NOVA SCHOOL OF SCIENCE & TECHNOLOGY

III Encontro Português de **Biomatemática**

3rd Portuguese Meeting in Biomathematics

FCT NOVA **13-14 julho 2022**

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About

EPB

The Portuguese Meeting on Biomathematics (EPB) is a biannual event, which aims to bring together national researchers interested in Biomathematics and, at the same time, to promote interaction between mathematicians working on models arising from the field of biology, with other researchers working in areas of biology and who use mathematics as an important tool in their investigation.

III EPB

The III EPB, will take place on the 13th and 14th of July, at NOVA School of Science and Technology, and is a joint organization of the NOVA MATH (Center for Mathematics and Applications) of the NOVA School of Science and Technology, NOVA University of Lisbon and the Center for Research and Development in Mathematics and Applications of the University of Aveiro (CIDMA), integrated in its thematic lines Mathematical Biology and Biomathematics.

Organizing committee

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Paulo Doutor	FCT NOVA & NOVA MATH

Timetable

SC: Short Course, IS: Invited Speaker, CT: Contributed Talk.

Tuesday, 12 of July

14:30–17:30	SC	**Nico Stollenwerk & Maíra Aguiar** Bilbao, Spain	Stochastic processes theory and applications

Wednesday, 13 of July

9:00–9:30	**Registration**		
9:30–9:45	**Opening Session**		
9:45–10:30	IS	**Jean Clairambault** Paris, France	From mathematical modelling by structured cell population dynamics with cancer plasticity to philosophy of cancer
10:30–10:50	CT	**Carlos A. Braumann** Évora, Portugal	General autonomous population growth models with and without harvesting in random environments: the effect of Allee effects
10:50–11:10	CT	**Patrícia Filipe** Évora, Portugal	Weighted maximum likelihood estimation method for SDE individual growth models
11:10–11:40	**Coffee break**		
11:40–12:00	CT	**Alberto Pinto** Porto, Portugal	Immune responses by CD4+ T cells
12:00–12:20	CT	**Diogo Cabanas** Lisbon, Portugal	Entropy and the arrow of time in population dynamics
12:20–12:40	CT	**José Martins** Leiria, Portugal	Dynamics of vaccination strategies
12:40–14:15	**Lunch**		
14:15–15:00	IS	**Cristiana Silva** Aveiro, Portugal	Mathematical modeling of epidemics: ODE's, complex networks hybrid models
15:00–15:20	CT	**Vanessa Steindorf** Bilbao, Spain	Modelling secondary infections with temporary immunity and disease enhancement factor: mechanisms for complex dynamics in simple epidemiological models

15:20–15:40	CT	**Vizda Anam** Bilbao, Spain	Understanding the immunological responses mediated by antibodies during primary and secondary dengue infection
15:40–16:00	CT	**Akhil Kumar Srivastav** Bilbao, Spain	Optimal control of multi-strain host-vector dengue model
16:00–16:30	**Poster session**		
16:30–17:15	**Coffee break**		
17:15-18:00	IS	**Maíra Aguiar** Bilbao, Spain	On the origin of complex dynamics in multi-strain dengue models

Thursday, 14 of July

9:00–9:30	**Registration**		
9:30–9:45	**Opening Session**		
9:45–10:30	IS	**Carlos Ramos** Évora, Portugal	Kinematics, dynamics and complex motion in biology
10:30–10:50	CT	**Paulo Rebelo** (1) Covilhã, Portugal	An optimal control problem for non autonomous crop growth with Richards Logistic growth and predation
10:50–11:10	CT	**Diogo Baptista** Leiria, Portugal	Measure the complexity of Nicholson-Bailey type biological dynamical systems using symbolic dynamics
11:10–11:40	**Coffee break**		
11:40–12:00	CT	**Davide Cusseddu** Lisbon, Portugal	Cell polarisation and cytosolic protein diffusion in the bulk-surface wave-pinning model
12:00–12:20	CT	**Tony Humphries** Montreal, Canada	Modeling Iron Metabolism and Erythropoiesis of Blood Donors
12:20–12:40	CT	**Jorge Cabral** Aveiro, Portugal	Modelling the functional status of people with COPD – a comparison of feature selection methods
12:40–14:15	**Lunch**		
14:15–15:00	IS	**Ana Jacinta Soares** Braga, Portugal	Kinetic modelling and analysis of autoimmune diseases
15:00–15:20	CT	**Paulo Rebelo** (2) Covilhã, Portugal	An optimal control problem for a non-autonomous model consisting of two prey, one predator with weak Allee effect on the strong prey
15:20–15:40	CT	**Silvério Rosa** Covilhã, Portugal	Fractional Modelling and Optimal Control of the third wave of COVID-19 in Portugal

15:40–16:00	CT	**Bruno V. Guerrero B.** Bilbao, Spain	A pragmatic view on chaotic dynamics and ergodicity in a SIR-like epidemic model
16:00–16:30	CT	**Carla Pinto** Porto, Portugal	Assessing the fallout of different control measures for dengue disease
16:30–17:15	**Coffee break**		
17:15-18:00	IS	**Jorge Orestes Cerdeira** Lisbon, Portugal	The Max-Out Min-In Problem: A Tool for Data Analysis in Biomathematics

Friday, 15 of July

14:30–17:30	SC	**Nico Stollenwerk & Maíra Aguiar** Bilbao, Spain	Stochastic processes theory and applications

List of Abstracts – Talks

Wednesday 13th

From mathematical modelling by structured cell population dynamics with cancer plasticity to philosophy of cancer

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In this talk, I will suggest that cancer is fundamentally a disease of the control of cell differentiation in multicellular organisms, uncontrolled cell proliferation being a mere consequence of blockade, or unbalance, of cell differentiations. Cancer cell populations, that can reverse the sense of differentiations, are extremely plastic and able to adapt without mutations their phenotypes to transiently resist drug insults, which is likely due to the reactivation of ancient, normally silenced, genes. Stepping from mathematical models of non genetic plasticity in cancer cell populations and questions they raise, I will propose an evolutionary biology approach to shed light on this problem both from a theoretical viewpoint by a description of multicellular organisms in terms of multi-level structures, which integrate function and matter from lower to upper levels, and from a practical point of view oriented towards cancer therapeutics, as cancer is primarily a failure of multicellularity in animals and humans. This approach resorts to the emergent field of knowledge named philosophy of cancer

General autonomous population growth models with and without harvesting in random environments: the effect of Allee effects

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In a randomly varying environment, a general autonomous model for the growth of a closed population under harvesting assumes that the (*per capita*) growth rate follows the stochastic differential equation (SDE) $\frac{dX(t)/dt}{X(t)} = f(X(t)) + \sigma\varepsilon(t) - qE(X(t))$ with initial condition $X(0) = x_0 > 0$, where $X(t)$ is the population size at time $t \geq 0$, $f(x)$ of class C^1 is the (*per capita*) arithmetic average natural growth rate when population size is x, $\sigma\varepsilon(t)$ is the deviation of the natural growth rate from its average due to environmental fluctuations (approximated by a standard white noise $\varepsilon(t)$ multiplied by an intensity parameter $\sigma > 0$), and $qE(x)$ is the mortality rate caused by harvesting ($E(x) \geq 0$ being the harvesting effort when the population size is x and assumed of class C^1 and $q > 0$ being the catchability coefficient). We assume $\lim_{x\to 0^+} xf(x) = 0$ and $f(+\infty) < 0$. Denoting by $W(t) = \int_0^t \varepsilon(s)ds$ the standard Wiener process, we can write the SDE in the form

$$dX(t) = f(X(t))X(t)dt - qE(X(t))X(t)dt + \sigma X(t)dW(t). \tag{0.1}$$

If there is no harvesting, we have $E(x) \equiv 0$. Model (0.1) is very general since we do not assume a specific form for $f(x)$, only that it satisfies reasonable general biological assumptions.

