Workshop on population models in biology

Granada. November 26-28.

ABSTRACTS

Tomás Alarcón

Mathematical modelling of cancer treatment with transgenic oncolytic viruses

Oncolytic viruses (OV) provide an emerging class of cancer therapeutics based on replication-competent viruses that selectively infect and eradicate malignant cells. Their restricted replication within tumor tissue enables their use as targeted gene therapy vectors, for example, by encoding prodrug-converting enzymes that locally activate cytotoxic agents. Despite recent advances in this area, the synergistic combinations of lytic activity and processes tied to OV-targeted gene delivery remain poorly understood. We present a spatially structured, multi-patch model of cancer populations infected by an OV engineered to deliver a prodrug-activating enzyme. Our model describes how the OV propagates over the tumor and eradicates cancer cells. As infection progresses, the prodrug is activated by the OV within the infected cancer cells. This allows for the combined effects of the lytic and cytotoxic effects. Using spectral dimension reduction, we analyze a non-spatial ODE model and derive a basic reproduction number, R_0, that predicts OV spread. Notably, R_0 depends on only a subset of parameters, highlighting the key biological processes that enhance viral infection capacity and thus defining the parameters that should be considered to optimize OV-based therapies. Further numerical simulations show that the predictions of the diffusionless model extend to the case when cells are motile.

Javier Buceta Fernández

Tracing Ebola's Ecological Footprint: From Bat Habitats to Spillover Risk

Filovirus spillover emerges from a complex interplay of bat ecology, environmental drivers, and local stochastic dynamics. Here I will present different studies that cover enviroclimatic models of bat migration and infection, the socio-behavioral predictors of spillover exposure, and the stochastic analyses of Ebola persistence in small zoonotic niches. Together, these approaches reveal when and where risk is highest, and why some infections in populations fade out while others spark outbreaks. This multi-scale perspective highlights how ecological and social factors can be combined to improve prediction and guide targeted surveillance.

Sílvia Cuadrado

On ecological and epidemic structured model

The basic reproduction number $\mathcal{R}_0$ is a fundamental concept in epidemic and ecological modeling, typically computed as the spectral radius of the so-called *next-generation operator*. However, this approach fails when considering continuously structured populations with concentrated states at birth. We present a methodology to compute $\mathcal{R}_0$ in such settings as the limit of a sequence of models where the operator is well-defined. Several examples will be discussed, including an epidemic model with asymptomatic transmission, for which we also analyze the final infection size. Finally we will briefly explore some mathematical models of therapeutic virus treatments, including models of encapsulated bacteriophages in the grastrointestinal tract.

Gissell Estrada Rodriguez

Cell-cell adhesion models: mean-field limits and parameter estimation

This work presents a mathematical and computational framework for estimating parameters in cell–cell adhesion models. The study builds upon a macroscopic, nonlocal PDE model involving two interacting cell populations influenced by attractive and repulsive forces, incorporating both adhesion dynamics and volume exclusion effects. Starting from a stochastic particle system, the nonlinear PDE system for the cell densities is formally derived through mean-field limits. The parameter estimation problem is addressed by minimising an error functional that combines macroscopic densities and individual trajectories. The model parameters are estimated using a Bayesian approach, which involves sampling from the posterior distribution of the parameters given observed data. To efficiently sample from this distribution, the pre-conditioned Crank–Nicolson (pCN) Markov Chain Monte Carlo method is used. This algorithm is derivative-free, well-suited for high-dimensional spaces, and has a single tunable parameter to optimize performance.

Jordi Garcia-Ojalvo

Spatiotemporal modeling of dense bacterial populations

In this talk I give an overview of different types of mathematical models that we have used over the years to represent the dynamics of bacterial populations in space and time, focusing on the case of the dense bacterial aggregates known as biofilms. The examples discussed include a variety of growth geometries and conditions, and special emphasis is put on how the models are chosen as a function of the experimental information available, and how they are constrained by the experimental observations.

Erida Gjini

From confection SIS models with many strains to replicator dynamics: a new framework for theory and data

Despite extensive research, modelling and understanding biodiversity remains a challenge across fields such as ecology, epidemiology and microbiology. In the last years, we have approached biodiversity by developing and studying an N-strain SIS system with co-colonization and interactions, leading to a replicator equation. Using mathematical techniques, we have simplified this high-dimensional eco-epidemiological system, finding organizing principles for stability, complexity and coexistence, and parallels across biological scales: from microbial transmission at the population level to multi-species microbiota dynamics within host. In this talk, I will present the model, its key properties, and our most recent extensions, and describe ways to link this replicator framework to epidemiological or microbiological data. Overall our work opens new theoretical avenues for investigation and fresh perspectives for applying this replicator equation to biological data.

