

Preface

This book deals with modelling, analysis and simulation of problems arising in the life sciences, in particular, biological processes. Such problems play a very important role in many scientific and technological areas and is a truly interdisciplinary research topic. Indeed the models and results obtained in this book are a result of very useful and intensive discussions with microbiologists, doctors and medical personnel, physicists, chemists, as well as industrial engineers. Our results give a better understanding of the problems of life sciences considered in this book and explain their experimental findings. We especially emphasize that, due to strong interactions with colleagues in the topics mentioned above, the governing equations of life science models we have derived are based on experimental data and lead to a new class of degenerate density-dependent nonlinear reaction-diffusion-convective equations comprising two kinds of degeneracy: porous-medium and fast-diffusion type degeneracy. It is worth mentioning that such a class of degenerate evolution partial differential equations (PDEs), comprising simultaneously two kinds of degeneracy, is so far inadequately understood in the mathematical literature. This shows how useful such interdisciplinary research topics are for both mathematicians and representatives of other fields.

In this book we not only derive realistic life science models and their governing equations of the degenerate types mentioned above, but at the same time systematically study these classes of equations. In each concrete case we study their well-posedness, dependence of solutions on boundary conditions, which reflects some properties of our environment and the large-time behaviour of solutions; we also include some numerical analysis.

The book consists of six chapters. Chapter 1 has more of a teaching aid character and is dedicated to some basic concepts of linear elliptic boundary value problems (BVPs), properties of Nemytskii operators in Sobolev spaces (fractional as well) and Hölder spaces which we use in the analysis of deriving models in the next chapters.

Chapter 2 is concerned with large time behaviour of solutions of evolution equations in terms of the global attractor, its existence and properties.

In deriving evolution models of the problems of life sciences we are usually dealing with the temporal evolutions of non-negative quantities like concentrations

of nutrients and chemicals, population densities, temperature, pressure etc. Each model is some approximation of a real situation and therefore it is not clear beforehand, that the obtained models will obey the following crucial properties for the modellers: the solutions of continuous evolution equations remain non-negative if the initial data are non-negative. We emphasize that numerical simulations cannot answer the question whether the model in this sense is valid or not; even though numerical simulations can provide empirical evidence we can never be sure. Hence it is extremely important for modellers to have such criteria, that is necessary and sufficient conditions for solutions of parabolic systems containing diffusion, transport (convection) and interaction of species (nonlinear term) to preserve positive cones. It is worth noting, that so far such a criterion, in full generality, has only been found for scalar equations, which criterion is based on the maximum principle. It is well-known that for a system of parabolic PDEs the maximum principle fails. At present in the mathematical literature there exist many sufficient conditions for parabolic systems preserving positive cones. However this is not satisfactory for modellers. They need to have an algorithm to know whether or not the derived realistic models satisfy this property before starting to do analysis and carrying out simulations. Therefore in Chap. 3 (which in turn consists of three sections) we derive a criterion for positivity of solutions for quite large classes of deterministic parabolic systems containing diffusion, transport (advection or convection) and interaction of species (nonlinear term).

Chapter 4 is devoted to the positivity of solutions of a class of semilinear parabolic systems of stochastic partial differential equations by considering random approximations. For the family of random approximations we derive explicit necessary and sufficient conditions such that solutions preserve positivity. These conditions imply the positivity of the solutions of the stochastic system for both Ito's and Stratonovich's interpretation of stochastic differential equations. We emphasize that this result is also of independent interest for the mathematical community, since in this generality such a criteria for the systems mentioned in Chap. 3 and Chap. 4 were not previously known.

Chapter 5 is devoted to biofilm modelling (meso-scale level), analysis and simulation which is one of the most active areas in modern microbiology. To this end it is enough to refer to: "It is the best of times for biofilm research" (Nature 76, vol. 15, pp. 76–81, 2007). In contrast to existing biofilm models, which are based mostly on discrete rules or hybrid models, we are mainly interested in a deterministic and continuous model which is described by PDEs.

