ABSTRACT

Pure Strong Competition for Two Nutrients by Two Microbial Populations in a Chemostat

by
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The dynamics of pure, strong, double competition between two microbial populations in an ideal chemostat have been investigated by using mathematical and numerical analysis. The two nutrients competed for have been assumed to be complementary for both competitors. Inter active models have been used for the specific growth rates. Two cases have been considered; one in which neither of the two substrates exerts inhibitory effects on the growth of either one of the competing populations, and one in which the growth of one population is inhibited by only one of the two substrates. The primary focus of this investigation was on the coexistence steady state and the ability to maintain a mixed culture in a chemostat. It has been found that except for rare cases, there are regimes in the operating parameters space of a chemostat where coexistence is possible. Conditions for stability have been derived, situations where multiple states are possible have been found, and the main results are presented in the form of characteristic two-dimensional diagrams.

PURE STRONG COMPETITION FOR TWO NUTRIENTS BY TWO MICROBIAL POPULATIONS IN A CHEMOSTAT

by
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This Thesis is dedicated to
my Grandparents

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CHAPTER 1
INTRODUCTION

Microorganisms are responsible for many human diseases, and are also known as agents that spoil food. Even though they can be harmful to humans, microorganisms can also be beneficial to mankind by producing useful products [13] and by destroying harmful materials [25]. Dionysus (Greek ancient god) was credited by the ancient Greeks with the invention of *Fermentation* for the production of wine. What the Greeks back then most probably did not know is that microorganisms were the biological agents responsible for their wine production. Fermentation products, such as food (cheese, yoghurt, bread, etc), beverages (wine, etc), vitamins, antibiotics, aminoacids, and many more, are essential for life. It was not until the late nineteenth century that Pasteur and Tyndall identified microorganisms as the active agents in the up till then primitive fermentation technology. Further work in the early twentieth century from various researchers led to the development of processes for the production of chemicals such as ethanol. But microorganisms find application not only in fermentation technology. In *Environmental engineering* microorganisms decompose municipal and industrial wastes and thus decrease the negative impact of these materials on the environment. In *Genetic engineering* existing species are cloned for the production of new strains having specified desired properties. Microorganisms can be employed even in the *Mining industry* (e.g. leaching of sulfur from coal). Microorganisms are also used by nature itself for the formation of coal, oil, for the mineralization of dead organic matter, for the regeneration of the atmosphere, etc. It is not possible for the biosphere to function without microorganisms.

The 1940's mark the birth of systematic biochemical engineering. In that period humanity entered the era of antibiotics which gave relief to man's suffering from disease.

Microbial populations in order to grow and reproduce need a number of materials which are essential in their cellular economy. These materials include: (1) an energy source (energy can be obtained by breaking chemical bonds or from light); (2) a carbon source (which can be the same as the energy source); (3) a nitrogen source; (4) minerals such as phosphorus, potassium, sulfur, magnesium (major minerals) and iron, copper, cobalt, zink, manganese, molybdenum (minor minerals); (5) growth factors such as vitamins, which the cell may be able to synthesize and if not, they have to be externally supplied; (6) dissolved gases such as oxygen.

Depending on how microbial populations meet their needs for the above mentioned materials, they are divided into osmotrophic (bacteria, yeasts, molds, microalgae) and phagotrophic (protozoa) microorganisms. Based on how they satisfy their needs for specific elements, species are divided into heterotrophic and autotrophic (which are divided into photoautotrophs and chemoautotrophs) microorganisms.

Various environmental factors such as temperature, pressure, and medium properties (pH, toxins, inhibitors) may affect the growth of microorganisms.

In industrial operations, either pure or mixed cultures are used. Pure cultures are predominant in the fermentation industry while mixed cultures are useful for waste treatment. When several populations of microorganisms share a common environment they will interact with one another. Fredrickson [10] classifies interactions into positive and negative, direct and indirect.

Competition is the most common microbial interaction, and its patterns have been discussed by Fredrickson and Stephanopoulos [11]. The same authors have defined competition between two species as follows: Two populations X and Y compete for a resource s_1, if and only if: (1) both populations use, but do not necessarily require, s_1; (2) s_1 has a dynamical effect on at

least one of X and Y. If competition is the only interaction between two species and if it occurs for a single resource, the pattern is called pure and simple competition. Competition may be single or double depending upon the number of resources competed for. Competition between two populations is strong when all resources competed for have a dynamical effect on both populations.

Regarding nutrients, they are classified as complementary when they fulfill different needs in the cellular economy or as substitutable when they fulfill the same needs in the cellular economy (e.g. two different carbon sources). This topic has been addressed by various authors, see for example Baltzis and Fredrickson [5].

In order to understand the dynamics of a microbial system we must: (1) identify the populations involved; (2) identify the population-changing processes; (3) identify the environmental factors and study how they affect the population-changing processes; and (4) identify how the population-changing processes affect the environment. Over the years a large number of models describing microbial growth has been derived. Most of them are highly idealized expressions describing only some aspects of the problem. This is the result of the fact that it is almost impossible to formulate a model which includes and takes into account every aspect of the problem. After a model is derived, its predictions should be tested experimentally. If the model is valid, it can be improved by incorporating neglected aspects of the problem and the scheme model-experimental testing-improved model should be repeated. First, one needs a model for describing growth. Having an adequate such model, maintenance, lysis, variability of yield coefficients are some of the species related phenomena which need to be investigated. Moving then to the reactors used, one can relax the assumption of ideal chemostats and consider effects of mixing, of cell attachment to the walls of the reactor etc.

Very fast the picture becomes too complicated.

Even though models can be simplistic at times, they nevertheless can help us get valuable insight in key aspects of dynamics, and guide us in developing a proper experimental plan. The present study does not involve experiments. It is a theoretical investigation of the possibility to maintain a mixed culture at steady state in an ideal chemostat. Two populations are considered, and they compete for two complementary resources. There is no other interaction, hence competition is pure. Since it occurs for two resources, competition is not simple but double. Furthermore, it is assumed that the availability of both nutrients exerts dynamical effects on both species hence, competition is strong. Two cases are considered. In the first, neither substrate is inhibitory for either population while in the second one of the substrates is inhibitory for one of the two competitors. A number of results have been obtained analytically , while the investigation has been completed by extensive numerical studies.

CHAPTER 2
LITERATURE REVIEW

The question regarding the proper way to express the specific growth rate of a population when more than one resource is present at relatively low levels in the environment where growth occurs, started being of interest to researchers in the late sixties and to date, has not been completely resolved. This is due to the fact that it is not easy to understand cellular regulatory processes as has been discussed by various investigators [e.g., [12] and [25] with regard to biodegradation of pollutants].

With regard to substitutable resources, organisms have been found to use substrates sequentially or simultaneously. For example, Lee et al. [21] have reported that when a medium containing glucose and lactate is inoculated with *P.shermanii*, lactate is consumed first and then glucose utilization begins. This is a typical case where a species exhibits diauxic growth.

Yoon et al. [35] assumed that two (or more) substitutable resources are simultaneously used, but the uptake of each resource is inhibited (in a competitive fashion) by the other substrates. By modifying the Monod model to include the postulated inhibitory effects and by using a sequence of "microbial reactions", they applied the pseudo-steady-state approximation for intermediates to develop a generalized expression for the specific growth rate. They tested their model in two series of experiments. In both series they used mixtures of glucose and fructose in batch experiments. In the first series of experiments they used the species *Bacillus cereus*, while in the second series they used *Candida tropicalis*. In both cases they found good agreement between experimental data and their proposed model.

Ramkrishna [26] introduced a completely new concept, that of cybernetic approach, for modelling growth of microorganisms on multiple substitutable resources. In this approach, the use of substrates is based on the principle

of optimal allocation of existing resources as microbes have the capability to control their regulatory processes in order to maximize their growth rate. In this approach, a fundamental question is whether optimization can be done at every instant, or if microbes need a finite time period for achieving optimization.

Kompala et al. [15] have developed cybernetic models assuming that optimization can be accomplished at every instant of time (also known as short-term perspective). In one case the assumed objective was maximum biomass productivity, while in a second case they used the "matching law". In the first approach, the model assumes that at any instant of time the organism synthesizes the key enzyme required for the utilization of a given substrate in order to maximize biomass growth at that instant of time. This model does not account for inhibition or activation of existing enzymes and thus, it would not necessarily predict the maximum average productivity if any changes in the environment are with respect to enzymes which have not been accounted for in the optimization approach. The "matching law" approach takes into consideration inhibition and activation of the existing enzymes and can predict more phenomena. The model has been tested in batch experiments [16] when *Klebsiella oxytoca* was fed with various mixtures made of the following carbon/energy sources: glucose, xylose, arabinose, lactose, and fructose. Good agreement was found between experimental data and model predictions. In fact, when sequential use of the substrates was observed, the model not only predicted the diauxic growth but the order in which the substrates were removed as well.

Dhurjati et al. [9] considered a cybernetic model assuming that optimization is not an instantaneous process as Kompala et al. [15] assumed, but that it is accomplished over a finite period of time. Using *Klebsiella pneumoniae* growing in batch culture on mixtures of D-glucose and D-xylose, they were

able to get limited agreement between their data and their model predictions.

Regarding complementary resources, two schools of thought have developed over the years. Some researchers have argued that when two complementary resources are present at low concentrations, both exhibit a dynamical effect on the growth of a population. These researchers have used what are known as interactive models. A second group of researchers has argued that under no conditions can more than one substrate exert rate limitation on the growth of a population. These researchers have used what are known as non-interactive models.

Megee et al. [23] have used an interactive model to describe the growth of *Lactobacillus casei* in glucose and riboflavin minimal media. Their model is essentially a product of two Monod-type expressions, one involving the concentration of glucose while the other that of riboflavin. They had excellent agreement between data and model predictions.

Cooney and Wang [8] also used an interactive model to describe the growth of *Enterobacter aerogenes NCTC 418* in nitrogen and phosphate minimal media. They found good agreement between model and data, except in cases where one of the nutrients was supplied in excess. Namely, when the cells were provided with ammonia (in a pulse fashion) sufficient to remove nitrogen limitation, the maximum specific growth rate achieved was not what the model predicted in the limit where nitrogen would not be limiting.

Sinclair and Ryder [28] used two interactive models for describing the growth of *Candida utilis* in oxygen and glucose minimal media. The first model was the expression of Megee et al. [23] discussed previously, while the second was a product of a Monod-type expression involving the oxygen concentration and a Contois-type expression involving the glucose concentration. They concluded that the second model could describe the data more accurately than the first one. In an earlier study with the same system but

different concentration levels of glucose and oxygen, the same authors introduced a non-interactive model. This model descsribed in Ryder and Sinclair [27], assumes that the specific growth rate is given by either a Monod model involving the oxygen concentration or a Monod model involving the glucose concentration. Which one of the two expressions should be used is determined by which one predicts the lowest biomass production at steady state, and under the given operating conditions of the chemostat. This model cannot be correct since it cannot work in a batch situation. Probably because of this problem, these researchers used an interactive model in their batch studies [28] discussed above.

Sykes [30] proposed a non-interactive model which assumes that the specific growth rate is given by a Monod model involving either one or the other of the substrates. Up to this point, the model is identical to that of Ryder and Sinclair [27]. The difference is with regard to which of the two expressions should be actually used. Sykes proposed that the expression having the smaller value should be used (the comparison being made at every instant of time). He was able to show that in the operating parameters space of a chemostat, the regions where growth occurs under limitation of either nutrient do not overlap.

In an effort to resolve the controversy between proponents of interactive models and proponents of non-interactive models, Bader [3] used conceptual and mathematical descriptions to argue that a unique model describing all cases of growth under conditions where two complementary nutrients are present in less than saturation levels may not exist. In fact, he argued that there must be operating regimes where growth cannot be described but by an interactive model, and other regimes where a non-interactive model is needed.

Baltzis and Fredrickson [5] observed that all non-interactive models pro-

posed up-till then, assumed that yield coefficients were constant regardless of what substrate was rate-limiting. For example the yield of *Candida utilis* on glucose was assumed constant regardless of whether glucose was the rate-limiting substrate or not [27]. From a number of published experimental results they found that the assumption of constant yield coefficients was not correct. Relaxing this assumption, and using a model practically the same as that of Sykes [30] they were able to show that even if a non-interactive mobel is used, there are domains in the operating parameters space (for a chemostat) where growth actually occurs under dual limitation. This model although too simplistic in the sense that it assumes for the yield coefficient a switch from one value to another as the identity of the rate-limiting nutrient changes, it has nevertheless shown that dual limitation does exist and it does not require, as Bader [3] suggested, an interactive model to express it.

This concludes the literature review on how to express growth rates when more than one nutrient is present at relatively low concentrations in the environment of growth. In the present thesis, interactive models have been employed.

Regarding competition, the literature is fairly extensive especially for the pattern which is pure and simple, and for the case of non-inhibitory growth. A good review of this subject can be found in Fredrickson and Stephanopoulos [11]. Aris and Humphrey [2] have studied competition between two species for a single inhibitory substrate, when the specific growth rate is expressed via an Andrews [1] expression. The main conclusion is that pure and simple competitors cannot coexist at a steady state in an ideal chemostat. Steady state coexistence of two pure and simple competitors has been found to be possible in two interconnected chemostats [17, 18]. These results cannot be extended to any number of competitors since it has been found that three pure and simple competitors cannot coexist in three interconnected chemostats [7].

Competition between two species for two resources has been studied up to a certain extent.

When two species compete for two substitutable resources, it has been found that coexistence can occur at steady state in a chemostat. For example, Yoon et al. [35] in a study which has been already mentioned earlier in this review, studied competition between *Bacillus cereus* and *Candida tropicalis* for a mixture of fructose and glucose. They found coexistence to be possible, and in fact their proposed model predicts that it is possible to maintain a mixed culture at a steady state in a chemostat even when the competitors exhibit strong preference for one of the substrates competed for. León and Tumpson [22] have concluded that when two species compete for two perfectly or imperfectly substitutable resources, coexistence is possible at a stable equilibrium point provided that at that point a different resource contributes more to the growth of each competitor

In the aforementioned study by León and Tumpson [22], competition for two complementary nutrients between two species has been also considered. In this study a non-interactive model was essentially used and it was concluded that coexistence can occur at a stable equilibrium point provided that at that point each competitor consumes its own rate limiting resource at a rate faster than the other species. In this case, although both species utilize both substrates, a different nutrient is rate limiting for each one of the populations, hence competition is not strong.

Using the interactive model of Megee et al. [23] which has been discussed earlier in this review, Yoon and Blanch [34] and Taylor and Williams [31] have studied competition between two species for two complementary resources. These studies have concluded that stable coexistence of the two competitors is possible in a chemostat. Yoon and Blanch [34] have concluded that coexistence depends on the saturation constants, the maximum specific

growth rates, and on the yield coefficients of the two competitors on the two substrates. Taylor and Williams [31] have concluded that in general, in order to maintain a mixed population at steady state at least an equal number of growth limiting substrates is required. Thus, two species competing for two resources can in fact coexist. Using the model of Megee et al. [23] they have also concluded that two coexistence steady states could arise, but they have not been able to determine whether both could be meaningful and stable under the same operating conditions. Using topological considerations and Hopf's index theorem, Stephanopoulos [29] was able to show that it is impossible to obtain two meaningful and stable coexistence steady states in any domain of the operating parameters space when the system equations of Taylor and Williams [31] are valid. The same topic has been considered in a section of the present thesis. Although the results are basically the same with those already reported in the literature, it is the first time that operating diagrams have been constructed for this system and the effects of system and operating parameters on the domain of coexistence have been investigated in detail.

In experimental studies, Tilman [32] and Titman [33] have reported data on the competition between *Asterionella formosa* and *Cyclotella meneghiniana* for phosphate and silicate. Although they have observed coexistence, they have found *A.formosa* to be competitively dominant under phosphate limiting conditions and *C.meneghiniana* to dominate under silicate limiting conditions. It should be mentioned of course, that when only one substrate is present at limiting conditions the pattern of competition is pure and simple rather than double strong and thus, the results are in agreement with the pertiment theory.

Although this thesis is on pure competition in an ideal reactor, a few things need to be mentioned in order to emphasize the fact that the picture

can be completely altered when the reactor is not ideal and when interactions other than competition are also occuring in a competitive system.

For example, although pure and simple competitors cannot coexist in an ideal reactor, Baltzis and Fredrickson [6] and Lagonikos [19] have shown that attachment of cells to solid surfaces (reactor walls, impeller, etc.) can lead to steady state coexistence. Furthermore, pure and simple competitors can coexist in an ideal chemostat in a state of sustained oscillations when the competing species are members of a more complex food chain. For example, Jost et al. [14] have studied competition between *Escherichia coli* and *Azotobacter vinelandii* for glucose in a chemostat. They observed that while *A.vinelandii* was always excluded from the chemostat, it could be maintained in it, along with *E.coli* when a third protozoan population of *Tetrahymena pyriformis* was introduced in the same vessel. The protozoa preyed upon both bacterial species and all three populations could coexist in a state of sustained oscillations.

When the competing species are also involved in commensalistic or mutualistic interactions, chances for stable steady state coexistence are increased.

For example, Megee et al. [23] have studied competition for glucose between *Lactobacillus casei* and yeast. When riboflavin was present in the feed, *L.casei* won the competition. When the feed was riboflavin free, the two competitors coexisted at steady state as riboflavin, needed for growth of *L.casei*, was produced by the yeast. In this case competition was complicated by the commensal dependence of *L.casei* on yeast and allowed for coexistence. In another study, Lee et al. [20] examined competition between *Lactobacillus plantarum* and *Propionibacterium shermanii* for glucose. This pure and simple competitive pattern should lead to exclusion of *P.shermanii* from the reactor since it grows slower than *L.plantarum* on glucose. Nonetheless, it was found that the two species coexisted at steady state. This was due to

the fact that actually competition did not occur as *P.shermanii* did not use glucose but it preferred lactic acid, a by-product of *L.plantarum* metabolism on glucose. Hence, instead of pure and simple competiton the two species preferred to interact via a pure commensal pattern. As has been shown by Meyer et al. [24], mutualism can also lead to coexistence of two species which compete (not purely) for a single resource in an ideal chemostat.

Microbial systems are very complex, but as argued at the end of the Introduction modelling of idealized systems can provide some important basic information on dynamics. Thus, although relatively simple systems have been considered in the present study, it is believed that the results contibute towards a better understanding of microbial competition.

CHAPTER 3
MATHEMATICAL DESCRIPTION OF THE UNINHIBITED SYSTEM

This chapter describes competition for two complementary nutrients by two microbial populations in a chemostat, when inhibitory effects are not included in the analysis, and when the growth rates follow a Monod dependence on both nutrients.

3.1 Model Equations

In order to have a fully described system, one needs to derive four mass balances, two of which are written for the biomass of the two populations and two for the rate-limiting substrates. When an interactive model is used, the equations describing the system are the following:

$$\frac{db_1}{dt} = -Db_1 + \mu_1 b_1 \tag{3.1}$$

$$\frac{db_2}{dt} = -Db_2 + \mu_2 b_2 \tag{3.2}$$

$$\frac{ds_1}{dt} = D(s_{1f} - s_1) - \frac{1}{Y_{11}}\mu_1 b_1 - \frac{1}{Y_{21}}\mu_2 b_2 \tag{3.3}$$

$$\frac{ds_2}{dt} = D(s_{2f} - s_2) - \frac{1}{Y_{12}}\mu_1 b_1 - \frac{1}{Y_{22}}\mu_2 b_2 \tag{3.4}$$

where,

b_j, $j = 1, 2$: biomass concentration of species j, in the chemostat

D: dilution rate (inverse of the holding time) defined as q/V

q: volumetric flow rate of medium externally fed to chemostat

V: working volume of chemostat

s_{if}, $i = 1, 2$: concentrations of the rate-limiting substrates in the feed to the

chemostat

s_i, $i = 1, 2$: concentrations of the rate-limiting substrates in the chemostat

Y_{ij}: yield coefficient of species j on substrate i; $i = 1, 2$ and $j = 1, 2$

μ_j: specific growth rate of species j; $j = 1, 2$

For this part of the study it is assumed that

$$\mu_j = \frac{\hat{\mu}_j s_1 s_2}{(K_{1j} + s_1)(K_{2j} + s_2)}, \quad j = 1, 2 \tag{3.5}$$

with,

$\hat{\mu}_j$: characteristic constant for species j, having units of inverse time

K_{1j} and K_{2j}: kinetic constants for species j having units of concentration.

By introducing the following dimensionless quantities:

$$x = \frac{b_1}{Y_{11}K_{11}} \qquad y = \frac{b_2}{Y_{22}K_{21}} \qquad \theta = t\hat{\mu}_1$$

$$\alpha = \frac{D}{\hat{\mu}_1} \qquad v_f = \frac{s_{2f}}{K_{21}} \qquad u = \frac{s_1}{K_{11}}$$

$$v = \frac{s_2}{K_{21}} \qquad \varphi = \frac{\hat{\mu}_2}{\hat{\mu}_1} \qquad \delta = \frac{K_{12}}{K_{11}}$$

$$\sigma = \frac{K_{22}}{K_{21}} \qquad u_f = \frac{s_{1f}}{K_{11}} \qquad \varepsilon = \frac{K_{21}}{K_{11}}\frac{Y_{22}}{Y_{21}}$$

$$\gamma = \frac{K_{11}}{K_{21}}\frac{Y_{11}}{Y_{12}}$$

equations (3.1) through (3.4) can be written in dimensionless form as:

$$\frac{dx}{d\theta} = -\alpha x + \mu_1' x \tag{3.6}$$

$$\frac{dy}{d\theta} = -\alpha y + \mu_2' y \tag{3.7}$$

$$\frac{du}{d\theta} = \alpha(u_f - u) - \mu_1' x - \varepsilon \mu_2' y \tag{3.8}$$

$$\frac{dv}{d\theta} = \alpha(v_f - v) - \gamma \mu_1' x - \mu_2' y \tag{3.9}$$

with,

$$\mu_1' = \frac{uv}{(1+u)(1+v)} \tag{3.10}$$

$$\mu_2' = \frac{\varphi uv}{(\delta+u)(\sigma+v)} \tag{3.11}$$

3.2 Dimensional Reduction of the Model

Although the sustem is described by four differential equations, its actual dimensionality is two, according to the arguments of Aris and Humphrey [2]. In fact, one can easily show that equations (3.8) and (3.9) can be substituted for by the following two algebraic expressions:

$$u = u_f - x - \varepsilon y \tag{3.12}$$

$$v = v_f - \gamma x - y \tag{3.13}$$

The dimensional reduction from 4 to 2 actually implies that 2 of the 4 eigenvalues of the unreduced system are always equal to $-\alpha$, and thus they need not be further considered.

3.3 Possible Steady States

By setting the left-hand side of equations (3.6) and (3.7) equal to zero, and by using eqns (3.12) and (3.13), one can see that the system can have the following types of steady states:

- SS1: x=y=0

  Both populations wash out of the chemostat.

- SS2: x=0, $y > 0$

  Population 1 washes out of the chemostat, while population 2 survives.

- SS3: $x > 0$, y=0

  Population 2 washes out of the chemostat, while population 1 survives.

- SS4: $x > 0$, $y > 0$

  Both competing population coexist in a steady state.

3.4 Stability Analysis

The local stability character of any meaningful steady state can be determined by the eigenvalues of the Jacobian matrix of the system. Using eqns (3.6), (3.7) , (3.12), and (3.13), the Jacobian is the following 2×2 matrix:

$$J = \begin{bmatrix} J_{11} & J_{12} \\ J_{21} & J_{22} \end{bmatrix}$$

where,

$$J_{11} = -\alpha + \mu_1' + x\frac{d\mu_1'}{x} \tag{3.14}$$

$$J_{12} = x\frac{d\mu_1'}{dy} \tag{3.15}$$

$$J_{21} = y\frac{d\mu_2'}{dx} \tag{3.16}$$

$$J_{22} = -\alpha + \mu_2' + y\frac{d\mu_2'}{dy} \tag{3.17}$$

with,

$$\frac{d\mu_1'}{dx} = \left[\frac{\partial\mu_1'}{\partial u}\right]_v \frac{du}{dx} + \left[\frac{\partial\mu_1'}{\partial v}\right]_u \frac{dv}{dx} \tag{3.18}$$

$$\frac{d\mu_2'}{dy} = \left[\frac{\partial\mu_2'}{\partial v}\right]_u \frac{dv}{dy} + \left[\frac{\partial\mu_2'}{\partial u}\right]_v \frac{du}{dy} \tag{3.19}$$

$$\frac{d\mu_2'}{dx} = \left[\frac{\partial\mu_2'}{\partial u}\right]_v \frac{du}{dx} + \left[\frac{\partial\mu_2'}{\partial v}\right]_u \frac{dv}{dx} \tag{3.20}$$

$$\frac{d\mu_1'}{dy} = \left[\frac{\partial\mu_1'}{\partial u}\right]_v \frac{du}{dy} + \left[\frac{\partial\mu_1'}{\partial v}\right]_u \frac{dv}{dy} \tag{3.21}$$

and,

$$\frac{du}{dx} = -1 \tag{3.22}$$

$$\frac{du}{dy} = -\varepsilon \tag{3.23}$$

$$\frac{dv}{dx} = -\gamma \tag{3.24}$$

$$\frac{dv}{dy} = -1 \tag{3.25}$$

$$\left[\frac{\partial\mu_1'}{\partial u}\right]_v = \frac{v}{(1+u)^2(1+v)} = M \tag{3.26}$$

$$\left[\frac{\partial\mu_1'}{\partial v}\right]_u = \frac{u}{(1+u)(1+v)^2} = N \tag{3.27}$$

$$\left[\frac{\partial\mu_2'}{\partial u}\right]_v = \frac{\varphi\delta v}{(\delta+u)^2(\sigma+v)} = K \tag{3.28}$$

$$\left[\frac{\partial \mu_2'}{\partial v}\right]_u = \frac{\varphi \sigma u}{(\delta + u)(\sigma + v)^2} = \Lambda \tag{3.29}$$

3.5 Analysis of Steady State 1 (SS1)

The stoichiometric relations, i.e eqns (3.12) and (3.13), imply that u=u_f and v=v_f. This steady state is always meaningful, since the conditions $0 < u \leq u_f$ and $0 < v \leq v_f$ are unconditionally satisfied.

