

PREFACE

This volume contains papers presented at the workshop *Stochastic Models in Biological Sciences* held at the Stefan Banach International Mathematical Center in Warsaw, 29 May–2 June 2006. The workshop was organized in the framework of the European Science Foundation program “Phase Transitions and Fluctuation Phenomena for Random Dynamics in Spatially Extended Systems”.

For several years now, biology has attracted the renewed interest of mathematicians and physicists. Apart from the development of new statistical algorithmic procedures to organize huge data sets, there is a need for analytical methods helping to understand physical and biochemical processes on the molecular level. The aim of our exploratory workshop on stochastic models in biology was to broaden the area of research of the mathematical statistical mechanics/stochastic processes community and to learn about issues and problems in biology which could be addressed by mathematics and theoretical physics. The workshop had a strong tutorial character. It attracted about 40 Ph.D. students and post-docs and introduced them to new interdisciplinary topics and research problems. All invited talks were pedagogical introductions to particular fields and such are the papers presented in this volume.

The leading motif of the workshop was the analysis of stochastic dynamics of finite populations. Stochastic effects can be modeled by Markov chains, stochastic processes or stochastic differential equations. Such stochastic models are analyzed from mathematical, physical and biological points of view. We identified five research areas which in our opinion are mature enough to allow an application of mathematical methods of stochastic analysis. More specifically, in many biological models we deal with systems of many interacting entities like genes in population genetics, species in evolutionary ecology, proteins in regulatory biochemical networks, or players in evolutionary games. The number of interacting objects is finite and often very small and therefore their stochastic fluctuations play a decisive role in the time evolution of a given system. Topics discussed during the workshop have included evolutionary genetics and ecology, molecular motors, genetic regulatory networks and evolutionary game theory.

Regulation of gene expression is a chemical process involving many coupled elementary chemical reactions. For this reason, it is frequently modeled by using classical chemical kinetics in which the system is represented by a set of differential equations describing the time evolution of molecular concentrations. However, gene expression processes occur in

very small volumes and involve very small numbers of molecules. Therefore, it is expected that significant random fluctuations occur.

Ofer Biham *et al.* present Monte-Carlo simulations of the master equation for certain regulatory systems. They show that in some cases, deterministic equations produce only steady state solutions but in the stochastic dynamics the system exhibits bistability and therefore functions as a switch.

Adam Bobrowski describes similar regulatory systems by piece-wise deterministic Markov processes—stochastically coupled ordinary differential equations. He discusses asymptotic (in time) behaviour of such processes and a limiting behaviour when certain parameters are large.

Long-run behaviour of different populations can be often described within game-theoretic models. In replicator dynamics, infinite populations evolve deterministically toward stationary points. However, we have to take into account random matching of players, random perturbations of their rationality in social models, and mutation and recombination in genetic models.

Jens Christian Claussen describes various stochastic dynamics of finite populations of interacting players such as the Moran process or a local update process. He then performs the infinite population limit of appropriate Fokker-Planck equations and obtains respectively a replicator dynamics or an adjusted replicator dynamics.

György Szabó discusses mechanisms of cooperation in evolutionary games of the Prisoner's Dilemma. He studies effects of pay-offs and noise on the level of cooperation in various stochastic dynamics of finite populations. In particular, he shows that in some models, the noise actually enhances the cooperative behaviour.

The construction of nonequilibrium statistical mechanics is expected to take great advantage from the study of biological models where nonequilibrium fluctuations are important. Most relevant studies are those of biological transport and its modeling via variations of exclusion models, and of molecular motors which are often seen as the small-scale chemical engines by which life processes are sustained. Physically inspired questions of efficiency and of the balances between dissipation and production can be studied here in a fully biological context.

The paper of Mauro Mobilia *et al.* discusses variations on nonequilibrium interacting particle systems as they are known in the literature on stochastic lattice gases. Here, however, their biological realization and relevance is stressed and it is sought to identify some generic principles of active transport.

The paper by Reinhard Lipowsky and Steffen Liepelt addresses molecular motors in the framework of models of nonequilibrium statistical mechanics. In particular, the thermodynamics of the motor systems and its ATP hydrolysis is discussed in the framework of recent developments in the understanding of entropy production.

Population genetics is concerned with the study of the genetic composition of populations. This composition may be changed by selection, mutation, recombination, mating structure, migration, and other genetic, ecological, and evolutionary factors. Major themes are the investigation of the mechanisms that generate and maintain genetic variability, the study of how this variation affects evolutionary change, and the inference

of past evolutionary events from contemporary DNA sequence data. Thus, population genetics provides the basis for understanding biological evolution.

Ellen Baake and Robert Bialowons study two stochastic population models with mutation and selection, the first relying on a multitype branching process, the second being the Moran model in which lineages are no longer independent. They analyze the properties of the stationary distributions forwards in time, which result from evolution, and the asymptotic distributions backwards in time. In both backwards models, the authors concentrate on the ancestry of single individuals rather than the genealogies of samples of individuals.

Michael Baake investigates the evolution of genetic sequences with repeated units, such as microsatellites. The copy numbers of these units vary within and between species. Baake analyzes a class of recombination models with single crossovers and studies the resulting equilibrium distributions. The nonlinear and infinite-dimensional nature of these models makes them interesting from a purely mathematical point of view: they can be viewed as nonlinear analogues of Markov chains.

Alison Etheridge's contribution also focuses on the interplay between forwards-in-time and backwards-in-time models. She starts by describing Kingman's, now classical, coalescent process which provides an elegant description of the genealogical relationship among individuals under neutral evolution. Then, she treats various important generalizations which include selection, spatial structure, or large-scale extinction-recolonization events.

Paul Higgs considers the way in which population genetics and phylogenetics are linked. In phylogenetics, species are typically represented by a single DNA sequence and properties of the substitution process are used to infer evolutionary (species) trees. This is clearly an over-simplification because species are genetically variable. The author demonstrates how phylogenetic modeling can benefit by taking population-genetic considerations into account.

Reinhard Bürger
Christian Maes
Jacek Miękisz