References:

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[4] Le, T. M. T., Madec, S., Gjini, E. (2025). Inference of Pairwise Interactions from Strain Frequency Data Across Settings and Context-Dependent Mutual Invasibilities. Bulletin of Mathematical Biology, 87(6), 1-29.

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Antonio Gómez Corral

Erlangian approximations of epidemic models with time-varying contact and recovery rates

In the stochastic framework, epidemic models with time-varying contact and recovery rates can easily be formulated as time-inhomogeneous level-dependent quasi-birth-death (LD-QBD) processes, i.e., multi-dimensional continuous-time Markov chains with time-varying transition rates and a block-tridiagonal q-matrix. By using the well-known Widder's inversion formula for a non-negative function on $(0, \infty)$ from its Laplace transform, we present a general-purpose computational method to evaluate the transient distribution and moments of first-passage times to higher levels, and related hitting probabilities, at a fixed finite horizon T for a time-inhomogeneous LD-QBD process. We also show how to apply the method to SIR models with sinusoidal forcing of transmission, with special emphasis on technical details to demonstrate the effectiveness of the approximation.

Toni Guillamon

Optimal generalization and synchronization of neural oscillations through response functions

Periodic sustained oscillations are typically represented as limit cycles in dynamical systems, whereas damped oscillations correspond to stable foci. We present two examples of optimal control in oscillatory systems – both in the sustained and the damped regimes–using the so-called augmented phase reduction, which combines phase and amplitude response functions.

In the first example, we show how to design an external input capable of inducing sustained oscillations in a damped oscillator. We show that our optimal control strategy effectively enhances the oscillatory regime of realistic neuron models, rendering them excitable even under low-intensity external stimulation.

In the second example, we focus on the paradigm of Communication Through Coherence, a theory proposing that macroscopic oscillations in the brain regulate information flow between neural populations, thereby supporting effective communication. For this mechanism to operate, neural populations must synchronize their oscillatory activity so that input volleys from the presynaptic population arrive when the postsynaptic one is at its phase of maximum excitability. Using an excitatory-inhibitory population network, we explore strategies to design a periodic control signal that entrains the target population to the optimal phase, synchronizing its activity with a specific presynaptic input and establishing communication.

The presentation includes results made in collaboration with G. Huguet, M. Orieux, K. Martínez-Anhom and R. Moreno.

Gemma Huguet Casades

Emergence of complex spatio-temporal oscillations in large-scale brain networks of coupled exact mean field models

Macroscopic oscillatory patterns are a ubiquitous feature of brain dynamics and have been linked to diverse cognitive functions. Large-scale brain models aim to explain how such dynamics emerge from the brain's complex structure, but their analysis remains challenging due to the inherent complexity of these systems. In this study, we investigate a model of 90 interconnected brain regions coupled through empirical anatomical connectivity, where each region is described by a next-generation neural mass model (NG-NMM) that explicitly captures excitatory and inhibitory population activity. We identify homogeneous resting and oscillatory states and analyze their stability under both uniform and non-uniform perturbations. To assess stability with respect to heterogeneous perturbations, we decompose them on a suitable basis and compute a dispersion relation—or, in the case of periodic orbits, a Master Stability Function—that links spatial modes to perturbation growth rates. Simulations and analysis of Lyapunov exponents reveal that destabilization of homogeneous solutions drives the large-scale model toward heterogeneous activity patterns, including traveling and chaotic waves. Our findings show that NG-NMM provide a richer dynamical repertoire—both within homogeneous states and in heterogeneous regimes—than classical neural mass models, suggesting that next-generation approaches are not only more biophysically grounded but also particularly well-suited to capture the complexity of large-scale brain dynamics.

This is joint work with Rosa Delicado (UIB) and Pau Clusella (UPC).

Bartolo Luque Serrano

Los eucariotas emergieron en el punto crítico de una transición de fase algorítmica

Analizando estadísticamente las longitudes de los genes y las proteínas de 33.000 especies que recorren el árbol de la vida desde las bacterias a los humanos, hemos descubierto que sus distribuciones son log-normales, que sus longitudes medias han crecido exponencialmente a lo largo de la evolución y que existe una relación invariante de escala, una ley de potencias, entre la longitud media y la varianza de las longitudes de los genes y proteínas de todos los organismos.

En la charla mostraremos cómo todas estas características surgen de manera natural a partir de un sencillo proceso estocástico de crecimiento multiplicativo de los genes que la evolución ha mantenido desde el origen de la vida. Combinar este proceso con la proporción de intrones en los genomas nos conduce a entender la aparición de organismos multicelulares como resultado de una transición de fase algorítmica. Esta interpretación nos permite, a partir del momento de aparición y tamaño medio del genoma de LUCA (nuestro primer ancestro común con regulación génica) predecir el momento y el tamaño medio del genoma de las primeras células eucariotas que permitieron un crecimiento espectacular de la complejidad de los seres vivos.