The terms J_{12} and J_{21} of the Jacobian stability matrix are equal to zero while J_{11}=$-\alpha+\mu_1'$ and J_{22}=$-\alpha+\ \mu_2'$. The eigenvalues are: λ_1=$-\alpha+\mu_1'$, λ_2=$-\alpha+\mu_2'$.

It is obvious that both eigenvalues are real, while both of them are negative if and only if $\alpha > \mu_1'$ and $\alpha > \mu_2'$. Hence SS1 is stable if and only if:

$$\alpha > max[f(u_f, v_f), g(u_f, v_f)] \tag{3.30}$$

where,

$$f(u_f, v_f) = \frac{u_f v_f}{(1 + u_f)(1 + v_f)} \tag{3.31}$$

and,

$$g(u_f, v_f) = \frac{\varphi u_f v_f}{(\delta + u_f)(\sigma + v_f)} \tag{3.32}$$

3.6 Analysis of Steady State 2 (SS2)

In this steady state population 2 wins the competition while population 1 washes out of the chemostat.

Equations (3.7), (3.12) and (3.13) imply that

$$\alpha = \mu_2' \tag{3.33}$$

$$y = \frac{u_f - u}{\varepsilon} \tag{3.34}$$

$$y = v_f - v \tag{3.35}$$

Equation (3.33) implies that

$$v = \frac{\alpha\sigma(\delta + u)}{u(\varphi - \alpha) - \alpha\delta} \tag{3.36}$$

It is easy to see that the condition $0 < u < u_f$ (necessary for meaningfulness of SS2) will not be satisfied unless

$$\frac{u}{\delta + u} < \frac{u_f}{\delta + u_f} \tag{3.37}$$

Similarly, the condition $0 < v < v_f$ will not be satisfied unless

$$\frac{v}{\sigma + v} < \frac{v_f}{\sigma + v_f} \tag{3.38}$$

When conditions (3.37) and (3.38) are satisfied, taking into consideration equation (3.33), one can easily conclude that SS2 cannot be meaningful unless

$$\alpha < g(u_f, v_f) \tag{3.39}$$

where $g(u_f, v_f)$ is defined by expression (3.32).

One can easily see that when condition (3.39) is satisfied, it is also true that $\alpha < \varphi$ which in turn combined with expression (3.36) implies that v will be positive only if a meaningful value of u satisfies the following condition:

$$u > \frac{\alpha\delta}{(\varphi - \alpha)} \tag{3.40}$$

Equations (3.34) and (3.35) imply that

$$v = \frac{u - u_f + \varepsilon v_f}{\varepsilon} \tag{3.41}$$

One can easily observe that a meaningful value of u will imply [through (3.41)] that $v < v_f$. Using equations (3.33) and (3.41) one can show that the value of u is given as a solution to the following quadratic:

$$F(u) = a_1 u^2 - b_1 u - c_1 = 0 \tag{3.42}$$

where,

$$a_1 = \varphi - \alpha \tag{3.43}$$

$$b_1 = (\varepsilon v_f - u_f + \varepsilon\sigma)\alpha - (\varphi\varepsilon v_f - \varphi u_f - \alpha\delta) \tag{3.44}$$

$$c_1 = \alpha\delta(\varepsilon v_f - u_f + \varepsilon\sigma) \tag{3.45}$$

One can show that the following inequalities hold, when condition (3.39) is satisfied:

$$F(u_f) > 0 \tag{3.46}$$

and

$$F\left(\frac{\alpha\delta}{\varphi - \alpha}\right) < 0 \tag{3.47}$$

Case 1: $c_1 > 0$

In this case, $F(0) < 0$ and hence, if (3.39) is satisfied (implying that $\alpha < \varphi$), $F(u) = 0$ has one positive and one negative root. Call u_1 the positive root. Because of relations (3.46), (3.47) and (3.40), one can conclude that $u_1 < u_f$ and that $v > 0$. Furthermore, due to (3.41) and (3.34) one can see that $v < v_f$ and $y > 0$. Hence, when $c_1 > 0$, and when condition (3.39) is satisfied, there is a meaningful and unique steady state 2.

Case 2: $c_1 < 0$

In this case, due to (3.47) one can conclude that the quadratic $F(u) = 0$ has two positive roots, u_1 and u_2. Assuming that $u_1 < u_2$, due (3.47) and (3.40) only u_2 will lead to a positive value for v. When (3.39) is satisfied, one can easily show that

$$u_f > \frac{\alpha\delta}{\varphi - \alpha} \tag{3.48}$$

Relations (3.46) through (3.48) imly that

$$0 < u_1 < \frac{\alpha\delta}{\varphi - \alpha} < u_2 < u_f \tag{3.49}$$

Hence, when $c_1 < 0$ there is one and only one meaningful SS2, provided that (3.39) is satisfied.

The general conclusion from the foregoing analysis is that there is a meaningful and unique SS2 whenever (3.39) is satisfied.

3.6.1 Stability analysis of steady state 2

The terms of the Jacobian stability matrix are:

$$J_{11} = -\alpha + \mu_1' \tag{3.50}$$

$$J_{12} = 0 \tag{3.51}$$

$$J_{21} = y\frac{d\mu_2'}{dx} \tag{3.52}$$

$$J_{22} = y\frac{d\mu_2'}{dy} \tag{3.53}$$

The eigenvalues are: $\lambda_1 = -\alpha + \mu_1'$, $\lambda_2 = y(d\mu_2'/dy)$, where $(d\mu_2'/dy)$ is given by eqn (3.19).

Looking at (3.23), (3.25), (3.28) and (3.29) one can easily see that λ_2 is always negative. Thus, the necessary and sufficient condition for a stable SS2

is that $\alpha > \mu_1'$.

3.7 Analysis of Steady State 3 (SS3)

In this steady state population 1 wins the competition by excluding population 2 from the chemostat. Since SS3 is a case symmetric to that of SS2, the analysis is not repeated and only the results are presented.

When

$$\alpha < \frac{u_f v_f}{(1+u_f)(1+v_f)} \tag{3.54}$$

there is a unique meaningful SS3 which is stable if and only if $\alpha > \mu_2'$. In this case, as in SS2 all eigenvalues are real and thus, no oscillatory behavior is exhibited by the system during transients.

3.8 Analysis of Steady State 4 (SS4)

This is the steady state where the two competitors coexist.

From eqns (3.6) and (3.7) at steady state it follows that $\alpha = \mu_1' = \mu_2'$. Equations (3.12) and (3.13) can be viewed as a system of two equations in two unknowns x and y. The solution of the system, using Kramer's rule, is:

$$x = \frac{(u_f - u) - \varepsilon(v_f - v)}{1 - \gamma\varepsilon} \tag{3.55}$$

$$y = \frac{(v_f - v) - \gamma(u_f - u)}{1 - \gamma\varepsilon} \tag{3.56}$$

In order to have meaningful values for x and y one of the following two inequalities must be valid:

either

$$\frac{1}{\gamma} > \frac{u_f - u}{v_f - v} > \varepsilon \tag{3.57}$$

or

$$\varepsilon > \frac{u_f - u}{v_f - v} > \frac{1}{\gamma} \tag{3.58}$$

Since $\mu_1' = \mu_2'$, one can write:

$$u = \frac{\delta\sigma - \varphi + v(\delta - \varphi)}{\varphi - \sigma + (\varphi - 1)v} \tag{3.59}$$

and,

$$v = \frac{\delta\sigma - \varphi + u(\sigma - \varphi)}{\varphi - \delta + (\varphi - 1)u} \tag{3.60}$$

By substituting eqn (3.59) into $\alpha = \mu_1'$ the following quadratic in u is obtained:

$$G(u) = au^2 + bu + c = 0 \tag{3.61}$$

where,

$$a = \alpha(\sigma - 1) - (\sigma - \varphi) \tag{3.62}$$

$$b = \alpha(\sigma - 1)(\delta + 1) - (\delta\sigma - \varphi) \tag{3.63}$$

$$c = \alpha(\sigma - 1)\delta \tag{3.64}$$

To get the values of the state variables at steady state, one has to solve $G(u) = 0$ to determine the value(s) of u. Then, using eqns (3.59), (3.55), and (3.56) the values of v, x, and y are determined. In this case it is possible that there are two SS4.

It should be mentioned that since $\alpha = \mu_1' = \mu_2'$ and since one must have $u < u_f$, and $v < v_f$ a necessary (but not sufficient) condition for meaningfulness of SS4 is that

$$\alpha < min[f(u_f, v_f), g(u_f, v_f)] \tag{3.65}$$

where $f(u_f, v_f)$ and $g(u_f, v_f)$ are defined by relations (3.31) and (3.32), respectively.

One can also observe that when (3.65) is satisfied, condition (3.30) is violated. This implies that SS1 and SS4 are mutually exclusive steady states, in the sense that it is impossible for them to be both meaningful and stable for the same operating parameter values. Actually, SS1 is also mutually exclusive with both SS2 and SS3 since condition (3.30) is violated when (3.39) and/or (3.54) is satisfied.

3.8.1 Stability analysis of steady state 4

The eigenvalues of SS4 are given as roots to the following quadratic equation:

$$G(\lambda) = \lambda^2 + d_1\lambda + d_2 = 0 \tag{3.66}$$

where,

$$d_1 = xM + \gamma xN + y\Lambda + \varepsilon yK \tag{3.67}$$

$$d_2 = xy(1 - \varepsilon\gamma)(\Lambda M - KN) \tag{3.68}$$

M, N, K, and Λ are defined by relations (3.26) through (3.29) and because of (3.10) and (3.11) they are all positive. The discriminant of eqn (3.66) is:

$$\Delta = (xM + \gamma xN - y\Lambda - \varepsilon yK)^2 + 4(yK + \gamma y\Lambda)(xN + \varepsilon xM) \tag{3.69}$$

Since $\Delta > 0$, the roots of (3.66) are real.

Let λ_1 and λ_2 to be the two roots. Then

$$\lambda_1 + \lambda_2 = -(xM + \gamma xN + y\Lambda + \varepsilon yK) \tag{3.70}$$

$$\lambda_1\lambda_2 = xy(1 - \varepsilon\gamma)(\Lambda M - KN) \tag{3.71}$$

It is clear that $\lambda_1 + \lambda_2 < 0$, hence the necessary and sufficient condition for a stable SS4 is $d_2 > 0$.

Using the expressions (3.26) through (3.29) one can show that

$$\Lambda M - KN = \frac{\varphi uvL}{(1+u)(1+v)(\delta+u)(\sigma+v)} \tag{3.72}$$

where

$$L = \frac{\sigma}{(1+u)(\sigma+v)} - \frac{\delta}{(\delta+u)(1+v)} \tag{3.73}$$

Using (3.73) one can write

$$L = \frac{uv(\sigma-\delta) + u\sigma(1-\delta) + \delta v(\sigma-1)}{(1+u)(\sigma+v)(\delta+u)(1+v)} \tag{3.74}$$

If $\sigma < 1 < \delta$, (3.74) implies that L, and consequently $\Lambda M - KN$ is negative. If $\sigma > 1 > \delta$, (3.74) and (3.72) imply that $\Lambda M - KN$ is positive. Since $\alpha = \mu_1' = \mu_2'$, (3.73) can be brought into the form

$$L = \frac{\alpha R}{uv(1+u)(\delta+u)} \tag{3.75}$$

where

$$R = \sigma(\delta+u)^2 - \delta(1+u)^2 \tag{3.76}$$

If $\sigma < \delta < 1$, (3.76) implies that

$$R < \delta[(\delta+u)^2 - (1+u)^2] = \delta(\delta-1)(\delta+1+2u) < 0 \tag{3.77}$$

Hence, (3.77), (3.75) and (3.72) imply that $\Lambda M - KN < 0$ when $\sigma < \delta < 1$. If $\sigma > \delta > 1$, (3.76) implies that

$$R > \delta[(\delta+u)^2 - (1+u)^2] = \delta(\delta-1)(\delta+1+2u) > 0 \tag{3.78}$$

Hence, (3.78), (3.75) and (3.72) imply that $\Lambda M - KN > 0$ when $\sigma > \delta > 1$. Since $\alpha = \mu_1' = \mu_2'$, (3.73) can be also brought into the form

$$L = \frac{\alpha Q}{uv(\sigma+v)(1+v)} \tag{3.79}$$

where

$$Q = \sigma(1+v)^2 - \delta(\sigma+v)^2 \tag{3.80}$$

If $1 < \sigma < \delta$, (3.80) implies that

$$Q < \delta[(1+v)^2 - (\sigma+v)^2] = \delta(1-\sigma)(1+\sigma+2v) < 0 \tag{3.81}$$

Hence, (3.81), (3.79) and (3.72) imply that $\Lambda M - KN < 0$ when $1 < \sigma < \delta$. If $1 > \sigma > \delta$, (3.80) implies that

$$Q > \delta(1-\sigma)(1+\sigma+2v) > 0 \tag{3.82}$$

Hence, (3.82), (3.79) and (3.72) imply that $\Lambda M - KN > 0$ when $1 > \sigma > \delta$.

From the foregoing considerations, one can conclude the following:

$$1.\ \ if\ \ \sigma < \delta\ \ then\ \ \Lambda M - KN < 0 \tag{3.83}$$

$$2.\ \ if\ \ \sigma > \delta\ \ then\ \ \Lambda M - KN > 0 \tag{3.84}$$

Relations (3.83) and (3.84) when combined with relation (3.71) lead to the final conclusions:

- If $\sigma < \delta$, a meaningful SS4 is stable if and only if $\varepsilon\gamma > 1$

- If $\sigma > \delta$, a meaningful SS4 is stable if and only if $\varepsilon\gamma < 1$

It should be emphasized here, that the results show that the stability

of a meaningful coexistence steady state is independent of operating parameters (α, u_f, v_f), and is determined only by the system parameters (σ, δ, ε, γ).

3.9 Conclusions from the Analysis of Steady States

From the analysis performed in the previous sections, one can conclude the following:

- The system never exhibits an oscillatory (damped or sustained) response.
- Only SS4 may exhibit multiplicity.
- SS1 is mutually exclusive with every one of the remaining steady states.
- The analytical work has not shown if in fact SS4 can have two equilibrium points, and if there is a regime in the operating parameter space where SS4 (at least one) can be meaningful and stable. Furthermore , the analysis could not show if SS2, SS3, and SS4 are mutually exclusive with one another.

These answers have to be found via numerical studies.

The analysis has shown that there are two curves, $f(u_f, v_f)$ and $g(u_f, v_f)$ defined via relations (3.31) and (3.32), respectively, which play a very important role for the rise and/or stability of the various steady states. Actually, the relations $\alpha = f(u_f, v_f)$ and $\alpha = g(u_f, v_f)$ define surfaces in the $\alpha - u_f - v_f$ space. Since three dimensional diagrams are neither easy to construct nor to read (in some cases), one can decide to construct projections of these surfaces on a 2-dimensional plane. Here it has been decided to show things on the $\alpha - u_f$ plane for most of the cases considered. Also, without loss of generality one can assume that $\varphi > 1$. Then, for a fixed v_f-value, the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves may or may not cross each other. In the later case, for a given v_f-value it will be $g(u_f, v_f) > f(u_f, v_f)$ for any u_f value. If crossing occurs, it does so at a single point only, namely at

$$u_{fc} = \frac{\delta\sigma - \varphi + v_f(\delta - \varphi)}{\varphi - \sigma + v_f(\varphi - 1)} \tag{3.85}$$

Crossing of the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves occurs in the following cases (when $\varphi > 1$):

1. $\varphi > \sigma$, $\delta\sigma > \varphi$, $\delta > \varphi$, for any v_f

2. $\varphi > \sigma$, $\delta\sigma < \varphi$, $\delta > \varphi$, for $v_f > (\varphi - \delta\sigma)/(\delta - \varphi)$

3. $\varphi < \sigma$, $\delta\sigma > \varphi$, $\delta > \varphi$, for $v_f > (\sigma - \varphi)/(\varphi - 1)$

4. $\varphi < \sigma, \delta\sigma > \varphi, \delta < \varphi, \delta > 1$, for $(\delta\sigma - \varphi)/(\varphi - \delta) > v_f > (\sigma - \varphi)/(\varphi - 1)$

5. $\varphi < \sigma$, $\delta\sigma < \varphi$, $\delta < \varphi$, for $v_f < (\sigma - \varphi)/(\varphi - 1)$

Crossing of the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves does not occur in the following cases (when $\varphi > 1$):

1. $\varphi > \sigma$, $\delta\sigma < \varphi$, $\delta > \varphi$, for $v_f < (\varphi - \delta\sigma)/(\delta - \varphi)$

2. $\varphi > \sigma$, $\delta\sigma < \varphi$, $\delta < \varphi$, for any v_f value

3. $\varphi < \sigma$, $\delta\sigma > \varphi$, $\delta > \varphi$, for $v_f < (\sigma - \varphi)/(\varphi - 1)$

4. $\varphi < \sigma$, $\delta\sigma > \varphi$, $\delta < \varphi$, $\delta < 1$, for any v_f value

5. $\varphi < \sigma$, $\delta\sigma > \varphi$, $\delta < \varphi$, $\delta > 1$, for $v_f < (\delta\sigma - \varphi)/(\varphi - \delta)$

or $v_f > (\sigma - \varphi)/(\varphi - 1)$

6. $\varphi < \sigma$, $\delta\sigma < \varphi$, $\delta < \varphi$, for $v_f > (\sigma - \varphi)/(\varphi - 1)$

3.10 Results of Numerical Studies and Operating Diagrams

A number of important results have been obtained analytically as discussed

in the preceeding sections of this thesis. Nonetheless, some important questions could not be answered but through numerical studies. Among these questions, the most important ones were the following:

- Under what conditions can a coexistence steady state really arise?
- Can the coexistence steady state really exhibit multiplicity?
- When coexistence is possible, does it occur in a domain of the operating parameters space, or does it occur only for discrete values of the parameters in which case it would not be possible to get it practically (in an experimental or actual process)?
- Do the results of the local stability analysis hold globally or not?
- Do the pairs of SS2 and SS3, SS2 and SS4, SS3 and SS4 constitute pairs of mutually exclusive steady states or not?

Answers to the foregoing questions have been found through extensive numerical studies. The main results are the following:

- The necessary and sufficient condition for SS4 (coexistence) to arise is that the $f(u_f, v_f)$ and $g(u_f, v_f)$ [defined by relations (3.31) and (3.32)] curves, cross each other. For a given v_f value, crossing of the curves occurs at a specific value of u_f, called u_{fc} and defined by relation (3.85). The value of u_{fc} is the minimum value of u_f for which coexistence is possible. At u_{fc}, the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves cross each other at $f(u_f, v_f) = g(u_f, v_f) = \alpha_c$. For a given v_f value, the point (α_c, u_{fc}) defines the point in the $\alpha - u_f$ plane from which the region of SS4 arises. If $\sigma < \delta$, coexistence occurs for values of α less than α_c in the $\alpha - u_f$ plane, and for values of α larger than α_c in the $\alpha - v_f$ plane. If $\sigma > \delta$, the opposite is true, i.e., in the $\alpha - u_f$ plane coexistence occurs

at values of α higher than α_c and in the $\alpha - v_f$ plane at values of α less than α_c. It should be mentioned here, that α_c in the $\alpha - v_f$ plane is not the same as in the $\alpha - u_f$ plane. In the $\alpha - v_f$ plane, α_c critical is defined as $\alpha_c = f(u_f, v_{fc}) = g(u_f, v_{fc})$ for a given value of u_f, while v_{fc} is defined by an expression similar (analogous) but not identical to (3.85).

- The coexistence steady state does not exhibit multiplicity. Since the absence of multiplicity has been excluded (analytically) for the other steady states as well, it can be now concluded that for the uninhibited system none of the possible steady states exhibits multiplicity.

- Whenever coexistence arises, it does so in a domain of the $\alpha - u_f - v_f$ space except for the special case where $\varepsilon\gamma = 1$. In this special case, coexistence arises on a surface in the $\alpha - u_f - v_f$ space or on a curve in the $\alpha - u_f$ plane (see Figures 3.5 and 3.7).

- SS2 and SS4 as well as SS3 and SS4 constitute pairs of mutually exclusive steady states in the sense that there is no domain where both steady states of these pairs can be meaningful and stable.

- As has been proved analytically, if $\sigma < \delta$, SS4 is stable provided that $\varepsilon\gamma > 1$. Similarly, if $\sigma > \delta$, SS4 is stable provided that $\varepsilon\gamma < 1$. In such cases, SS2 and SS3 are mutually exclusive.

- As has been proved analytically, if $\sigma < \delta$ a meaningful SS4 is unstable if $\varepsilon\gamma < 1$. Similarly, if $\sigma > \delta$ a meaningful SS4 is unstable if $\varepsilon\gamma > 1$. In such cases, SS2 and SS3 are not mutually exclusive. In fact, in the region where SS4 is meaningful but unstable, both SS2 and SS3 are meaningful and stable.

- The results of the local stability analysis hold globally as well except

in regions where SS2 and SS3 are both meaningful and stable. In such cases, the outcome of competition (i.e., exclusion of population 1 or 2) will depend on the initial conditions, that is on how the system is started-up. It should be also mentioned that if one is interested in maintaining a mixed culture but SS4 is unstable whenever meaningful, proper control action could stabilize SS4 and prevent exclusion of either one of the two species.

- When the $f(u_f, v_f)$ and $g(u_f, v_f)$ do not cross each other, coexistence is impossible. In such cases, the system has only two possible outcomes. If $\varphi > 1$, there is a total washout for $\alpha > g(u_f, v_f)$ while SS2 is meaningful and stable for $\alpha < g(u_f, v_f)$. In such cases, SS3 is unstable whenever meaningful. If $\varphi < 1$, there is a total washout for $\alpha > f(u_f, v_f)$ while SS3 is meaningful and stable for $\alpha < f(u_f, v_f)$. In such cases, SS2 is unstable whenever meaningful

The numerical work was done as follows: For fixed values of the system parameters (φ, σ, δ, ε, γ) the equations developed in earlier sections were used in order to determine the regions in the $\alpha - u_f - v_f$ space [or in a projection of it on either the $\alpha - u_f$ or $\alpha - v_f$ plane] where each steady state is meaningful and stable or unstable. Some simulations were also performed by integrating the state model in order to check the global validity of the results of the local stability analysis. The main programs used in this study are given in the Appendix of the thesis. Some characteristic results are shown in the operating diagrams of Figures 3.1 through 3.9. The values of the parameters used in constructing these diagrams are given in Table 3.1. Since the most important question in this study was to explore the possibility of coexistence, no diagrams are shown for cases where the $f(u_f, v_f)$ and $g(u_f, v_f)$ do not cross each other, since in such cases coexistence is impossible as has been discussed earlier. As has been discussed in an earlier section of the thesis,

one can assume without loss of generality that $\varphi > 1$. Thus, all diagrams presented here are for $\varphi = 1.25$.

Diagrams 3.1 and 3.2 are for cases where $\sigma < \delta$ and $\varepsilon\gamma < 1$. In such cases, there is a region where SS4 is meaningful but unstable, and in that same region both SS2 and SS3 are meaningful and stable. The only difference between the diagrams of Figures 3.1 and 3.2 is that $\varepsilon < \gamma$ in 3.1 while $\varepsilon > \gamma$ in 3.2. One can observe that when $\varepsilon > \gamma$ the region where SS4 is meaningful but unstable is larger than when $\varepsilon < \gamma$ and the region shifts to the right, i.e., to larger u_f values.

As has been already discussed, when $\sigma < \delta$ but $\varepsilon\gamma > 1$ there is a region where SS4 is meaningful and stable, while all possible steady states are mutually exclusive. These characteristics can be seen in Figures 3.3 and 3.4. Once again, when $\varepsilon > \gamma$ (Figure 3.4) the region of coexistence is larger than when $\varepsilon < \gamma$ (Figure 3.3), and the region shifts to larger u_f values (at low α values).

When the value of $\varepsilon\gamma$ decreases while it remains larger than 1 the region of SS4 becomes smaller and eventually reduces to a curve. This can be seen from Figures 3.3 and 3.5. Similarly, when the value of $\varepsilon\gamma$ increases while it remains less than 1 the region where SS4 is meaningful but unstable becomes smaller and eventually reduces to a curve as can be seen from Figures 3.1 and 3.5. The foregoing considerations are true when $\sigma < \delta$.

When $\sigma < \delta$ and $\varepsilon\gamma > 1$ the region where SS4 is meaningful and stable arises for $\alpha < \alpha_c$. The opposite is true when $\sigma > \delta$ and $\varepsilon\gamma < 1$. These observations can be made for the cases of Figures 3.3 and 3.6.

