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The theory of the chemostat

Dynamics of microbial competition

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The Simple Chemostat

1. Introduction

Competition modeling is one of the more challenging aspects of mathematical biology. Competition is clearly important in nature, yet there are so many ways for populations to compete that the modeling is difficult to carry out in any generality. On the other hand, the mathematical idea seems quite simple: when one population increases, the growth rate of the others should diminish (or at least not increase), a concept that is quite easily expressed by partial derivatives of the specific growth rates. If an ecosystem is modeled by a system of ordinary differential equations – for example, by

$$y_i' = y_i f_i(y),$$

where $i = 1, 2, \ldots, n$, f_i is a continuously differentiable function defined on $\mathbb{R}^n$, and $y = (y_1, y_2, \ldots, y_n)$ – then competition is expressed by the condition

$$\frac{\partial f_i}{\partial y_j} \leq 0$$

when $i \neq j$. Dynamical systems with such properties have been studied extensively; see Hirsch [Hi1; Hi2] and Smith [S3].

Such models easily reflect the direct impact of one population upon the other – for example, the production by one population of a metabolic product that inhibits the growth of the other. The simplest form of competition, however, occurs when two or more populations compete for the same resource, such as a common food supply or a growth-limiting nutrient. This is called *exploitative competition*. A simple example of this type of competition occurs in a laboratory device, called a *chemostat* or

a *continuous culture*, that models competition in a very simple lake. This device is important in ecological studies because the mathematics is tractable and the relevant experiments are possible (although by no means easy). Its place in theoretical ecology is well documented in the surveys of Bungay and Bungay [BB], Cunningham and Nisbet [CN2], Fredrickson and Stephanopoulos [FSt], Jannash and Mateles [JM], Taylor and Williams [TW], Veldcamp [V], Waltman [W1; W2], and Waltman, Hubbell, and Hsu [WHH]. The chemostat model also plays a role in wastewater treatment problems - two examples are D'Ans, Kokotović, and Gottlieb [DKG] and La Riviere [La] - and in the study of recombinant problems in genetically altered organisms, for example, in Stephanopoulis and Lapidus [SLa] and Stewart and Levin [SL2]. Moreover, the chemostat model is the starting point for many variations that yield more realistic biological models and interesting mathematical problems. The following quotations reflect the importance of the chemostat.

> The chemostat is the best laboratory idealization of nature for population studies. It is a dynamic system with continuous material inputs and outputs, thus modeling the open system character and temporal continuity of nature. The input and removal of nutrient analogs the continuous turnover of nutrients in nature. The washout of organisms is equivalent to non-age specific death, predation or emigration which always occurs in nature. [Wi]

> An ecosystem is so complex, so difficult to comprehend, that any attempt to understand the interactions of the component parts *in situ* is frequently doomed to failure because of a lack of rigorous controls. Under such circumstances the behavior displayed by one component may be ascribed to any number of phenomena. Consequently, if we wish to understand the mechanisms by which populations interact we must study them under simplified, controllable laboratory conditions. These should be modeled for theoretical insight, and under ideal circumstances the behavior displayed should be predictable under a variety of conditions imposed by the experimentalist.
>
> From such a perspective, mixed microbial cultures inhabiting simple continuous culture devices are ideal model systems for the study of many ecological phenomena. Unfortunately, population biology has neglected this whole field of research for far too long and without good reason; for micro-organisms are not only economically and ecologically important, their world is every bit as fascinating as that of higher forms of life that are the stable diet of our researchers. Indeed, they can provide unique insights unavailable from almost any other experimental approach. [De]

The name "chemostat" seems to have originated with Novick and Szilard [NS].

In this monograph the basic literature on competition in the chemostat is collected and explained from a common viewpoint. The subject is by

no means complete, but sufficient progress has been made to warrant exposition in a single place. There are also many biological situations that can be modeled by similar techniques. It is also hoped that successful analysis of the models presented here will help to convince biologists of the importance and utility of modern mathematics in ecological studies.

2. Derivation of the Basic Equations of Growth

The apparatus consists of three connected vessels as shown in the schematic in Figure 2.1. The leftmost vessel is called the *feed bottle* and contains all of the nutrients needed for growth of a microorganism – all in excess except for one, which is referred to as the *limiting* nutrient. The second vessel is called the *culture vessel*, and it is here that the "action" takes place. The third vessel is the overflow or *collection* vessel; it is here that the products of the culture vessel are collected. It will contain nutrient, organisms, and perhaps products produced by those organisms. Note that measurements can be made on the contents of the collection vessel without disturbing the action in the culture vessel. Since some nutrient is always in shortest supply, we focus on that limiting nutrient, hereafter simply called the nutrient, and ignore the others that are present in surplus quantities. We emphasize that Figure 2.1 is a schematic; the actual realization of the device can take many forms.

