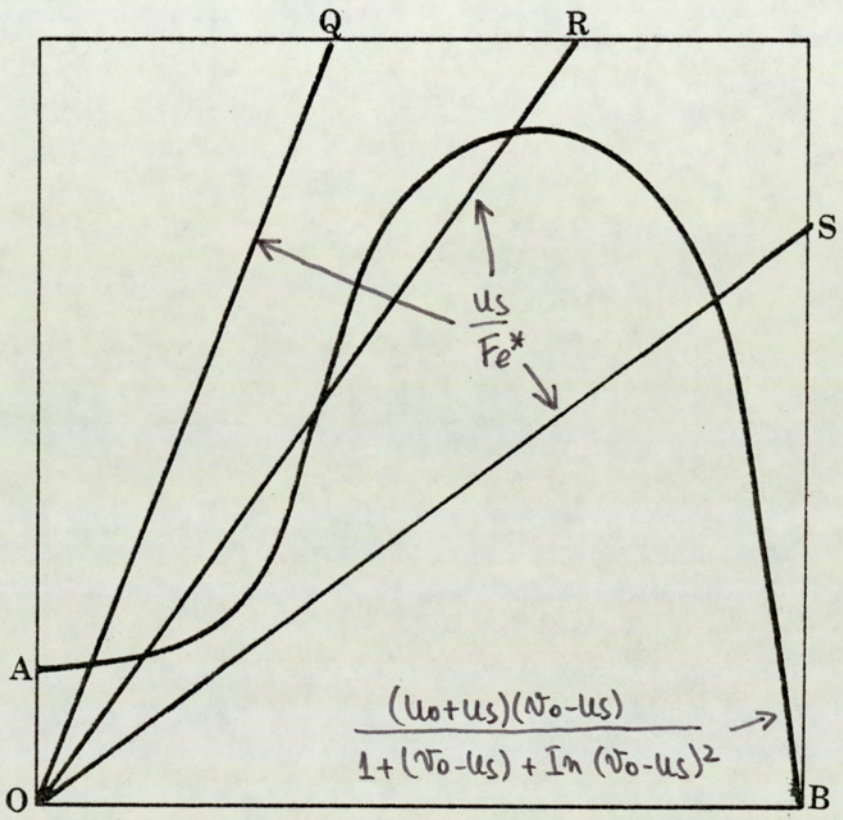
Inhibitory fermentation process under non-sterile feed conditions.
Effects of U_o for In = 0.5.

F I G U R E (4.6.12)



Inhibitory fermentation process under non-sterile feed conditions.
Effects of Bo for a non-gaseous limiting substrate.

F I G U R E (4.6.13)



Graphical analysis of a inhibitory fermentation process under non-sterile feed conditions.

which allows physical interpretation of the results for all cases. Finally, the results obtained are plotted graphically.

The results obtained in this chapter can also be used in the analysis of the well-mixed reactor for which they are exact. The aim of the work, however, is the analysis of the tubular reactor used as a fermenter. In this situation the results obtained must be considered as first approximations, especially when high values of Bo are considered.

V - NUMERICAL ANALYSIS FOR THE EXACT PROBLEM FOR A NON-GASEOUS LIMITING SUBSTRATE

5.1) INTRODUCTION

In this chapter the equation governing a fermentation process involving a non-gaseous limiting substrate will be analyzed by using a numerical method. The goal of this analysis is to compare exact solutions with those obtained in the last chapter using the lumped approximation method.

In order to solve the exact problem the "shooting method" has been used. This method reduces the boundary value problem to an initial value problem by introducing an estimate of the steady-state microbial concentration at the fermenter outlet. The initial value problem may then be solved by a RUNGE-KUTTA marching technique, and the solution can be tested against the boundary condition at the inlet. If the solution does not satisfy this boundary condition a new estimate of the microbial concentration at the outlet is introduced and the procedure repeated until the boundary condition at the inlet is satisfied. It is possible to associate this procedure with any method for finding the roots of non-linear equations. KUBICEK and HLAVACEK [55][56] have shown how this is possible with the Newton and Richmond methods in order to obtain second and third order convergence, respectively. Unfortunately, due to time limitations some precision had to be sacrificed and a simplified method used.

5.2) NUMERICAL CALCULATIONS.

For a non-gaseous limiting substrate the steady-state equation is

$$\frac{1}{Bo}\frac{d^2u_s}{dy^2} + \frac{du_s}{dy} + Fe\,\frac{(u_o+u_s)(v_o-u_s)}{1+(v_o-u_s)+In(v_o-u_s)^2} = 0 \qquad (5.2.1)$$

together with the boundary conditions

$$y = 0 \Longrightarrow \frac{du_s}{dy} = 0 \qquad (5.2.2)$$

$$y = 1 \Rightarrow u_s + \frac{1}{Bo}\frac{du_s}{dy} = 0 \qquad (5.2.3)$$

From (3.5.10) it is possible to conclude that

$$0 \leq u_s \leq v_o \qquad (5.2.4)$$

After choosing

$$u_s = \alpha \qquad 0 \leq \alpha \leq v_o \qquad (5.2.5)$$

at $y = 0$, the above boundary value problem reduces to the initial-value problem

$$\frac{1}{Bo}\frac{d^2u_s}{dy^2} + \frac{du_s}{dy} + Fe\,\frac{(u_o+u_s)(v_o-u_s)}{1+(v_o-u_s)+In(v_o-u_s)^2} = 0 \qquad (5.2.6)$$

$$y = 0 \Rightarrow \begin{cases} u_s = \alpha \\ \dfrac{du_s}{dy} = 0 \end{cases} \qquad (5.2.7)$$

This problem may be solved by using the RUNGE-KUTTA marching technique from $y = 0$ to $y = 1$ to obtain

$$\delta(\alpha) = \left[u_s + \frac{1}{Bo}\frac{du_s}{dy}\right]_{y=1} = 0 \qquad (5.2.8)$$

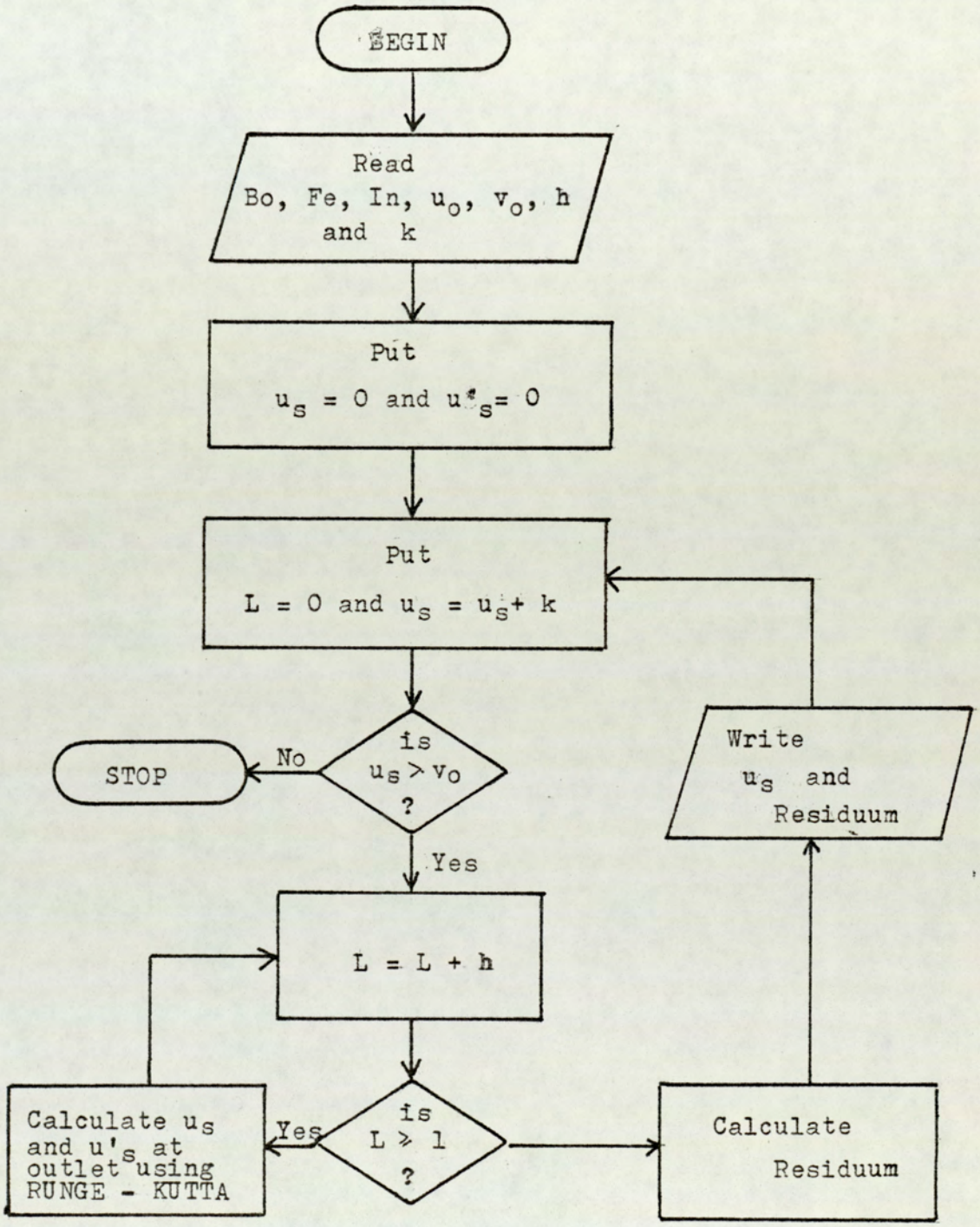
In order to find the values of α for which (5.2.8) is satisfied a sequence of equally spaced values of α in the interval $[0, v_o]$ is chosen and $\delta(\alpha)$ calculated for each value of α.

The computer problem used was based on the FLOWCHART (5.2.1). The RUNGE-KUTTA method employed can be found in the text by ABRAMOWITZ and STEGUN [79].

An example of the results obtained by the computer are given in TABLE (5.2.1). Values of u_s at the fermenter outlet can then be found graphically as shown in FIGURE (5.2.1).