When $\sigma > \delta$ and $\varepsilon\gamma$ increases while it remains less than 1, the region of SS4 eventually reduces to a curve (Figures 3.6 and 3.7). This observation is analogous to the one made for the case of Figures 3.3 and 3.5.

Selecting the $\alpha - u_f$ as opposed to the $\alpha - v_f$ plane for the graphs is not

important. The only difference is that whatever is observed (regarding SS4) in the $\alpha - u_f$ plane for $\alpha < \alpha_c$ is also observed in the $\alpha - v_f$ plane for $\alpha > \alpha_c$ (Figures 3.1 and 3.8).

Lastly, one can without loss of generality assume that $\sigma < \delta$. In the same plane, e.g., $\alpha - u_f$, whatever is observed for $\alpha < \alpha_c$ when $\sigma < \delta$, it is observed for $\alpha > \alpha_c$ when $\sigma > \delta$ (e.g., Figures 3.3 and 3.6). When the inequality $\sigma < \delta$ is reversed, whatever is observed in the $\alpha - u_f$ plane is now observed in the $\alpha - v_f$ plane (Figures 3.1 and 3.9; actually an identical picture would require inversing the value of $\varepsilon\gamma$ as well).

3.11 Main Conclusion

The main conclusion from this part of the present thesis is the following: Two populations competing purely and strongly for two non-inhibitory complementary substrates can coexist in a chemostat in a steady state which is either stable by itself or can be stabilized by the use of proper control action. Coexistence occurs in a domain of the operating parameters space $(\alpha - u_f - v_f)$. There are two exceptions: (1). When $\varepsilon\gamma = 1$, the domain of coexistence becomes a surface in the $\alpha - u_f - v_f$ space and thus, coexistence is practically unattainable due to the ever existing fluctuations in the operating parameter values; (2). When the $f(u_f, v_f)$ and $g(u_f, v_f)$ surfaces do not cross each other for any values of u_f and v_f; the latter, when $\varphi > 1$ occurs when $\varphi > \sigma$, $\delta\sigma < \varphi$ and $\delta < \varphi$. It should be mentioned here that exclusion of coexistence is decided by the system parameters (ε, γ, σ, δ, φ) which physically means that it depends on the identity of the competitors and of the two substrates competed for.

Table 3.1

Uninhibited System-Parameter values used for operating diagrams 3.1-3.9

Figure	ε	γ	φ	σ	δ	v_f
3.1	0.2	0.5	1.25	1.1	1.82	4.0
3.2	0.5	0.2	1.25	1.1	1.82	4.0
3.3	1.3	1.7	1.25	1.1	1.82	4.0
3.4	1.7	1.3	1.25	1.1	1.82	4.0
3.5	4.0	0.25	1.25	1.1	1.82	4.0
3.6	0.5	0.2	1.25	1.82	1.1	4.0
3.7	4.0	0.25	1.25	1.82	1.1	4.0

Figure	ε	γ	φ	σ	δ	u_f
3.8	0.2	0.5	1.25	1.1	1.82	4.0
3.9	0.2	0.5	1.25	1.82	1.1	4.0

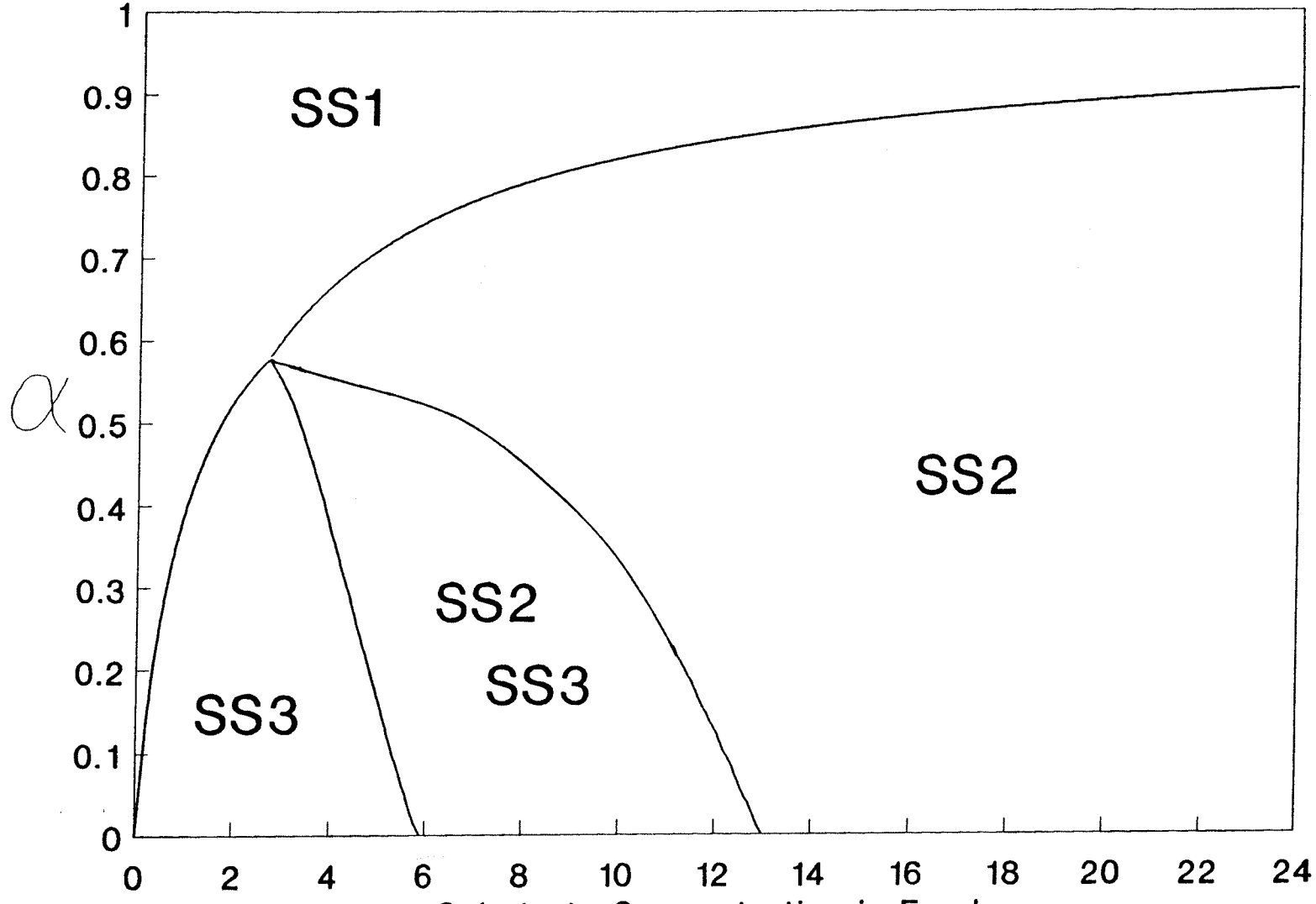

SS1
SS2
SS2
SS3
SS3
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u_f

Figure 3.1

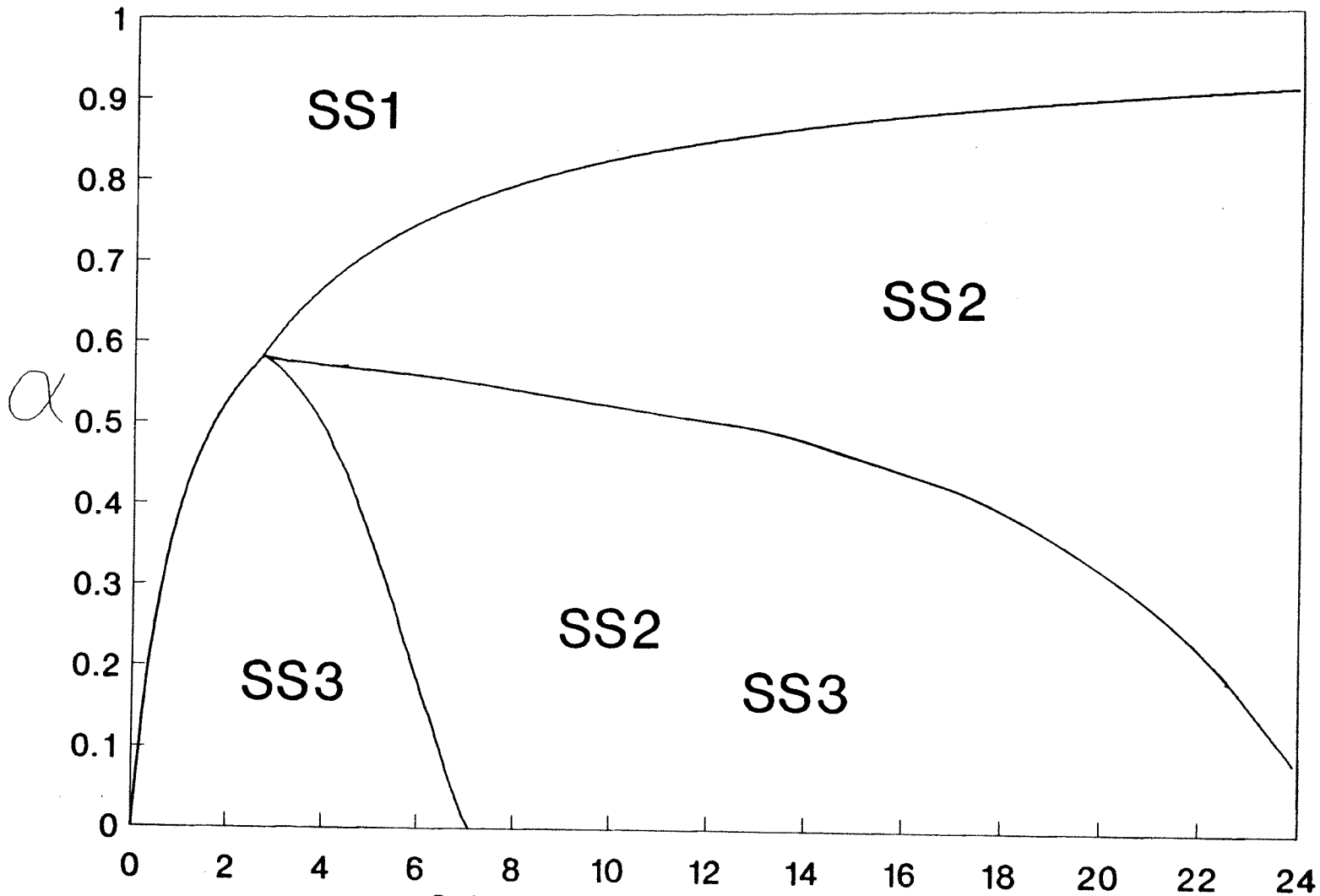

SS1
SS2
SS2
SS3
SS3
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed, u_f

Figure 3.2

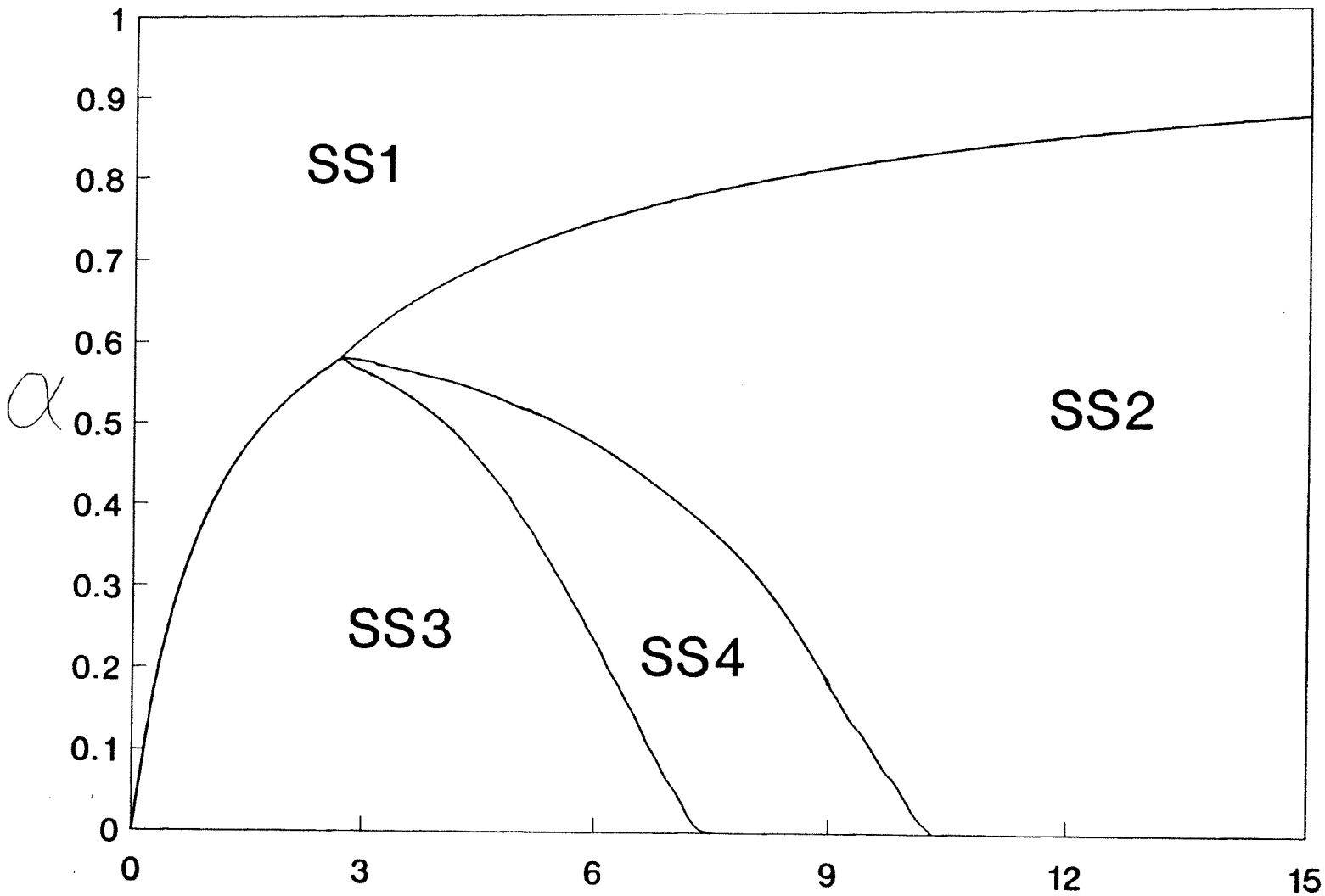

1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
α
SS1
SS2
SS3
SS4
0
3
6
9
12
15
Substrate Concentration in Feed,u_f

Figure 3.3

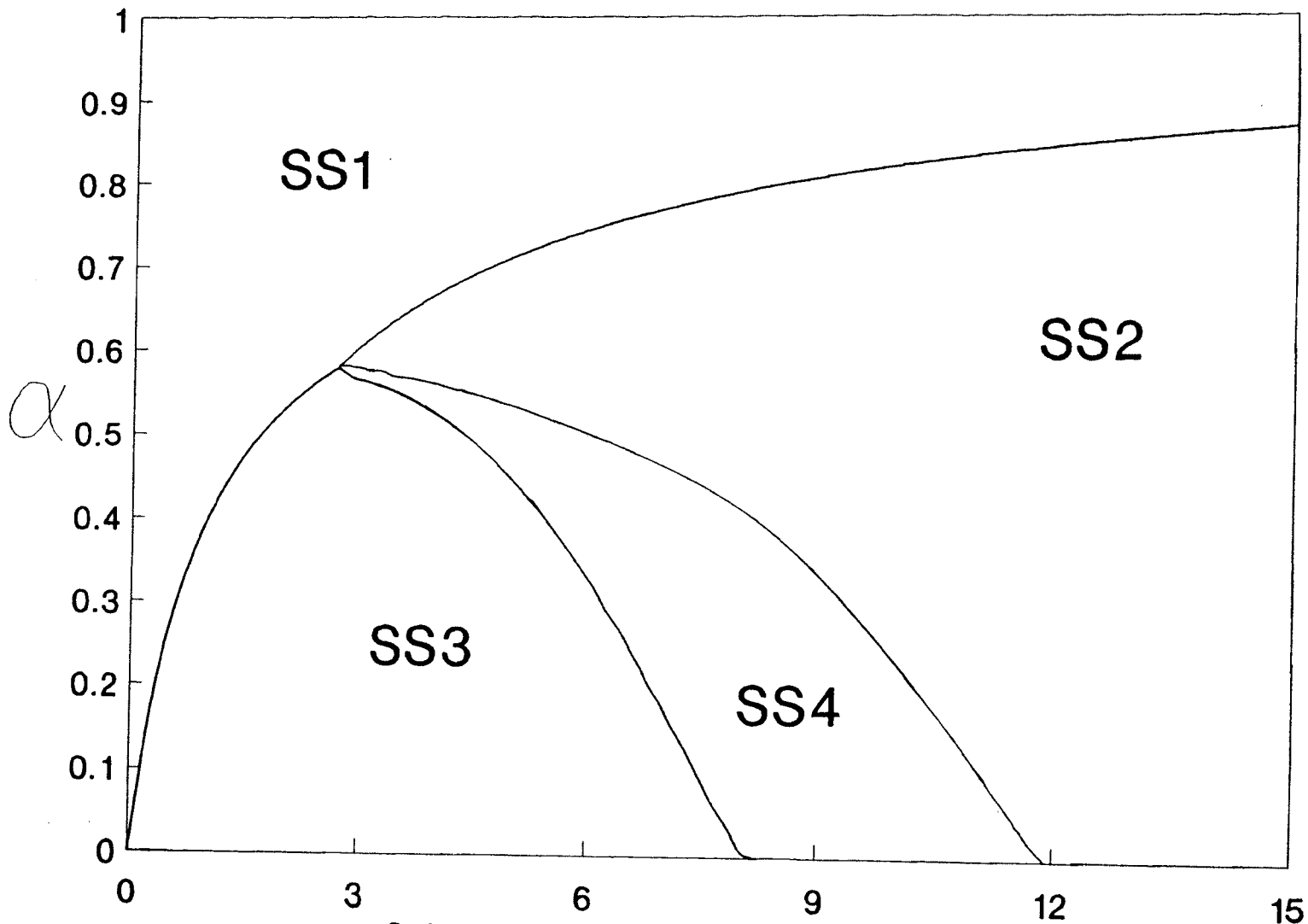
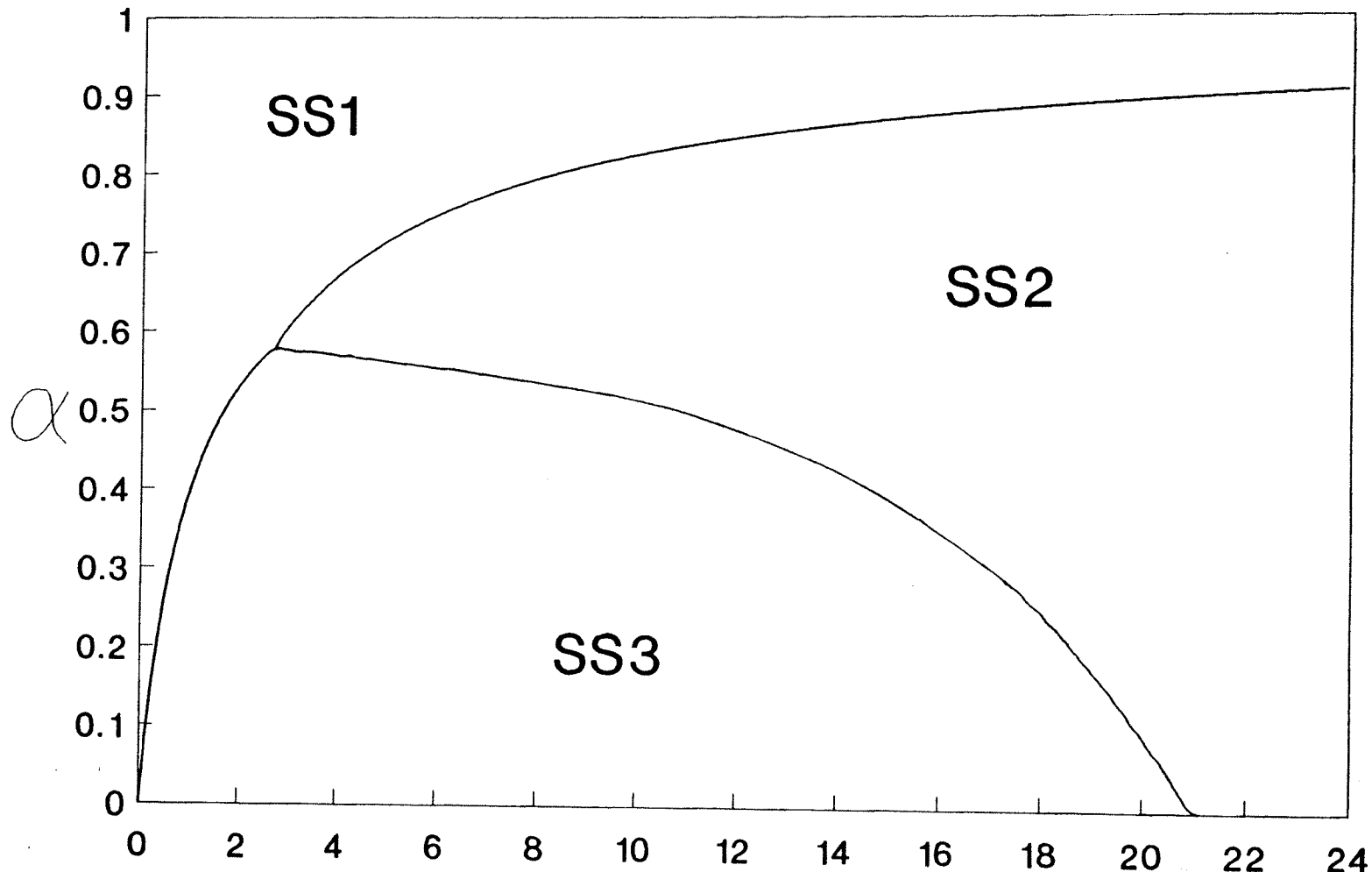

SS1
SS2
SS3
SS4
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
3
6
9
12
15
Substrate Concentration in Feed,u f

Figure 3.4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SS2
SS3
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
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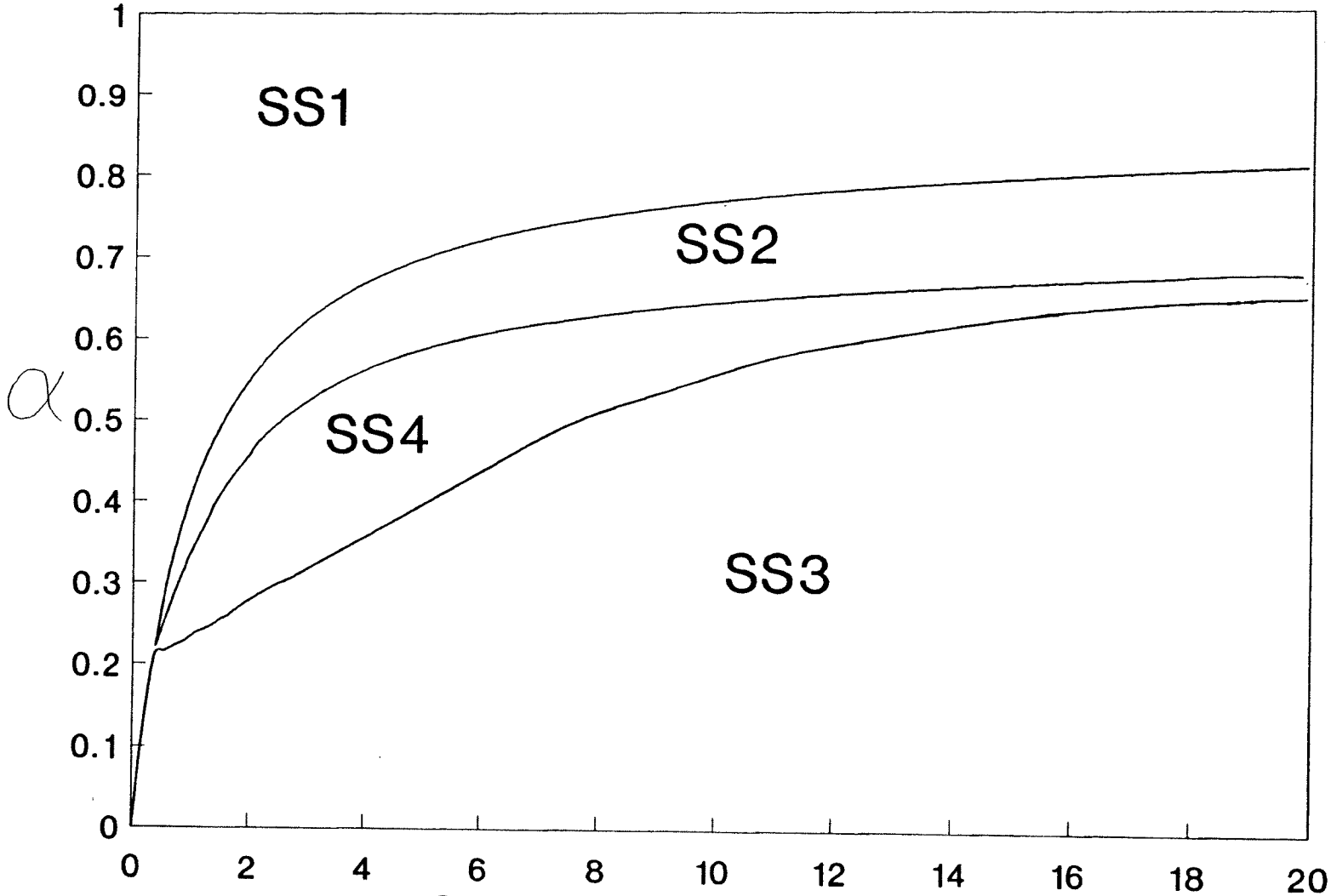
22
24
Substrate Concentration in Feed,u f

