## Preface

Our aim in this monograph is to present an essentially self-contained account of the theory of mathematical model building of microbial populations. The emphases and selection of topics reflect our own involvement in the field over the past 10 years and our intent has been to stress the ideas and methods of analysis besides describing the most general and far-reaching results possible. This monograph includes published work as well as work presented at various seminars and conferences. There has been much ferment in this field during the past 15 years resulting in numerous publications with various methods and theoretical arguments. Much experience has been gained from this research during the past decade by researchers that include mathematicians, biologists, limnologists, and chemical and civil engineers. Now it is time to crystallize these concepts into a simple ready-to-use format to enable the implementation of these models by practicing field scientists. Thus, the first and foremost aim of the authors is to encourage others to consider and apply the results and the tools discussed in this book. Also, it is an attempt by the authors, a mathematician with an enthusiasm for biology and a biologist with an interest in mathematics, to encourage and promote the quintessential aspects of a collaborative dialogue between their respective disciplines. Mathematical models that describe the growth of microorganisms feeding on a nutrient in limited supply in a continuous cultured environment are very popular among researchers in mathematical biology. In this case, the mathematical predictions may be tested in a laboratory using a device known as a chemostat. The models are therefore called chemostat models. Chemostat models are identified as instances where mathematics precedes biology. On the basis of similarities, researchers viewed a chemostat as a replica of a simple, natural lake. But a chemostat is a closed system in which some of the key parameters can be controlled. This is not the case with a lake that is influenced by external factors, mainly seasonal changes. A variety of Lyapunov function(al)s are provided and this forms the main approach for the stability studies in most situations. The construction of Lyapunov function(al)s is described step-by-step. Enough care is taken to see that these results actually contribute to the continuity and completeness of the basic line of thinking that we began with. The book consists of eight chapters. The following is an outline of the book.

The first chapter presents an introduction to basic chemostat models. Global qualitative analysis of the stability of equilibria is carried out and this covers all recent literature. This approach forms a basis for the techniques in later chapters and makes a good starting point for subsequent chapters.

In Chap. 2, attention is drawn toward a lake. The device chemostat is compared with a natural lake. Such a lake has some extra features in addition to those of the closed environment of a chemostat, and the models introduced in Chap. 1 are appropriately modified to suit to a lake. Keeping in view the observations of biologists, time delays are introduced into the models of Chap. 1. Various combinations of time delays, both discrete and distributed, as studied by researchers are explained in this chapter in detail. These models are popularly known as chemostat-like models. A complete analysis of each of these models starting from the existence and uniqueness of solutions to the local and global stability of equilibria (implying the extinction/survival of species) is presented. Imbalances and disturbances are common in nature. Thus, species in lakes are prone to these disturbances caused by environmental conditions and exhibit instability characteristics unlike the models of Chap. 1, which are structurally stable. It is observed that time delays and variations in nutrient supply and its supply rate (due to seasonal changes) influence the dynamics of the system and tend to destabilize it. Unbounded growth or extinction are the characteristics observed. These instability characteristics of the models are discussed in Chap. 3. How to combat such an unstable situation is the content of the next three chapters, identifying the root cause of instability in each case. Having a good grasp of how a season cycle tends to infuse instability in a system, we study the natural response of consumer species (system) in each case. We consider the system in its most possible general form and study the behavior (response) of species.

Chapter 4 introduces the self-regulation of species due to a low supply of the nutrient (during summer months) and lack of support from the environment. This may also be understood as the effect of finite carrying capacity or overcrowding on the system. In Chap. 5 the behavior of species when the inflows and outflows in a lake are very high (during the rainy season) is studied. In this case, the nutrient is freely available to the species but there is always a danger of a species being washed out of the system. How the species survive the high washout is the point of interest here. The concept of wall growth (species finding a safer place in the same environment) is introduced and its influence studied in this chapter.

The survival and growth of microbial populations depends upon the consumption levels of the nutrient and this leads to another interesting phenomenon. We discuss the following prominent situations that have a direct bearing on the modeling perspective of these species. The first represents the natural tendency of a species to maintain the consumption levels at equilibrium values showing a natural inactive state of the consumer species. The second state may be understood as a regulation of the supply of the nutrient during the transition from high supply to low supply and vice versa. These are defined as the zones of no activation for the consumer species. The influence of this zone on the behavior of the system is the content of Chap. 6.

