XII BIFI25 National Conference

January 15th - 17th 2025

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Cátedra EXOBIOPHARMA de Nanomedicina
Universidad Zaragoza

Book of Abstracts

Instituto Universitario de Investigación
de Biocomputación y Física
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Foreword

Welcome to the XII National Conference of BIFI 2025, hosted at the Institute for Biocomputation and Physics of Complex Systems (BIFI) in Zaragoza, Spain. This event continues our tradition of biennial National Conferences, serving as a dynamic platform for BIFI members to showcase their latest work, exchange ideas, and foster new collaborations between the various research lines and areas of the Institute as well as with external colleagues.

The conference program features a variety of sessions, including short presentations by students and trainees, two poster sessions, and keynote talks by the principal Investigators of most of the institute's active research lines, as well as several external contributions from other research centers in Spain.

Hoping that this event will be of interest, and enjoyable to all of you, and that it will provide invaluable opportunities for our scientific community to reconnect, and generate innovative ideas, and new partnerships, we wish you a fruitful and inspiring experience at the XII National Conference BIFI 2025.

The BIFI2025 Organizing Committee
Zaragoza, 2025

Program

BIOCHEMISTRY AND BMC

BIOPHYSICS

COMPUTATION AND DATA SCIENCE

PHYSICS

EXTERNAL CONTRIBUTIONS

Wednesday January 15th

Session 1: 08:30-11:00

Chairperson: Olga Abián

08:30-08:45	REGISTRATION
08:45-09:00	OPENING
09:00-09:15	**PROTEIN FOLDING & MOLECULAR DESIGN** Helena García-Cebollada: reMoDA: An automated workflow for unfolding detection in relaxation Molecular Dynamics
09:15-09:30	Ritwik Maity: Knowledge-Based Enzyme Engineering for PKU Therapy in the Era of Generative AI
09:30-09:45	Ana Flores Charlez: GlobalPred: Whole-genome variant calling towards personalized medicine
09:45-10:00	Antonio Hidalgo: Increasing the thermal stability of a stable flavodoxin
10:00-10:15	**SIGNAL TRANSDUCTION AND MEMBRANE PROTEIN THERAPIES** Javier García Nafría: Controlling the function of G protein-coupled receptors
10:15-10:30	Iris del Val García: Study of the orphan receptor GPR32
10:30-10:45	Ángela Carrión-Antolí: Structural Insights into GPR15 Coupled to G Proteins: Unique Features Driving Arrestin Bias

10:45-11:00	Sandra Arroyo Urea: Selectivity in the dopamine D3 Receptor: Insights from a bitopic agonist

11:00-11:30	COFFEE BREAK

Session 2: 11:30-13:45. Track 1: Biochemistry and MCB.

Chairperson: M. Teresa Bes

11:30-12:15	**INVITED SPEAKER** David Pacheu Grau: Elucidating determinants of mitochondrial translation within the cellular context.
12:15-12:30	**PLANT EVOLUTIONARY AND GENETIC BIOLOGY** Chunlin Chen: Genome assembly of two Brachypodium perennials and insights into Brachypodium evolution
12:30-12:45	Miguel Campos Cáceres: Life-history traits and environmental isolation genomics of recurrently originated allotetraploid Brachypodium hybridum lineages and its progenitor species
12:45-13:15	**COMPUTATIONAL GENOMICS AND SYSTEMS BIO-MEDICINE** Ignacio Marchante: Sex and age modulate immune activation and tissue regeneration pathways in celiac disease, independently of tissue damage severity.
13:15-13:30	Jorge Alberto Cárdenas-Pestana: Integrating Carbon Source and Iron Availability: Transcriptomic Insights into Growth Arrest in *Mycobacterium tuberculosis (MTB)*
13:30-13:45	Noelia Ferrer-Luzón: Overcoming the limitations of classical RNA-seq normalization methods in regimes of pervasive expression variance across samples

13:45-15:45	LUNCH

Session 3: 15:45-17:00
Chairperson: Javier García-Nafría

15:45-16:15	**BIOMOLECULAR INTERACTIONS** David Ortega-Alarcón: Harnessing Disorder: Small-Molecule Modulation of Intrinsically Disordered Proteins
16:15-16:30	Marta Asensio del Río: Investigating LpxC as a Zinc-Dependent Target for Novel Antibiotic Development Against MDR Gram-Negative Bacteria
16:30-16:45	Paula María García Franco: Inhibition of HDAC8 as a Therapeutic Approach to Combat Melanoma Progression and Drug Resistance
16:45-17:00	**CLINICAL DIAGNOSIS AND DRUG DELIVERY** Francisco Javier Falcó-Martí: Advancing clinical diagnosis and drug discovery with computational approaches

