

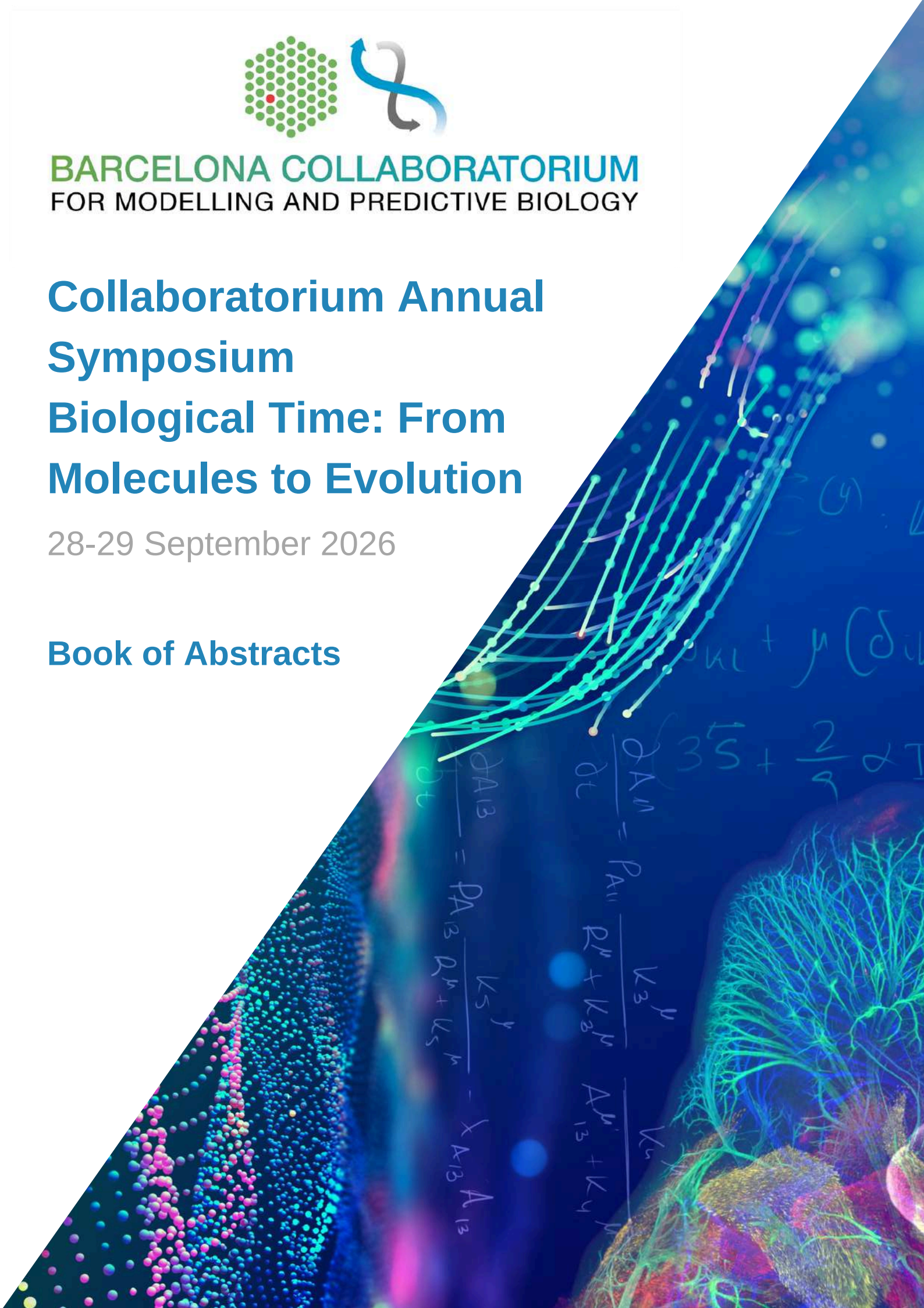
BARCELONA COLLABORATORIUM
FOR MODELLING AND PREDICTIVE BIOLOGY

Collaboratorium Annual Symposium

Biological Time: From Molecules to Evolution

28-29 September 2026

Book of Abstracts



FUNDERS:



Biological Time: From Molecules to Evolution

Time is fundamental to all biological processes — from the molecular oscillations governing gene expression to the evolutionary timescales shaping species. This symposium will explore the many temporal dimensions of life, examining how biological systems measure, respond to, and are constrained by time.

We will move from the precise developmental tempos orchestrating embryogenesis, through the cyclical rhythms that maintain homeostasis in living systems, to the temporal disruptions associated with aging and disease. Bringing together leading researchers from developmental biology, biophysics, chronobiology, systems biology, and computational oncology, the symposium aims to foster new perspectives on how time shapes living systems across scales.

The symposium follows the collaborative spirit of the Barcelona Collaboratorium, combining scientific excellence with strong integration of early-career researchers through discussion sessions, networking opportunities, and community-building activities.

