

CIMPA SCHOOL
Mathematical Models in Biology and Related
Applications of Partial Differential Equations

Havana (Cuba)

June 9th - June 20th, 2025

Welcome Address & Schedule

Mathematical modelling in biology and related domains is becoming of increasing importance in the mathematical community as well as for biologists, physicians, engineers in environmental science from the point of view of possible applications. The recent progress in the development and the analysis of these mathematical models have to be shared with Cuba and other countries of the Caribbean area.

The school aims at presenting some of the current approaches in PDE, modelling biological phenomena or related domains by covering a wide class of models and applications including dynamics of intracellular and extracellular phenomena, neuronal networks, pattern formation, chemotaxis and their implications in developmental biology, epidemiology or neurosciences.

| | Monday, 9.6. | Tuesday, 10.6. | Wednesday, 11.6. | Thursday, 12.6. | Friday, 13.6. |
|-------|---|---|--|---|---|
| 9:00 | Transport Bouin (I) | Transport Bouin (II) | Transport Bouin (III) | Neurobiology Caceres (III) | Transport Bouin (IV) |
| 10:30 | Coffee-break | Coffee-break | Coffee-break | Coffee-break | Coffee-break |
| 11:00 | Neurobiology Caceres (I) | Neurobiology Caceres (II) | Mosquito Estrada Hernández & Alvarez Borges (II) | Mosquito Estrada Hernández & Alvarez Borges (III) | Neurobiology Caceres (IV) |
| 12:30 | Lunch | Lunch | Lunch | Lunch | Lunch |
| 14:00 | Mosquito Estrada Hernández & Alvarez Borges (I) | Garcia-Martinez Hubert | TD: Transport Fonte | Lage Castellanos Moyano | Mosquito Estrada Hernández & Alvarez Borges (III) |
| 15:30 | Coffee-break | Coffee-break | Coffee-break | Coffee-break | Coffee-break |
| 16:00 | Open discussion / Working groups | Student presentations: Nurdan Kar Damon Jorge Rubio Jefferson Prada | Open discussion / Working groups | TD: Mosquito Estrada Hernández & Alvarez Borges | TD: Neurobiology Fonte |

| | Monday, 16.6. | Tuesday, 17.6. | Wednesday, 18.6. | Thursday, 19.6. | Friday, 20.6. |
|-------|--|------------------------------------|--------------------------------------|---------------------------------------|---|
| 9:00 | Numerical Methods (I) Peurichard | Singular Limits Hecht (I) | Singular Limits Hecht (II) | Singular Limits Hecht (III) | Singular Limits Hecht (IV) |
| 10:30 | Coffee-break | Coffee-break | Coffee-break | Coffee-break | Coffee-break |
| 11:00 | Diffusion Lam (I) | Diffusion Lam (II) | Numerical Methods (II) Peurichard | Numerical Methods (III) Peurichard | Numerical Methods (IV) Peurichard |
| 12:30 | Lunch | Lunch | Lunch | Lunch | Lunch |
| 14:00 | Hernandez Mederos Mischler | Soresina Coville | Trescases Kanzler | Diffusion Lam (III) | Diffusion Lam (IV) |
| 15:30 | Coffee-break | Coffee-break | Coffee-break | Coffee-break | Coffee-break |
| 16:00 | Student presentations: Loidel Barrera Rodríguez Sofía Albizu-Campos Camilo Medina González | TD: Diffusion Estrada Hernández | Open discussion / Working groups | TD: Singular Limits Alvarez Borges | TD: Numerical Methods Alvarez Borges |