Under usual density-dependent conditions, the larger is the population size, the shorter is the availability of resources required for survival and reproduction of each indiviual and so $f(x)$ is assumed to be strictly decreasing and to have a carrying capacity $K > 0$ such that $f(K) = 0$. This situation was studied in [1]. The particular cases of f following the logistic and the Gompertz models were treated, in terms of profit optimization, in [4, 5], comparing a more general non-autonomous variable harvesting effort $E(t; X(t))$ with constant harvesting effort $E(X(t)) \equiv E$.

However, the strictly decreasing assumption for f may fail if there are Allee effects that depress $f(x)$ for small x sizes, effects that are stronger for smaller population sizes. They may be due to difficulties in encountering mating partners. They can also happen when a prey population is insufficient to mount an effective group defense against predators or when a predator population is insufficient to mount an effective group attack against prey. With Allee effects, for small population sizes x, say for $0 < x < L < K$, $f(x)$ increases with x, but still decreases for $x > L$ when Allee effects are overcome by density-dependence. Allee effects can be strong or weak depending on whether the geometric average natural growth rate $f(x) - \frac{\sigma^2}{2}$ when $x \to 0^+$ is negative or positive. The general Allee effects stochastic model without fishing was studied in [8]. With harvesting, the particular case of f being a logistic-like model with weak Allee effects was studied in [6, 7], comparing non-autonomous different variable effort policies with the constant effort policy.

Here, we treat the general stochastic Allee effects model with general autonomous harvesting effort. Under the assumptions made above, we show that strong Allee effects always lead to population extinction with probability one, even without harvesting. The same happens with harvesting when there is overharvesting, i.e. when, for very low population sizes ($x \to 0^+$), the harvesting mortality rate $qE(x)$ is larger than the geometric average natural growth rate $f(x) - \frac{\sigma^2}{2}$. Assuming that, for very low population sizes, $qE(x)$ is smaller than $f(x) - \frac{\sigma^2}{2}$, then there is no "mathematical" extinction and the process is ergodic, with the probability distribution of $X(t)$

[2]The CEMAPRE/REM is supported through national funds by FCT, Project UIDB/05069/2020.

converging as $t \to +\infty$ to a stationary distribution with stationary density (which we determine). For the particular case of constant effort policies, we also determine the harvesting effort that maximizes the steady-state profit per unit time. For a more realistic extinction concept, extinction still occurs and extinction time moments can be obtained using the techniques in [2, 3].

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Weighted maximum likelihood estimation method for SDE individual growth models

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We model individual growth in a randomly varying environment through a general and flexible class of SDE models that takes the form of a variant of the Ornstein-Uhlenbeck model. Adequate transformation of the size allows us to work with this general SDE model, that includes stochastic versions of the monomolecular, the logistic, the Gompertz and the Bertallanffy-Richards models, among others. We have applied such class of models using real weight data of males of the Mertolengo cattle breed. Focused on our application, we have seen that one of the most adequate transformations of the animals weight was the logarithm, which lead us to the Stochastic Gompertz model. Based on this model, we estimate the model parameters through the maximum likelihood (ML) method. In most applications, the available observations are equidistant in time, are taken at the same instant for all trajectories and there are large time observations, sufficient for a reasonable knowledge of the complete growth curve. However, in our case, it is often not feasible to obtain animal's observations at equally spaced ages nor even at the same ages for different animals and, since the animals are raised for the meat market, there is typically a small number of observations at older ages. For these reasons, maximum likelihood estimates of the growth model parameters can be quite inaccurate, and with the goal of improving the estimation when there are a small number of observations at older ages, we propose to consider in the likelihood function a weight function associated to the elapsed times between two consecutive observations of each animal, which results in the weighted maximum likelihood (WML) method.

This method was proposed in [2] and we have, using simulations, performed in [1] a study on the optimization of the weight function and the comparison of the performance of both estimation methods, ML and WML, under several scenarios. We have worked with simulated data for scenarios corresponding to weights measured at equally spaced ages using different spacings and different maximum ages. The "real" ages scenario was also considered with simulation of weights at the effective observed ages of a group of 100 animals randomly selected from the 16029 animals on the database. We also compared the estimation methods for different homogeneous age schemes of observation, using equidistant observations, taken at every 15 or every 30 days, and until a maximum age of 2, 4 or 6 years. Simulated weights, under what we have called ´´realistic" age scheme, was also considered. This age scheme is the same age scheme of a new random sample of 100 animals extracted from the database, but restricting the choice to animals that have at least 4 observations with the last observation at the maximum age of 18 months. Notice that this is in fact the scenario we face in the Breeders Association ACBM (Associação de Criadores de Bovinos Mertolengos), since the purpose of the Association is to perform the growing and finishing phases

of young Mertolengo males to sell in the meat market, and according to the dataset the mean selling age of a bovine male is about 14 months old.
For small sample sizes, ML estimates may have non-negligible biases and the confidence intervals obtained from the Fisher information matrix may be quite unreliable. In such case, bootstrap methods can be used. Since that was the case of the "real" ages scenario, a parametric bootstrap estimation method was also applied to the corresponding simulated data set, allowing us to correct the bias and improve the standard error of the ML estimates.

We concluded that, when the age scheme of observations is homogeneous with equidistant observation ages common to all animals and there are a reasonable number of observations, the ML estimates are recommended and the accuracy of the estimates improves as the range of observations reaches older ages. For heterogeneous age schemes, like the ones available in our application data for the evolution of bovine weight of Mertolengo cattle breeds, the estimation methods become much more imprecise. A sample of animals with an heterogeneous age scheme of observations, but with a large number of observations and some of them for animals with older ages, is enough for a similar performance of both methods. However, if in the dataset all the observations are for animals at younger ages, the WML method performs a lot better than the ML method, being the recommended method.

When we are dealing with real data, since the ML and the WML methods can estimate the parameters with bias and high variability, we applied the Bootstrap estimation method to correct the bias. We have seen that the estimation error decreases significantly using this method when dealing with heterogeneous "real" ages scenario where some animals have weight observations at older ages. As for the heterogeneous "realistic" age scheme with only very young animals, the Bootstrap method improved significantly the ML estimation method, but, compared with the WML method, the estimates have similar or even worse precision.

