
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.

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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.

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