

# Preface to the First Edition

The theory of branching processes is an area of mathematics that describes situations in which an entity exists for a time and then may be replaced by one, two or more entities of a similar or different type. It is a well developed and active area of research with theoretical interests and practical applications.

The theory of branching processes has made important contributions to biology and medicine since Francis Galton considered the extinction of names among the British peerage in the nineteenth century. More recently, branching processes have been successfully used to illuminate problems in the areas of molecular biology, cell biology, developmental biology, immunology, evolution, ecology, medicine, and others. For the experimentalist and clinician, branching processes have helped to understand observations that seem counter-intuitive, has helped develop new experiments and clinical protocols, and has provided predictions which have been tested in real life situations. For the mathematician, the challenge of understanding new biological and clinical observations has motivated the development of new mathematics in the field of branching processes.

The authors of this monograph are a mathematician and a cell biologist who have collaborated on investigations in the field of branching processes for more than a decade. In this monograph, we have collected examples of applications of branching processes from our own publications, and from publications of many other investigators. Each example is discussed in the context of the relevant mathematics. We have made an effort to collect and review much of the published literature which has applied branching processes to problems in molecular and cellular biology, as well as selected examples from the fields of human evolution and medicine.

The intended audiences for this monograph are mathematicians and statisticians who have had an introduction to stochastic processes but have forgotten much of their college biology, and biologists who wish to collaborate with mathematicians and statisticians. Both audiences will find many examples of successful applications of branching processes to biological and medical problems. As an aid to understand the specific examples, we have provided two introductory chapters one with background material in mathematics, and the other with background material in biology, as well as two glossaries.

The book is organized as follows: Chapter 1 provides a mathematical background and motivating examples of branching processes. Chapter 2 provides an introduction to biological terms and concepts. The subsequent chapters are divided into specific areas of branching processes. Each of these chapters develops the appropriate mathematics and discusses several applications from the published literature. Chapter 3 discusses the Galton-Watson process, the oldest, simplest and best known branching process. Chapter 4 discusses the age dependent process—Markov case, the time continuous branching process with exponential life-time distributions. Chapter 5 discusses the Bellman–Harris process, an age-dependent process. Chapter 6 gives a more systematic treatment of multitype processes, in which progeny may be of many types. Chapter 7 discusses branching processes with infinitely many types, stressing interesting properties which are different from the finite multitype situation. Appendices provide information on probability generating functions, construction of the probability space for the Bellman–Harris process as well as a brief introduction to the Jagers–Crump–Mode process (the general branching process).

We have made an effort to broadly review the published literature on branching processes applied to biology. However, we had to select specific examples and we wish to apologize to our colleagues whose work has not been cited. We welcome comments from colleagues and students who are interested the field of branching processes.

A search of any university library or an internet bookstore will reveal a number of volumes devoted to branching processes. Among the most important, we may cite the fundamental books by Harris (1963), and by Athreya and Ney (2004). Multitype branching processes were first covered in the book by Mode (1971). General branching processes, in a systematic way, were explored by Jagers (1975). Each of these classics, particularly Jagers (1975) includes some biological applications. An important book concerning estimation of branching processes is Guttorp (1991). Asmussen and Herring (1983) involve a very mathematical approach. In addition, there exist at least a dozen or two of collections of papers and more specialized volumes. Recently, Pakes (2000) prepared a report on biological applications of branching processes, which is wider in scope (it has a lot spatial branching and ecology, for example), but less detailed, although an area of overlap with our book exists. We believe that the scope of the present volume is unique in that it illustrates a paradigm, in which theoretical results are stimulated by biological applications and biological processes are illuminated by mathematics.

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for its mathematical correctness. His critical remarks improved it significantly. Remaining inaccuracies are our fault. Generations of graduate students at the Statistics Department at Rice University provided welcome feedback. Professor Jim Thompson encouraged teaching this material at Rice and Rice and provided much constructive criticism. Professor Peter Jagers of the Chalmers University in Gotheborg, Sweden, hosted Marek Kimmel on several occasions and provided much needed feedback. Our families showed warmth and patience during the gestation of this book.

We dedicate this book to our students, our teachers, and our families.

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# Preface to the Second Edition

The first edition of “Branching Processes in Biology” published in 2002 has been well received by mathematicians, statisticians, and biologists. Both established investigators and advanced students have indicated to us that its inclusion of both theory and applications has been informative.

This second expanded edition adds new material published during the last decade. In addition to the work that the authors were aware of, an extensive search of the mathematical literature covered by the MatSciNet database and the biomedical literature covered by the Medline database was surveyed and relevant publications were selected. Nearly 200 new references have been added. These have been reviewed either as subsections within existing chapters, or as a new chapter.

Chapter 2, Biological Background, includes additional material on Cell Growth, Division and Death, Stem Cells, and Tumor Progression. The subsection on Textbooks and Monographs in Biology has been updated.

Chapter 3, The Galton-Watson Process, includes a new application section on Cancer Mutations, and subsections on Modeling Driver and Passenger Mutations, and a subsection on Distribution of Mutational Events in Various Phases of Tumor Growth.

Chapter 4, The Age-Dependent Process: The Markov Case. Mostly left unchanged.

Chapter 5, The Bellman-Harris Process, includes new subsections on Cell Proliferation, and on Branching Processes and Cancer Therapy.

Chapter 6, Multitype Processes, includes new subsections on Robust Modified Median Estimator of Mutation Rates, Robust Modified Median Estimator Versus Data, and Recent Developments in Theory and Application of Fluctuation Analysis.

Chapter 7, Branching Processes with Infinitely Many Types, includes a new section on Generalized Linear-Fractional Distributions and Their Applications, with subsections on Definitions and Basic Properties, and Applications in Branching Processes. A new section Application of Branching Process with Infinite-Allele Mutations includes subsections on Proliferation of Alu Repeats, and Modeling Telomeres.

Chapter 8, Genealogies of Branching Processes and Their Applications, is a new chapter, with a subsection on Robustness of Mitochondrial Eve Dating.

Chapter 9, References. Nearly 200 new recent references have been added, bringing the total to over 460 references.

Chapter D, Glossaries. New entries have been added to define or explain new terms.

In addition to the revised subject index, a new author index has been added.

New applications have been added in appropriate chapters. They discuss recent advances in several areas, including cancer mutations, cancer therapy, cell proliferation, estimation of mutation rates, fluctuation analysis, *Alu* repeats, and telomeres, among others.

During the past decade two of our colleagues, who had made major contributions to this field, have died, Ovide Arino and Andrey Yakovlev. We hope that their work, and the other work reviewed in this edition, will inspire new investigators to explore this active field of branching processes in biology.

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Branching Processes in Biology

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