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Immune responses by CD4+ T cells

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We use a a set of ordinary differential equations (ODE) to study mathematically the effect of regulatory T cells (Tregs) in the control of immune responses by CD4+ T cells. T cells trigger an immune response in the presence of their specific antigen, while regulatory T cells (Tregs) play a role in limiting auto-immune diseases due to their immune-suppressive ability. We fitted this model to quantitative data regarding the CD4+ T cell numbers from the 28 days following the infection of mice with lymphocytic choriomeningitis virus LCMV. We observed the proliferation of T cells and, to a lower extent, Tregs during the immune activation phase following infection and subsequently, during the contraction phase, a smooth transition from faster to slower death rates. Furthermore, we have obtained explicit exact formulas that give the relationship between the concentration of T cells, the concentration of Tregs, and the antigenic stimulation of T cells, when the system is at equilibria, stable or unstable. We found a region of bistability, where 2 stable equilibria exist. Making a cross section along the antigenic stimulation of T cells parameter, we observe an hysteresis bounded by two thresholds of antigenic stimulation of T cells. Moreover, there are values of the slope parameter of the tuning, between the antigenic stimulation of T cells and the antigenic stimulation of Tregs, for which an isola-center bifurcation appear and, for some other values, there is a transcritical bifurcation.

Entropy and the arrow of time in population dynamics

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Time reversal symmetry is one of the fundamental symmetry in physical laws; as a simple, but clear example, second Newton's law is preserved by the time reversal $t \to -t$. In classical Hamiltonian mechanics, we frequently assume $H(p,q) = H(p,-q)$ and, therefore $(q(t), p(t))$ solves Hamilton's equations if and only if $(q(-t), -p(-t))$ solves the same system.

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However, at human scale (i.e., when considering the number of interacting agents in a given system at the order of 10^{23} particles), physics is full of irreversible phenomena. A clear example of dissutation happens when a drop of ink dissolves in a bucket of water. Nothing prevents an spontaneous concentration of ink from a previously homogeneous mixture; however this phenomena is expected to happen — even with almost negligible probability – after a interval of time larger that the age of universe.

The irreversibility of a certain class of physical phenomena is natural only in the realm of statistical mechanics — the area of physics that deals with a large number of interacting constituents. One of the aims of the present work is to use techniques from statistical mechanics to understand irreversible phenomena in models used in population genetics.

Population genetics has no equivalent of the second Newton's law. Furthermore, most models based on microscopic description of a population (e.g., the Moran, and the Wright-Fisher processes, Individual based dynamics, to name a few models used in the study of biological evolution) are first-order in time, and therefore does not posses the symmetry $t \to -t$. Therefore, it is not unexpected that population based mathematical models do not present, generally, the time-reversal symmetry. Example of such models are the replicator dynamics, the Kimura equation, the canonical equation of adaptive dynamics etc.

On the other hand, both classical particle physics and population genetics starts with the description of the dynamics at individual level. However, the relevant features are measured in completely different scales – in fact, at population level, although this expression is not used in physics.

In this work we propose to explore one of the central concepts of the micro-macro asymmetry in physics, the *entropy*, in the context of evolutionary dynamics. We will use the term as close as possible to its meaning in statistical mechanics.

The concept of entropy was introduced in physics within the framework of the study of efficiency in thermal machines; later on, Boltzmann reinterpreted this concept as a measure of the number of microstates consistent with a given macroscopic state of a system with a large number of degrees of freedom. The understanding of entropy and the associated second law of thermodynamics is fundamental to understand the asymmetry between past and future — the so called *arrow of time*, cf.

The implications of the concept of entropy went far beyond physics; in a further development, Shannon extended Boltzmann ideas to what is now called *information theory*. Currently, many reinterpretations of this concept are studied in general biology, including.

Here, we are concerned with understanding non-equilibrium dynamics, and, in particular, irreversibility, in population dynamics. More precisely, we start this work by considering a population of interacting individuals, in which individuals are replaced by newborns over time, according to certain dynamics. These newborns inherit the characteristics from its parents.

In population dynamics, as discussed above, we are not concerned with the precise characterization of individuals, but with macroscopic descriptions, i.e., descriptions at population level. In particular, we study how allele frequency — the fraction of the population that shares a given allele — varies over time when the population evolves according to certain rules defined at individual level.

We claim that the entropies introduced in are the relevant quantities to characterize the irreversibility feature of evolutionary dynamics. More precisely, they form a class of functions obtained naturally from the mathematical theory of gradient flows and optimal transport; therefore, they are not only monotonous in time, but they increase in an efficient way. We will proceed with a detailed study of this concept for populations evolving according to the Moran process and discuss the application of the concept in models in which the mathematical theory does not apply directly.

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Dynamics of vaccination strategies

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In this work, we study the evolution of vaccination decisions in a homogeneous population depending on the morbidity risks of the vaccine, the morbidity risks of the disease, and also depending on the decisions of all other individuals. In 2017 [1], Martins and Pinto introduced the evolutionary vaccination dynamics of the population vaccination strategy for the basic reinfection SIRI model. We analyze the changes provoked in the vaccination dynamics when the morbidity risks also evolve with the course of the disease.

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Mathematical modeling of epidemics: ODE's, complex networks and hybrid models

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This talk is divided in three parts. We start by presenting a SICA (Susceptible–Infectious–Chronic–AIDS) mathematical model given by a system of ordinary differential equations (ODE's) for the transmission dynamics of human immunodeficiency virus (HIV), considering real data from Cape Verde [3, 4].

After, we propose a complex network built with non identical instances of the SICA model, in heterogeneous geographical areas. We analyze the effect of different coupling and intensity of migratory movements between nodes and explore the effect of human displacement and behavior [1].

Finally, we built hybrid models by coupling epidemic models given by ODE's systems and agent-based models. These hybrid models intend to integrate the microscopic dynamics of individual behaviors into the macroscopic evolution of various population dynamics models. We apply the hybrid model general framework to the COVID-19 pandemic in Portugal [2].

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Modelling secondary infections with temporary immunity and disease enhancement factor: mechanisms for complex dynamics in simple epidemiological models

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With the outbreak of COVID-19, which quickly spread across the world and became a pandemic, modelling, understanding, and foreseeing the transmission of diseases became a key source for controlling disease spread and preventing mortality caused by those infections. In this work, a SIR model-type is studied, considering two subsequent infections, no strain structure and two features: cross-immunity protection between infections and an effect known as antibody-dependent enhancement (ADE), both of which are present in dengue fever. The model exhibits rich dynamical behavior, including fixed points, limit cycles, and chaotic dynamics. We also investigate the role of those two main features included in the model. The ADE effect and cross protection play an important role in changing the dynamical behavior of the model, generating backward bifurcation in a set region of parameters.