As the stability of equilibria implies the eventual survival of species, sufficient conditions are provided for the stability of the equilibria of the system equations. The tendencies toward instability introduced by the presence of time delays and

## Preface

variations in nutrient supply/consumption are then controlled by the mechanisms henceforth termed as "biocontrol mechanisms." The switch from instability to stability is thus explained and established. A number of examples are provided at each stage that help one understand how each of these mechanisms works on the system.

In the final chapter, we present some of the latest techniques to realize the mathematical results obtained. This forms a direct link between a mathematician and a biologist, which is the main objective of the study of chemostat(-like) models. This is achieved by finding ways to easily estimate the control (key) parameters that influence the dynamics of the system. Dynamic optimization algorithms are employed for this purpose. Such an approach is entirely new to the researchers working in this area.

Research articles that motivated the preparation of the book are cited in the section on "Notes and Remarks" at the end of each chapter. Scope for further research is discussed and gaps in the literature are pointed out. Examples are provided at every stage to illustrate, to compare the results, and to realize the underlying biological situation. It is hoped that this book will serve as a basis for further research for new entrants interested in this interdisciplinary area of research. It is our strong belief that this type of interdisciplinary work will not only be stimulating but will also open up many more new vistas, offering exciting prospects. This book is suitable for a one to two semester course for senior undergraduate and graduate students of mathematics, biology, agriculture, limnology, and chemical and civil engineering. Moreover, the reader feels throughout the reading of this monograph that the basic motif behind chemostat models, that is, "theory(mathematics) precedes experiment(biology)," is always cherished. Writing this book has been both interesting and challenging. Challenging, particularly, because it is not easy for us, as the authors, to judge whether we have succeeded in the aims we set for ourselves. Have we provided an accessible and informative overview of the subject? Have we managed to strike a balance between theory and application? Have we interested the readers enough that they can move on and build new mathematical models? We are honest enough to realize that answers to these and similar questions cannot be an unequivocal yes. We would therefore encourage readers to respond with ideas for further improvements.

## Acknowledgments

*VSHR*. It is a pleasure to express my appreciation to those who have directly or indirectly influenced this work. Over the years, I have benefited from interaction and collaboration with numerous people within the scientific community. In particular, I express my gratitude to the late Professor M. Rama Mohan Rao (Indian Institute of Technology, Kanpur), who supervised my doctoral thesis in nonlinear differential equations. Also, I am extremely grateful to Professor Herbert I. Freedman (University of Alberta, Edmonton), who first introduced me to the fascinating field of mathematical biology. Further, I take this opportunity to thank my friends and

## Preface

collaborators, Professors Lynn H. Erbe (University of Nebraska, Lincoln), the late Geoffrey J. Butler (University of Alberta, Edmonton), V. Lakshmikantham (Florida Institute Technology, Melbourne), Bindhyachal Rai (University of Allahabad, India), Rajiv S. Mishra, Chelluri A. Sastri and Martin Bohner (Missouri University of Science and Technology, Rolla), Dr. Srinivas Pyda (Oracle Corporation, Redwood Shores, CA) and Dr. Rama Krishna Tadi (CALTRANS, San Bernardino, CA). Final parts of this work were completed at the Missouri University of Science and Technology in the years 2007–2009 and I wish to thank Professor Leon M. Hall for his generous help and support which indeed have facilitated my visit to Rolla.

Finally, I wish to thank my wife Mrs. Prameela (Scientist, Defence Research and Development Laboratory, Hyderabad, India) and my sons Sree Krishna Chaitanya (University of California, Davis) and Sree Sesha Aravind (University of Washington, Seattle) for their unconditional support and encouragement.

*PRSR.* I wish to thank my family for their patience and unstinting support during the preparation of this book.

Both of us wish to thank our colleagues from around the world who have provided feedback and review on the material presented in this monograph. We would like to take this opportunity to express our warm gratitude to the editorial staff at Springer, New York. In particular our special thanks go to Mr. Jeffrey Ciprioni, Editor, Genetics and Evolution and Ms. Melanie Wilichinsky, Associate Editor, Springer Science and Business Media, New York, for their very efficient handling of this manuscript.

We gratefully acknowledge support from the Foundation for Scientific Research and Technological Innovation – a constituent division of Sri Vadrevu Seshagiri Rao Memorial Charitable Trust, Hyderabad, India.

Hyderabad, India Guntur, India V. Sree Hari Rao P. Raja Sekhara Rao