Contents

| | |
|--|------------|
| Welcome Address & Schedule | iii |
| Courses | 1 |
| Transport phenomena in Mathematical Biology (<i>Émeric Bouin</i>) | 1 |
| Simulation and numerical treatment of PDEs in Mathematical Biology (<i>Diane Peurichard</i>) | 1 |
| Mathematical Models in Neurobiology (<i>Maria José Caceres</i>) | 2 |
| Singular limits arising in mechanical models of tissue growth (<i>Sophie Hecht</i>) | 3 |
| Mathematical models in population dynamics: applications in agroecology (<i>Frank Ernesto Alvarez Borges, Jorge Estrada Hernández</i>) | 3 |
| Reaction-diffusion equations in Mathematical Ecology (<i>Adrian Lam</i>) . . . | 4 |
| Research Talks | 5 |
| How to construct travelling wave in homogeneous reaction dispersion equation (<i>Jérôme Coville</i>) | 5 |
| How tumors dynamically evolve during interaction with T cells?: Implications for immunotherapies efficacy (<i>Karina Garcia-Martinez</i>) | 5 |
| Isogeometric approach to the study of focused ultrasound induced heating in biological tissues (<i>Victoria Hernández Mederos</i>) | 6 |
| Growth Fragmentations Models (<i>Florence Hubert</i>) | 6 |
| Modelling the evolution of the size-distribution in aquatic ecosystems (<i>Laura Kanzler</i>) | 7 |
| Inference of hidden processes in first waves of COVID in Cuba (<i>Alejandro Lage Castellanos</i>) | 7 |
| Semigroup techniques and applications to evolution PDE (<i>Stéphane Mischler</i>) | 8 |
| Derivation of cross-diffusion models in population dynamics: dichotomy, time-scales, and fast-reaction (<i>Cinzia Soresina</i>) | 8 |
| A viscous multi-tissue model for vertebrate embryo growth (<i>Ariane Trescases</i>) | 8 |
| Short Presentations | 9 |
| Reaction-Diffusion Formalism for Glioma Growth (<i>Nuridan Kar</i>) | 9 |
| Evaluation of the reproductive behavior of the mosquito <i>Aedes aegypti</i> incorporating polyandry (<i>Damon Jorge Rubio</i>) | 9 |
| On the Controllability of Systems Involving Chemotaxis Phenomena (<i>Jefferson Prada</i>) | 10 |
| Solving Helmholtz equation for ultrasound propagation with Isogeometric analysis (<i>Loidel Barrera Rodríguez</i>) | 10 |

| | |
|---|----|
| An isogeometric approach to the solution of the one-dimensional Westervelt equation (<i>Sofía Albizu-Campos Rodríguez</i>) | 11 |
| Heated Pathways: Examining the Influence of Temperature Rise on Leaf Vein Patterns (<i>Camilo Medina González</i>) | 11 |

Courses

Transport phenomena in Mathematical Biology

Émeric Bouin

Université Paris Dauphine

Many phenomena in mathematical biology can be described by using the mathematical properties of the transport equation and more generally a kinetic description of a large population of individuals. One main example is the pattern formation that occurs naturally while observing a flock of birds, a school of fish or a swarm of bees. A possible mathematical description of this behaviour uses the kinetic gas description of statistical mechanics to describe the interaction of a large number of individuals. With this perspective, swarming would be a consequence of an equilibrium between large-range attraction between moving individuals of the same species and a long-range repulsion intended to avoid collisions. The mathematical framework of these models involves the use of the transport equation and the associated collision and alignment models, based on the Boltzmann equation. The goal of this course is to give an introduction to these tools.

Teaching assistant: Claudia Fonte Sanchez (INRIA Grenoble)

Simulation and numerical treatment of PDEs in Mathematical Biology

Diane Peurichard

INRIA Paris

The partial differential equations describing biological phenomena may or may not possess exact solutions, and even if they do, they are frequently difficult to compute. For practical purposes it is sometimes enough to produce accurate simulations that describe a fair approximation of the original model and possibly give some useful qualitative or quantitative information about the biological model itself. In order to produce these computational approximations, a number of numerical methods can be used, all with some particular advantages and flaws depending on the underlying partial differential equation dynamics. The goal of this course is to introduce some basic numerical methods, such as finite differences, finite volumes and Monte-Carlo methods, that can be very useful to get a complementary insight into the equations

introduced in the courses and simulation.

Teaching assistant: Frank Ernesto Alvarez Borges (LJLL, Sorbonne Université)

Mathematical Models in Neurobiology

Maria José Caceres
Universidad de Granada

In recent decades, mathematical models employed by the neuroscience community—whose properties were not yet well understood—have been studied in greater depth. Modeling the behavior of large populations of neurons using microscopic approaches often entails a high computational cost. To overcome this, models based on partial differential equations (PDEs) have been developed, which describe the dynamics of neuron populations at the mesoscopic or macroscopic scale. These advancements are providing deeper insights into brain functioning and its disorders, such as neurodegenerative diseases and neuropsychiatric conditions. In this course, we will focus on the mathematical study of some of these PDE-based models. The course is structured as follows:

1. **Introduction to Neuronal Physiology.** We begin with an introduction to the fundamental aspects of neuronal physiology, discussing how neurons transmit signals through action potentials and how these signals can be mathematically modeled. This physiological context is essential for understanding the models we will study later.

