THEORETICAL AND EXPERIMENTAL INVESTIGATIONS OF MICROBIAL COMPETITION IN CONTINUOUS CULTURE

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SHORT HISTORY OF THE CLASSICAL THEORY OF ECOLOGICAL COMPETITION

The classical theory of ecological competition between two or more species, attributed to Lotka and Volterra [60], is an extension of the basic logistic model of single-species growth that dates from Verhulst [59]. The dynamical equations for this theory for two competitors, 1 and 2, are often written as:

$$\frac{dN_1}{dt} = r_1 N_1 \left[1 - \frac{N_1 + \alpha N_2}{K_1} \right]$$

$$\frac{dN_2}{dt} = r_2 N_2 \left[1 - \frac{\beta N_1 + N_2}{K_2} \right]$$

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where N_i is the number of the ith competing species, r_i and K_i are the intrinsic rate of increase and the carrying capacity of the ith competitor, respectively, and α and β are the interaction or "competition" coefficients, expressing the per capita competitive effects of species 2 on 1, and 1 on 2, on the growth rate and realized carrying capacity of the rival species. In the absence of competition ($\alpha = \beta = 0$), each population grows to its respective carrying capacity. In the presence of competition, one or the other rival may survive while its competitor dies out, or else the rivals may coexist. In the two-species case, there are four possible outcomes provided that the initial populations are both positive; which outcome occurs depends on the carrying capacities and competition coefficients. Competitive stability (coexistence) occurs when $\alpha < K_1/K_2$ and $\beta < K_2/K_1$, competitive instability (initial number of each rival determines winner) occurs when these inequalities are both reversed, and competitive dominance (one or the other species wins regardless of initial numbers) occurs when one but not both of these inequalities are reversed.

This classical theory of competition and its extension to n competing species has been the subject of a great amount of theoretical (cf. review, [61, 17]) and experimental [23, 37, 40, 44, 57, 63] work in the last 40 years. However, in recent years there has arisen a widespread feeling that the subject of competition is ready for a new theoretical framework. A pervasive problem with classical theory is that it is "phenomenological," seeking to describe how the numbers of competitors change without ever being specific about which resources are the focus of competition, nor about how efficiently the rivals exploit or control these limited resources. While the lasting appeal of Lotka-Volterra theory has come from its generality and simplicity, this same generality has also made it very difficult for the experimentalist to measure the theory's critical parameters. It has proved especially difficult to estimate the competition coefficients independently of actually growing the competing species together. Usually they have been estimated by fitting the equations to the growth curves of the species in competition (e.g., [57]). Whenever these coefficients can only be estimated from the dynamics of populations already in competition, the value of the theory for prediction is much diminished. It then becomes at best an *ex post facto* description of the outcome of competition [47, 61], and at worst an unsuccessful exercise in curve fitting.

There are a number of other problems with the classical theory which concern its biological assumptions. These include the assumptions of a constant carrying capacity, ecological equivalence of all individuals within

each population (no age-dependent differences in birth or death rates or in resource use, for example), no time lags, and constant, linear per-capita effects on population growth rates within and between species. The organisms which best meet these assumptions in general are microorganisms, which as single-celled organisms usually reproduce by simple binary fission, producing clones of genetically identical daughter cells. It is not surprising, therefore, that the experimental work best supporting the theory has been done on microorganisms, beginning with the pioneering work of Gause [7] and continuing until quite recently [8, 40, 56]. In the work with metazoans, however, the theory has with a few possible exceptions (e.g., [23]) not proved adequate [37, 44, 48, 49, 62].

During the last 20 years increasing attention has been given to the details of the processes underlying consumer-resource interactions, with the goal of constructing more mechanistic theories of interspecific competition. Research has been focused on three principal questions. First of all, do the rival species compete only indirectly by lowering the shared pool of limited resources (exploitative competition), or do they also compete more directly by harming their rivals or by sequestering some of the resources for their exclusive use (interference competition) [33]? Secondly, how efficiently do the rivals exploit these limiting resources? In particular, how do the per capita consumption rates of each species respond to a change in resource concentration (nutrients, prey, etc.) in the environment ("functional" response)? Finally, how do these resources, once consumed, translate into a particular rate of population growth ("numerical" response)? There are other questions as well, such as competition within and between age-structured populations (e.g., [39]), and genetic considerations (e.g., [41]), that as yet have not received much attention.

In this chapter we focus exclusively on *exploitative competition*. Interference competition, while common in nature, is mediated through a diversity of mechanisms. As yet there is little consensus about the way that interference should be modeled mathematically given that the effects of toxins or injury are so varied, and are different from the effects of resource sequestering. In any event, it is not a trivial exercise to consider the consequences of exploitative competition, which occurs more universally than interference. Unless one species can totally exclude its rivals from access to the limiting resources, consumption of these resources by both species occurs, and exploitative competition is a reality.

Moreover, there is greater agreement on the biology and mathematics of exploitative competition. Extensive studies have been made on the functional

response of a great variety of organisms to resource density, including microorganisms (e.g., [9]), protozoa [46], insect predators [10, 15] and parasitoids [10, 11], fish [24, 36], birds [45, 56], and mammals [13], and others. Functional responses of all organisms are saturating functions of increasing resource density, such that the consumption rate reaches some maximum at high resource density. At low resource density, consumption rate may increase in a nearly linear fashion with resource density (typical of filter-feeding organisms consuming prey much smaller than themselves; e.g., clams, baleen whales); consumption rate may increase nonlinearly, decelerating smoothly to a maximum feeding rate asymptote (most invertebrate predators and many vertebrate predators feeding on one prey type at a time); or consumption rate may increase slowly at low resource density and faster at higher resource density in an S-shaped curve (typical predators that develop learned "search images" as a function of prey encounter rate, and which actively switch between alternate prey, or between non-feeding and feeding behavior, as some threshold prey density). These classes of functional responses have been classified by Holling [14] as Types I, II, and III, respectively. Type II is the most common type of functional response among microorganisms and small invertebrates. In microorganisms, resource uptake occurs at the level of enzyme-mediated transport of specific nutrients across the cell wall, and uptake rates are generally characterized by the Michaelis-Menten equations for enzyme-catalyzed reactions [6, 42]. Types II and III functional responses in higher organisms follow identical mathematics, as has been explored in some detail by Real [43].

Once the limiting resources have been consumed, they may interact in a variety of ways to promote population growth. Leon and Tumpson [30] have distinguished two important classes or resources: complementary and substitutable. Complementary resources are substances which are metabolically independent requirements for growth, such as a carbon and a nitrogen source for a bacterium, or silica and phosphorus for a diatom. Substitutable resources are substances which are metabolically interchangeable in the organism, such as two carbon sources, or two sources of phosphorus. In the case of growth limited by complementary resource, only one such resource can be limiting growth at any given time, and which complementary resource is limiting is determined by the relative rate of supply of the resources in relation to the required proportional demand of the organism. On the other hand, in the case of substitutable resources, growth on any one of the resources is possible because each substitutable resource is actually

an alternative form of supply of the same basic nutrient for which there is a requirement. Thus, a given complementary resource can be supplied in a variety of substitutable "packages." For example, planktonic algae obtain their phosphorus from both inorganic sources such as orthophosphate as well as from dissolved organic molecules containing phosphorus. Resources may also be "imperfectly substitutable" if they can be interconverted by the organism to meet various metabolic demands but only by augmenting energy expenditure and generally at the expense of a reduced growth rate.

The developing theories of resource-based ecological competition will, almost certainly, first be tested in the laboratory with systems of competing microorganisms and protozoa. The advantages of the laboratory environment for controlling extraneous variables are clear. Furthermore, microorganisms offer the advantages of (a) rapid generation time, so that experiments can be carried to completion in a short time; (b) small size, so that competitive communities can be economically housed and replicated; (c) clonal homogeneity of individuals, so that genetic differences among individuals within species, barring mutation, are absent; (d) reproduction by binary fission, so that ecological differences due to size and age are minimal; and (e) simple functional responses to resource density, so that the complex behavioral patterns of higher predators (such as searching images, learning, switching behavior, etc.) can be initially ignored.

Consequently, in this chapter we develop the theory of exploitative competition for microbial organisms competing in mixed-growth laboratory cultures. The theory is developed for a culturing technique known as "continuous culture," the most widely used laboratory idealization of a constant carrying capacity environment. The remaining sections of the chapter are organized as follows: First, the technique of continuously culturing microorganisms is briefly described, followed by a section detailing the mathematical model of single-species and multiple-species growth in continuous culture on a single limiting resource. The next section presents the mathematical analysis of the n-species, 1-resource model. This is followed by two sections which give some experimental results of tests of the model, and then generalize by analogy to competition among unicellular planktonic algae in lakes and oceans. Next we consider what happens when two competitors are predators feeding on the same population of prey, a different situation insofar as the "resource" is now capable of self-renewal. We conclude with a brief look at some of our theoretical work in progress.

ORIGINS OF THE CONTINUOUS CULTURE TECHNIQUE

Most natural environments are inhabited by a great diversity of interacting microorganisms, but the ecology of these organisms and their competitive, mutualistic, or predator-prey relationships are almost always very difficult to study in nature because of the highly complex structure of natural environments and because of the limitations in ability to make accurate estimates of natural population densities. In order to study these organisms and their interactions in any detail, it was necessary to develop various isolation procedures so that individual species or strains of microorganisms could be cultured separately in the laboratory. At present laboratory cultures exist for literally thousands of bacteria, fungi, protozoa, and unicellular planktonic and benthic algae, from environments as diverse as lakes, streams, oceans, hot springs, soil, root nodules of plants, and the intestinal tracts of man and a host of other animals.

Many of the pure cultures of these organisms were isolated from so-called "batch enrichment" cultures, in which a small sample of the environmental medium or substrate is incubated with an enriched mixture of nutrients in a closed culture vessel. One or more of the microorganisms present in the sample grow to very large numbers under such conditions, making it easier to isolate individual cells of the organisms into pure culture. These batch cultures are also widely used in studies on the energy metabolism and nutrient requirements of different species of microorganisms.

From an ecological perspective, however, the batch culture environment has some serious drawbacks as a model of natural microbial environments [25, 51, 58]. For one thing, in nature microorganisms almost never encounter the very high nutrient levels that characterize batch cultures. Generally the concentrations of limiting nutrients in soils and natural waters are several orders of magnitude lower than in batch culture (although this is less the case for intestinal environments). Thus, the question arises as to whether the species isolated from batch culture are likely to be representative of the microorganisms that are of a major functional importance in the natural ecosystem. Indeed, one of the significant points of this chapter is that there are both theoretical and experimental grounds for expecting profound differences between the organisms which become abundant under nutrient-rich, batch-culture conditions, and those which are abundant under the much lower nutrient conditions in nature. In batch culture there is also the problem that nutrient conditions are in continual flux with the

possibility that growth is not always limited by the same nutrient. This can make the study of the dependence of growth rate on nutrient concentration very difficult, and can obscure the competitive relationships among organisms growing in mixed culture.

The concept of a "continuous" culture was introduced in the late 1940s, and came into widespread application in the 1950s. Continuous cultures were mainly developed so that microbial growth could be studied under nutrient limitation in a controlled nutrient environment. The elementary design and theory of continuous culture was first described by Monod [35] and independently by Novick and Szilard [38], who called their culture device a "chemostat."

The basic concept of a chemostat is to supply the culture continuously with a constant input of sterile medium, and to remove medium plus cells and byproducts from the culture at the same rate, maintaining culture volume constant. Initially the culture is inoculated with a small number of cells; and these multiply until a steady-state cell density is achieved. The influent medium provides all nutrients essential for growth in excess of demand except for one, which is supplied in growth-limiting amounts. Herein lies the principal advantage of continuous culture over batch culture: the rate of dilution controls the rate of microbial growth via the concentration of the growth-limiting nutrient in the medium. As long as the dilution rate is lower than the maximum growth rate attainable by the microorganisms, the cell density will grow to a point at which the cell division rate ("birth" rate) exactly balances the cell washout rate ("death" rate). This steady-state cell density is characterized by a constancy of all metabolic and growth parameters. On the other hand, if the dilution rate exceeds the maximum cell division rate, then total washout of the entire cell population occurs.