The contents of the feed bottle are pumped at a constant rate into the culture vessel; the contents of the culture vessel are pumped at the same constant rate into the collection vessel. Let V denote the volume of culture vessel (V has units of l^3, where l stands for length), and let F denote the volumetric flow rate (F has units of l^3/t, where t is time). The concentration of the input nutrient, denoted by $S^{(0)}$, is kept constant. Concentration has units of mass$/l^3$.

The culture vessel is charged with a variety of microorganisms, so it contains a mixture of nutrient and organisms. The culture vessel is well

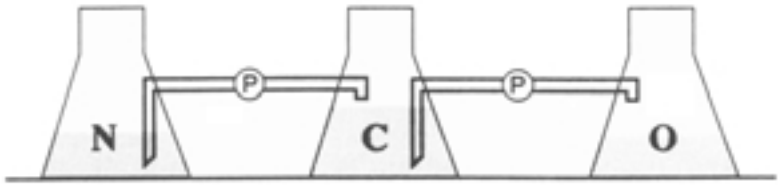

Figure 2.1. A schematic of the simple chemostat. (From [W2], Copyright 1990, Rocky Mountain Mathematics Consortium. Reproduced by permission.)

stirred, and all other significant parameters (e.g. temperature) affecting growth are kept constant. Since the output is continuous, the chemostat is often referred to as a "continuous culture" in contrast with the more common "batch culture."

We seek to write differential equations for this model, and begin by considering just one organism growing in the chemostat. (A more complete derivation can be found elsewhere; see e.g. Herbert, Elsworth, and Telling [HET].) The rate of change of the nutrient can be expressed as

$$\text{rate of change} = \text{input} - \text{washout} - \text{consumption},$$

while that of the organism can be expressed as

$$\text{rate of change} = \text{growth} - \text{washout}.$$

Let $S(t)$ denote the concentration of nutrient in the culture vessel at time t. Thus $VS(t)$ denotes the amount of nutrient in the vessel at that time. The rate of change of nutrient is the difference between the amount of nutrient being pumped into the vessel per unit time and the amount of nutrient being pumped out of the vessel per unit time. If there were no organisms, and hence no consumption, then the equation for the nutrient would be

$$(VS)'(t) = S^{(0)}F - S(t)F,$$

where the prime denotes the derivative with respect to time. Note that the units on each side are mass/time. Since V is constant, the quantity on the left can be written as $VS'(t)$ and both sides divided by V. The quantity F/V, called the *dilution* (or *washout*) *rate*, is denoted by D and has units of $1/t$. The equation then becomes

$$S'(t) = S^{(0)}D - S(t)D.$$

The formulation of the consumption term, based on experimental evidence, goes back at least to Monod [Mo1; Mo2]. The term takes the form

$$\frac{mSx}{a+S},$$

where x is the concentration of the organism (units are mass$/l^3$), m is the maximal growth rate (units are $1/t$), and a is the Michaelis–Menten (or half-saturation) constant with units of concentration. The form (and the terminology) of the consumption term is that of enzyme kinetics, where S would be a substrate. Both a and m can be measured experimentally. Since it is generally accepted by microbial ecologists, and since it contains

parameters that can be measured, the Michaelis–Menten (or Monod) formulation is most often used as the uptake function, but the mathematical results are valid for much more general functions. Simple monotonicity in S, with a limit as S tends to infinity, is usually sufficient. Trying to squeeze the greatest mathematical generality from the theorems could interfere with our presentation, so the emphasis here is on the Monod formulation. (A partial justification is given in Chapter 2, where it is shown that – for the simple chemostat – a more general response function does not introduce any new types of behavior.)

As noted, the form of the consumption term depends on experimental evidence and does not rest on any physiological basis. The uptake of nutrient is a very complex phenomenon from the standpoint of molecular biology. Indeed, the transport of the nutrient through the cell wall is itself a very complex phenomenon. Dawes and Sutherland [DSu] give a descriptive (i.e. nonmathematical) introduction to microbial physiology and its complexities. Koch [Ko] considers the uptake and the factors affecting growth in considerable detail. The Monod and other similar formulations give an aggregate description of the nutrient uptake; to do otherwise would make the modeling problem very difficult. One can, however, take into account that the uptake by "larger" cells is more than that of "smaller" ones [Cu2].

The differential equation for S takes the form

$$S' = (S^{(0)} - S)D - \frac{mS}{a+S}\frac{x}{\gamma}, \tag{2.1}$$

while that of the corresponding equation for the microorganism, assuming growth is proportional to consumption, is

$$x' = x\left(\frac{mS}{a+S} - D\right), \tag{2.2}$$

where γ is a "yield" constant reflecting the conversion of nutrient to organism. The constant γ can be determined (in batch culture) by measuring

$$\frac{\text{mass of the organism formed}}{\text{mass of the substrate used}}$$

and hence is dimensionless. (We will scale it out in the simple chemostat, but it is important for multiple-nutrient problems.) That γ is a constant is a hypothesis; this hypothesis will be reconsidered in Chapter 8. The assumption that reproduction is proportional to nutrient uptake is a vast simplification. The cell cycle is a very complex phenomenon, and entire

books have been devoted to its description (see e.g. Murray and Hunt [MH]). Incorporating the essentials of the cell cycle into the chemostat model would be an interesting problem. From the mathematical point of view, this introduces a delay between nutrient uptake and cell division. Comments on the delay models can be found in Chapter 10, and their proper incorporation in microbial models is very much an open problem.

