

## Workshop

### Mathematical Perspectives in Biology

February 3-5, 2016, ICMAT, Madrid

[www.icmat.es/congresos/2016/BBVA/](http://www.icmat.es/congresos/2016/BBVA/)

**Organizers:** Francisco J. Cao (UCM, Madrid)  
Kurusch Ebrahimi-Fard (ICMAT-CSIC, Madrid)  
W. Steven Gray (Old Dominion Univ, Norfolk, USA)

The purpose of this interdisciplinary workshop is to bring together leading international researchers sharing a common interest in mathematical perspectives in modern biology. The aim is to discuss a broad spectrum of new and important results as well as interact and foster new research at the ICMAT.

This event is part of the Project “Mathematical Methods for Ecology and Industrial Management”<sup>1</sup>, which received generous funding from the *Ayudas Fundación BBVA a Investigadores, Innovadores y Creadores Culturales*.

#### Speakers:

- 1) Elena Akhmatskaya (Bilbao, Spain)
- 2) Tomás Alarcón (Barcelona, Spain)
- 3) Elena Beltrán-Heredia (Madrid, Spain)
- 4) Steinar Engen (Trondheim, Norway)
- 5) Javier Jarillo (Madrid, Spain)
- 6) W. Steven Gray (Norfolk, USA)
- 7) Laurie Kell (Madrid, Spain)
- 8) Emilio Marañón (Vigo, Spain)
- 9) José María Maroto (Madrid, Spain)
- 10) Mihaly Petreczky (Lille, France)
- 11) Bernt-Erik Sæther (Trondheim, Norway)
- 12) Joan Saldana (Girona, Spain)

---

<sup>1</sup> [www.icmat.es/research/bbva-mmeim/](http://www.icmat.es/research/bbva-mmeim/)

## Schedule:

### FEBRUARY 3:

**Start:** Lunch 13:30 - 15:30  
**15:30 - 16:25:** Mihaly Petreczky  
**16:30:** coffee break  
**17:00 - 17:55:** Elena Akhmatskaya

### FEBRUARY 4:

**10:00 - 10:55:** Emilio Marañón  
**11:00:** coffee break  
**11:30 - 12:25:** Tomás Alarcón  
**12:30:** lunch  
**15:00 - 15:55:** Bernt-Erik Sæther  
**16:00:** coffee break  
**16:30 - 17:25:** Steinar Engen  
*Special Session:* short communications  
**20:30:** Dinner

### FEBRUARY 5:

**10:00 - 10:55:** Laurie Kell  
**11:00:** coffee break  
**11:30 - 12:25:** José María Maroto  
**12:30:** lunch  
**15:00 - 15:55:** W. Steven Gray  
**16:00:** coffee break  
**16:30 - 17:25:** Joan Saldana  
Discussions  
**20:00:** Dinner

**Venue:** Aula Naranja, ICMAT, C/ Nicolás Cabrera 13-15  
Campus Cantoblanco – UAM  
28049 Madrid, [www.icmat.es](http://www.icmat.es)

**Accommodation:** *Residencia de Estudiantes*  
Pinar 21-23, 28006 Madrid  
[www.residencia.csic.es/](http://www.residencia.csic.es/)  
[www.residencia.csic.es/pres/localiza\\_maps.html](http://www.residencia.csic.es/pres/localiza_maps.html)

**How to arrive:** [www.icmat.es/facilities/howtoarrive](http://www.icmat.es/facilities/howtoarrive)  
to ICMAT

**Google-Maps:** <https://goo.gl/maps/VzaeN9q9rQ62>

## **Titles and Abstracts:**

**Elena Akhmatskaya**

BCAM - Basque Center for Applied Mathematics, Bilbao, Spain

Title: *Mix & Match Hamiltonian Monte Carlo*

Abstract: Hamiltonian (Hybrid) Monte Carlo (HMC) method, initially proposed in High Energy Physics, is becoming a popular tool for solving complex and intractable problems of statistical inference.