The dependence of microbial growth rate on the concentration of limiting nutrient was originally described by Monod [34] as simply a data-fitting curve. Later the relationship was frequently interpreted in terms of Michaelis-Menton kinetics. This explanation is undoubtedly too simplistic for most growth-limiting substances in that the model of a single enzyme-mediated reaction as the one rate-limiting step may not be completely accurate. It now appears that some deviations from the Monod relationship in microorganisms may depend on whether the limiting substrate is an energy source or is an essential nutrient such as a vitamin or mineral [25].

The most common deviation from the classical Monod formulation is that the yield coefficient is not independent of growth rate. This is usually due to the fact that cell volume in many microbial species is a function of steady-state growth (division) rate, and therefore depends on the particular dilution rate that is used in the continuous culture experiment [25, 58]. Other deviations may occur if growth rate falls to zero at some nonzero concentration of the limiting substrate, producing a threshold phenomenon in growth, or it may be found that growth on one substrate is inhibited by the presence of a second substrate. Bacteria, for example, commonly exhibit "diauxic" growth in the presence of two sugars as energy and carbon sources. The presence of glucose in the medium completely inhibits the uptake and metabolism of lactose in *Escherichia coli* via the lac operon [1], until the supply of glucose in the medium is exhausted.

Finally, the cells may be capable of "luxury" consumption of certain nutrients, such that there is uptake and storage of the nutrient in excess of the amounts that are currently needed for growth. This can lead at least to transient departures from the Monod growth rate predictions because growth rate is no longer a strict function of external concentration. Until steady state is reached, growth rates may remain higher than predicted from the Monod relationship or from the concentration of the external nutrient pool. For example, many planktonic algae are capable of considerable luxury consumption of orthophosphate, stored as polyphosphate in the cells; and elevated growth rates can be maintained on these internal stores for some time after external phosphate concentrations have fallen virtually to zero [5].

In spite of departures in detail from the original microbial growth model proposed by Monod, this model remains the simplest and the most widely applicable theory for nutrient-limited growth in microorganisms. Moreover, the theory, as extended to cover n-species microbial competition, now appears sufficient to make qualitatively accurate predictions of the outcomes of microbial competition in continuous culture. For example, Tilman [52], in studying the ability of the Monod model to predict the winning species among diatoms competing for silica and phosphorus, found that the Monod model did as well or better than a more complex "internal stores" model developed by Droop [5], which allows for luxury consumption and uncouples growth rate from external phosphorus concentrations. We also report in the present article and elsewhere [9] that the Monod formulation successfully predicts the outcome of competition between auxotrophic strains of bacteria grown in continuous culture.

Consequently, we feel that competition theory developed from the microbial growth equations of Monod remains the most general theory available, and will serve as the most practical tool for probing the mechanics of microbial competition for some time to come. We also feel that this theory will serve as the foundation for the development of much more mechanistic theories of competition among higher organisms as well, theories which make explicit the interaction of the competitors with each other and with their shared, limited resources.

DERIVATION OF THE MODEL EQUATIONS

The equations for the chemostat for one population were originally derived by Monod [35]. Here we give a simpler derivation following Herbert, Elsworth, and Telling [12], but based on Monod's observations. Let $x(t)$ denote the concentration of the organism and $S(t)$ the concentration of the substrate at time t.

If the organism were grown in a batch culture then the rate of consumption of the substrate and rate of growth of the organism are directly proportional (Monod, [34]):

$$\begin{Bmatrix}\text{rate of growth}\\ \text{of organism}\end{Bmatrix} = y\begin{Bmatrix}\text{rate of consumption}\\ \text{of resource}\end{Bmatrix} \tag{1}$$

y is called the yield constant and is determinable over a finite period of time by

$$y = \frac{\text{weight of the organism formed}}{\text{weight of the substrated used}}$$

The rate of growth of the organism may be simply expressed as

$$\text{increase} = \text{growth} - \text{output}$$

or

$$\frac{dx}{dt} = \mu x - Dx \tag{2}$$

where μ is a function (defined below) and D is a constant. The change in the substrate is slightly more complicated in that

$$\text{increase} = \text{input} - \text{output} - \text{consumption}$$

or

$$\frac{dS}{dt} = DS^{(0)} - DS - \frac{\mu x}{y} \tag{3}$$

where Eq. (1) has been used to model the consumption (keeping in mind that the rate of growth in the concentration of the organism is μx). Finally, μ is assumed (or known experimentally, Monod [34]) to have the form

$$\mu = m \frac{S}{a + S}$$

where m is the maximum growth rate and a is the half-saturation, or Michaelis-Menton, constant, numerically equal to the substrate concentration at which $\mu = m/2$. Combining the above yields the equations of the chemostat:

$$\begin{aligned} S' &= (S^{(0)} - S)D - \frac{1}{y}\frac{mxS}{a + S} \\ x' &= \frac{mxS}{a + S} - Dx \\ x(0) &> 0, \qquad S(0) > 0 \end{aligned} \tag{4}$$

Taylor and Williams [50] extended the derivation to cover n populations existing on one resource, obtaining

$$\begin{aligned} S' &= (S^{(0)} - S)D - \sum_{i=1}^{n} \frac{1}{y_i}\frac{m_i x_i S}{a_i + S} \\ x_i' &= \frac{m_i x_i S}{a_i + S} - Dx_i \\ x_i(0) &= x_{i0} > 0, \qquad S(0) = S_0 > 0, \qquad i = 1, \ldots, n \end{aligned} \tag{5}_n$$

ANALYSIS OF THE CHEMOSTAT

The system $(5)_n$ was investigated numerically by Taylor and Williams [50] who found that only one population survived. To describe which one, let $b_i = m_i/D$ and if $b_i > 1$, let $\lambda_i = a_i/(b_i - 1)$. If $b_i > 1$, $i = 1,\ldots, n$, Taylor and Williams found that one the population with the smallest value of λ_i survived. A mathematical proof of this result was given by Hsu, Hubbell, and Waltman [18], and a much shorter proof given by Hsu [16]. Before describing these results precisely we note first that the model is biologically reasonable.

THEOREM 1 The solutions $S(t)$, $x_i(t)$, $i = 1,\ldots, n$ are positive and bounded.

Proof The positivity of the x_i's follows from the uniqueness of solutions of initial value problems and the fact that each $x_i = 0$ face is invariant under the flow given by $(5)_n$. The positivity of $S(t)$ follows from the inequality

$$S(t) > S(0)\exp\int_0^t \left\{ - D - \sum_{i=1}^{n} \frac{m_i}{y_i} \frac{x_i(\xi)}{a_i + S(\xi)} \right\} d\xi$$

and the boundedness of solutions from the relation

$$S(t) + \sum_{i=1}^{n} \frac{x_i(t)}{y_i} = A_n e^{-Dt} + S^{(0)} \tag{6}$$

where

$$A_n = S_0 + \sum_{i=1}^{n} \frac{x_{i0}}{y_i} - S^{(0)}$$

Eq. (6) is obtained by forming a linear differential equation for the quantity

$$S(t) + \sum_{i=1}^{n} \frac{x_i(t)}{y_i}$$

Next it is convenient to eliminate "inadequate" competitors.

THEOREM 2 If

(i) $b_i \leq 1$,

or

(ii) $\lambda_i > S^{(0)}$ if $b_i > 1$,

then $\lim_{t\to\infty} x_i(t) = 0$.

This theorem states that if the maximum growth rate m_i of the ith organism is less than or equal to the dilution rate D or if the parameter $a_i/(b_i - 1) > S^{(0)}$, the organism will become extinct in the culture. Note that the resulting behavior is competition-independent and reflects excessive dilution or, given the dilution rate, the inability to uptake sufficient nutrient. Since $(5)_n$ is a dynamical system, analyzing $(5)_n$ with the ith equation eliminated (analyzing an appropriate $(5)_{n-1}$) is equivalent to studying the omega limit set of the original $(5)_n$ with $\lim_{t\to\infty} x_i(t) = 0$.

Proof First observe that from (6) if $\varepsilon > 0$ there exists a t_0 such that if $t \geq t_0$, $S(t) \leq S^{(0)} + \varepsilon$. $x_i(t)$ may be written

$$x_i(t) = x_{i0}\exp \int_0^t \frac{(m_i - D)S(\xi) - a_i D}{a_i + S(\xi)}\, d\xi \tag{7}$$

If $b_i \leq 1$, then

$$x_i(t) \leq x_{i0}\exp \int_0^t \frac{-a_i D}{a_i + S(\xi)}\, d\xi$$

$$\leq Cx_{i0}\exp \frac{-a_i D}{a_i + S^{(0)} + 1}(t - t_0)$$

where t_0 is chosen so that for $t \geq t_0$, $S(t) \leq S^0 + 1$ and

$$C = \exp \int_0^{t_0} \frac{-a_i D}{a_i + S(\xi)}\, d\xi$$

Since the exponent is negative and $x_i(t) > 0$, $\lim_{t\to\infty} x_i(t) = 0$.

Rearranging (7) yields

$$x_i(t) = x_{i0}\exp\int_0^t \frac{m_i - D}{a_i + S(\xi)}\left[S(\xi) - \frac{a_i}{b_i - 1}\right]d\xi \tag{8}$$

If $b_i > 1$, then the first factor of the integrand is positive. Let $0 < \xi < (a_i/(b_i - 1)) - S^{(0)}$, and choose $t_0 > 0$ such that $S(t) \leq S^{(0)} + \varepsilon$ for $t \geq t_0$. Then for an appropriate constant C, it follows that

$$x_i(t) \leq Cx_{i0}\exp\left\{\left[S^{(0)} + \varepsilon - \frac{a_i}{b_i - 1}\right]\left[\frac{m_i - D}{a_i + S^{(0)} + 1}\right](t - t_0)\right\}$$

The first factor in the exponent is negative, and the other two positive so $\lim_{t\to\infty} x_i(t) = 0$.

For $b_i > 1$, as noted above, we define $\lambda_i = a_i/(b_i - 1)$. The basic hypothesis is

$$\lambda_1 < S^{(0)} \tag{H}_n$$

$$0 < \lambda_1 < \lambda_2 \leq \lambda_3 \leq \cdots \leq \lambda_n$$

The equations may be relabeled without loss of generality, so that the parameters $\lambda_i = a_i/(b_i - 1)$ are nondecreasing in i. $(H)_n$ excludes equality of this parameter for the first and any other population.

THEOREM 3 Let $(H)_n$ hold. The solutions of $(5)_n$ satisfy

$$\lim_{t\to\infty} S(t) = \lambda_1,$$

$$\lim_{t\to\infty} x_1(t) = x_1^* = y_1(S^{(0)} - \lambda_1)$$

$$\lim_{t\to\infty} x_i(t) = 0, \qquad 2 \leq i \leq n$$

This theorem states that under the hypothesis $(H)_n$ only one type of organism survives, the one with the lowest value of λ, and gives the limiting

concentrations. For a given system, the parameter λ depends on two characteristics, the growth rate and the Michaelis-Menten constant. It is biologically reasonable to assume that for two distinct species, the corresponding parameter will be different. Hence $(H)_n$ (with all strict inequalities) is a biologically reasonable assumption.

Proof of Theorem 3 (Hsu, [16]) Let F denote the positive cone in R^{n+1} and define there a Liapunov function

$$V(S, x_1, \ldots, x_n)$$

$$= S - \lambda_1 - \lambda_1 \ln\left(\frac{S}{\lambda_1}\right) + c_1\left[(x_1 - x_1^* - x_1^*)\ln\left(\frac{x_1}{x_1^*}\right)\right] + \sum_{i=2}^{n} c_i x_i$$

where $c_i = m_i/[y_i(m_i - D)]$. Along solutions of the equation

$$\frac{d}{dt} V(S(t), x_1(t), \ldots, x_n(t))$$

$$= \text{grad } V \cdot (S', x_1', \ldots, x_n')^T$$

$$= \begin{bmatrix} 1 - \dfrac{\lambda_1}{S} \\ c_1\left(1 - \dfrac{x_1}{x_1}\right) \\ c_2 \\ \cdot \\ \cdot \\ \cdot \\ c_n \end{bmatrix} \begin{bmatrix} (S^{(0)} - S)D - \displaystyle\sum_{i=1}^{n} \frac{m_i}{y_i} \frac{x_i S}{a_i + S} \\ \dfrac{(m_1 - D)}{a_1 + S}(S - \lambda_1)x_1 \\ \dfrac{m_2 - D}{a_2 + S}(S - \lambda_2)x_2 \\ \cdot \\ \cdot \\ \cdot \\ \dfrac{m_n - D}{a_n + S}(S - \lambda_n)x_n \end{bmatrix}$$

$$= (S - \lambda_1)\left[\frac{(S^{(0)} - S)}{S} D - \frac{k_1 x_1^*}{a_1 + S}\right] + \sum_{i=2}^{n} \frac{m_i}{y_i}(\lambda_1 - \lambda_i)\frac{x_i}{a_i + S}$$

where $k_1 = m_1/y_1$.