PROGRAM

DAY 1

14:00	 Registration, MNT Auditorium Plaça del Gas 1 - Torre A - 08003 Barcelona, Spain
14:15	WELCOME AND PRESENTATION by James Sharpe (Collaboratorium - EMBL Barcelona) and Monica Bettencourt (CRG) Scientific introduction by Eric Latorre Crespo (Collaboratorium - CRM - CRG) and Jordi García-Ojalvo (Collaboratorium - UPF)
14:30	Session I: The Beginning of Life 14:30 - Felix Ritort – University of Barcelona: <i>Heatomics</i> 15:10 - Miki Ebisuya – TU Dresden: <i>Stem Cell Zoo: a platform for studying species-specific developmental time and shape</i> 15:50 - 16:00 FLASH TALKS (Manuela Giraud, Giacomo Bartolucci, Akhilesh Nandan) 16:00 - 16:20 BREAK 16:20 - Vikas Trivedi – EMBL Barcelona: <i>Metabolic control of multicellular transitions</i>
17:00	END OF DAY I by Jordi García-Ojalvo (Collaboratorium - UPF)
17:30	Reception and Networking at the Collaboratorium Barcelona Collaboratorium

PROGRAM

DAY 2

09:00	 Registration, MNT Auditorium Plaça del Gas 1 - Torre A - 08003 Barcelona, Spain
09:15	SUMMARY OF DAY 1 AND INTRODUCTION TO DAY 2 by Eric Latorre Crespo (<i>Collaboratorium</i> - CRM - CRG)
9:20	Session II: Time and Function – Systems in Balance 9:20 - Thomas Höfer – DFKZ: <i>Breakdown of the hematopoietic hierarchy in the evolution of leukemia</i> 10:00 - Alejo Rodriguez-Fraticelli – IRB Barcelona: <i>Origins and dynamics of non-genetic blood stem cell diversity</i> 10:40 - 10: 50 FLASH TALKS (Julia Rius I Bonet, Irene Gravili, Daniele Scarcella) 10: 50 - 11: 20 BREAK 11:20 - Kirsty Wan – University of Exeter: <i>Embodied motility in single-celled organisms</i> 12:00 - Didier Gonze – Université Libre de Bruxelles: <i>Biological clocks: design principles and physiological roles</i>
12:40	LUNCH and POSTER SESSION
14:00	Session III: Aging – When Time is Perturbed 14:00 - Ala Trusina – Niels Bohr Institute, University of Copenhagen: <i>Low-dimensional models of robust patterning in early embryo development</i> 14:40 - Donate Weghorn – CRG: <i>From early development to evolution: the temporal dynamics of a human germline mutational hotspot</i> 15:20-15:50 BREAK 15:50 - Melike Donertas – Graduate School of Informatics – METU & Leibniz Institute on Aging (FLI): <i>Ageing where selection declines - from genomes to populations</i> 16:30 - Manuel Collado – CIMUS: <i>Rejuvenate or Die: New Approaches Targeting Cellular Senescence</i>
17:10	END OF DAY II Scientific Summary by Eric Latorre Crespo (<i>Collaboratorium</i> - CRM - CRG) and Jordi García-Ojalvo (<i>Collaboratorium</i> - UPF) CLOSING REMARKS by Mafalda Dias (<i>Collaboratorium</i> - CRG)