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Understanding the immunological responses mediated by antibodies during primary and secondary dengue infection

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With more than a half of the world's population being at risk of dengue infection, at present dengue fever is a major public health problem in the tropics and subtropics. Nevertheless, a threat of possible outbreaks in Europe should not be underestimated. It is caused by four antigenically related but distinct serotypes (DENV-1 to DENV-4), infection by one serotype confers life-long immunity to that serotype and a period of temporary cross-immunity (TCI) to other serotypes. Although most of the cases recover following a self-limiting non-severe clinical course, there is good evidence that sequential infection increases the risk of developing severe disease, due to a process described as antibody-dependent enhancement (ADE). There is no specific treatment for dengue, and severe cases require hospitalization. A safe, effective and affordable dengue vaccine against the four strains would represent a significant advance for the control of the disease and could be an important tool for reducing disease transmission and mortality.
Mathematical modeling is often used for understanding infectious diseases dynamics and to evaluate the introduction of intervention strategies like vector control and vaccination. A within-host framework is built to describe viral replication and antibody responses affecting the disease outcome in primary and recurrent infections. Understanding the immunopathogenesis of severe illness during recurring infections is critical for future research directions to evaluate the impact of dengue vaccines.
In this work, we analyse the deterministic and stochastic models describing the immunological responses mediated by antibodies during a primary dengue infection. A detailed sensitivity analysis of the parameters involved in the model is performed. The deterministic framework is extended to its stochastic counterpart for a better understanding of the variation observed in the available data. Using numerical simulations, we investigate features of viral replication, antibody production and infection clearance over time. Results presented here will be used as baseline to investigate a more complex within-host dengue model, giving insights into the immunopathogenesis of severe diseases during secondary infections caused by heterologous serotypes.

Optimal control of multi-strain host-vector dengue model

CT

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Dengue fever is caused by four dengue virus serotypes: DEN-1, DEN-2, DEN-3, and DEN-4. This study presents a mathematical host-vector model considering multiple strains of dengue fever and the dynamics between human and mosquito population. For this model, the sensitivity analysis (PRCC Method) is conducted in order to identify the key parameter that has more influence in the transmission of dengue. Further, in order to find the optimal strategies for suitable control interventions that reduce the dengue prevalence and economic burden, an optimal control problem is proposed by considering vaccination, use of preventive measures and killing mosquito population as control interventions. A weighted sum of various costs incurred in applied controls and the cost due to dengue disease (productivity loss) is incorporated in the proposed cost functional. The analysis of control system using Pontryagins Maximum Principle leads the existence of the optimal control profiles. Further, an exhaustive comparative study for three different control strategies is conducted numerically. Our findings ensure that every individual control strategy has their own impact on reducing the cumulative count of infection. The combined impact of all control interventions is highly effective in controlling the prevalence of dengue. We observed that the comprehensive use of controls keeps a strong tab on the infectivity even if the severity of epidemic is high.

ON THE ORIGIN OF COMPLEX DYNAMICS IN MULTI-STRAIN DENGUE MODELS

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Dengue fever epidemiological dynamics shows large fluctuations in disease incidence, and several mathematical models describing the transmission of dengue viruses have been proposed to explain the irregular behavior of dengue epidemics. Multi-strain dengue models are often modeled with SIR-type models where the SIR classes are labeled for the hosts that have seen the individual strains. The extended models show complex dynamics and qualitatively a very good result when comparing empirical data and model simulations. However, modeling insights for epidemiological scenarios characterized by chaotic dynamics, such as for dengue fever epidemiology, have been largely unexplored. The problem is mathematically difficult and to make the urgently needed progress in our understanding of such dynamics, concepts from various fields of mathematics as well the availability of good data for model evaluation are needed.

In this talk, I will present a set of models motivated by dengue fever epidemiology and compare different dynamical behaviors originated when increasing complexity into the model framework.

Thursday 14th

Kinematics, dynamics and complex motion in biology

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We present a study on complex motion in biology. From a descriptive point of view, we have kinematics. Introducing the causes of movement or an interaction with the environment we have a dynamical point of view. Our main objective is the classification of complex patterns of motion.

We consider a two-parameter family of bimodal interval maps which determines the displacements through iteration. A trajectory is, therefore, composed of patches of linear motions, intertwined by changes of direction.

The characterization of the types of movements is obtained from the topological classification of the interval map family. Techniques from symbolic dynamics and topological Markov chains are used, and the main classifying tool is the kneading invariant - the symbolic itinerary of the critical orbits of the interval maps.

We present part of a catalogue or dictionary of typical trajectories.

We further discuss ongoing work on multiple organism motion with interactions and dependence on the environment.

An optimal control problem for non autonomous crop growth with Richards Logistic growth and predation

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The aim of this work is to study an optimal control problem for a non autonomous crop growth model with Richards Logistic growth. Preys are divided in two compartments: one represents the susceptible individuals (S) and another one represents the infected individuals (I). The natural predators of the preys (P) and the level of awareness (A) are also considered.

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Predators biomass depends only on the preys and we consider predators death is caused by intra-specific competition and natural causes but is not affected by the infection. Competition among preys is also considered.

Non autonomous Richards growth logistic law has the form

$$X' = r\left(t\right) X \left(1 - \left(\frac{X}{k}\right)^{q}\right),\ q \in \mathbb{R}R^{+},\ t \in [0, t_f]$$

where $r\left(t\right), 0 < r_1 \leqslant r\left(t\right) \leqslant r_2 < \infty$, is the growth and k is the carrying capacity of the system. This law is more suitable than the usual logistic growth model to simulate crops biomass growth, as we can see in [3] and [4].

Our goal is to maximize the crop biomass and awareness, minimizing simultaneously the preys, both susceptible and infected.

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Measure the complexity of Nicholson-Bailey type biological dynamical systems using symbolic dynamics

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In this work is characterized the complexity of bidimensional discrete dynamical systems with chaotic behavior and limit cycles, which appear from the Nicholson-Bailey model. This class of bidimensional continuous maps that we will consider has the particularity of admitting periodic critical orbits and strange attractors obtained from the critical orbits which makes possible, through the kneading theory, construct the Markov partitions in its phase space and consequently the definition of a rigorous method to calculate the topological entropy.

The Nicholson-Bailey model [1], which investigates the complex dynamics between a parasitoid and its host has been widely studied. In 1975, Beddington, Free and Lawton [6] presented a generalization of the initial Nicholson-Bailey model and based on that generalization [2], we study the dynamics of the bidimensional map $F(x,y) = (f(x,y), g(x,y))$ with four parameters defined by

$$\begin{cases} f(x,y) = x\left(e^{r\left(1-\frac{x}{k}\right)-by}\right) \\ g(x,y) = x\left(1-e^{ay}\right) \end{cases}, \tag{0.2}$$

with $x, y > 0$, where x represents the population of the hosts, y the population of the parasitoids before they die, and the real parameters a, b, r and k are all positive.

The dynamics described by the model 0.2 are studied using the tools of symbolic dynamics, kneading sequence, Lyaponov exponent and bifurcation diagram developed for two specific types of bidimensional maps, the bidimensional triangular maps and Lozi-Hénon-type maps

In the case of the bidimensional triangular maps, which are a continuum maps of the form

$$T(x,y) = (f(x), g(x,y)), b = 0$$

we follow the work developed by Diana Mendes and J. Sousa Ramos [7].