In order to control the error in the computer calculations

PROGRAM FLOWCHART



```
0001          C THIS PROGRAM CALCULATES THE OUTLET MICROBIAL CONCENTRATION VERSUS RESIDUUM FOR
0002          C ORGANIC SUBSTRATE
0003          C
0004          C
0005          C READ NUMBER OF SPACING
0006          C
0007               READ (1,1) M1,N1
0008             1 FORMAT (2I10)
0009          C
0010          C
0011          C READ VALUES OF PARAMETERS
0012          C
0013               5 READ (1,10) XB,XI,XU,XV
0014              10 FORMAT (5F15.5)
0015          C
0016               IF (XB .EQ. 0.) STOP
0017          C
0018          C
0019               DO 160 N = 1,10
0020               XF = FLOAT(N)
0021          C WRITE VALUES OF PARAMETERS
0022          C
0023               WRITE (2,20)
0024             20 FORMAT(1H1,17X,25H DIMENSIONLESS PARAMETERS)
0025               WRITE (2,30) XF
0026             30 FORMAT (1HO,18X,22H FERMENTATION NUMBER =,F10.5)
0027               WRITE (2,40) XB
0028             40 FORMAT (1HO,20X,20H BODENSTEIN NUMBER =,F10.5)
0029               WRITE (2,50) XI
0030             50 FORMAT (1HO,20X,20H INHIBITION NUMBER =,F10.5)
```

```
0031                  WRITE (2,60) XU
0032               60 FORMAT (1H0,8X,32H INLET MICROBIAL CONCENTRATION =,F10.5)
0033                  WRITE (2,70) XV
0034               70 FORMAT (1H0,8X,32H INLET SUBSTRATE CONCENTRATION =,F10.5)
0035            C
0036            C
0037            C WRITE NUMBER OF SPACING
0038            C
0039                  WRITE (2,80)
0040               80 FORMAT (1H0,31X,18H NUMBER OF SPACING)
0041                  WRITE (2,90) M1
0042               90 FORMAT (1H0,5X,35H NUMBER OF AXIAL DISTANCE SPACING =,I5)
0043                  WRITE (2,100) N1
0044              100 FORMAT (1H0,6X,34H NUMBER OF CONCENTRATION SPACING =,I5)
0045            C
0046            C
0047            C RUNGE-KUTTA METHOD
0048            C
0049            C CALCULATION OF MICROBIAL CONCENTRATION VERSUS RESIDUUM
0050            C
0051            C
0052                  WRITE (2,110)
0053              110 FORMAT (1H0,17X,47H OUTLET MICROBIAL CONCENTRATION VERSUS RESIDUUM
0054                 1)
0055            C
0056            C
0057            C
0058                  XH = XV/FLOAT(N1)
0059                  XK = 1./FLOAT(M1)
0060                  DO 150 J1 = 1,N1
```

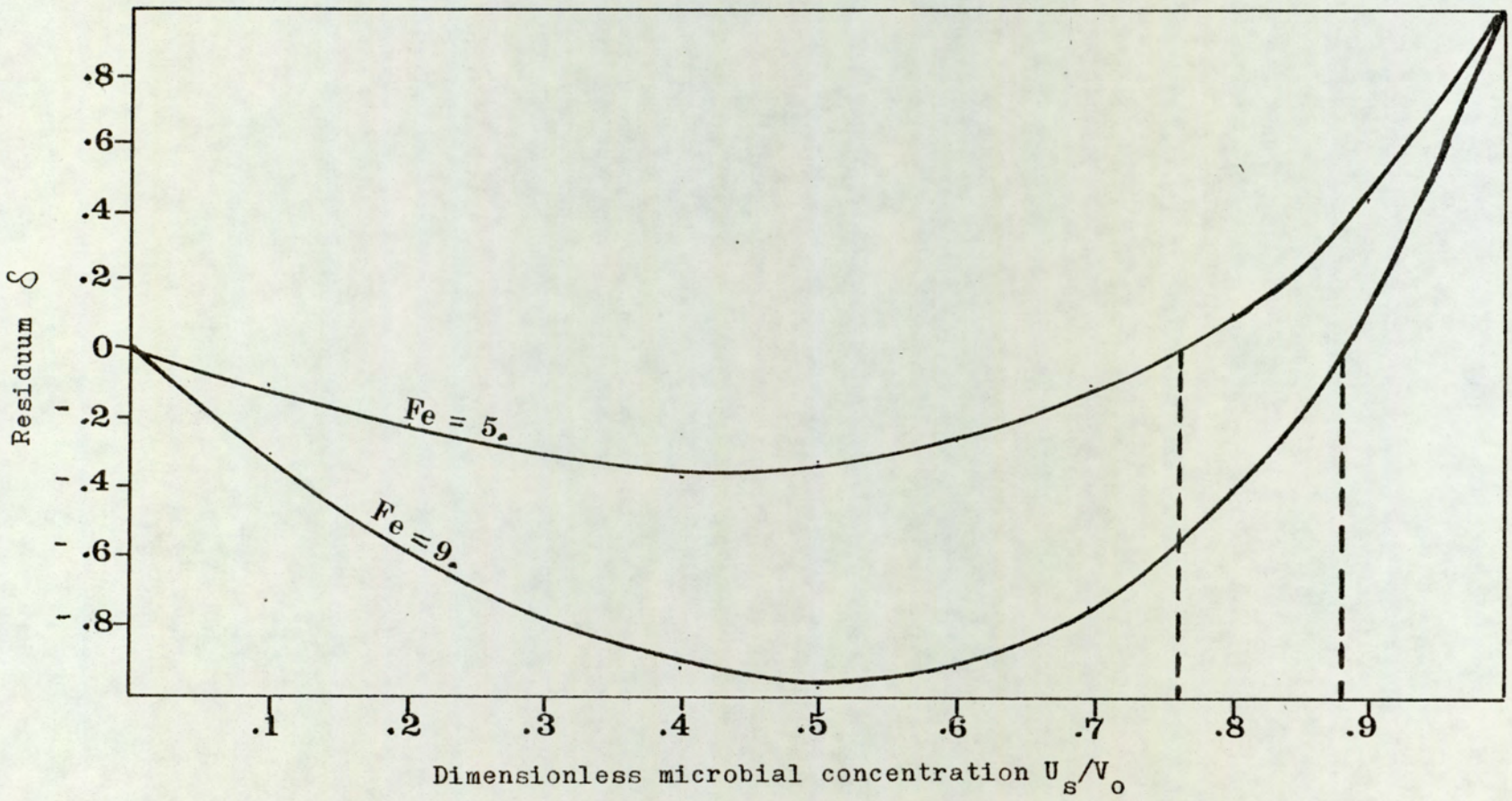
```
0061                    Y1=FLOAT(J1)*XH
0062                    R1=Y1
0063                    R2=0.
0064                    DO 130 J2 = 1,M1
0065                      X1=R1
0066                      X2=R2
0067                      XK1 = -XB*(X2 + XF*(XU + X1)*(XV - X1)/(1. + (XV-X1)*
0068                   1  (1. + XI*(XV - X1))))*XK
0069                      X1 = X1 + X2*XK + XK1*XK/2.
0070                      X2 = X2 + XK1/2.
0071                      XK2 = -XB*(X2 + XF*(XU + X1)*(XV - X1)/(1. + (XV - X1)*
0072                   1  (1. + XI*(XV - X1))))*XK
0073                      X2 = X2 + XK2/2.
0074                      XK3 = -XB*(X2 + XF*(XU + X1)*(XV - X1)/(1. + (XV - X1)*
0075                   1  (1. + XI*(XV - X1))))*XK
0076                      X1 = X1 + X2*XK + XK3*XK/2.
0077                      X2 = X2 + XK3
0078                      XK4 = -XB*(X2 + XF*(XU + X1)*(XV - X1)/(1. + (XV - X1)*
0079                   1  (1. + XI*(XV - X1))))*XK
0080                      R1 = R1 + XK*(X2 + (XK1 + XK2 + XK3)/6.)
0081                      R2 = R2 + (XK1 + 2.*XK2 + 2.*XK3 + XK4)/6.
0082                130   CONTINUE
0083                    XD = R1 + R2/XB
0084                    WRITE (2,140) Y1,XD
0085                140   FORMAT (F10.5,30X,F10.5)
0086                150 CONTINUE
0087                160 CONTINUE
0088                    GO TO 5
0089                    END
```

T A B L E (5.2.1)

u_s/v_o	FERMENTATION NUMBER	
	5.0	9.0
0.1	-0.12632	-0.30612
0.2	-0.22782	-0.56800
0.3	-0.29879	-0.77565
0.4	-0.33215	-0.91575
0.5	-0.31893	-0.97279
0.6	-0.24767	-0.92589
0.7	-0.10351	-0.74808
0.8	0.13317	-0.40352
0.9	0.48884	0.15650
1.0	1.00000	1.00000

Numerical example for $N_0 = 1.0$, $B_0 = 0.01$, $I_m = 0.0$ and $u_0 = 0.0$.

F I G U R E (5.2.1)



Example of graphical calculation of the outlet microbial concentration.

T A B L E (5.2.2)

	AXIAL DISTANCE STEP	
u_s/v_o	1×10^{-2}	2×10^{-3}
0.1	-0.11832	-0.12202
0.2	-0.23411	-0.24119
0.3	-0.34603	-0.35601
0.4	-0.45189	-0.46400
0.5	-0.54781	-0.56087
0.6	-0.62633	-0.63838
0.7	-0.67128	-0.67894
0.8	-0.64122	-0.63818
0.9	-0.39471	-0.36947
1.0	1.00000	1.00000

Error control for $Fe = 10.0$, $Bo = 1.0$, $Im = 0.5$ $u_o = 0.0$ and $v_o = 1.0$.

we ran the problem for

Fe = 10.0, Bo = 1.0; In = 0.5; u_o = 0.0; v_o = 1.0

initially considering steps of 10^{-2} and then 0.2×10^{-2} to obtain the results shown in TABLE (5.2.2).

It may be concluded that steps of 10^{-2} are dangerously near the point where the results become meaningless, but due to time limitations we have used it. The trial runs suggest that steps of 10^{-3} or smaller should be used especially if a sophisticated method of calculation is to be used.