2. **Microscopic Models for Neuronal Dynamics.** We examine how neurons are modeled at the microscopic scale, beginning with the detailed Hodgkin-Huxley model and moving towards simpler approaches, such as the integrate-and-fire model.

3. **Some PDE-based Models (Meso/Macroscopic Scale).** In this part of the course, we focus on two models formulated as partial differential equations (PDEs) that describe the dynamics of neuronal networks at the mesoscopic macroscopic level: the Nonlinear Leaky Integrate-and-Fire (NNLIF) model and the Age-Structured Equation model. We will study their stability and asymptotic behavior, focusing on the system's equilibria and how they depend on various parameters such as synaptic delay and network connectivity. To analyze these models, we will use advanced mathematical tools, including the entropy dissipation method, commonly used in kinetic theory, as well as a new technique that involves rewriting the problem as a Volterra-type equation. This allows us to explore the long-term behavior and stability of the system in a more powerful way. Throughout the course, students will explore how microscopic models at the neuronal level can be translated into macroscopic descriptions of neural networks, and how mathematical techniques provide a deep understanding of the asymptotic behavior in these systems.

Teaching assistant: Claudia Fonte Sanchez (INRIA Grenoble)

Singular limits arising in mechanical models of tissue growth

Sophie Hecht

CNRS & LJLL - Sorbonne Université

Based on the mechanical viewpoint that living tissues present a fluid-like behaviour, PDE models inspired by fluid dynamics are nowadays well established as one of the main mathematical tools for the macroscopic description of tissue growth. Depending on the type of tissue, these models link the pressure to the velocity field using either Brinkman's law (visco-elastic models) or Darcy's law (porous-medium equations (PME)). Moreover, the stiffness of the pressure law plays a crucial role in distinguishing density-based (compressible) models from free boundary (incompressible) problems where saturation of the density holds. This course aims to analyse how to relate different mechanical models of living tissues through singular limits. In particular, we will address the inviscid limit towards the PME, the incompressible limit from the PME towards Hele-Shaw free boundary problems and their joint limit for equations including convective effects as well as for systems of coupled nonlinear equations. The techniques that will be employed during the course include classical tools in the theory of the PME (Aronson-Bénilan estimate, uniform BV-bounds, energy bounds) as well as techniques that are reminiscent of the theory of gradient flows, such as, for instance, the energy dissipation inequality (EDI) formulation.

Teaching assistant: Frank Ernesto Alvarez Borges (LJLL, Sorbonne Université)

Mathematical models in population dynamics: applications in agroecology

Frank Ernesto Alvarez Borges, Jorge Estrada Hernández

LJLL - Sorbonne Université, Universidad de la Habana

Due to the high number of diseases that they transmit, mosquito is considered as the most dangerous animal species for human. In particular, *Aedes* mosquitoes are one of the main vector for diseases like dengue, chikungunya and zika. Due to climate change, such mosquitoes are present and invasive on every continent in the world. Since there is no vaccine available for such diseases, one of the most promising techniques to limit the transmission consists in acting on the mosquitoes population. Several techniques of control of the mosquitoes dynamics are under study, among them we may cite the sterile insect technique (SIT) and the replacement technique. These two techniques consist in releasing specific mosquitoes which will interact with the host population to reduce the size of the population (SIT) or to replace it by a population carrying a bacteria blocking the transmission of arboviruses. Obviously, a safe, proper and optimal use of such techniques requires a careful mathematical analysis. In this course we will review the main aspect of the life cycle of mosquitoes and present the main techniques that may be used to control the mosquitoes population. Then, we will present some mathematical models and mathematical tools that will be useful to answer to several questions: How to

optimize such strategies of control ? How to guarantee the success of such strategies ? What could be the influence of the spatial heterogeneities on the success of these control strategies?