17:00-19:30	COFFEE BREAK & POSTER SESSION

Thursday January 16th

Session 4: 09:00-11:00
Chairperson: Alejandro Tejedor

09:00-09:30	**HIGH PERFORMANCE & CLOUD COMPUTING** Daniel Martínez: Advanced Computing Architectures and Operations at CESAR
09:30-09:45	Sergio Martínez-Losa del Rincón: The Quantum Era: Transforming Computation and Beyond
09:45-10:15	**STATISTICAL-PHYSICS MODELING OF BIOMOLECULES** Pierpaolo Bruscolini: The "Physical Modeling of Biomolecules" research line at BIFI
10:15-10:30	David Luna-Ceralbo: CertPrime: a new oligonucleotides design tool for gene synthesis
10:30-10:45	Marco Mendivil-Carboni: Polymer model for nuclear chromatin: simulation of chromatin structure and dynamics.
10:45-11:00	Alejandro Sáinz-Agost: Revealing Human G-quadruplex unfolding Intermediates through Complex Markov Networks

11:00-11:30	COFFEE BREAK

Session 5: 11:30-13:45
Chairperson: Fernando Falo Forniés

11:30-12:15	**INVITED SPEAKER** Saúl Ares: Boundary conditions play a key role in pattern formation in nitrogen-fixing filamentous cyanobacteria
12:15-12:30	**GENETIC REGULATION AND PHYSIOLOGY OF CYANOBACTERIA** Ana Alonso-Simón: Coculture with Anabaena PCC7120: a tool to mitigate lindane toxicity in rice (Oryza sativa L.) seedlings
12:30-12:45	Irene Oliván-Muro: To biofilm or not to biofilm: insights into biofilm formation and its link to stress response in cyanobacterium Anabaena sp. PCC7120
12:45-13:15	**STRUCTURAL BIOLOGY OF NEURONAL MEMBRANE RECEPTORS** Beatriz Herguedas: Understanding the AMPA receptor proteome: insights from structural studies
13:15-13:30	Carlos Vega-Gutiérrez: Molecular architecture and gating of GluA4-containing AMPA Receptors
13:30-13:45	Irene Sánchez-Valls: Building of AMPA Glutamate receptors in the endoplasmic reticulum

13:45-15:30	LUNCH

Session 6: 15:30-17:00
Chairperson: Jesús Gómez-Gardeñes

15:30-16:00	**DATA ANALYSIS, ADVANCED VISUALIZATION & TECH. TRANSFER** Gonzalo Ruiz: Addressing the IND problem (Institution Name Disambiguation) in affiliation data extracted from research production repositories
16:00-16:15	Francisco Bauzá Mingueza: Predictive models for estimating the risk of bone mineral loss in Gaucher disease
16:15-16:30	Sonia Herrero Luna: Does Digitalization Enhance Firm Performance Among Science and Technology Park Enterprises?

16:30-16:45	**DIGITAL SCIENCE** María José Luzón: From research papers to tweetorials: How researchers are transforming scientific publications into engaging social media narratives
16:45-17:00	María Ángeles Velilla Sánchez: From research to reach: How video abstracts connect science with broader Audiences

17:00-19:30	COFFEE BREAK & POSTER SESSION (BIFI council: 18:30-19:30; for bifi members only)

Friday January 17th

Session 7: 09:00-11:00

Chairperson: David Yllanes

09:00-09:30	**COMPLEX SYSTEMS AND NETWORKS** Alberto Aleta: Beyond the Graph: Computational Perspectives on Human, Economic, and Animal Behavior
09:30-09:45	Hugo P. Maia: Rumor-Spreading Dynamics on Polarized Networks: Theoretical Predictions and Empirical Observations
09:45-10:00	Marco Fernández: Consider a spherical cow...
10:00-10:30	**GROUP OF THEORETIC AND ADVANCED MODELING** Hugo Pérez-Martínez: The Role of Higher-Interactions in the Processes of Opinion Formation
10:30-10:45	Pablo Gallarta-Sáenz: Emergence of technological innovations under reputation-driven interactions
10:45-11:00	Santiago Lamata-Otín: Group overlap drives explosive collective behaviors in dynamical systems