SCIENTIFIC ORGANISERS

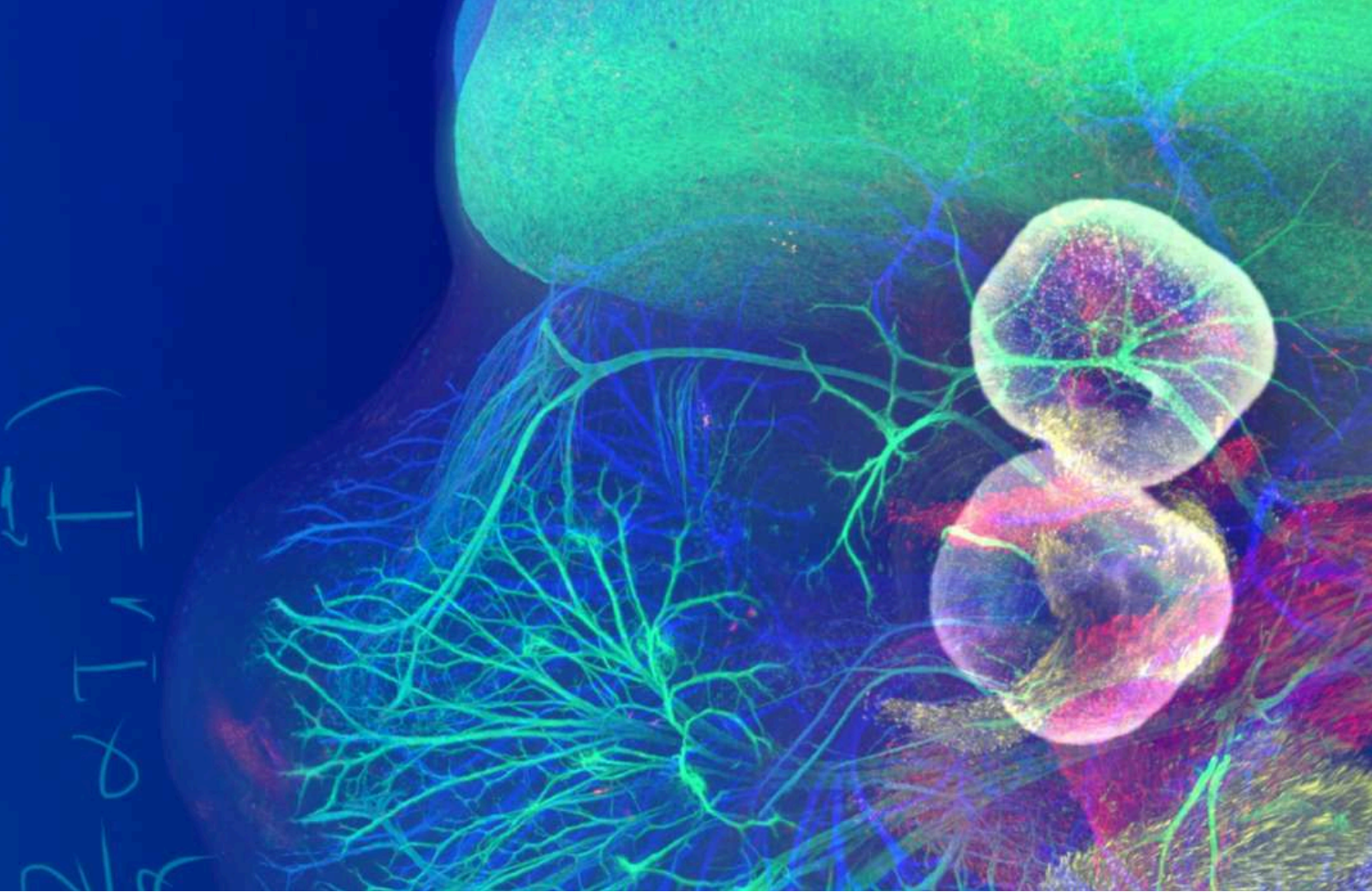
Jordi García Ojalvo

Jordi Garcia-Ojalvo, a Senior Fellow at the Barcelona Collaboratorium and head of the Dynamical Systems Biology Lab at Pompeu Fabra University (UPF), studies how living systems use their dynamics to process information and adapt to changing environments. His research explores oscillations, synchronization, and noise-driven behavior across bacteria, mammalian cells, tissues, the immune system, and the brain, linking these dynamics to cellular decision-making and natural computation.

Eric Latorre Crespo

Eric Latorre Crespo, an Independent Fellow at the Centre for Genomic Regulation (CRG) and the Barcelona Collaboratorium, and a Junior Group Leader at the Centre de Recerca Matemàtica (CRM), develops mathematical models to understand how stem cell dynamics shape cellular aging, health, and lifespan. His research combines evolutionary models of mutation accumulation with stochastic models of epigenetic changes to explain how cellular turnover and individual microenvironments contribute to differences in aging and disease progression.

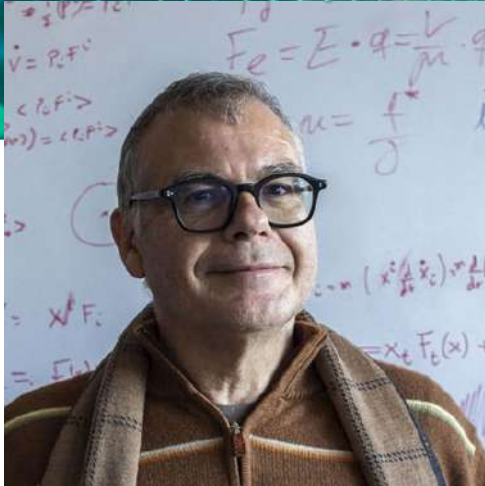




Speakers and abstracts



BARCELONA COLLABORATORIUM
FOR MODELLING AND PREDICTIVE BIOLOGY



Felix Ritort

Universitat de Barcelona (UB), Spain

Heatomics

Heat is essential for life. In living organisms, the generation of mechanical and chemical work to accomplish specific tasks inevitably leads to energy dissipation in the degraded form of heat—the most fundamental signature of life. Despite major progress in processing large biological data sets across all omics layers, we still lack a clear understanding of how to measure heat generation at the nanoscale, known as the entropy production rate, σ . In this talk, I present a recently introduced variance sum rule for measuring σ with attowatt sensitivity ($1 \text{ aW} = 10^{-18} \text{ Watts}$) from the flickering motion of a microscopic probe. We apply it to produce the first heat map of human red blood cells and to derive σ from hidden degrees of freedom in molecular processes. The variance sum rule provides a new resource for energy inference, enabling σ measurements in living and active matter.

