Preface

The primary focus of this book is the mathematical theory of persistence. The theory is designed to provide an answer to such questions as which species, in a mathematical model of interacting species, will survive over the long term. In a mathematical model of an epidemic, will the disease drive a host population to extinction or will the host persist? Can a disease remain endemic in a population? Persistence theory can give a mathematically rigorous answer to the question of persistence by establishing an initial-condition-independent positive lower bound for the long-term value of a component of a dynamical system such as population size or disease prevalence.

Mathematically speaking, in its simplest formulation for systems of ordinary or delay differential equations, and for a suitably prescribed subset I of components of the system, persistence ensures the existence of $\epsilon > 0$ such that $\liminf_{t\to\infty} x_i(t) > \epsilon,\ i \in I$ provided $x_i(0) > 0,\ i \in I$. We say that these components persist uniformly strongly, or, more precisely, that the system is uniformly strongly ρ-persistent for the persistence function $\rho(x) = \min_{i\in I} x_i$. This *persistence function* $\rho(x)$ may be viewed as the distance of state x to a portion of the boundary of the state-space $\mathbb{R}^n_+$, namely the states where one or more of species $i \in I$ are extinct.

The adjective "strong" is often omitted; uniform weak ρ-persistence is defined similarly but with limit superior in place of limit inferior. The adjective "uniform" emphasizes that the lower bound ϵ is independent of initial data satisfying the restriction $x_i(0) > 0,\ i \in I$. Similarly, as in the definition of Lyapunov stability, the precise value of ϵ is unspecified and usually difficult to estimate. Uniform persistence is a qualitative notion, not a quantitative one. However, in rare cases, ϵ can be related to system parameters; this ideal situation is referred to as "practical persistence" [**24, 25, 26, 28, 27, 35**].

Weaker notions of weak and strong persistence drop the "uniformity with respect to initial data" (i.e., ϵ), requiring merely positivity of the limit superior, respectively, the limit inferior.

The definition of persistence and the related concept of permanence (uniform persistence plus an upper bound on limit superior of all components) evolved in the late 1970s from the work of Freedman and Waltman [**75**], Gard [**80, 81**] Gard and Hallam [**82**], Hallam [**96**], and Schuster, Sigmund, Wolff [**196**]. Most of these early papers show weak persistence, but Schuster, Sigmund, and Wolff [**196**] prove uniform strong ρ-persistence for the hypercycle equation in the n-simplex with $\rho(x) = x_1 \cdots x_n$ as persistence function.

The notion of a persistence function seems to have been introduced by Gard and Hallam [**82, 80**], though with a more technical intention than here. It was later superseded by a more general concept which combines the usual Lyapunov function methods with time averages [**104**] and became known as average Lyapunov function [**109**]. "Persistence function" (together with the ρ-symbol [**80, 82**]) is revived here as a means to make precise which parts of a system persist; in applications ρ has a very concrete and intuitive interpretation like the number of infected individuals to describe disease persistence in an epidemic model. Such a "hands on" interpretation would be lacking for a typical average Lyapunov function like $x_1^{p_1} \cdots x_n^{p_n}$ [**81, 82**]. Zhao [**238**] uses the notion *generalized distance function* to stress the idea that ρ measures the distance to the brink of extinction.

Persistence theory developed rapidly in the 1980s because the necessary machinery from dynamical systems, a theory of attractors and repellers, was already in place. Early work focused on persistence of components of systems of ordinary differential equations. Later, this was extended to discrete time or difference equations, and then to infinite dimensional dynamical systems generated by delay differential equations and partial differential equations. Application of the theory was initially slow to catch on in the applied literature on population biology and epidemiology, but it has more recently become an accepted tool in theoretical population dynamics.