11:00-11:30	COFFEE BREAK

Session 8: 11:30-13:45
Chairperson: Patricia Ferreira & Pierpaolo Bruscolini

11:30-12:00	**PROTEIN MISFOLDING AND AMYLOID AGGREGATION** Nunilo Cremades: Protein phase transitions in neurodegenerative diseases: from basic research to diagnosis
12:00-12:15	David Polanco: Dynamic arrest in protein phase separation: the case of tau and alpha synuclein complex coacervation
12:15-12:30	Laura Asín: Development and characterization of cellular models for studying the formation of molecular condensates in neurodegenerative diseases
12:30-13:00	**PROTEIN GLYCOSYLATION AND ITS ROLE IN DISEASE** Ramón Hurtado-Guerrero: A family of di-glutamate mucin-degrading enzymes that bridges glycan hydrolases and peptidases
13:00-13:15	Irene Ginés Alcober: Recognizing Tn and STn Epitopes in Protein Context
13:15-13:45	**SPECIAL PURPOSE COMPUTERS** Sergio Pérez-Gaviro: Spin glass traveller guide for a Janus journey

13:45-15:30	LUNCH

Session 9: 15:30-17:30
Chairperson: Pierpaolo Bruscolini & Javier Sancho

15:30-16:00	**SPIN GLASSES** David Yllanes: Memory in spin glasses: overview of results by the Janus Collaboration
16:00-16:30	Javier Moreno-Gordo: Numerical evidences of a second order phase transition in the six-dimensional Ising spin glass on a field
16:30-17:00	**FLAVOENZYMES: ACTION MECHANISMS AND BIOTECHNOLOGY** Marta Martínez-Júlvez: Insights into functional and structural features of Ferredoxin NADP$^+$ Reductase (FPR) from *Brucella ovis*
17:00-17:15	Paula Cinca-Fernando: Two novel Bacterial Aryl-Alcohol Oxidases: Expanding the Toolbox for Greener Synthesis

17:15-17:30	Maribel Rivero: Non-equivalent active sites in homodimeric flavoenzymes
17:30-17:35	CLOSING REMARKS

Talks

reMoDA: An automated workflow for unfolding detection in relaxation Molecular Dynamics

García-Cebollada, Helena[1,2,3], Galano-Frutos, Juan José[1,2,3,*], Sancho Sanz, Javier[1,2,3]

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Next Generation Sequencing techniques are becoming increasingly used in diagnostics. However, the significance of many variants remains unknown. For this purpose, the variant effect prediction field is significantly growing. The most commonly-used predictors include sequence- and structure-based approaches, but few of them consider mutation effects on protein dynamics. One of the main limitations of relaxation Molecular Dynamics, besides its high computational cost, is the lack of a standard metric to detect unfolding. For this purpose, we have developed a workflow composed of four different modules for analysis: 2D-RMSD-based clustering, Energetics, Multianalysis and PCA, using distance metrics to generate structure clusters along the simulation, monitoring the forces affecting the protein, calculating conventional metrics and summing them up in a 2-dimensional plot, respectively. These methods have already proven useful in previous investigations on hypertrophic cardiomyopathy and hereditary breast cancer, and it has been fine-tuned and validated in a set of simulations from five different proteins at different temperatures and with destabilizing variants. The resulting algorithm, named reMoDA (**re**laxation **Mo**lecular **D**ynamics **A**nalysis) is already available at https://github.com/elhectro2/reMoDA

Knowledge-Based Enzyme Engineering for PKU Therapy in the Era of Generative AI

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Human phenylalanine hydroxylase (hPAH) catalyzes the hydroxylation of L-phenylalanine (L-Phe) to L-tyrosine, initiating a catabolic pathway that subsequently feeds into neurotransmitter synthesis. Phenylketonuria (PKU) arises from an hPAH deficiency, resulting in toxic levels of L-Phe and a reduction in neurotransmitter precursors within the central nervous system, which together cause cognitive disabilities and neurological damage. While therapeutics such as Kuvan and Pegvaliase have significantly advanced PKU treatment, current pharmaceutical interventions face limitations in pan-specificity, age restrictions, and immunogenicity. Enzyme replacement therapy (ERT) is among the most discussed approaches in this area, with hPAH being a favorable candidate due to its low immunogenicity. In this work, we present the development of engineered hPAH with improved thermostability and enzymatic activity, offering potential for ERT in PKU patients.