It is time therefore to abandon the idea that genes are the blueprint for life (Noble, 2024), and to replace the Central Dogma of Molecular Biology with causal diagrams of functional physiological networks (Noble, 2025a, b) that show how organisms use stochasticity at molecular and other lower levels of organisation to generate functional physiological outcomes. With that information, physiological multi-scale modelling may develop the solution to the gene-centric impasse in finding cures for complex polygenic diseases.



Miki Ebisuya

Technische Universität Dresden (TU
Dresden), Germany

Stem Cell Zoo: a platform for studying species-specific developmental time and shape

Different animal species exhibit distinct developmental timing and morphology. For example, human embryonic development proceeds 2-3 times more slowly than in mice, and the human brain undergoes markedly greater expansion compared to other species. Our group investigates the mechanisms underlying these species-specific differences using in vitro models derived from the “Stem Cell Zoo,” a collection of pluripotent stem cells from a wide range of mammalian species.

In this talk, I will present our findings on species-specific segmentation clock periods and brain tissue mechanics, highlighting how the Stem Cell Zoo platform enables comparative analysis of developmental tempo and biophysical parameters across species.



Vikas Trivedi

European Molecular Biology Laboratory
Barcelona (EMBL Barcelona), Spain

Metabolic control of multicellular transitions

Metabolism supplies more than energy: by controlling biosynthesis, redox balance and signalling, it can set the timing and dynamics of cellular transitions. Yet whether metabolic state helped govern the emergence of multicellularity remains unexplored. The filasterean *Capsaspora owczarzaki*, a close unicellular relative of animals, provides a tractable model through its cystic, proliferative filopodiated and aggregative stages. Using lipidomic and metabolomic profiling, we identify metabolic remodelling across these transitions. In the dormant unicellular stage, cells store fats and use little energy. As unicellular cells become active, their mitochondria switch on and their lipids change. During the transition to a multicellular state, cells increase specific membrane lipids and antioxidant pathways, helping them manage the stress of increased respiration. Pharmacological inhibition shows that pentose phosphate pathway activity is required to form and maintain multicellular aggregates. Our findings identify metabolism as a regulator of multicellular-state dynamics and suggest that metabolic innovation contributed to the evolutionary emergence of animal multicellularity.



Thomas Höfer

German Cancer Research Center (DKFZ),
Germany

Breakdown of the hematopoietic hierarchy in the evolution of leukemia

Tumor evolution is a dynamic process of mutation and clonal competition and selection. While this evolutionary process is not directly observable before diagnosis, it nevertheless leaves traces in the mutation spectrum of the tumor that allow us to reconstruct the underlying clonal dynamics. In this way, we have birthdated a range of pediatric and adult cancers, and I will review recent results. Moreover, the genetic analyses of both non-malignant tissues and tumors have shown abundance of driver mutations, raising the question under which conditions drivers become selected to sustain malignant transformation. Using a mouse model of spontaneous leukemogenesis and human data, I will describe a route to driver selection that originates in the disruption of the stem cell-progenitor hierarchy.



Alejo Rodriguez-Fraticelli

Institut de Recerca Biomèdica Barcelona
(IRB Barcelona), Spain

Origins and dynamics of non-genetic blood stem cell diversity

Haematopoietic stem cells (HSCs) are commonly viewed as a functionally interchangeable population whose clonal behaviour is shaped largely by stochastic events or acquired genetic mutations. However, lineage-tracing studies increasingly reveal stable and heritable differences between genetically unperturbed HSCs.

Our initial studies using Sleeping Beauty transposon barcoding uncovered extensive clonal heterogeneity during native haematopoiesis. Subsequent single-cell lineage tracing with LARRY linked these differences in clonal fate to molecular states present before differentiation, demonstrating that the future behaviour of individual stem and progenitor cells is already biased (and partially predictable) from their initial state.

We next developed EPI-Clone, which uses naturally occurring somatic DNA methylation changes as endogenous clonal barcodes. This enabled transgene-free lineage tracing in mice and humans and revealed that age-related clonal expansion is not restricted to cells carrying known genetic drivers. Instead, ageing produces a continuum of clonal behaviours, while many functionally young-like clones persist into old age.

To investigate when this diversity is established, we recently generated a fetal-to-neonatal LARRY atlas of HSC fate. These data point to the perinatal transition as a critical window during which distinct and heritable clonal programmes emerge. In situ tracing identifies a developmentally defined population of Tppp3-expressing HSCs whose clones progressively expand throughout life while retaining distinctive functional outputs.

Together, these findings suggest that clonal selection in blood is not exclusively stochastic or genetically driven. Developmentally encoded, non-genetic states may constrain HSC behaviour in a reproducible (and partially deterministic) manner. Similar mechanisms may contribute to unexplained clonal expansions and age-associated blood-cell biases in humans.