Although the theory is now quite "user friendly" in the sense that a user does not need to be an expert to use it, it is a mathematically sophisticated theory. Our motivation for writing this monograph grew out of the problem of teaching the theory to our graduate students. There are very few sources where one can find self-contained treatments that are accessible to graduate students. The survey articles by Waltman [**231**] and by Hutson and Schmitt [**110**] remain useful, although they do not contain more recent refinements of the theory which are scattered in the literature. Recent monographs by Cantrell and Cosner [**25**], Hofbauer and Sigmund [**106**], Thieme [**217**], and Zhao [**238**] are good sources, but their focus is broader than persistence theory.

This monograph began as a set of lecture notes for graduate students in a team-taught course on Dynamical Systems in Biology offered by the authors in fall 2005, spring 2007, and spring 2009 at Arizona State University. It contains a large number of homework exercises. A description of the contents of the chapters follows.

Chapters 1 through 8 contain our main results on persistence theory for autonomous dynamical systems.

Chapter 1 begins with a review of metric spaces, the natural abstract setting or "state space" for finite and infinite dimensional dynamics. The notion of a semiflow on a metric space is developed; it gives the dynamics. We distinguish discrete and continuous time semiflows simply by the time set: nonnegative integers in the former case, the nonnegative reals in the latter case. The basic properties of a semiflow are independent of the time set. This unified treatment of discrete time and continuous time semiflows allows us to unify the later treatment of persistence theory for discrete time and continuous time dynamics. In the literature, the theory developed separately for discrete and continuous time systems, but we have been largely successful in our attempt to present a unified treatment, avoiding as much as possible separate approaches. Persistence theory often requires that the underlying dynamics are dissipative in some sense. The strongest sense is that there is a compact attractor of bounded subsets. Although the trend of recent work, and one of our goals here, is to weaken these compactness requirements where possible, we present the theory of attractors in Chapter 2.

Chapter 3 begins with the definitions of persistence, both uniform weak and uniform strong persistence relative to a persistence function. However, its main focus is on uniform weak persistence and on elementary methods for establishing it. Several examples illustrating such methods are introduced. These include the continuous time model of an SEIRS infectious disease in a meta-population with host travel between patches, the classical May-Leonard system of three competing populations, and discrete time nonlinear matrix models of population dynamics. The latter include the LPA model of flour beetle dynamics and nonlinear versions of the well-studied Leslie-type demographic models.

Uniform strong persistence is the desired conclusion; uniform weak persistence is more easily obtainable. It has long been known that uniform weak persistence plus suitable compactness properties of the dynamical system give uniform strong persistence. See Freedman and Moson [**72**] for flows on locally compact metric spaces, Freedman, Ruan, and Tang [**73**] for flows, and Thieme [**215**] for semiflows on general metric spaces. In Chapter 4, we present a number of such results. Some of these have relatively weak compactness assumptions at the expense of lengthy and seemingly technical hypotheses. Others require more compactness assumptions but are more easily and concisely formulated. A number of applications are treated in detail, including those introduced in the previous chapter.

The choice of a persistence function may be not obvious; several different choices may be appropriate. The question then naturally arises as to whether, and how to prove that, persistence with respect to one such function implies persistence with respect to another persistence function. This issue is treated in Chapter 4.6.

For semiflows that are dissipative in a suitable strong sense and that are uniformly ρ-persistent, there is an elegant decomposition of the attractor into an extinction attractor, a persistence attractor, and a family of total trajectories whose α limit sets are contained in the extinction attractor and whose ω limit sets are contained in the persistence attractor. This result, versions of which were first proved by Hale and Waltman [**95**] and later by Zhao [**238**] and Magal and Zhao [**158**], is proved in Chapter 5.

The brief Chapter 6 explores various scenarios whereby one may establish that persistence implies the existence of a "persistence equilibrium", that is, an equilibrium x^* for which $\rho(x^*) > 0$ where ρ denotes the persistence function. This provides an extra incentive for taking the trouble to establish persistence. The monograph by X.-Q. Zhao [**238**] contains a nice summary of the history of results in this direction. See the notes to Chapter 1 of [**238**]. Newer results also appear in the recent paper by Magal and Zhao [**158**].