GlobalPred: Whole-genome variant calling towards personalized medicine

Ana Flores Charlez[2,3], Helena García-Cebollada[1,2,3], Juan José Galano-Frutos[1,2,3,*], Javier Sancho Sanz[1,2,3]

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Precision Medicine, one of the main goals of Biomedical Sciences, aims to adapt each patient's treatment to their genetic particularities, increasing the probability of success while reducing potential side effects and healthcare costs associated with inefficient treatments.

The group previously developed Pirepred, an interpretation tool displaying the genotype/phenotype relationships of clinical variants found in 58 genes related to neonatal diseases. Pirepred includes a metapredictor for variant calling based on the most commonly used predictors.

The current goal is to develop GlobalPred, a tool for genetic variant interpretation including a new artificial intelligence model with high predictive value for classifying any single nucleotide variant (SNV) in the coding human genome as either pathogenic or benign.

The dataset is constructed by retrieving all the annotated and classified SNVs in ClinVar per gene, and searching their corresponding predictions in the dbNSFP database, which contains prediction scores for non-synonymous SNVs from multiple prediction algorithms. A subset of those predictors is selected avoiding low-quality and redundant information in the predictions. The curated dataset is used for training and selecting the optimal model among majority-vote, linear regression, random forest, and neural network approaches.

The final metapredictor will be implemented into a user-friendly web server for healthcare professionals.

Increasing the thermal stability of a stable flavodoxin

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To study the function and the processes in which a protein is involved, it is desirable to determine its (thermo)stability.
Furthermore, even if they are modified in certain regions, proteins have the ability to remain functional. Thanks to this feature, and using site directed mutagenesis, it is possible to increase protein stability without losing function. This means that by changing some residues the protein could be more stable at higher temperatures. This concept is used by Protposer, a server that proposes stabilizing mutations for any protein sent to it as a PDB file.
Using this server, different stabilizing mutations have been predicted for an already highly hyperstabilized flavodoxin. The best proposed mutations have been combined into different mutants and introduced by site-directed mutagenesis. From these mutants we selected those that showed an increased T_m and studied their point mutations to determine the stability increase produced by each of them. The most stabilizing point mutations were then grouped. Finally, we obtained a mutant with a higher stability that presented an 8ºC T_m increase relative to pseudo WT (which was already a highly stabilized version of the original WT).

Controlling the function of G protein-coupled receptors

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G protein-coupled receptors (GPCRs) form the largest family of membrane proteins in the human body, are present in all major organs as well as being the target for 34% of the drug in the clinic. GPCRs sense a variety of molecules (lipids, hormones, neurotransmitters…etc) and transduce the signal to the intracellular milieu by coupling to and activating heterotrimeric G-proteins and b-arrestins, which activate a diverse set of signaling cascades that result in a cell-specific response. Controlling the function of GPCRs has great potential to generate new and improved therapeutics, however, we still lack an understanding on the functional mechanisms on these receptors as well as lack of tools to finely control their function. I will provide an overview of the ongoing work at the *Signal Transduction and Membrane protein therapeutics* research group, focusing on test cases of dopamine receptor control by bitopic molecules.

Study of the orphan receptor GPR32

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G protein-coupled receptors (GPCRs) without identified endogenous ligand are classified as *orphan GPCRs (oGPCRs)*. GPCRs are the largest family of receptors in the human body and approximately 34% of FDA-approved drugs modulate GPCRs[1]. Hence, the study of oGPCRs presents an enormous potential for the discovery of new therapeutic targets. *GPR32* is an oGPCR abundant in immune cells. Its study is crucial for understanding certain processes involved in the resolution of inflammation and for the rational development of small molecules with an anti-inflammatory function[2].
In this study we aim to de-orphanize and understand the functional mechanisms of GPR32. For this purpose, we use an integrated approach of structural biology techniques, highlighting the use of single-particle cryo-electron microscopy (cryo-EM) as well as cell signaling assays. In this work, the structure of GPR32 bound to a G protein heterotrimer has been determined. A density is observed at the orthosteric site, however, it probably corresponds to an unknown endogenous ligand and not to the synthetic ligand proposed in the literature. The receptor has structural motifs and characteristics that correspond to lipid receptors. Additional electron microscopy, cell signaling assays and mass spectrometry studies are currently being carried out for the de-orphanization of the receptor.

[1] Santos R, et al. A comprehensive map of molecular drug targets. Nature Reviews Drug Discovery. 2016; 16(1):19–34.
[2]. Mena HA and Spite M. Proresolving receptor tames inflammation in atherosclerosis. J Clin Invest. 2021 Dec 15.