Figure 3.5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SS2
SS4
SS3
α
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0.7
0.6
0.5
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0.1
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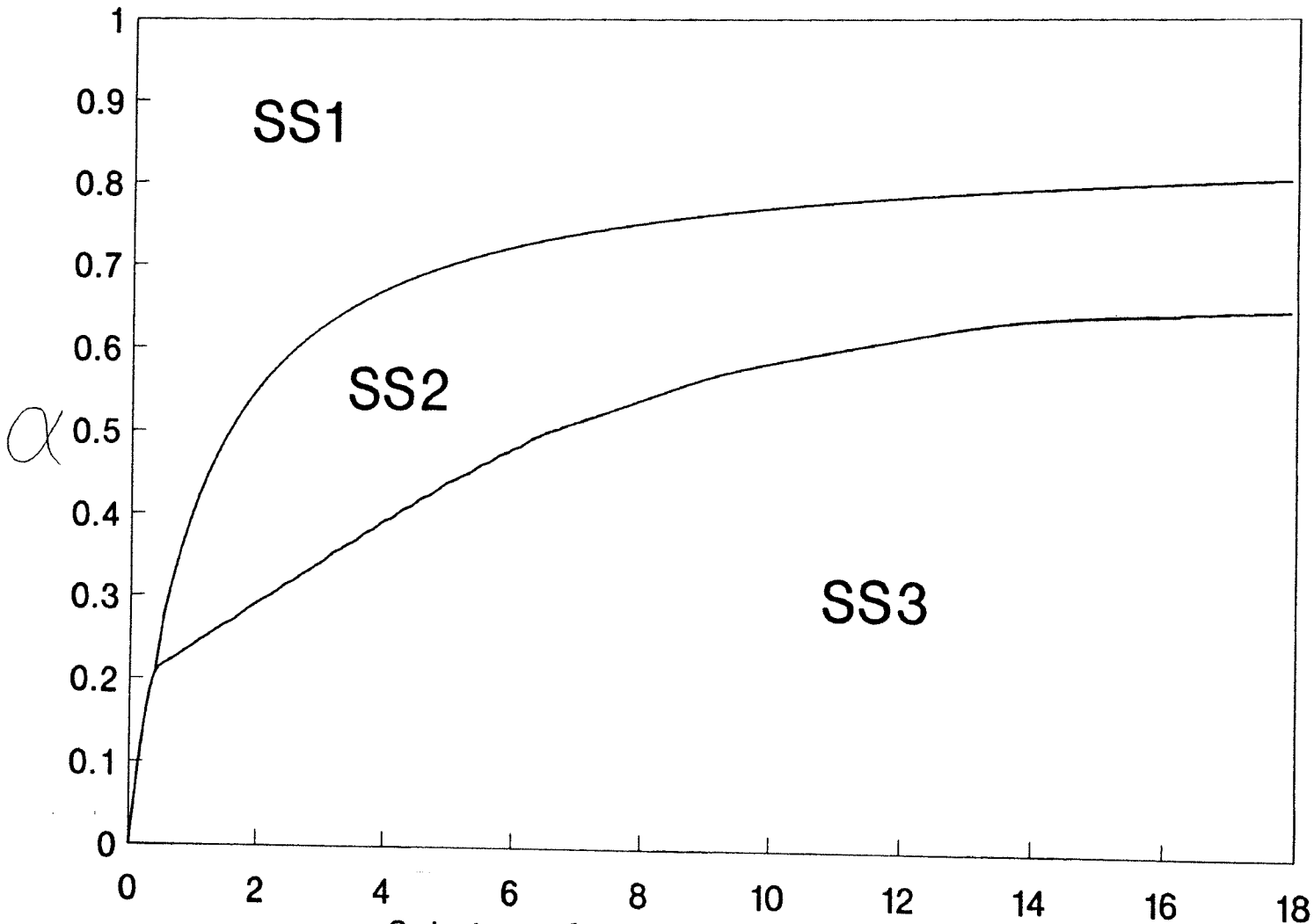
Substrate Concentration in Feed,u_f

Figure 3.6


SS1
SS2
SS3
α
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0.6
0.5
0.4
0.3
0.2
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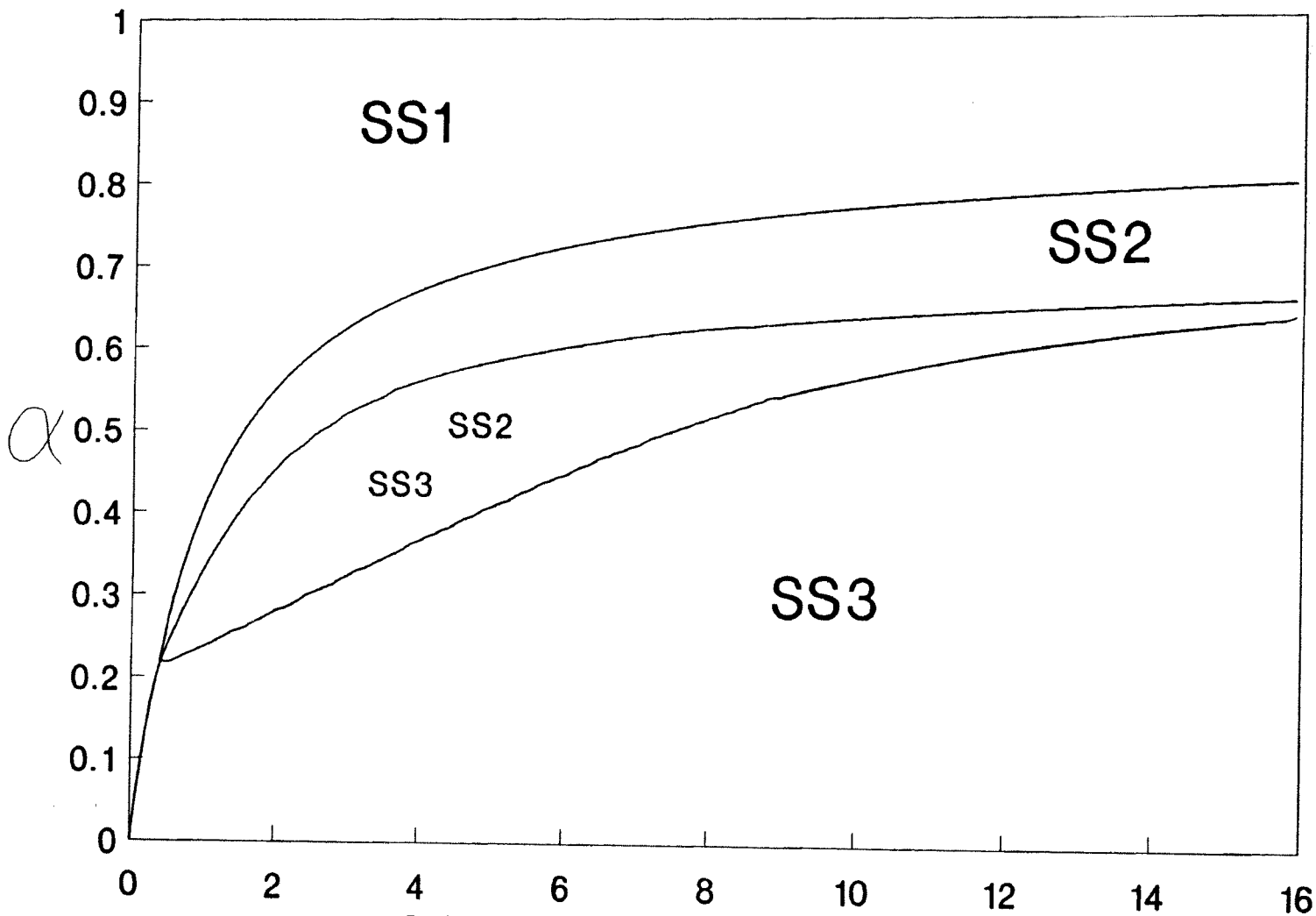
Substrate Concentration in Feed,u f

Figure 3.7


SS1
SS2
SS2
SS3
SS3
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
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6
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10
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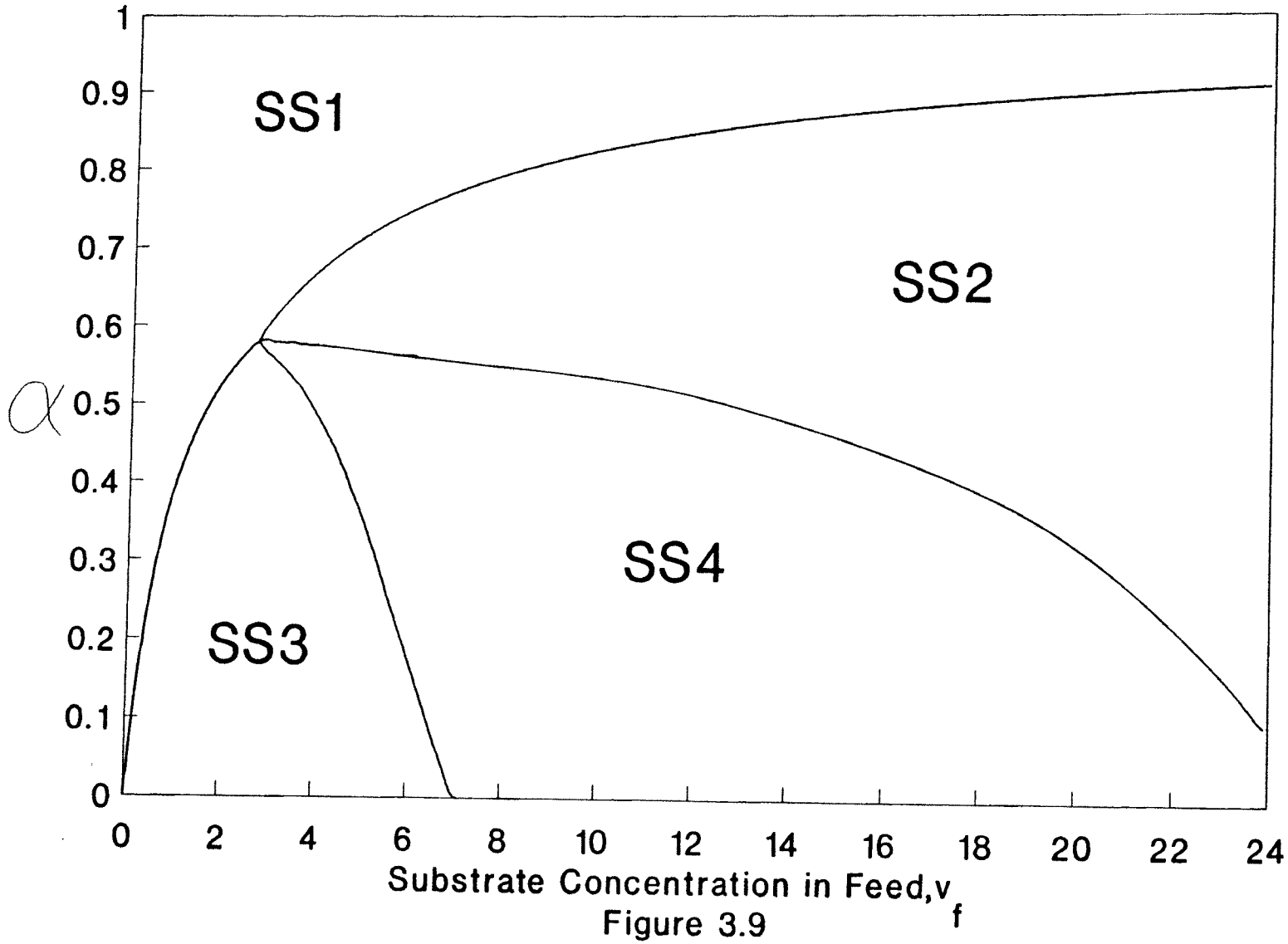
14
16
Substrate Concentration in Feed, v_f

Figure 3.8


SS1
SS2
SS3
SS4
α
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
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24
Substrate Concentration in Feed, v_f

Figure 3.9

CHAPTER 4
MATHEMATICAL DESCRIPTION OF A PARTIALLY INHIBITED SYSTEM

This chapter describes competition for two complementary nutrients by two microbial populations in a chemostat, when the growth of one competitor is inhibited by only one of the two substrates. Using interactive expressions for the specific growth rates, the case is described by one expression which can be viewed as a product of two Monod expressions, and one which can be viewed as a product of one Monod-type and one Andrews-type expression.

4.1 Model Equations

In order to have a fully described system, one needs to derive four mass balances, two of which are written for the biomass of the two populations and two for the rate-limiting substrates. When an interactive model is used, the equations describing the system are the following:

$$\frac{db_1}{dt} = -Db_1 + \mu_1 b_1 \tag{4.1}$$

$$\frac{db_2}{dt} = -Db_2 + \mu_2 b_2 \tag{4.2}$$

$$\frac{ds_1}{dt} = D(s_{1f} - s_1) - \frac{1}{Y_{11}}\mu_1 b_1 - \frac{1}{Y_{21}}\mu_2 b_2 \tag{4.3}$$

$$\frac{ds_2}{dt} = D(s_{2f} - s_2) - \frac{1}{Y_{12}}\mu_1 b_1 - \frac{1}{Y_{22}}\mu_2 b_2 \tag{4.4}$$

where,

b_j, $j = 1, 2$: biomass concentration of species j, in the chemostat

D: dilution rate (inverse of the holding time) defined as q/V

q: volumetric flow rate of medium externally fed to chemostat

V: working volume of chemostat

s_{if}, $i = 1, 2$: concentrations of the rate-limiting substrates in the feed to the chemostat

s_i, $i = 1, 2$: concentrations of the rate-limiting substrates in the chemostat

Y_{ij}: yield coefficient of species j on substrate i; $i = 1, 2$ and $j = 1, 2$

μ_j: specific growth rate of species j; $j = 1, 2$

For this part of the study it is assumed that

$$\mu_1 = \frac{\hat{\mu}_1 s_1 s_2}{(K_{11} + s_1 + (s_1^2/K_{I11}))(K_{21} + s_2)} \tag{4.5}$$

$$\mu_2 = \frac{\hat{\mu}_2 s_1 s_2}{(K_{12} + s_1)(K_{22} + s_2)} \tag{4.6}$$

with,

$\hat{\mu}_j$: characteristic constant for species j, having units of inverse time

K_{ij}: kinetic constant having units of concentration; it refers to species j and substrate i ($i = 1, 2$; $j = 1, 2$); it is known as the half -saturation constant

K_{I11}: kinetic constant having units of concentration; it refers to species 1 and the inhibitory substrate 1; it is known as the Andrews inhibition constant

By introducing the following dimensionless quantities:

$$x = \frac{b_1}{Y_{11}K_{11}} \qquad \theta = t\hat{\mu}_1 \qquad v_f = \frac{s_{2f}}{K_{21}}$$

$$y = \frac{b_2}{Y_{22}K_{21}} \qquad v = \frac{s_2}{K_{21}} \qquad \delta = \frac{K_{12}}{K_{11}}$$

$$\varepsilon = \frac{K_{21}}{K_{11}}\frac{Y_{22}}{Y_{21}} \qquad u_f = \frac{s_{1f}}{K_{11}} \qquad \sigma = \frac{K_{22}}{K_{21}}$$

$$\gamma = \frac{K_{11}}{K_{21}}\frac{Y_{11}}{Y_{12}} \qquad u = \frac{s_1}{K_{11}} \qquad \omega = \frac{K_{11}}{K_{I11}}$$

$$\varphi = \frac{\hat{\mu}_2}{\hat{\mu}_1} \qquad \alpha = \frac{D}{\hat{\mu}_1}$$

equations (4.1) through (4.4) can be written in dimensionless form as:

$$\frac{dx}{d\theta} = -\alpha x + \mu_1' x \tag{4.7}$$

$$\frac{dy}{d\theta} = -\alpha y + \mu_2' y \tag{4.8}$$

$$\frac{du}{d\theta} = \alpha(u_f - u) - \mu_1' x - \varepsilon \mu_2' y \tag{4.9}$$

$$\frac{dv}{d\theta} = \alpha(v_f - v) - \gamma \mu_1' x - \mu_2' y \tag{4.10}$$

with,

$$\mu_1' = \frac{uv}{(1 + u + \omega u^2)(1 + v)} \tag{4.11}$$

$$\mu_2' = \frac{\varphi uv}{(\delta + u)(\sigma + v)} \tag{4.12}$$

This system is in many ways similar to the one analyzed in Chapter 3 of this thesis. It has the same type of steady states as those discussed in section 3.3. Furthermore, the stoichiometric relations (3.12) and (3.13) are valid for the present case as well, implying again that two of the four eigenvalues of the system are equal to $-\alpha$ and that the actual dimensionality of the system is 2. The local character of the stability of each steady state is decided by the eigenvalues of the 2×2 Jacobian matrix J presented in section 3.4. Relations (3.14) through (3.25) hold for the present case as well, the only difference being that the expressions for M, N, K, and Λ are not those given by relations

(3.26) through (3.29); for the system studied here, the expressions for M, N, K, and Λ are the following:

$$\left[\frac{\partial \mu_1'}{\partial u}\right]_v = \frac{v(1-\omega u^2)}{(1+u+\omega u^2)^2(1+v)} = M \tag{4.13}$$

$$\left[\frac{\partial \mu_1'}{\partial v}\right]_u = \frac{u}{(1+u+\omega u^2)(1+v)^2} = N \tag{4.14}$$

$$\left[\frac{\partial \mu_2'}{\partial u}\right]_v = \frac{\varphi \delta v}{(\delta+u)^2(\sigma+v)} = K \tag{4.15}$$

$$\left[\frac{\partial \mu_2'}{\partial v}\right]_u = \frac{\varphi \sigma u}{(\delta+u)(\sigma+v)^2} = \Lambda \tag{4.16}$$

4.2 Analysis of Steady State 1 (SS1)

The stoichiometric relations, i.e., eqns (3.12) and (3.13), imply that $u=u_f$ and $v=v_f$. This steady state is always meaningful, since the conditions $0 < u \leq u_f$ and $0 < v \leq v_f$ are unconditionally satisfied.

The terms J_{12} and J_{21} of the Jacobian stability matrix are equal to zero while $J_{11}=-\alpha+\mu_1'$ and $J_{22}=-\alpha+\mu_2'$. The eigenvalues are: $\lambda_1=-\alpha+\mu_1'$, $\lambda_2=-\alpha+\mu_2'$.

It is obvious that both eigenvalues are real, while both of them are negative if and only if $\alpha > \mu_1'$ and $\alpha > \mu_2'$. Hence SS1 is stable if and only if:

$$\alpha > max[f(u_f, v_f), g(u_f, v_f)] \tag{4.17}$$

where,

$$f(u_f, v_f) = \frac{u_f v_f}{(1+u_f+\omega u_f^2)(1+v_f)} \tag{4.18}$$

and,

$$g(u_f, v_f) = \frac{\varphi u_f v_f}{(\delta + u_f)(\sigma + v_f)} \tag{4.19}$$

4.3 Analysis of Steady State 2 (SS2)

In this steady state population 2 wins the competition by excluding population 1 from the chemostat. One can easily observe that SS2 of the system studied here, is described by equations identical with those describing SS2 of the system studied in Chapter 3. Hence, the analysis is not repeated and only the results are presented. When

$$\alpha < \frac{\varphi u_f v_f}{(\delta + u_f)(\sigma + v_f)} \tag{4.20}$$

there is a unique, meaningful SS2 which is stable if and only if $\alpha > \mu_1'$. The eigenvalues are real and thus, no oscillatory behavior is exhibited by the system during transients.

4.4 Analysis of Steady State 3 (SS3)

In this steady state population 1 wins the competition, while population 2 washes out of the chemostat. Equations (4.7), (3.12), and (3.13) imply that

$$\alpha = \mu_1' \tag{4.21}$$

$$x = u_f - u \tag{4.22}$$

$$x = \frac{v_f - v}{\gamma} \tag{4.23}$$

Equation (4.21) implies that the values of u and v will not be meaningful, unless the following condition is met:

$$\alpha < 1 \tag{4.24}$$

Using equations (4.21) through (4.23), one can show that the value of x is given as a solution to the following cubic equation:

$$F(x) = a_1 x^3 - b_1 x^2 + c_1 x - d_1 = 0 \tag{4.25}$$

where,

$$a_1 = \alpha\gamma\omega \tag{4.26}$$

$$b_1 = \gamma(\alpha - 1) + \alpha\omega(1 + v_f + 2\gamma u_f) \tag{4.27}$$

$$c_1 = \alpha(\gamma + 1) + \gamma u_f(\alpha - 1) + v_f(\alpha - 1) + \alpha\omega u_f(2 + 2v_f + \gamma u_f) \tag{4.28}$$

$$d_1 = \alpha(1 + v_f + u_f) + u_f v_f(\alpha - 1) + \alpha\omega u_f^2(1 + v_f) \tag{4.29}$$

One can show that the following statements are true:

$$if \quad \alpha < \frac{u_f v_f}{(1 + u_f + \omega u_f^2)(1 + v_f)}, \quad then \quad F(0) > 0 \tag{4.30}$$

$$if \quad \alpha > \frac{u_f v_f}{(1 + u_f + \omega u_f^2)(1 + v_f)}, \quad then \quad F(0) < 0 \tag{4.31}$$

$$if \quad u_f > \frac{1 + v_f}{\gamma}, \quad then \quad F(u_f) > 0 \tag{4.32}$$

$$if \quad u_f < \frac{1 + v_f}{\gamma}, \quad then \quad F(u_f) < 0 \tag{4.33}$$

$$if \quad u_f > \frac{1 + v_f}{\gamma}, \quad then \quad F\left(\frac{1 + v_f}{\gamma}\right) < 0 \tag{4.34}$$

$$if \quad u_f < \frac{1 + v_f}{\gamma}, \quad then \quad F\left(\frac{1 + v_f}{\gamma}\right) > 0 \tag{4.35}$$

$$if \;\; u_f > \frac{v_f}{\gamma}, \quad then \quad F\left(\frac{v_f}{\gamma}\right) < 0 \tag{4.36}$$

It should be mentioned here that $u_f < (v_f/\gamma)$ does not necessarily imply that $F(v_f/\gamma) > 0$.

Case 1:

$$\alpha < \frac{u_f v_f}{(1 + u_f + \omega u_f^2)(1 + v_f)}$$

From (4.30) one can conclude that $d_1 < 0$. From (4.26) it is obvious that $a_1 > 0$. Let x_1, x_2, and x_3 be the roots of (4.25). The product of the three roots is equal to d_1/a_1 which is negative, thus implying that at least one of the three roots is negative. Let $x_3 < 0$.

Case 1a: $u_f > (1 + v_f)/\gamma$

In this case, (4.34) and (4.36) imply that there are positive values of x for which $F(x) < 0$. Hence, x_1 and x_2 are both real and positive. Let $x_1 < x_2$. Relations (4.32) and (4.36) imply that

$$x_1 < v_f/\gamma < x_2 < u_f.$$

Now, taking into consideration relations (4.22) and (4.23) one can conclude that only x_1 leads to meaningful values for both u and v. Hence, in this case there is a unique meaningful SS3.

Case 1b: $v_f/\gamma < u_f < (1 + v_f)/\gamma$

In this case, (4.33) and (4.36) imply that there are positive values of x for which $F(x) < 0$. Hence, x_1 and x_2 are both real and positive. Let $x_1 < x_2$. Relations (4.33), (4.35) and (4.36) imply that

$$x_1 < v_f/\gamma < u_f < x_2$$

Now, taking into consideration relations (4.22) and (4.23) one can conclude that only x_1 leads to meaningful values for both u and v. Hence, again in this case there is a unique meaningful SS3.

Case 1c: $u_f < v_f/\gamma$

In this case, (4.33) impies that there is at least one positive value of x for which $F(x) < 0$. Hence, x_1 and x_2 are real and positive. Let $x_1 < x_2$. Relations (4.33) and (4.35) imply that either

$$x_1 < u_f < v_f/\gamma < x_2 < (1 + v_f)/\gamma$$

or

$$x_1 < u_f < x_2 < v_f/\gamma$$

In either case, when relations (4.22) and (4.23) are taken into consideration, the conclusion is that only x_1 leads to meaningful values for both u and v. Hence, again in this case there is a unique meaningful SS3.

The following conclusion can be reached: SS3 is meaningful and unique, provided that

$$\alpha < \frac{u_f v_f}{(1 + u_f + \omega u_f^2)(1 + v_f)} \tag{4.37}$$

Case 2:

$$\alpha > \frac{u_f v_f}{(1 + u_f + \omega u_f^2)(1 + v_f)}$$

In this case, following the reasoning of Case 1, one can show that (4.25) has at least one positive root which leads to meaningless values for u and v. It is not possible to show analytically that there is no meaningful SS3 when (4.37) is violated but numerical calculations have shown that in fact this is the case.