Since

$$x_1^* = y_1(S^{(0)} - \lambda_1)$$

$$= \frac{(S^{(0)} - \lambda_1)(a_1 + \lambda_1)Dy_1}{m_1\lambda_1}$$

then

$$\frac{k_1x_1^*}{a_1 + S} = \frac{k_1\lambda_1x_1^*}{\lambda_1(a_1 + S)} = \frac{(S^{(0)} - \lambda_1)(a_1 + \lambda_1)D}{\lambda_1(a_1 + S)}$$

Thus

$$\frac{(S^{(0)} - S)D}{S} - \frac{k_1x_1^*}{a_1 + S}$$

$$= \frac{D[S^{(0)}\lambda_1a_1 + S^{(0)}\lambda_1S - (S^{(0)} - \lambda_1)(a_1 + \lambda_1)S - \lambda_1S^2] - \lambda_1a_1S}{S(a_1 + S)\lambda_1}$$

$$= \frac{-D(S - \lambda_1)(\lambda_1S + a_1S^{(0)})}{S(a_1 + S)\lambda_1}$$

Using this in the computation of dV/dt yields

$$\frac{dV}{dt} = \frac{-D(S - \lambda_1)^2(\lambda_1S + a_1S^{(0)})}{(a_1 + S)S\lambda_1} = \sum_{i=2}^{n} k_i(\lambda_1 - \lambda_i)\frac{x_i}{a_i + S} \leq 0$$

since $0 < \lambda_1 < \lambda_i$, $i \geq 2$, and $S > 0$. The set $E = \{(S, x_1, \ldots, x_n) | \dot{V} = 0\}$ is given by

$$E = \{\lambda_1, x_1, 0, 0, \ldots, 0)\}$$

Since $\lambda_1 < S^{(0)}$, the only invariant set in E is

$$S = \lambda_1$$

$$x_1 = x_1^* = y_1(S^{(0)} - \lambda_1)$$

$$x_i = 0, \quad i = 2, \ldots, n$$

An application of LaSalle [29, p. 30] completes the proof. The proof in [16] is more general in that it allows unequal death rates.

Only one coexistence result was obtained.

THEOREM 4 Let $b_1 > 1$ and $0 < \lambda_1 = \lambda_2 = \ldots = \lambda_n < S^{(0)}$. Then

$$\lim_{t\to\infty} S(t) = \lambda_1$$

and

$$\lim_{t\to\infty} x_i(t) = x_i^* > 0$$

where

$$\lambda_1 + \sum_{i=1}^{n} \frac{x_i^*}{y_i} = S^{(0)}$$

EXPERIMENTAL RESULTS

Theorem 3 makes an explicit prediction when several populations are grown in a chemostat--it predicts a unique surviving population and the steady state concentration levels for the nutrient and for the survivor. The experiments corresponding to this prediction have been made by Hansen and Hubbell [9] and will be summarized here. Before giving the details, however, we pause to observe several features of the model. First of all, two of the parameters, $S^{(0)}$, the input concentration, and D, the dilution parameter, are controlled by the experimenter. The yield constants, y_i, are measured by growing the organisms one at a time in batch culture, or (preferably) in

continuous culture, and estimating cell concentrations at steady state for a given input of limiting nutrient. Since each equation for a population x_i contains only the variables x_i and S, the nutrient concentration, the remaining parameters, m_i and a_i can also be obtained by growing each population, in the absence of the other organisms, on the limiting nutrient. The most widely used method of computing m_i and a_i is a graphical technique known as a "Lineweaver-Burk Plot" [31]. While the biological details of such parameter estimation are not of interest to mathematicians, the important point is that the determination of m_i and a_i is *independent* of the other populations. For this reason it is possible to make the measurements of each organism and predict the outcome when the two are mixed together and grown in a chemostat.

The λ criterion for competitive ability is nonobvious and requires experimental verification. It could not have been predicted from classical theories of ecological competition. *A priori* it might have been expected that the winner would always be the organism with the highest affinity and lowest a_i, for the limiting nutrient, or perhaps the organism with the highest intrinsic rate of increase. In the Monod model of competition, the intrinsic rate of increase of organism x_i is given by the difference between the maximal birth rate, m_i, and the death rate, D, and is denoted by r_i. The theory, however, asserts that the critical parameter to competitive success is actually a weighted a_i. This weighted a_i is the parameter λ_i which can be rewritten from the fourth section as $\lambda_i = a_i(D/r_i)$. Thus the biologically interesting prediction can be made that a species may actually lose in competition even with a lower half-saturation constant a_i and thus a higher affinity for the resource, if it also has a lower intrinsic rate of increase r_i than its rivals. The theory also asserts that winning will not depend in any way on the growth efficiency or yield of the competing organisms from the limiting resource.

To make a rigorous test of the λ criterion in continuous culture requires proof that (i) if two organisms have equal r_i's and D's, the organism with the lower a_i wins; that (ii) if two organisms have identical a_i's and D's, the organism with the higher r_i wins; and that (iii) if two organisms have different a_i's and r_i's but in spite of this still have identical λ's, then the organisms should coexist. Hansen and Hubbell [9] have conducted all three of these tests in competition experiments with mutant strains of bacteria which must be supplied with an external source of the amino acid, tryptophan, in order to grow and divide. In the first set of tests, the

competing strains were of different species and differed primarily in their a_i values for tryptophan uptake. In the second and third tests, the competing organisms were strains of the same species, and of the same mating type so that conjugation between strains and gene exchange were prevented. In the second set of tests, the strains had identical a_i values but differed considerably in maximal specific growth rates and in r_i's. In the third set, the strains had identical λ's although they differed in both their a_i's and r_i's.

Each set of experiments was conducted in two sequential parts. The first part consisted of measuring the a_i's and m_i's for each bacterial strain grown alone in batch culture on a limiting amount of tryptophan. The values of λ were calculated to predict the outcomes of the subsequent competition experiments. The yield constants were measured in pure-strain continuous cultures at steady state.

The measured parameters for each bacterial strain are shown in Table 4.1, in addition to other run parameters for each experiment. Figure 4.1 shows the result of the first experiment. In this case, *Escherichia coli* C-8 was opposed by *Pseudomonas aerogenosa* PAO-283. The a_i values for tryptophan for these two bacterial species differ by nearly two orders of magnitude, and as a result the λ value for *E. coli* is much smaller than for *P. aerogenosa*. The predicted winner, *E. coli*, actually did win, effectively eliminating *P. aerogenosa* in the space of 60 hr. Note that *P. aerogenosa* lost to *E. coli* in spite of having a higher intrinsic rate of increase, and in spite of having a starting 200:1 numerical advantage. That initial densities as different as these do not influence the outcome can be taken as evidence supporting the view that competition for tryptophan between these two bacteria is purely exploitative.

The first experiment confirms the importance of having high affinity (low a_i) for the limiting resource, but the second and third experiments confirmed that it is a weighted a_i (i.e., λ) which is critical to the outcome. In both of these sets of experiments, competition occurred between two clones of *E. coli*. The strains were artificially selected for a cross pattern of drug resistance (strain 1 resistant to drug a, sensitive to drug b; strain 2 with the reverse pattern). These drugs cause a lowering of cell growth rate--a linear depression of growth rate at low drug concentrations (see Figure 4.2). By adding small amounts of a drug to the culture medium flowing into the chemostat, it was possible to alter the intrinsic rate of increase, r_i, of the sensitive strain while leaving the r_i of the resistant

TABLE 4.1

Uptake and Growth Parameters for Competing Bacterial Strains[a]

Experiment Number	Bacterial Strain	Yield Cells/g	a_i g/l	m_i hr^{-1}	r hr^{-1}	λ g/l
1	C-8[b]	2.5×10^{10}	3.0×10^{-6}	0.81	0.75	2.40×10^{-7}
	PAO283[c]	3.8×10^{10}	3.1×10^{-4}	0.91	0.85	2.19×10^{-5}
2	C-8 $nal^r spec^s$	6.3×10^{10}	1.6×10^{-6}	0.68	0.61	1.98×10^{-7}
	C-8 $nal^s spec^r$	6.2×10^{10}	1.6×10^{-6}	0.96	0.89	1.35×10^{-7}
3[d]	C-8 $nal^r spec^s$	6.3×10^{10}	1.6×10^{-6}	0.68	0.61	1.98×10^{-7}
	C-8 $nal^s spec^r$	6.2×10^{10}	0.9×10^{-6}	0.41	0.34	1.99×10^{-7}

Other Run Parameters

Experiment Number	S_0 g/l	D hr^{-1}	Volume ml
1	1×10^{-4}	6.0×10^{-2}	200
2	5×10^{-6}	7.5×10^{-2}	200
3	5×10^{-6}	7.5×10^{-2}	200

[a]The limiting nutrient is the amino acid, tryptophan, needed by both strains. The superscripts "r" and "s" refer to drug resistance or sensitivity, respectively.

[b]*Escherichia coli*

[c]*Pseudomonas aerogenosa*

[d]0.5 μg/ml nalidixic acid added
Metabolic inhibitors (drugs): nal = nalidixic acid
spec = spectinomycin

strain unaffected. This technique was used in the second set of experiments. In these tests, although both strains had identical half-saturation constants, the strain with the lower intrinsic rate of increase lost (see Figure 5.3). In the final set of experiments, the two *E. coli* strains chosen also differed in their half-saturation constants. By lowering the intrinsic rate of increase of the strain with the lower half-saturation constant with a drug, it was possible to make the λ's of the two strains equal. The result of the thrice-replicated experiment (see Figure 4.4) was coexistence of the competing bacteria, as predicted by the theory [18].

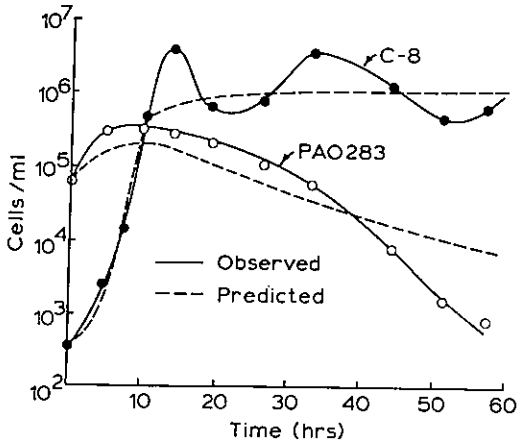

Fig. 4.1. Observed and predicted time course of cell density for the strains PAO283 and C-8 competing in mixed culture for limiting tryptophan in continuous culture. Parameters for the run are listed in Table 4.1. The predicted curves were obtained by numerical solution of equations $(5)_2$. In this experiment, the strains differ principally in their half-saturation constants for tryptophan.

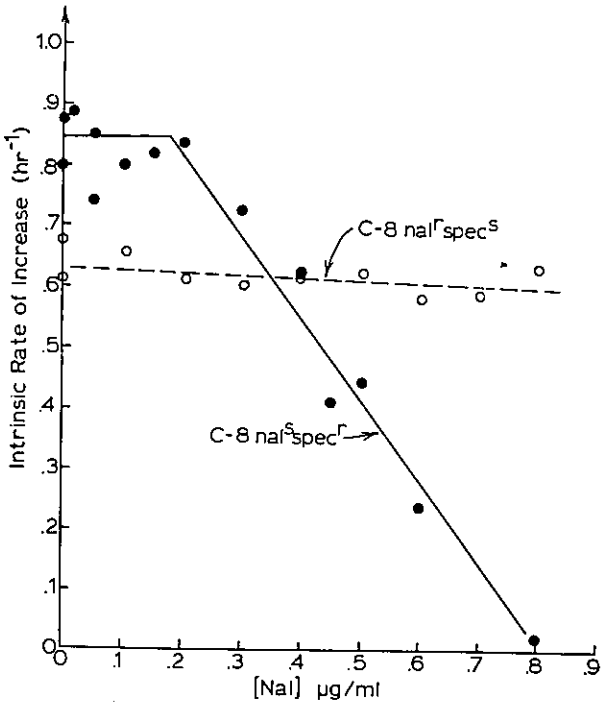

Fig. 4.2. Effect of nalidixic acid concentration on the intrinsic rate of increase of two strains of *E. coli* growing alone. Growth rate of the nal-sensitive strain in linearly depressed with increasing concentration between 0.2 and 0.8 g/ml nalidixic acid. Growth rate of the nal-resistant strain is virtually unaffected. In the figure, read "+" as "resistant" and "-" as "sensitive."