5.3) NUMERICAL ANALYSIS FOR A NON-GASEOUS LIMITING SUBSTRATE.

Considering a non-inhibitory fermentation process under sterile feed conditions for which v_o = 1.0 and Bo = 0.01 the results shown in TABLE (5.3.1) were obtained. FIGURE (5.3.1) compares the results obtained in the previous chapter with those obtained in this chapter: there is a very good agreement. - FIGURES (5.3.2) and (5.3.3) compare the results for Bo = 1.0 and Bo = 5.0 respectively. The former shows good agreement, but the latter show only "poor agreement" for small values of Fe. These figures were constructed using the data shown in TABLES (5.3.2) and (5.3.3), respectively.

Finally considering an inhibitory fermentation process under sterile feed conditions we obtain the results shown in FIGURES (5.3.4) and (5.3.5) for Bo = 0.01 and Bo = 5.0 respectively.

5.4) DISCUSSION AND CONCLUSIONS.

The method used to obtain the above results was somewhat cumbersome and the precision was relatively low. The use of a high precision method, such as that proposed by KUBICEK and HLAVACEK [35] requires more computer time than was available to the author.

For inhibitory fermentation process under sterile feed

T A B L E (5.3.1)

	FERMENTATION NUMBER						
u_s	2·0	3.0	4·0	5.0	6.0	7.0	8.0
0.1	0.01	-0.04	-0.08	-0.13	-0.18	-0.23	-0.27
0.2	0.02	-0.06	-0.15	-0.24	-0.33	-0.41	-0.50
0.3	0.05	-0.07	-0.19	-0.31	-0.44	-0.56	-0.68
0.4	0.10	-0.04	-0.20	-0.34	-0.50	-0.64	-0.79
0.5	0.16	0.00	-0.16	-0.33	-0.50	-0.66	-0.83
0.6	0.25	0.08	-0.08	-0.25	-0.43	-0.60	-0.77
0.7	0.37	0.21	0.05	-0.10	-0.27	-0.43	-0.59
0.8	0.53	0.40	0.26	0.13	0.00	-0.13	-0.27
0.9	0.73	0.65	0.57	0.48	0.40	0.32	0.23
1.0	1.00	1.00	1.00	1.00	1.00	1.00	1.00

RESIDUUM

Numerical data used in FIGURE (5.3.1)

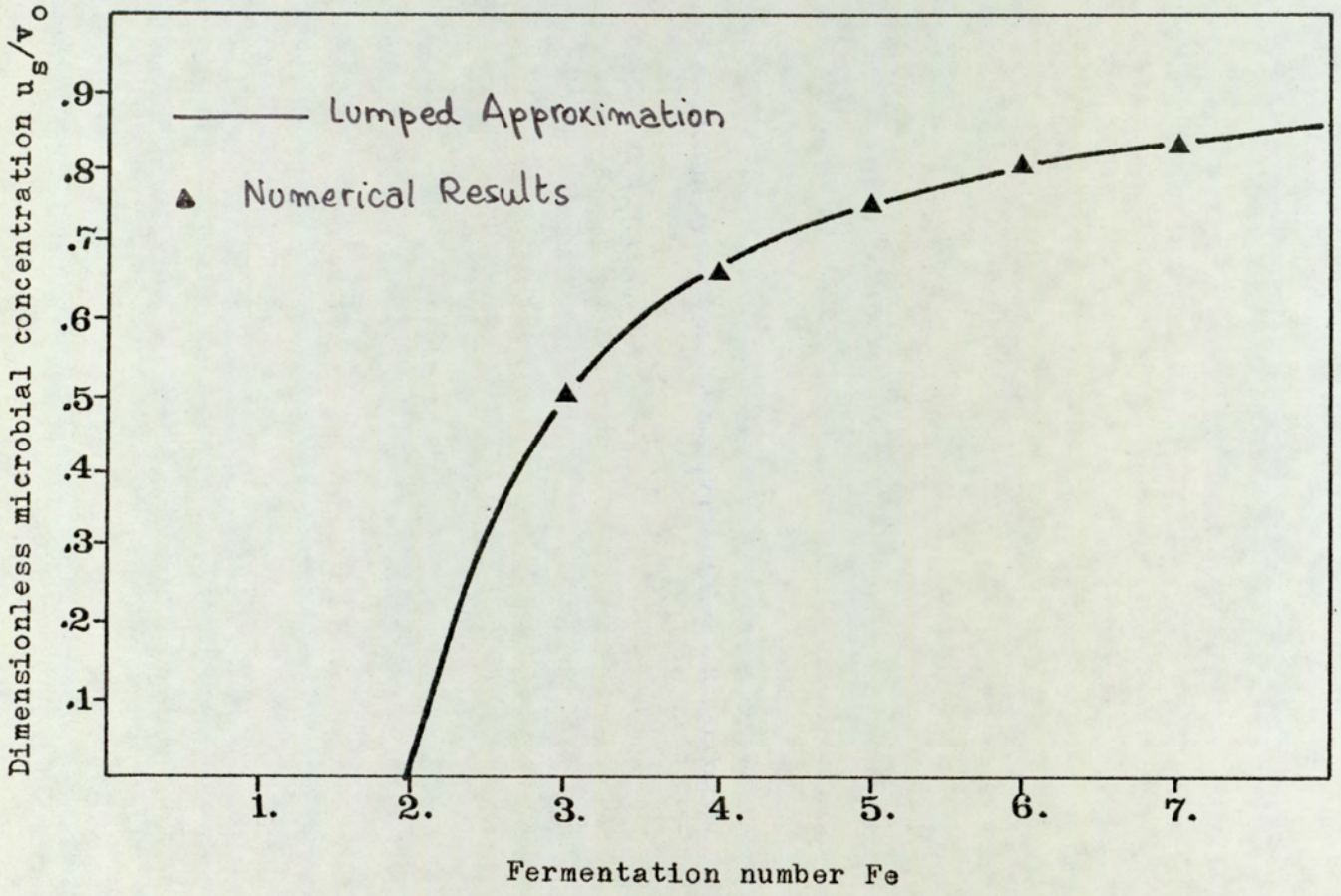
$B_0 = 0.01$

$I_n = 0.0$

$u_0 = 0.0$

$N_0 = 1.0$

F I G U R E (5.3.1)



Comparison between lumped approximation and numerical results.
Non-inhibitory fermentation process under sterile feed conditions
(Bo = 0.01).

TABLE (5.3.2)

	FERMENTATION NUMBER						
u_s	2.0	3.0	4.0	5.0	6.0	7.0	8.0
0.1	0.01	-0.04	-0.09	-0.14	-0.18	-0.23	-0.28
0.2	0.02	-0.06	-0.15	-0.24	-0.33	-0.42	-0.50
0.3	0.05	-0.07	-0.19	-0.31	-0.43	-0.56	-0.68
0.4	0.10	-0.05	-0.20	-0.35	-0.50	-0.64	-0.79
0.5	0.16	0.00	-0.16	-0.33	-0.50	-0.66	-0.83
0.6	0.26	0.08	-0.08	-0.25	-0.42	-0.60	-0.77
0.7	0.38	0.21	0.05	-0.11	-0.27	-0.43	-0.59
0.8	0.53	0.39	0.26	0.13	-0.00	-0.13	-0.27
0.9	0.74	0.65	0.57	0.49	0.40	0.32	0.23
1.0	1.00	1.00	1.00	1.00	1.00	1.00	1.00

RESIDUUM

Numerical data used in FIGURE (5.3.2)

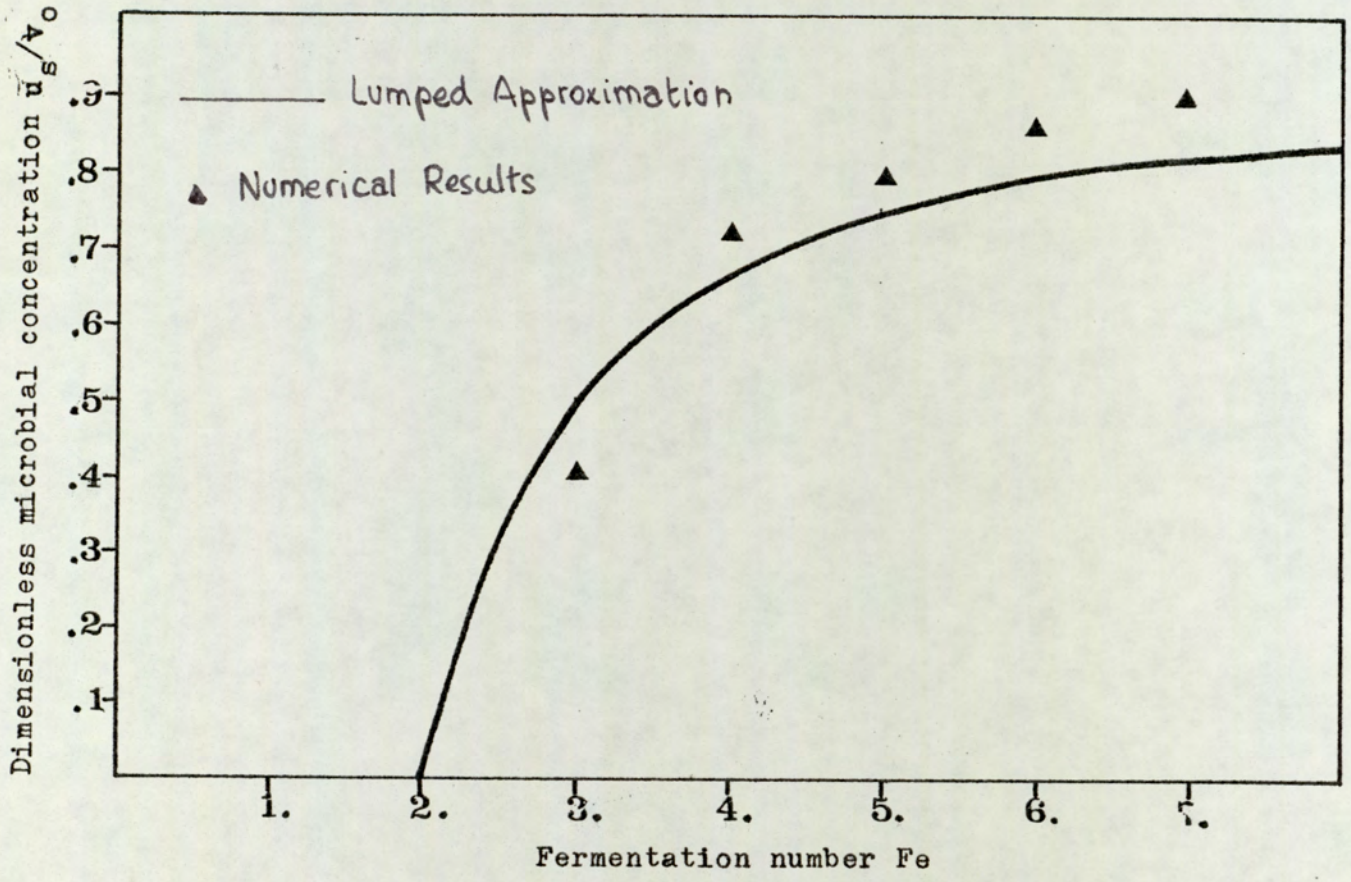
$B_0 = 1.0$

$I_m = 0.0$

$u_0 = 0.0$

$N_0 = 1.0$

F I G U R E (5.3.2)



Comparison between lumped approximation and numerical results.
Non-inhibitory fermentation process under sterile feed conditions
(Bo = 1.0).