We introduce multiple modifications in the original formulation of the HMC in order to enhance sampling from high-dimensional or strongly correlated target densities. The new features include the modified Metropolis test, the updated momentum refreshment step, the novel numerical integrating scheme. All alterations have been formulated and implemented within the Generalized Shadow Hybrid Monte Carlo framework, earlier proposed by the authors for simulation of molecular systems.

The sampling efficiency of the resulting method is assessed by performing inference on standard statistical benchmark models, and compared with Random Walk Metropolis- Hastings Monte Carlo, the original Hamiltonian Monte Carlo and Riemannian Manifold Hamiltonian Monte Carlo methods.

Coauthor: Tijana Radivojević (BCAM Mathematics, Spain)

**Tomas Alarcón**

Centre de Recerca Matemàtica, Barcelona, Spain

Title: *Population and evolutionary dynamics of tumour growth*

Abstract: There is a current, growing school of thought that puts forward that concepts borrowed from population dynamics and evolutionary and ecological theory are instrumental to understand complex dynamical processes in tumour growth, such as emergence of drug resistance. In this talk, I will review the state-of-the-art of the subject and present new results, particularly regarding the effects of random fluctuations.

**Elena Beltrán-Heredia**

Dept. de Física Atòmica, Molecular y Nuclear, Univ. Complutense de Madrid, Spain

Title: *Phytoplankton size and porter scaling: optimal net nutrient uptake*

Abstract: We derive for phytoplankton a phenomenological size scaling relation as a function of nutrient concentration. This scaling relation is obtained combining a trait based model with previous experimental data. We also obtain phenomenological trait scaling relations for the number of porters and handling time as a function of size. Using a trait based model of uptake,

these relations are obtained from experimental data of half-saturation constant and maximal uptake rate at different nutrient concentration and for different phytoplankton sizes. Introducing a maintenance cost of the porters in the model leads to an optimal number of porters as a function of the dominant size at the given environmental nutrient concentration. We found that the phenomenological relations obtained from experimental data are accounted for when the porter maintenance cost scales approximately with  $n^{1.6}$ .

## **Steinar Engen**

Department of Mathematical Sciences, NTNU, Trondheim, Norway

Title: *Evolution of density-dependent dynamics of a fluctuating population caused by non-selective harvesting*

Abstract: Evolutionary changes in many adaptive phenotypic characters like body mass, age at maturation and timing of breeding, often occur in populations subject to aggressive harvesting over long periods. One explanation for these changes may be that harvesting is selective, for example biased toward larger individuals. Here we analyze evolutionary responses to non-selective harvest, using a model for evolution of a quantitative character in a fluctuating density-dependent population, giving the joint diffusion approximation for the mean phenotype and log population size. We show how non-selective harvesting influences evolution of all parameters determining the dynamics of the population, in particular r-selection governed by genetic variation in strength of density-regulation and the magnitude of population fluctuations. The short-term response to selection is proportional to the harvest fraction averaged over the stationary distribution of population size conditioned on mean phenotype. The short-term as well as long-term evolutionary impact of non-selective harvesting can therefore be compared for different harvesting strategies, simply by comparing mean harvest fraction for strategies with the same mean annual yield. This comparison is performed for three different harvesting strategies, constant, proportional and threshold harvesting. The more ecologically sustainable strategies also produce smaller evolutionary changes.

## **W. Steven Gray**

Electrical & Computer Engineering, Old Dominion University, Norfolk, VA, USA

Title: *Analytic Left Inversion of Multivariable Lotka-Volterra Models*

There is great interest in managing populations of animal species that are vital food sources for humans. A classical population model is the Lotka-Volterra

system, which can be viewed as a nonlinear input-output system when time-varying parameters are taken as inputs and the population levels are the outputs. If some of these inputs can be actuated, this sets up an open-loop control problem where a certain population profile as a function of time is desired, and the objective is to determine suitable system inputs to produce this profile. Mathematically, this is a left inversion problem. In this talk we present a solution to the general left inversion problem for multivariable input-output systems that can be represented in terms of Chen-Fliess series using concepts from combinatorial Hopf algebras. The method is then applied to a three species, two-input, two-output Lotka-Volterra system. The biological goal is to change the population dynamics of the top-level predator species in a food chain in order to prevent extinction.