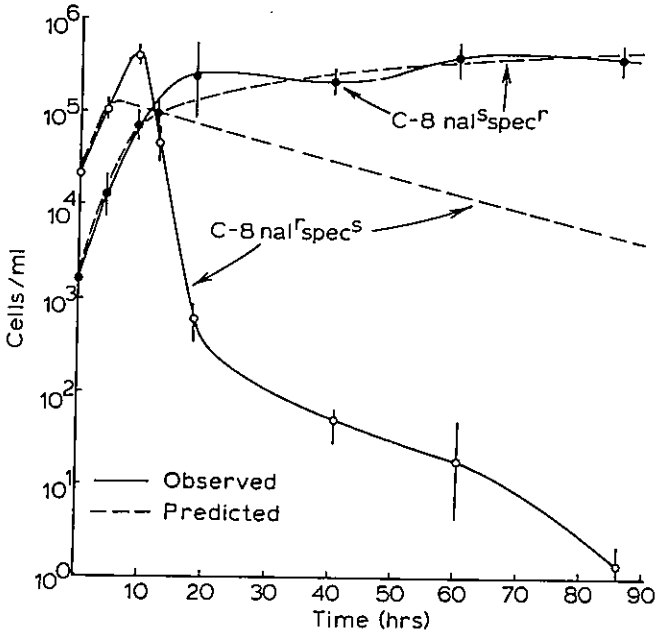

Fig. 4.3. Observed and predicted time course of cell density for two strains of *E. coli* competing for limiting tryptophan. Strains differ in their intrinsic rates of increase, but not in their half-saturation constants (Table 4.1). Dots represent mean cell densities for 3 replicate runs; bars are the ranges of cell densities.

It should be noted that although the qualitative outcomes of the theory are correctly matched by experiment, there are some quantitative deviations of the experimental results from the theoretical trajectories forecast by the system of equations in (5). For example, sometimes oscillations (Figure 4.1) in the approach to steady-state cell density occur in the culture. These could be caused by time delays present in the system that are not reflected in the model. How to formulate the delays so as to give a better fit appears to be an interesting open question. It seems likely that changing cell volume during the growth and plateau phases of population increase could contribute some of the delay. Cell death over and above losses in the effluent could also account for the faster-than-expected decline in the losing strains.

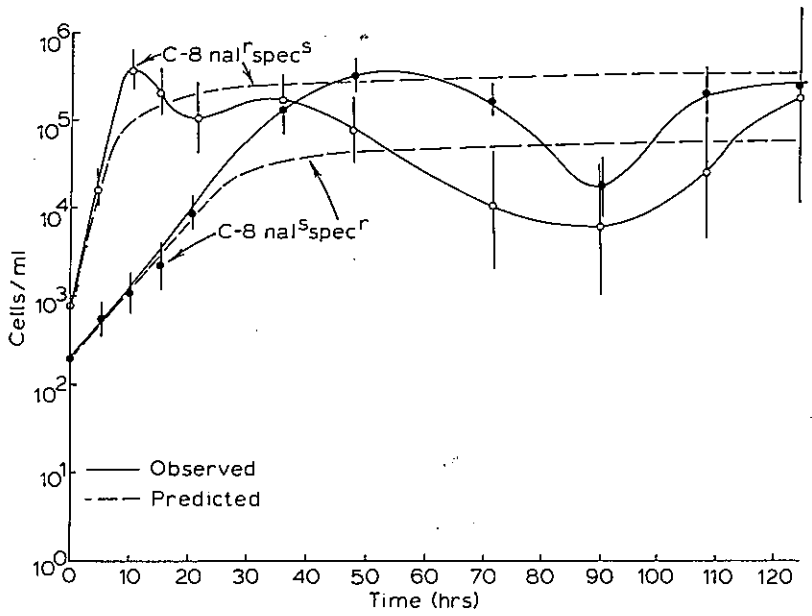

Fig. 4.4. Time course of cell density for two strains of *E. coli* competing for limiting tryptophan in continuous culture. Strains differ in their half-saturation constants and in their intrinsic rates of increase, but are identical in their T values. The strains coexisted for the length of the run.

RELEVANCE TO THE ECOLOGY OF LAKES AND OCEANS

Naturally occurring bodies of water such as lakes and oceans are inhabited by a diverse array of microscopic organisms such as bacteria and unicellular algae that form complex planktonic communities. Because these organisms share many of the same nutrient requirements, the question naturally arises as to the extent to which such ecosystems are analogs of continuous cultures in the laboratory. The surface waters of almost all lakes and oceans, where these planktonic organisms occur, receive nutrient inputs from eroding watersheds or upwelling water rich in nutrients from bottom sediments. Indeed, the planktonic community is wholly dependent on sustained nutrient inputs for continued persistence in the sunlit surface waters [22].

In the temperature zone at least, the biggest departure from the chemostat results from the periodic forcing of natural ecosystems by seasonal weather changes. Lakes and oceans, although in part thermally buffered by the high heat capacity of water, nevertheless do not escape the influence of the seasons. Nutrient levels experienced by phytoplankton change

profoundly from one season to the next. For example, in deeper lakes and oceans, gradients of water density established in summer prevent complete mixing of the water column, thereby cutting off the supply of nutrients to surface waters from bottom sediments or nutrient-rich older and denser waters below. In the spring and fall, however, heating and cooling of the surface waters, respectively, equalize the water densities throughout the water column, and more nearly complete mixing occurs. Therefore, these times of the year in temperate bodies of water are characterized by nutrient enrichment of the surface waters. These spring and fall "turnovers" are accompanied by phytoplankton "blooms" for a few weeks during and after turnover. As summer and winter progress, respectively, the nutrient levels decline as a direct result of their consumption and removal by the plankton. The nutrients are slowly lost from the upper waters because the plankton gradually sinks to the bottom, decomposes, and liberates the nutrients once again, to be refluxed to the surface during the next lake overturn. These seasonal changes in nutrient and phytoplankton levels in the surface waters of lakes and oceans are well documented in the limnological literature [22, 26].

In addition to these almost periodic seasonal drivers, natural "cultures" of microorganisms, especially smaller bodies of water, receive stochastic nutrient pulses of varying amplitude and duration. These pulses are caused by nutrient input during precipitation and the resulting, fairly abrupt, increased inflow from the surrounding watershed. Pulses of this type have been measured for a number of important limiting nutrients on several occasions [26].

In spite of the fact that natural planktonic ecosystems often depart from the ideal laboratory chemostat, both in the inconstancy of nutrient input and in the lack of achievement of a steady state, nevertheless a number of predictions about the composition of these communities based on chemostat studies have been very successful. This has been particularly true among planktonic algal communities. The success of these predictions appears due to the fact that, in spite of natural fluctuations in nutrients, the same nutrients remain limiting to the plankton throughout, or else quickly become limiting once again after the pulse is over.

These successes can be illustrated by recent work on freshwater diatoms. These unicellular algae are encased in a siliceous shell, which imposes on all diatoms a requirement for silica. Silicate has a fairly low solubility in water, and as a result diatoms are frequently limited by the availability

of this mineral. Kilham [27] was able to relate the dominance of particular diatom species in a series of African lakes to the concentration of silicate in the streamwater flowing into the lake, and to the amount of silica in the bedrock of the watershed. Diatom species with lower half-saturation constants for uptake of silicate were dominant in lakes with lower input concentrations of silicate. Kilham also found, however, that lakes with a higher silicate input were dominated with diatom species having higher half-saturation constants for silicate. This result would not be expected from chemostat theory if all diatoms in these lakes were limited by silicate.

Later work by Tilman and Kilham [53] and Tilman [52, 55] suggests a very simple explanation: limitation by different complementary nutrients in the different lakes. They studied two species of diatom, *Asterionella* and *Cyclotella*, growing first under silicate limitation and then under phosphate limitation. *Cyclotella* not only has the lower half-saturation constant, but also the higher intrinsic rate of increase, under silicate limitation, and the converse is true under phosphate limitation. Therefore, when these diatoms are placed in competition in mixed-growth continuous culture, *Cyclotella* wins when both species are silicate-limited, whereas *Asterionella* wins when both species are phosphate-limited. Tilman also found a region of coexistence, corresponding to nutrient ratios of phosphate to silicate in the influent medium for which *Asterionella* was silicate-limited but *Cyclotella* was phosphate-limited. These results were fully predicted by chemostat theory extended to two complementary resources.

These two diatom species are abundant in the Great Lakes, and Tilman [52] went on to show that chemostat theory could predict the relative abundance of these species with reasonable accuracy. To make these predictions he assumed that the sampled lake waters were at or near steady state. Then the observed phosphate/silicate ratios in the water samples were used to predict the relative proportion of *Cyclotella* cells in the water sample. When this ratio is high, generally in inshore waters where phosphate levels are at their highest, the predicted percentage of *Cyclotella* was zero, due to exclusion by *Asterionella*. In midlake water samples, where phosphate levels are at their lowest, the expected percentage of *Cyclotella* was 100%, resulting from the competitive elimination of *Asterionella*. In the region of intermediate phosphate/silicate ratios, the theory predicted intermediate percentages of *Cyclotella*. The fit of the expected percentages to the observed percentages of *Cyclotella* was remarkably good: more than 70% of the variance was explained. This is a very high percentage of variance

explained, given that many other variables also affect diatom abundance in nature, and the further fact that steady-state conditions were assumed in order to make the predictions.

As mentioned in the second section, Tilman also discovered that a model of luxury consumption of phosphate by the diatoms, which takes into account internal stores of phosphate in the cells, generally fit the data no better than the simpler Monod model. In any event, at steady state the predictions were virtually identical for the Monod formulation and the "internal stores model" proposed by Droop [5] for unicellular algae. Recently, it has been shown that there is a good theoretical basis for steady-state equivalence between these two models [3].

These studies have been presented for illustrative purposes to show how well the theory is being adapted to natural ecosystems. Because the theory and its biological testing are still in their infancy, we can expect many more theoretical and biological contributions to resource-based competition theory in the near future.

TWO COMPETITORS AND A SELF REVIEWING RESOURCE

The Equations

The chemostat has forced resource input, but in many ecological systems the resource is not a chemical but a reproducing organism. Thus it is desirable to change the system (5) to reflect this phenomenon. However, doing so introduces serious mathematical complications. The simplest model of limited population growth of a simple organism is the logistic equation. Replacing the chemostat input with logistic terms, keeping the Michaelis-Menten dynamics (here, more appropriately, called Holling dynamics [13]), and limiting n to be 2, yields a system of the form

$$S' = \gamma S\left(1 - \frac{S}{K}\right) - \sum_{i=1}^{2} \frac{m_i}{y_i} \frac{x_i S}{a_i + S}$$

$$x_i' = \frac{m_i S x_i}{a_i + S} - D_i x_i \tag{9}$$

$$x_i(0) = x_{i0} > 0, \quad S(0) = S_0 > 0, \quad i = 1, 2$$

γ is the intrinsic growth rate for the resource, now appropriately viewed as the prey population, and K is the carrying capacity--the natural limit of the population size without predators--and all of the other constants are as before except that now there is an individual death rate rather than a simple washout rate. The use of D_i reflects the fact that this parameter may be different for each population. We seek to analyze the system (9). Where a rigorous analysis has not been achieved, computer simulation has been utilized to indicate the behavior of the system. The mathematical proofs and a more complete biological discussion can be found in Hsu, Hubbell, and Waltman [19] and [20]. In this section we summarize the basic results of these papers.