The appropriate initial conditions are $S(0) \geq 0$ and $x(0) > 0$. The number of parameters in the system is excessive, so some scaling is in order. First of all, note that $S^{(0)}$ and D (the input concentration and the washout rate) are under the control of the experimenter. The $S^{(0)}$ term has units of concentration and D has units of reciprocal time. Equations (2.1) and (2.2) may be rewritten as

$$\frac{S'}{S^{(0)}} = \left(1 - \frac{S}{S^{(0)}}\right) D - \frac{mS/S^{(0)}}{a/S^{(0)} + S/S^{(0)}} \frac{x}{S^{(0)}\gamma};$$

$$\frac{x'}{S^{(0)}\gamma} = \left(\frac{x}{S^{(0)}\gamma}\right)\left(\frac{mS/S^{(0)}}{a/S^{(0)} + S/S^{(0)}} - D\right).$$

By measuring S, a, and x/γ in units of $S^{(0)}$ and time in units of D^{-1}, one obtains the following nondimensional differential equations (note that m and a have changed their meanings):

$$\begin{aligned} S' &= 1 - S - \frac{mSx}{a+S}, \\ x' &= x\left(\frac{mS}{a+S} - 1\right), \\ S(0) &\geq 0, \quad x(0) > 0. \end{aligned} \tag{2.3}$$

This sort of scaling will occur frequently in the problems that follow. The constants m and a can be regarded as the "natural" parameters of the organism in this particular environment. We have standardized the environment, scaling out the factors that can be changed by the experimenter; hence the use of natural parameters expressed in (2.3). This unclutters the mathematics from the "real" world and focuses attention on the selection of the parameters a and m. This, of course, is in marked contrast to the point of view of a person who wishes to perform an experiment. There the parameters a and m are given; they come from the organism selected. An experimenter wishes to tune the chemostat to make the organisms grow. Thus, particularly in the engineering literature, one finds an emphasis on presenting results in the form of "operating diagrams," graphs that show where to operate the chemostat. Since the emphasis here is

theoretical, the scaling just described will be used whenever possible; results in terms of the original parameters can easily be obtained by reinterpreting the parameters.

3. Dynamical Systems

Although the system of equations (2.3) is simple enough to handle directly, we pause here to introduce some mathematical material that will be important in the remainder of the book. The reader who is not interested in mathematical tidiness may just note the definitions and go on to the next section. [CL] and [H2] are standard references for the material presented here. The focus throughout the book will be on the "dynamical systems" point of view. Dynamical systems are used primarily as a language, not because we need many deep results from that subject. The language, however, does seem natural for the problems considered. The dynamical system will be defined in terms of $\mathbb{R}^n$, but the natural (and most efficient) formulation is that of a metric space. In a later chapter we will use the space $C[0,1]$, the space of continuous functions on the interval $[0,1]$ with the usual sup norm, and the definition will be expanded at that time.

The most basic concept is that of a dynamical (or a semidynamical) system. Let $\pi: M \times \mathbb{R} \to M$ be a function of two variables, where M is $\mathbb{R}^n$ and $\mathbb{R}$ denotes the real numbers. (We use M for the first variable or state space to suggest that the results are true in greater generality.) The function π is said to be a *continuous dynamical system* if π is continuous and has the following properties:

(i) $\pi(x, 0) = x$;
(ii) $\pi(x, t+s) = \pi(\pi(x, t), s)$.

An ordinary differential equation of the form

$$y' = f(y), \tag{3.1}$$

with $y \in \mathbb{R}^n$ and $f: \mathbb{R}^n \to \mathbb{R}^n$ and where f is continuously differentiable, generates such a system by defining $\pi(x, t)$ to be the value $y(t)$, where $y(t)$ is the solution of (3.1) satisfying the initial condition $y(0) = x$. (We are tacitly assuming, of course, that all initial value problems for (3.1) exist for all time.) When (ii) holds only for positive s and t, π is said to be a *semidynamical system*.

Given a point x, the set $\{\pi(x, t), t \geq 0\}$ is called the *positive orbit* or *positive trajectory* through the point and is denoted by $\gamma^+(x)$. If only

nonpositive t are considered, the set is called the *negative orbit* or *negative trajectory* through the point and is denoted by $\gamma^-(x)$. The union of the positive and negative orbits is simply called the *orbit* or *trajectory* through the point, denoted by $\gamma(x)$. For emphasis, the latter is sometimes called the *full* orbit. For biological systems one wants to determine the eventual behavior - the asymptotic properties - of trajectories. Biological models require that trajectories remain positive (concentrations or populations are positive numbers) and that trajectories do not tend to infinity with increasing time. If a set S is such that all trajectories that begin (have their initial condition) in S remain in S for all positive time, then S is said to be *positively invariant*. (If trajectories remain in S for both positive and negative time, S is said to be *invariant*.) Hence the basic condition for positivity (of the dependent variables) can be stated as "the positive cone is positively invariant for the dynamical system generated by (3.1)." The dynamical system is said to be *dissipative* if all positive trajectories eventually lie in a bounded set. This is sufficient to ensure that all solutions of (3.1) exist for all positive time.