Chapter 5 consists of five sections. The first two sections, 5.1 and 5.2 are concerned with the single species/single substrate models. In Sect. 5.1 we derive governing equations which describe spatial spreading mechanisms of biomass. The feature of these equations is that they are highly nonlinear density-dependent degenerate reaction-diffusion systems comprising two kind of degeneracy: porous medium and fast diffusion. We prove the well-posedness of the obtained equations and study the long-time dynamics of their solutions in terms of a global attractor. Moreover we analyze dependence of solutions on boundary conditions. Our numerical simulations of derived equations lead to mushroom patterns which were observed in the experimental studies.

Section 5.2 is concerned with biofilm growth in a porous medium (e.g. soil) which changes the hydraulic conductivity of the medium (bioclogging), which in turn changes substrate transport, and as a result, the food supply of bacteria. This naturally occurring nonlinear phenomenon is used by engineers to devise microbially based technologies for groundwater protection and soil remediation. We derive bioclogging models that account for the spatial expansion of the bacterial population in the soil and make a numerical analysis of the corresponding reaction-diffusion-convective parabolic systems describing the behaviour of this model. More precisely, it consists of a density-dependent, doubly degenerate diffusion equation that is coupled with the Darcy equations and a transport-reaction equation for growth limiting substrates. It is worth mentioning that, in contrast to previous existing bioclogging models, our model allows bacteria to move into neighbouring void regions when the space becomes locally limited and the environmental conditions are such that further growth of the bacterial population is sustained.

Sections 5.3–5.5 are devoted to multi-species/multi-substrate biofilm models. More precisely in Sect. 5.3 we are interested in antibiotic disinfection of biofilms. In this case the biofilm system consists of the particulate volume fraction of active and inert biomass and the dissolved substrates of nutrients and antibiotics. We derive governing equations describing antibiotic disinfection of biofilms and study the model both analytically and numerically. We prove global in time existence of solutions, but, in contrast to the single species/single substrate model, the uniqueness of solutions remains an open problem. This proof uses among other techniques a positivity criterion, which is formulated and proved in Chap. 3. Moreover, using the difference in characteristic time-scales of the components of our model in the one-dimensional case we derive a dimensionless parameter, the disinfection number, that provides information for the net biomass production preventing antibiotic disinfection.

Section 5.4 deals with a mathematical model that describes how a “good” bacterial biofilm controls the growth of harmful pathogenic bacterial biofilm. The underlying mechanism is a modification of the local protonated acid concentration, which in turn decreases the local pH and, thus, makes growth conditions for the pathogens less favourable, while the control-agent itself is more tolerant to these changes. We give an existence proof for the resulting degenerated mixed-culture biofilm model. Neither a uniqueness nor non-uniqueness result is obtained. We illustrate in our numerical simulations workings of these bio-control mechanisms. In particular, it is shown that pathogens are eradicated first in the deeper layers of the biofilm, close to the substratum, whereas in traditional antibiotic biofilm control first the cells in the outer layers are deactivated.

Section 5.5 is concerned with the role of quorum sensing in biofilm formation. Quorum sensing is a cell-cell communication mechanism used by bacteria to coordinate gene expression and behaviour in groups based on the local density of the bacterial population. We present a model of quorum sensing in biofilm communities, which extends the mono-species biofilm growth model derived in Sect. 5.1 and combines it with a mathematical model of quorum sensing for suspended populations. The dependent model variables are the volume fraction occupied by down-regulated

and up-regulated cells, concentration of signalling molecules, and concentration of the growth limiting nutrient. We prove the well-posedness of the model. In particular, we present for the first time a uniqueness result for this type (multi-component) of problem. Moreover, we illustrate the behaviour of model solutions in numerical simulations.

In the last Chap. 6, we shall illustrate the use of mathematical modelling in the pharmaceutical industry by an example from the development of a blood coagulation treatment with a coagulation factor. More specifically we derive a mathematical model for a blood coagulation cascade set up in a perfusion experiment conducted at the pharmaceutical company Novo Nordisk A/S in Denmark. We investigate the influence of blood flow and diffusion on the blood coagulation pathway by deriving a model consisting of a system of partial differential equations, taking into account the spatial distribution of the biochemical species. The validity of the model is established via positivity criteria proved in Chap. 3. The model is solved using a finite element code in order to illustrate the influence of diffusion and convection on the coagulation cascade with dynamic boundary condition modelling adhesion of blood platelets to a collagen coated surface.

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