Teaching assistant: Frank Ernesto Alvarez Borges (LJLL, Sorbonne Université)
& Jorge Estrada Hernández (Universidad de la Habana)

Reaction-diffusion equations in Mathematical Ecology

Adrian Lam
The Ohio State University

Reaction-diffusion equations are ubiquitous in describing many spatio-temporal phenomena in biology, such as in the studies of persistence and competition of species, and spatial propagation phenomena. The first part of this course covers the mathematical theory for population model in a bounded domain, we will investigate the effect of diffusion, environmental source and sink patterns, and the boundary conditions on the persistence of species. The second part of the talk will be devoted to propagation phenomena of a variant of Fisher-KPP equation on the real line which is proposed by Bewick et al., and we will study the asymptotic spreading of a species when the environmental quality is shifting at a constant speed using the notion of generalized super/subsolutions.

Teaching assistant: Jorge Estrada Hernández (Universidad de la Habana)

Research Talks

How to construct travelling wave in homogeneous reaction dispersion equation

Jérôme Coville
INRAE, Avignon

Travelling wave solutions are an essential tools for understanding the spreading properties of population dynamics models. The existence and properties of these solutions have been studied in various local and nonlocal semilinear equations. In all these examples, the dispersal operator can be linked to the generator of a particular Levy process: Brownien, α -stable processes, compound Poisson processes, ... A natural question to ask is whether such solutions still exist when a generic generator is considered. I will present some recent work with E. Bouin that provides a methodology offering an almost complete answer to this question for symmetric generators of Levy processes. I will detail our approach when the nonlinearity is bistable and the dispersal operator is purely a nonlocal with a diffuse Levy measure.

How tumors dynamically evolve during interaction with T cells?: Implications for immunotherapies efficacy

Karina Garcia-Martinez
Center of Molecular Immunology

I will present a mathematical model developed in our group to study the evolution of tumors in interaction with the immune response. After a brief biological introduction, I will present the ODE system and the algebraic equations that allowed us to predict the different modes of tumor growth. We were able to characterize the dynamic properties of tumor clones during evolution. Finally, we predicted the impact of tumor evolution on the efficacy of different immunotherapies.

Isogeometric approach to the study of focused ultrasound induced heating in biological tissues

Victoria Hernández Mederos

Instituto de Cibernética, Matemática y Física

Ultrasound medical treatments are non-invasive, repeatable, and non-toxic methods that can be used to treat muscle, bone, and skin tissue. Focused ultrasound systems for medical therapy must be carefully designed, implemented, and applied to avoid tissue damage. In this talk we discuss a study of the heating of a biological tissue induced by the ultrasonic pulse emitted by a curved transducer. The thermal diffusion effect of the ultrasound is computed solving Helmholtz and Pennes partial differential equations. Isogeometric analysis (IgA) is proposed as an effective tool to compute the acoustic pressure field, solution of Helmholtz equation. In combination with the method of lines, IgA is also used to compute the temperature field, solution of Pennes bioheat equation. Numerical experiments are performed with a biological tissue composed of three layers: skin, fat and muscle and a fixed value of the frequency of the pulse, in order to determine the intensity at which ultrasound effectively stimulates the tissues while avoiding tissue injury, according to the time-temperature combinations recommended in the literature.

Growth Fragmentations Models

Florence Hubert

Aix-Marseille Université

Growth fragmentations models are often used in structured population dynamics to model for example cell division, polymerization. The classical form of the equation is

$$\begin{cases} \partial_t \rho(t, x) + \partial_x (g(x) \rho(t, x)) = -B(x) \rho(t, x) + \int_x^\infty B(y) k(y, x) \rho(t, y) dy, & t > 0, x > 0 \\ \rho(t, 0) = 0, & t > 0 \\ \rho(0, x) = \rho^0(x), & x > 0 \end{cases}$$

The wellposedness of a solution globally defined to this equation as well as its asymptotic behaviour has been widely studied. We will first give some contexts where this model is used and recall the main results. We will also propose extensions of such equation in the context of metastasis spreading and in the context of microtubule dynamical instabilities. We will make a point on the properties of these models and the remaining challenges.