Let $\{t_n\}$ be a sequence of real numbers which tends to infinity as n tends to infinity. (Such a sequence is sometimes called an *extensive* sequence.) If $P_n = \pi(x, t_n)$ converges to a point P, then P is said to be an *omega limit point* of x. (More correctly, P is an omega limit point of the positive trajectory $\gamma^+(x)$; both references will be used, but since there is a unique trajectory through each point x, the abuse of terminology will cause no confusion when dealing with systems of the form (3.1).) The set of all such omega limit points is called the *omega limit set* of x, denoted $\omega(x)$. If the system is dissipative, the omega limit set is a non-empty, compact, connected, invariant set. Moreover, the orbit $\gamma^+(x)$ is asymptotic to the omega limit set of x in the sense that the distance from $\pi(x, t)$ and $\omega(x)$ tends to zero as t tends to infinity.

Now let $\{t_n\}$ be a sequence of real numbers which tends to negative infinity as n tends to infinity. If $P_n = \pi(x, t_n)$ converges to a point P, then P is said to be an *alpha limit point* of x. The set of all such alpha limit points is called the *alpha limit set* of x, denoted $\alpha(x)$. It enjoys similar properties if the trajectory lies in a compact set for $t < 0$.

A particularly important class of solutions are the constant ones, which are called steady states, *rest points*, or equilibrium points. In terms of (3.1), such a solution is a zero of $f(y)$, that is, a vector $y^* \in \mathbb{R}^n$ such that $f(y^*) = 0$. In the terminology of dynamical systems, a rest point is an element $p \in M$ such that $\pi(p, t) = p$ for all $t \in \mathbb{R}$. Similarly, a periodic orbit is one that satisfies $\pi(p, t+T) = \pi(p, t)$ for all t and for some fixed number T. The corresponding solution of (3.1) will be a periodic function.

If the omega limit set is particularly simple – a rest point or a periodic orbit – this gives information about the asymptotic behavior of the trajectory. An invariant set which is the omega limit set of a neighborhood of itself is called a (local) *attractor.* If (3.1) is two-dimensional then the following theorem is very useful, since it severely restricts the structure of possible attractors.

THEOREM (Poincaré–Bendixson). *If* (3.1) *is two-dimensional and if* $\gamma^+(x)$ *remains in a closed and bounded region of the plane without rest points, then either* $\gamma^+(x)$ *is a periodic orbit (and* $\gamma^+(x) = \omega(x)$*) or* $\omega(x)$ *is a periodic orbit.*

Although this is the classical statement of this theorem, a simple consequence is often useful. This is sometimes called the Poincaré–Bendixson trichotomy.

THEOREM. *Let* $\gamma^+(y_0)$ *be a positive semi-orbit of* (3.1) *which remains in a closed and bounded subset* K *of* $\mathbb{R}^2$*, and suppose that* K *contains only a finite number of rest points. Then one of the following holds:*

(i) $\omega(y_0)$ *is a rest point;*
(ii) $\omega(y_0)$ *is a periodic orbit;*
(iii) $\omega(y_0)$ *contains a finite number of rest points and a set of trajectories* γ_i *whose alpha and omega limit sets consist of one of these rest points for each trajectory* γ_i.

Figure 3.1 illustrates the possibilities. Additionally, if a two-dimensional system has a periodic orbit then it must have a rest point "inside" that orbit. These simple facts (and their generalizations) play an important role in the analysis presented here.

While the Poincaré–Bendixson theorem yields the existence of limit cycles, it is often important to know when limit cycles do *not* exist. For two-dimensional systems, a result in this direction which complements the Poincaré–Bendixson theorem is called the Dulac criterion. Its proof is a direct application of the classical Green's theorem in the plane (after an assumption that the theorem is false) and will not be given here; a good reference is [ALGM].

THEOREM (Dulac criterion). *Suppose that* (3.1) *is two-dimensional. Let* Γ *be a simply connected region in* $\mathbb{R}^2$ *and let* $\beta(x)$ *be a continuously differentiable scalar function defined on* Γ. *If* $\nabla(f(x)\beta(x))$ *is of one sign (excluding zero) in the region* Γ *then there are no periodic orbits in* Γ.

