

# CRM-CRAG Workshop

Monday 28 January 2019, CRAG Auditorium

## PROGRAMME

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- 09:00 – 09:15 | Overview of CRAG and its research  
**José Luis Riechmann**, CRAG Director
- 09:15 – 09:30 | Overview of CRM and its research  
**Lluís Alsedà**, CRM Director
- 09:30 – 10:10 | Almost magic: how math can help uncover biology  
**Martí Bernardo**, Head of Data Analysis at the Bioinformatics Core Unit at CRAG, & **Isabel Serra**, Technology Transfer Manager at CRM
- 10:10 – 10:35 | Network Mechanisms Underlying the Role of Oscillations in Cognitive Tasks<sup>1</sup>  
**Alex Roxin**, Principal Investigator at the Computational Neuroscience Unit at CRM
- 10:35 – 11:00 | Brassinosteroid signaling in plant development and adaptation to stress<sup>2</sup>  
**Ana I. Caño-Delgado**, Group Leader at the Brassinosteroid Signalling in Plant Development Research Group at CRAG
- 11:00 – 11:30 | Coffee break\*
- 11:30 – 11:55 | Mathematical modelling of pattern formation, morphogenesis and evolution<sup>3</sup>  
**Isaac Salazar**, Principal Investigator at the Mathematics of Development and Evolution Unit at CRM
- 11:55 – 12:20 | Molecular mechanisms of circadian clock function in plants<sup>4</sup>  
**Paloma Mas**, Group Leader at the Molecular Mechanisms of Circadian Clock Function Research Group at CRAG
- 12:20 – 12:45 | Mathematical and computational approaches for plant virus dynamics and evolution<sup>5</sup>  
**Josep Sardanyés**, Senior Research Fellow at the Nonlinear Dynamics and Evolution Laboratory Unit at CRM
- 12:45 – 13:10 | Base-frequency caller for the analysis of genome variability in Pooled data and in autopolyploid species<sup>6</sup>  
**Sebastián Ramos-Onsins**, Researcher at the Statistical and Population Genomics Research Group at CRAG
- 13:10 – 13:30 | Final remarks  
**Martí Bernardo**, Head of Data Analysis at the Bioinformatics Core Unit at CRAG, & **Isabel Serra**, Technology Transfer Manager at CRM
- 13:30 – 14:30 | Networking lunch\*  
For CRM and CRAG researchers
- 14:30 – 15:00 | CRAG visit  
For CRM guests

## ABSTRACTS OF THE TALKS

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### 1. Network Mechanisms Underlying the Role of Oscillations in Cognitive Tasks - Alex Roxin (CRM)

Oscillatory activity robustly correlates with task demands during many cognitive tasks. However, not only are the network mechanisms underlying the generation of these rhythms poorly understood, but it is also still unknown to what extent they may play a functional role, as opposed to being a mere epiphenomenon. Here we study the mechanisms underlying the influence of oscillatory drive on network dynamics related to cognitive processing in simple working memory (WM), and memory recall tasks. Specifically, we investigate how the frequency of oscillatory input interacts with the intrinsic dynamics in networks of recurrently coupled spiking neurons to cause changes of state: the neuronal correlates of the corresponding cognitive process. We find that slow oscillations, in the delta and theta band, are effective in activating network states associated with memory recall by virtue of the hysteresis in sweeping through a saddle-node bifurcation. On the other hand, faster oscillations, in the beta range, can serve to clear memory states by resonantly driving transient bouts of spike synchrony which destabilize the activity. We leverage a recently derived set of exact mean-field equations for networks of quadratic integrate-and-fire neurons to systematically study the bifurcation structure in the periodically forced spiking network. Interestingly, we find that the oscillatory signals which are most effective in allowing flexible switching between network states are not smooth, pure sinusoids, but rather burst-like, with a sharp onset. We show that such periodic bursts themselves readily arise spontaneously in networks of excitatory and inhibitory neurons, and that the burst frequency can be tuned via changes in tonic drive. Finally, we show that oscillations in the gamma range can actually stabilize WM states which otherwise would not persist.