Statement of the Mathematical Results

As with $(5)_n$ it follows easily that all solutions with initial conditions in the positive octant are bounded and remain in the positive octant. In the analysis of (9) the carrying capacity K plays the role of the input nutrient $S^{(0)}$ in $(5)_n$ in the sense that if the maximum attainable amount of resource, K, is inadequate, survival is not possible. Also one expects that if the death rate is larger than the maximum possible birth rate, survival is not possible. This is the content of the following:

THEOREM 5 If $b_i \leq 1$ or if $K \leq \lambda_i$, $\lim_{t\to\infty} x_i(t) = 0$.

If one of the above conditions is satisfied, then the behavior of the solutions of (9) is determined from the analysis of the remaining two equations whose solutions form the omega limit set of the entire dynamical system. (Of course if for each i = 1 and 2, one of the above conditions is satisfied, the omega limit set of every trajectory is the critical point (K, 0, 0).) The interesting behavior of the two dimensional system

$$\begin{aligned} S' &= \gamma S\left(1 - \frac{S}{K}\right) - \frac{m}{y}\frac{xS}{a+S} \\ x' &= \frac{mxS}{a+S} - Dx \\ x(0) &= x_0 > 0, \qquad S(0) = S_0 > 0 \end{aligned} \tag{10}$$

is contained in the following statement.

LEMMA 6 If in (10) $K < a + 2\lambda$, where $\lambda = aD/(m - D)$, then (10) has no limit cycles in the first quadrant. If $K > a + 2\lambda$, there exists a limit cycle in the first quadrant.

The proof of the first statement follows from the Dulac Criterion; the second, from boundedness of solutions, the Poincaré-Bendixon Theorem, and the instability of the interior critical point. When one competitor is "inadequate" ($b_i \leq 1$ or $\lambda_i \geq K$), then with relatively little additional effort one obtains:

THEOREM 7 Let (a) $0 < \lambda_1 < K$, and

(b) $\lambda_2 > K$ or $b_2 \leq 1$

If

$$K < a_1 + 2\lambda_1$$

then

$$\lim_{t\to\infty} S(t) = S^* = \lambda_1$$

$$\lim_{t\to\infty} x_1(t) = x_1^* = \frac{\lambda\left(1 - \frac{S^*}{K}\right)(a_1 + S^*)}{(m_1/y_1)}$$

$$\lim_{t\to\infty} x_2(t) = 0$$

If $K > a_1 + 2\lambda_1$, then the omega limit set of the trajectory of $(S(t), x_1(t), x_2(t))$ lies in the $S - x_1$ plane (i.e., $\lim_{t\to\infty} x_2(t) = 0$) and contains a periodic trajectory except for one distinguished orbit which approaches the critical point $(S^*, x_1^*, 0)$.

The interesting case, of course is when both competitors can survive alone on the resource. To have competitive exclusion hold, one seeks conditions which make the omega limit set two dimensional. One such criterion is the following:

LEMMA 8 If $0 < \lambda_1 < \lambda_2$ and if $b_2 \leq b_1$, then $\lim_{t\to\infty} x_2(t) = 0$.

This lemma provides the technical bases for our principal result on competitive exclusion for the system (9).

THEOREM 9 Suppose that $0 < \lambda_1 < \lambda_2 < K$ and $b_1 \geq b_2 > 1$. Then the conclusions of Theorem 7 hold as $K < a_1 + 2\lambda_1$ or $K > a_1 + 2\lambda_1$.

Thus coexistence is possible only if $\lambda_1 < \lambda_2$, $a_1 < a_2$, and $b_1 < b_2$. (Note that these conditions are not independent.) We also have the following result on the persistence of x_1.

THEOREM 10 Suppose that $0 < \lambda_1 < \lambda_2 < K$, $a_1 < a_2$ and $K < a_2 + 2\lambda_2$. Then $\limsup_{t\to\infty} x_1(t) > 0$.

In the numerical simulation, the following result was useful, particularly when $b_2 - b_1$ was small.

THEOREM 11 Suppose that $0 < \lambda_1 < \lambda_2 < K$, $a_1 < b_1$, $b_1 < b_2$, and $K < (b_1a_2 - b_2a_1)/(b_2 - b_1)$. Then $\lim_{t\to\infty} x_2(t) = 0$.

Numerical Studies

The preceding theorems yield sufficient conditions for one predator population to survive and the ordering $\lambda_1 < \lambda_2$ favors the first predator. In view of the results presented in the third section one might expect that this is the only outcome possible. Extensive computer simulation shows this not to be the case; in fact, not only may coexistence occur but if K is sufficiently large (relative to other parameters) predator two can win the competition. A coexistence model of two predators which can survive on a single resource have been constructed by McGehee and Armstrong [32] and numerical studies by Koch [28] proceed ours. We summarize our computer results with three graphs from [20].

The data in Figure 4.5 was obtained by fixing all of the parameters except a_1 and K and letting these vary subject to $\lambda_1 < \lambda_2$. The designations

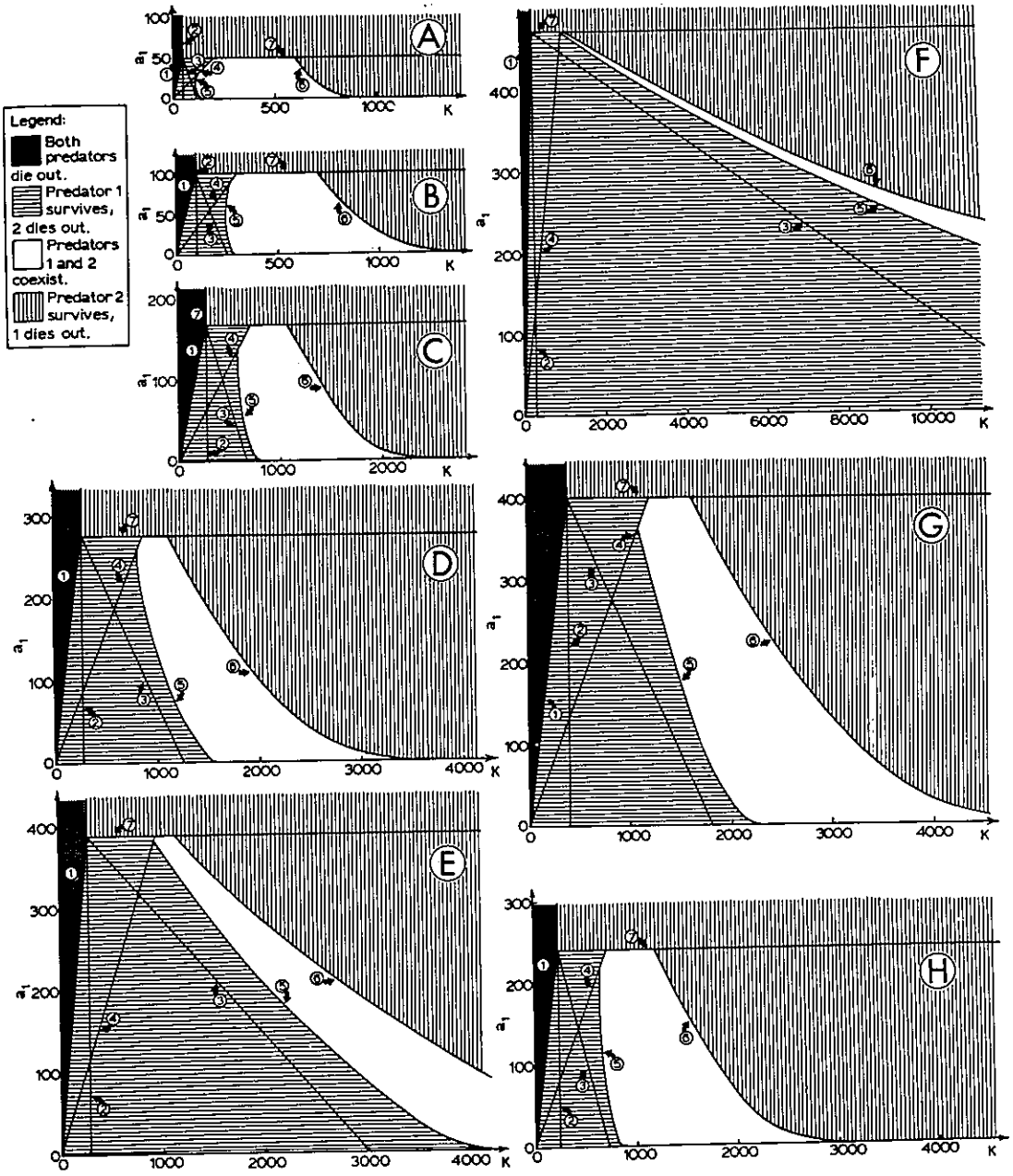

Fig. 4.5. Coexistence region illustrated for 2 predator species competing for a single prey species. Parameter space is a plot of prey carrying capacity, K, on the x-axis against the half-saturation constant for predator 1, a_1, on the y-axis. Parameters fixed for all graphs: $\gamma = 20.1n2$; $d_1 = 1$, $d_2 = \ln2/2$; $y_1 = \ln2$; $y_2 = 0.1$; $y_2 = 1.14$. Parameters for each case: A: $a_2 = 500$, $m_1 = \ln2$ ($b_1 = 2$), $m_2 = 11 \cdot \ln2$ ($b_2 = 11$); B: $a_2 = 500$, $m_1 = \ln2$

($b_1 = 2$), $m_2 = 6 \cdot \ln 2$ ($b_2 = 6$); C: $a_2 = 500$, $M_1 = 0.8 \cdot \ln 2$ ($b_1 = 1.6$), $m_2 = 2.8 \cdot \ln 2$ ($b_2 = 2.8$); D: $a_2 = 500$, $m_1 = \ln 2$ ($b_1 = 2$), $m_2 = 2.8 \cdot \ln 2$ ($b_2 = 2.8$); E: $a_2 = 500$, $m_1 = 1.2 \cdot \ln 2$ ($b_1 = 2.4$); $m_2 = 2.8 \cdot \ln 2$ ($b_2 = 2.8$); F: $a_2 = 500$, $m_1 = 1.35 \cdot \ln 2$ ($b_2 = 2.7$), $m_2 = 2.8 \cdot \ln 2$ ($b_2 = 2.8$); G: $a_2 = 720$, $m_1 = \ln 2$ ($b_1 = 2$), $m_2 = 2.8 \cdot \ln 2$ ($b_2 = 2.8$); H: $a_2 = 720$, $m_1 = \ln 2$ ($b_1 = 2$), $m_2 = 4 \cdot \ln 2$ ($b_2 = 4$). Numbered lines are as follows: (1): $\lambda_1 = K$; (2): $\lambda_2 = K$; (3): $K = (a_2 b_1 - a_1 b_2)/(b_2 - b_1)$; (4): $\lambda_1 = (K - a_1)/2$; (5): Lower $k - a_1$ boundary for coexistence region (known from numerical analysis); (6): Upper $K - a_1$ boundary for coexistence region (known from numerical analysis); (7): $\lambda_1 = \lambda_2$.

A - H indicate different parameters (see the figure caption). The numbered lines 1-4 correspond to analytically known results whereas curves 5 and 6 are numerically determined, and line 7 corresponds to $\lambda_1 = \lambda_2$. The horizontally shaded area to the left of curve 5 and below line 7 corresponds to the (numerically determined) region in $a_1 - K$ space where predator 1 wins the competition. The vertically shaded area to the right of curve 6 and below line 7 corresponds to the region where predator 2 wins the competition. In the unshaded area between curves 5 and 6, coexistence was found to occur as a globally asymptotically stable limit cycle. That the coexistence region is nonempty is a consequence of the work of G. Butler [2]. That the solutions corresponding to parameters in the coexistence region tend to a periodic solution is an open mathematical question. Figure 4.6 shows such a periodic solution and its projection onto $x_1 - x_2$ space.