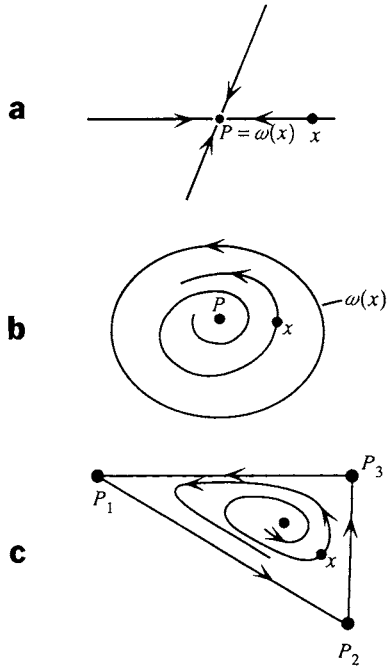

Figure 3.1. Examples of limit sets for planar systems: **a** a rest point; **b** a periodic orbit; **c** multiple rest points with connecting orbits.

By ∇ is meant the gradient of the resulting two-dimensional vector function.

Local stability considerations also play a role in the analysis. For simplicity denote the solution of the autonomous system (3.1) through the point y_0 at time $t=0$ by $\phi(t, y_0)$. Let $\|\cdot\|$ denote the Euclidean norm in $\mathbb{R}^n$. The solution $\phi(t, y_0)$ is said to be *stable* if, for any $\epsilon > 0$, there exists a $\delta > 0$ such that if $\|y_0 - x_0\| < \delta$ then $\|\phi(t, y_0) - \phi(t, x_0)\| < \epsilon$ for all $t > 0$. The solution $\phi(t, y_0)$ is said to be *asymptotically stable* if it is stable and if there is a neighborhood N of y_0 such that if $x_0 \in N$ then $\lim_{t\to\infty} \|\phi(t, x_0) - \phi(t, y_0)\| = 0$. We shall be concerned with the case where $\phi(t, y_0)$ is a constant solution or rest point, that is, where $\phi(t, y_0) = y_0$ for all t. We usually use y^* to denote a rest point. Note that a rest point y^* is asymptotically stable if it is stable and an attractor.

The system

$$x' = f_y(y^*)x \tag{3.2}$$

is said to be the *linearization* of (3.1) around the rest point y^*, where $f_y(y^*)$ is the Jacobian matrix

$$\left[\frac{\partial f_i}{\partial x_j}\right]\Big|_{y=y^*}.$$

This matrix is called the *variational matrix* at y^*.

If all of the eigenvalues of the variational matrix have negative real parts, then y^* is an asymptotically stable rest point of (3.1). When this happens it is possible to find an arbitrarily small neighborhood around the rest point such that, on the boundary of the neighborhood, all trajectories cross the boundary from outside to inside.

If an omega limit set contains an asymptotically stable rest point P, then that point is the entire omega limit set. If all of the eigenvalues of the variational matrix have positive real part then the rest point is said to be a *repeller*; such a rest point cannot be in the omega limit set of any trajectory other than itself. If k eigenvalues have positive real part and $n-k$ eigenvalues have negative real part then there exist two sets: $M^+(P)$, called the *stable* manifold and defined by

$$M^+(P) = \{x \mid \lim_{t\to\infty} \pi(x,t) = P\};$$

and $M^-(P)$, called the *unstable* manifold and defined by

$$M^-(P) = \{x \mid \lim_{t\to-\infty} \pi(x,t) = P\}.$$

The sets $M^+(P)$ and $M^-(P)$ are locally manifolds of dimension $n-k$ and k, respectively, and all trajectories with initial conditions on these sets tend to the rest point as t tends to infinity (stable) or as t tends to negative infinity (unstable). One should think of these manifolds as surfaces in the appropriate space. On these surfaces, trajectories tend to the rest point as t tends either to positive or to negative infinity. (To assist with the notation, the reader should associate the plus sign on M^+ with positive time and the minus sign on M^- with negative time.) In particular, a single eigenvalue with positive real part makes the rest point unstable. The corresponding eigenvectors generate the tangent space to the respective manifolds. When no eigenvalue of the variational matrix has zero real part, the rest point is said to be *hyperbolic*.

Let P, Q be hyperbolic rest points (not necessarily distinct). P is said to be *chained* to Q, written $P \to Q$, if there exists an element x, $x \notin P \cup Q$, such that $x \in M^-(P) \cap M^+(Q)$. A finite sequence $P_1, P_2, \ldots, P_k$ of hyperbolic rest points will be called a *chain* if $P_1 \to P_2 \to \cdots \to P_k$ ($P_1 \to P_1$ if $k = 1$). The chain will be called a *cycle* if $P_k = P_1$. A chain reflects the connections between equilibrium states. A cycle will turn out to be an "undesirable" type of connection.

The following theorem is often useful.

