

Lecture Notes in Mathematics

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Multiscale Problems in the Life Sciences

From Microscopic to Macroscopic

Lectures given at the Banach Center
and C.I.M.E. Joint Summer School
held in Będlewo, Poland
September 4–9, 2006

Editors:
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Preface

*“... It also happens...
that branches which were thought
to be completely disparate
are suddenly seen to be related ...”*

Michiel Hazewinkel, 1977

During September 4–9, 2006 the Stefan Banach International Center (BC) of the Institute of Mathematics of the Polish Academy of Sciences and the (Italian) International Summer Institute for Mathematics (CIME) jointly organized at the Mathematical Research and Conference Center (MRCC), Będlewo, Poland, the School *From a Microscopic to Macroscopic Description of Complex Systems*. In addition to the main speakers, whose contributions are included in this volume, there were a significant number of participants from 11 countries. In parallel with the School, a workshop on *Modelling Cellular Systems with Applications to Tumor Growth* was organized in the framework of the activity of the EU MCRTN “MRTN-CT-2004-503661”. The courses were targeted at Ph.D. students and young researchers and have had an educational character, whereas the workshop offered presentations on particular applications to modelling tumour growth phenomena.

The aim of the School has been to offer a broad presentation of updated methods suitable to provide a mathematical framework for the development of a hierarchy of models of complex systems in the natural sciences, with special attention to biology and medicine. The mastering of complexity implies the sharing of different tools which require a much higher level of communication between different mathematical and scientific schools, for solving classes of problems of the same nature. Nowadays, more than ever, one of the most important challenges derives from the bridging of parts of a system evolving at different time and space scales, especially with respect to computational affordability. Therefore, the courses have had a rather general character and

method; the main role is played here by stochastic processes, positive semi-groups, asymptotic analysis, continuum theory and game theory.

For many biological systems only non-negative states or solutions make sense. The theory of Banach lattices and positive operators, developed in the series of lectures *Positivity in the Natural Sciences* by Jacek Banasiak, provides a mathematical framework to address such problems. The lectures show how the interplay of positivity and compactness yields very strong results in many fields ranging from well-posedness of the problem at hand, through long time behaviour of solutions (including emergence of chaos), to asymptotic analysis of systems displaying multiple scale phenomena. Theoretical results are applied to a variety of specific problems occurring in natural sciences, including birth-and-death type models that describe the development of drug resistance in cancer cells, blood cells' evolution equation, singularly perturbed models of sole migration, or diffusion approximation of the Fokker–Planck equation.

As a paradigmatic microcosm for all of biology, i.e. as an observable system where mutation and evolution take place, in the course on *Cancer* by Mark Chaplain, the different aspects of the growth phases of a tumour are described (raise query?) solid tumours (the most frequent of all cancers) progress through several key stages of growth from a single transformed/mutated cell, to a multicell spheroid (avascular growth), vascular growth in connection with blood vessels, and finally invasive growth of the local tissue and metastasis to distant sites where secondary tumours occur. Modelling these growth phases involves a mixture of continuum models (ordinary, delay and partial differential equations – reaction–diffusion–taxis equations) and individual-based models (cellular automata, discrete modelling techniques). The lecture notes present a range of mathematical techniques to examine a family of models (qualitative analysis of DEs, asymptotic analysis, numerical analysis and computation) and provide a general framework for developing quantitative and predictive models.

The mathematical framework for searching for links between solutions related to equation modelling at the microscopic, mesoscopic and macroscopic levels is the topic of the course *Links between microscopic and macroscopic description* by Mirosław Lachowicz. Usually, the description of biological populations is carried out on a macroscopic level of interacting sub-populations. The mathematical structures are deterministic reaction–diffusion equations. They describe the (deterministic) evolution of densities of subpopulations rather than the interactions between their individual entities. However, in many cases the description on a micro-scale of interacting entities (e.g. cells) seems to be more appropriate. The problem of relationships between the various scales of description seems to be one of the most important problems of the mathematical modelling of complex systems, e.g. in the modeling of tumour growth. The following strategy can be applied. One starts with the deterministic macroscopic model for which the identification of parameters by an experiment is easier. Then one provides the theoretical framework for modelling at the

microscopic scale in such a way that the corresponding models at the macro- and micro-scales are asymptotically equivalent, i.e. the solutions are close to each other in a properly chosen norm. Then, if the microscopic model is chosen suitably, one may hope that it covers not only the macroscopic behaviour of the system in question, but also some of its microscopic features. The microscopic model by its nature is richer and it may describe a larger variety of phenomena. In mathematical terms, we are interested in the links between the following mathematical structures: at the micro-scale of stochastically interacting entities (cells, individuals,...), in terms of continuous stochastic semigroups, the meso-scale of statistical entities, in terms of continuous nonlinear semigroups related to the solutions of Boltzmann-type nonlocal kinetic equations, and the macroscale of densities of interacting entities in terms of dynamical systems related to reaction–diffusion equations.