Structural Insights into GPR15 Coupled to G Proteins: Unique Features Driving Arrestin Bias

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GPR15 is a G protein-coupled receptor (GPCR) with crucial roles in immune system regulation, including lymphocyte homing to epithelial barriers and modulating inflammatory responses. Despite its significance, the structural basis for its function and signaling bias remains poorly understood.

Using cryo-electron microscopy, we have determined the structure of GPR15 in complex with a heterotrimeric Ga_O protein, unveiling unique features that distinguish it from other GPCRs in the same family. Our study reveals that the G protein inserts at an atypical angle relative to the receptor, diverging from canonical coupling modes. Additionally, we observed that the peptide ligand binds in a "hook-like" configuration, providing new insights into receptor activation and signaling.

A striking discovery is the role of Proline 288 in the transmembrane helix 7 (TM7), which induces a kink in TM7. This structural peculiarity appears to favor arrestin coupling over G protein signaling, suggesting a potential bias toward arrestin-mediated pathways. Ongoing studies are focused on characterizing this proline's contribution to the receptor's signaling dynamics.

These findings provide novel insights into GPR15 structural and functional biology, offering a framework for understanding its immune functions and paving the way for therapeutic targeting of this receptor.

Selectivity in the dopamine D3 Receptor: Insights from a bitopic agonist

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Although aminergic GPCRs are the target for ~25% of approved drugs, developing subtype selective drugs is a major challenge due to the high sequence conservation at their orthosteric binding site. Bitopic ligands are covalently joined orthosteric and allosteric pharmacophores with the potential to boost receptor selectivity and improve current medications by reducing off-target side effects. However, the lack of structural information on their binding mode impedes rational design. Here we determine the cryo-EM structure of the hD_3R:$G\alpha_O\beta\gamma$ complex bound to the D_3R selective bitopic agonist FOB02-04A. Structural, functional and computational analyses provide insights into its binding mode and point to a new TM2-ECL1-TM1 region, which requires the N-terminal ordering of TM1, as a major determinant of subtype selectivity in aminergic GPCRs. This region is underexploited in drug development, expands the established secondary binding pocket in aminergic GPCRs and could potentially be used to design novel and subtype selective drugs.

Elucidating determinants of mitochondrial translation within the cellular context

Ana Vela Sebastian [1,2,3], Saioa Aguas [1], **David Pacheu Grau**[1,2,3,4]

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The mitochondrial proteome has a dual genetic origin. From approximately 1200 proteins functioning in mitochondria, only 13 are encoded in the mitochondrial DNA (mtDNA) and are synthesized inside the organelle, whereas the vast majority of them are encoded in the nuclear DNA, synthesized in cytoplasmic ribosomes, and translocated into mitochondria. Genetic defects in either mtDNA or nuclear genes encoding mitochondrial proteins have been linked to disease, mainly caused by defects in oxidative phosphorylation and decreased energy production. It is remarkable that even though some mutations causing mitochondrial diseases are present in all body cells, only some tissues, or cell types, are affected by the energetic defect and contribute to the patients´ phenotype. The causes of this tissue specificity are still under debate. Interestingly, mitochondrial translation is not only maintaining balance between the synthesis of mtDNA-encoded proteins and availability of imported subunits, but it is also integrated in the cellular environment. How mitochondrial gene expression is regulated in the context of cellular physiology is little understood. Here, we will present evidence to elucidate determinants that might regulate mitochondrial translation in the context of the cell and also explain the tissue specificity of mitochondrial diseases with defects in protein synthesis.

Genome assembly of two *Brachypodium* perennials and insights into *Brachypodium* evolution

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Brachypodium represents a model system for studying the evolution of Poaceae. However, the genomes resource for this genus is scarce. Here we generated chromosome-level genome assemblies for *B. mexicanum* and *B. arbuscula*, representing the most ancestral species with the biggest genome and core perennial group of *Brachypodium* genus respectively. We assembled the genome of *B. arbuscula* into 9 chromosomes with a scaffold N50 of 30.19Mb and a total of 33,605 gene were annotated, which covers 99.10% complete BUSCOs. The assembled genome of *B. mexicanum* contains 20 chromosomes with a scaffold N50 of 78.41 Mb and a total of 70,845 protein-coding genes were annotated, which covers 99.5% of the complete BUSCOs. In addition, *B. mexicanum* were further revealed to be an allopolyploid with two different subgenomes that diverged successively. We further identified that the biggest genome of *B. mexicanum* is partially attributable to its high quantities of TE insertion, especial the Retland LTR retrotransposons. The genomes assembled here provide valuable resource for further exploration of the evolution of *Brachypodium.*