Susanna Manrubia

Hierarchical genotype networks condition sequence space search and evolution of viral quasispecies

Understanding how viral mutant spectra organize and explore genotype space is essential for elucidating the mechanisms that drive molecular evolution. We have used deep-sequencing data of the RNA bacteriophage Qbeta to reconstruct genotype networks with tens of thousands of haplotypes. The study of populations evolved under different temperature regimes reveals robust, reproducible patterns that arise from the interplay between fundamental structural motifs of sequence spaces and population dynamics. Mutant swarms exhibit a self-similar, hierarchical organization in which sequences cluster around

a highly connected and abundant sequence core that continuously regenerates diversity along evolution. The immediate neighborhood of this core is rapidly rebuilt and extensively sampled, showing only weak signs of selection, while a few mutations away sampling becomes dynamical and sparse. This population structure, shared by other viruses, emerges from a dynamic, out-of-equilibrium balance between replication and exploration, and suggests that viral populations do not rely primarily on neutral networks for navigation or for generating diversity. Our research underscores the usefulness of genotype networks as an enlightening visualization of the organization of mutant swarms.

Joan Saldaña Meca

Epidemic models with varying infectiousness, vaccination and waning immunity

Traditional ODE-based models of infectious disease dynamics, such as the SIS and SIR models, assume that infected individuals have a constant level of infectiousness. However, the viral load of individuals, and therefore their infectiousness, varies over the course of infection, depending on the time elapsed since they became infected, often referred to as the age of infection. Additional factors, including the individual's chronological age and behavioural changes during the infectious period, also affect the level of an individual's infectiousness.

In this talk, we will present a Susceptible-Infected-Recovered-Vaccinated-Susceptible (SIRVS) epidemic model with waning immunity which includes the contact pattern between age groups. We will see that, with a limited supply of vaccines, a vaccination strategy based on minimizing the basic reproduction number allows for the deployment of vaccine doses lower than those required to maximize vaccination coverage of the population. Secondly, we will structure individuals into each epidemic class according to their age of infection if they are in the infected class, or to their age of immunity if they are immunized or recovered. The analysis of the resulting PDE model shows that only the basic reproduction number, R_0, and the mean immunity period of the vaccinated individuals have an impact on the critical vaccination rate needed to achieve herd immunity. Moreover, we will show different behaviours of the solutions obtained from the numerical integration of the system of PDEs that defines the model.

Samir Suweis

Archetypal Decomposition of Metagenomic Profiles for Cross-Study Diagnostic Classification

Shotgun metagenomics enables the quantitative profiling of microbial communities in biological samples, providing a rich, high-dimensional description of microbiota composition. These microbial profiles are increasingly used to investigate associations with host health. However, the high dimensionality of such data—thousands of microbial or functional features per sample—and the heterogeneity introduced by cross-study aggregation pose significant challenges for data analysis and interpretation.

In this work, we explore the use of Archetypal Analysis (AA) as a geometry-aware dimensionality reduction method to extract interpretable low-dimensional structure from metagenomic data, with particular application to inflammatory gastrointestinal conditions. AA approximates each sample as a convex combination of a small number of archetypes, corresponding to extreme points in the data cloud. Compared to PCA, which captures directions of maximal variance, AA emphasizes the boundary geometry of the dataset, enabling the identification of meaningful data directions in terms of compositional extremes.

We apply AA to an aggregated dataset of metagenomic profiles drawn from multiple independent studies, uniformly reprocessed through a common pipeline. Archetypes specific to individual studies can be removed to improve cross-study comparability, allowing for the construction of a robust shared representation that preserves biologically relevant information. In this reduced space, the healthy/diseased status of samples emerges naturally as a prominent axis of separation, enabling the training of a classifier with good generalization performance across studies.

These results suggest that archetypal geometry can serve as a powerful tool in microbiome-based

diagnostics, particularly when data integration across studies is necessary.

This is joint work with Marcello Seppi, Jacopo Pasqualini and Guido Zampieri.

Nicolás Torres Escorza

On the local stability of the elapsed-time model in terms of the transmission delay and interconnection strength

The elapsed-time model describes the behavior of interconnected neurons through the time since their last spike. It is an age-structured non-linear equation in which age corresponds to the elapsed time since the last discharge, and models many interesting dynamics depending on the type of interactions between neurons. We investigate the linearized stability of this equation by considering a discrete delay, which accounts for the possibility of a synaptic delay due to the time needed to transmit a nerve impulse from one neuron to the rest of the ensemble. We state a stability criterion that allows to determine if a steady state is linearly stable or unstable depending on the delay and the interaction between neurons. Our approach relies on the study of the asymptotic behavior of related Volterra-type integral equations in terms of theirs Laplace transforms. The analysis is complemented with numerical simulations illustrating the change of stability of a steady state in terms of the delay and the intensity of interconnections.