Nonlinear matrix models, such as those introduced in Chapter 3, are increasingly being used in population modeling as indicated by the recent monographs [**29, 44, 39**]. Therefore, we devote Chapter 7 to applying the results of the previous chapters to them.

Chapter 8 treats the mathematically more sophisticated topological approach to persistence and its consequences. As Josef Hofbauer [**79, 104**] has repeatedly pointed out, the theory of attractors and repellers, formulated by several mathematicians including Zubov, Ura, Kimura, and Conley, lead directly to proofs of many of the results of persistence theory. See [**79**] for many historical references to the work of Zubov and Ura and Kimura; the monograph of Bhatia and Szegő [**16**] contains some of this work. The notion of chain recurrence and chain transitivity of Conley [**33**] has also proved to be very useful. These notions were originally established for flows on locally compact spaces but are needed for semiflows on potentially infinite dimensional Banach spaces for persistence theory. We give here a self-contained treatment of these ideas and how they are used in the theory. Most notable among the results implied by these ideas are the Butler-McGehee Theorem and the acyclicity theorem establishing uniform weak persistence.

These were first formulated by Butler, Freedman and Waltman [**22, 23**] for flows on locally compact spaces, extended to discrete time systems by Freedman and So [**74**] and Hofbauer and So [**107**]. They were later generalized to semiflows on infinite dimensional spaces by Hale and Waltman [**95**] assuming the existence of a compact attracting set, an assumption that was relaxed in [**215**].

Several more or less straightforward applications of the acyclicity approach to persistence are included. These include the classical three-level (ODE) food chain model considered by Hastings and collaborators, nonlinear matrix models for biennial species, and a metered epidemic model — a hybrid of both discrete and continuous time.

Finally, we show how classical Lyapunov exponents may be used to establish one of the key hypotheses in the acyclicity theorem, namely, that a compact invariant set, belonging to the "extinction set", is uniformly weakly repelling in directions normal to the extinction set. The use of Lyapunov exponents in the study of biological models was pioneered by Metz et al. [**168**], who proposed that the dominant Lyapunov exponent gives the best measure of invasion fitness, and by Rand et al. [**180**] who used it to characterize the invasion "speed" of a rare species. Roughly, a positive dominant Lyapunov exponent corresponding to a potential invading species in the environment set by a resident species attractor implies that the invader can successfully invade. Our treatment is patterned after the approach taken by Paul Salceanu in his thesis [**186**] and [**187, 188, 189, 190**].

Chapter 9 focuses on an SI epidemic model where infectives are structured by age since infection and where the force of infection depends on an age-since-infection weighted average of current infectives. The model can be reduced to a system of integral equations; existence and uniqueness of solutions, and boundedness of solutions are proved. The host is shown to (uniformly) persist, the basic replacement number $\mathcal{R}_0$ is identified, disease extinction is shown to occur if $\mathcal{R}_0 < 1$, and uniform weak persistence of the disease is shown if $\mathcal{R}_0 > 1$. In order to obtain uniform persistence of the disease, it is useful to reformulate the dynamics as a semiflow on a suitable Banach space. This is done by showing that solutions satisfy a weakly formulated semilinear Cauchy problem. One can then show the existence of a compact attractor of bounded sets under suitable restrictions. This in turn facilitates the argument for uniform persistence of the disease when $\mathcal{R}_0 > 1$. The existence of an endemic equilibrium is also established, and rather unrestrictive conditions for its global stability are derived. It should be noted that persistence is indispensable for doing the latter because the Lyapunov function that is used is not defined on the whole state space but only on the persistence attractor (see also [**155**]).