The notes on *Rescaling Stochastic Processes: Asymptotics*, by Vincenzo Capasso and Daniela Morale, investigate the links among different scales, from a more probabilistic point of view. As already mentioned, particular attention is being paid to the mathematical modelling of the social behaviour of interacting individuals in a biological population, on the one hand because there is an intrinsic interest in the dynamics of population herding, and on the other hand, as agent-based models are being used in complex optimization problems. Among other interesting features, these systems lead to self-organization phenomena, which exhibit interesting spatial patterns. Here, we show how properties on the macroscopic level depend on interactions at the microscopic level; in particular, suitable laws of large numbers are shown to imply the convergence of the evolution equations for empirical spatial distributions of interacting individuals to nonlinear reaction–diffusion equations for a so-called mean field, as the total number of individuals becomes sufficiently large. As a working example, an interacting particle system modelling social behaviour has been proposed, based on a system of stochastic differential equations, driven by both aggregating/repelling and external forces. To support a rigorous derivation of the asymptotic nonlinear integro-differential equation, compactness criteria for convergence in metric spaces of measures, and problems of existence of a weak/entropic solution have been analyzed. Further the temporal asymptotic behaviour of the stochastic system of a fixed number of interacting particles has been discussed. This leads to the problem of the existence of nontrivial invariant probability measures.

These microscopic interactions between individuals can often be described within game-theoretic models. This theme has been discussed in the notes on *Evolutionary Game Theory and Population Dynamics* by Jacek Miękiś. In such evolutionary models, individuals adapt to a changing environment and are subject to selection pressure and mutations. We will present deterministic and stochastic models of adaptive dynamics and discuss the stability of equilibria in appropriate dynamical systems such as time-delay equations and Markov chains.

VIII Preface

As Co-Directors, we are pleased to thank both institutions, BC and CIME, in particular the former Director of the Institute of Mathematics and founder of MRCC, Professor Bogdan Bojarski, and the Director of CIME Professor Pietro Zecca, for letting us organize the joint school, and for their continuous support. It has had a special meaning at the time of extension of Europe towards the East; in this way a concrete occasion has been offered to the young participants to contribute actively in building a common European Research Area. They have had the chance of experiencing directly that different Schools in Europe may actively contribute to making the European Union a highly competitive scientific community.

Our special thanks are due to our Colleagues, Professors Banasiak, Chaplain and Miękisz, for their careful preparation and stimulating presentation of the material, both at the school and in these Lecture Notes. We thank Dr Gabriela Lorelai Litcanu for her work in preparation of the workshop organized in connection with the courses. All the participants contributed to the creation of an exceptionally friendly atmosphere which also characterized the various social events organized in the beautiful environment of the Będlewo Palace. We thank the Director and the whole staff of MRCC in Będlewo for their warm and efficient hospitality. Thanks are due to Dr Daniela Morale for her editorial assistance during the preparation of this volume.

Milan, Warsaw,
March 2007

Vincenzo Capasso
Miroław Lachowicz

Contents

Positivity in Natural Sciences

<i>Jacek Banasiak</i>	1
1 Introduction	1
1.1 What can go Wrong?	3
1.2 And if Everything Seems to be Fine?	3
2 Spectral Properties of Operators	4
2.1 Operators	5
2.2 Spectral Properties of a Single Operator	7
3 Banach Lattices and Positive Operators	13
3.1 Defining Order	13
3.2 Banach Lattices	15
3.3 Positive Operators	19
3.4 Relation Between Order and Norm	20
3.5 Complexification	23
3.6 Spectral Radius of Positive Operators	24
4 First Semigroups	25
4.1 Around the Hille–Yosida Theorem	27
4.2 Dissipative Operators	28
4.3 Long Time Behaviour of Semigroups	29
4.4 Positive Semigroups	37
4.5 Generation Through Perturbation	39
4.6 Positive Perturbations of Positive Semigroups	42
5 What can go Wrong?	45
5.1 Applications to Birth-and-Death Type Problems	52
5.2 Chaos in Population Theory	59
6 Asynchronous Growth	61
6.1 Essential Growth Bound	61
6.2 Peripheral Spectrum of Positive Semigroups	63
6.3 Compactness, Positivity and Irreducibility of Perturbed Semigroups	67