Assuming that the quantity of the population y can be given by a percentage population x, i.e. $y = bx$, with $0 < b \leq 1$, and following the work developed by Diogo Baptista [4, 5, 3], we will work on the Lozi-Hénon-type map defined by

$$LH(x,y) = (f(x,y), g(x)).$$

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Cell polarisation and cytosolic protein diffusion in the bulk-surface wave-pinning model

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The *bulk-surface wave-pinning (BSWP) model* is a reaction-diffusion system for studying cell polarisation in three-dimensional domains [1] and it represents a multi-dimensional extension of the classical *wave-pinning model*, originally proposed in [2]. Both models describe the switching between the active and inactive states of a representative protein from the GTPase family. The bulk-surface extension of the wave-pinning model is motivated by the fact that active proteins are bounded to the cell membrane, while inactive proteins are generally found internally within the cytosol. Hence, the BSWP model is constituted by the following surface reaction-diffusion equation

$$\frac{\partial a}{\partial t}(\mathbf{x},t) = D_a \Delta_\Gamma a(\mathbf{x},t) + f(a,b), \quad \mathbf{x} \in \Gamma, \tag{0.3}$$

coupled to a bulk diffusion equation with a non-linear boundary condition:

$$\frac{\partial b}{\partial t}(\mathbf{x},t) = D_b \Delta b(\mathbf{x},t), \quad \mathbf{x} \in \Omega, \tag{0.4}$$

$$-D_b \frac{\partial b}{\partial \mathbf{n}}(\mathbf{x},t) = f(a,b), \quad \mathbf{x} \in \Gamma. \tag{0.5}$$

Here, Δ is the classical Laplace operator, Δ_Γ is the Laplace-Beltrami operator, $\mathbf{n}$ is the outward vector to Ω on Γ, D_b and D_a are the bulk and surface diffusion coefficients, respectively. The function f is defined as

$$f(a,b) = \left(k_0 + \frac{\gamma a^2}{K^2 + a^2}\right) b - \beta a \tag{0.6}$$

and indicates the reaction between the active proteins $a(\mathbf{x},t)$ and the inactive counterparts $b(\mathbf{x},t)$, which takes place at the boundary of Ω. The constant parameters $k_0 > 0$ and $\beta > 0$ represent,

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respectively, the basal activation and inactivation rates, while $\gamma > 0$ weights a nonlinear term describing a positive feedback loop in activation, in the form of a Hill function. At saturation of a, the extent of this term tends to γb, while K represents the half-activation concentration of a.

Cell polarisation arises as the surface component forms specific patterns, by developing propagating front solutions with non-constant speed. Since proteins diffuse much faster in the cell interior than on the membrane, in the literature, the bulk component is often assumed to be spatially homogeneous, see for example [3]. Therefore the model reduces to a single surface equation. However, a spatially non-uniform bulk component might be an important player to take into account. In this work, we study, through numerical computations based on the bulk-surface finite element method [1, 4], the role of the bulk component and, more specifically, how different bulk diffusion rates might affect the polarisation response. We find that the bulk component is indeed a key factor in defining the final position of the polarised surface area. Moreover, for certain geometries, it is the spatial heterogeneity of the bulk component that triggers the polarisation response, which might not be possible in a minimal surface model. Understanding how polarisation depends on bulk diffusivity might be crucial when studying models of migrating cells, which are naturally subject to domain deformation.

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Modeling Iron Metabolism and Erythropoiesis of Blood Donors

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In the United States and Canada, blood donors are allowed to give blood every 56 days (8 weeks).

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This interval is based on old studies investigating only the recovery of hemoglobin after blood donation. Recent experimental studies, which measure other iron parameters after blood donation, have shown that this interval is very short to prevent iron deficiency in frequent blood donors. Possible interventions can be lengthening the interval between donations, giving iron supplementation, or combination of both.

In this talk, we present a mathematical model which we propose for erythropoiesis and iron metabolism and apply it to this problem. The model consists of six coupled delayed differential equations (DDEs). The first four equations track iron during erythropoiesis, including: the hemoglobin iron within erythrocytes, iron in the recycling macrophages, iron in circulating plasma, and iron in the storage. The last two equations in the model describe the dynamics of the major regulating hormones: hepcidin and erythropoietin (EPO). Hepcidin is produced in the liver, and regulates iron uptake for hemoglobin synthesis during erythropoiesis. EPO is produced principally in the kidney in adult humans, and regulates erythroid cells proliferation. Mathematically, the inclusion of delays in our model has the advantage of minimizing the number of variables in the model in order to circumvent issues with parameter identifiability that arise in ODE many-compartment models. The use of distributed delays allows us to capture the effect of the hormones on precursor cells. We show how to reformulate the distributed DDEs so that solutions can be simulated using standard MATLAB solver. We present numerical simulation of a single and multiple blood donations with and without iron supplementation, compare with experimental data from the literature, and show some conclusions.

Modelling the functional status of people with COPD - a comparison of feature selection methods

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Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive, treatable and preventable respiratory disease. The 2020 imposed lockdown due to the Coronavirus Disease 2019 (COVID-19) pandemic is likely to have influenced funcional status of people with COPD. Linear models (LMs) aim to predict outcomes given p features. The following measures can be used to quantify the fit: (i) mean squared error (MSE); (ii) coefficient of determination (R^2); (iii) adjusted R^2; (iv) Akaike's information criterion (AIC); (v) Bayesian information criterion (BIC). Criteria to choose appropriate methods to select features are unclear. Information theory provides criteria for setting up probability distributions on the basis of partial knowledge [1]. Normalized entropy [2] measures the information content of a particular model or feature. It was defined based on the consistent and asymptotically normal generalized maximum entropy estimator [3]. Features with normalized entropy approximately equal to one should be excluded. We aimed to compare feature selection (FS) methods and describe the effect of the COVID-19 lockdown, sociodemographic and clinical features on the functional status of people with COPD.

Methods

Data from stable people with COPD were used. Functional status was assessed using the one-minute sit-to-stand test at baseline and 5 months after. The minimal clinically important difference (MCID) is 3 repetitions. FS was performed in standardized data: (i) LASSO used the λ that produced the lowest 5-fold cross-validation MSE; (ii) AIC/BIC based stepwise automatic selection consisted of a backward elimination of terms from a LM with all features in order to obtain the lowest AIC/BIC; (iii) normalized entropy procedure with optimization of the support. Ordinary least squares (OLS) LMs and fit measures were applied. A LM with the features selected by the entropy algorithm that returned the lowest AIC was computed.

Results

A total of 39 participants were included. $\lambda = -1.34$ minimized the MSE and selected BORG Dyspnoea, sex and pack years. The AIC algorithm removed 14 features. With decreasing importance, the features sex, BORG Dyspnoea, pack years, St. George's respiratory questionaire (SGRQ), modified British medical research council dyspnoea (mMRC), smoking status and FEV1/FVC were kept. Using BIC, BORG Dyspnoea and pack years remained. Sex had the lowest normalized entropy (0.948) followed by pack years (0.966). BORG Dyspnoea, SGRQ and BORG Fatigue registered a value under 0.98. No significant differences between models were found. The LM using the features selected by LASSO and the entropy algorithm with 3 features was the same and had the lowest AIC. It shows that a unit increase in the BORG Dyspnoea scale tended to increase the difference of repetitions by 1.25 repetitions (CI95=[0.14,2.38]). Male participants with scores of 3 and 4 tended to recover above the MCID.

