CEMRACS 2018

Numerical and Mathematical Modeling for Biological and Medical Applications: Deterministic, Probabilistic and Statistical Descriptions

CIRM, Luminy
Marseille, Bouches du Rhône
16 July - 24 August 2018

Summer School Courses
July 16-20, 2018

Thierry Colin (SOPHiA GENETICS)
Tuesday 20:00
Industrial experience testimonial
Abstract: La modélisation en oncologie est en pleine expansion au niveau de la recherche internationale et de nombreux résultats, de nombreuses techniques, de nombreux modèles sont disponibles pour exploiter les données disponibles pour les études précliniques, cliniques ou bien issus de la routine. Néanmoins, pour l'instant, force est de constater que pour ainsi dire aucun de ces modèles n'est arrivé jusqu'au patient. Je tenterai de montrer à travers le transfert du projet "Nenuphar" chez SOPHiA GENETICS quels sont les obstacles et comment on peut espérer les contourner.

Pierre Degond (Imperial College, London)
Tuesday 17:30 – 19:00, Friday 9:00 – 10:30

Modeling emergence in biology
Abstract: Emergence is a process by which coherent structures arise through interactions among elementary entities without being directly encoded in these interactions. In this course, we will address some of the key questions of emergence such as the deciphering of the hidden relation between individual behavior and emergent structures. We will start with presenting biologically relevant examples of microscopic individual-based models (IBM). Then, we will develop a systematic coarse-graining approach and derive corresponding coarse-grained models (CGM) using mathematical kinetic theory as the key methodology. We will highlight that novel kinetic theory concepts need to be developed as new mathematical problems arise with emergent systems such as the lack of conservations, the build-up of correlations, or the presence of phase transitions (or bifurcations). Our goal is to show how kinetic theory can be used to provide better understanding of emergence phenomena taking place in a wide variety of biological contexts.

Jean-Frédéric Gerbeau (Inria Paris)
Thursday 15:30 – 17:00, Friday 13:30 – 15:00

Fluid-Structure Interaction and Hemodynamics
Abstract: In these lectures, I will review various concepts useful to Fluid-Structure Interaction algorithms: energy conservation, added-mass effect, implicit and explicit coupling. I will show the progress achieved in the coupling algorithms over the last decade, with recent results for cardiac valves, and I will address some inverse problems issues in hemodynamics.

Florence Hubert (Université Aix–Marseille)
Monday 14:00 – 15:30, Tuesday 9:00 – 10:30

Introduction to pharmacokinetics and pharmacodynamics of anticancer drugs
Abstract: This course aims to present some deterministic models used in oncology to understand the efficiency of anticancer drugs. Drugs are first transformed by body, before to produce an effect on the disease. The study of the drug's transformation is called pharmacokinetics, whereas the study of drug's efficiency or toxicity is called pharmacodynamics. We will present examples ODE's systems used to model the pharmacokinetics of anticancer drugs and examples of simple ODE's or PDE's systems used to predict a cancer evolution in a preclinical or clinical setting.

Nathalie Krell (Université Rennes 1)
Monday 17:30 – 19:00, Tuesday 15:30 – 17:00

When PDMP naturally appear to model biological problems (grow of bacteria, interacting spiking neurons)
Abstract: I will first present PDMP's (Piecewise Deterministic Markov Processes) thanks to biological models: the growth of bacteria, interacting spiking neurons, the moving of bacteria. After giving the definition and some classical properties of PDMP, I will make some statistical inferences. Through the case of colony of growing bacteria, I will show how to deal with a process which takes its value in $\mathbb{R}^{\mathbb{N}}$ and no only in $\mathbb{R}$. This case is not so complicated since conditionnally on the size at birth the bacteria evolve independently, which enables us to use a many to one formula. Using the example of systems of interacting neurons, I will explain how we can get through more dependency: here when a neuron spikes, the spike changes the membrane potential of the other neurons.

References

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Bertrand Maury (Université paris Sud)
Thursday 11:00 – 12:30, Wednesday 17:30 – 19:00, Thursday 20:00 Start up presentation

Mathematics behind some phenomena in crowd motion : Stop and Go waves and Capacity Drop.

Abstract: This minicourse aims at providing tentative explanations of some specific phenomena observed in the motion of crowds, or more generally collections of living entities. The first lecture shall focus on the so-called Stop and Go Waves, which sometimes spontaneously emerge and persist in crowds in motion. We shall present a general class of dynamical systems which are likely to exhibit this type of instabilities, and emphasize the critical role of two basic ingredients: the asymmetry of interactions, and any sort of delay in the transmission of information through the network of entities. The second lecture will address the Capacity Drop Phenomenon (decrease of the flux though a bottleneck when the upstream density becomes too high), and the more paradoxical Faster is Slower Effect (in some regimes, attempts to go quicker may slow down the overall process). We shall in particular detail how an accurate description of the relative position of entities (at the microscopic level) is crucial to recover and understand those effects.