Life-history traits and environmental isolation genomics of recurrently originated allotetraploid Brachypodium hybridum lineages and its progenitor species

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The genus *Brachypodium*, comprising the diploids *B. distachyon* and *B. stacei* and their allotetraploid hybrid *B. hybridum*, provides an exceptional model for studying polyploid genome evolution and adaptation in grasses. Integrating genomic, phylogenomic, and ecological data from 308 individuals across the circum-Mediterranean region, we explored syntenic single nucleotide polymorphisms (SNPs), hybridization dynamics, introgression, and genomic divergence. Our analysis confirmed the three independent origins of *B. hybridum* from local parents, supported by nuclear and plastome phylogenies. Genomic structure revealed three clusters for, respectively, the ancestral western Mediterranean and the two recent western and eastern Mediterranean hybridization events. These findings underscore subgenome-specific responses to selection, mutation, and hybridization events. Genomic islands of divergence highlight adaptive pathways associated with energy metabolism, reproduction, and stress responses, reflecting lineage-specific adaptations to diverse Mediterranean habitats. Environmental factors emerged as significant drivers of genomic variation, with isolation-by-environment (IBE) models outperforming isolation-by-distance (IBD) in explaining genetic differentiation. This study showcases the complex interplay between hybridization, genomic stability, and environmental adaptation in shaping the evolution of *B. hybridum* and advance our understanding of polyploid genome evolution and establish *Brachypodium* as a valuable model for exploring plant adaptation and resilience in dynamic environments.

Sex and age modulate immune activation and tissue regeneration pathways in celiac disease, independently of tissue damage severity

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Celiac disease (CD) is a chronic autoimmune disorder triggered by gluten in genetically predisposed individuals, with a global prevalence of circa ~1%. The disease manifests through heterogeneous clinical presentations and morbidity, and the effectiveness of the only available treatment—a gluten-free diet (GFD)—varies significantly between patients. This variability underscores the need for a deeper understanding of CD's underlying mechanisms, which remain incompletely characterized.

In this study, we compiled a large transcriptomic dataset from gastroduodenal mucosa in CD patients, capturing data during both active disease and GFD-induced remission. Our aim was to characterize interindividual differences in immune activation, metabolic shifts, tissue damage, and regeneration, considering patient sex and age.

Our findings reveal a marked sex bias in CD pathophysiology: women exhibit higher immune activation during active disease, whereas men display more robust tissue regeneration responses. Pediatric patients show a stronger reversal of immune activation upon gluten withdrawal, alongside sustained tissue renewal signals.

These results provide a comprehensive molecular map of interindividual variation in CD, offering critical insights into the disease's heterogeneity. By advancing our understanding of the immune, metabolic, and regenerative processes in CD, this work lays the groundwork for developing personalized therapeutic strategies to improve patient outcomes.

Integrating Carbon Source and Iron Availability: Transcriptomic Insights into Growth Arrest in *Mycobacterium tuberculosis* (MTB)

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Mycobacterium tuberculosis (*Mtb)* adapts to diverse host environments by transitioning from active growth to dormancy. This process is regulated by transcriptional regulatory programs that are triggered, among other factors, by changes in the availability of different carbon sources and key nutrients like iron. While iron deprivation is a well-known trigger of the transcriptional adaptation to dormancy in *Mtb*, our understanding on how it interacts with the environmental availability of different carbon sources remains limited. To shed light on this question, we collected RNA-seq data from *in vitro* cultures of *Mtb* subject to different iron levels and carbon sources (glycerol, dextrose, and fatty acids), from exponential to stationary growth phases. As a result, we found that gene expression was significantly affected by iron deprivation during the stationary phase, while showing minimal sensitivity during exponential growth, where only a limited number of genes coding mycobactins showed iron-dependent expression. This phase-dependent effects of iron deprivation on gene expression translate into an iron-dependent modulation of the magnitude of the response to growth arrest. Unexpectedly, most of the effects of iron deprivation on the magnitude of growth arrest responses were positive, implying stronger transcriptional changes during the transition to dormancy in iron-deprived media, particularly in cultures lacking fatty acids as a carbon source. Considering that, our results suggest an "OR-like" logic where bacteria integrate the sensing of both iron deprivation and lipid availability as relevant signaling cues to modulate the magnitude of its transcriptional adaptation to dormancy.