In Figure 4.7 shows a cut through Figure 4.5H, $a_1 = 100$. We interpret this figure in the language of bifurcation theory. For values of $K < \lambda_1$, the critical point (K, 0, 0) is globally asymptotically stable (no predator survives). As K passes through λ_1, a second critical point enters the positive octant, (K, 0, 0) loses its stability (it has a one dimensional stable manifold) and the new critical point (λ_1, x^*, 0) is globally asymptotically stable. At $K = a_1 + 2\lambda_1$, this critical point bifurcates (a Hopf bifurcation) into a globally asymptotically stable limit cycle, lying in the $S - x_1$ plane and (λ_1, x_1^*, 0) becomes unstable (has a two dimensional unstable manifold). The upper and lower curves in Figure 4.7 show the maximum and minimum of the periodic solution. At a higher value of K--determined only numerically--this limit cycle bifurcates (not a Hopf bifurcation) into two periodic solutions, one remaining in the $S - x_1$ plane and one in the open, positive octant. This is the region of coexistence. For even higher values of K,

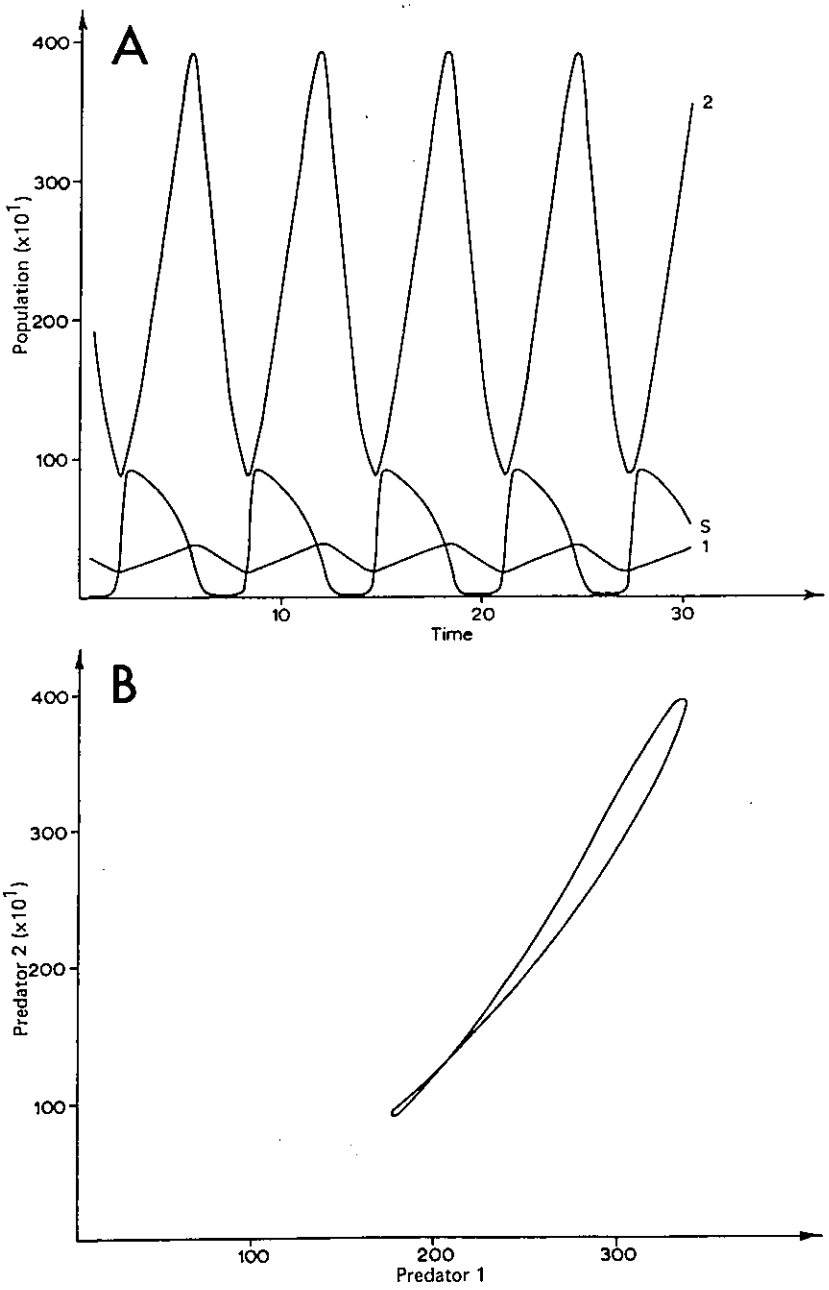

Fig. 4.6. Case in which there is oscillatory coesistence of 2 predator species (1 and 2) on a single prey species, S. Parameters are the same in Figure 1D with a_1 = 200 and K = 1100. A: Oscillations as in a function of time. B: Limit cycle of numbers of predator 1 plotted against numbers of predator 2. Initial values: x_1 = 307.13, x_2 = 2684.95, S = 8.60.

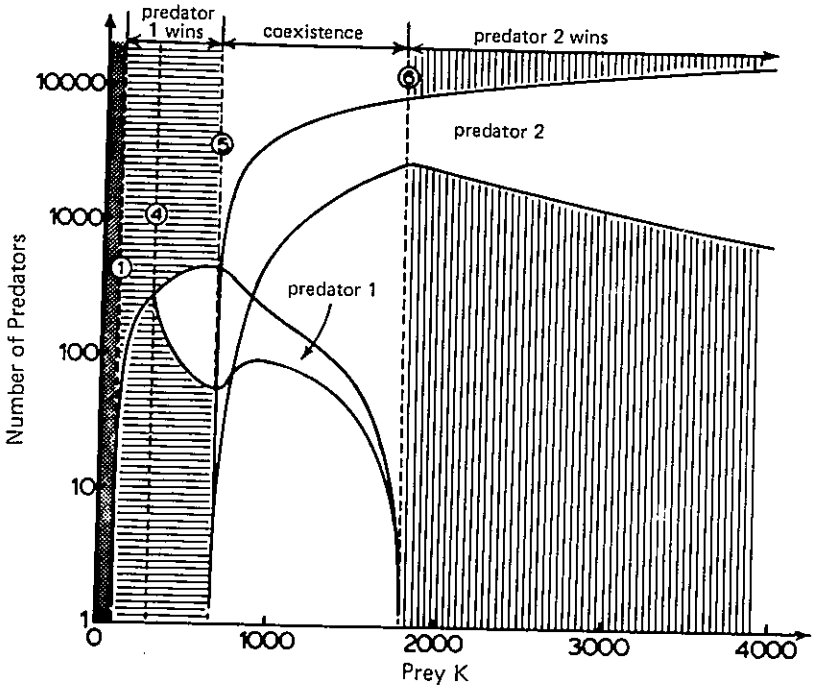

Fig. 4.7. Limiting behavior of 2 competing predators, one of which is a "K-strategist" (predator 1) and the other of which is an "r-strategist," preying upon a single prey population. Outcome as a function in Figure 4.5H with $a_1 = 100$. Shaded and hatched areas and numbered lines are codes as indicated in the legend and caption for Figure 4.5. Lines for predators 1 and 2 indicate the periodic maximal and minimal population sizes in the limiting oscillations.

the limit cycle in the open positive octant--which appears to be globally asymptotically stable--collapses into a limit cycle in the S - x_2 plane, retaining its global stability properties. This is the region where x_2 wins the competition. Proof that the two dimensional limit cycle bifurcates into a globally asymptotically stable limit cycle in the open octant is an open mathematical question and would appear to require information about the Poincaré map before existent bifurcation theorems could be applied. The collapse into the S - x_2 plane is the same problem viewed as K being sufficiently large but decreasing.

EXTENSION TO TWO RESOURCES

When the theory is extended to cover exploitative competition for two or more resources, it becomes necessary to consider how the resources, once consumed, interact to promote growth. Leon and Tumpson [30] and Hubbell and Hsu [21] have considered the cases of competition for two perfectly complementary or substitutable resources. The criteria for the outcomes for each case are given in [21]. We summarize these results in this section.

Before presenting the competition models for two species on two resources, it is necessary to discuss how the functional responses of the consumer species have been generalized from one to two resources. In the one-resource case, the per capita consumption rate, according to the Type II functional response, is given by $(m_{ri}/y_{ri})(R/a_{ri} + R))$ if the resource is R, or is given by $(m_{si}/y_{si})(S/a_{si} + S))$ if the resource is S. These one-resource per capita consumption rates can be rewritten as:

$$\frac{m_{ri}/a_{ri}}{y_{ri}} \frac{R}{1 + R/a_{ri}} \quad \text{and} \quad \frac{m_{si}/a_{si}}{y_{si}} \frac{S}{1 + S/a_{si}}$$

respectively. The generalization of two perfectly substitutable resources is well known, and corresponds in Michaelis-Menten theory to reaction rates with competitive inhibition--consumption of resource R acts as a competitive inhibitor in the consumption of resource S. In Holling's terminology, handling time devoted to processing a unit of resource R is time not available for the processing of resource S, and this competitive effect is linear. Therefore, the per capita consumption rates of resource R in the presence of substitutable resource S, and of S in the presence R, are given by:

$$\frac{m_{ri}/a_{ri}}{y_{ri}} \frac{R}{1 + R/a_{ri} + S/a_{si}} \quad \text{and} \quad \frac{m_{si}/a_{si}}{y_{si}} \frac{S}{1 + R/a_{ri} + S/a_{si}}$$

respectively. Note that the above expressions simplify to the previous case if one of the resources is absent.

The generalization of the functional response to two complementary resources is different. In this case, the per capita consumption rate of whichever resource is currently limiting growth is identical to the one-resource per capita consumption rate for the appropriate resource. The

question then arises: At what rate is the nonlimiting resource consumed? This question can be answered by considering the yield of consumer produced per unit of resource consumed. When the yield factors, y_{ri} and y_{si} are constants, then it follows that there must be a fixed ratio of the growth-essential substances provided by resources R and S in a unit of consumer. Moreover, this also implies that the per capita consumption rate of the nonlimiting resource must be proportional to the per capita consumption rate of the limiting resource. If it were not, then the ratio of essential growth substances in the consumer would be changing, and the yield factors would no longer be constant. The proportionality constant is the ratio of the yield constants for the two resources. For example, suppose species i is S-limited. Then the per capita consumption rate of S, call it $f_1(S)$, is:

$$f_1(S) = \frac{m_{si}}{y_{si}} \frac{S}{a_{si} + S} \tag{11}$$

whereas the concurrent per capita consumption rate of the nonlimiting resource R is given by:

$$\left(\frac{y_{si}}{y_{ri}}\right) \cdot f_1(S) = \frac{m_{si}}{y_{ri}} \frac{S}{a_{si} + S} \tag{12}$$

Note that this expression does not contain the concentration of the nonlimiting resource R. Thus, it should be noted that: *For complementary resources R and S, when a species is S-limited, its per capita consumption rate of R is independent of the concentration of R; whereas, when the species is R-limited, its per capita consumption rate of S is independent of the concentration of S.*

For complementary resources, R and S, the species 1 and 2, competing exploitatively for them, the system of equations then is:

$$\frac{dS}{dt} = (S_0 - S)D_s - f_1(S, R)x_1 - f_3(S, R)x_x$$

$$\frac{dR}{dt} = (R_0 - R)D_r - f_2(S, R)x_1 - f_4(S, R)x_2$$

$$\frac{dx_1}{dt} = \left[\min\left(\frac{m_{s_1} S}{a_{s_1} + S}, \frac{m_{r_1} R}{a_{r_1} + R}\right) - D_1\right] x_1$$

$$\frac{dx_2}{dt} = \left[\min\left(\frac{m_{s_2} S}{a_{s_2} + S}, \frac{m_{r_2} R}{a_{r_2} + R}\right) - D_2\right] x_2$$

where S, R, N_1, and N_2 are all positive at time 0, and where:

$$f_1(S, R) = \begin{cases} \dfrac{m_{s_1}}{y_{s_1}} \dfrac{S}{a_{s_1} + S} & \text{if } \dfrac{m_{s_1} S}{a_{s_1} + S} \leq \dfrac{m_{r_1} R}{a_{r_1} + R} \\ \dfrac{m_{r_1}}{y_{s_1}} \dfrac{R}{a_{r_1} + R} & \text{if } \dfrac{m_{s_1} S}{a_{s_1} + S} \geq \dfrac{m_{r_1} R}{a_{r_1} + R} \end{cases}$$

$$f_2(S, R) = \begin{cases} \dfrac{m_{s_1}}{y_{r_1}} \dfrac{S}{a_{s_1} + S} & \text{if } \dfrac{m_{s_1} S}{a_{s_1} + S} \leq \dfrac{m_{r_1} R}{a_{r_1} + R} \\ \dfrac{m_{r_1}}{y_{r_1}} \dfrac{R}{a_{r_1} + R} & \text{if } \dfrac{m_{s_1} S}{a_{s_1} + S} \geq \dfrac{m_{r_1} R}{a_{r_1} + R} \end{cases}$$

$$f_3(S, R) = \begin{cases} \dfrac{m_{s_2}}{y_{s_2}} \dfrac{S}{a_{s_2} + S} & \text{if } \dfrac{m_{s_2} S}{a_{s_2} + S} \leq \dfrac{m_{r_2} R}{a_{r_2} + R} \\ \dfrac{m_{r_2}}{y_{s_2}} \dfrac{R}{a_{r_2} + R} & \text{if } \dfrac{m_{s_2} S}{a_{s_2} + S} \geq \dfrac{m_{r_2} R}{a_{r_2} + R} \end{cases}$$

$$f_4(S, R) = \begin{cases} \dfrac{m_{s_2}}{y_{r_2}} \dfrac{S}{a_{s_2} + S} & \text{if } \dfrac{m_{s_2} S}{a_{s_2} + S} \leq \dfrac{m_{r_2} R}{a_{r_2} + R} \\ \dfrac{m_{r_2}}{y_{r_2}} \dfrac{R}{a_{r_2} + R} & \text{if } \dfrac{m_{s_2} S}{a_{s_2} + S} \geq \dfrac{m_{r_2} R}{a_{r_2} + R} \end{cases}$$