Chapter 10 is devoted to a brief treatment of the semilinear Cauchy problem $u' = Au + F(u),\ u(0) = u_0$ in a Banach space setting. Here A is a closed linear operator and F is a nonlinear map. Notions of classical, integral, and mild solutions are defined, and the equivalence of mild and integral formulation is shown. Globally defined integral solutions are shown to define a semiflow, and local existence is established by the contraction mapping principle when F satisfies a Lipschitz condition. If F is suitably bounded, global in time existence is also shown. Conditions for the induced semiflow to be asymptotically smooth, a key requirement for showing the existence of a compact global attractor, are identified. As we have biological examples in mind, positivity of solutions must be satisfied. Conditions which ensure positivity of solutions are formulated.

Chapter 11 treats microbial growth on a growth-limiting nutrient in a tubular bioreactor. Fresh nutrient enters the left side of the tube, and unused nutrient and microbes leak out the right side of the tube in proportion to their concentration. Both nutrient and microbes are assumed to diffuse throughout the tube. The issue is whether or not the influx of nutrient is sufficient to allow the microbes to persist in the bioreactor. Relying heavily on the machinery of Chapter 10, we show that the system of reaction-diffusion equations generates a dissipative semiflow. Linearized stability analysis of the so-called washout equilibrium solution (no microbes) leads to a basic reproduction number $\mathcal{R}_0$. If $\mathcal{R}_0 < 1$, the microbes are "washed out" of the bioreactor, and, if $\mathcal{R}_0 > 1$, they uniformly persist and there is a unique colonization equilibrium.

Chapter 12 considers a model of microbial growth in a chemostat where microbial cells of different age take up nutrient at differing rates and divide at an age-dependent rate. Ignoring growth and uptake, focusing only on demographics of cell division, we begin by obtaining a renewal equation for cell population division rate and showing that it has a unique solution. This leads to the definition of a semigroup of operators and ultimately to a formulation of the full model, including growth and uptake, as an abstract ODE in a Banach space setting. Its mild solutions are shown to generate a semiflow. Consideration of the "washout state", absent microbes, allows identification of the basic "biomass production number" for the model. When it is less than one, and an additional condition satisfied, the microbes are washed out;

when it exceeds one, the cell population persists uniformly weakly. Proofs of these results make use of the Laplace transform. In fact, uniform persistence of the cell population holds when the basic production number exceeds one under additional assumptions, but the proof is deferred to a later chapter. The problem is in establishing sufficient compactness of the semiflow. A different approach provides another route from uniform weak to uniform strong persistence, which succeeds for this model.

Chapter 13 is devoted to persistence for nonautonomous systems. Practical persistence is established, under suitable conditions, for a population of micro-organisms growing in a chemostat with time-dependent dilution rate using elementary arguments. It is also established that all positive solutions are asymptotic to each other. The abstract notion of a nonautonomous semiflow is introduced, corresponding definitions of persistence are given, and several results giving conditions under which uniform weak persistence implies uniform strong persistence are proved. Special attention is devoted to the case of periodic nonautonomous semiflows and nonautonomous semiflows that are asymptotic to such semiflows. The implication that uniform weak persistence implies uniform persistence for these cases is specialized. Finally, uniform persistence is established for the (autonomous) cell division model treated in Chapter 12 by using the methods developed for nonautonomous semiflows.

As noted in our description of Chapter 3 above, persistence functions were introduced early on in the history of persistence theory as a means to obtain uniform persistence (permanence) in much the same way that they are used in Lyapunov stability theory to obtain stability results for equilibria of dynamical systems [**82**], and there is now a well-developed approach to establishing persistence using so-called average Lyapunov functions (a generalization of persistence functions in the sense of Gard and Hallam [**82**]). The works of Fonda [**71**], Gard [**80**], Hofbauer [**103**], Hutson [**109**], and Schuster, Sigmund and Wolff [**196**] have been very influential. Some of their ideas, as well as later work, have been reviewed in the paper of Hutson and Schmitt [**110**] and the monograph of Sigmund and Hofbauer [**106**]. However, so far in this work, we have used persistence functions primarily as a means to precisely define what is meant by persistence, not as a tool with which to establish it.