Overcoming the limitations of classical RNA-seq normalization methods in regimes of pervasive expression variance across samples

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Since its emergence in the early 2000s, RNA-seq has become an indispensable tool in modern genomics. It is a powerful technique that identifies the presence and quantity of RNA within a biological sample. However, technical biases such as gene length, sequencing depth and library composition must be corrected to accurately compare within and/or across samples.

Crucially, all differential expression pipelines rely on the assumption that a majority of features under analysis in a given experiment can be safely considered to be non-differentially expressed, and thus used as "reference beacons" for normalizing datasets across-samples by estimating the total output -number of basepairs of all expressed transcripts-, in each sample, compared to a reference. Yet, many experimental contexts and methods where this assumption does not hold are increasingly gaining importance in a number of applications. One of such is GRAD-seq (Gradient Fractionation and Sequencing), which is a method used to profile the RNA localization within subcellular compartments by separating cellular components based on their sedimentation rates in a gradient, followed by sequencing to identify RNA distribution.

In this talk, we will illustrate how classical normalization methods like TMM (Trimmed Mean of M-values), when dealing with datasets with high inter-sample variability, such as those produced by Grad-seq, are affected by a significant lack of transitivity, leading to inconsistent results depending on the identity of the reference sample, which can lead to inaccuracies in downstream analyses, if not alleviated.

Finally, we will present two independent approaches to deal with this issue, in order to improve the consistency of the coefficients, both in regular RNA-seq as in Grad-seq experiments.

Harnessing Disorder: Small-Molecule Modulation of Intrinsically Disordered Proteins

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Intrinsically disordered proteins (IDPs) are critical in diverse biological processes and disease mechanisms, yet their lack of stable structures has traditionally hindered drug development. Our group explores innovative strategies to target IDPs, aiming to expand the boundaries of druggable targets.

We focus on IDPs of high therapeutic relevance, such as MeCP2, implicated in Rett syndrome and pancreatic cancer, targeted through modulators of its DNA-binding complex; c-MYC, a driver of cell proliferation in various cancers, where folding induction in its nuclear localization sequence (NLS) blocks nuclear entry and activity; and NUPR1, a stress-response protein involved in pancreatic and colorectal tumor progression, disrupted by compounds that induce allosteric folding to impair its interactions.

The biophysical characterization of the protein targets, using calorimetric and spectroscopic techniques, and the screening method should be applied to IDPs,

Preliminary results reveal selective binding and regulatory effects of these compounds in cellular models, showcasing the feasibility of targeting IDPs.

Our work underscores the therapeutic potential of IDPs, presenting novel approaches to tackle diseases where they play central roles. By overcoming traditional challenges associated with IDP druggability, we pave the way for new therapeutic strategies in cancers and other pathologies.

Investigating LpxC as a Zinc-Dependent Target for Novel Antibiotic Development Against MDR Gram-Negative Bacteria

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Bacterial infections caused by multi-drug-resistant (MDR) gram-negative pathogens have become a serious public health threat, highlighting the urgent need for new drugs. The enzyme LpxC (UDP-3-O-(R-3-hydroxymyristoyl)-N-acetylglucosamine deacetylase) is broadly conserved in all gram-negative bacteria and lacks sequence homology with other deacetylases. LpxC is involved in the biosynthesis of lipid A, the membrane anchor of lipopolysaccharides (LPS), and it is essential for bacterial viability. Therefore, it represents an attractive target for the development of new antibacterial agents.

LpxC is a zinc-dependent deacetylase. Zinc is required for structural stability and functions but needs to be tightly controlled through different mechanisms depending on the requirements of the cell. Like other zinc-dependent proteins, LpxC can adopt well-folded functional states in the presence of zinc, whereas, it adopts partially unfolded inactive states in the absence of zinc. This characteristic presents a strategic vulnerability in LpxC that can be exploited through the design of a new pharmacological strategy.

LpxC deacetylase has been purified and characterized from different gram-negative bacteria to compare the structural stability of the protein. Several biophysical techniques such as Differential Scanning Fluorimetry (DSF), Differential Scanning Calorimetry (DSC) and Circular Dichroism (CD), were employed to collect thermal denaturation data, with and without zinc.

