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Pasquale Ciarletta • Thomas Hillen • Hans Othmer •
Luigi Preziosi • Dumitru Trucu

Mathematical Models and Methods for Living Systems

Levico Terme, Italy 2014

Luigi Preziosi • Mark Chaplain • Andrea Pugliese
Editors

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Preface

Understanding the mechanisms used by cells to move, to self-organise and to develop in tissues is not only fundamental in embryogenesis but is also relevant in tissue engineering and in other environmental and industrial processes involving the growth and homeostasis of biological systems, e.g. biofilm growth. Growth and organisation processes are also important in many diseases and tissue degeneration and regeneration processes, such as tumour growth, tissue vascularization, heart and muscle functionality and cardiovascular diseases.

In the last decade there has been a burst in the development of mathematical models aimed at studying the behaviour of such biological systems. In doing that, the most difficult point to be taken care of is that by definition biological systems are alive which means that, for instance, they do not respond in a passive way to external chemical and mechanical stimuli, but react actively. They are also able to modify their internal state according to the surrounding environment. Modelling this aspect requires to deeply question and re-analyse whether the classical tools used to model inert matter are proper enough to describe active behaviours. For instance, in continuum mechanics, the concept of evolving natural configurations was proposed to describe the active behaviour of cells, cell ensembles and entire tissues, e.g. muscle and heart (see, for instance, Chap. 4).

In some cases, it is necessary to link mathematical techniques that appear very different. For instance, the study of networks describing chemical reactions occurring inside the cells is interlinking more and more with kinetic theories and continuum mechanics. In fact, more in general what happens at a certain spatial scale, i.e. subcellular, cellular or tissue scale, is logically and functionally linked with what happens at other scales (see, for instance, Chap. 5). For instance, the behaviour of a cell depends on the one hand on the interaction it has with the surrounding environment (see, for instance, Chap. 3) and on the other hand on the chemical reactions occurring inside it (see, for instance, Chap. 1). The two aspects are then related through feedback loops, so that describing a phenomenon without considering what happens at a smaller or at a larger scale results in a strong oversimplification. From the mathematical point of view, this leads to the need of using multiscale methods and upscaling techniques to connect phenomena occurring at different scales, like the diffusive limits described in Chap. 2.

Keeping this in mind, the aim of the C.I.M.E.-C.I.R.M. summer school on Mathematical Models and Methods for Living Systems was to give an introduction to several mathematical models and methods used to describe the behaviour of living systems. In more detail, then

- Chapter 1, authored by Hans Othmer, deals with models of cell motion starting from the reaction networks occurring at the cytoskeleton level to end with the motion of cell aggregates. In particular, the chapter gives an overview of how chemical and mechanical signals are integrated, how spatial differences in signals are produced and how propulsive and adhesive forces are controlled.
- Chapter 2, authored by Thomas Hillen and Amanda Swan, having in mind the modelling of cell motion, deals with transport models and their relations with individual-based random walk models and reaction-diffusion equations. The model is then applied to bacterial movement, amoeboid movement of cells and the spread of metastasis in anisotropic tissues like the growth of glioblastoma in the brain.
- Chapter 3, authored by Luigi Preziosi and Marco Scianna, focuses on the interaction of cells with the surrounding environment, taking into account several phenomena occurring at the cellular level, such as the role of the nucleus stiffness and the adhesion mechanisms between cells and the fibre network forming the extracellular matrix. With this aim in mind, several mathematical models are introduced, e.g. age-structured models, cellular Potts models and continuum mechanics models.
- Chapter 4, authored by Pasquale Ciarletta and Valentina Balbi, deals with a continuous chemomechanical approach to morphogenesis. The basic evolution laws for both volumetric and interfacial processes are derived and then applied to the study of pattern formation in biological systems treated either as fluids or as solids.
- Chapter 5, authored by Dumitru Trucu, Pia Domschke, Alf Gerisch, and Mark A.J. Chaplain, deals with a multiscale model of cancer invasion. The main focus of the modelling is how the molecular processes occurring at the level of individual cells (micro-scale) and the processes occurring at the tissue level (cell population or macro-scale) are connected and affect each other. Initially a single tissue scale model of cancer invasion is presented based around a system of non-local partial differential equations where the specific roles of cell-cell adhesion and cell-matrix adhesion are explored. This leads naturally to the development of a general spatio-temporal-structured cell population modelling framework which considers the role of cell-receptor dynamics in cancer invasion. Finally, a multiscale moving boundary modelling framework for cancer invasion is developed. In each case, computational simulations are presented which all aim to predict how far cancer cells can invade into healthy normal tissue.

As a concluding remark, we express our deepest gratitude to all the people that have contributed to the success of this C.I.M.E.-C.I.R.M. summer school: the

lecturers, the authors that have contributed to this volume, the participants and all the persons in charge of the organisation. We thank both C.I.M.E. and C.I.R.M. for their financial support, without which the school and therefore this lecture note would have never been possible.

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