Kirsty Wan

University of Exeter

Embodied motility in single-celled organisms

How do diverse organisms coordinate complex movement without centralized control? In this talk, I will explore how microscale motility and navigation emerge from the oscillatory dynamics of motile cilia across multiple species. Connecting sub-cellular biophysics to whole-organism behavior, we combine live imaging, micro-manipulation, and computational modelling to dissect the complex waveform dynamics of ciliary beats and their impact on swimming and flow generation. We will discuss physical and biological mechanisms of interaction that lead to different forms of (including metachronal) coordination among diverse ciliated structures, and the influence of mechanical and electric field perturbations. We will explore how systematic variations in these waveforms across a low-dimensional manifold of shapes produce self-propulsion. We examine how symmetry-breaking within these dynamic ciliary gaits enables steering in both 2D and 3D, offering a generalized framework to predict how distinct appendage actuation strategies shapes locomotion across ciliated systems.



Didier Gonze

Université Libre de Bruxelles, Belgium

Biological clocks: design principles and physiological roles

Circadian clocks govern the timing of a wide range of physiological and behavioral processes, allowing organisms to anticipate the 24h day-night cycle. In mammals, the suprachiasmatic nucleus (SCN) of the hypothalamus acts as the central pacemaker: it receives light input from the retina and synchronizes peripheral clocks in the liver, pancreas, kidney, heart, and other organs. Within each SCN neuron, interlocked transcriptional-translational feedback loops drive rhythmic expression of clock genes. In dispersed cell culture, however, these oscillations are highly heterogeneous: many cells show damped rhythms with cell-to-cell variability in period. Intercellular coupling, mediated by periodic neurotransmitter release, synchronizes these disparate cellular rhythms into a coherent tissue-level output. In this talk, I will show how computational modeling provides insights into the design principles underlying circadian oscillations, focusing on how the SCN's complex architecture confers robustness and entrainability, and how aging impairs synchronization. I will then show how these modeling concepts have been revisited to interpret clock gene expression data in diabetic patients, raising hypotheses on how intercellular coupling within peripheral oscillators may be affected in diabetic patients.



Ala Trusina

Niels Bohr Institute, University of
Copenhagen (NBI), Denmark



Low-dimensional models of robust patterning in early embryo development

In mammalian development, the embryo is robustly patterned in the absence of maternal cues. What are the key mechanisms and principles underlying this robust development? While tremendous biological knowledge on the molecular level has been accumulated, it is unclear whether explicitly accounting for the multitude of discovered molecular players and mechanisms is necessary — or whether robust development can emerge from a handful of simple rules. In other words, is this an intrinsically high-dimensional problem, or do a few effective dimensions suffice to fully describe the system? Does accounting for realistic morphology and/or feedback between molecular signaling and morphological changes naturally reduce the dimensionality? We take steps toward addressing these questions using biophysical models of embryo patterning during the first four days of embryogenesis and in early gastrulation. During the first few days of mouse development, a homogeneous population of cells differentiates and becomes a patterned blastocyst — a pattern that can scale and is robust to perturbations in cell fates. In early mouse gastrulation, a stage in development when the body plan is laid out, the head-tail axis is established in an initially radially symmetric embryo by a migrating population of cells (DVE) expressing "head"-like signals that inhibit tail-like signals. Disrupting the movement of this population does not deterministically disrupt axis formation; instead, one or multiple axes can form in a fraction of embryos, suggesting that there may be another symmetry-breaking mechanism working in concert with DVE migration. For both cases, we find that models embedded in realistic 3D morphologies and based on a few simple rules can successfully capture the majority of experimental observations of wild-type and mutant phenotypes. Specifically, for the blastocyst stage, in addition to robust patterning of the three cell types in wild-type, we capture scaling, changes in cell proportions with varying durations of FGF signaling, and the rates of apoptosis. For the case of symmetry breaking in early gastrulation (work in progress), the polarized particle model of cup-shaped VE and EPI epithelia enables modeling PCP-driven collective DVE migration within the VE epithelia. In addition to reproducing the experimental observations of emergent flow patterns and intercalation statistics in VE cells, we show that co-existence of single- and multiple-streak phenotypes in DVE-disrupted mutants may be an outcome of Turing patterning acting in parallel with the consensus DVE migration.



Donate Weghorn

Centre for Genomic Regulation (CRG),
Spain

From early development to evolution: the temporal dynamics of a human germline mutational hotspot

Mutation is not uniform in either space or time. New heritable mutations can arise at different stages of an individual's life history, from early embryonic development to gametogenesis. Once transmitted, these variants enter the population, where selection and other evolutionary processes reshape their frequencies over generations. Here, using extremely rare variants from gnomAD and the UK Biobank, we identify a pronounced mutational hotspot at human transcription start sites (TSSs) and trace its origin and fate across these distinct biological timescales.