Discussion and Conclusion

Some features can be considered relevant by significance tests in regression models where relationships between outcome and features do not exit [4]. Elimination algorithms can overestimate the effect size of features and should not be used if $p > n$ [5][6]. OLS may be biased and lead to unstable solutions [7]. Normalized entropy estimation is appealing because it imposes no structure on data [3]. Nevertheless, the LM obtained with 3 features selected by the entropy approach was at least not worse than the remaining. Our model suggests that lockdown had no effect in the functional status of participants with COPD but male with a severe dyspnoea tend to clinically improve.

Acknowledgements

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Kinetic modelling and analysis of autoimmune diseases

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We consider a mathematical model for autoimmune disease based on a kinetic theory approach. The model describes not only the cellular dynamics and the biological expression of cells but also the global behaviour of the interacting populations that are involved in the disease. We investigate relevant properties of the model solution and study interesting problems related to the chronicity and impact of drug therapies on the development of the disease.

We perform some numerical simulations which show the ability of the model to reproduce different aspects of the disease and to investigate optimal treatment strategies.

An optimal control problem for a non-autonomous model consisting of two prey, one predator with weak Allee effect on the strong prey

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The aim of this paper is to formulate an optimal control problem for a non autonomous model with two prey species, one strong and the other weak, and a predator. The proposed model incorporates a weak Allee effect in the strong prey and seasonal breeding in both preys. We consider a death rate for predators that leads to a decrease in their biomass. An optimal control problem related to predators biomass is formulated. Existence and uniqueness of optimal solutions are established. Uniqueness on the whole interval is also obtained using an inductive argument. Simulation results show the usefulness of the proposed model in the control of predators biomass.

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Fractional Modelling and Optimal Control of the third wave of COVID-19 in Portugal

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A fractional-order compartmental model was quite recently used to describe real data of the first wave of the COVID-19 pandemic in Portugal [1]. After time dimensions correction of the model, it is used to investigate the third wave of COVID-19 which occurred in Portugal from December 2020 till February 2021. That wave surpassed all previous ones, both in numbers and consequences. A new fractional optimal control problem is then formulated and numerically solved, with vaccination and preventive measures as controls. A cost-effectiveness analysis is carried out, and the obtained results are discussed.

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A pragmatic view on chaotic dynamics and ergodicity in a SIR-like epidemic model

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Epidemiological models, such as the prototypical compartmental SIR model, are widely used to describe the evolution of infectious diseases. Even though this kind of simplistic models fairly capture the phenomenology of the spreading disease, under certain circumstances are not capable of describing its long-term behavior. Sometimes, this lack of reproducibility of real data is not due to a deficiency of the model but to the non-linear nature of the phenomenon itself (associated with the emergence of chaos). A theoretical tool used to determine the stability of the solution and to define the prediction horizon are the Lyapunov's exponents λ_j (equal in number to the dimensionality of the phase space). In general, the solution is stable when the largest exponent is negative, while if at least one of the exponents is positive, it entails an exponential instability: infinitesimally close orbits in the phase space tend to separate exponentially in time with a rate λ (a hallmark of deterministic chaos). In particular, the unpredictability of chaos and the onset of complex dynamics that arises as consequence of the seasonally modulation in the transmission rate [1, 1] poses a challenge when it comes to establishing timely seasonal control measures (such as seasonal vaccination campaigns or lock-downs) for recurrent disease outbreaks (i.e. influenza, dengue or COVID-19).

Stochastic versions of deterministic models are used to explore the effects of external noise or random environments (introduced as stochastic terms in the differential equations system or as fluctuations in the parameter values) in the simulated population dynamics. On average, the stochastic solution should match the deterministic one (mean-field approximation). But, when the system is not ergodic, *time*-averages of a given observable may not correspond with the obtained when using *ensemble*-averages (also known as *phase-space* averages).

In practice, the ergodicity of the problem is a feature often overlooked. However, the ergodicity breaking has implications that must be taken into account in order not to reach misleading or erroneous conclusions [3]. Here, from a practical point of view, the direct consequences of

the non-ergodicity will be shown in a concrete physical example. From experimental measurements (physical observables of a granular system and some time variables), the ergodicity has been quantified in statistical terms (by means of diffusive properties) and rationalized (through a Continuous-Time Random Walk (CTRW) sub-diffusive model) [2].

Finally, our ongoing research will be presented and some preliminary results on the stability of a seasonally-driven SIR model with waning immunity and imported infected population, which has been characterized in terms of the Lyapunov spectrum, and to bring some thoughts on ergodicity from a merely pragmatic perspective.

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Assessing the fallout of different control measures for dengue disease

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Mathematical models are ubiquitous tools in epidemiological studies [[1], [2], [3]], as this COVID-19 pandemic clearly documented, with thousands of papers on mathematical models for SARS-CoV-2 transmission dynamics being published. In this paper, we introduce a non-integer order model for the transmission dynamics of dengue fever in a susceptible population. We intend to assess the influence of four different control strategies in disease spread. The controls include existence of sterile male mosquitoes, the use of pesticides for larvae, the use of pesticide for adult mosquitoes, and vaccination against dengue virus (DENV). The numerical results suggest that our model is well-posed, and epidemiological inferences are drawn, which may help define health policy measures.

Keywords: DENV, Dengue fever, mathematical model, control strategies.

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The Max-Out Min-In Problem: A Tool for Data Analysis in Biomathematics

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Let $N = \{1, 2, \ldots, n\}$ be a set of *entities* and $W = [w_{ij}]$ a non-negative symmetric matrix of weights expressing quantified relations between pairs of elements of N, with $w_{ii} = 0$, for $i = 1, \ldots, n$. For $S \subseteq N$, we define $\phi(S)$ to be the sum of the weights of pairs of elements where an element is in S and the other is in $\bar{S} = N \setminus S$, minus the sum of the weights of pairs of elements in S. We consider the problem of finding $S \subseteq N$ for which $\phi(S)$ is maximized. We call this combinatorial optimization problem the max-out min-in problem (MOMIP). In this talk I will present two alternative formulations of MOMIP, discuss the application of MOMIP in the selection of variables in exploratory data analysis and in the identification of clusters in the context of cluster analysis, and report preliminary results of its applicability in priority area selection for species coping with climate change, an urgent issue in Conservation Biology.

This is a joint work with Maria João Martins (ISA, ULisboa), Marcos Raydan (CMA, FCT-NOVA) and Diogo Alagador (UÉvora)

List of Posters

Optimal control strategies for the HIV/AIDS epidemic in the Philippines

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The Human Immunodeficiency Virus (HIV) impairs a person's immune system, which can lead to Acquired Immunodeficiency Syndrome (AIDS), a condition marked by co-infection of other severe diseases. In the Philippines, HIV infections have more than doubled from 2010 to 2016, and a sterilizing cure is yet to be discovered. Here, we have constructed a mathematical model to capture the HIV dynamics in the Philippines. The model equilibria and basic reproduction number have been calculated, and public data have been used to identify model parameters. Under the framework of optimal control theory, the efficiency of precautionary measures, HIV screening, Anti-Retroviral Therapy, and Pre-Exposure Prophylaxis (PrEP) as disease controls has also been investigated. Each strategy, and combinations thereof have been compared in terms of their cost-effectiveness and ability to reduce infections. The PrEP-only scenario has been shown to be the most cost-effective strategy among all the possible combinations.