T A B L E (5.3.3)

	FERMENTATION NUMBER						
u_s	2.0	3.0	4.0	5.0	6.0	7.0	8.0
0.1	0.03	0.01	0.00	-0.00	-0.00	-0.01	-0.00
0.2	0.06	0.02	0.00	-0.00	-0.01	-0.01	-0.01
0.3	0.10	0.04	0.00	-0.01	-0.02	-0.02	-0.01
0.4	0.15	0.07	0.01	-0.01	-0.02	-0.03	-0.02
0.5	0.20	0.10	0.03	-0.00	-0.03	-0.04	-0.03
0.6	0.27	0.15	0.05	-0.00	-0.03	-0.05	-0.05
0.7	0.36	0.21	0.10	0.01	-0.03	-0.06	-0.06
0.8	0.47	0.31	0.17	0.06	-0.01	-0.06	-0.08
0.9	0.65	0.50	0.33	0.19	0.07	-0.02	-0.07
1.0	1.00	1.00	1.00	1.00	1.00	1.00	1.00

RESIDUUM

Numerical data used in FIGURE (5.3.3)

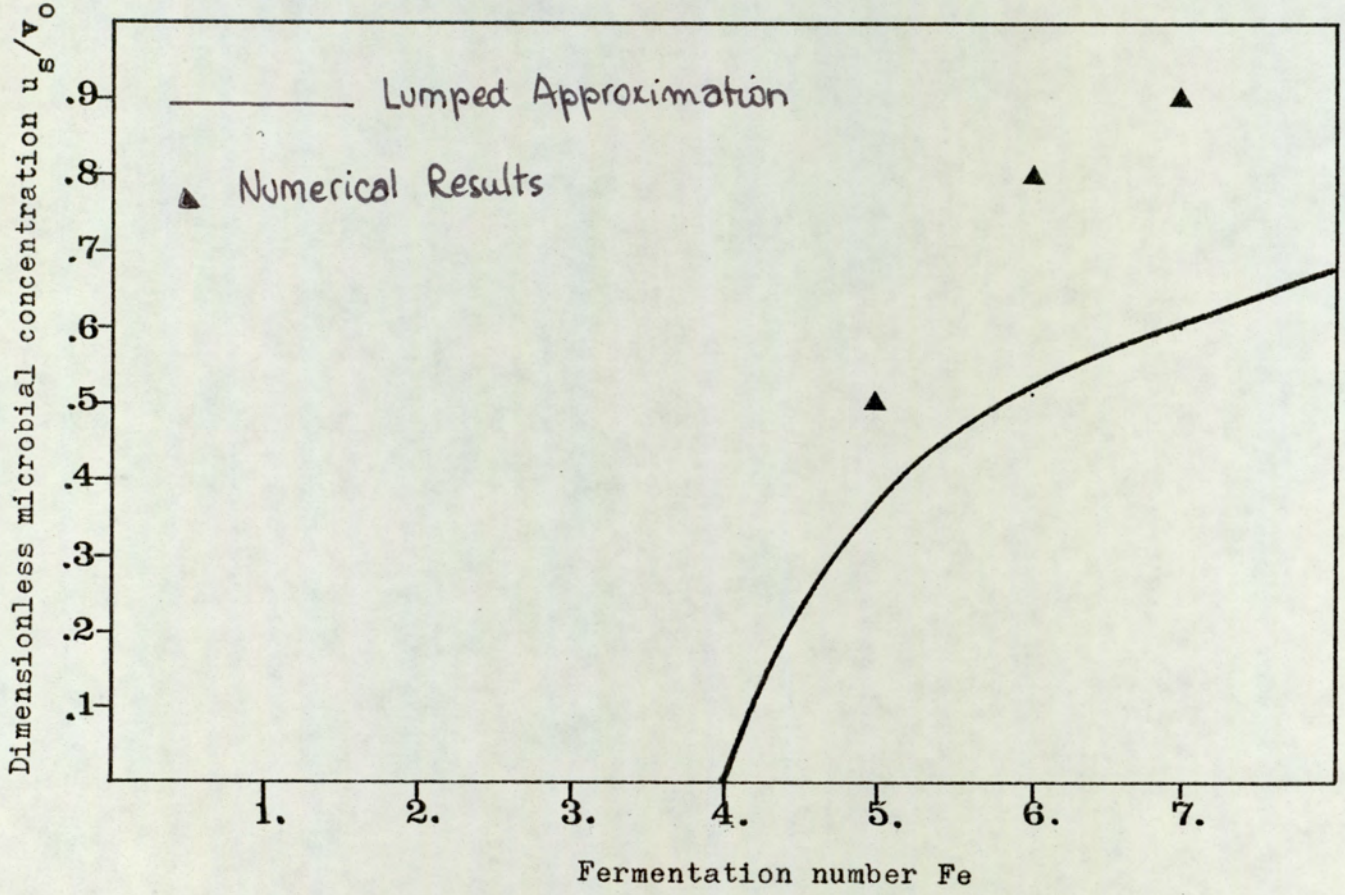
$B_0 = 5.0$

$I_m = 0.0$

$u_0 = 0.0$

$N_0 = 1.0$

F I G U R E (5.3.3)



Comparison between lumped approximation and numerical results. Non-inhibitory fermentation process under sterile feed conditions (Bo = 5.0).

conditions agreement between the exact and approximate method is very good for small values of Bo (Bo = 0.01): this is to be expected since the fermenter tends to behave like a well-mixed tank reactor. When the Bo increases (Bo = 1.0 and Bo = 5.0) the graphs show increasing degrees of deviation. It is difficult to assess the extent of this disagreement because values of u_s calculated in the last chapter are somewhere within the fermenter and the values of u_s calculated in this chapter corresponds to that at the outlet.

For an inhibitory fermentation process the agreement is good for both Bo = 0.01 and Bo = 5.0 as shown in FIGURES (5.3.4) and (5.3.5).

The results show that the region of wash-out predicted in the last chapter tends to be conservative, i.e., smaller than that predicted by numerical calculations. Also, the disagreement between the methods appears to be greater for small values of Fe: such values are associated with the frontier between the wash-out region and the "active" fermentation regions and with the multiplicity regions. The disagreement between the methods decreases as Fe increases, but this can be attributed to the fact that both solutions converge to $u_s = 1$ as $Fe \to \infty$.

For the range of values of Bo reported by the Tower Fermenter Group [27], i.e., Bo < 1.0, the results obtained by using the approximate analytical method appear to be satisfactory. To achieve high values of Bo in practice a tubular fermenter would need to be fitted with special baffles to prevent back-mixing of the liquid-phase and microbial suspension.

The next obvious step in the research appears to be a more numerical analysis. But before rushing into an exploration of this area, it might be prudent to work and see if experimentalists can confirm some of the prediction of the mathematical model.

For a gaseous limiting substrate the situation becomes

TABLE (5.3.4)

	FERMENTATION NUMBER						
u_s	2.0	3.0	4.0	5.0	6.0	7.0	8.0
0.1	0.01	- 0.48	- 0.98	- 1.47	- 1.96	- 2.46	- 2.95
0.2	-0.07	- 1.10	- 2.13	- 3.16	- 4.20	- 5.22	- 6.25
0.3	-0.24	- 1.86	- 3.48	- 5.09	- 6.70	- 8.31	- 9.91
0.4	-0.51	- 2.76	- 5.01	- 7.25	- 9.49	-11.72	-13.95
0.5	-0.86	- 3.79	- 6.70	- 9.61	-12.52	-15.41	-18.30
0.6	-1.25	- 4.87	- 8.47	-12.07	-15.66	-19.24	-22-80
0.7	-1.55	- 5.81	-10.07	-14.32	-18.55	-22.78	-27.00
0.8	-1.40	- 6.10	-10.80	-15.49	-20.18	-24.86	-29.54
0.9	0.38	- 3.94	- 8.30	-12.67	-17.06	-21.46	-25.89
1.0	10.00	10.00	10.00	10.00	10.00	10.00	10.00

RESIDUUM

Numerical data used in FIGURE (5.3.4)