Regarding the stability of SS3, one can show that the eigenvalues are given as: $\lambda_1 = -x(M + \gamma N)$, $\lambda_2 = -\alpha + \mu_2'$. From expressions (4.13) and (4.14) one can see that for a meaningful SS3, $N > 0$. The sign of M cannot be analytically predicted here. Hence, there are two conditions for stability of a meaningful SS3; namely $\alpha > \mu_2'$ and $M + \gamma N > 0$. Once again, the eigenvalues are real, and thus the system will always approach this steady

state in an exponential fashion.

4.5 Analysis of Steady State 4 (SS4)

For this coexistence steady state, eqns (4.6) and (4.7) imply that $\alpha = \mu_1' = \mu_2'$. In this case one can see that a meaningful SS4 requires that $\alpha < g(u_f, v_f)$ but it does not necessarily require that $\alpha < f(u_f, v_f)$. One can conclude that SS4 and SS1 are mutually exclusive. Since the stoichiometric relations are the same for both cases considered in Chapters 3 and 4, the values of x and y (when u and v are known) will be given for the system considered in this Chapter, by eqns (3.55) and (3.56).

Since $\mu_1' = \mu_2'$, one can show that the value of v (when u is known) will be given by the following expression:

$$v = \frac{(\delta\sigma - \varphi) + (\sigma - \varphi)u - \varphi\omega u^2}{(\varphi - \delta) + (\varphi - 1)u + \varphi\omega u^2} \tag{4.38}$$

Using the eqn. $\alpha = \mu_1'$ and substituting for v the expression (4.38) one can show that the value of u is given as a solution to the following cubic equation:

$$F(u) = a_3u^3 + b_3u^2 + c_3u + d_3 = 0 \tag{4.39}$$

where,

$$a_3 = \varphi\omega(\alpha\sigma - \alpha + \varphi) \tag{4.40}$$

$$b_3 = \alpha\delta\varphi\omega(\sigma - 1) + \sigma\varphi(\alpha - 1) + \varphi(\varphi - \alpha) \tag{4.41}$$

$$c_3 = \alpha\sigma\varphi(\delta + 1) - \delta\varphi(\alpha + \sigma) + \varphi(\varphi - \alpha) \tag{4.42}$$

$$d_3 = \alpha\delta\varphi(\sigma - 1) \tag{4.43}$$

It is clear that there may be up to three different steady states 4. The expressions are too complex for the analysis to proceed any further. As

discussed in the following section, numerical results have shown that there are cases where in the $\alpha - u_f - v_f$ space there is a domain where two different SS4 actually arise. So, in this case SS4 can in fact exhibit multiplicity. It should be mentioned that three SS4 have never been found during the numerical studies.

Regarding the stability of SS4, its two eigenvalues are again given as solutions to the equation (3.66). In this case though, the expressions (values) of M, N, K, and Λ are those described by relations (4.13) through (4.16). Since it cannot be exluded that M may be negative, for the partially inhibited system considered here we cannot conclude (as in the case studied in Chapter 3) that the eigenvalues of SS4 are always real, or that the stability of SS4 is determined only by the values of ε and γ. In fact, numerical studies have shown that the latter is not always true.

4.6 Numerical Results and Operating Diagrams

As in the case of the uninhibited system discussed in Chapter 3, a number of questions regarding the partially inhibited system had to be answered numerically. In this section, results of extensive numerical studies are discussed and some operating diagrams in the $\alpha - u_f$ plane are presented. The programs used in these studies are given in the Appendix of this thesis; they are based on the expressions which have been developed in the preceeding sections while for getting the roots of cubic equations the subroutine ZPORC of the IMSL/Math Library was employed.

The main conclusions from the numerical studies on the partially inhibited system are as follows:

- The surfaces defined by relations (4.18) and (4.19) play a very important role on the outcome of competition. In the $\alpha - u_f$ plane, the

$f(u_f, v_f)$ and $g(u_f, v_f)$ surfaces become curves. Unless the $f(u_f, v_f)$ and $g(u_f, v_f)$ surfaces (or curves) cross each other, coexistence of the two competitors is not possible.

- When $\alpha > f(u_f, v_f)$, SS3 cannot arise.
- The coexistence SS4 arises only if $\alpha < min[f(u_f, v_f), g(u_f, v_f)]$.
- The total washout steady state (SS1) is mutually exclusive with each one of the remaining three types of steady states.
- The coexistence steady state (SS4) is the only type of steady state which exhibits multiplicity. In fact, although theoretically one can have up to three different SS4, numerically only up to two different SS4 have been found under the same operating conditions (i.e., α, u_f, v_f). It should be also mentioned that when two SS4 arise, one is stable while the other is unstable. Furthermore, under the same operating conditions there is a meaningful and stable SS2 (e.g., Figures 4.14 and 4.16).
- The pairs of SS2 and SS3; SS2 and SS4 are not mutually exclusive in the sense that there are domains in the $\alpha - u_f - v_f$ space where both steady states of each pair are meaningful and stable. Whenever this happens, there is a meaningful but unstable SS4 in the same domain. Based on the calculations performed for this study, it seems that SS3 and SS4 are mutually exclusive.

As can be seen from the expressions (4.18) and (4.19), for a given v_f, the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves may cross each other at a single u_f-value; they may cross each other at two u_f-values; or they may not cross each other for any u_f-value. Since the last case never leads to coexistence of the two competitors, no operating diagrams are presented here for such situations.

The diagrams of Figures 4.1 through 4.9 are for cases where the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves cross each other at a single u_f-value, while the diagrams of Figures 4.10 through 4.19 are for cases where the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves cross each other at two u_f-values.

When the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves cross each other at a single u_f-value (in the $\alpha - u_f$ plane), the results are identical with those obtained for the uninhibited case (Chapter 3). The coexistence steady state does not exhibit multiplicity, and its stability is determined by the system parameters only (i.e., φ, σ, δ, ε, and γ).

When $\sigma > \delta$, and $\varepsilon\gamma < 1$ (Figures 4.1, 4.3, 4.7 through 4.9) there is a region where both SS2 and SS3 are meaningful and stable. In the same region, there is a unique, meaningful but unstable SS4. The extent of this region reduces as the value of $\varepsilon\gamma$ increases (Figures 4.1 and 4.3) towards 1, and when $\varepsilon\gamma = 1$ the region becomes a curve (Figure 4.6). The region where SS4 is meaningful but unstable, shifts to higher u_f values and its extent increases considerably as the value of v_f increases (Figures 4.1 and 4.7). The opposite is true when v_f decreases (Figures 4.1 and 4.8). As the value of ω increases (i.e, inhibitory effects are more pronounced), the region of SS4 shifts to lower u_f values (Figures 4.1 and 4.9). It seems that a decreasing ω-value and an increasing v_f-value have the same impact on the system.

When $\sigma > \delta$, and $\varepsilon\gamma > 1$ (Figures 4.2, 4.4, and 4.5), there is a region of a unique, meaningful and stable SS4. When ω increases, the region of coexistence shifts to lower u_f-values and the extent of the region decreases.

When the $f(u_f, v_f)$ and $g(u_f, v_f)$ curves cross each other at two u_f-values in the $\alpha - u_f$ plane, the situation is much different from the uninhibited case and the system exhibits much more complex dynamics. In such cases, the possibility of maintaining a mixed culture (coexistence) increases significantly. In fact, one can always find a region where at least one SS4 is

meaningful and stable, provided that $\varepsilon\gamma \neq 1$. When $\varepsilon\gamma = 1$ coexistence is not possible, neither regions where SS2 and SS3 are both meaningful and stable can be found (Figure 4.19).

When $\sigma > \delta$, and $\varepsilon\gamma < 1$ (Figure 4.10), a region of stable SS4 arises from the lower of the two u_f-values for which $f(u_f, v_f) = g(u_f, v_f)$, while a region of an unstable SS4 [with both SS2 and SS3 meaningful and stable] arises from the larger of the two u_f-values. Exactly the opposite is true when $\varepsilon\gamma > 1$ (Figure 4.11).

Comparing the diagrams of Figures 4.10, 4.14, and 4.15 one can see that when $\sigma > \delta$ and $\varepsilon\gamma < 1$, at low v_f-values the regions where SS4 arises are further apart and their extent is small. At large v_f-values (Figure 4.14) the two regions overlap and give rise to a new one. This is a very interesting region since there are two meaningful SS4 only one of which is stable, and a stable SS2 as well. Comparing the diagrams of Figures 4.10, 4.16, and 4.17 one can see that the effect of an increased ω-value on the system is the same as that of an increased v_f.

The effects of v_f and ω on the system when $\varepsilon\gamma > 1$ are the same with the ones already discussed for $\varepsilon\gamma < 1$. From Figures 4.11 and 4.12 one can see that as v_f increases the two regions of SS4 come closer. From Figures 4.11 and 4.13 one can see that as ω decreases, the two regions of SS4 become more separated from one another.

The main conclusion here is that coexistence is possible in most cases when the system is partially inhibited. The dynamics can be quite complex with a number of different steady states arising in the same domain of the operating parameters space, something which may imply that control is required for maintaining a mixed culture at the desired concentration levels.

Table 4.1

Partially Inhibited System-Parameter values used for operating diagrams 4.1-4.19

Figure	ε	γ	φ	σ	δ	ω	v_f
4.1	0.2	0.5	0.6	1.2	0.8	0.1	2.0
4.2	1.3	1.7	0.6	1.2	0.8	0.1	2.0
4.3	0.45	1.0	0.6	1.2	0.8	0.1	2.0
4.4	1.3	1.7	0.6	1.2	0.8	0.5	2.0
4.5	1.3	1.7	0.6	1.2	0.8	0.05	2.0
4.6	4.0	0.25	0.6	1.2	0.8	0.1	2.0
4.7	0.2	0.5	0.6	1.2	0.8	0.1	5.0
4.8	0.2	0.5	0.6	1.2	0.8	0.1	1.0
4.9	0.2	0.5	0.6	1.2	0.8	0.3	2.0
4.10	0.2	0.5	0.6	1.1	0.4	0.1	4.0
4.11	1.3	1.7	0.6	1.1	0.4	0.1	4.0
4.12	1.3	1.7	0.6	1.1	0.4	0.1	5.0
4.13	1.3	1.7	0.6	1.1	0.4	0.05	4.0
4.14	0.2	0.5	0.6	1.1	0.4	0.1	8.0
4.15	0.2	0.5	0.6	1.1	0.4	0.1	1.0
4.16	0.2	0.5	0.6	1.1	0.4	0.2	4.0
4.17	0.2	0.5	0.6	1.1	0.4	0.05	4.0
4.18	0.2	0.5	0.6	1.1	0.4	0.05	8.0
4.19	4.0	0.25	0.6	1.1	0.4	0.1	2.0

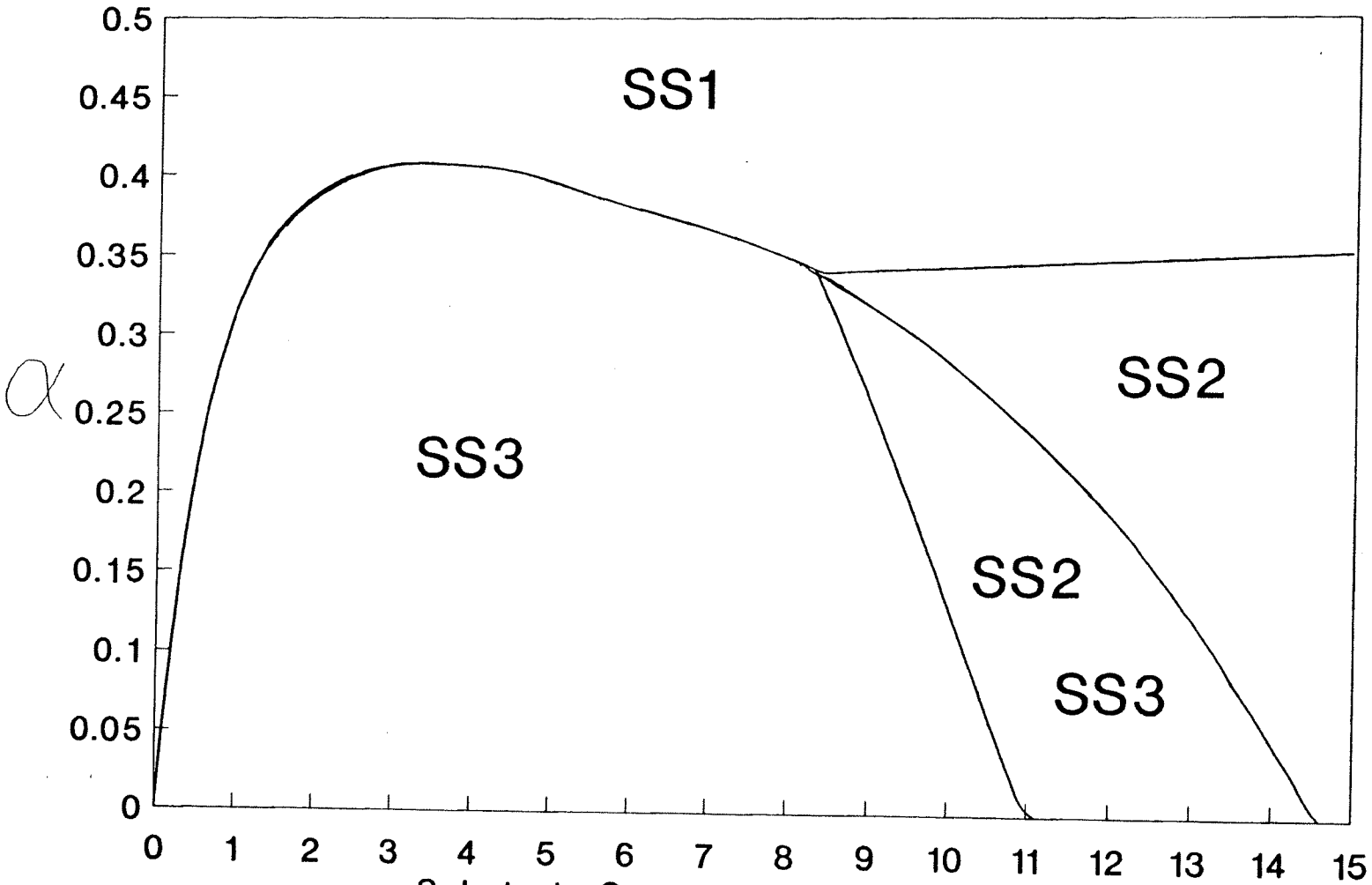
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2
SS3
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Substrate Concentration in Feed, u_f

Figure 4.1

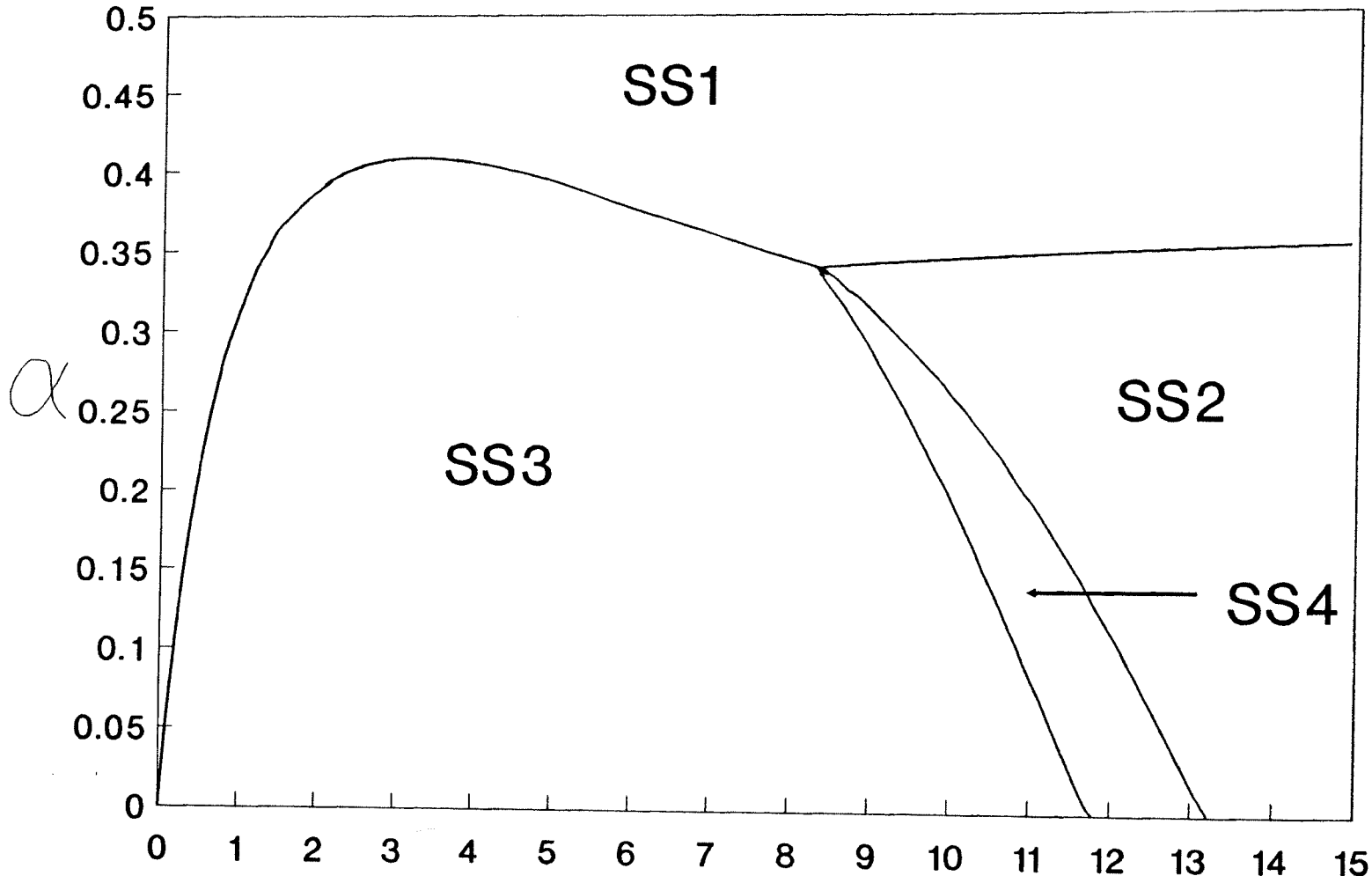
SS1
SS2
SS3
SS4
α
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Substrate Concentration in Feed,u f

Figure 4.2

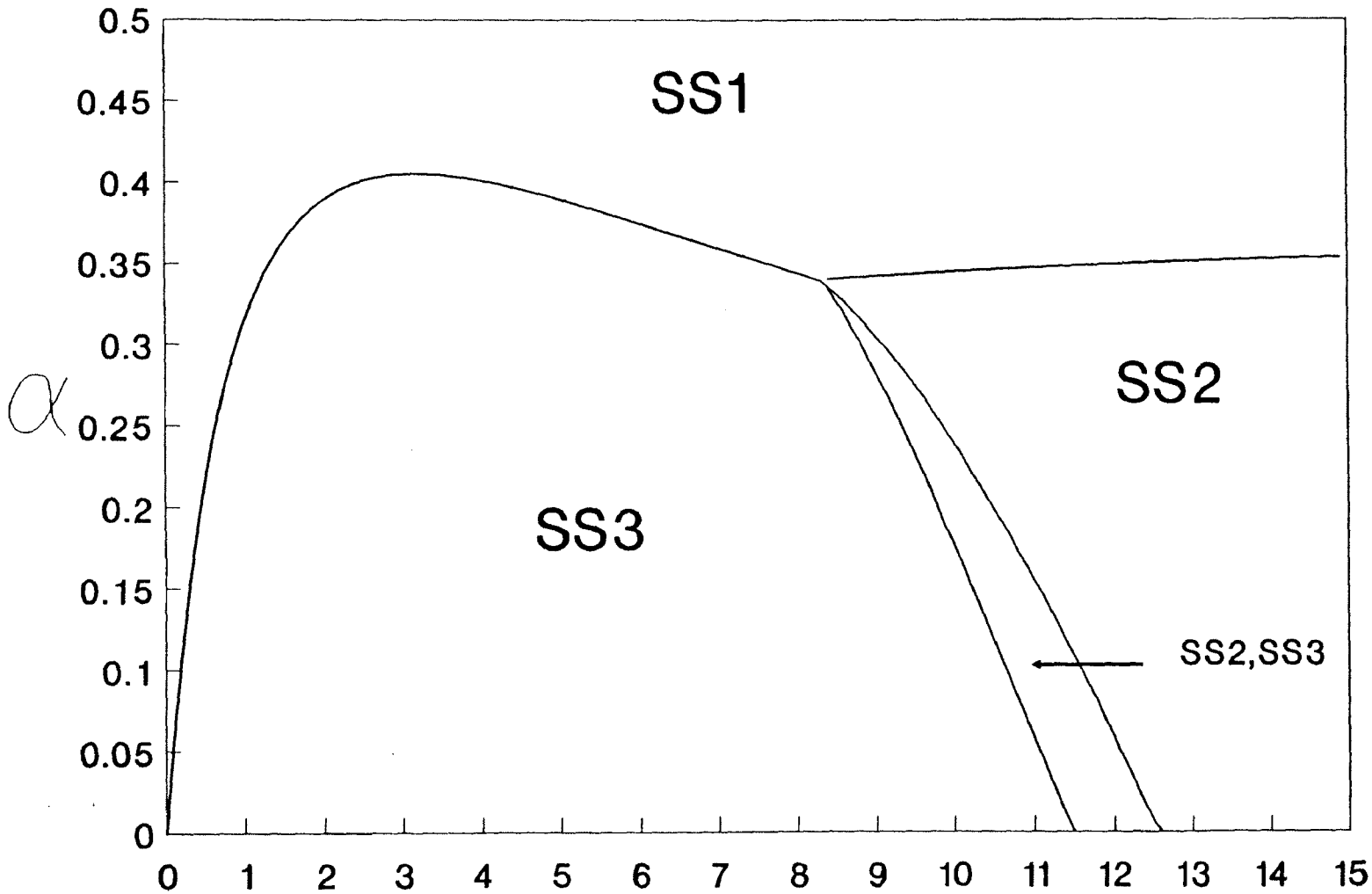
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2,SS3
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Substrate Concentration in Feed,u_f

Figure 4.3

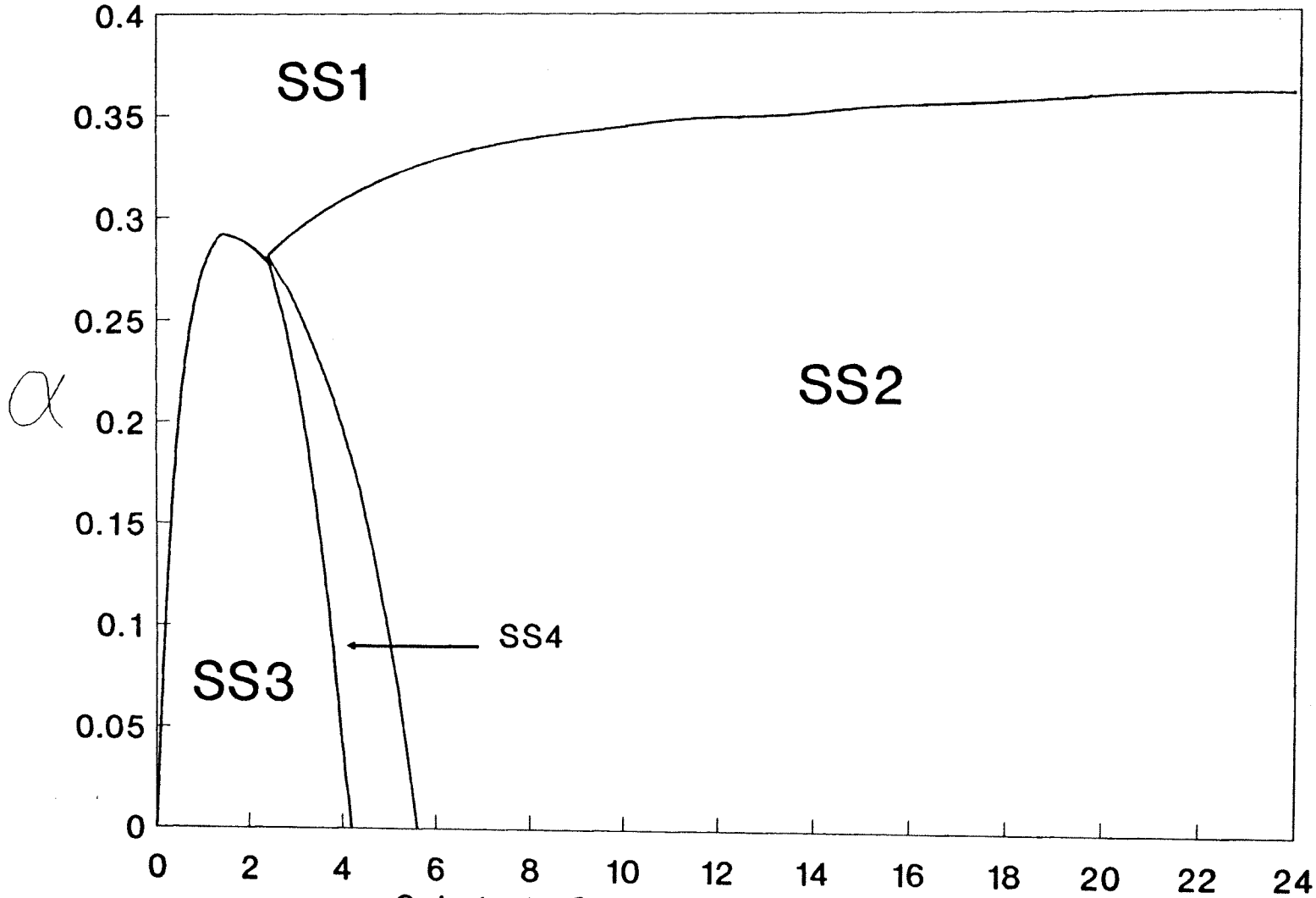
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS4
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.4