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Identification of transcriptomic markers of intertumoral heterogeneity in gliomas via sparse logistic regression with the elastic net penalty

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Given that glioma is the most common primary brain tumor, understanding heterogeneity among its subtypes is relevant to the improvement in the procedures applied to each patient, mainly diagnosis and treatment. The application of Machine Learning techniques has shown to be useful in this understanding, handling well with the complexity of biological data in order to produce efficient results [1]. In particular, sparse logistic regression has been applied for both classification of glioblastoma (GBM) patients and selecting the relevant features that separate the different patient and cell groups [2].

In this work two methodologies were applied to RNA sequencing data from glioma patients obtained from The Cancer Genome Atlas (TCGA) database. The first one was the application of t-distributed stochastic neighbor embedding (t-SNE) for visualization of patients attributed to different gliomas, namely astrocytoma, oligodendroglioma, oligoastrocytoma – low-grade-gliomas (LGG) – and GBM, the most common and aggressive subtype. The second one was the fitting of a sparse logistic regression model using elastic net with different parameters to optimize the strength of the penalty and the best compromise between the Lasso and Ridge penalties, in the identification of genes as potential biomarkers of intertumoral heterogeneity in gliomas, in particular, LGG subtypes. Both methodologies were implemented and tested using the R software [4].

t-SNE showed a good separability between GBM and LGG, but the separation of LGG histological types was not so evident. Among the genes selected by sparse logistic regression with the elastic net penalty, *TXNDC12* was selected for all fitted models. Previous reports have shown a significantly high expression of this gene in gliomas [3], highlighting the suitability of the present approach to disclose relevant genes and foster the biological validation of non-reported genes.

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Disclosing sparse transcriptomics networks in gliomas using the graphical lasso

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Glioma is one of the most common brain tumor. There are several glioma subtypes, among which glioblastoma (GBM) represents the most aggressive one, with a median survival time of 1 year. Glioma is characterized by both intertumoral and intramural heterogeneity [1], which often leads to bad prognosis, and therefore further treatments need to be developed. To this end, the search for new molecular biomarkers can be fundamental to design novel targeted therapies.

The recent advances in sequencing technology allow for the collection of a huge amount of data coming from multi-omics layers, holding the promise of disclosing new therapeutic direction. However, the analysis of these information is not trivial, due to the high dimensionality of the data, the unknown relations between the variables in each level, and between different omics. Several methods have been proposed to analyze single and multi-omics data with the aim of classifying patients, understanding underlying unknown mechanisms or discovering new biomarkers [2], and some of them have been applied to glioma [3, 4, 6, 5].

The work we are presenting applies the graphical lasso (glasso) algorithm [7] to RNA-sequencing dataset extracted from TCGA, referring to two different glioma subtypes: GBM and low-grade glioma (LGG). The idea of glasso method is generalizing the classical lasso, by assuming that, given N samples of p normally distributed variables, the theoretical and the empirical covariance matrices are different. Due to the presence of a regularization term, glasso provides a sparse covariance matrix and, as a consequence, a sparse inverse of the covariance matrix, also known as precision matrix. The precision matrix can be considered a good estimate for the adjacent matrix of the network between the p variables [8]. The goal of our work is estimating sparse transcriptomic networks describing the relations between the genes. Using these information, we define different measures, which allow us to identify key variables. We compare the variables selected from the different glioma subtypes, analyzing differences and similarities.

Since it has been shown that integrating more than one omics leads to better results [9, 10], in the next future, we plan to extend this work by using the information provided by glasso as prior knowledge for a multi-omics analysis. We believe that considering trans-omic relations is an essential step to identify potential biomarkers associated to different glioma subtypes, in order to improve patients prognosis, diagnosis and therapies.

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Genomic prediction using machine learning methods: performance comparison on synthetic and empirical data

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The accurate prediction of genomic breeding values is central to genomic selection (GS) in both plant and animal breeding studies. Genomic prediction (GP) involves the use of thousands of molecular markers spanning the entire genome and therefore requires methods able to efficiently handle high dimensional data. Machine learning (ML) methods, which encompass different groups of supervised and unsupervised learning methods, are becoming widely advocated for and used in GP studies. Although several studies have compared the predictive performances of individual methods [1], studies comparing the predictive performance of different groups of methods are rare. However, such studies are crucial for identifying (i) groups of methods with superior predictive performance and assessing (ii) the merits and demerits of such groups of methods relative to each other and to the established classical methods. Here, we comparatively evaluate the genomic predictive performance of several groups of supervised ML methods using one simulated dataset (animal breeding population) and three empirical maize breeding datasets. Our results show that the relative predictive performance of the groups of ML methods depends upon both the data and target traits and that for classical regularized methods, increasing model complexity can incur huge computational cost but does not necessarily always substantially improve predictive accuracy. This rules out selection of one benchmark procedure among ML methods for genomic prediction.

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Estimating life expectancy and years of life lost in 2020 associated with the COVID-19 pandemic in the Basque Country

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Life Expectancy at Birth (LEB) is one of the most frequently used health status indicators, estimating the average number of additional years that a person of a given age can expect to live. It is estimated from the number of age-specific deaths during a particular period of time, divided by the total observed population alive at a given point within that interval. Higher death rates lowers the average life expectancy. Investment on public health systems improving health care, is essential to increase life expectancy worldwide.

According to recent estimations, the decline in life expectancy between 2019 and 2020 can primarily be attributed to deaths from the COVID-19 pandemic. In this work, which is part of the "Mathematical modelling Applied to Health" project, we estimate the life expectancy loss in Basque Country between 2019 and 2020. With the objective to measure the impact of the COVID-19 during the first year of the pandemic in terms of health, a survival analysis is carried out for the Basque population. Three different age-group intervals were considered: 0 to 110, 5 to 95 and 30 to 90 years of age. For those ranges, we used lineal regression predictors to create three parametric models based on the Gompertz survival function. We studied their fitting regression line with the R^2 parameter, and compared their survival function results with the survival empirical data. Finally we compared our predictions with the results available from the Spanish Statistics Institute (INE). We evaluate separately women, men and the total population.

Although the LEB has been rising over the last few years, the pandemic had an important impact in the health indicators of the Basque population. Our results show that the COVID-19 has affected men more than women, with a LEB loss of 0.95 and 0.87 years respectively, with a significant impact on older ages. Population older than 85 years presented a relative life expectancy loss higher than 5%, while population younger than 25 years had a relative loss lower than 1.5%.

Short Course

Stochastic processes theory and applications

12 and 15 Jully, from 14:30 to 17:00

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We present a concise introduction of stochastic processes, including its consequences in terms of parameter estimation from empirical data and model comparison, from basic notions on mathematics. Basic notions of probability theory are introduced, following the application to dynamic stochastic processes, from discrete maps via the Perron-Frobenius type equations to time continuous state discrete systems and approximations via the Fokker-Planck equations derived via Kramers-Moyal expansion. Maximum likelihood and Bayesian methods of parameter estimation in stochastic processes will be demonstrated, and model comparison in Bayesian frameworks discussed. If time permits, spatially extended stochastic processes will be described, leading in mean field approximation to partial differential equations, including ordinary diffusion and in the framework of fractional calculus also superdiffusive processes. All material will be complemented with examples from population biology and especially epidemiology, now in the wider public attention due to the COVID-19 pandemic experienced in recent years. The examples allow a hands on approach to current research questions in stochastic processes, well beyond the demonstated examples of the course.