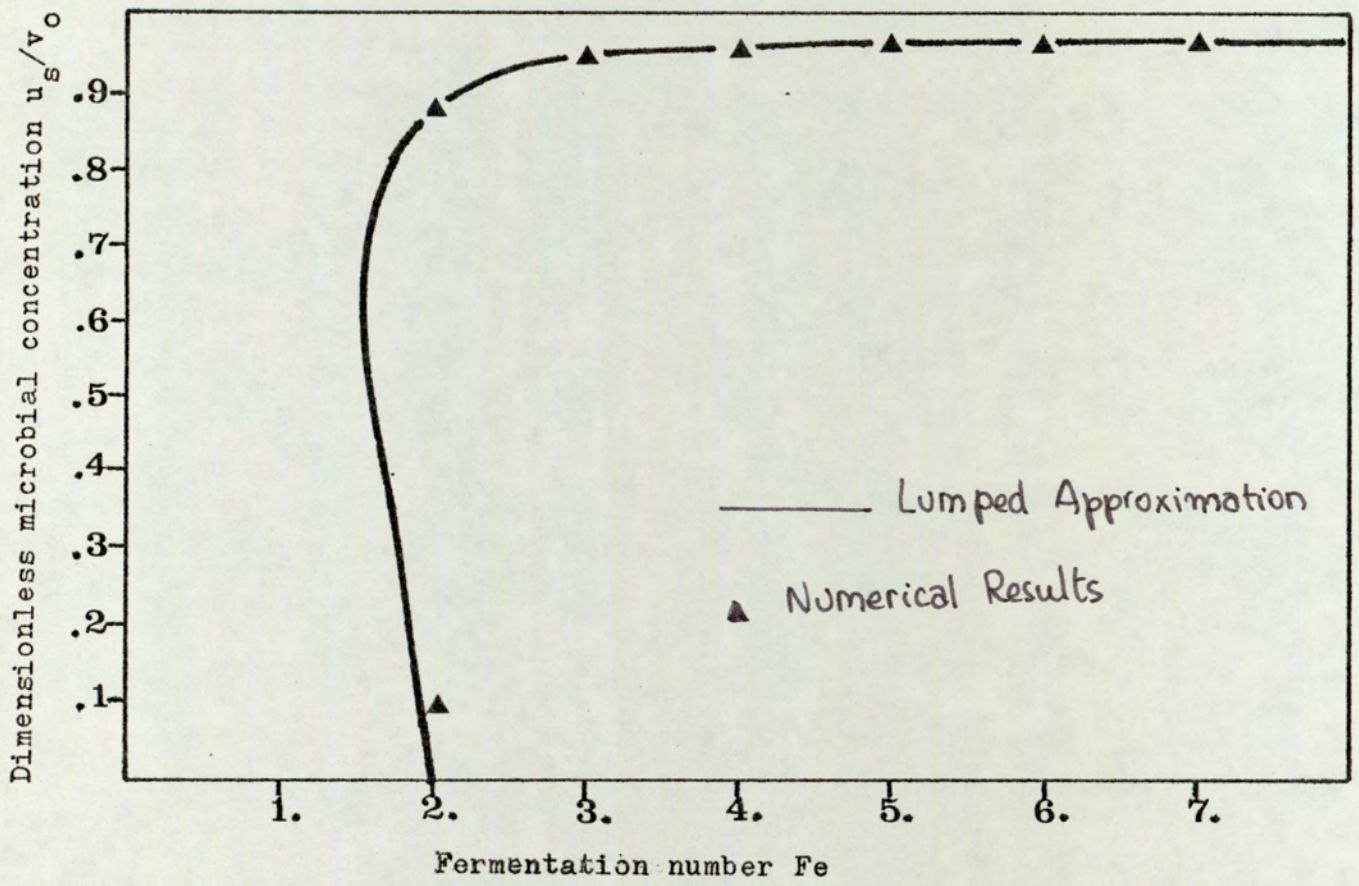
$B_0 = 0.01$

$I_m = 0.1$

$u_0 = 0.0$

$N_0 = 10.0$

F I G U R E (5.3.4)



Comparison between lumped approximation and numerical results.
Inhibitory fermentation under sterile feed conditions (Bo = 0.01).

T A B L E (5.3.5)

	FERMENTATION NUMBER						
u_s	2.0	3.0	4.0	5.0	6.0	7.0	8.0
0.1	0.30	0.12	0.01	-0.05	-0.07	-0.07	-0.06
0.2	0.57	0.21	0.01	-0.10	-0.14	-0.13	-0.10
0.3	0.81	0.29	-0.00	-0.16	-0.21	-0.20	-0.15
0.4	1.03	0.35	-0.03	-0.22	-0.28	-0.28	-0.19
0.5	1.23	0.40	-0.06	-0.28	-0.35	-0.35	-0.23
0.6	1.41	0.43	-0.10	-0.35	-0.42	-0.42	-0.27
0.7	1.59	0.45	-0.15	-0.42	-0.50	-0.49	-0.30
0.8	1.77	0.48	-0.19	-0.50	-0.58	-0.57	-0.35
0.9	2.04	0.56	-0.22	-0.58	-0.67	-0.67	-0.42
1.0	10.00	10.00	10.00	10.00	10.00	10.00	10.00

RESIDUUM

Numerical data used in FIGURE (5.3.5)

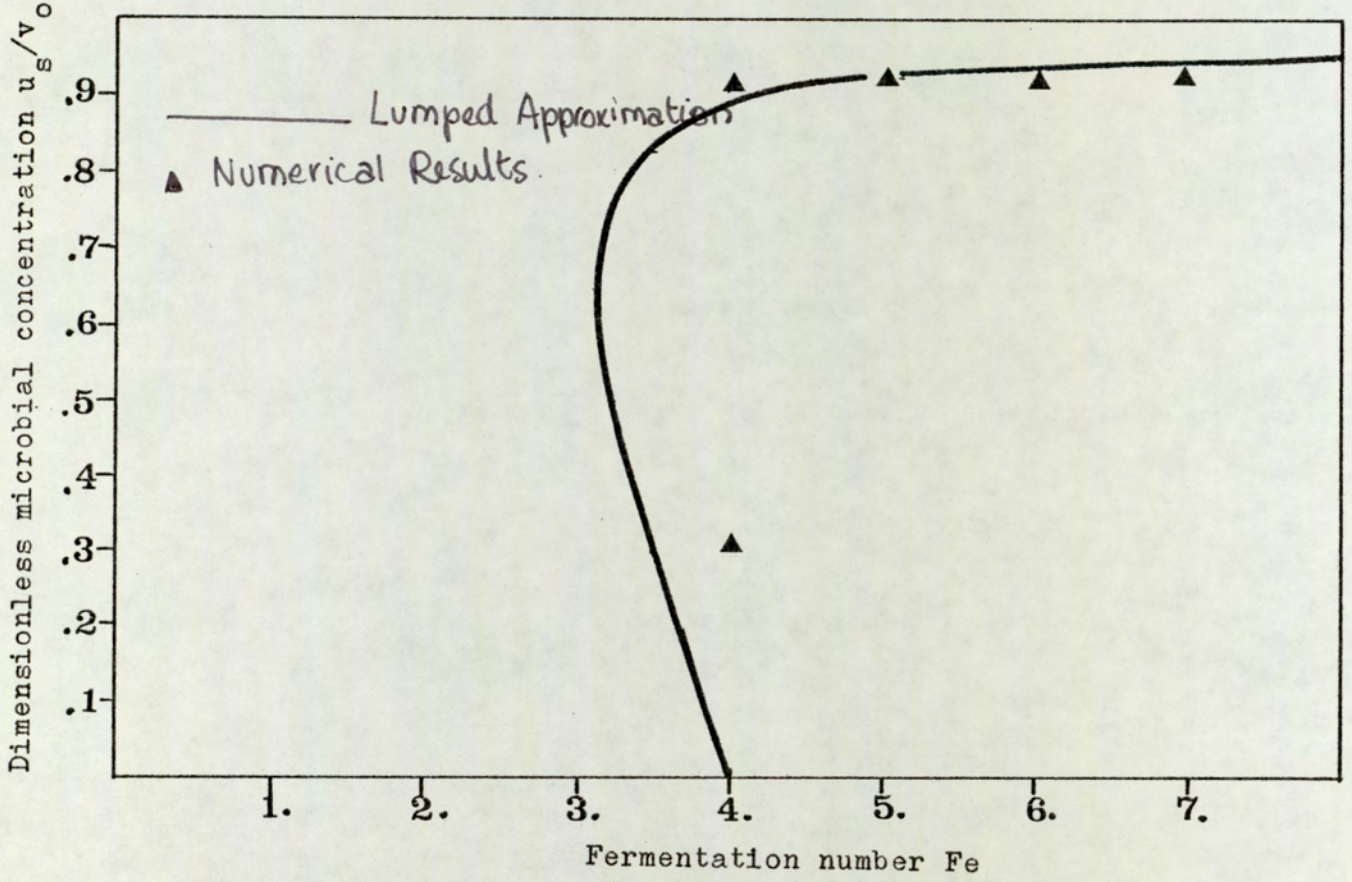
$B_0 = 1.0$

$I_M = 0.1$

$u_0 = 0.0$

$N_0 = 10.0$

F I G U R E (5.3.5)



Comparison between lumped approximation and numerical results.
Inhibitory fermentation under sterile feed conditions (Bo = 5.0).

a little more complicated. We need to solve two non-linear second order ordinary differential equations and calculate two residuals which are function of two estimates at the outlet. This would require a more sophisticated method of searching for the roots and possibly more time on the computer.

VI - FINAL COMMENTS AND SUGGESTIONS FOR FUTURE WORK.

In this chapter we take stock of the results already obtained in order that the importance of future work can be assessed. This assessment will allow us to optimize the theoretical and the practical research.

So far in considering a single cell fermentation process only substrate-limited fermentation processes have been analyzed. It is also possible to consider product-inhibited fermentation processes. In such problems three balance equations have to be solved - one for the micro-organism, one for the limiting substrate and one for the product. A possible kinetic model for such a process may be expressed by the relationship

$$R_g = \mu m \tag{6.1}$$

where

$$\mu = \frac{\mu^* s}{K_s + s + p^2/K_i} \tag{6.2}$$

and

$$R_s = \frac{1}{Y_s} R_g \tag{6.3}$$

and

$$R_p = \frac{1}{Y_p} R_p \tag{6.4}$$

In meetings of the Tower Fermenter Research Group at Aston mention has frequently been made of the importance of the so-called secondary metabolites. This word was coined by micro-biologists to describe products of fermentation processes in the non-growth phase. However, the absence of a widely accepted model for such processes precludes any possibility of theoretical analysis at the present time, although it could be a profitable area in the future.