Modelling the evolution of the size-distribution in aquatic ecosystems

Laura Kanzler

CNRS & LJLL - Sorbonne Université

Trophic interactions between animals in the ocean were matter of interest since the 1960ies, where it was quickly discovered that the body size of an individual acts as 'master trait' in food webs of animals, giving rise to emergent distributions of biomass, abundance and production of organisms. We propose and investigate a deterministic jump-growth model, which is given by a kinetic equation for coalescing particles, aiming to capture this emergence phenomenon in aquatic ecosystems. The equation of interest is derived from individual based dynamics governed by a stochastic process. Following the observation of the body mass being the crucial trait in these dynamics it is based on the assumption that binary interactions between individuals in the ecosystem take place: A predator feeding on a prey, which then results in growth of the predator with assimilating a certain (usually very small) amount of its prey's mass as well as plankton production. Analytical results in various parameter regimes are discussed and numerical simulations underlying these observations are given.

Inference of hidden processes in first waves of COVID in Cuba

Alejandro Lage Castellanos

Universidad de la Habana

I'll discuss two researches carried in our group at the early onset of COVID in Cuba. They both deal with the possibility of inferring what lies behind the surface of the public data of new cases.

First I'll discuss the inference of the number of undetected cases in Cuba's first waves of COVID. This research, published in Revista Cubana de Matematica, <https://arxiv.org/pdf/2008.03332>, was inspired by some similar work done in France (L. Roques). The idea is Not to fix SIR models to the public data of cases. Instead, understand that such reports are a stochastic sample from the real epidemic, that evolves as SIR but is not detected. So, we fit two models, one stochastic for the detection process and one mechanistic for the underlying epidemic, to match the public data.

Second, I'll discuss how to treat the contact tracing of cases in an epidemic as a cascade process. Cuba's public report of cases separated the primary from secondary cases. Notably, there was a much higher number of secondary cases than primary cases. We built a cascade model of contact tracing to try to fit this data and understand the efficiency of the Cuban health system in detecting cases. This approach is similar to results from the group of Ferguson in the early 2000's, and somehow is a rediscovery of their results.

Semigroup techniques and applications to evolution PDE

Stéphane Mischler

Université Paris-Dauphine

I will give a short overview about more or less recent semigroup techniques such as the change of the functional space technique, the (principal) spectral mapping theorem, the Weyl's Theorem, the stability under small perturbations theorem, the Doblin-Harris and the Krein-Rutman theorems. I will then show some possible applications to evolution PDEs encountered in a biological context such as the growth-fragmentation equation for proteins dynamics, the Keller-Segel equation and the runs and tumbles equation for bacteria dynamics and the time elapsed equation, the FitzHugh-Nagumo equation and the Voltage-Conductance kinetic equation for neuron network.

Derivation of cross-diffusion models in population dynamics: dichotomy, time-scales, and fast-reaction

Cinzia Soresina

University of Trento

In population dynamics, cross-diffusion describes the influence of one species on the diffusion of another. A benchmark problem is the cross-diffusion SKT model, proposed in the context of competing species to account for stable inhomogeneous steady states exhibiting spatial segregation. Even though the reaction part does not present the activator-inhibitor structure, the cross-diffusion terms are the key ingredient for the appearance of spatial patterns. From the modelling perspective, cross-diffusion terms naturally appear in the fast-reaction limit of a “microscopic” model (in terms of time scales) presenting only standard diffusion and fast-reaction terms, thus incorporating processes occurring on different time scales. In this talk, recent applications of this approach will be presented, e.g., predator-prey and mutualistic interactions, plant dynamics with autotoxicity effects, and epidemiology.

A viscous multi-tissue model for vertebrate embryo growth

Ariane Trescases

CNRS & Institut de Mathématiques de Toulouse

During elongation of the vertebrate embryo, live imaging reveals cellular turbulence in the embryonic tissues. We propose a 2D mechanical model for tissue growth during embryo elongation, which recovers these turbulent movements and addresses the question of the mechanism of segregation between tissues. Having (formally) determined the incompressible limit, we study the qualitative behavior at the limit and discuss a ghost effect, then deduce new biological hypotheses.