For substitutable resources, R and S, and species 1 and 2 competing exploitatively for them, the system of equations is:

$$\frac{dS}{dt} = (S_0 - S)D_s - g_1(S, R)x_1 - g_3(S, R)x_2$$

$$\frac{dR}{dt} = (R_0 - R)D_r - g_2(S, R)x_1 - g_4(S, R)x_2$$

$$\frac{dx_1}{dt} = \left[\frac{(m_{s_1}/a_{s_1})S + (m_{r_1}/a_{r_1})R}{1 + S/a_{s_1} + R/a_{r_1}} - D_1 \right] \cdot x_1$$

$$\frac{dx_2}{dt} = \left[\frac{(m_{s_2}/a_{s_2})S + (m_{r_2}/a_{r_2})R}{1 + S/a_{s_2} + R/a_{r_2}} - D_2 \right] \cdot x_2$$

where S, R, N_1, and N_2 are all positive at time 0, and where:

$$g_1(S, R) = \frac{m_{s_1}/a_{s_1}}{y_{s_1}} \frac{S}{1 + S/a_{s_1} + R/a_{r_1}}$$

$$g_2(S, R) = \frac{m_{r_1}/a_{r_1}}{y_{r_1}} \frac{R}{1 + S/a_{s_1} + R/a_{r_1}}$$

$$g_3(S, R) = \frac{m_{s_2}/a_{s_2}}{y_{s_2}} \frac{S}{1 + S/a_{s_2} + R/a_{r_2}}$$

$$g_4(S, R) = \frac{m_{r_2}/a_{r_2}}{y_{r_2}} \frac{R}{1 + S/a_{s_2} + R/a_{r_2}}$$

where,

S_0, R_0 = input concentrations of resource S and R, respectively,
D_s, D_r = input-output flow rate of medium containing S or R,
D_i = per capita death rate for the ith species,
m_{si}, m_{ri} = per capita birth rate of species i on resource S or R,
y_{si}, y_{ri} = yield of species i per unit of resource S on R consumed, and
a_{si}, a_{ri} = half-saturation constant for species i on resource S or R.

In the one-resource case, λ, the subsistence resource concentration for each competing species, was sufficient to predict the outcome of competition. The λ criterion is also important in the two-resource case, but in general it no longer provides sufficient information by itself to predict competitive outcomes, except in the case where one species has the lower λ's for both resources (this species wins regardless of initial abundance). In particular, additional competition criteria are required when species 1 has the lower subsistence concentration on one resource, but species 2 has the lower subsistence concentration on the second resource, because in this situation there are a number of possible outcomes. To discriminate between these additional outcomes, it becomes necessary to introduce two new parameters, T* and C_i, which differ depending on whether or not the resources are complementary or substitutable. The parameter C_i is species specific. These parameters for complementary resources are:

$$T^* = \frac{(R_0 - \quad_{r_2})D_r}{(S_0 - \quad_{s_1})D_s}, \qquad C_1 = \frac{1/y_{r_1}}{1/y_{s_1}}, \qquad C_2 = \frac{1/y_{r_2}}{1/y_{s_2}}$$

where λ_{r_i} and λ_{s_i} are the λ parameters of species i on resources r and s, respectively.

For substitutable resources, the corresponding values of T*, C_1, and C_2 are:

$$C_1 = \frac{m_{r_1}/y_{r_1}}{m_{s_1}/y_{s_1}}, \qquad C_2 = \frac{m_{r_2}/y_{r_2}}{m_{s_2}/y_{s_2}}$$

$$T^* = \frac{\frac{(R_0 - R^*_{12})}{R^*_{12}} D_r}{\frac{(S_0 - S^*_{12})}{S^*_{12}} D_s}$$

where

$$R^* = \frac{\lambda_{r_1}\lambda_{r_2}(\lambda_{s_2} - \lambda_{s_1})}{\lambda_{r_1}\lambda_{s_2} - \lambda_{r_2}\lambda_{s_1}} \tag{13}$$

and

$$S^*_{12} = \frac{\lambda_{s_1}\lambda_{s_2}(\lambda_{r_1} - \lambda_{r_2})}{\lambda_{r_1}\lambda_{s_2} - \lambda_{r_2}\lambda_{s_1}}$$

The parameter T* represents the ratio of the steady-state resource regeneration rates, R over S, when both species 1 and 2 are present at equilibrium. The C_1 and C_2 parameters represent the ratios of demand for resources R and S by species 1 and 2, respectively. In the case when one species has a lower λ for one of the resources, and the second species has the lower λ for the other resources, the outcome of competition depends on the relative rates of resource supply compared with the rates of resource demand by the two species. The 3-way inequalities involving T*, C_1, and C_2 constitute criteria to resolve all remaining cases of exploitative competition for two resources. The T* and C_i parameters differ in the cases of complementary and substitutable resources. In the complementary-resource case, the C_i's are ratios of the yield constants because the uptake rate of the nonlimiting resource is proportional to, and determined by, the uptake rate of the limiting resource. However, in the substitutable-resource

case, the C_i's are ratios of per capita consumption rates instead. Since each substitutable resource is actually just an alternate source for the same essential nutrient, what becomes important to competitive outcomes in this case are the per capita rates of resource consumption by each species, in relation to the specific rates of resource regeneration. Relative rates of consumption are now important because neither species can be limited solely by one of the resources; thus, there is no simple refuge from competition by separate resource limitation in the two species.

When the present theory is extended from one resource to two, additional outcomes of competition not found in one-resource situations, are predicted. Two-resource theory predicts that there will be a broad region of parameter space for which the competing species can coexist, unlike the "knife-edge" condition of precisely equals λ's in one-resource theory. Moreover, two-resource theory predicts that, under certain conditions, the initial abundance of the competing species will determine which species is the eventual winner. Finally, the two-resource theory generates each of the classical outcomes of two-species competition in more than one way. These outcomes are compared in Table 4.2.

To our knowledge no one has yet reported a case of competition for two known complementary or substitutable resources in which the outcome depended on the initial abundances of the competitors. Tilman and Kilham [53] and Tilman [52] have performed interesting competition studies in semicontinuous cultures between two freshwater diatoms, *Asterionella formosa* Hass., and *Cyclotella meneghiniana* Kutz. for the complementary resources, phosphate and silicate. They did not report any cases in which the outcomes were dependent on initial numbers. However, they did find a broad region of coexistence over a range of ratios of silicate/phosphate in the influent supply to semicontinuous cultures of the two diatom species.

The data provided by Tilman [52] has been analyzed to see if there is any possibility of a case in which the initial number of *Asterionella* or *Cyclotella* could determine the outcome of competition. Let λ_{AP} and λ_{AS} be the λ criteria for *Asterionella* on phosphate and silicate, respectively; and let λ_{CP} and λ_{CS} be the λ criteria for *Cyclotella*, correspondingly. Assuming that all cell death was due to washout from the culture in the effluent, then the maximum death rate they studied experimentally was 0.5/day. If we use this rate, then the values of the λ criteria are: λ_{AP} = 0.25μM (micromole), λ_{AS} = 3.28μM, λ_{CP} = 0.417μM, and λ_{CS} = 0.90μM. Thus, $\lambda_{AP} < \lambda_{CP}$, so that *Asterionella* has a lower subsistence concentration on

phosphate than *Cyclotella* by more than an order of magnitude, but $\lambda_{CS} < \lambda_{AS}$, so that *Cyclotella* has a lower subsistence concentration on the silicate than *Asterionella*.

TABLE 4.2

Biological Classification of the Outcomes of Two-Resource Exploitative Competition Between Two Species

Biological Case	Lotka-Volterra Competition Criterion	Two-Resource Exploitative Competition Criteria
1. Species 1 always wins, regardless of initial density; species 2 dies out.	$\alpha < \frac{K_1}{K_2}$, $\beta > \frac{K_2}{K_1}$	(a) $\lambda_{s_1} < \lambda_{s_2}$, $\lambda_{r_1} < \lambda_{r_2}$ (b) $\lambda_{s_1} > \lambda_{s_2}$, $\lambda_{r_1} < \lambda_{r_2}$, $T^* < C_1, C_2$ (c) $\lambda_{s_1} < \lambda_{s_2}$, $\lambda_{r_1} > \lambda_{r_2}$, $T^* > C_1, C_2$
2. Species 2 always wins, regardless of initial density; species 1 dies out.	$\alpha > \frac{K_1}{K_2}$, $\beta < \frac{K_2}{K_1}$	(a) $\lambda_{s_1} > \lambda_{s_2}$, $\lambda_{r_1} > \lambda_{r_2}$ (b) $\lambda_{s_1} > \lambda_{s_2}$, $\lambda_{r_1} < \lambda_{r_2}$, $T^* > C_1, C_2$ (c) $\lambda_{s_1} < \lambda_{s_2}$, $\lambda_{r_1} > \lambda_{r_2}$, $T^* < C_1, C_2$
3. Species 1 and 2 persist in a stable coexistence.	$\alpha < \frac{K_1}{K_2}$, $\beta < \frac{K_2}{K_1}$	(a) $\lambda_{s_1} > \lambda_{s_2}$, $\lambda_{r_1} < \lambda_{r_2}$, $C_1 < T^* < C_2$ (b) $\lambda_{s_1} < \lambda_{s_2}$, $\lambda_{r_1} > \lambda_{r_2}$, $C_1 > T^* > C_2$
4. Species 1 wins, or species 2 wins, while rival species dies out; initial densities determine eventual winner.	$\alpha > \frac{K_1}{K_2}$, $\beta > \frac{K_2}{K_1}$	(a) $\lambda_{s_1} > \lambda_{s_2}$, $\lambda_{r_1} < \lambda_{r_2}$, $C_1 > T^* > C_2$ (b) $\lambda_{s_1} < \lambda_{s_2}$, $\lambda_{r_1} > \lambda_{r_2}$, $C_1 < T^* < C_2$

Next, it is necessary to compute T*, C_A, and C_C, where C_A and C_C are the criteria for *Asterionella* and *Cyclotella*, respectively, and

$$T^* = \frac{(P_0 - \lambda_{CP})D_P}{(S_0 - \lambda_{AS})D_S}$$

where P_0 and S_0 are the input phosphate and silicate concentrations, respectively D_P and D_S are the input flow rates of phosphate and silicate, which in this case are equal (taken as 0.5/day), and the point $(\lambda_{AS}, \lambda_{CP})$ is the intersection of the *Asterionella* and *Cyclotella* isoclines on the silicate-phosphate resource plane. Of the range of values of P_0 and S_0 tested by Tilman, we chose P_0 = 10μM and S_0 = 100μM. This gives a value for T* = 0.100.

Finally, it is necessary to compute the C criteria for the two diatoms. The yield constants for *Asterionella* are reported by Tilman (1977) to be: $Y_{AP} = 2.18 \times 10^8$ cells/μM on phosphate, and $Y_{AS} = 2.51 \times 10^6$ cells/μM on silicate. Therefore, $C_A = (1/Y_{AP})/(1/Y_{AS}) = 1.15 \times 10^{-2}$. The yield constants for *Cyclotella* are: $Y_{CP} = 2.59 \times 10^7$ cells/μM on phosphate, and $Y_{CS} = 4.20 \times 10^6$ cells/μM on siiicate. Thus $C_C = (1/Y_{CP})/(1/Y_{CS}) = 1.62 \times 10^{-1}$.