7	Asymptotic Analysis of Singularly Perturbed Dynamical Systems . . .	75
7.1	Compressed Expansion	77
	References	87

Rescaling Stochastic Processes: Asymptotics

	<i>V. Capasso and D. Morale</i>	91
1	Introduction	91
1.1	First Examples of Rescaling	95
2	Stochastic Processes	97
2.1	Processes with Independent Increments	100
2.2	Martingales	100
2.3	Markov Processes	103
2.4	Brownian Motion and the Wiener Process	109
3	Itô Calculus	110
3.1	The Itô Integral	110
3.2	The Stochastic Differential	112
3.3	Stochastic Differential Equations	113
3.4	Kolmogorov and Fokker-Planck Equations	115
3.5	The Multidimensional Case	117
4	Deterministic Approximation of Stochastic Systems	118
4.1	Continuous Approximation of Jump Population Processes	118
4.2	Continuous Approximation of Stochastic Interacting Particle Systems	120
4.3	Convergence of the Empirical Measure	122
5	A Specific Model for Interacting Particles	128
5.1	Asymptotic Behavior of the System for Large Populations: A Heuristic Derivation	130
5.2	Asymptotic Behavior of the System for Large Populations: A Rigorous Derivation	134
6	Long Time Behavior: Invariant Measure	137
A	Proof of the Identification of the Limit ρ	141
	References	144

Modelling Aspects of Cancer Growth: Insight from Mathematical and Numerical Analysis and Computational Simulation

	<i>Mark A.J. Chaplain</i>	147
1	Introduction	147
1.1	Macroscopic Modelling	148
1.2	Cancer Growth and Development	149
2	Modelling Avascular Solid Tumour Growth	150
2.1	Introduction	150
2.2	Linearised Stability Theory	151
2.3	The Role of Pre-Pattern Theory in Solid Tumour Growth and Invasion	153

2.4	Model Extension: Application to a Growing Spherical Tumour	156
2.5	Discussion and Conclusions	157
3	Mathematical Modelling of T-Lymphocyte Response to a Solid Tumour	160
3.1	Introduction	160
3.2	The Mathematical Model	161
3.3	Travelling Wave Analysis	173
3.4	Discussion	178
4	Mathematical Modelling of Cancer Invasion	180
4.1	Introduction	180
4.2	Cancer Invasion of Tissue and Metastasis	182
4.3	Proteolysis and Extracellular Matrix Degradation	182
4.4	The Mathematical Model of Proteolysis and Cancer Cell Invasion of Tissue	184
4.5	Nondimensionalisation of the Model Equations	187
4.6	Model Analysis	188
4.7	Spatially Uniform Steady States	188
4.8	Taxis-Driven Instability and Dispersion Curves	188
4.9	Numerical Results	189
4.10	Numerical Technique	190
4.11	Computational Simulation Results	191
4.12	Discussion and Conclusions	191
5	Summary	195
	References	195

Lins Between Microscopic and Macroscopic Descriptions

	<i>Miroslaw Lachowicz</i>	201
1	Introduction	201
2	Microscopic (Stochastic) Systems	205
3	Generalized Kinetic Models	213
4	Diffusive Limit	227
5	Links in the Space-Homogeneous Case	231
6	Coagulation-Fragmentation Equations	243
7	The Space-Inhomogeneous Case: Reaction-Diffusion Equations	245
8	Reaction-Diffusion-Chemotaxis Equations	252
	References	262

Evolutionary Game Theory and Population Dynamics

	<i>Jacek Miękisz</i>	269
1	Short Overview	269
2	Introduction	270
3	A Crash Course in Game Theory	273
4	Replicator Dynamics	277
5	Replicator Dynamics with Migration	280

XII Contents

6	Replicator Dynamics with Time Delay	285
6.1	Social-Type Time Delay	285
6.2	Biological-Type Time Delay	288
7	Stochastic Dynamics of Finite Populations	290
8	Stochastic Dynamics of Well-Mixed Populations	292
9	Spatial Games with Local Interactions	298
9.1	Nash Configurations and Stochastic Dynamics	298
9.2	Ground States and Nash Configurations	300
9.3	Ensemble Stability	303
9.4	Stochastic Stability in Non-Potential Games	306
9.5	Dominated Strategies	310
10	Review of Other Results	311
	References	312
	List of Participants	317
	Index	319