School schedule

Benoît Perthame: 2x2 hours Monday, Tuesday
Nicolas Vauchelet: 2x2 hours Monday, Tuesday
James Sneyd: 4x1 hour Monday, Tuesday, Thursday, Friday
José Antonio Carrillo: 2x2 hours Thursday, Friday
Nikolaos Sfakianakis: 2x2 hours Friday, Saturday

More precisely, keeping in mind that informal talks and discussions should occur after dinner, to be proposed every day on the spot:

Sunday September 1

18:00 Registration, welcome and dinner at 20:00

On the other days, coffee breaks will occur at 10:30-11:00 and 16:30-17:00, lunch breaks at 12:00-14:30, dinner at 20:00

Monday 2

9:30-10:30 + 11:00-12:00 Perthame // 14:30-15:30 Sneyd // 15:30-16:30 + 17:00-18:00 Vauchelet

18:00 Welcome drink (Samos wine)

Tuesday 3

9:30-10:30 + 11:00-12:00 Vauchelet // 14:30-15:30 Sneyd //15:30-16:30 + 17:00-18:00 Perthame

Wednesday 4

Break (planned: 9:30-17:30 excursion)

Thursday 5

9:30-10:30 + 11:00-12:00 Carrillo // 14:30-15:30 Sneyd // 15:30-16:30 Sfakianakis

20:00 Conference dinner

Friday 6

9:30-10:30 + 11:00-12:00 Carrillo // 14:30-15:30 Sneyd // 15:30-16:30 Sfakianakis

Saturday 7

9:30-10:30 + 11:00-12:00 Sfakianakis
12:00 End of the school and farewell lunch

Abstracts of lectures

Benoît Perthame's abstract:
Adaptive evolution and concentrations in nonlocal parabolic PDEs

Living systems are subject to constant evolution through the three processes, stated by C. Darwin, of population growth, selection and mutations. The goal of this series of lectures is to formalize them and to discuss the exemple of resistance to therapy in cancer treatment; can an injection protocol diminish adaptation of cancer cells to the drug?

In a very simple, general and idealized description, the environment can be considered as a nutrient shared by all the population. This alllows certain individuals, characterized by a 'phenotypical trait', to proliferate faster because they are better adapted to use the environment. This leads to select the 'fittest trait' in the population (singular point of the system). On the other hand, the new-born individuals can undergo small variations of the trait under the effect of genetic mutations. In these circumstances, is it possible to describe the dynamical evolution of the current trait? A new area of population biology that aims at describing mathematically these processes is born in the 1980's under the name of 'adaptive dynamics' and, compared to population genetics, considers usually asexual reproduction, a continuous phenotypical trait and population growth.

We will give a self-contained mathematical model of such dynamics, based on parabolic equations, and show that an asymptotic method allows us to formalize precisely the concepts of monomorphic or polymorphic population and describe the evolution of the 'fittest trait'. Mathematically, the interest comes from concentration effects after an appropriate rescaling. The solution converges to a (sum of) Dirac mass(es) supported on a hypersurface that results from the nonlinearity. The difficulty is to evaluate the weight and position of the moving Dirac mass(es) that desribe the population. We will show that a new type of Hamilton-Jacobi equation, with constraints, naturally describes this asymptotic. Some additional theoretical questions as uniqueness for the limiting H.-J. equation will also be addressed.

This course is based on collaborations with G. Barles, J. Clairambault, O. Diekmann, P.-E. Jabin, T. Lorenzi, A. Lorz, S. Mirahimmi, S. Mischler and P. E. Souganidis.

Ch 1. Principles of adaptation/evolution modeling for large populations
Ch 2. The constrained Hamilton-Jacobi equations
Ch 3. The smooth concave case and point dynamics on the hypersurface
Ch 4. Evolution without proliferating advantage

Nicolas Vauchelet's abstract:
Mathematical modeling of control techniques for vector borne diseases and their epidemics.

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, zika. Since there is no vaccine available for such diseases, one of the most promising technique 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 presentation we will review the main aspect of the life cycle of mosquitoes and 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 techniques ?
(sterilized mosquitoes for the SIT or mosquitoes carrying a bacteria blocking the transmission of arboviruses

James Sneyd's abstract:

Talk 1: Enzyme kinetics, cell volume control and water transport

Cells need to control their volume so that they don't burst, and they do this by controlling very carefully the osmotic balance across the cell membrane. A wide range of ion channels and transporters allow the flow of ions in or out of the cell, and the fluxes through these pathways are actively controlled in order for the cell to survive.

