Mathematical models for bio-medical sciences

Lake Como School of Advanced Studies, June 20-24, 2022

Home

Mathematical Models for Bio-Medical Sciences

June 20-24, 2022

In the scientific community a growing interest arises on the mathematical formulation and study of evolution systems stemming from Biology and Health Sciences, focusing in particular on tumor growth models, bio-materials and complex systems.

This subject turns out to be particularly significant for Mathematical Biology especially during these years, in which a joint venture of the European Mathematical Society (EMS) and the European Society for Mathematical and Theoretical Biology (ESMTB) started. It results that applications of Mathematics in Bio-medical sciences are completely opening new pathways of interactions and they constitute a huge source of new mathematical problems.

The school aims to gather well-known experts in modeling of Bio-medical systems and mathematicians directing their research to the analysis of qualitative properties of solutions of the related partial differential equations and their implication on the biological behaviour. The main objective is to attract students interested in mathematical modeling and analysis in applied sciences.

- ***School Directors***:
  Pierluigi Colli – pierluigi.colli@unipv.it
  Elisabetta Rocca – elisabetta.rocca@unipv.it

  Dipartimento di Matematica "*F. Casorati*", Università degli Studi di Pavia.
  Scuola di Dottorato di Milano Bicocca

- ***Organizing Committee:***

Abramo Agosti (Università degli Studi di Pavia)
Andrea Aspri (Università degli Studi di Milano)
Matteo Fornoni (Università degli Studi di Pavia)

- ***Invited speakers:***
  Helen Byrne (Oxford University)
  José Antonio Carrillo (Oxford University)
  Harald Garcke (University of Regensburg)
  John Lowengrub (University of California, Irvine)

UNIVERSITÀ DI PAVIA
Dipartimento di Matematica "F. Casorati"

Università degli Studi di Milano Bicocca
Scuola di Dottorato

Gruppo Nazionale per l'Analisi Matematica
la Probabilità e le loro Applicazioni – INDAM

European Mathematical Society

Mathematical models for bio-medical sciences

Lake Como School of Advanced Studies, June 20-24, 2022

Courses

Helen Byrne (University of Oxford) https://www.maths.ox.ac.uk/people/helen.byrne

Approaches to modelling the growth and response to treatment of solid tumours

Abstract
There is a long tradition of developing mathematical and computational models that describe the growth and response to treatment of Solid tumours. Such models range from simple, phenomenological models to detailed mathematical and computational models. The phenomenological models typically contain small numbers of parameters and, as a result, can be Validated and parameterised against available experimental and/or clinical data. By contrast, more detailed models Are typically too complex to be fully validated against data, although they can generate valuable mechanistic insight into the processes that regulate tumour growth. In this lecture course, I will introduce a range of mathematical approaches that have been used to study different aspects of tumour growth, highlighting their relative strengths And weaknesses, while also identifying directions for future investigation.

Lecture 1, will focus on one-dimensional, continuum models of avascular tumour growth, formulated as non-standard systems of partial and integro differential equations. We will learn how the earliest models of avascular tumour growth can be derived from more complex, multiphase models PDE models and also discuss their extension to account for Vascular tumour growth.

Lecture 2, we will extend the models from Lecture 1 to investigate tumour responses to treatment with, e.g., radiotherapy, chemotherapy and immunotherapy. We will also compare the predictions of the PDE models with those generated from simpler, phenomenological ones. Attention will then turn to PDE models of tumour angiogenesis, the process by which avascular tumours stimulate the growth of a new blood vessels from pre-existing ones, And transition from relatively harmless, localised masses to rapidly growing and potentially life-threatening vascular tumours. Accordingly, in

Lecture 3, we will study the classical, snail-trail model of angiogenesis, focussing on the assumptions on which it is based, its solutions and its relationship to alternative mesoscopic and microscopic models The course will conclude, in

Lecture 4, with an introduction to hybrid, multi scale models of avascular and vascular tumour growth. We will learn How these computationally intensive models couple sub cellular processes (such as cell cycle progress and protein production) with cell scale processes (such as cell death and proliferation) And macro scale phenomena (such as the transport of nutrients and drugs within the tumour microenvironment). We will discuss the insight that these models can generate and the challenges associated with their validation.

José Antonio Carrillo (University of Oxford)
http://www.maths.ox.ac.uk/people/jose.carrillodelaplata

Cell-cell Adhesion micro-and macroscopic models via Aggregation-Diffusion systems

Abstract
We discuss microscopic and continuum cell-cell adhesion models and their derivation based on the underlying microscopic assumptions. We analyse the behavior of these models at the microscopic level based on the concept of H-stability of the interaction potential. We will derive these macroscopic limits via mean-field assumptions. We propose an improvement on these models leading to sharp fronts and intermingling invasion fronts between different cell type populations. The model is based on basic principles of localized repulsion and nonlocal attraction due to adhesion forces at the microscopic level. The new model is able to capture both qualitatively and quantitatively experiments by Katsunuma et al. (2016) [J. Cell Biol. 212(5), pp. 561–575]. We also review some of the applications of these models in other areas of tissue growth in developmental biology. We will analyse the mathematical properties of the resulting aggregation-diffusion and reaction-diffusion systems based on variational tools. We will discuss the numerical methods used for their simulation in the discussion sessions.