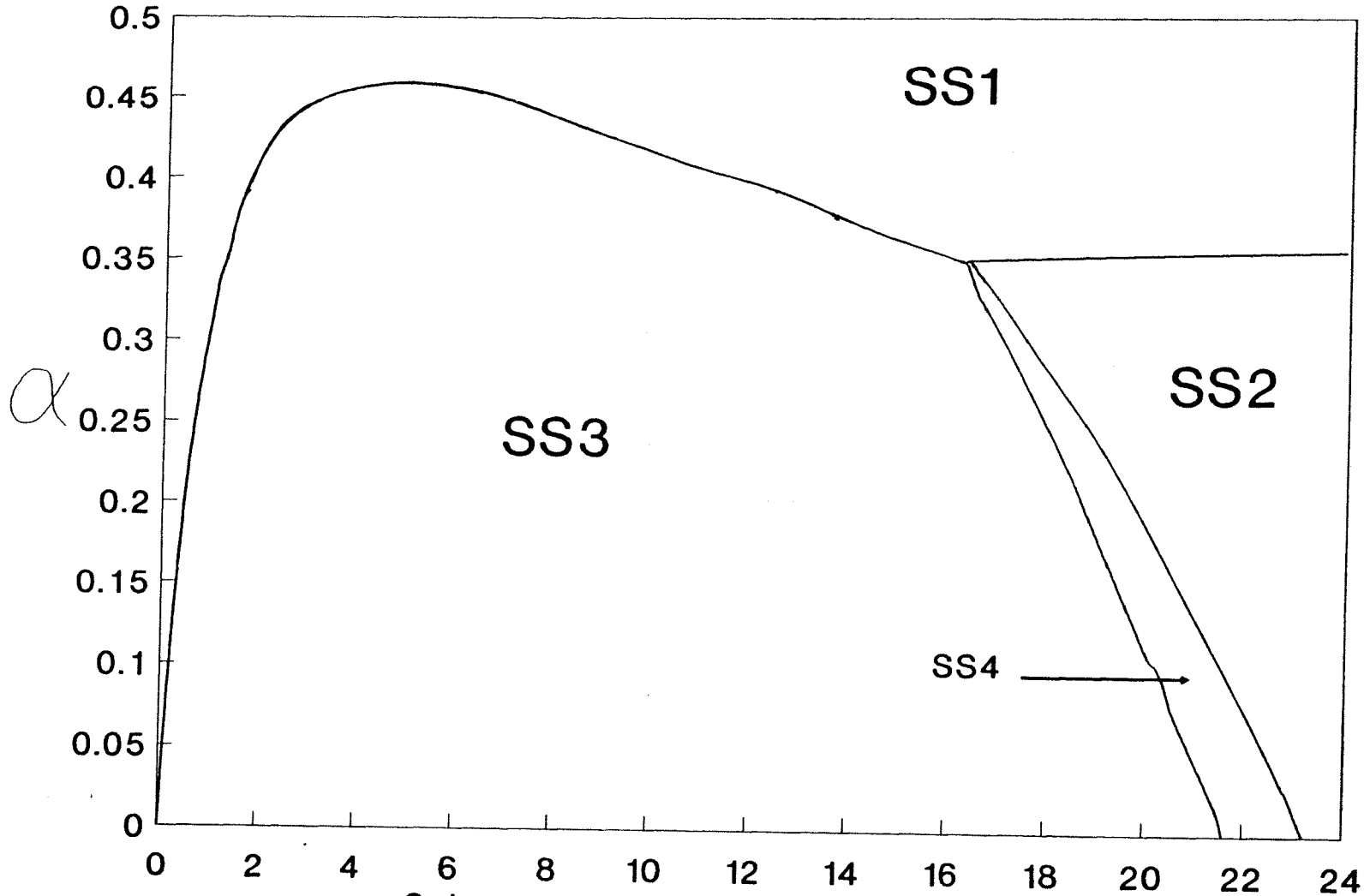
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS4
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.5

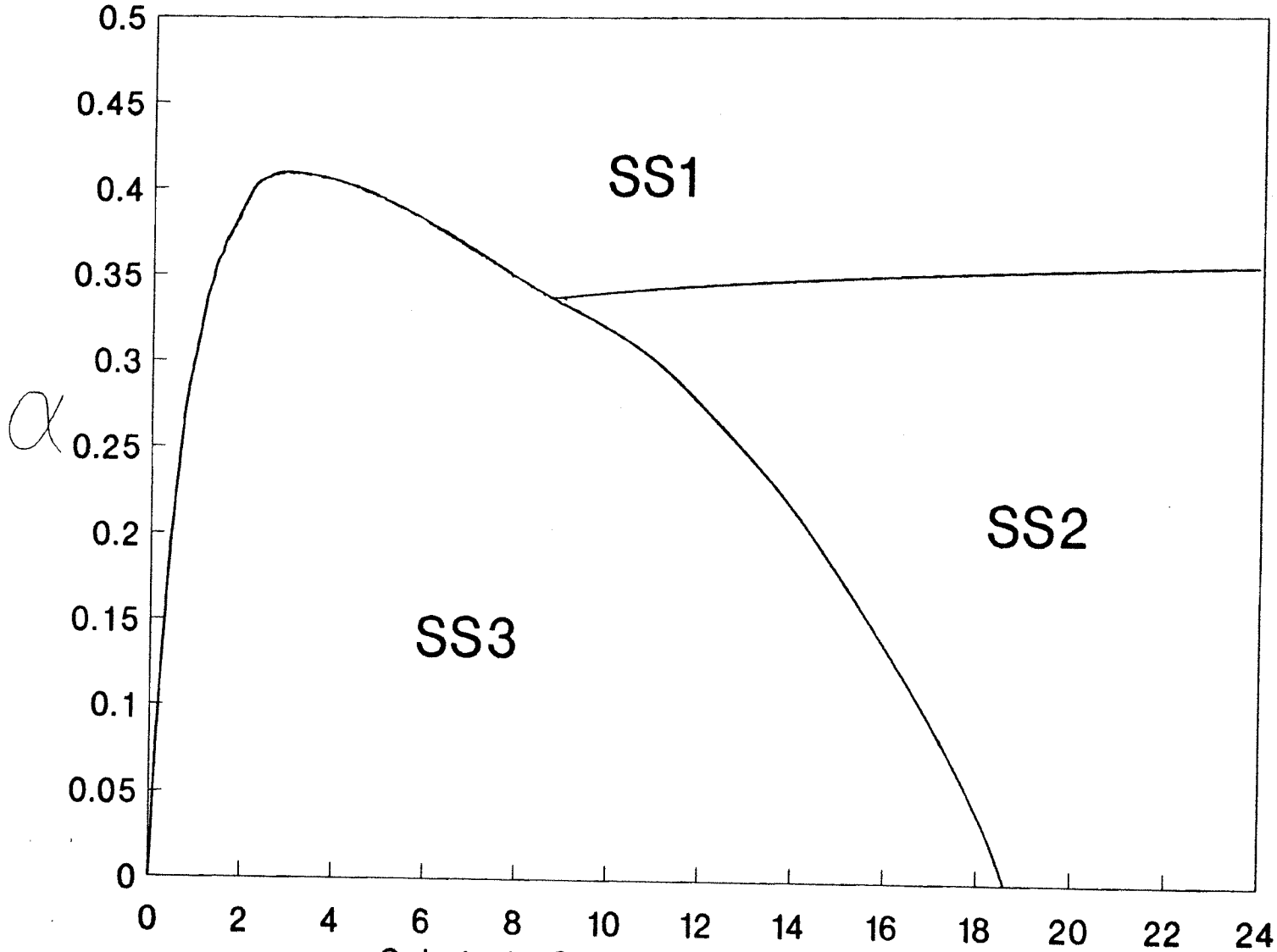
0.5
0.45
0.4
0.35
0.3
α
0.25
0.2
0.15
0.1
0.05
0
SS1
SS2
SS3
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.6

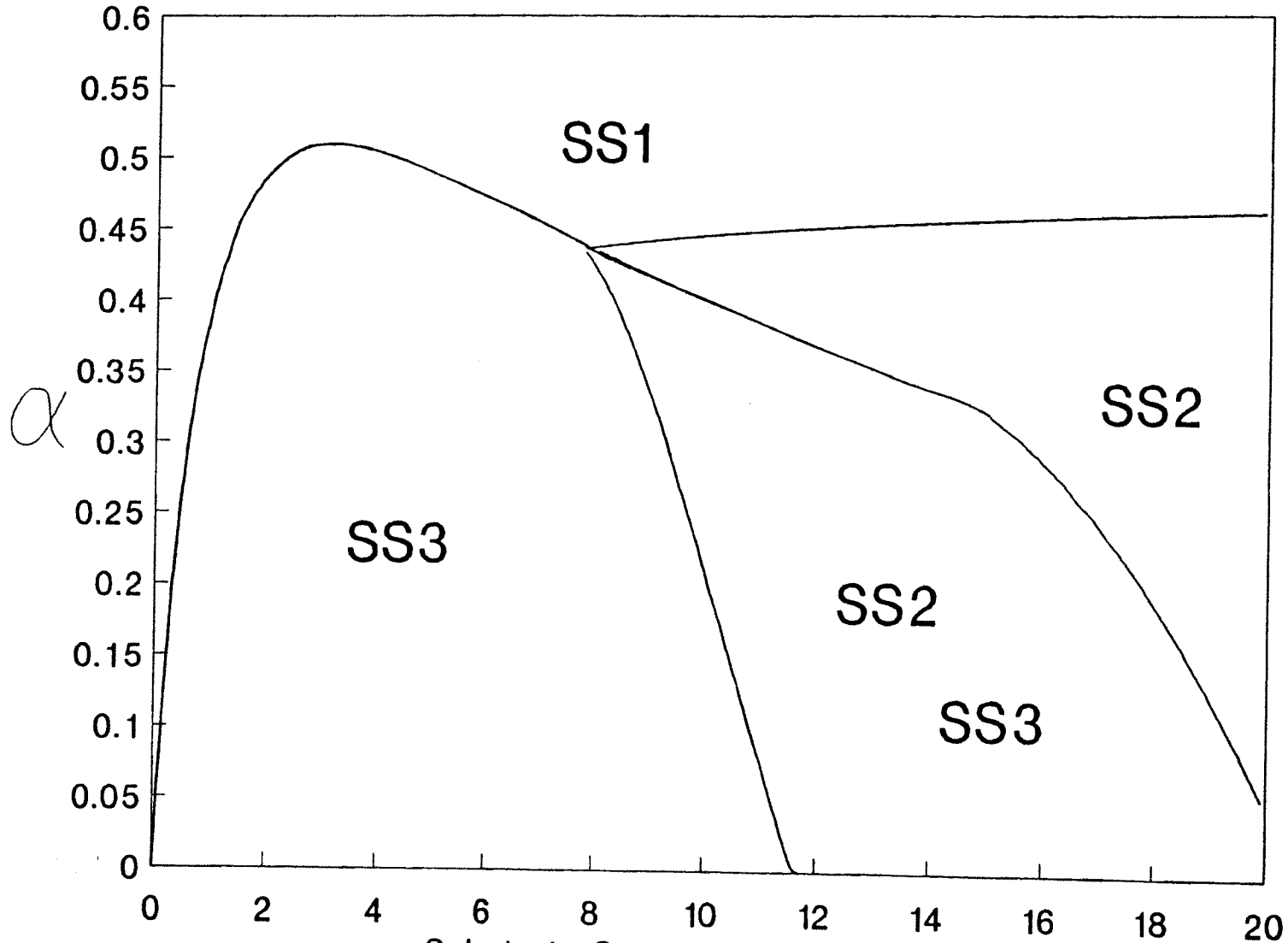
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2
SS3
0
2
4
6
8
10
12
14
16
18
20
Substrate Concentration in Feed,u_f

Figure 4.7

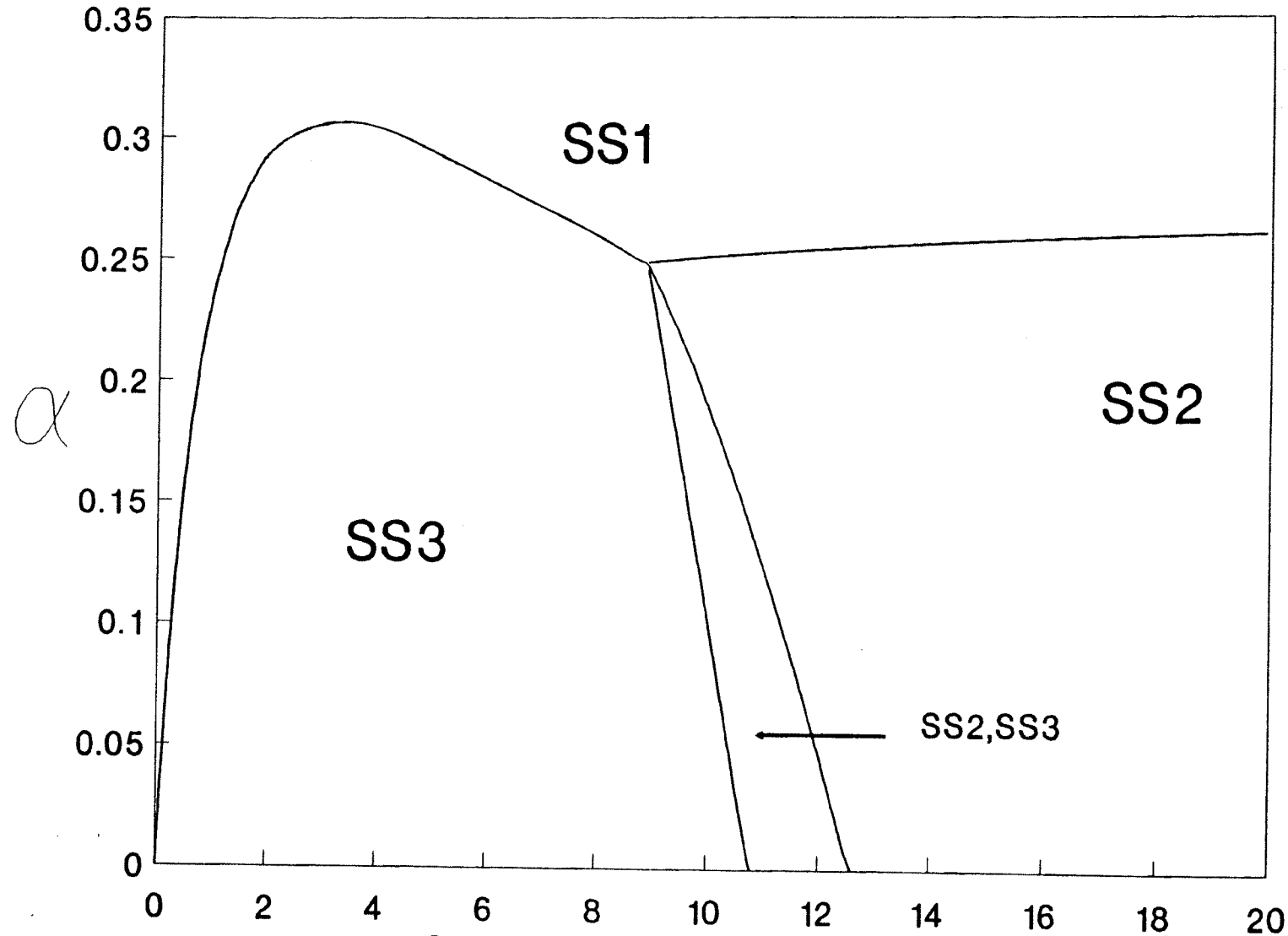
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2,SS3
0
2
4
6
8
10
12
14
16
18
20
Substrate Concentration in Feed,u_f

Figure 4.8

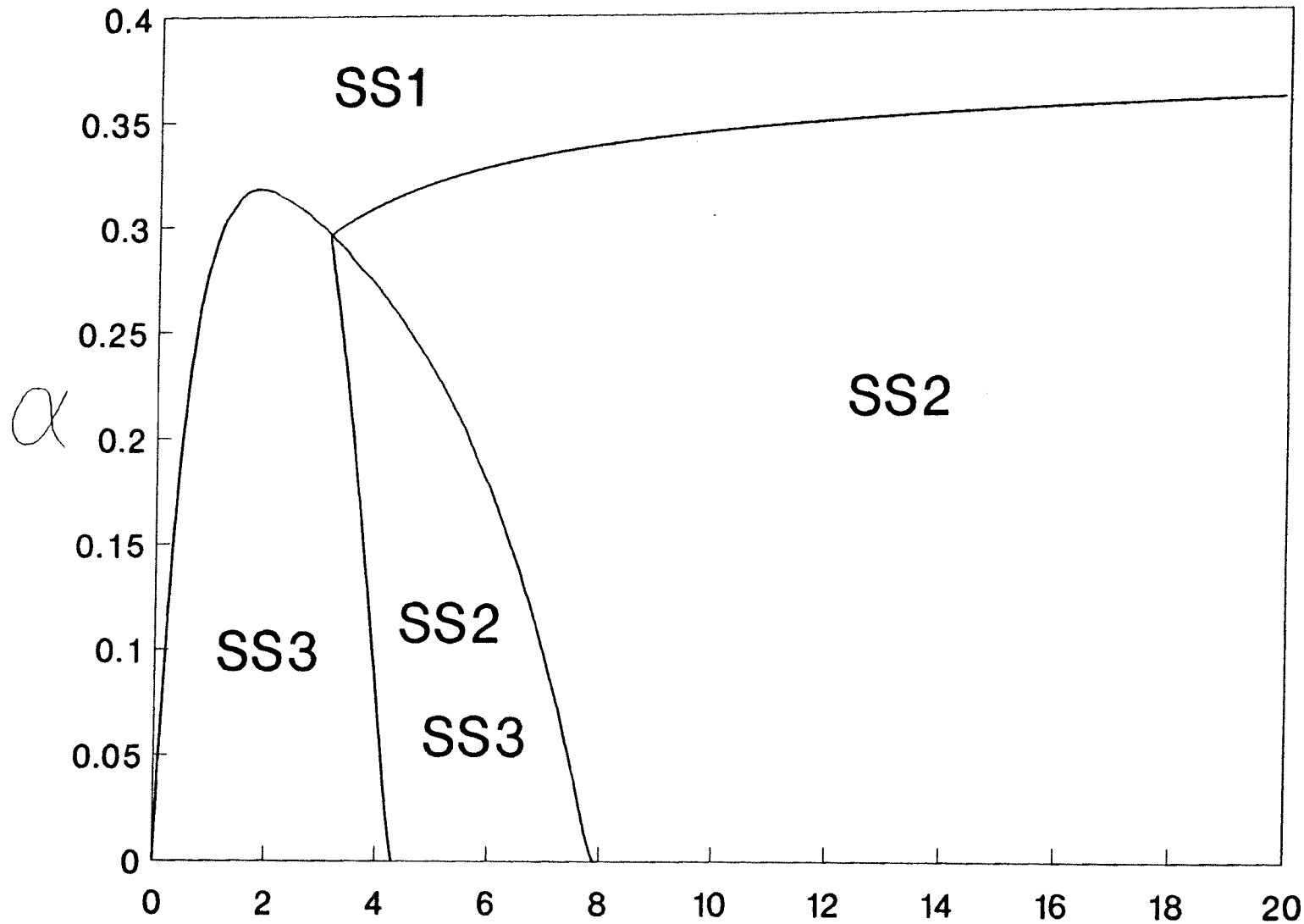
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2
SS3
0
2
4
6
8
10
12
14
16
18
20
Substrate Concentration in Feed,u_f

Figure 4.9

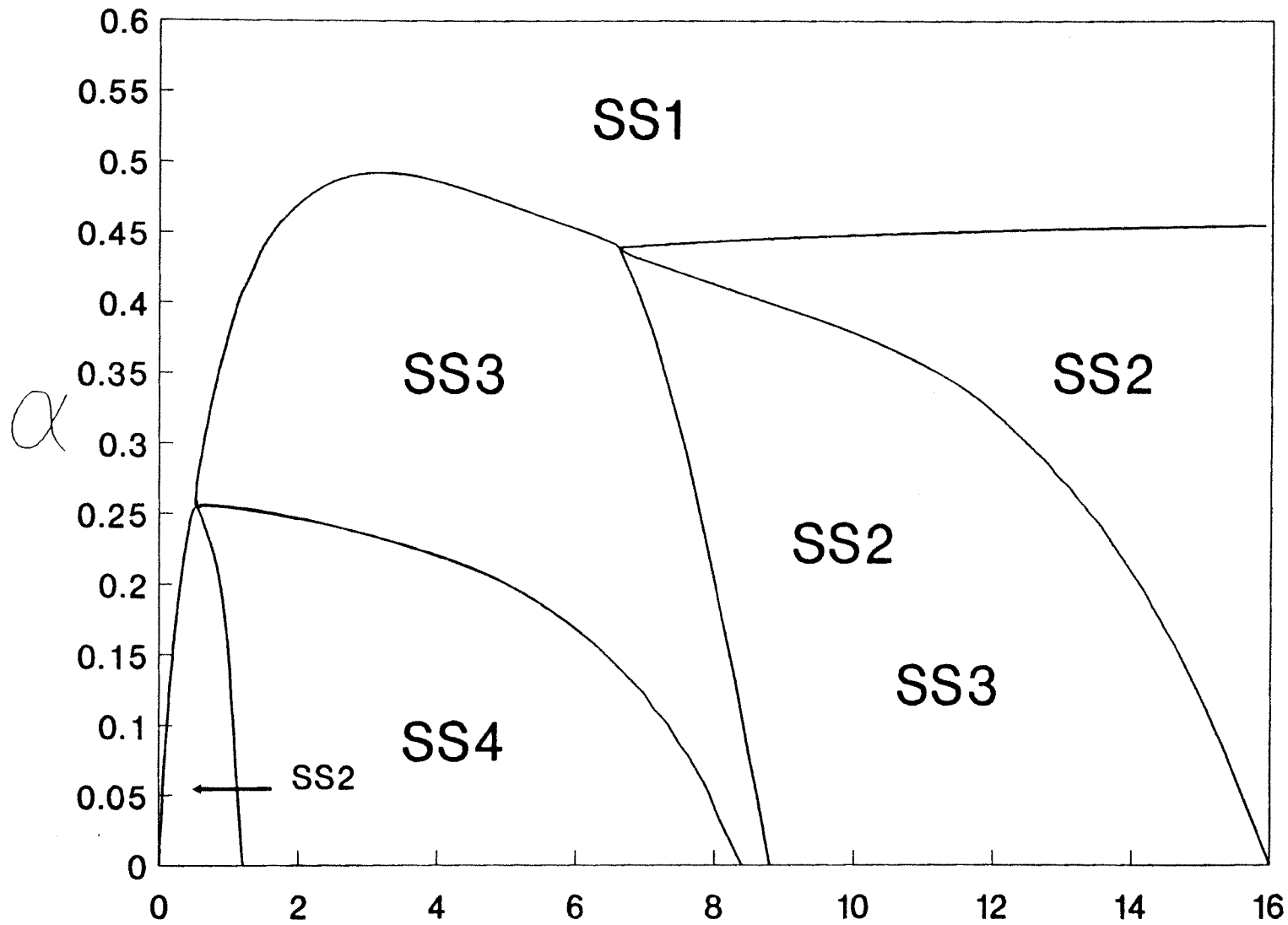
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS3
SS2
SS2
SS3
SS4
SS2
0
2
4
6
8
10
12
14
16
Substrate Concentration in Feed,u_f

