NUMERICAL TREATMENT OF DELAY DIFFERENTIAL EQUATIONS IN BIOSCIENCE

A thesis submitted to the University of Manchester
for the degree of Doctor of Philosophy
in the Faculty of Science

April 2000

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Abstract

Many real-life phenomena involve a delayed rather than instantaneous reaction, with a dependence on a memory of past events. Examples occur in biology, economics, immunology, materials with memory, physiology, and population dynamics, where there is a time-lag or after-effect. Models of such phenomena frequently involve retarded functional differential equations (RFDEs).

This thesis presents the author's research in the numerical treatment of some delay differential equations (DDEs) and neutral DDEs (NDDEs) that occur in certain areas of bioscience. The main novelty concerns parameter estimation in DDEs, and a sensitivity analysis of the solution with respect to the parameters and of the parameters with respect to the observations. When modelling in bioscience, DDEs and NDDEs are frequently more consistent with real phenomena than differential equations with no time-lag.

The outline of this thesis is as follows:

In chapter I, we indicate the scope for applications of delay differential models in biological systems. We show how delay differential models, of real-life phenomena, have potentially more interesting dynamics than equations that lack memory effects.

In chapter II, we review some features of DDEs, such as existence and uniqueness of the solution; propagation and location of discontinuities in DDEs. We investigate how ODEs formulae (in particular continuous Runge-Kutta formulae) can be adapted to solve various types of DDEs. We also recall the methods of steps

and θ-methods for DDEs. We describe, in brief, the theory of accuracy and some issues related to numerical solutions of DDEs.

In chapter III, we examine the stability of delay models described by linear and nonlinear DDEs and NDDEs, and conditions that ensure stable behaviour. In particular we study, and get some new results in, numerical stability regions of the solutions. Sufficient conditions for contractivity of the solutions are also discussed.

In chapter IV, we produce a numerical method (using a least squares approach) for parameter identification in DDEs and NDDEs. We also discuss some related problems in parameter estimation in DDEs and NDDEs, such as discontinuities arising in the objective function via the solutions of DDEs. We describe, in some detail, some numerical models in cell proliferation phenomena and make a comparison between the exponential and time-lag growth models for *pre-B-cell* growth in 'fetal calf serum' and growth of 'fission yeast'. Numerical results illustrate that (compared with ODEs) DDEs provide better consistency with the nature of cell proliferation phenomena.

In chapter V, we formulate an approach to sensitivity analysis of delay differential modes, covering (i) the sensitivity of the state variables to the parameter estimates (that is, to measure the sensitivity of the solution with respect to changes in the parameter estimates), (ii) the sensitivity of the parameter estimates to the observations (to estimate the change in parameter estimates due to a change in the data) and (iii) the nonlinearity effect. Sensitivity coefficients are used to determine the covariance matrix of parameter estimates and hence to determine the standard deviations. Numerical results, based on the growth of *E.coli* colonies, illustrate that the sensitivity of the parameter estimate to the observation is *low* if the sensitivity of the state variable to the parameter estimate is *high*.

In the last chapter, we give a general summary and discussion of our results, and provide some suggestions for further investigation that could be used to extend the present work.

Declaration

No portion of the work referred to in this thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institution of learning.

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To my parents,

to my wife, and

to my children, Bassel & Nouran

Acknowledgements

I would like to express my sincere gratitude to my supervisor Prof. Christopher T.H. Baker for his suggestion of the field of study. His constant help, encouragement, fruitful discussions, and advice have been of great help.

I would also like to thank Prof. Joan Walsh for her great help. I learned much about my project from my discussion with Prof. Gennadii Bocharov during his visit to Manchester University. I gratefully acknowledge his collaboration. I also express my deep appreciation to Dr Chris Paul for his comments and his assistance. Furthermore, I have to thank all the staff and the fellow students in the department of Mathematics, as I spent a nice time with them.

This work was generously supported by the Egyptian Government.