Although this an interesting problem in itself, it becomes even more interesting when you realise that these mechanisms of cell volume control result in a potential difference across the cell membrane, which can itself be modulated to allow cells to communicate with one another. Furthermore, many cells need to control their volume while simultaneously transporting (relatively) large amounts of water. It's not easy to do this, in a wide range of conditions, while controlling volume.

In this (relatively introductory) talk I'll cover the basic mechanisms of ion transport and cell volume control, and show how this results in a membrane potential difference, and how water transport occurs in salivary gland cells.

Background reading for this talk is chapters 1 and 2 of Keener and Sneyd, Mathematical Physiology, Ed. 2, Springer, 2008.

Chapter 1
Chapter 2

Talk 2: The dynamics of calcium: oscillations and waves, experiments and theory.

Oscillations in the cytoplasmic concentration of calcium is one of the most ubiquitous cellular signalling mechanisms, being used to control a wide variety of cellular processes, including muscular contraction, fluid transport, gene expression and cell differentiation. In

cells that are large enough, these oscillations can form periodic waves, or even spiral waves, of increased calcium concentration.

Because of such complex dynamics, over the past 20 years mathematical modelling has played an important role in the study of calcium signalling. I shall present an overview of the field, as well as a more in-depth look at a small number of particular questions. In particular, I shall look at the properties of isolated and periodic waves of calcium, the importance of homogenisation and microdomains, the role of Markov Chain Monte Carlo approaches to fitting single-channel data, and the possible importance of homoclinic bifurcations for understanding some of the most recent experimental results. Each of these topics will require a detailed consideration of experimental data, thus illustrating the close interplay between theoretical and experimental approaches.

Background reading for this talk is chapter 7 of Keener and Sneyd, Mathematical Physiology, Ed. 2, Springer, 2008.

Chapter 7

Talk 3: The Hodgkin-Huxley equations and their extension to neuroendocrine cells

In my first talk I will have shown how cell volume control results in a potential difference across the cell membrane. In this talk I'll show how this membrane potential is actively modulated, and (briefly) derive the famous Hodgkin-Huxley model of an action potential in a neuron. Then I'll show how these membrane based mechanisms can interact with cytosolic calcium dynamics to give a wide range of complex rhythmic activity such as bursting oscillations.

I'll also very briefly touch on the mathematical methods used to analyse these models, and how these methods can be used to understand experimental data.

Background reading for this talk is chapters 5 and 9 of Keener and Sneyd, Mathematical Physiology, Ed. 2, Springer, 2008.

Chapter 5
Chapter 9

Talk 4: Photoreceptors and the retina

One of the most important features of the visual system is that it responds to changes rather than to absolute levels. This becomes clear when one thinks about how camouflage works only if the hidden item remains quite still. As soon as it starts to move, the eye can pick up the resultant changes, which it couldn't do before. This is such an important property of the visual system that it is mediated at multiple levels, beginning at the lowest level, in the photoreceptor cells that detect light.

In my final talk I'll look at some features of the visual system, focusing almost entirely on photoreceptors and the retina. I'll look at some things as adaptation in photoreceptors, Weber's law, contrast detection, and the Hartline-Ratliff equations. Solutions of some simple models will be discussed.

Background reading for this talk is chapter 19 of Keener and Sneyd, Mathematical Physiology, Ed. 2, Springer, 2008.

Chapter 19

José Antonio Carrillo's abstract:
Cell-cell Adhesion micro- and macroscopic models via Aggregation-Diffusion systems.

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.

Nikolaos Sfakianakis's abstract:
Mathematical problems in evolutionary theory and associated numerical questions

As opposed to physical systems, biological systems have the tendency to reproduce their uniqueness. This property is encompassed in the mathematical studies of the corresponding problems and is a source of significant difficulties in the model development, analysis, and numerical investigations.

This tendency is not confined in a single class of biological problems nor in a single space and time scale. It extends from sub-cellular processes of milliseconds, to cellular activities of minutes, to tissue and organ dynamics of hours, to organism processes of days and weeks, and population dynamics of years and millennia.

In these lectures we address the manifestation of this tendency by visiting biological problems from several of the above scales. We discuss the derivation of the mathematical models and some of the difficulties emanating from the inherent biological nature.

We will split these lectures in 4 parts:

Part 1: Gap gene system
Part 2: Cell migration and limb formation
Part 3: Cancer growth and invasion
Part 4: Darwinian evolution of dinosaur birds