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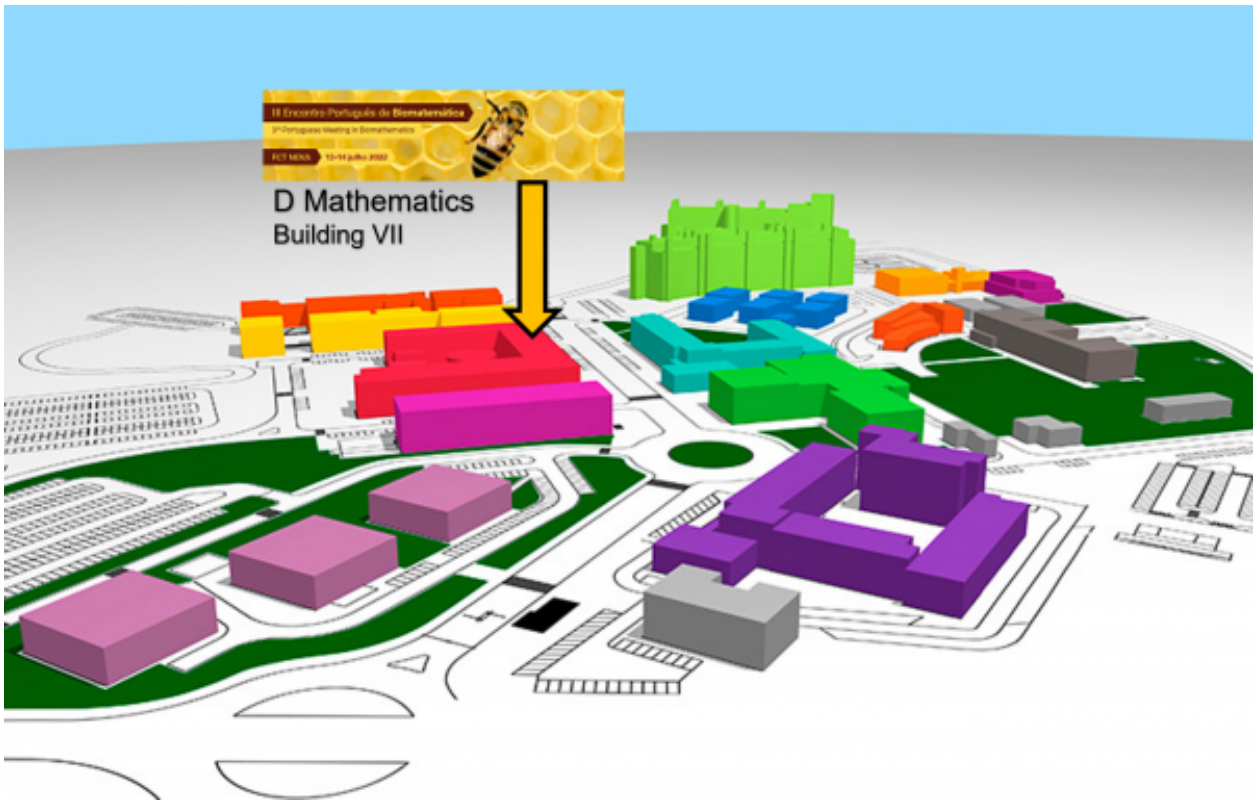
Willie Otávio Bueno Bernardi	São Paulo, Brazil

Useful Information

Talks will be held at the **Auditorium 1A-VII** in Building VII of NOVA School of Science and Technology | FCT NOVA (The Department of Mathematics is located in this building). The auditorium is situated on the ground floor of the west half of the building.



Coffee breaks will be offered next to Auditorium 1A-VII.

The **poster session** will be held on Tuesday next to Auditorium 1A-VII.

Open access to Wi-Fi will be available during the conference. Please choose the Open FCT or eduroam-guest networks. FCT NOVA also provides access to an eduroam network.

How to get to NOVA School of Science and Technology | FCT NOVA?

The campus is served by a wide transport network, including combined services (bus, train, ferry) and by tram, which terminus ("University") is located along one of the NOVA School of Science and Technology entrances. See this webpage for an useful map on how to get to FCT NOVA.

Here are some suggestions, although there are other possibilities, combining public transportation.

- From Lisbon (Humberto Delgado Airport)

  - By Metro (subway). The Lisbon airport has a underground station (metro) with a direct line to the city centre. The Red Line (Aeroporto – S. Sebastião) takes you to the downtown in about 20 minutes. The Metro network will allow you to move around the city at ease. To arrive at NOVA School of Science and Technology we advise you to exchange routes at Alameda (swaping from Red to Green Line), towards Cais do Sodré, where you can find the "Cais do Sodré" Ferry Station. Here you can take a ferryboat to "Cacilhas". Once in Cacilhas you take a tram (MTS) to "Universidade", hopping off on its terminus (located near one of the campus entrances).

  - By Shuttle. With frequent departures from the airport, this bus provides a link between the main city points, the Sete Rios bus terminal, the Entrecampos railway terminal, Cais do Sodré and the two terminals at the Lisbon Airport (1 and 2). AEROBUS 1: from the Aeroporto to Cais do Sodré, with stops at: Entrecampos, Campo Pequeno, Saldanha, Picoas, Marquês, Av. Liberdade, Restauradores, Rossio and Praça do Comércio. More information here.

  - By Taxi. There are always plenty of taxis at the Arrivals and Departures Halls. All the taxis have meters, a ride to NOVA School of Science and Technology costs approximately €20, depending on the traffic. During weekends, nights, and holidays there is a 20

  - By Bus. Several bus lines stop at the airport arrivals terminal, taking you to different parts of the city. However, please note that the maximum baggage size allowed in these buses is 50x40x20cm. If your baggage exceeds this size, you must take the airport's specific buses (Aerobus and Airport Shuttle).More information here and here.Please be advised that most of the routes provided here are only for Lisbon. From Lisbon you can take the Buses 3710 (Sete Rios - Costa da Caparica, with exit at Monte da Caparica IC20 Casas Velhas) or 3711 (Sete Rios - Monte da Caparica FCT Rotunda). New routes may be available soon.

- From Lisbon (Downtown)

  - By Car. Follow the directions to "A2 Sul". Cross the "25 de Abril" bridge towards south ("Sul"), take the first exit after the bridge, entering the expressway to Caparica (IC20), follow the sign "Universidade".

  - By Ferry. In the "Cais do Sodré" Ferry Station, you can take a ferryboat to "Cacilhas". Once in Cacilhas, you take a tram to "Universidade", hopping off on its terminus (located near one of the campus entrances).

  - By Bus. From Lisbon you can take the Buses 3710 (Sete Rios - Costa da Caparica, with exit at Monte da Caparica IC20 Casas Velhas) or 3711 (Sete Rios-Monte da Caparica FCT Rotunda). New routes may be available soon.

  - By Taxi. There are always plenty of taxis in the city. All the taxis have meters, a ride to FCT NOVA costs approximately €20, depending on the traffic. During weekends, nights, and holidays there is a 20

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