THEOREM (Butler–McGehee). *Suppose that P is a hyperbolic rest point of* (3.1) *which is in $\omega(x)$, the omega limit set of $\gamma^+(x)$, but is not the entire omega limit set. Then $\omega(x)$ has nontrivial (i.e., different from P) intersection with the stable and the unstable manifolds of P.*

Figure 3.1c, where P is any of the three equilibria, illustrates the theorem. A short proof (due to McGehee) can be found in the appendix of [FW2], but it requires some advanced concepts from dynamical systems. The result is very general and theorems in the same spirit can be found in [BW], [BFW], [DRS], [T1], or [HaW] in very abstract settings. Note that the linearization around such a point P cannot have all of its eigenvalues with negative real part else $P = \omega(x)$; it also cannot have all eigenvalues with positive real part, for a repeller cannot be in the omega limit set of a point other than itself. Hence the stable and unstable manifolds are not empty. The intuition behind the result is that an orbit cannot "sneak" into and out of a neighborhood of P infinitely often without having accumulation points on the stable and unstable manifolds. The proof simply makes this idea precise. (The proof may be skipped on first reading.)

Proof of the Butler–McGehee Theorem. Since P is a hyperbolic equilibrium, there exists a bounded open set U containing P, but not x, with the property that if $\pi(y,t) \in U$ for all $t > 0$ ($t < 0$), then y belongs to the local stable (unstable) manifold $M^+(P)$ ($M^-(P)$); see [H2]. (P is the largest invariant set in U, or U isolates P from any other invariant sets.) By taking a smaller open set V, $P \in V \subset \bar{V} \subset U$, we have that $\pi(y,t) \in \bar{V}$ for all $t > 0$ ($t < 0$) implies $y \in M^+(P)$ ($M^-(P)$).

Since $P \in \omega(x)$, there exists a sequence $\{t_n\}$, $\lim_{n\to\infty} t_n = \infty$, such that $\lim_{n\to\infty} x_n = \lim_{n\to\infty} \pi(x, t_n) = P$. It follows that $x_n \in V$ for all large n. Since $x \notin M^+(P)$, else $\omega(x) = P$, from the property of the neighborhood V one may conclude that there exist positive numbers r_n, s_n such that $r_n < t_n$, $\pi(x_n, t) \in V$ for $-r_n < t < s_n$, and $\pi(x_n, -r_n)$, $\pi(x_n, s_n) \in \partial V$. By the continuity of $\pi(x,t)$, solutions that start near P must remain near P; hence it follows that r_n and s_n tend to infinity as n tends to infinity. However, $\bar{V}$ is compact, so (passing to a subsequence if necessary) one may conclude that $\lim_{n\to\infty} \pi(x_n, -r_n) = q \in \bar{V}$ and $\lim_{n\to\infty} \pi(x_n, s_n) = \hat{q} \in \bar{V}$. We continue the proof for q; the other case is similar.

It is claimed that $\pi(q,t) \in \bar{V}$ for all $t > 0$. Recall that $\lim_{n\to\infty} q_n = q$ where $q_n = \pi(x_n, -r_n)$. Fix $t > 0$. By the continuity of π, $\lim_{n\to\infty} \pi(q_n, t) = \pi(q,t)$. Since $-r_n < t - r_n < 0$ for all large n, $\pi(q_n, t) = \pi(x_n, t - r_n) \in V$

for all large n. It follows that $\pi(q,t) \in \bar{V}$. Since $t > 0$ was arbitrary, the claim is established.

Since $\pi(q,t) \in \bar{V}$ for all $t > 0$, we have $q \in M^+(P)$ by the isolating property of V cited in the first sentence of the proof. However, $q \in \overline{\gamma^+(x)} = \gamma^+(x) \cup \omega(x)$. Since $q \in M^+(P)$, $q \notin \gamma^+(x)$ and hence $q \in \omega(x)$, which establishes one case of the theorem. □

For many of the systems of interest here, the dynamics restricted to the various boundaries of the positive cone in $\mathbb{R}^n$ will be dynamical systems in their own right – the boundaries will be invariant sets. It may happen that a rest point P will be asymptotically stable when regarded as a rest point of the lower-dimensional dynamical system and yet have unstable components when the full system is considered. If the entire stable manifold is contained in the boundary, then the Butler–McGehee theorem can be used to conclude that no trajectory from the interior of the positive cone can have P as an omega limit point. Indeed, the omega limit set cannot equal P because the initial point does not belong to the stable manifold of P. If the limit set contains P then it would also contain a point of the stable manifold distinct from P, by the Butler–McGehee theorem, and would therefore contain the closure of the entire orbit through this point since the omega limit set is closed and invariant. However, this typically leads to a contradiction, since orbits in the stable manifold of P are either unbounded or their limit sets contain equilibria that can be readily excluded from the original limit set (e.g. are repellors). Section 5 will use the theorem in this way.