When considering fermentation processes where microbial aggregates occur we find that extensive use has been made of the

analogy between floes/films and catalyst pellets/slabs (See the work of ATKINSON and co-workers [75]-[76]. The idea is appealing, but the quasi-steady state situation is far from real and the agreement that it is a reasonable assumption does not satisfy the desire for a more exact approach. The latter can be started by abandoning the above analogy and considering models which describe more realistically the microbial growth phenomena. The correct mathematical problem for a microbial film, assuming MONOD kinetics, is

$$\frac{\partial s}{\partial t} = D \frac{\partial^2 s}{\partial y^2} - \frac{K_{max}\, s}{K_s + s} \tag{6.5}$$

$$s - s_o = D \frac{\partial s}{\partial y} \text{ at } y = \ell(t);\ t \geq 0 \tag{6.6}$$

$$\frac{\partial s}{\partial y} = 0 \text{ at } y = 0;\ t \geq 0 \tag{6.7}$$

$$\frac{d\ell}{dt} = -K \frac{\partial s}{\partial y} \text{ at } y = \ell(t);\ t \geq 0 \tag{6.8}$$

and for a spherical floc

$$\frac{\partial s}{\partial t} = \frac{D}{r^2} \frac{\partial}{\partial r} \left[r^2 \frac{\partial s}{\partial r} \right] = \frac{K_{max}\, s}{K_s + s} \tag{6.9}$$

$$s - s_o = D \frac{\partial s}{\partial r} \text{ at } r = \ell(t);\ t \geq 0 \tag{6.10}$$

$$\frac{\partial s}{\partial r} = 0 \text{ at } r = 0\ ;\ t \geq 0 \tag{6.11}$$

$$\ell^2 \frac{d\ell}{dt} = -K \frac{\partial s}{\partial r} \text{ at } r = \ell(t);\ t \geq 0 \tag{6.12}$$

The above mathematical problem constitutes a non-linear Stefan Problem with the non-linearity due to the source term. A preliminary search in the mathematical literature appears to indicate that this kind of problem has never been considered before. The non-linear Stefan Problems already studied are due to the presence of a non-linear coefficient, i.e., $D = D(s)$. FIGURES (6.1) and (6.2) show the meaning of $\ell(t)$ for film and flocs respectively. In the construction of the above equations the microbial concentration inside of the film/floc is assumed constant.

FIGURE (6.1)

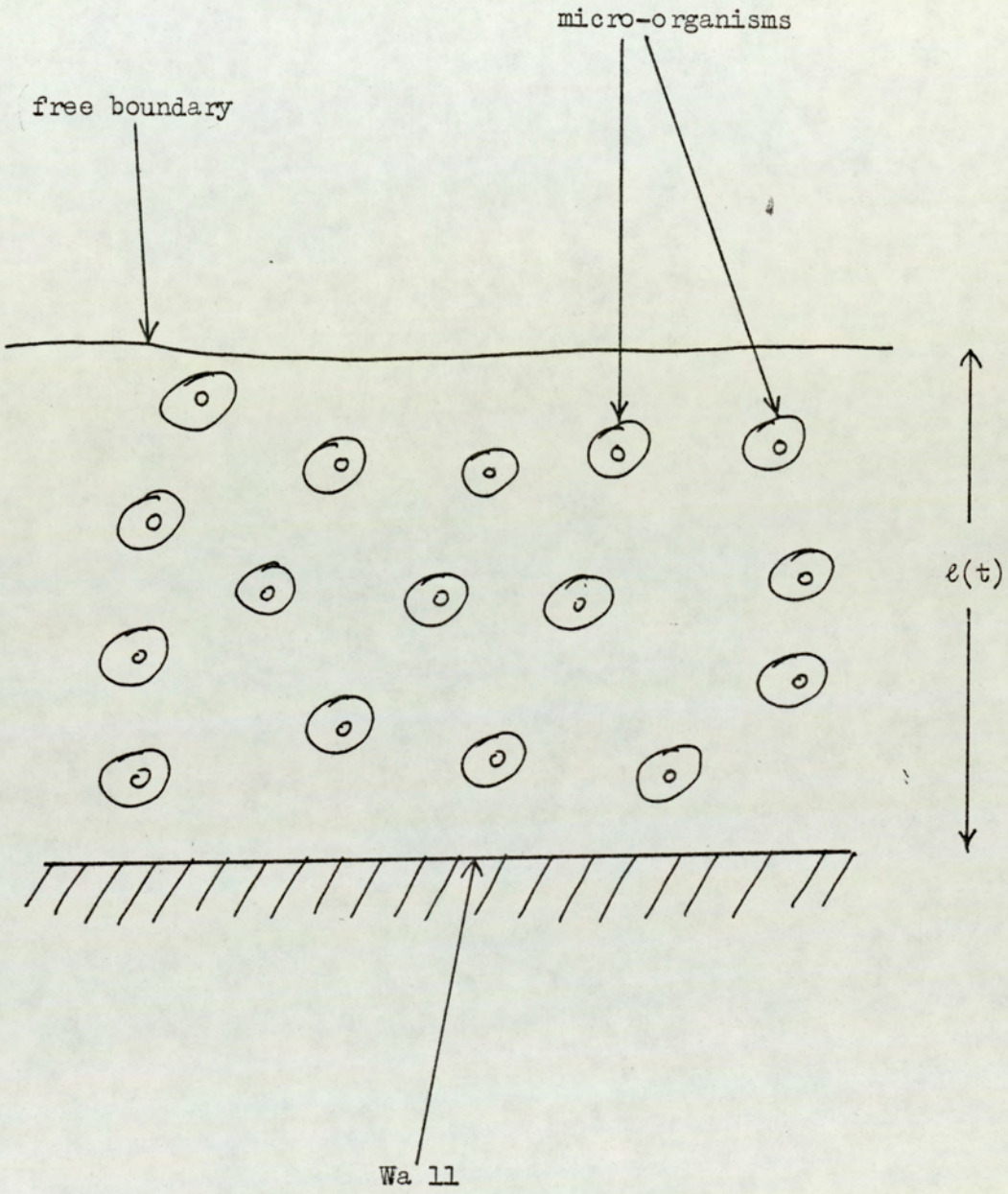


Diagram of a microbial film.

FIGURE (6.2)

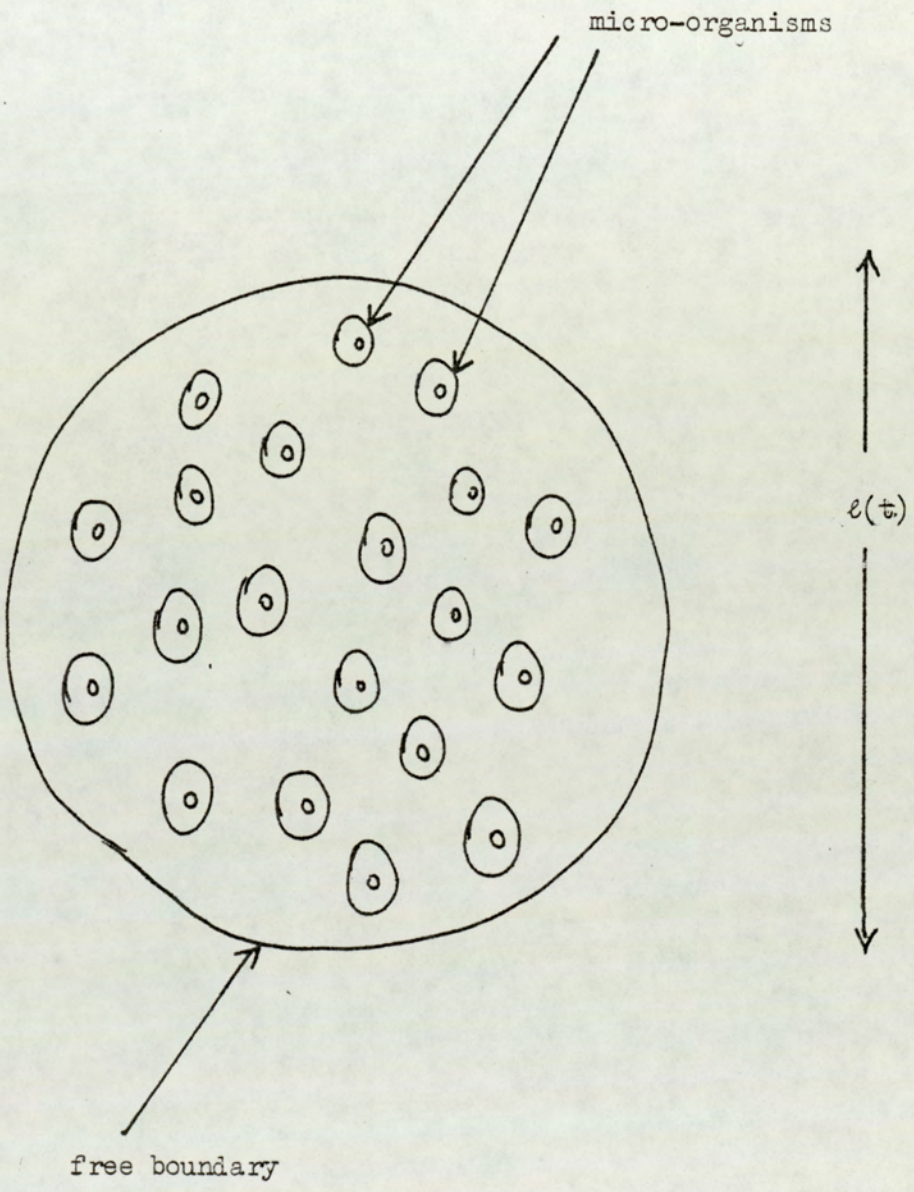


Diagram of a microbial floc.

Another possibility for future work is to consider the dispersion coefficients of the nutrient and microbial phases to be different. This is a natural continuation of the present research and only time constraints prevented us from including such an analysis in the thesis. Such a case appears to be important when flocculation occurs, but as yet there are no experimental data to support such modelling approaches. For a non-gaseous limiting substrate it is possible to take advantage of the relation

$$u_s = v_s \quad \text{at } y = 0 \tag{6.13}$$

to simplify the numerical calculations.