The hotspot extends several hundred base pairs around TSSs, but surprisingly it is largely absent from conventional de novo mutation data. We reconcile this discrepancy by showing that TSSs are strongly enriched for early mosaic variants, many of which are systematically excluded during de novo mutation calling, implicating early development in the generation of the hotspot. Mechanistically, we find that TSS mutagenesis is associated with divergent transcription, RNA polymerase II stalling, R-loops and mitotic double-strand breaks. Strikingly, these associations differ across developmental time: early mosaic mutation density is associated with double-strand breaks, whereas late mosaic mutation density is associated with RNA polymerase II stalling. Mutational signatures further implicate transcription-associated mutagenesis and non-canonical double-strand-break repair.

The hotspot is subsequently reshaped over evolutionary time. While pronounced among extremely rare variants, it progressively disappears among higher-frequency polymorphisms. Consistently, dN/dS reveals measurable purifying selection already among extremely rare variants and a substantially stronger signature of purifying selection among common variants, supporting evolutionary erosion of the hotspot over generations.



Melike Donertas

Graduate School of Informatics – METU &
Leibniz Institute on Aging – Fritz Lipmann
Institute (FLI)

Ageing where selection declines - from genomes to populations

Natural selection weakens over the course of adulthood, and functions that act late in life are therefore under weaker constraint than those that act early. This decline has consequences at every level of biological organisation, from the genome to the population. In genomes, genes acting late in life are expected to accumulate deleterious variation and to show relaxed constraint across species. Within individuals, ageing is accompanied by increasing heterogeneity between cells and between individuals, a weakening of the coordination between molecular features, and a loss of the features that distinguish cell types and tissues. In populations, the decline of selection with age can be quantified directly from survival and fertility schedules and compared across species, and across human populations whose survival has changed markedly over recent decades. Our work combines comparative analyses in model organisms with large-scale human data to test these evolutionary predictions. In this talk I will present examples from our recent and ongoing work at each of these levels and discuss what they tell us about how ageing evolves and how it varies across species and individuals.



Manuel Collado

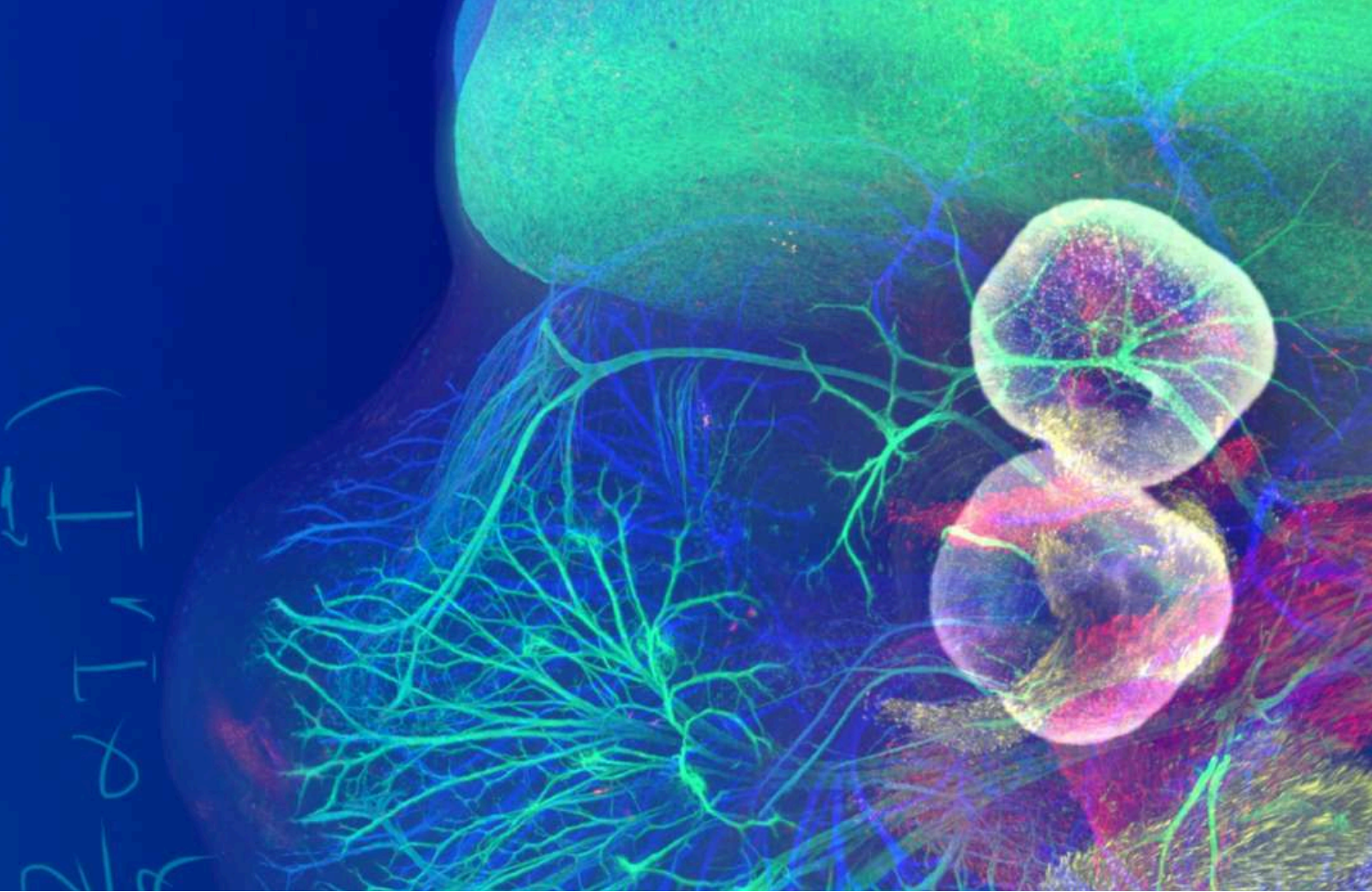
Centro de Investigación en Medicina Molecular y Enfermedades Crónicas (CIMUS), Spain

