European teams in mathematical biology

In each issue we present some of the European groups working in the field of mathematical biology. We try to cover different subjects and geography. If you think some group should be portrayed in the next issue, please let us know. Enjoy!

Applied Analysis and Modelling in Biosciences Group headed by Anna Marciniak-Czochra is located at the Institute of Applied Mathematics (IAM), Interdisciplinary Center of Scientific Computing (IWR) and BIOQUANT Center, Heidelberg University.

Research focus: The interdisciplinary expertise of the group lies in the areas of applied mathematics and mathematical and computational biosciences. Specifically, our field of focus is the dynamics of self-organisation and structure formation in developmental and regeneration processes and in cancer. The aim of our research is to develop and analyse mathematical models of the dynamics of structure formation in multicellular systems and to develop new mathematical methods of modelling of such complex processes. Accordingly, we collaborate closely with experimentalists and clinicians, and pursue mathematical problems arising in modelling of biological processes, both analytically and computationally.

Mathematical areas of groups focus are partial differential equations, dynamical systems, and multiscale and singular perturbation analysis. Methods of mathematical analysis are used to formulate the models and to study the spatio-temporal behaviour of solutions, such as stability and dependence on characteristic scales, geometry, and sensitivity to initial data and key parameters. Our analytical research includes (1) analysis of pattern formation mechanisms in the systems of reaction-diffusion type; (2) analysis of nonlinear structured population models; linking continuous and discrete structures; (3) derivation of effective models from first-principles to describe transport of cells and molecules through heterogeneous media such as biological tissues. Particular attention is paid to methods of model upscaling and reduction.

Applications in biology and medicine: Mathematical models and methods developed by the group are applied to specific problems of developmental and cell biology, as listed further on.

(1) Pattern formation

The first area of focus is modeling, analysis and simulation of symmetry breaking and pattern formation in developmental biology. Together with the experimental group of Thomas Holstein (Center for Organismal Studies (COS), Heidelberg University), we investigate the role of different components of the complex spatio-temporal Wnt signaling in development and regeneration of the fresh water polyp Hydra. We focus on models coupling non-diffusive cellular processes with diffusing signaling factors, which we derived using homogenization techniques. Our results transcend the classical Turing theory. We investigate how the structure of nonlinearities determines model dynamics and lead to pattern formation phenomena. We explore multistability and hysteresis in signaling, diffusion-driven instability or interplay between the two mechanisms. We also investigate a new pattern-formation mechanism based on coupling of chemical signaling with tissue mechanics, described by 4th order PDEs. Numerical simulations of the mechano-chemical models show symmetry breaking and formation of patterns similar to those observed in experiments. Currently, we work on a new approach to model identification combining statistical methods of parameter estimation with singular perturbation analysis of the hypothetical mechanisms.
(2) Stem cell dynamics in development, regeneration and cancer

The second, related, line of our studies is mathematical modeling, analysis, and simulation of dynamics of stem cell self-renewal, differentiation, and clonal evolution in different contexts. In close collaboration with developmental biologists (Lazar Centanin and Jan Lohmann, COS, Heidelberg University), we established multi-scale models of stem cell-initiated organogenesis. We built models of plant meristem development providing mechanistic understanding of meristem regulations and mutant phenotypes. Furthermore, we proposed models identifying functional heterogeneity of stem cells in development of the fish respiratory organ.

The role of intercellular heterogeneity is also the topic of our research in aging and regeneration in adult neurogenesis (collaboration with experimental labs of Ana Martin-Villalba, DKFZ, Heidelberg and Francois Guillemot, Francis Crick Institute, London). Integrating mathematical models with experimental data allows identifying stem cell properties that change with age to compensate reduction of the stem cell pool and to maintain life-long neurogenesis.

In a collaboration with hematologists (Anthony D. Ho, Carsten Müller-Tidow and Christoph Lutz, Heidelberg Medical Clinic), we develop multi-compartment and structured population models that allow explaining observations on regeneration processes in hematopoiesis, development of leukemia, clonal selection and resulting therapy resistance in blood cancers. The study reveals different scenarios of possible cancer initiation and provides qualitative hints to treatment strategies. The models, combined with clinical data, may serve as a tool of personalised (targeted) therapy and provide insight into healthy and leukemic stem...
cell behavior in addition to molecular or biological classification of these cells.

Different areas of applications require diversified mathematical methods ranging from stochastic models to partial differential equations, integro-differential and ordinary differential equations. Development and comparison of different models often requires new mathematical and computational approaches and leads to new analytical results.

(3) Systems Medicine

We find it important to develop models that may contribute not only to a mechanistic understanding of the underlying processes but also to integration of this knowledge with experimental and patient data and providing a tool for patient stratification, risk prediction and treatment planning. We focus on mathematical hematology projects, working on applications of mathematical models to acute myeloid leukemia and multiple myeloma (collaboration with Heidelberg Medical Clinic V). Our blood production models have been also applied to predict onset of sepsis and SIRS in intensive care patients. The latter is a collaboration with Mannheim University Clinic within the SCIDATOS Consortium (Scientific Computing For Improved Detection And Therapy of Sepsis).

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More about our research, projects and publications can be found at http://www.biostruct.uni-hd.de.

Meeting Reports

The International Conference “Dynamical Systems Applied to Biology and Natural Sciences - DSABNS” is a well established international scientific event, organized every year since 2010, in February. The DSABNS conferences present both methods from the theory of dynamic systems, stochastic processes and statistical inference and practical applications to research topics in population dynamics, eco-epidemiology, epidemiology of infectious diseases, molecular and antigenic evolution and other fields in the natural sciences.

Without registration fee, this series of conferences favours the participation of researchers and students from different countries of the world in order to present their recent scientific results. The 11th DSABNS Conference was held in a friendly atmosphere at the Department of Economics and Management of the University of Trento, from 4 to 7 February 2020, with the participation of 168 researchers and students from 40 different countries.

The Conference programme (see http://www.dsabns2020.maths.unitn.it/index.html) included:

- 2 Public Lectures and 10 Plenary Talks:
  - Maíra Aguiar, University of Trento, Trento, Italy & Basque Center For Applied Mathematics (BCAM), Bilbao, Spain
  - Gianfranco Anfora, University of Trento, Trento, Italy
  - Konstantin Blyuss, University of Sussex, Sussex, UK (online lecture)
  - Susanne Ditlevsen, University of Copenhagen, Copenhagen, Denmark
  - Bob W. Kooi, VUUniversity Amsterdam, Amsterdam, The Netherlands
  - Bas Kooijman, VU University Amsterdam, Amsterdam, The Netherlands