### 2. Brassinosteroid signaling in plant development and adaptation to stress - Ana I. Caño-Delgado (CRAG)

Brassinosteroids (BRs) are steroid hormones essential for plant growth and development. These hormones control the division, elongation and differentiation of various cell types throughout the entire plant life cycle. Our current understanding of the BR signalling pathway has mostly been attained via studies using *Arabidopsis* as a model. In this context, the membrane steroid receptor BRI1 (BRASSINOSTEROID INSENSITIVE 1) binds directly to the BR ligand, triggering a signal cascade in the cytoplasm that leads to the transcription of BR-responsive genes that drive cellular growth. However, our recent studies in the primary root have revealed distinct BR signalling pathways in different cell types and have highlighted cell-specific roles for BR signalling in controlling adaptation to stress. In this seminar, I will summarize the current knowledge of the spatiotemporal control of BR action in plant growth and development, focusing on BR functions in primary root development and growth, in stem cell self-renewal and death, and in plant adaptation to environmental stress.

### 3. Mathematical modelling of pattern formation, morphogenesis and evolution - Isaac Salazar (CRM)

In this talk I will give a short overview of the search we have been doing on how the mechanisms of pattern formation and morphogenesis in animals affects their morphological evolution. In the first part of the talk I will outline our current understanding of how cell-cell signalling and tissue bio-mechanics determine the morphology of teeth, their population level variation and their evolution. In the second part of my talk I will outline general insights about how the way cell-cell signalling and tissue bio-mechanics are coordinated during development affects the range of possible morphological variation in populations. Then I will explain how this latter thing affects the outcome of morphological evolution and the evolution of development.

#### **4. Molecular mechanisms of circadian clock function in plants - Paloma Mas (CRAG)**

Circadian clocks are ubiquitous in nature and control the rhythms of multiple biological processes with a period of exactly 24 hours. Proper circadian function in plants is essential for growth, development and adaptation to harsh environmental conditions. In my seminar at the CRAG-CRM Workshop, I will provide a glimpse of our recent results showing the molecular mechanisms responsible for the generation of rhythms. I will present data demonstrating how the rhythmic recruitment of the transcriptional machinery controls circadian gene expression and discuss the function of chromatin remodelling in this regulation. I will also present our results showing the mechanistic insights of circadian clock control of metabolic pathways, responses to drought as well as plant growth through tight regulation of the cell cycle.

#### **5. Mathematical and computational approaches for plant virus dynamics and evolution - Josep Sardanyés (CRM)**

In this talk we will introduce mathematical tools from dynamical systems theory to characterise the population and evolutionary dynamics of plant RNA viruses. This includes both analytical and computational tools, which allow to identify equilibria solutions and bifurcations causing RNA virus extinctions. The topics of the talk, within the framework of plant-virus systems biology, will range from the modelling of experimental viral RNA silencing to the modelling of viral RNA amplification modes from experiments. Finally, some advances within the framework of spatial infection dynamics will be also discussed.

#### **6. A Base-frequency caller for the analysis of genome variability in Pooled data and in autopolyploid species - Sebastián Ramos-Onsins (CRAG)**

Research in population genetics mostly requires an unbiased estimate of the levels of variability and of the frequency distribution of mutations (the Site Frequency Spectrum, SFS) in order to infer the evolutionary forces that have been acting on the species. The high-performance NGS methods for genome sequencing produce a high number of reads for each base but also generate similar or higher ratios of sequencing errors, that are confounded with real mutations which are the focus of our study. This effect becomes worst in case of having several numbers of lines per NGS lane. For diploid data, several methods to produce accurate results have been already developed. Nevertheless, in case of using several or many lines within each NGS lane (e.g., pooled data of a number of samples), the site frequency spectrum is difficult to calculate, especially for low frequency variants, which are the most abundant class of mutations, and allow to determine the recent evolutionary processes.

We propose a Bayesian model approach in which we added an additional parameter to estimate the SFS: the contributing number of samples per position, which permits to estimate the frequencies of mutations by considering a different "contributing" sample size per position, in relation to the fixed initial sample size. In order to estimate the parameters distributions, the probabilities of the model can be divided in three main parts: combinatorics, evaluation of the sample frequency and sequencing error.

Computer simulations show that this model is able to estimate unbiasedly the levels and the patterns of variability in a wide range of ploidy or sample size used, even having low sequencing read depths ratios (that is, low ratio of read depth versus sample size) but also with very low sequencing read depth values (on the levels of 1-2 reads per position). Analysis having empirical sequencing data are on evaluation.