Rejuvenate or Die: New Approaches Targeting Cellular Senescence

PAs the burden of age-related diseases continues to rise, cellular senescence has emerged as a key driver of tissue dysfunction, chronic inflammation, and loss of regenerative capacity. The accumulation of senescent cells during aging contributes to a deleterious secretory phenotype (SASP) that disrupts tissue homeostasis and promotes the progression of multiple pathologies. Consequently, strategies aimed at targeting senescent cells have become a major focus of geroscience, either by eliminating these cells through senolytic interventions or by reprogramming them into a less harmful state through senomorphic approaches.

In my talk I will expose recent advances in both directions developed in our lab. First, I will discuss the discovery of novel senolytic compounds using high-throughput screening platforms, highlighting how unbiased chemical screening approaches are expanding the repertoire of agents capable of selectively eliminating senescent cells across different cellular contexts. Second, I will present emerging evidence that partial cellular reprogramming, achieved through genetic and chemical interventions, can act as a rejuvenation strategy by suppressing key features of senescence and attenuating SASP production without necessarily inducing cell death nor pushing senescent cells back into the cell cycle.

Together, these approaches illustrate complementary paths toward restoring tissue function and promoting healthy aging, bringing us closer to effective interventions that can either remove or rejuvenate senescent cells.



SELECTED POSTERS



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FLASH TALK PROGRAM

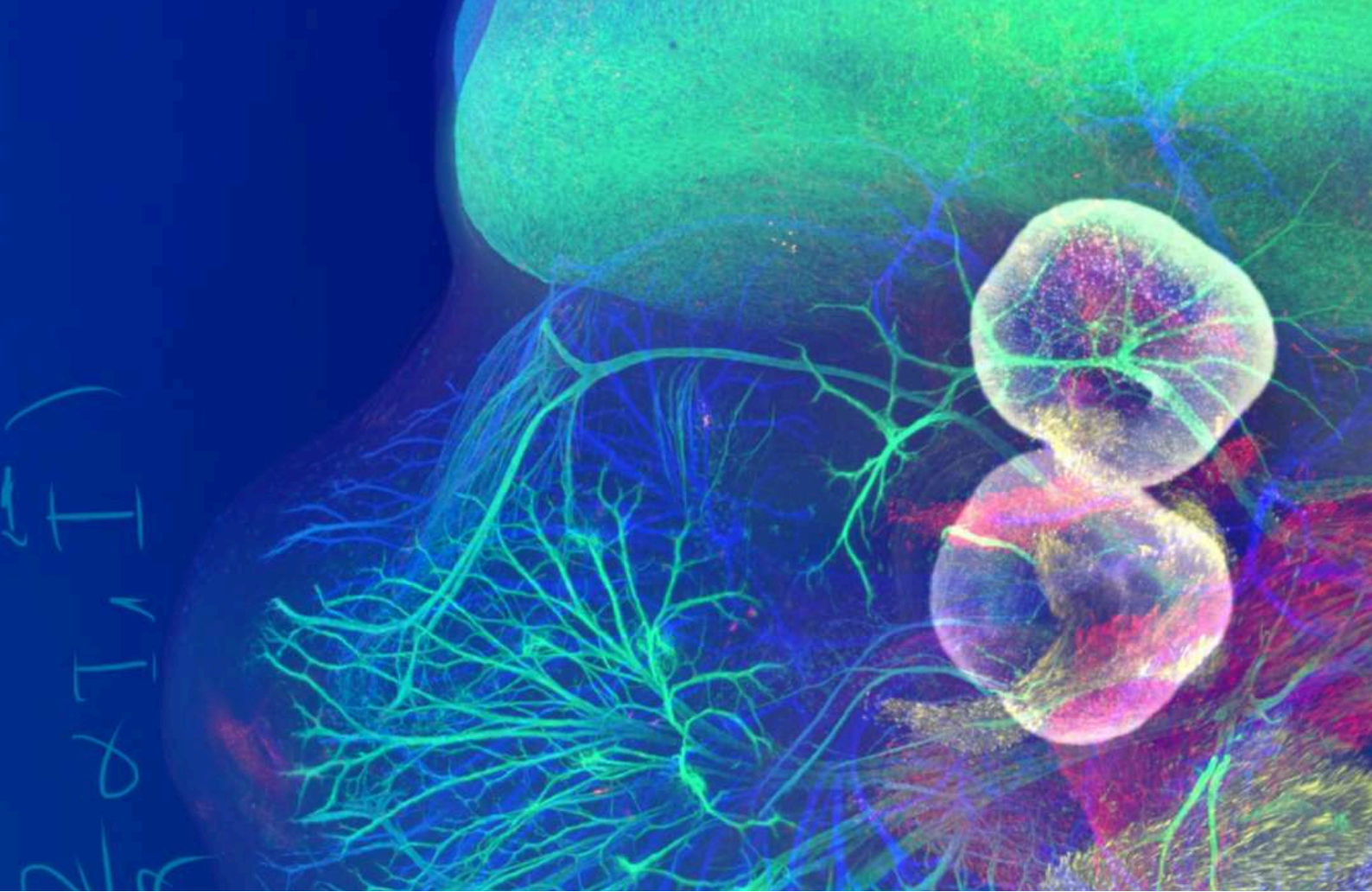
Time slot	Presenter	Institution	Title
Day 1 · 15:50–16:00	Manuela Giraud	Centre for Genomic Regulation (CRG)	Insertions and Deletions contribute to new dynamics of phenotypic variation
Day 1 · 15:50–16:00	Giacomo Bartolucci	Universitat de Barcelona (UB)	Spatiotemporal Organization of Chemical Oscillators via Phase Separation
Day 1 · 15:50–16:00	Akhilesh Nandan	EMBL	Multiple tipping points in multispecies ecosystems with cross-feeding
Day 2 · 10:40–10:50	Julia Rius i Bonet	Barcelonaβeta Brain Research Center (BBRC)	Lifelong senescence modulation by BTK inhibitor extends lifespan and delays molecular brain ageing in mouse
Day 2 · 10:40–10:50	Irene Gravili	Scuola Normale Superiore	Transcriptomic clock in the short-lived African Killifish predicts mortality and detects longevity interventions
Day 2 · 10:40–10:50	Daniele Scarcella	Helmholtz Munich	Bayesian inference of clonal fitness, age and lineage bias from snapshot single-cell hematopoiesis