Figure 4.10

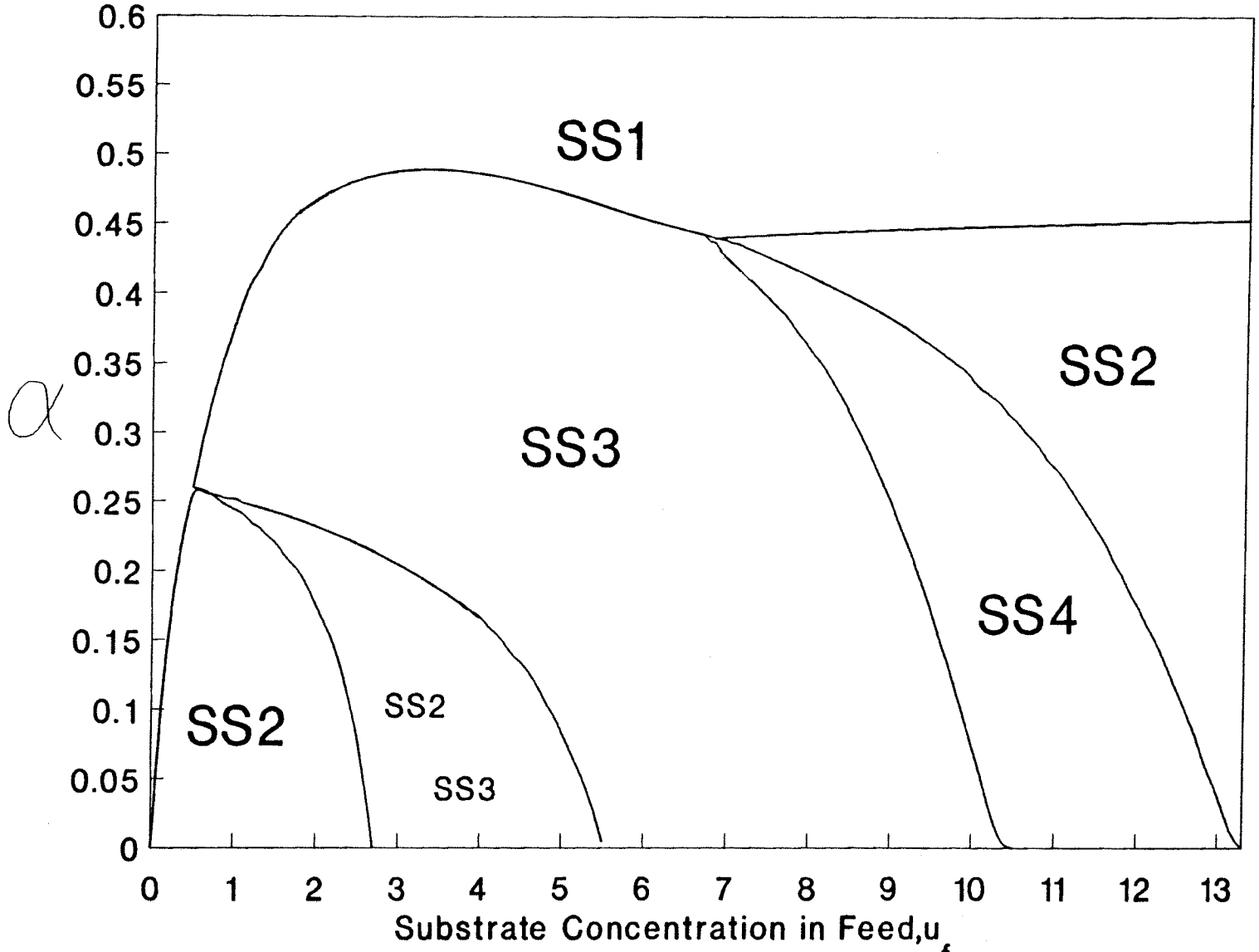
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS4
SS2
SS2
SS3
0
1
2
3
4
5
6
7
8
9
10
11
12
13
Substrate Concentration in Feed,u_f

Figure 4.11

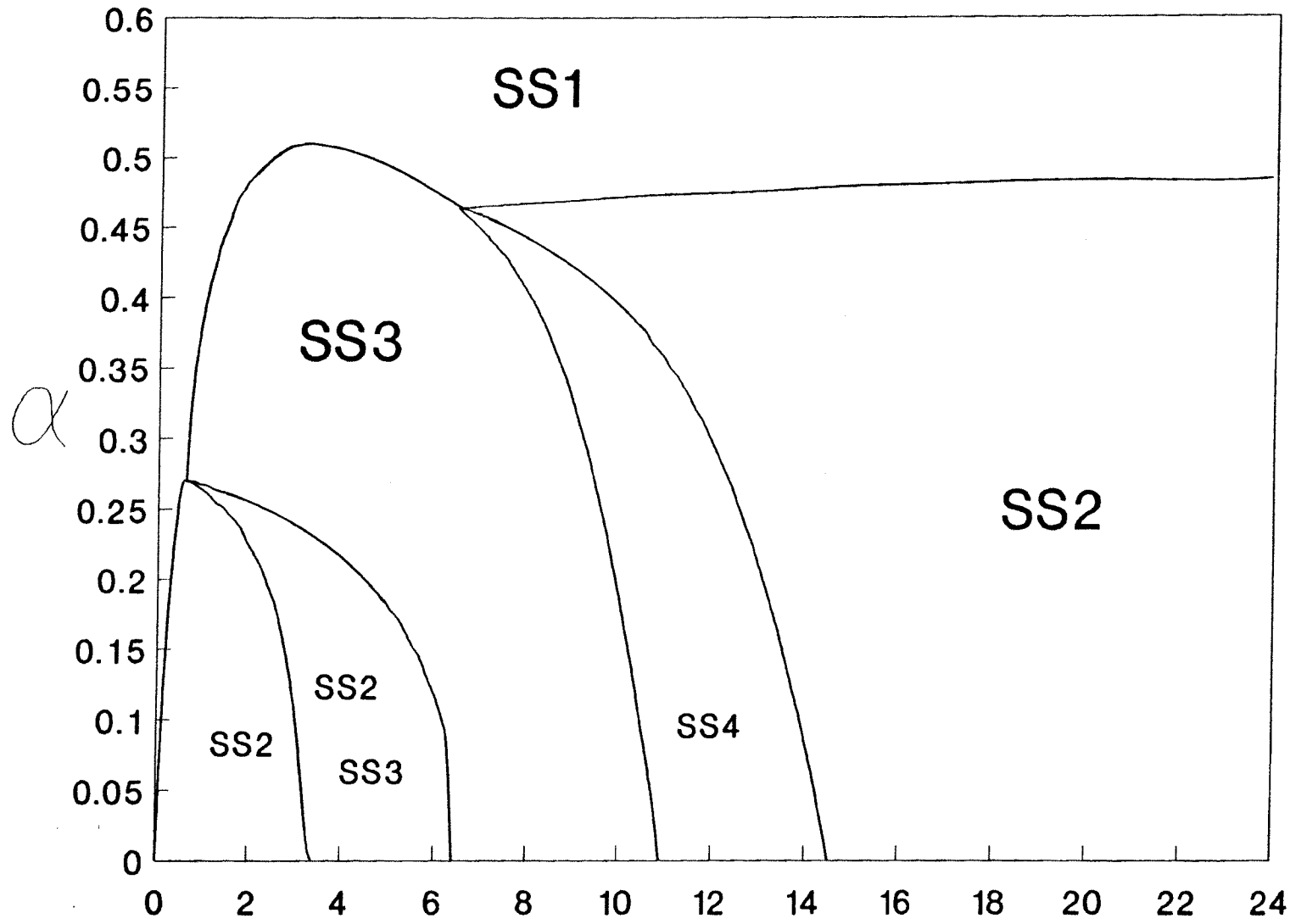
SS1
SS3
SS2
SS2
SS3
SS2
SS4
α
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.12

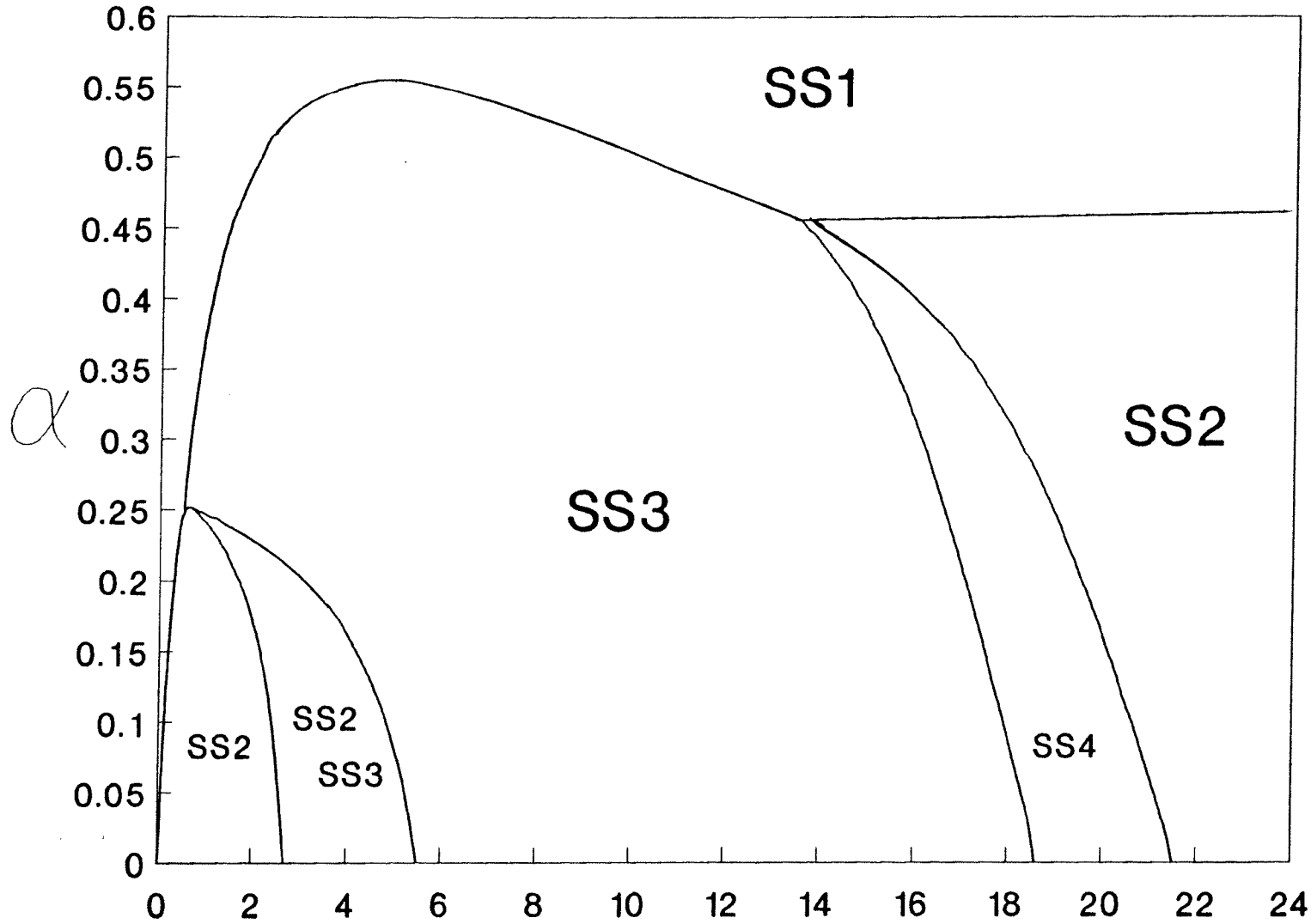
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS2
SS3
SS2
SS2
SS3
SS4
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.13

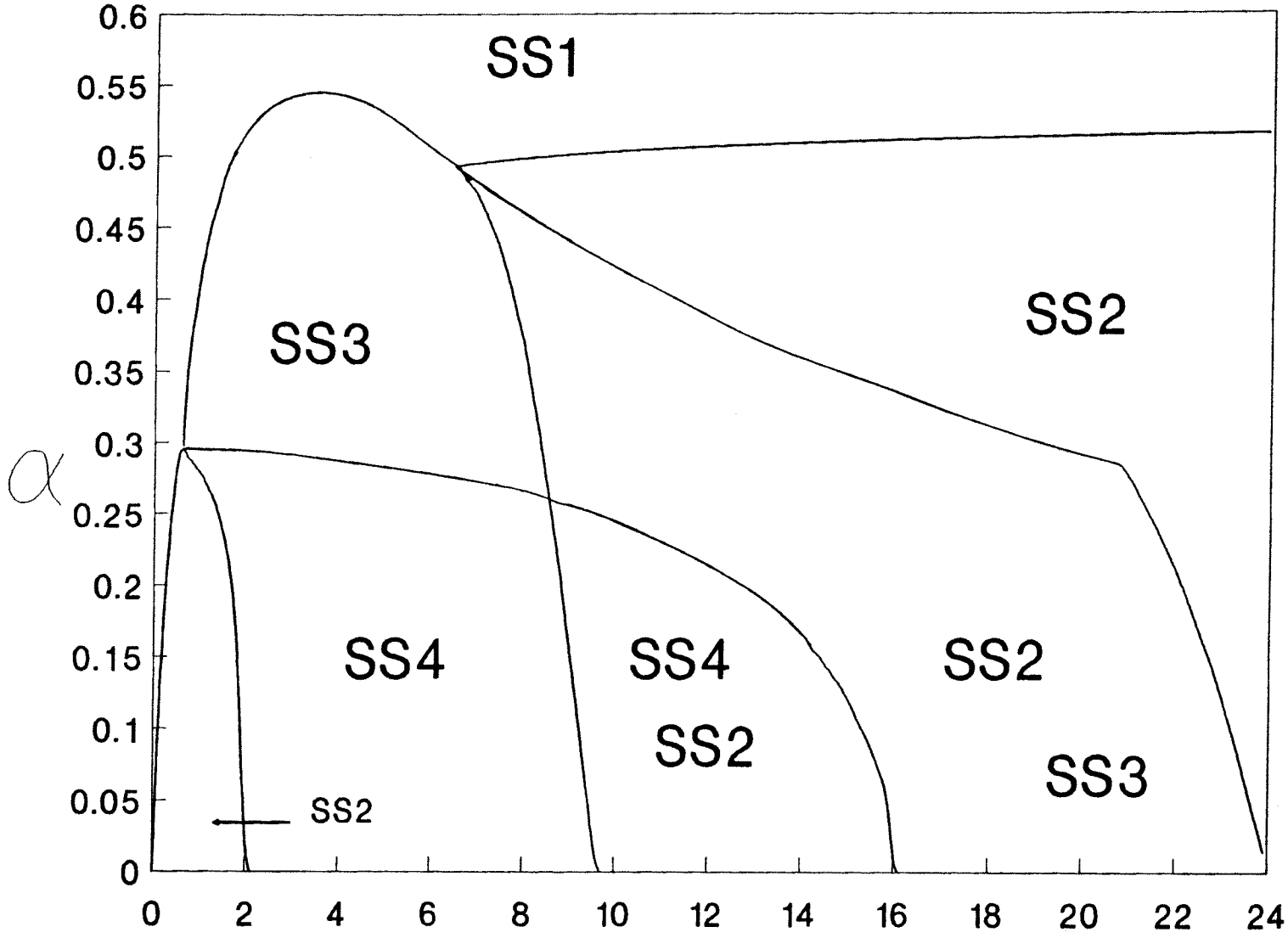
SS1
SS2
SS3
SS4
SS4
SS2
SS2
SS3
SS2
α
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.14

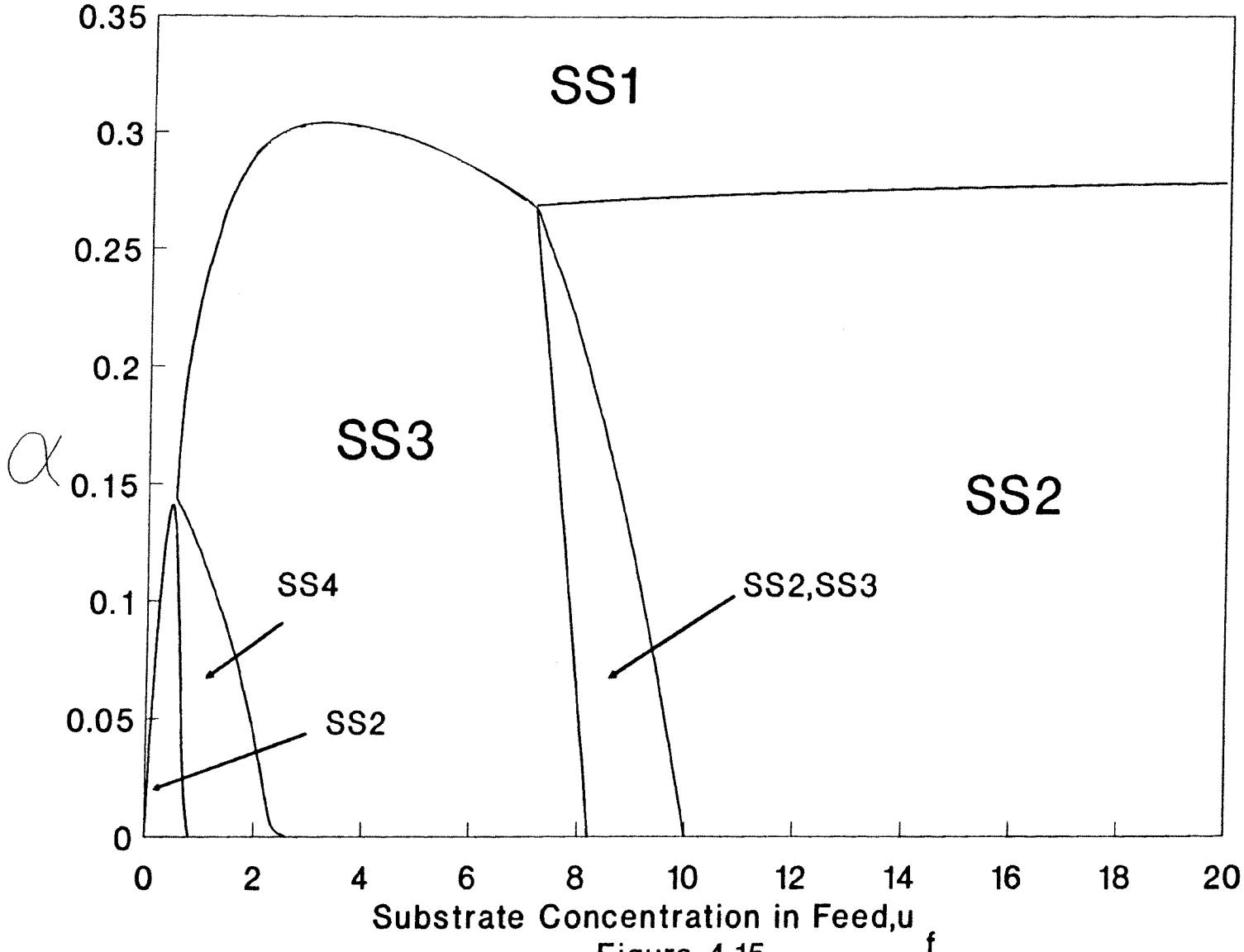
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
α
SS1
SS3
SS2
SS4
SS2
SS2,SS3
0
2
4
6
8
10
12
14
16
18
20
Substrate Concentration in Feed,u f

Figure 4.15

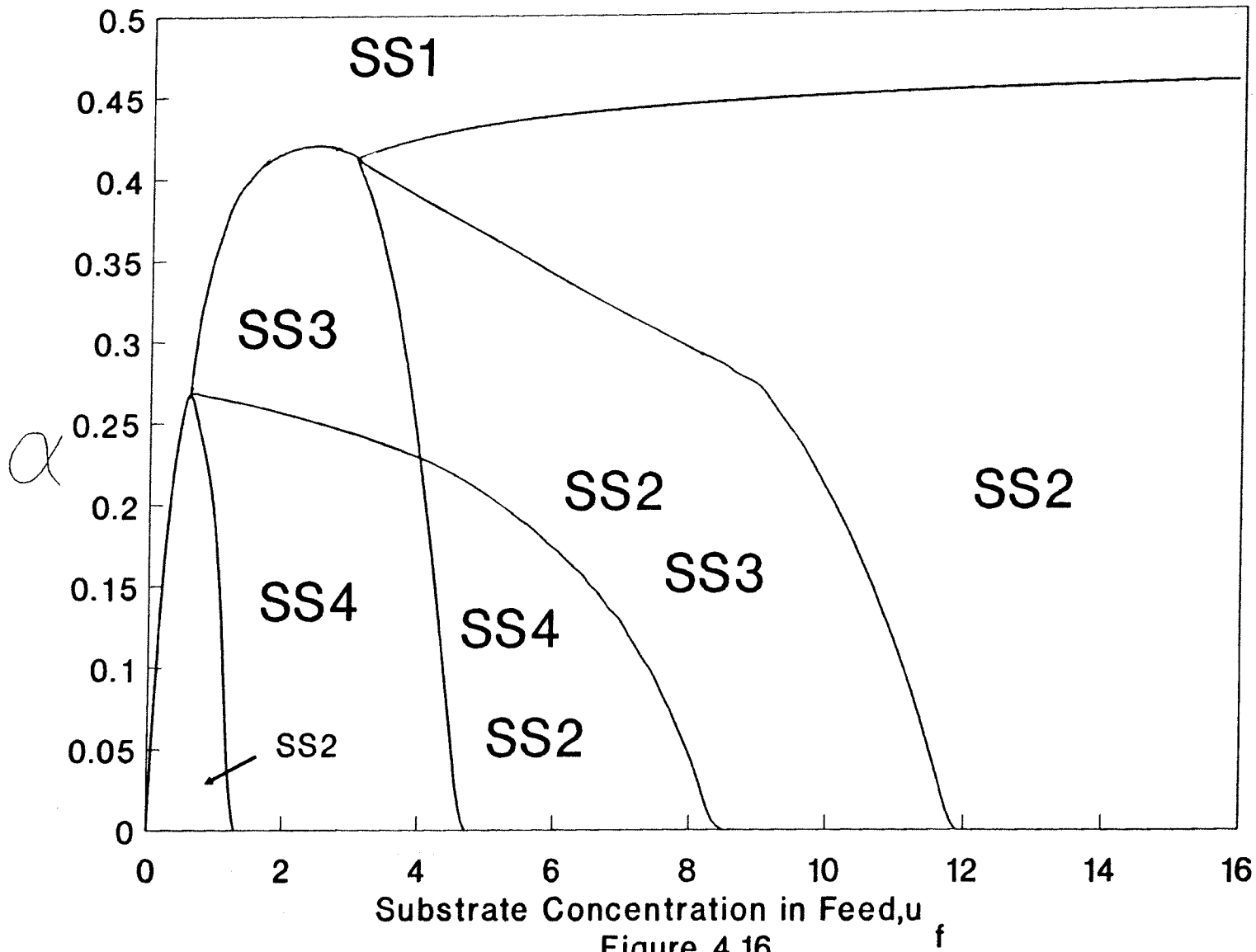
SS1
SS3
SS4
SS2
SS4
SS2
SS3
SS2
SS2
α
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
Substrate Concentration in Feed,u f

Figure 4.16

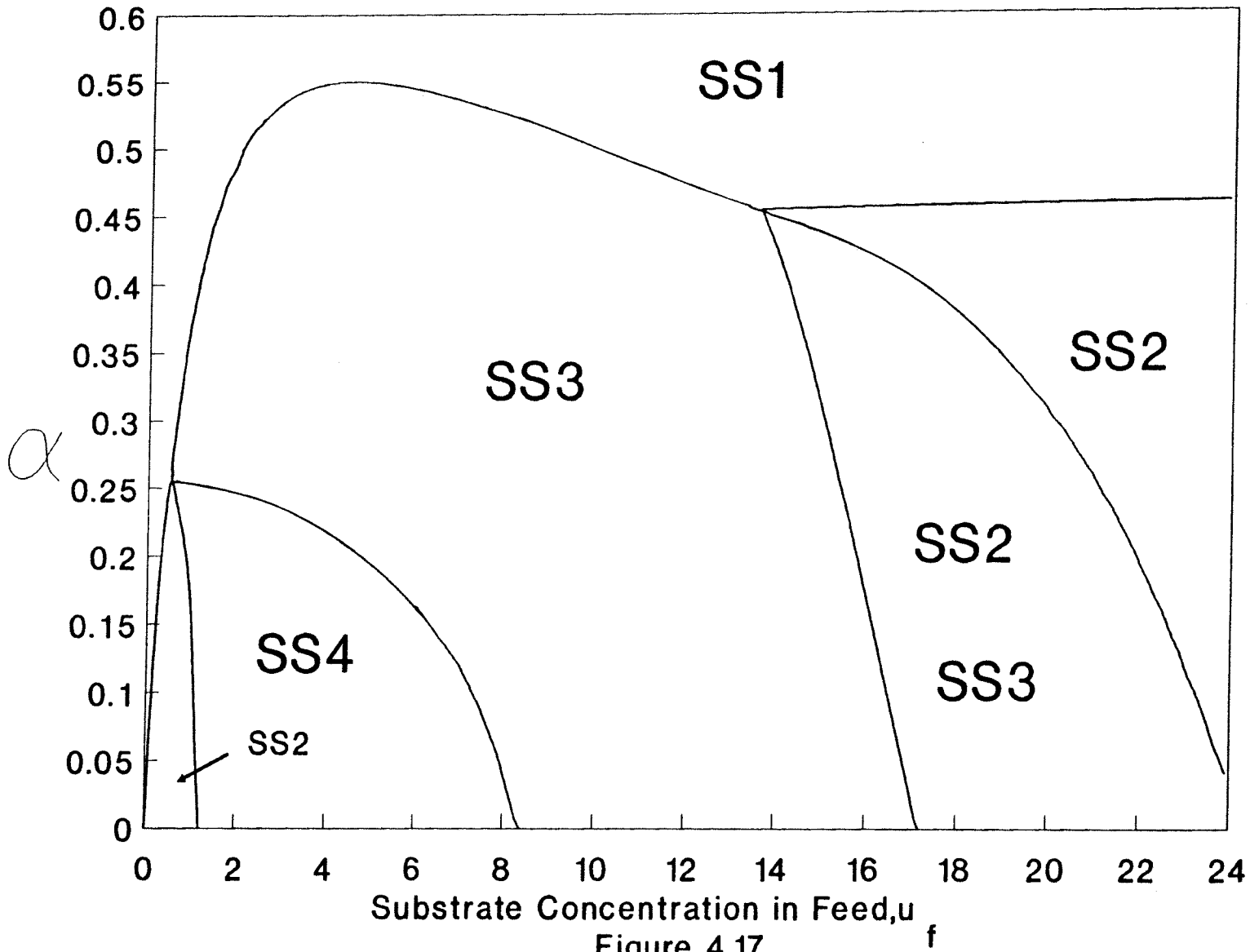
SS1
SS2
SS3
SS2
SS3
SS4
SS2
α
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.17

