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

– Monograph –

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## 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.

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# Contents

<b>1</b>	<b>Introduction</b> .....	1
1.1	Examples of Delay Differential Equations .....	1
1.2	Some Terminology .....	9
1.3	Solving Delay Equations Using a Computer .....	11
<b>2</b>	<b>Delayed Negative Feedback: A Warm-Up</b> .....	13
2.1	Preliminaries .....	13
2.2	The Simplest Delay Equation .....	16
2.3	Oscillation of Solutions .....	20
2.4	Solutions Backward in Time .....	22
<b>3</b>	<b>Existence of Solutions</b> .....	25
3.1	The Method of Steps for Discrete Delay Equations .....	25
3.2	Positivity of Solutions .....	27
3.3	A More General Existence Result .....	29
3.4	Continuation of Solutions .....	36
3.5	Remarks on Backward Continuation .....	37
3.6	Stability Definitions .....	38
<b>4</b>	<b>Linear Systems and Linearization</b> .....	41
4.1	Autonomous Linear Systems .....	41
4.2	Laplace Transform and Variation of Constants Formula .....	43
4.3	The Characteristic Equation .....	45
4.4	Small Delays Are Harmless .....	48
4.5	The Scalar Equation $x'(t) = Ax(t) + Bx(t-r)$ .....	49
4.6	Principle of Linearized Stability .....	54
4.7	Absolute Stability .....	56
<b>5</b>	<b>Semidynamical Systems and Delay Equations</b> .....	61
5.1	The Dynamical Systems Viewpoint .....	61
5.2	Semiflows and Omega Limit Sets .....	64

5.3	SemiDynamical Systems Induced by Delay Equations	65
5.4	Monotone Dynamics	70
5.5	Delayed Logistic Equation	73
5.6	Delayed Microbial Growth Model	76
5.7	Liapunov Functions	78
5.7.1	Logistic Equation with Instantaneous and Delayed Density Dependence	80
<b>6</b>	<b>Hopf Bifurcation</b>	<b>87</b>
6.1	A Canonical Example	87
6.2	Hopf Bifurcation Theorem	89
6.3	Delayed Negative Feedback	91
6.3.1	Computation of the Hopf Bifurcation	92
6.3.2	Series Expansion of Hopf Solution	94
6.3.3	The Logistic Equation	97
6.4	A Second-Order Delayed Feedback System	99
6.4.1	Delayed Feedback Dominates Instantaneous Feedback	101
6.4.2	Instantaneous Feedback Dominates Delayed Feedback	104
6.4.3	Stabilizing the Straight-Up Steady State of the Pendulum	106
6.5	Gene Regulation by End-Product Repression	111
6.6	A Poincaré-Bendixson Theorem for Delay Equations	115
<b>7</b>	<b>Distributed Delay Equations and the Linear Chain Trick</b>	<b>119</b>
7.1	Infinite Delays of Gamma Type	119
7.1.1	Characteristic Equation and Stability	120
7.1.2	The Linear Chain Trick	123
7.2	A Model of HIV Transmission	126
7.3	An ODE Approximation to a Delay Equation	129
<b>8</b>	<b>Phage and Bacteria in a Chemostat</b>	<b>131</b>
8.1	Model	131
8.2	Positivity and Boundedness of Solutions	133
8.3	Basic Reproductive Number for Phage	134
8.4	Persistence of Host and Phage Extinction	135
8.5	The Coexistence Equilibrium	137
8.6	Another Formulation of the Model	141
<b>A</b>	<b>Results from Real and Complex Analysis</b>	<b>149</b>
A.1	Analytic Functions	149
A.2	Implicit Function Theorem for Complex Variables	151
A.3	Rouché's Theorem	152
A.4	Ascoli-Arzela Theorem	153
A.5	Fluctuation Lemma	154
A.6	General Implicit Function Theorem	155
A.7	Gronwall's Inequality	155

<b>B</b>	<b>Hopf Bifurcation for Delayed Negative Feedback</b> .....	157
B.1	Basic Setup and Preliminaries .....	157
B.2	The Solution .....	160
B.2.1	Solve for $q$ .....	161
B.2.2	Solve for $\mu$ and $\delta$ .....	163
	<b>References</b> .....	167
	<b>Index</b> .....	171

In mathematics, delay differential equations (DDEs) are a type of differential equation in which the derivative of the unknown function at a certain time is given in terms of the values of the function at previous times. DDEs are also called time-delay systems, systems with aftereffect or dead-time, hereditary systems, equations with deviating argument, or differential-difference equations. They belong to the class of systems with the functional state, i.e. partial differential equations (PDEs) which