POSTERS

Surname	First name	Institution	Poster title
Bartolucci	Giacomo	Universitat de Barcelona (UB)	Spatiotemporal Organization of Chemical
Bugrim	Andrej	Silver Beach Analytics, Inc.	Distributional Geometry of Cell Populations as a Readout of
Carmona Campos	Diego	Universitat Pompeu Fabra (UPF)	A dynamical systems perspective on
García Ortiz	Enrique	Universitat de Barcelona (UB)	A mechanism for self-organization at criticality for M. Polymorpha
Giraud	Manuela	Centre for Genomic Regulation (CRG)	Insertions and Deletions contribute to new dynamics of
Gravili	Irene	Scuola Normale Superiore	Transcriptomic clock in the short-lived African Killifish predicts
Isildak	Ulas	Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)	Aging as an Evolutionary Timescale: Genome-Resolved Ecology and
Jordan	Ansgar	Centre for Genomic Regulation (CRG) /	The Ticking Epigenetic Clock: Modelling Aging in
López Zancajo	Judith	Universitat de Barcelona (UB)	The effects of promiscuity, redundancy and stochasticity on
Macwan	Eric	Centre for Genomic Regulation (CRG)	Can DNA Sequence Predict Age-Associated

POSTERS

Surname	First name	Institution	Poster title
Manso	Victor	IDIBELL	Mathematical modeling of BRCA1 associated
Matyjaszkiewicz	Antoni	EMBL Barcelona	Böllpark: online multicellular
Nandan	Akhilesh	EMBL	Multiple tipping points in multispecies
Prista von Bonhorst	Francisco	Universitat Pompeu Fabra	Information Theory and Gene
Rius i Bonet	Julia	Barcelonaβeta Brain Research Center (BBRC)	Lifelong senescence modulation by BTK inhibitor extends lifespan and
Santos Pujol	Eloy	Barcelonaβeta Brain Research Center (BBRC)	Challenging biological time: The multiomics blueprint of the
Scarcella	Daniele	Helmholtz Munich	Bayesian inference of clonal fitness, age and lineage bias from
Sen	Aritra	Centre for Genomic Regulation (CRG)	3D computer simulation of anaphase midzone
Soldatkina	Oleksandra	Barcelona Supercomputing Center (BSC)	Multimodal data analysis reveals asynchronous aging dynamics
Soler Sanchis	Xavier	Centre for Genomic Regulation (CRG)	Does unsupervised outlier identification uncover hidden



Event management

ANNA MARTA BORRELL PAGES (CRG)

BASTIEN DEBIÈVE (EMBL Barcelona)



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Modelling Biology Across Scales