Texts in Applied Mathematics 57

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An Introduction to Delay Differential Equations with Applications to the Life Sciences

Springer

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ISSN 0939-2475
ISBN 978-1-4419-7645-1 e-ISBN 978-1-4419-7646-8
DOI 10.1007/978-1-4419-7646-8
Springer New York Dordrecht Heidelberg London

Library of Congress Control Number: 2010936520

Mathematics Subject Classification (2010): 34K05, 34K20, 92D25

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

Preface

This book is intended to be an introduction to delay differential equations for upper-level undergraduates or beginning graduate mathematics students who have a reasonable background in ordinary differential equations and who would like to get to the applications quickly. I used a preliminary version of this manuscript in teaching such a course at Arizona State University over the past two years. Existing texts on the subject by Diekmann et al. [26] and by Hale and Lunel [41], while excellent on the theory, are heavy on functional analytic background and light on applications. In my experience, most graduate students do not have the requisite background to read such texts profitably. A more applications oriented text by Kuang [48] is, unfortunately, out of print.

Both theory and applications of delay differential equations require a bit more mathematical maturity than its ordinary differential equations counterparts. Primarily, this is because the theory of complex variables plays such a large role in analyzing the characteristic equations that arise on linearizing around equilibria. Ideal prerequisites for this book include a second course in ordinary differential equations such as in the text [78, 10], some familiarity with complex variables, and some elementary analysis. Results from the calculus of several variables are routinely used, especially, the implicit function theorem.

This book focuses on the key tools necessary to understand the applications literature involving delay equations and to construct and analyze mathematical models involving delay differential equations. It begins with a survey of mathematical models involving delay equations. These are primarily from the biological literature, in keeping with my own prejudices, and due to the relative frequency of delay models in that literature relative to others. This is followed by a "warm-up" chapter on the simplest possible delay equation $u'(t) = -\alpha u(t-r)$. This simple example illustrates many of the complexities that arise with delays and has the advantage that results may be easily and explicitly worked out. Its main message is that delays naturally induce oscillations. Standard existence and uniqueness results are taken up in Chapter 3. The method of steps is introduced and exploited for discrete delay equations. For the reader interested mainly in applications, this may suffice. A more general approach follows but no fixed point theorems are used: the method of successive approximations works fine. A key notation is introduced here, one that takes a bit of getting used to, namely the state variable x_t which appears throughout the remainder of the book. In addition to continuous dependence of solutions on initial data, continuation of solutions, positivity, and comparison of solutions are also discussed because many applications come from biology where positivity restrictions are inherent to the models. Linear equations are taken up next with the primary aim being stability. In applications, linear delay equations arise through linearization of a nonlinear equation about an equilibria so the focus is on linear stability analysis and the characteristic equation the roots for which determine stability. Proof of the validity of linearized stability would require too much additional mathematics and therefore it is not given.

The following chapter is an introduction to abstract dynamical systems theory, using ordinary differential equations, discrete-time difference equations, and now delay differential equations as examples. It is shown that a delay differential equation induces a semidynamical system on the space of continuous functions on the delay interval. The focus then turns to omega limit sets, the usual results familiar from ODEs continue to hold but with some nuances due to the infinite-dimensional state space. Applications to the delayed logistic equation and the delayed chemostat model are treated. The LaSalle invariance principle is established and an application is given. Next, the Hopf bifurcation theorem, critical for applications, is treated. A simple canonical example is considered where the bifurcation can be explicitly computed. Following this, the Hopf bifurcation theorem is stated without proof. It is applied to the standard delayed negative feedback system $x'(t) = -f(x(t-1))$ where $xf(x) > 0$. In this case, a formal expansion for the periodic solution in terms of a small parameter (this is fully justified in an appendix) is given. Applications to various second-order delay equations are then considered, one of which is stabilizing the up position of a damped pendulum with delayed feedback; another is a model of a gene regulatory network. Finally, the beautiful Poincaré–Bendixson theory for monotone cyclic feedback systems, obtained recently by Mallet-Paret and Sell, is stated.

The following brief chapter is an introduction to equations with infinite delay and to the linear chain trick by which certain special kinds of infinite delays can lead to ordinary differential equations. These arise often in the modeling literature so an example is discussed in some detail. The final chapter focuses on a model of virus predation on a bacterial host in the setting of a chemostat where the bacteria subsist on a supplied nutrient. The delay corresponds to the latent period following virus infection during which new virus particles are manufactured within the cell. Most of the theoretical results of previous chapters are used in the analysis of this system of delay equations.

Two brief appendices should help those readers needing additional background on complex variables and analytic functions including the very useful Rouché's theorem, and implicit function theorems. The Ascoli–Arzela theorem is stated and discussed and the useful fluctuation method is described. A second appendix is devoted to a rigorous proof of Hopf bifurcation for the delayed negative feedback systems.

The impatient reader could skim the applications in Chapter 1, jump over Chapter 2, and start with Chapter 3. A note on notation: we use $\mathbb{R}$ for the set of real numbers, $\mathbb{C}$ for the set of complex numbers, and f' denotes the derivative of a function f.

I would like to acknowledge the influence of Yang Kuang, a collaborator on much of the author's own work in delay differential equations, on this work and to thank him for providing several figures used in the book. Several students, colleagues, and anonymous reviewers read portions of the manuscript and provided valuable feedback. Among these, the author would like to thank Patrick de Leenheer, Thanate Dhirasakdanon, Zhun Han, and Harlan Stech. Most of what I know about delay differential equations, I learned from Jack Hale, a giant in the field.

Finally, I have been supported by the NSF during the time this book took shape, recently by award DMS 0918440.

Tempe, Arizona *Hal Smith*
July, 2010

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