4. Analysis of the Growth Equations

For system (2.3) the positive cone is positively invariant (see Appendix B, Proposition B.7). In simpler terms, if the system is given positive initial conditions then the two components of the solution remain positive for all finite time. Moreover, if one adds the two equations and defines $\Sigma = 1 - S - x$, then one obtains a single equation

$$\Sigma' = -\Sigma$$

with $\Sigma(0) > 0$. It follows at once that $\lim_{t\to\infty} \Sigma(t) = 0$ and that the convergence is exponential. This not only gives the required dissipativeness but also leads to the simplification of the system by the elimination of one variable. From $\lim_{t\to\infty}[S(t) + x(t)] = 1$, one can conclude that the omega limit set of the system (2.3) must lie in this set, and trajectories on the omega limit set must satisfy

$$x' = x\left[\frac{m(1-x)}{1+a-x} - 1\right], \quad 0 \le x \le 1. \tag{4.1}$$

It might seem at first that it was extremely fortuitous that the aforementioned limit should exist. However, there is a simple, intuitive explanation. If there were no organisms in the model - that is, if only nutrient were present in the equation - then the nutrient would satisfy

$$S' = 1 - S \quad \text{and} \quad \lim_{t\to\infty} S(t) = 1.$$

The scaling in the system has expressed the concentration of organism in terms of its "nutrient equivalent." Since nothing is created or destroyed in the system, the sum should satisfy the same equation. The quantity Σ (more accurately, $1-\Sigma$) reflects this. Indeed, if all of the variables in the model are properly accounted for, this will always be true for the sum of the variables in a chemostat.

Since all trajectories of the original system are asymptotic to their omega limit set, in analyzing this equation it is sufficient to determine the asymptotic behavior of (2.3). From a more intuitive viewpoint this is merely starting on the manifold $S+x=1$, to which all solutions must tend; the mathematical support for this is rigorously established later (see the proof of Theorem 5.1 or Appendix F). Define, for $m > 1$,

$$\lambda = \frac{a}{m-1};$$

λ is called the *break-even* concentration. Equation (4.1) has two rest points, $x = 0$ and $x = 1-\lambda$, and the equation can be rewritten as

$$x' = x\left[\frac{m-1}{1+a-x}\right][1-\lambda-x]. \tag{4.2}$$

Clearly, if $m < 1$ or $m > 1$ and $\lambda > 1$, then $\lim_{t\to\infty} x(t) = 0$ ($x'(t)$ is negative and $x(t)$ is bounded below by zero). On the other hand, if $\lambda < 1$ and $m > 1$, then $\lim_{t\to\infty} x(t) = 1-\lambda$ (and hence $\lim_{t\to\infty} S(t) = \lambda$). If $m < 1$, the organism is washing out faster than its maximal growth rate, whereas if $\lambda \ge 1$ there is insufficient nutrient available for the organism to survive. In either case, extinction is not a surprising outcome. The case $m = 1$ is handled by using (4.1) directly.

5. Competition

To study competition in the chemostat, introduce two different microorganisms into the system, labeled x_1 and x_2, with corresponding parameters

a_i and m_i, $i = 1, 2$. We assume that the corresponding lambdas, λ_1 and λ_2, are different. The overall system becomes

$$\begin{aligned} S' &= 1 - S - \frac{m_1 S x_1}{a_1 + S} - \frac{m_2 S x_2}{a_2 + S}, \\ x_1' &= x_1\left(\frac{m_1 S}{a_1 + S} - 1\right), \\ x_2' &= x_2\left(\frac{m_2 S}{a_2 + S} - 1\right), \\ S(0) &\geq 0, \quad x_1(0) > 0, \quad x_2(0) > 0. \end{aligned} \tag{5.1}$$

Again, let $\Sigma(t) = 1 - S(t) - x_1(t) - x_2(t)$, and rewrite the system as

$$\begin{aligned} \Sigma' &= -\Sigma, \\ x_1' &= x_1\left(\frac{m_1(1 - \Sigma - x_1 - x_2)}{a_1 + 1 - \Sigma - x_1 - x_2} - 1\right), \\ x_2' &= x_2\left(\frac{m_2(1 - \Sigma - x_1 - x_2)}{a_2 + 1 - \Sigma - x_1 - x_2} - 1\right), \\ \Sigma(0) &\leq 1, \quad x_1(0) > 0, \quad x_2(0) > 0. \end{aligned} \tag{5.1'}$$

In the same manner as before, one has that

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

where the convergence is exponential. Again this shows that the system is dissipative and that, on the set $\Sigma = 0$, trajectories satisfy

$$\begin{aligned} x_1' &= x_1\left(\frac{m_1(1 - x_1 - x_2)}{a_1 + 1 - x_1 - x_2} - 1\right), \\ x_2' &= x_2\left(\frac{m_2(1 - x_1 - x_2)}{a_2 + 1 - x_1 - x_2} - 1\right), \\ x_1(0) &> 0, \quad x_2(0) > 0, \quad x_1 + x_2 \leq 1 \end{aligned} \tag{5.2}$$

or

$$\begin{aligned} x_1' &= x_1\left[\frac{m_1 - 1}{1 + a_1 - x_1 - x_2}\right][1 - \lambda_1 - x_1 - x_2], \\ x_2' &= x_2\left[\frac{m_2 - 1}{1 + a_2 - x_1 - x_2}\right][1 - \lambda_2 - x_1 - x_2], \\ x_1(0) &> 0, \quad x_2(0) > 0, \quad x_1 + x_2 \leq 1. \end{aligned}$$

The system (5.2) has three rest points:

$$E_0 = (0,0), \quad E_1 = (1-\lambda_1, 0), \quad E_2 = (0, 1-\lambda_2).$$

If λ_1 is different from λ_2 then there is no "interior" rest point, that is, a rest point with both components positive. In view of the results for growth without a competitor, the only interesting cases are where $m_i > 1$ and $0 < \lambda_i < 1$ for $i = 1$ and 2. If not, the corresponding population washes out of the chemostat even without a competitor (and hence is called an inadequate competitor).