### **Javier Jarillo**

Dept. de Física Atómica, Molecular y Nuclear, Univ. Complutense de Madrid, Spain

Title: *Effects of harvesting and strength of competition on the spatial scales of population fluctuations of two competing species*

Abstract: We show that proportional harvesting and competition modify the spatial structure of population fluctuations of two competing species using a perturbative expansion around the deterministic equilibrium point. Harvesting always increases the spatial scale of population synchrony, whilst the effect of competition is more involved. In some cases, competition is found to increase the population synchrony scale of one of the species, while it decreases the synchrony scale of the other one. However, in other cases competition increases or decreases the spatial synchrony scales of both species. These results provide corrections to the spatial scale of single-species population synchrony, which is known to be given by the spatial scale of environmental fluctuations (the Moran effect) plus a term proportional to the quotient of the migration capacity and the rate of the return to equilibrium.

### **Laurie Kell**

ICCAT, Madrid, Spain

Title: *Reframing stock assessment as risk management*

Abstract: TBA

### **Emilio Marañón**

Departamento de Ecología y Biología Anima, Univ. de Vigo, Spain

Title: *Size-scaling of phytoplankton metabolic rates and growth*

Abstract: Phytoplankton size structure controls the trophic organization of marine planktonic communities and their ability to sequester atmospheric CO<sub>2</sub> in the the ocean's interior. Body size is a major determinant of metabolic rate and growth in all living organisms, as described by the  $\frac{3}{4}$ -power rule (Kleiber's rule).

Using laboratory and field measurements, we have assessed whether phytoplankton metabolism and growth conform to this general size-scaling pattern. Our results show that phytoplankton metabolism and growth do not follow Kleiber's rule. Biomass-specific production and growth rates are similar in both small and large cells, but peak at intermediate cell sizes. We have also found that the maximum nutrient uptake rate scales isometrically with cell volume and superisometrically with the minimum nutrient quota. The unimodal size scaling of phytoplankton growth arises from ataxonomic, size-dependent trade-off processes related to nutrient requirement, acquisition, and use. The superior ability of intermediate-size cells to exploit high nutrient concentrations explains their dominant role in the ecology and biogeochemistry of the ocean.

#### References

Marañón E (2015) *Cell size as a key determinant of phytoplankton metabolism and community structure*. Annual Review of Marine Science, 7, 241-264.

Marañón E, Cermeño P, López-Sandoval DC, Rodríguez-Ramos T, Sobrino C, Huete-Ortega M, Blanco JM, Rodríguez J (2013) *Unimodal size scaling of phytoplankton growth and the size dependence of nutrient uptake and use*. Ecology Letters, 16, 371-379.

Marañón, E., Cermeño, P., Rodríguez, J., Zubkov, M. V., Harris, R. P. (2007) *Scaling of phytoplankton photosynthesis and cell size in the ocean*. Limnology and Oceanography, 52, 2190-2198.

#### **José María Maroto**

Departamento de Estadística e Investigación Operativa II Facultad de Ciencias Económicas y Empresariales, Universidad Complutense de Madrid, Madrid, Spain

Title: *Seasonality in fisheries: A bridge between continuous and discrete-time bioeconomic models*

Abstract: We develop a discretization method of continuous-time bioeconomic models, which consists of two steps: first we estimate a proper growth function for the continuous-time model through the ensemble Kalman Filter. Then we use the Runge-Kutta method to analyze the optimal management of seasonal fisheries in a discrete-time setting. We analyze both the case of quarterly harvest and the case of monthly harvest, and we compare these to the case of annually harvest. We find that seasonal

harvesting is a win-win optimal solution with higher harvest, higher optimal steady state equilibrium, and higher economic value. We also demonstrate that the discretization method overcomes the economic and biological weakness and preserves the strengths of both continuous and discrete-time bioeconomic models.