Harald Garcke (University of Regensburg)
http://www.mathematik.uni-regensburg.de/Mat8/lst/

Phase field approaches for tumour growth

Abstract
Modelling of tumour growth is one of the challenging frontiers of applied mathematics. In the last years, phase field models for tumour growth have been studied intensively. Alike classical free boundary models they use a continuum approach to describe the growth of tumours. However, an advantage to free boundary models is that phase field models allow for topology changes like break up and coalescence. In addition, phase field methods can be used numerically without an explicit tracking of the interface which is necessary for free boundary models. In my talks I will introduce several macroscopic models for tumour growth in which cell-cell adhesion effects are taken into account with the help of a Ginzburg–Landau type energy. The resulting evolution equation is a Cahn-Hilliard equation taking source and sink terms into account. In addition, nutrient diffusion is incorporated by a coupling to a reaction-equation diffusion. I will show existence, uniqueness and regularity results. In addition, several continuous dependence results are shown. I will also discuss how to couple the system to an internal velocity field which either solves a Darcy-type or a (Navier-)Stokes system or a viscoelastic system. Using matched asymptotics, the phase-field systems are related to classical free boundary problems. Finally, using optimisation theory and reduced order modelling I will describe how parameter in the system can be estimated in a patient specific way. In all lectures properties of solutions will be illustrated with the help of numerical simulations.

John Lowengrub (University of California, Irvine)
https://www.math.uci.edu/people/john-lowengrub

Multiscale models of complex biological systems: Growth, patterning and morphogenesis

Complex biological systems such as developing tissues and growing tumors are characterized by nonlinear interactions among many dynamic components. Therefore, it is now clear more than ever that relying on experimental tools alone to understand these complex systems is not sufficient — mathematical, statistical, and computational approaches are becoming increasingly indispensable. In this course, we will develop and analyze mathematical models of selected complex biological and biomedical systems and show how these models can be simulated numerically. We demonstrate how to constrain and calibrate the models using experimental data and how both the models and their solutions provide insight into biological and biomedical systems. A major challenge in such studies is to properly integrate information across multiple scales that is increasingly more feasible to collect from experiments. We will discuss this point as well as advantages and disadvantages of various modeling approaches, which point the way to future studies.

Lecture 1. *Image-based modeling*. Here, we focus on Fisher-Kolmogorov-based models that can account for proliferation, invasion, deformation and mass effects. We apply the models to brain tumors and we demonstrate how multimodal medical scans can be used to calibrate the models. We discuss how the models can be personalized and can be used for treatment planning.

Lecture 2. *Multiscale model development.* Here, we discuss strategies for coarse-graining systems of individual cells to obtain continuum models at a variety of scales by borrowing ideas from statistical physics, materials science and applied mathematics. We present continuum models at the cell scale and demonstrate how to obtain new continuum models at the tissue-scale with parameters that can be directly obtained from cell scale measurements. We relate the new systems with previously developed models.

Lecture 3. *Multiscale models of morphogenesis.* The regulation of cell division, cell sizes and cell arrangements is central to tissue growth and morphogenesis. Here, we discuss mathematical modeling approaches of tissue morphogenesis. We account for feedback regulation of cell lineage progression and demonstrate how the emergence of patterned growth from which sharply-demarcated buds and fingers readily emerge, either spontaneously or in response to transient external signals.

Lecture 4. *Multiscale models of tumor growth.* Cancer arises in cells that are actively engaged in collective, coordinated, and tightly controlled behaviors that have been exquisitely tailored to ensure reliable size control, homeostasis, and response to injury. Many of the distinctive characteristics of cancers result from the fact that transformed cells continue to be bound by constraints and rules associated with such collective behaviors, even as they progressively escape from some of them. We develop, analyze and simulate mathematical models of the spatiotemporal dynamics of heterogeneous cell populations and dysregulated cell-to-cell signaling. We use the models to investigate the emergence and consequences of non-genetic heterogeneity, focusing on colon cancer as an example.

Mathematical models for bio-medical sciences

Lake Como School of Advanced Studies, June 20-24, 2022

Program

M2BS	Monday 20	Tuesday 21	Wednesday 22	Thursday 23	Friday 24
09.00-10.30		J.A. Carrillo	H. Garcke	J.A. Carrillo	H. Byrne
10.30-11.00		Coffee break	Coffee break	Coffee break	Coffee break
11.00-12.30		H. Garcke	J.A. Carrillo	H. Byrne	J. Lowengrub
12.30-14.00		Lunch	Lunch	Lunch	Lunch
14.00-14.15	Opening				
14.15-15.45	H. Byrne	H. Garcke	H. Byrne	J.A. Carrillo	
15.45-17.15	H. Garcke	J. Lowengrub	J. Lowengrub	J. Lowengrub	
17.15-17.45	Coffee break	Coffee break	Coffee break	Coffee break	
17.45-18.45	15 minutes talks by G.L. Celora, S. Cygan, D. Katsaounis, E. Leschiera	5 minutes poster presentations by K. Alexiou, J.-P. Bäcker, F. Ballatore, G. Chiari, A. Di Primio, C. Elbar, M. Fornoni, P. Hüttl	5 minutes poster presentations by E. Ipocoana, W. Martinson, A. Massimini, D. Morselli, A. Poiatti, L. Schmeller, J. Skrzeczkowski, W. van Oosterhout, S. Wolff-Vorbeck	15 minutes talks by Y. Liu, G. Lucci, A. Signori, C. Villa	