Short Presentations

Reaction-Diffusion Formalism for Glioma Growth

Nurdan Kar
Ankara University

More than 120 different types of tumors can occur in the human brain. In this talk, we discuss the modeling of glioma growth, a primary brain tumor that originates in the glial cells, using reaction-diffusion equations. We first provide a brief biological and mathematical foundation for glioma growth, then introduce a time-fractional partial differential equation for glioblastoma growth, the most aggressive subtype of glioma. We conclude with analysis of the fractional model's dynamics.

Evaluation of the reproductive behavior of the mosquito *Aedes aegypti* incorporating polyandry

Damon Jorge Rubio
Universidad de La Habana

The mosquito *Aedes aegypti* is the primary vector responsible for transmitting diseases such as yellow fever, dengue, chikungunya, and zika. Traditionally, it has been believed, mainly due to laboratory observations, that females of this species mate only once in their lifetime. Nonetheless, recent research has demonstrated the occurrence of polyandry both in controlled environments and in natural populations, where a single female may produce offspring sired by multiple males. This reproductive behavior has significant consequences for vector control strategies like the Sterile/Incompatible Insect Technique SIT/IIT, which often assume monandry as a key premise and overlook the possibility of multiple matings. In this study, we present biomathematical models that incorporate polyandry into the reproductive dynamics of *Aedes aegypti*, aiming to more accurately represent its biology for the development and assessment of vector control approaches.

On the Controllability of Systems Involving Chemotaxis Phenomena

Jefferson Prada

Pontificia Universidad Católica de Chile

Chemotaxis is a biological process in which organisms or cells move in response to chemical gradients. Mathematically, this behavior is often modeled by nonlinear partial differential equations, typically of parabolic-parabolic or parabolic-elliptic type. In this talk, we discuss recent results concerning the controllability of such systems, with a particular focus on the Keller Segel model from insensitizing approach. We present strategies based on Carleman estimates and duality techniques to address controllability problems and explore how the coupling and nonlinearity influence the control mechanisms. These results are relevant for understanding population dynamics, cancer modeling, and other applications where chemotaxis effects play a fundamental role.

This work is in collaboration with F.W. Chaves-Silva at Universidade Federal da Paraíba, Brasil.

Solving Helmholtz equation for ultrasound propagation with Isogeometric analysis

Loidel Barrera Rodríguez

ICIMAF

High-intensity focused ultrasound has now been used for clinical treatment of a variety of solid malignant tumors, including those in the pancreas, liver, kidney, bone, prostate, and breast, as well as uterine fibroids and soft-tissue sarcomas. The ultrasound radiation problem is modeled mathematically by means of the Helmholtz equation with mixed boundary conditions. Isogeometric analysis (IgA) is applied to compute the acoustic pressure field produced by a curved ultrasound transducer in a 2D nonconvex physical domain. A key step of the IgA approach is the parametrization of the domain, which plays in IgA a role similar to mesh generation in the classical Finite Element Method (FEM). The main goal of the research is to study the influence of the parametrization on the overall performance and accuracy of the numerical solution of Helmholtz equation with the Isogeometric method.

An isogeometric approach to the solution of the one-dimensional Westervelt equation

Sofía Albizu-Campos Rodríguez

Universidad de La Habana

The Westervelt equation is widely used to model the nonlinear propagation of waves, and it is obtained by introducing a nonlinear perturbation to the standard wave equation. It is convenient to study the behavior of ultrasonic waves due to the use of high-frequency sources, both in the context of imaging and non-invasive medical treatments. This work aims to obtain the numerical solution of the Westervelt equation in a one-dimensional physical domain through Isogeometric Analysis (IgA) and compare the results and numerical difficulties with those founded via the finite element method (FEM) using linear and quadratic Lagrange basis.

Heated Pathways: Examining the Influence of Temperature Rise on Leaf Vein Patterns

Camilo Medina González

Universidad Nacional de Colombia

The impact of temperature increases on the formation of venation architecture in leaves was investigated. A model of biological networks was employed, establishing a constant initial configuration for the networks and edges, and varying a metabolic coefficient as an equivalent to temperature variation to assess its impact. The results demonstrate an inversely proportional relationship between the vein conductivity and the metabolic coefficient value c_0 . The network structure remained unchanged, maintaining the same functional veins but varying in size, reducing as the metabolic coefficient increased.