The following is the principal theorem for competition between two adequate competitors under Michaelis-Menten dynamics. Proofs (with varying degrees of mathematical rigor) may be found in [AH; HHW; P; SL1]. Extensions will be discussed in the next chapter.

THEOREM 5.1. *Suppose that* $m_i > 1$, $i = 1$ *and* 2, *and that* $0 < \lambda_1 < \lambda_2 < 1$. *Then any solution of the system* (5.2) *with* $x_i(0) > 0$ *satisfies*

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

$$\lim_{t\to\infty} x_1(t) = 1-\lambda_1,$$

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

Proof. We begin by analyzing (5.2). The first step is to compute the stability of the rest points of system (5.2) by finding the eigenvalues of the Jacobian matrix evaluated at each of these rest points. At $(0,0)$ this matrix takes the form

$$\begin{bmatrix} \dfrac{(m_1-1)(1-\lambda_1)}{1+a_1} & 0 \\ 0 & \dfrac{(m_1-1)(1-\lambda_2)}{1+a_2} \end{bmatrix}.$$

Both eigenvalues are positive and the origin is a repeller. In particular, the origin is not in the omega limit set of any trajectory (other than itself).

At $(1-\lambda_1, 0)$, the variational matrix is of the form

$$\begin{bmatrix} \dfrac{(\lambda_1-1)(a_1 m_1)}{(\lambda_1+a_1)^2} & \dfrac{(\lambda_1-1)(a_1 m_1)}{(\lambda_1+a_1)^2} \\ 0 & \dfrac{(m_2-1)(\lambda_1-\lambda_2)}{\lambda_1+a_2} \end{bmatrix}.$$

Since $0 < \lambda_1 < \lambda_2$ and $m_2 > 1$, both eigenvalues are negative. Thus E_1 is (locally) asymptotically stable. At $(0, 1-\lambda_2)$, the variational matrix takes the form

$$\begin{bmatrix} \dfrac{(m_1-1)(\lambda_2-\lambda_1)}{\lambda_2+a_1} & 0 \\ \dfrac{(\lambda_2-1)(a_2m_2)}{(\lambda_2+a_2)^2} & \dfrac{(\lambda_2-1)(a_2m_2)}{(\lambda_2+a_2)^2} \end{bmatrix}.$$

One eigenvalue is negative since $\lambda_2 < 1$ and one is positive since $\lambda_1 < \lambda_2$. Thus the stable manifold is one-dimensional and, since E_2 attracts along the $x_1 = 0$ axis, the stable manifold lies there. In particular, the Butler-McGehee theorem (stated in Section 3) allows one to conclude that no trajectory with positive initial conditions can have E_2 as an omega limit point. Since the initial data are positive, the omega limit set cannot equal E_2. If it contained E_2, then it must also contain an entire orbit different from E_2 belonging to the stable manifold of E_2. There are only two possible orbits; one is unbounded, and the other has alpha limit set E_0. But the omega limit set cannot contain an unbounded orbit and it cannot contain E_0 since it is a repeller. Therefore, E_2 is not a limit point.

Since E_1 is a local attractor, to prove the theorem it remains only to show that it is a global attractor. This is taken care of by the Poincaré-Bendixson theorem. As noted previously, stability conditions preclude a trajectory with positive initial conditions from having E_0 or E_2 in its omega limit set. The system is dissipative and the omega limit set is not empty. Thus, by the Poincaré-Bendixson theorem, the omega limit set of any such trajectory must be an interior periodic orbit or a rest point. However, if there were a periodic orbit then it would have to have a rest point in its interior, and there are no such rest points. Hence every orbit with positive initial conditions must tend to E_1. (Actually, two-dimensional competitive systems cannot have periodic orbits.) Figure 5.1 shows the x_1-x_2 plane.

Although this argument resolves the asymptotic behavior on the set $\Sigma = 0$, there remains the question of whether the systems (5.1) and (5.2) have the same asymptotic behavior. This question is answered in considerable generality in Appendix F; however, we give a direct proof of the current case.

Although the stable manifold of E_0 was E_0 in the planar system, and the stable manifold of E_2 was one-dimensional in that system, these manifolds have an extra dimension when one considers the full system (5.1′) involving Σ. Specifically,