With this information, the question of whether there can exist a case in which the winning diatom species (*Asterionella* or *Cyclotella*) is determined by the initial cell density of each diatom can be answered. Note that $\lambda_{AP} < \lambda_{CP}$ and $\lambda_{AS} > \lambda_{CS}$. Also note that $C_A < T^* < C_C$. This corresponds to a case of coexistence, a fact that Tilman [52] confirmed experimentally. In order for there to be a case in which the initial diatom density determines the outcome in this competitive system for these λ's, it would be necessary that the inequalities among C_A, T*, and C_C be totally reversed: $C_A > T^* > C_C$. This, in turn, would require substantial changes in the yield constants for phosphate and silicate in these two diatom species. Since only the criterion variable T* involves parameters under experimental control, there is no possibility of a case in which initial cell densities affect the competitive outcome between *Asterionella* and *Cyclotella*.

OTHER THEORETICAL WORK IN PROGRESS

A Four Population, Three Level Food Chain

The system (9) presumes a carrying capacity K but does not indicate the mechanism by which it occurs. One way in the laboratory to create the effect of a carrying capacity for the population S would be to grow it in a chemostat on a single resource, call it R. The equations for S and R without a predator for S would be given by $(5)_1$. Combining this with the ideas in the seventh section produces a three level, four population food chain whose equations are

$$\begin{aligned} R' &= (R^{(0)} - R)D - \frac{m_3}{y_3}\frac{SR}{a_3 + R} \\ S' &= \frac{m_3 SR}{a_3 + R} - DS - \sum_{i=1}^{2} \frac{m_i}{y_i}\frac{x_i S}{a_i + S} \\ x_i' &= \frac{m_i x_i S}{a_i + S} - Dx_i, \qquad i = 1, 2 \\ R^{(0)} &= R_0 > 0,\ S(0) = S_0 > 0,\ x_i(0) = x_{i0} > 0, \qquad i = 1, 2 \end{aligned} \tag{14}$$

Since death is through washout all of the death rates are the same, although one might want to allow individual death rates for mathematical completeness. The system (14) is currently being studied by the authors.

Delays

All of the above models assume instantaneous reaction, that is, there are no delays. The oscillations found in the experimental data in the sixth section suggest that delays may be present. In an experiment with the chemostat Caperon [4] was forced to consider delays in the chemostat equations in order to fit his experimental data. In fact, simple constant delays were not adequate and Caperon was forced to consider distributed delays. Currently the use of delays in $(5)_2$ is being investigated.

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REFERENCES

1. J. R. Beckwith and D. Zipser (Eds.), *The Lactose Operon*. (Cold Spring Harbor Laboratories, Cold Spring Harbor, New York (1970).

2. G. Butler, "Coexistence in predator-prey systems," These Proceedings.

3. D. E. Burmaster, "The continuous culture of phytoplankton: mathematical equivalences among three steady state models," *Amer. Nat.* 113(1978), 123-134.

4. J. Caperon, "Time lag in population growth response of *Isochrysis galgana* to a variable nitrate environment," *Ecology* 50(1969), 188-192.

5. M. R. Droop, "The nutrient status of algal cells in continuous culture," *J. Marine Biol. Assoc. U. K.* 54(1974), 825-855.

6. R. W. Eppley and J. L. Coatsworth, "Uptake of nitrate and nitrite by *Pitylum brightwellii*--kinetics and mechanisms," *J. Phycol.* 4(1968), 151-158.

7. G. J. Gause, *The Struggle for Existence*. Williams and Wilkins, Baltimore, Maryland (1934).

8. D. E. Gill, "Intrinsic rates of increase, saturation densities, and competitive ability. I. An experiment with *Paramecium*," *Amer. Nat.* 106(1972), 461-471.

9. S. R. Hansen and S. P. Hubbell, "Single-nutrient microbial competition: agreement between experimental and theoretically forecast outcomes," Subm. *Science* (1979).

10. M. P. Hassell, *The Dynamics of Arthropod Predator-Prey Systems*. Princeton University, Princeton, New Jersey (1978).

11. M. P. Hassell, J. H. Lawton and J. R. Beddington, "Sigmoid functional responses by invertebrate predators and parasitoids," *J. Anim. Ecol.* 46(1977), 249-262.

12. D. Herbert, R. Elsworth and R. C. Telling, "The continuous culture of bacteria: a theoretical and experimental study," *J. Gen. Microbiol.* 14(1956), 601-622.

13. C. S. Holling, "The components of predation as revealed by a study of small mammal predation of the European pine sawfly," *Canad. Entomol.* 91(1959), 293-320.

14. C. S. Holling, "The functional response of predators to prey density and its role in mimicry and population regulation," *Mem. Entomol. Soc. Canada* 45(1965), 3-60.

15. C. S. Holling, "The functional response of invertebrate predators to prey density," *Mem. Entomol. Soc. Canada* 48(1966), 1-86.

16. S. B. Hsu, "Limiting behavior for competing species," *SIAM J. Appl. Math.* 34(1978), 760-763.

17. S. B. Hsu, "The application of the Poincaré-transform to the Lotka-Volterra model," *J. Math. Biology* 6(1978), 67-73.

18. S. B. Hsu, S. P. Hubbell and P. Waltman, "A mathematical theory of single-nutrient competition in continuous cultures of microorganisms," *SIAM J. Appl. Math.* 32(1977), 366-383.

19. S. B. Hsu, S. P. Hubbell and P. Waltman, "Competing predators," *SIAM J. Appl. Math.* 35(1978), 617-625.

20. S. B. Hsu, S. P. Hubbell and P. Waltman, "A contribution to the theory of competing predators," *Ecological Monographs* 48(1978), 337-349.

21. S. P. Hubbell and S. B. Hsu, "Exploitative competition for resources: multiple mechanistic origins for each outcome of classical competition theory," Subm. *Ecology*, 1979.

22. G. E. Hutchinson, *A Treatise on Limnology. II. Introduction to Lake Biology and Limnoplankton.* Wiley, New York (1967).

23. C. A. Istock, "Logistic interaction of natural populations of two species of water-boatmen," *Amer. Nat.* 111(1977), 279-287.

24. V. S. Ivlev, *Experimental Ecology of the Feeding of Fishes.* Yale University, New Haven, Connecticut (1961).

25. H. W. Jannash and R. T. Mateles, "Experimental bacterial ecology studied in continuous culture," *Advances in Microbial Physiology* 11(1974), 165-212.

26. J. Kalff and R. Knoechel, "Phytoplankton and their dynamics in oligotrophic and eutrophic lakes," *Ann. Rev. Ecol. Syst.* 9(1978), 475-495.

27. P. Kilham, "A hypothesis concerning silica and the freshwater planktonic diatoms," *Limnol. Oceanogr.* 16(1971), 10-18.

28. A. L. Koch, "Competitive coexistence of two predators utilizing the same prey under constant environmental conditions," *J. Theoret. Biol.* 44 (1974), 373-386.

29. J. P. LaSalle, *The Stability of Dynamical Systems*. Society for Industry and Appl. Math., Philadelphia (1976).

30. J. A. Leon and D. B. Tumpson, "Competition between two species for two complementary or two substitutable resources," *J. Theoret. Biol.* 50 (1975), 185-201.

31. H. R. Mahler and E. H. Cordes, *Biological Chemistry*. Harper and Row, New York (1966).

32. R. McGehee and R. A. Armstrong, "Some mathematical problems concerning the ecological principle of competitive exclusion," *J. Diff. Eq.* 23 (1977), 30-52.

33. R. S. Miller, "Pattern and process in competition," *Advances in Ecological Research* 4(1967), 1-74.

34. J. Monod, *Reserches sur la Croissance des Cultures Bacteriennes*. Hermann, Paris (1942).

35. J. Monod, "La technique de la culture continue: theorie et applications," *Ann. Inst. Pasteur* 79(1950), 390-410.

36. W. W. Murdoch, S. Avery and M. E. B. Smyth, "Switching in predatory fish," *Ecology* 56(1975), 1094-1105.

37. W. E. Neill, "The community matrix and interdependence of the competition coefficients," *Amer. Nat.* 108(1974), 399-408.

38. A. Novick and L. Szilard, "Description of the chemostat," *Science* 112 (1950), 215-216.

39. G. Oster and Y. Takahashi, "Models for age-specific interactions in a periodic environment," *Ecological Monographs* 44(1974), 483-501.

40. T. Park, "Beetles, competition, and populations," *Science* 138(1962), 1369-1375.

41. T. Park, P. H. Leslie and D. B. Mertz, "Genetic strains and competition in populations of *Tribolium*," *Physiol. Zoology* 37(1964), 97-162.

42. J. W. Payne, "Oligopeptide transport in *Escherichia coli*," *J. Biol. Chem.* 243(1968), 3395-3403.

43. L. A. Real, "The kinetics of functional response," *Amer. Nat.* 111(1977), 287-300.

44. R. C. Richmond, M. E. Gilpin, S. Perez Salas and F. J. Ayala, "A search for emergent competitive phenomena: the dynamics of multispecies *Drosophila* systems," *Ecology* 56(1975), 709-714.

45. T. Toyama, "Factors governing the hunting behavior and selection of food by the great tit (*Parus major L.*)," *J. Anim. Ecol.* 39(1970), 619-668.

46. G. W. Salt, "Predator and prey densities as controls of the rate of capture by the predator *Didinium nasutum*," *Ecology* 55(1974), 434-439.

47. T. W. Schoener, "Some methods for calculating competitive coefficients from resource utilization spectra," *Amer. Nat.* 108(1974), 320-340.

48. T. W. Schoener, "Alternatives to Lotka-Volterra competition models of intermediate complexity," *Theoret. Popul. Biol.* 10(1976), 309-333.

49. N. W. Taylor, "A mathematical model for two *Tribolium* populations in competition," *Ecology* 49(1968), 843-848.

50. P. A. Taylor and J. L. Williams, "Theoretical studies on the coexistence of competing species under continuous-flow conditions," *Canad. J. Microbiol.* 21(1975), 90-98.

51. D. W. Tempest, "The place of continuous culture in microbiological research," *Advances in Microbial Physiol.* 4(1970), 223-245.

52. D. Tilman, "Resource competition between planktonic algae: an experimental and theoretical approach," *Ecology* 58(1977), 338-348.

53. D. Tilman and S. S. Kolham, "Phosphate and silicate growth and uptake kinetics of the diatoms *Asterionella formosa* and *Cyclotella meneghiniana*," *J. Phycol.* 12(1976), 375-383.

54. L. Tinbergen, "The natural control of insects in pinewoods. I. Factors influencing the intensity of predation by songbirds," *Arch. Neerl. Zool.* 13(1960), 266-336.

55. D. Titman, "Ecological competition between algae: experimental confirmation of resource-based competition theory," *Science* 192(1977), 463-465.

56. P. van den Ende, "Predator-prey interactions in continuous culture," *Science* 181(1973), 562-564.

57. J. H. Vandermeer, "The competitive structure of communities: an experimental approach with protozoa," *Ecology* 50(1969), 362-371.

58. H. Veldcamp, "Ecological studies with the chemostat," *Advances in Microbiol Ecology* 1(1977), 59-95.

59. P. F. Verhulst, "Notice sur la loi que la population pursuit dans son accroissement," *Correspond. Math. Phys.* 10(1938), 113-121.

60. V. Volterra, "Variations and fluctuations of the number of individuals of animal species living together," in *Animal Ecology*, R. N. Chapman (Ed.), McGraw-Hill, New York (1926).

61. P. J. Wangersky, "Lotka-Volterra population models," *Ann. Rev. Ecol. Syst.* 9(1978), 189-218.

62. H. Wilbur, "Competition, predation and the structure of the *Ambystoma-Rana sylvatica* communitie," *Ecology* 53(1972), 3-21.

63. T. Yoshida, "Studies on the interspecific competition between bean weevils," *Mem. Fac. Liberal Arts Educ. Akita Univ. Natur. Sci.* 20(1966), 59-98.