Sylvie Méléard (Ecole Polytechnique)
Wednesday 11:00 – 12:30, Thursday 9:00 – 10:30

Stochastic dynamics for adaptation and evolution of microorganisms

Abstract: We present a model for the dynamics of a population of bacteria with a continuum of traits, who compete for resources and exchange horizontally (transfer) an otherwise vertically inherited trait with possible mutations. Competition influences individual demographics, affecting population size, which feeds back on the dynamics of transfer. We consider a stochastic individual-based pure jump process taking values in the space of point measures, and whose jump events describe the individual reproduction, transfer and death mechanisms. In a large population scale, the stochastic process is proved to converge to the solution of a nonlinear integro-differential equation. When there are only two different traits and no mutation, this equation reduces to a nonstandard two-dimensional dynamical system. We show how crucial the forms of the transfer rates are for the long-term behavior of its solutions. We describe the dynamics of invasion and fixation when one of the two traits is initially rare, and compute the invasion probabilities. Then, we study the process under the assumption of rare mutations. We prove that the stochastic process at the mutation time scale converges to a jump process which describes the successive invasions of successful mutants. We show that the horizontal transfer can have a major impact on the distribution of the successive mutational fixations, leading to dramatically different behaviors, from expected evolution scenarios to evolutionary suicide. Simulations are given to illustrate these phenomena.

Tâm Mignot
Monday 16:00 – 17:00

Modeling approaches to study the properties of genetic circuits
Abstract: Modeling approaches have recently proven powerful to model biological systems, especially to study the properties of genetic circuits. I will discuss how we applied such an approach to discover a new type of protein spatial oscillator regulating cell motility in bacteria.We initially started with a model and tested its key predictions experimentally only to discover that a key component was missing. The discovery of the missing component allowed the construction of a new model which revealed that cell motility is governed by a new type of relaxation oscillator with a gate. I will discuss the properties of this design and its implication for biology.

Lluis Mir
Friday 15:30 – 16:30

TBA

Philippe Moireau (Inria Saclay)
Thursday 17:30 – 19:00, Friday11:00 – 13:30

Inverse problems and data assimilation for applications in biology and medicine
Abstract: The question of using the available measurements to retrieve mathematical models characteristics (parameters, boundary conditions, initial conditions) is a key aspect of the modeling objective in biology or medicine. In a stochastic/statistical framework this question is seen as an estimation problems. From a deterministic point of view, we

classical talk about inverse problems as we recover classical model inputs from outputs. When considering evolution problems,this question falls in the realm of data assimilation that can be seen from a deterministic of statistical point of view. Our objective in this course is to introduce the mathematical principles and numerical aspects behind data assimilation strategies with an emphasis on the deterministic formalism allowing to understand why data assimilation is a specific inverse problem. Our presentation will include considerations on finite dimensional problems but also on infinite dimensional problems such as the one arising from PDE models. And we will illustrate the course with numerous examples coming from cardiovascular applications and population dynamics problems.

Luigi Preziosi (Politecnico di Torino)
Tuesday 9:00 – 10:30, Wednesday 9:00 – 10:30

Multi-level mathematical models for cell migration in dense fibrous environments

Abstract: Cell-extracellular matrix interaction and the mechanical properties of cell nucleus have been demonstrated to play a fundamental role in cell movement across fibre networks and micro-channels and then in the spread of cancer metastases. The lectures will be aimed at presenting several mathematical models dealing with such a problem, starting from modelling cell adhesion mechanics to the inclusion of influence of nucleus stiffness in the motion of cells, through continuum mechanics, kinetic models and individual cell-based models.

Olivier Seror (AP-HP)
Tuesday 13:30 – 14:30

Irreversible electroporation a new opportunity of curative treatment for HCC patients not amenable to thermal ablations

Abstract: Irreversible electroporation (IRE) is the sole physical ablative technology inducing tumorous cell death by process unrelated to thermal effect. This characteristic makes the technique suitable for the treatment of subtypes of liver tumors especially hepatocellular carcinoma (HCC) located next to critical structures leading to contraindications to thermal ablation like radiofrequency, microwave or cryotherapy. However, while IRE appears safe in such assumed challenging cases for thermal techniques, several issues remain to be addressed to make its use easier and more effective in clinical practice. First of all, tissue changes induced by IRE must be assessed keeping in mind that conversely to thermal techniques its efficacy is not limited to observable coagulative necrotic component of treatment zone. In addition, IRE which is multibipolar ablative technology requires meticulous demanding electrodes positioning to ensure proper magnitude of electric fields between each dipole. Finally, numerical simulations of IRE are mandatory to ease the setting of electrical pulses parameters to improve predictability of treatment in each individual case. In this setting of continue efforts to improve practicability of IRE the technique is routinely used in our institution since several years for the treatment of patients bearing early and locally advanced HCC not amenable to resection or thermal ablation. All along our experience with IRE, imaging appeared as a key point for addressing the specific issues listed above. For the 58 first patients 92% of complete ablation were achieved while the one-year local tumor progression free survival was 70% (95% CI: 56%, 81%). Indeed, despite the need of improvements IRE appears right now as a unique

opportunity to achieve complete sustained local tumor control for patient bearing early or locally advanced HCC not amenable to other curative treatments.