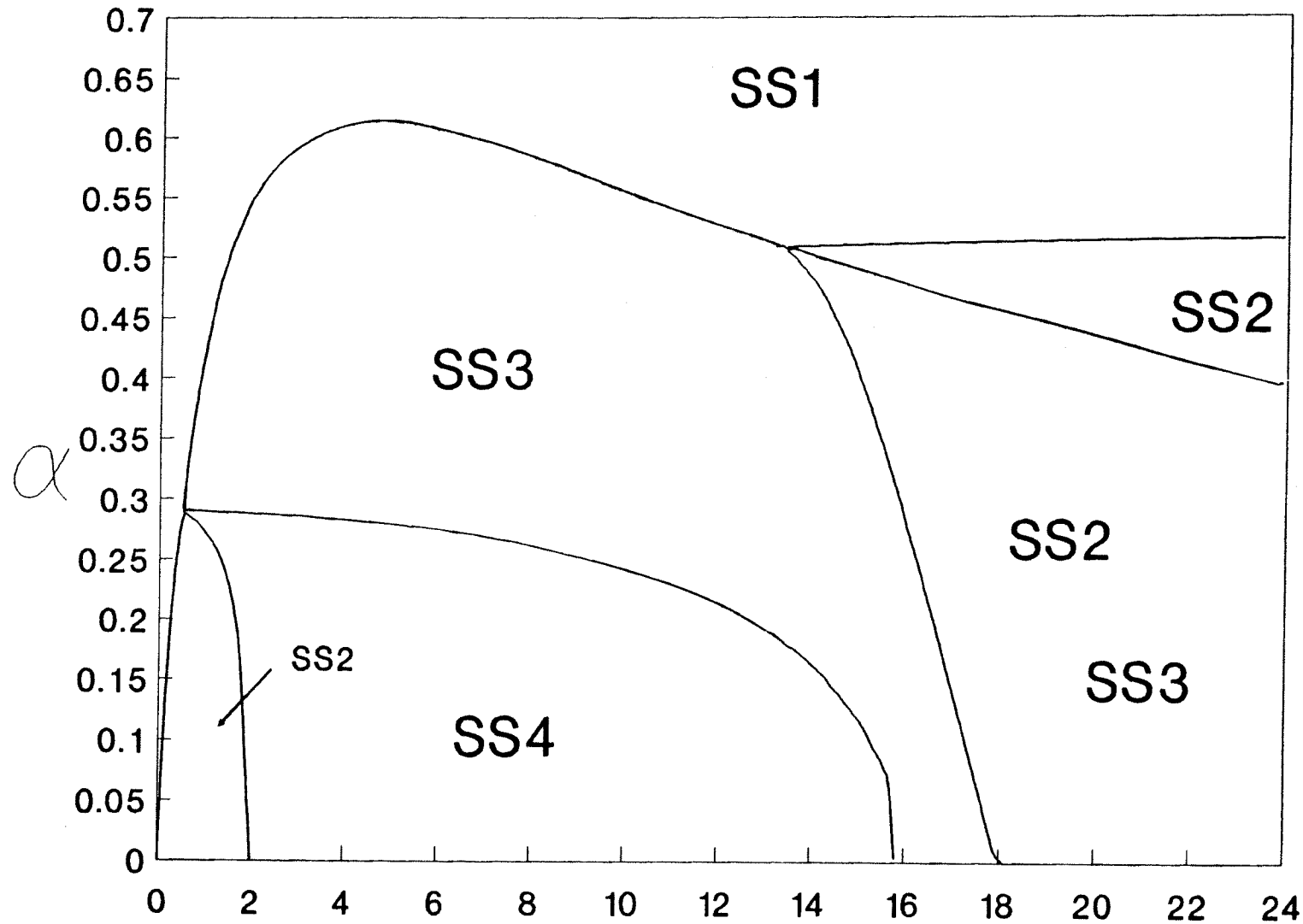
SS1
SS2
SS3
SS2
SS3
SS2
SS4
α
0.7
0.65
0.6
0.55
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.18

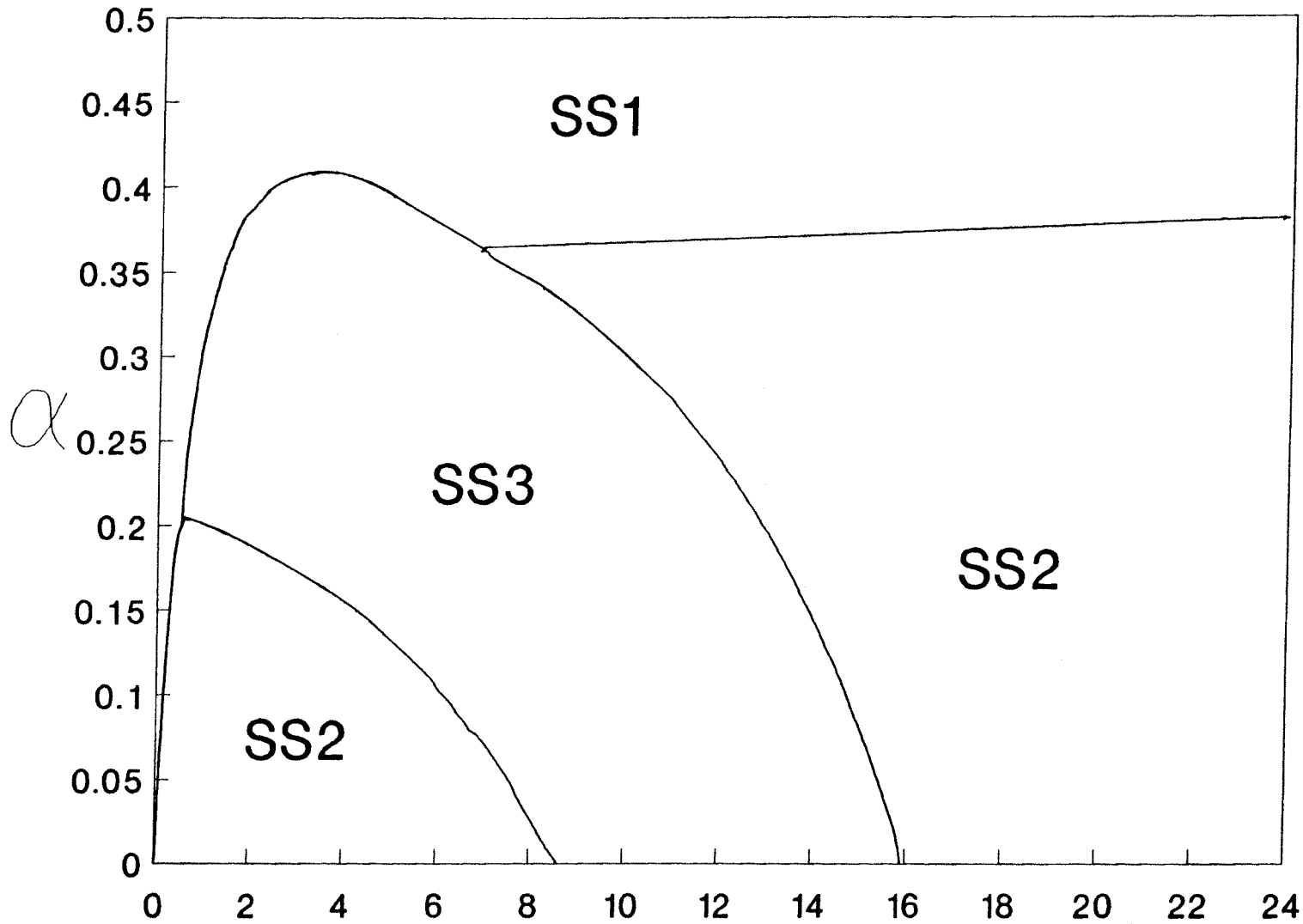
0.5
0.45
0.4
0.35
0.3
α
0.25
0.2
0.15
0.1
0.05
0
SS1
SS3
SS2
SS2
0
2
4
6
8
10
12
14
16
18
20
22
24
Substrate Concentration in Feed,u f

Figure 4.19

CHAPTER 5
CONCLUSIONS

In this thesis, aspects of a pure-double-strong competition pattern between two populations has been examined. The two resources competed for, have been assumed to be complementary and interactive models have been used for expressing the specific growth rates of the two species. Two cases have been examined: one in which neither of the two substrates exerts inhibitory effects on either population, and one in which only one of the substrates inhibits the growth of one of the two populations.

Based on analytical and numerical results, it has been found that the two competitors can coexist at a steady state in an ideal chemostat. Coexistence is excluded only if one of the competitors grows faster than the other under all operating conditions. This is determined by the system parameters (kinetic constants) appearing in the expressions of the specific growth rates.

Coexistence may arise at an unstable equilibrium point, in which case proper control of the chemostat will be necessary for maintaining a mixed culture. The stability of coexistence (for a given system) is determined solely from the yield coefficients when the system is not inhibited by either of the two substrates. In the case of partial inhibition, it has been found that the stability of coexistence may depend on the operating conditions (dilution rate, feed concentrations of the substrates) as well as on the yield coefficients.

Inhibition increases the complexity of the system and gives rise to domains where multiple outcomes and possible multiple coexistence states arise. The dynamics of such systems depend strongly on the way the chemostat is started-up.

There are other systems which need to be analyzed in further studies in order to complete the analysis of the double-strong competition pattern. Such systems are the following:

- both populations are inhibited by one, and the same substrate
- each population is inhibited by a different substrate
- only one population is inhibited by both substrates while the other is either not inhibited by any or at most by one of the two substrates
- both competitors are inhibited by both substrates

As the complexity of the system increases with the number of inhibition terms, it is anticipated that more and more one will have to rely on numerical results only. On the other hand, an increased complexity is expected to lead to more intriguing and interesting dynamics for this system.

APPENDIX

PROGRAM SOURCE FILE

The following source files are written in Fortran 77 and have been implemented on a VAX/VMS system.

```
c-----------------------------------------------------
c
c                UNINHIBITED SYSTEM
c
c-----------------------------------------------------
c       program to calculate numerically the regions
c       where SS2(x=0) is meaningful and stable
c
c       Parameters: e=epsilon, g=gamma, p=phi, s=sigma
c                   d=delta
c       Operating parameters: a=alpha, uf, vf
c
c-----------------------------------------------------
        integer vf,ufmax
        real d,e,p,s,g,a,uf,u,v,mu1,muo,y,ufin
        open(unit=2,file='ss2.2',status='new')
        open(unit=3,file='ss2.o',status='new')
        read *,e,g,p,s,d,vf,ufin,ufmax,deluf,ain
        uf=ufin
5       continue
        dela=(p*uf*vf/((d+uf)*(s+vf)))/100
        fina=100*dela
        a=ain
        count=1
25      continue
        Discr=(((p-a)*(uf+e*vf)-a*(d+e*s))**2)
      $ -4*e*(p-a)**2*uf*vf+4*e*a*(p-a)*(d*s+d*vf+s*uf)
        y=((p-a)*(uf+e*vf)-a*(d+e*s)-Discr**0.5)
        $ /(2*e*(p-a))
        u=uf-e*y
        v=vf-y
        mu1=u*v/((1+u)*(1+v))
        if(a.gt.mu1)then
        write(2,50)uf,a,y,u,v,mu1
        afin=a
        if(count.eq.1)then
        aar=a
        count=2
        endif
        endif
        muo=p*uf*vf/((d+uf)*(s+vf))
        a=a+dela
        if(a.lt.muo.and.a.lt.fina)then
        go to 25
        else
        write(3,60)uf,aar,afin
        endif
```

```
50      format(1x,f6.3,1x,5(f11.7,1x))
60      format(5x,f6.3,5x,2(f11.7,10x))
        uf=uf+deluf
        if(uf.gt.ufmax)go to 80
        go to 5
80      continue
        stop
        end
c-----------------------------------------------------
```

```
c-------------------------------------------------------------
c
c                    UNINHIBITED SYSTEM
c
c-------------------------------------------------------------
c          program to calculate numerically the regions
c          where SS3(y=0) is meaningful and stable
c
c          Parameters: e=epsilon, g=gamma, p=phi, s=sigma
c                      d=delta
c          Operating parameters: a=alpha, uf, vf
c
c-------------------------------------------------------------
           integer vf,ufmax
           real d,e,p,g,s,a,uf,u,v,mu2,muo,x,ufin
           open(unit=2,file='ss3.3',status='new')
           open(unit=3,file='ss3.o',status='new')
           read *,e,g,p,s,d,vf,ufin,ufmax,deluf,ain
           uf=ufin
5          continue
           dela=((uf*vf)/((1+uf)*(1+vf)))/100
           fina=100*dela
           a=ain
           count=1
25         continue
           Discr=(((1-a)*(vf+g*uf)-a*(g+1))**2)
         $ -4*g*((1-a)**2)*uf*vf+4*g*a*(1-a)*(1+uf+vf)
           x=((1-a)*(vf+g*uf)-a*(g+1)-Discr**0.5)/(2*g*(1-a))
           u=uf-x
           v=vf-g*x
           mu2=p*u*v/((d+u)*(s+v))
           if(a.gt.mu2)then
           write(2,50)uf,a,x,u,v,mu2
           afin=a
           if(count.eq.1)then
           aar=a
           count=2
           endif
           endif
           muo=uf*vf/((1+uf)*(1+vf))
           a=a+dela
           if(a.lt.muo.and.a.lt.fina)then
           go to 25
           else
           write(3,60)uf,aar,afin
           endif
50         format(2x,f6.3,2x,5(f11.7,2x))
60         format(10x,f6.3,5x,2(f11.7,10x))
```

```
          uf=uf+deluf
          if(uf.gt.ufmax)go to 80
          go to 5
80        continue
          stop
          end
c-----------------------------------------------------------
```

```
c-----------------------------------------------------------
c
c                    UNINHIBITED  SYSTEM
c
c-----------------------------------------------------------
c
c      program to calculate the regions where the
c      coexistence steady state is meaningful and stable
c
c-----------------------------------------------------------
       integer vf,ufmax
       real e,g,s,d,uf,ain,deluf,m1,m2,Discrv,Discr
       real M,N,K,L,L1,L2
       open(unit=2,file='ss4.out',status='new')
       open(unit=3,file='ss4.444',status='new')
c-----------------------------------------------------------
c
c      Parameters: e=epsilon,g=gamma,p=phi
c      L1,L2=eigenvalues(SS4), d=delta,s=sigma
c      Operating parameters: a=alpha, uf, vf
c
c-----------------------------------------------------------
       read *,e,g,p,s,d,vf,ufin,ufmax,deluf,ain
       uf=ufin
5      continue
       dela=p*uf*vf/((d+uf)*(s+vf))/160
       fina=p*uf*vf/((d+uf)*(s+vf))
       a=ain
25     continue
       Discrv=((a*(d-1)*(s+1)-(d*s-p))**2)
     $ -4*(a*(d-1)-(d-p))*(a*s*(d-1))
       if(Discrv.gt.0)then
       v=((d*s-p)-a*(d-1)*(s+1)-Discrv**0.5)
     $ /(2*(a*(d-1)-(d-p)))
       if(v.gt.0.and.v.lt.vf)then
       u=(d*s-p+v*(d-p))/(p-s+v*(p-1))
       if(u.gt.0.and.u.lt.uf)then
       x=((uf-u)-e*(vf-v))/(1-e*g)
       y=((vf-v)-g*(uf-u))/(1-e*g)
       if(x.gt.0.and.y.gt.0)then
       M=v/((1+u)**2*(1+v))
       N=u/((1+u)*(1+v)**2)
       K=p*v*d/((d+u)**2*(s+v))
       L=p*u*s/((d+u)*(s+v)**2)
       Discr=(x*M+g*x*N-y*L-e*y*K)**2+4*(y*K+g*y*L)
     $ *(x*N+e*x*M)
```

```
      L1=(-(x*M+g*x*N+y*L+e*y*K)+Discr**0.5)/2
      L2=(-(x*M+g*x*N+y*L+e*y*K)-Discr**0.5)/2
      write(2,60)uf,a,v,u,x,y,L1,L2
60    format(1x,f6.3,1x,7(f9.6,1x))
      write(3,70)uf,a,v,u,L1,L2
70    format(2x,f6.3,2x,5(f11.7,2x))
      endif
      endif
      endif
      endif
      a=a+dela
      if(a.lt.fina)go to 25
      uf=uf+deluf
      if(uf.gt.ufmax)go to 80
      go to 5
80    continue
      stop
      end
c-----------------------------------------------------------
```

```
c-----------------------------------------------------------
c
c                 PARTIALLY  INHIBITED SYSTEM
c
c-----------------------------------------------------------
c       program to calculate numerically the regions where
c
c       ss2(x=0) is meaningful and stable
c
c       Parametres: e=epsilon, g=gamma, p=phi, s=sigma
c                   d=delta, w1=omega
c
c       Operating Parameters: a=alpha , uf, vf
c
c-----------------------------------------------------------
        integer vf,ndeg,ufmax
        parameter(ndeg=2)
        real d,e,p,s,g,uf,ufin,u,v,y,mu1,w1,r(ndeg+1)
        real deluf,ain
        complex zero(ndeg)
        external wrcrn,zporc
        open(unit=2,file='x2.22',status='new')
        open(unit=3,file='x2.2',status='new')
        read *,e,g,p,s,d,w1,vf,ufin,ufmax,deluf,ain
        uf=ufin
 5      continue
        dela=((p*uf*vf)/((d+uf)*(s+vf)))/160
        fina=(p*uf*vf)/((d+uf)*(s+vf))
        a=ain
        count=1
 25     continue
        r(1)=((p-a)*uf*vf-a*(d*s+d*vf+s*uf))
        r(2)=(a-p)*(uf+e*vf)+a*(d+e*s)
        r(3)=((p-a)*e)
c-----------------------------------------------------------
c
c       Subroutine ZPORC (IMSL/Math Library)
c
c-----------------------------------------------------------
        call zporc(ndeg,r,zero)
        call wrcrn('the zeros found are',1,ndeg,zero,1,0)
        do 65,i=1,2
        if(aimag(zero(i)).eq.0.0)then
        y=real(zero(i))
        if(y.gt.0.0)then
        u=uf-e*y
        if(u.gt.0.0.and.u.lt.uf)then
```

```
      v=vf-y
      if(v.gt.0.0.and.v.lt.vf)then
      mu1=(u*v)/((1+v)*(1+u+w1*u**2))
c     q=(-1)*y*(((p*u*s)/((d+u)*(s+v)**2))+((e*u)
     $ /((d+u)**2*(s+v))))
      if(a.gt.mu1)then
      write(3,60)uf,a,y,u,v,mu1
      afin=a
      if(count.eq.1)then
      aar=a
      count=2
      endif
      endif
      endif
      endif
      endif
      endif
60    format(f10.7,5(f11.7))
65    continue
      a=a+dela
      if(a.lt.fina)then
      go to 25
      else
      write(2,70)uf,aar,afin
      endif
70    format(10x,f10.7,2(2x,f11.7))
      uf=uf+deluf
      if(uf.gt.ufmax)go to 80
      go to 5
80    continue
      stop
      end
c-----------------------------------------------------------
```

```
c-----------------------------------------------------------
c
c                 PARTIALLY INHIBITED SYSTEM
c
c-----------------------------------------------------------
c
c       program to calculate numerically the regions where
c       ss3(y=0)is meaningful and stable.
c
c       Parameters: e=epsilon, g=gamma, p=phi, s=sigma
c                   d=delta, w1=omega
c
c       Operating Parameters: a=alpha, uf, vf
c
c-----------------------------------------------------------
        integer vf,ufmax,ndeg
        parameter(ndeg=3)
        real e,g,p,s,d,w1,x,u,ufin,uf,v,deluf,a,r(ndeg+1)
        real mu2,q
        complex zero(ndeg)
        external wrcrn,zporc
        open(unit=2,file='x3.3',status='new')
        open(unit=3,file='x3.33',status='new')
        read *,e,g,p,s,d,w1
        read *,vf,ufin,ufmax,deluf,ain
        uf=ufin
5       continue
        dela=((uf*vf)/((1+uf+w1*uf**2)*(1+vf)))/160
c       fina=vf/((1+2*(w1**0.5))*(1+vf))
c       dela=((p*uf*vf)/((d+uf)*(s+vf)))/100
        fina=(uf*vf)/((1+uf+w1*uf**2)*(1+vf))
        a=ain
        count=1
25      continue
        r(1)=(uf*vf*(1-a)-a*(1+vf+uf)-a*w1*uf**2*(1+vf))
        r(2)=(a*(g+1)+g*uf*(a-1)+vf*(a-1)+a*w1*uf
      $ *(2+2*vf+g*uf))
        r(3)=(g*(1-a)-a*w1*(1+vf+2*g*uf))
        r(4)=(a*g*w1)
c-----------------------------------------------------------
c
c       Subroutine ZPORC (IMSL/Math Library)
c
c-----------------------------------------------------------
        call zporc(ndeg,r,zero)
        call wrcrn('the zeros are',1,ndeg,zero,1,0)
        do 65,i=1,3
```

```
      if(aimag(zero(i)).eq.0.0)then
      x=real(zero(i))
      if(x.gt.0)then
      u=uf-x
      if(u.gt.0.and.u.lt.uf)then
      v=vf-g*x
      if(v.gt.0.and.v.lt.vf)then
      mu2=(p*u*v)/((d+u)*(s+v))
      q=-x*((v*(1-w1*(u**2))/((1+v)*(1+u+w1*(u**2))**2))
     &  +((g*u)/((1+u+w1*(u**2))*((1+v)**2))))
      if(a.gt.mu2.and.q.lt.0.0)then
      write(3,60)uf,a,x,u,v,mu2,q
      afin=a
      if(count.eq.1)then
      aar=a
      count=2
      endif
      endif
      endif
      endif
      endif
      endif
      endif
60    format(1x,f6.3,1x,6(1x,f9.6))
65    continue
      a=a+dela
      if(a.lt.fina)then
      go to 25
      else
      write(2,70)uf,aar,afin
      endif
70    format(2x,f6.3,2(10x,f11.7))
      uf=uf+deluf
      if(uf.gt.ufmax)go to 80
      go to 5
80    continue
      stop
      end
c-----------------------------------------------------------
```

```
c-----------------------------------------------------------------
c
c                    PARTIALLY INHIBITED SYSTEM
c
c-----------------------------------------------------------------
c
c       program to calculate the regions where the coexistence
c       steady state is meaningful and stable
c
c       Parameters: e=epsilon, g=gamma, p=phi, s=sigma
c                      w1=omega, d=delta
c
c       Operating Parameters: a=alpha, uf, vf
c
c-----------------------------------------------------------------
        integer vf,ndeg
        parameter(ndeg=3)
        real e,g,p,s,d,w1,x,u,uf,ufmax,v,a,deluf,r(ndeg+1),L1,L2
        real m,nn,kk,l,d1,d2,DD
        complex zero(ndeg)
        external wrcrn,zporc
        open(unit=2,file='x4.4',status='new')
        open(unit=3,file='x4.44',status='new')
        read *,e,g,p,s,d,w1,vf,uf1,ufmax,deluf,ain
        uf=uf1
5       continue
        dela=(p*uf*vf/((d+uf)*(s+vf)))/30
c       dela=(vf/((1+2*(w1**0.5))*(1+vf)))/30
        fina=p*uf*vf/((d+uf)*(s+vf))
        a=ain
25      continue
        r(1)=a*d*p*(s-1)
        r(2)=a*s*p*(d+1)-d*p*(a+s)+p*(p-a)
        r(3)=s*p*(a-1)+a*p*d*w1*(s-1)+p*(p-a)
        r(4)=p*w1*(a*s-a+p)
c-----------------------------------------------------------------
c
c       Subroutine ZPORC (IMSL/Math Library)
c
c-----------------------------------------------------------------
        call zporc(ndeg,r,zero)
        call wrcrn(' the zeros are',1,ndeg,zero,1,0)
        do 65,i=1,3
        if(aimag(zero(i)).eq.0.0)then
        u=real(zero(i))
        if(u.gt.0.0.and.u.lt.uf)then
        v=((d*s-p)+u*(s-p)-p*w1*u**2)/((p-d)+u*(p-1)+p*w1*u**2)
```

```
      if(v.gt.0.0.and.v.lt.vf)then
      z=((uf-u)-e*(vf-v))/(1-e*g)
      y=((vf-v)-g*(uf-u))/(1-e*g)
      if(z.gt.0.and.y.gt.0)then
      m=v*(1-w1*u**2)/((1+u+w1*u**2)**2*(1+v))
      nn=u/((1+u+w1*u**2)*(1+v)**2)
      kk=p*v*d/((d+u)**2*(s+v))
      l=p*u*s/((d+u)*(s+v)**2)
      d1=z*m+g*nn*z+y*l+e*y*kk
c     d2=(y*l+e*y*kk)*(z*m+g*z*nn)-(y*kk+g*y*l)*(z*nn+e*z*m)
      d2=z*y*(l*m-kk*nn)*(1-e*g)
      DD=d1**2-4*d2
      L1=(-d1+DD**0.5)/2
      L2=(-d1-DD**0.5)/2
      if(L1.lt.0.0.and.L2.lt.0.0)then
      write(2,60)uf,a,u,v,z,y,L1,L2
60    format(1x,f6.3,7(1x,f8.5))
      endif
      endif
      endif
      endif
      endif
65    continue
      a=a+dela
      if(a.lt.fina)go to 25
      uf=uf+deluf
      if(uf.gt.ufmax)go to 80
      go to 5
80    continue
      stop
      end
c-----------------------------------------------------------------
```

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