### **Víctor M. Pérez García**

Mathematical Oncology Laboratory, Univ. de Castilla-La Mancha, Spain

Title: *Mathematical oncology against brain tumors: identifying clinical targets, indicators of response to therapies and therapeutical schedules*

Abstract: Mathematical oncology is a novel field of mathematical biology that intends to develop models and obtain results of direct use in the treatment of cancer. While many mathematical models inspired by cancer-related problems have been developed in the last 30 years, they usually (i) lack a solid bio-medical foundations; (ii) do not have a direct therapeutical value (i.e. there is no relevant question to solve using them); (iii) are not validated against real state-of-the-art knowledge or (iv) are too complicated to be useful. This is why mathematical models have been useless in Oncology up to now.

In the last few years there has been a strong interest in models of direct applicability in cancer. I will describe our own research on that kind of models and their applications to brain tumors. Specifically I will describe:

(i) A macroscopic model that predicts the relevance of certain tumor geometrical and heterogeneity measures obtained from pretreatment MRI images that are routinely used for diagnosis and therapy planning. The validation of the predictions will also be described.

(ii) A microscopic model, leading to the prediction that certain anti-oxidative therapies would be effective in combination with standard therapies. When tested on GBM cell cultures, xenografts and orthotopic transplants in nude mice and rats the designed therapy turns out to be able to completely suppress tumor growth. Recent progresses on the understanding of the effectivity of the therapy will be presented.

(iii) A model of radiation therapy for low grade glioma predicting a novel fractionation scheme with substantially improved effectiveness.

### **Mihaly Petreczky**

CNRS, Ecole Centrale de Lille, France

Title: *Realization Theory of Dynamical Systems for Systems Biology*

Abstract: Realization theory is a classical topic in mathematical control theory.

Suppose we have a set of trajectories (functions of time), which represent the observed behavior of a physical or biological system.

We would like to model this system by difference/differential equations, which may contain hidden variables, in such a way that the observed behavior of the system coincides with the observed behavior predicted by this model. Realization theory aims at finding out when it is possible to describe collections of trajectories as outputs of a dynamical system modeled by difference or differential equations of a certain class.

Realization theory provides the theoretical basis for estimating model parameters from data (known as system identification in mathematical control theory) and for model reduction (replacing a complex model by a simpler one). For biological systems, it is also important from a theoretical point of view, as it helps to understand the various explanations, which are consistent with the same experimental data.

In this talk I will briefly introduce realization theory, present the mathematical problem formulation and some basic results. Then I will concentrate on the following two problems, which are of particular interest for biology:

- 1) realization theory of differential equations whose right-hand side is semi-algebraic
- 2) realization theory of coordinated difference/differential equations, i.e. dynamical systems which can be represented as a certain type of interconnection of simpler subsystems.

The first problem is relevant for building monolithic models of biochemical and gene regulatory networks. The second problem is relevant for reverse engineering of the network structure of these networks.

## **Bernt-Erik Sæther**

Department of Biology, NTNU, Trondheim, Norway

Title: *Population dynamics in fluctuating environments: some key challenges*

Abstract: One of the central challenges for ecologists is to understand how changes in the environment affect the population dynamics at the local as well as the regional scale. Such knowledge is crucial for determining how different forms of human activities will affect the biological diversity in the future. Obtaining such an understanding must rely heavily on application of stochastic population models because stochastic variation is a central characteristic of all natural systems. A central goal for such population models that embed different forms of stochasticity is to disentangle the effects of different factors affecting the population dynamics such density dependence, demographic stochasticity and environmental stochasticity. In my talk I will provide some illustrations of how this can be done in practice, mainly using



examples based on analyses of bird and mammal populations. A central focus will to highlight key problems that still remain to be solved.

**Joan Saldana**

Dept. Informàtica, Matemàtica Aplicada i Estadística, Univ. de Girona, Spain

Title: *Behavioural responses and epidemic spread on networks*

Abstract: Human behavioural responses have an important impact on the spread of epidemics. One way to incorporate them into epidemic models has been to consider that individuals are aware of the risk of contagion and adopt preventive responses when get informed about the existence of the disease. The information dissemination can be modelled by means of a second network, with the same set of nodes as the contact network, over which awareness spreads. In this talk I present a toy model for epidemic spreading in the presence of awareness for which the epidemic threshold is expressed as a function of the overlap between these two networks. Finally, I will discuss the suitability of this measure of the interrelation between pairs of networks when distinct architectures are considered.