In Chapter 15, taking inspiration from this large literature, we formulate some general results which yield persistence using the average Lyapunov function approach. The adjective "average" in the terminology signifies that a time-average of the function over a sufficiently large interval should be positive. We formulate an approach which works for nonautonomous semiflows and, as usual, seeks to minimize compactness requirements. These goals force rather technical statements, but the main results are simple: The existence of a weak average Lyapunov function ρ implies weak ρ-persistence; the existence of a strong average Lyapunov function implies uniform ρ-persistence. As an application, the hypercycle equation, treated in Chapter 12 of [**106**] in the autonomous case, is extended to the case where replication rates may be time-dependent.

The book ends with two appendices. The first, Appendix A, covers some useful techniques in differential equations which are not usually covered in a basic course. Chief among these are differential inequalities, a key tool in applied dynamics. Here, we mean Kamke's comparison theorem for ODEs and the strong maximum principle for PDEs. The former result is proved, the latter is merely stated and references are given. Dynamical systems in biology typically deal with nonnegative quantities, and therefore one needs to establish that solutions that begin nonnegative, remain so in the future. Another essential tool for dealing with positivity and stability is the Perron-Frobenius theory which we state but do not prove. Finally, an elementary but powerful method which can sometimes establish persistence is the method of fluctuation. It provides the means to explicitly estimate the limit inferior and limit superior of bounded components of solutions of systems of ordinary and delay differential equations.

Appendix B introduces selected useful tools from functional analysis. Among them are compactness criteria in L^p spaces, inequalities for Volterra integral equations, proof of the equivalence of integral and mild solutions of linear differential equations in Banach spaces, and Fourier transform methods for integro-differential equations. The latter leads to conditions implying that any bounded solution of a class of integro-differential inequalities or equations vanishes identically, and this result may be used to establish global stability results. These tools are used in Chapter 9 and Chapter 12.

One should also disclose what is not in this book that a reader might expect given the title. One such omission is the notion of robust persistence, more precisely, the reasonable expectation that the notion of uniform persistence should be structurally stable to small changes in system dynamics in some topology. For example, if the dissipative system takes the Kolmogorov form $x_i' = x_i f_i(x)$ on $\mathbb{R}^n_+$, then small perturbations should mean small changes in the per capita growth rates f_i, say in the C^r-topology. Robust (C^r) ρ-persistence with $\rho(x) = \min_i x_i$ for this system would mean the existence of $\epsilon, \delta > 0$ such that $\liminf_{t\to\infty} x_i(t) > \epsilon$, $\forall i$ provided $x(t)$ satisfies $x_i' = x_i g_i(x)$ where $\|f - g\|_{C^r} < \delta$ and $x_i(0) > 0$, $\forall i$. Such results were first established by Schreiber [**193**]. See also Hirsch et al. [**101**]. We do not include these results since they are partly covered in the monograph of Zhao [**238**].

Finally, we have not included recent work on persistence for stochastic systems [**11, 105, 194**] or for skew-product semiflows [**169, 238**].

There is a huge body of literature on persistence theory, and this book does not span nearly all of it. We ask the forgiveness of our valued fellow scholars whose works we have failed to reference.

We would like to acknowledge the many students, especially Thanate Dhirasakdanon, who have contributed to this work through their questions, suggestions, and their homework solutions.

We thank our wives, Kathryn Smith and Adelheid Thieme, for their unwavering support, though this endeavor must have been shrouded in mystery for them.

As much as any other science, mathematics takes place in a tapestry of teachers, peers, and students; we gratefully dedicate this monograph to our Ph.D. advisors Willi Jäger (HRT) and Paul Waltman (HLS).

Hal Smith was supported in part by NSF Grant DMS-0918440.
Horst Thieme was supported in part by NSF Grant DMS-0715451.