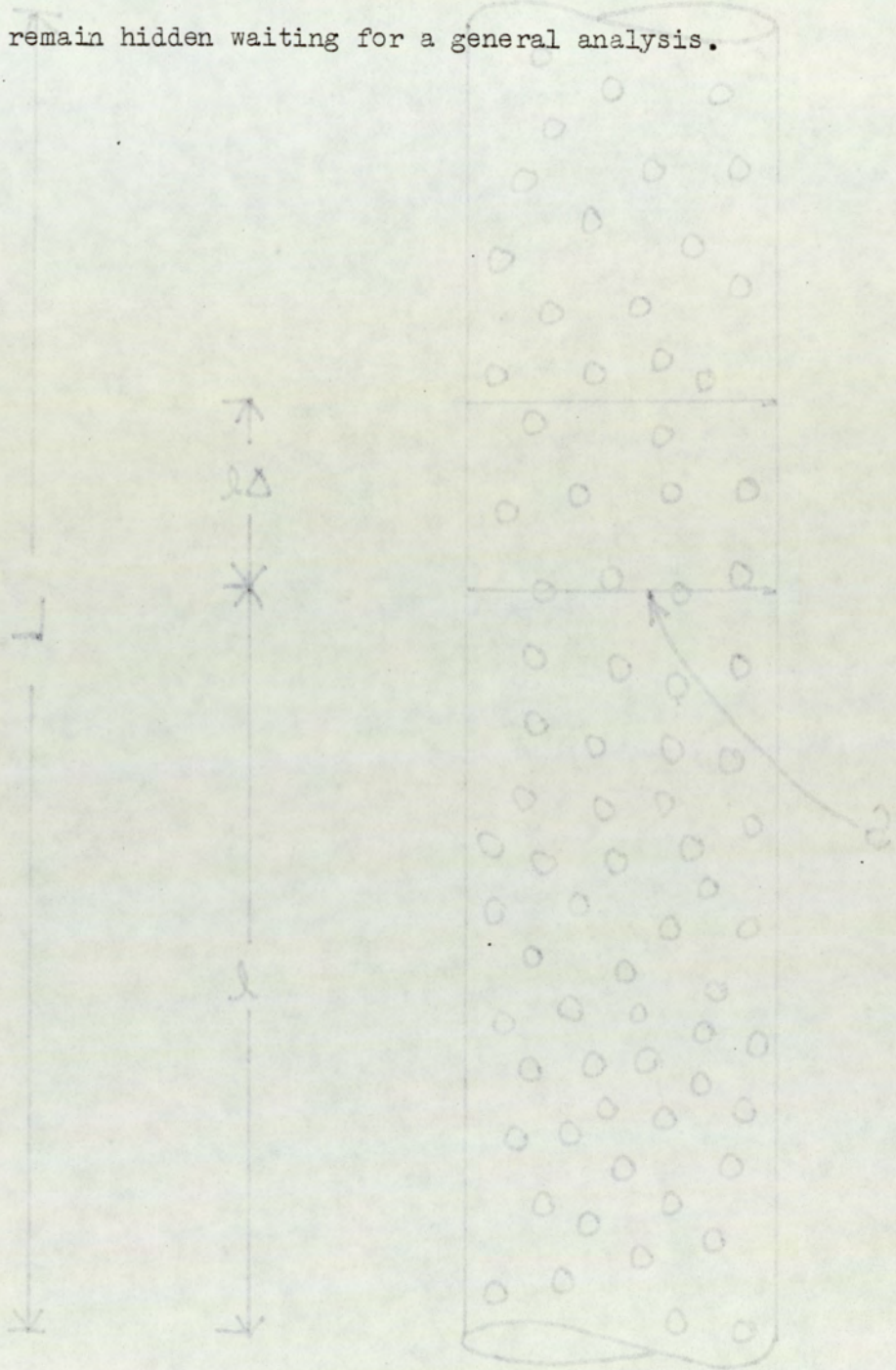
As far as numerical analysis is concerned the work is still incomplete. The results obtained to date are not as advanced as we expected, and the mathematical tools used are not as sophisticated as those employed in the analysis of tubular chemical reactors. Nevertheless the results are useful because they show that those obtained by the lumped approximation are not far from the truth, at least in qualitative terms.

For those looking for an analytical area of research it is worth pointing out that the equation which governs the steady-state for a non-gaseous limiting substrate, i.e., equation (3.5.11), belongs to a class of non-linear equations called non-linear equations of polynomial class [78]. It is possible that in a theoretical study of multiplicity this kind of non-linear equation might provide a fruitful starting point and, consequently, some general mathematical conclusions may be obtained if someone looks in this direction.

On experimental grounds we would like to see if the predictions of our analysis, especially those concerned with variations of Bo, are confirmed or refuted. In the case of disagreement between model and experiment the cause must be elucidated in order that the model be modified in the correct way. A comparison of the mixing

patterns of nutrient and microbial phases, especially when microbial flocs occur, may be useful in the design of tubular equipment.

The suggestions we have made in this section represent only the tip of the iceberg, and a large number of problems still remain hidden waiting for a general analysis.



APPENDIX A

MATERIAL BALANCE FOR AEROBIC FERMENTATION PROCESSES IN TUBULAR REACTORS.

Let us consider a tubular reactor in which an aerobic fermentation process is occurring. The reactor is shown diagrammatically in FIGURE (A-1). Its length is L and its cross sectional area is S.

The material balance equations are obtained by carrying out balances over a thin cylinder through which the culture and the air are flowing (See FIGURE (A-1)).

For unsteady-state conditions, the material balance is

$$\begin{bmatrix}\text{rate of mass}\\ \text{accumulation}\end{bmatrix} = \begin{bmatrix}\text{rate of mass}\\ \text{in}\end{bmatrix} - \begin{bmatrix}\text{rate of mass}\\ \text{out}\end{bmatrix} + \begin{bmatrix}\text{rate of mass}\\ \text{generation}\end{bmatrix} \qquad \text{(A-1)}$$

We begin applying the law of conservation to the microbial mass. The rates of microbial mass in through the face at ℓ due to convective motion and turbulent mixing are, respectively

$$\begin{bmatrix}\text{rate of microbial mass in}\\ \text{due to convective motion}\end{bmatrix} = m\Big|_{\ell} V(1-\varepsilon)S \qquad \text{(A-2)}$$

$$\begin{bmatrix}\text{rate of microbial mass in}\\ \text{due to turbulent mixing}\end{bmatrix} = J_m\Big|_{\ell} (1-\varepsilon)S \qquad \text{(A-3)}$$

and the rates if microbial mass out through the face at $\ell + \Delta\ell$ are

$$\begin{bmatrix}\text{rate of microbial mass out}\\ \text{due to convective motion}\end{bmatrix} = m\Big|_{\ell+d\ell} V(1-\varepsilon)S \qquad \text{(A-4)}$$

$$\begin{bmatrix}\text{rate of microbial mass out}\\ \text{due to turbulent mixing}\end{bmatrix} = J_m\Big|_{\ell+d\ell} (1-\varepsilon)S \qquad \text{(A-5)}$$

The rate of mass generation within the volume element is

$$\begin{bmatrix}\text{rate of microbial mass generation}\\ \text{within the volume element}\end{bmatrix} = R_g(1-\varepsilon)S\ \Delta\ell \qquad \text{(A-6)}$$

and finally the rate of microbial mass accumulation in the volume element is

$$\begin{bmatrix}\text{rate of accumulation of}\\ \text{microbial mass in the volume element}\end{bmatrix} = (1-\varepsilon)S\ \frac{\partial m}{\partial t}\ \Delta\ell \qquad \text{(A-7)}$$

Introducing (A-2)-(A-7) into (A-1) and dividing by $(1-\varepsilon)S\ \Delta\ell$ we get

$$\frac{\partial m}{\partial t} = -V\ \frac{m\big|_{\ell+\Delta\ell} - m\big|_{\ell}}{\Delta\ell} - \frac{J_m\big|_{\ell+\Delta\ell} - J_m\big|_{\ell}}{\Delta\ell} + \gamma_g \qquad \text{(A-8)}$$

Considering that

$$\lim_{\Delta\ell \to 0} \frac{m\big|_{\ell+\Delta\ell} - m\big|_{\ell}}{\Delta\ell} = \frac{\partial m}{\partial \ell} \qquad \text{(A-9)}$$

and

$$\lim_{\Delta\ell \to 0} \frac{J_m\big|_{\ell+\Delta\ell} - J_m\big|_{\ell}}{\Delta\ell} = \frac{\partial J_m}{\partial \ell} \qquad \text{(A-10)}$$

we obtain

$$\frac{\partial m}{\partial t} + V\ \frac{\partial m}{\partial \ell} = -\frac{\partial J_m}{\partial \ell} + R_g. \qquad \text{(A-11)}$$

Since

$$R_c = \frac{R_g(m,s)}{Y} \qquad \text{(A-12)}$$

we have to consider a material balance on the limiting substrate. The balance will be similar to the microbial balance. Consequently we can write

$$\begin{bmatrix}\text{rate of limiting substrate in}\\ \text{due to convective motion}\end{bmatrix} = s\big|_{\ell}\ V(1-\varepsilon)S \qquad \text{(A-13)}$$

$$\begin{bmatrix}\text{rate of limiting substrate in}\\ \text{due to mass transfer.}\end{bmatrix} = K_L a(s^*-s)S\ \Delta\ell \qquad \text{(A-14)}$$

$$\begin{bmatrix}\text{rate of limiting substrate out}\\ \text{due to convective motion}\end{bmatrix} = s\big|_{\ell+\Delta\ell}\ V(1-\varepsilon)S \qquad \text{(A-15)}$$

$$\begin{bmatrix}\text{rate of limiting substrate out}\\ \text{due to turbulent mixing}\end{bmatrix} = J_s\big|_{\ell+\Delta\ell}\ (1-\varepsilon)S \qquad \text{(A-16)}$$

$$\begin{bmatrix}\text{rate of limiting substrate consumption}\\ \text{within volume element}\end{bmatrix} = R_s(1-\varepsilon)S\ \Delta\ell \qquad \text{(A-17)}$$

and

$$\begin{bmatrix}\text{rate of accumulation of}\\ \text{limiting substrate in the volume element}\end{bmatrix} = (1-\varepsilon)S\ \frac{\partial s}{\partial t}\ \Delta\ell \qquad \text{(A-18)}$$

Introducing (A-13)-(A-18) into (A-1) and dividing by $(1-\varepsilon)S\ \Delta\ell$ we get

$$\frac{\partial s}{\partial t} = -V\ \frac{s\big|_{\ell+\Delta\ell} - s\big|_{\ell}}{\Delta\ell} - \frac{J_s\big|_{\ell+\Delta\ell} - J_s\big|_{\ell}}{\Delta\ell} + K_L a(s^*-s) + R_s \qquad \text{(A-19)}$$

But

$$\lim_{\Delta\ell \to 0} \frac{s\big|_{\ell+\Delta\ell} - s\big|_{\ell}}{\Delta\ell} = \frac{\partial s}{\partial \ell} \qquad \text{(A-20)}$$

and

$$\lim_{\Delta\ell \to 0} \frac{J_s\big|_{\ell+\Delta\ell} - J_s\big|_{\ell}}{\Delta\ell} = \frac{\partial J_s}{\partial \ell} \qquad \text{(A-21)}$$

so

$$\frac{\partial s}{\partial t} + V\ \frac{\partial s}{\partial \ell} = \frac{\partial J_s}{\partial \ell} + K_L a(s^*-s) + R_s. \qquad \text{(A-22)}$$

Assuming an analogy between mixing and molecular diffusion, we write

$$J_m = -D_m\ \frac{\partial m}{\partial \ell} \qquad \text{(A-23)}$$

and

$$J_s = -D_s\ \frac{\partial s}{\partial \ell} \qquad \text{(A-24)}$$

In spite of the lack of experimental values of D_m and D_s we would expect that

$$D_m \neq D_s \qquad \text{(A-25)}$$

However, in this work we will assume that

$$D_m = D_s = D \qquad \text{(A-26)}$$

leaving the former case to future studies. Introducing (A-23) and (A-24) into (A-11) and (A-22) we get

$$\frac{\partial m}{\partial t} + V \frac{\partial m}{\partial \ell} = D \frac{\partial^2 m}{\partial \ell^2} + R_g \qquad \text{(A-27)}$$

$$\frac{\partial s}{\partial t} + V \frac{\partial s}{\partial \ell} = D \frac{\partial^2 s}{\partial \ell^2} + K_L a(s^*-s) + R_s \qquad \text{(A-28)}$$

Finally, we assume that

$$R_g = \frac{\mu_{max}\, m\, s}{K_s + s + s^2/K_i} \qquad \text{(A-29)}$$

and

$$R_s = -\frac{1}{Y} \frac{\mu_{max}\, m\, s}{K_s + s + s^2/K_i} \qquad \text{(A-30)}$$

and on introducing these relationships into (A-27) and (A-28) we obtain

$$\frac{\partial m}{\partial t} + V \frac{\partial m}{\partial \ell} = D \frac{\partial^2 m}{\partial \ell^2} + \frac{\mu_{max}\, m\, s}{K_s + s + s^2/K_i} \qquad \text{(A-31)}$$

and

$$\frac{\partial s}{\partial t} + V \frac{\partial s}{\partial \ell} = D \frac{\partial^2 s}{\partial \ell^2} + K_L a(s^*-s) - \frac{1}{Y} \frac{\mu_{max}\, m\, s}{K_s + s + s^2/K_i} \qquad \text{(A-32)}$$

In developing the above mathematical model certain assumptions were made and these simplify the mathematical model considerably. They are:

a) flat velocity profile,

b) axial dispersion only,

c) the same dispersion coefficient for the nutrient and microbial phases,

d) Haldane enzyme kinetics.

Although in practice very few systems, if any, qualify to be described in this way, it is useful to examine this model to illustrate the principles which govern the use of a tubular reactor for fermentation processes.

APPENDIX B

ANALYSIS OF LOCAL STABILITY FOR NON LINEAR ORDINARY DIFFERENTIAL EQUATIONS USING THE FIRST METHOD OF LIAPUNOV

Since the work of BILOUS and AMUNDSON [B-1] in 1955, it has become a straightforward matter to evaluate the local stability of chemical reactors governed by an autonomous system of ordinary differential equations. The First Method of Liapunov provided a basis for the study of the local stability of the steady-states.

Consider the system

$$\frac{d\underline{x}}{dt} = \underline{f}(\underline{x}) \tag{B-1}$$

where

$$\underline{x} = \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} \tag{B-2}$$

and

$$\underline{f}(\underline{x}) = \begin{bmatrix} f_1(x_1, x_2) \\ f_2(x_1, x_2) \end{bmatrix} \tag{B-3}$$

A steady-state solution $\underline{x}_s$ of this system is one which satisfies

$$\underline{f}(\underline{x}_s) = \underline{0} \tag{B-4}$$

It was shown by LIAPUNOV [B-1] that the question of the stability of a steady-state could be answered by investigating the properties of equations (B-1) linearized about the steady-state. This system of linearized equations can be represented by

$$\frac{d\underline{Y}}{dt} = \underline{A}.\underline{Y} \tag{B-5}$$

where

$$\underline{Y} = \underline{x} - \underline{x}_s \tag{B-6}$$

and

$$\underline{A} = \nabla \underline{f}(\underline{x}) \Big|_{\underline{x} = \underline{x}_s} \tag{B-7}$$

$\nabla \underline{f}(\underline{x})$ is the gradient of the vector field $\underline{f}(\underline{x})$ and may be represented as

$$\nabla \underline{f}(\underline{x}) = \begin{bmatrix} \frac{\partial f_1(x_1,x_2)}{\partial x_1} & \frac{\partial f_1(x_1,x_2)}{\partial x_2} \\ \frac{\partial f_2(x_1,x_2)}{\partial x_1} & \frac{\partial f_2(x_1,x_2)}{\partial x_2} \end{bmatrix} \tag{B-8}$$

Let us represent the determinant and the trace of $\underline{A}$ as det $\underline{A}$ and tr $\underline{A}$ respectively. Then, according to HLAVACEK, KUBICEK and JELINEK [B-2] the critical point $\underline{y} = \underline{0}$ is classified as follows:

1. If det $\underline{A} < 0$, it is a saddle point and consequently always unstable.
2. If det $\underline{A} > 0$ and $(\text{tr } \underline{A})^2 - 4 \det \underline{A} \geq 0$, it is a node. It is a stable node if tr $\underline{A} < 0$ and an unstable node if tr $\underline{A} > 0$.
3. If det $\underline{A} > 0$ and $(\text{tr } \underline{A})^2 - 4 \det \underline{A} < 0$, it is a focus. It is a stable focus if tr $\underline{A} < 0$ and an unstable focus if tr $\underline{A} > 0$.

It is easy to see that the necessary and sufficient condition for the steady-state to be asymtotically stable is for the conditions

$$\det \underline{A} > 0 \tag{B-9}$$

$$\text{tr } \underline{A} < 0 \tag{B-10}$$

to be satisfied. In spite of the fact that no information is obtained about how large a perturbation can be tolerated before unstability will occur, the linear approximation analysis still remains as the most useful single approach to system stability.

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APPENDIX C.

EQUATIONS USED FOR PREPARING FIGURES (4.5.1) TO (4.5.12).

The following equations were used for preparing the graphs shown in Chapter IV:-

1. $$Fe^* = \frac{1 + (V_o - U_s)}{(V_o - U_s)} \qquad (C\text{-}1)$$

to plot the non-sterile steady state shown in FIGURE (4.5.1)-(4.5.3).

2. $$Fe^* = \frac{U_s[1 + (V_o - U_s)]}{(U_o + U_s)(V_o - U_s)} \qquad (C\text{-}2)$$

to build FIGURES (4.5.4)-(4.5.6)

3. $$Fe^* = \frac{1 + (V_o - U_s) + \ln(V_o - U_s)}{(V_o - U_s)} \qquad (C\text{-}3)$$

to calculate the non-sterile steady-state plotted in FIGURES (4.5.7)-(4.5.9).

4. $$Fe^* = \frac{U_s[1 + (V_o - U_s) + \ln(V_o - U_s)^2]}{(U_o + U_s)(V_o - U_s)} \qquad (C\text{-}4)$$

to obtain FIGURES (4.5.10)-(4.5.12).

NOMENCLATURE.

[ ] gives dimensions: ( ) defines symbol

$\underline{A}$ = matrix defined in Appendix A

Bo = Bodenstein number $\left(\frac{LV}{D}\right)$

D = dispersion coefficient $[L^2T^{-1}]$

Fe = fermentation number $\left(\frac{\mu^* L}{V}\right)$

In = inhibition number $\left(K_s/K_i\right)$

K_{La} = volumentric mass transfer coefficient $[T^{-1}]$

K_s = saturation constant $[ML^{-3}]$

K_i = inhibition constant $[ML^{-3}]$

ℓ = axial distance [L]

L = tube length [L]

m = microbial concentration $[ML^{-3}]$

Ma = mass transfer number $\left(\frac{K_{La}L}{V}\right)$

p = product concentration $[ML^{-3}]$

R_g = rate of microbial growth $[ML^{-3}T^{-1}]$

R_c = rate of substrate consumption $[ML^{-3}T^{-1}]$

s = substrate concentration $[ML^{-3}]$

t = time [T]

u = dimensionless microbial concentration $\left(\frac{m-m_o}{YK_s}\right)$

u_o = dimensionless inlet microbial concentration $\left(\frac{mo}{YK_s}\right)$

v = dimensionless substrate concentration $\left(\frac{s_o-s}{K_s}\right)$

v_o = dimensionless inlet microbial concentration $\left(\frac{s_o}{K_s}\right)$

V = axial velocity $[LT^{-1}]$

x = dimensionless time $\left(\frac{VT}{L}\right)$

y = dimensionless axial distance $\left(\frac{L-\ell}{L}\right)$

Y = yield coefficient

w = dimensionless variable $(w-u-v)$

λ_i = eigenvalue

μ_{max} = maximum specific growth rate $[T^{-1}]$

μ^* = maximum specific growth rate $[T^{-1}]$

ψ = modifying factor

ϕ = function

Subscripts

0 = inlet value

i = initial value

s = steady-state value

Superscripts

* = when used with variable means the value at the gas/culture interface

* = when used with dimensionless numbers means the modified number used with the lumped approximation method (see Chapter 4)

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