Inhibition of HDAC8 as a Therapeutic Approach to Combat Melanoma Progression and Drug Resistance

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Melanoma, the most lethal form of skin cancer, has been rapidly increasing in incidence over recent decades. It arises from melanocytes, highly specialized cells that produce melanin, a protective pigment against UV-induced damage. Despite of advancements in melanoma treatment, challenges such as cumulative toxicity and the development of drug resistance limit the effectiveness of current therapies. Recent studies have highlighted hypoacetylation as a common feature of various cancers, including melanoma. Histone deacetylases (HDACs) are enzymes that remove acetyl groups from lysine residues on histones, leading to chromatin remodelling and the suppression of gene expression. Among these, histone deacetylase 8 (HDAC8), a class I HDAC, plays a crucial role in melanoma progression by promoting cell proliferation and metastasis. HDAC8 participates in cancer development through interactions with both histone and non-histone proteins. Under stress conditions, such as hypoxia or UV damage, melanoma cells exhibit increased HDAC8 expression, driving the adoption of a drug-resistant phenotype. In this study, we identify several compounds that effectively interact with HDAC8, modulating its activity and stability. The development of potent HDAC8 inhibitors offers a promising strategy to reduce melanoma cell plasticity and enhance the response to treatment.

Advancing clinical diagnosis and drug discovery with computational approaches

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Computational approaches have become indispensable in modern biological and medical research at different levels, such as the development of tools that enable the early detection of diseases, especially those in which timely intervention is crucial, or the identification and optimization of bioactive molecules with therapeutic potential.
Our research focuses on these two main areas. First, in the field of clinical diagnosis, we are integrating serum analysis through Thermal Liquid Biopsy (TLB) with patient-specific clinical variables, enhanced by Machine Learning (ML) algorithms. This methodology has shown promising results in the early diagnosis of diseases such as ovarian and pancreatic cancers, where late detection significantly limits treatment options. Second, for drug development, we perform high-throughput screening of chemical libraries to identify compounds capable of modulating the stability of target protein conformations. The most promising candidates are subjected to molecular dynamics simulations and molecular docking analyses to elucidate their mechanisms of action and evaluate their viability as potential drugs. For example, we have applied these techniques to the HDAC8 protein, a potential therapeutic target that is involved in various pathologies.

Advanced Computing Architectures and Operations at CESAR

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The Aragón Supercomputing Center (CESAR), hosted in the BIFI datacenter in Zaragoza, Aragón, is a hub for high-performance computing and advanced system architectures. As the Caesaraugusta IV node of the Spanish Supercomputing Network (RES), CESAR integrates a robust infrastructure to meet the needs of scientific challenges.

At its core is the HPC supercomputer Agustina, featuring a 6,144-core CPU partition for diverse computational workloads and rasmIA, a GPU partition with 48 accelerators optimized for intensive data processing tasks. The legacy supercomputer Cierzo has been integrated as additional partitions, contributing 2,080 CPU cores, 8 GPUs, and 2 MICs, increasing the system's flexibility and capacity. Supporting these computing resources is Reposte, a CEPH-based distributed storage cluster offering 5.4 PB of raw capacity, enabling scalable and efficient data management. The Colossus cloud cluster, redeployed to implement an updated software version while retaining its original hardware, now features 1,800 CPU cores and a dedicated CEPH storage cluster with approximately 600 TB of capacity, providing robust support for virtualized and hybrid environments.

This presentation will cover advanced system architecture topics, including interconnect design and workload orchestration across heterogeneous platforms. It will also explore system administration strategies for resource allocation, fault tolerance, and managing large-scale infrastructures. Together, these insights reflect CESAR's pivotal role in driving innovation and computational efficiency.

The Quantum Era: Transforming Computation and Beyond

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Quantum computing represents a revolutionary new paradigm for computation that leverages the unique properties of quantum mechanics to solve certain problems exponentially faster than classical computers. This talk will introduce the fundamental concepts of quantum computing, including qubits, superposition, entanglement, quantum gates, and measurement.

We will explore how these principles enable quantum algorithms that can efficiently solve complex problems in fields like cryptography, optimization, and simulation. Key quantum computing architectures such as superconducting qubits, trapped ions, and topological quantum computers will be discussed.

The current state-of-the-art in quantum hardware and software development will also be examined, along with potential applications and future directions for this emerging technology. No prior knowledge of quantum mechanics is required, we will focus on intuitive explanations accessible to physicists and non-physicists alike. This introduction aims to provide a comprehensive overview of quantum computing for both experts and newcomers, highlighting its transformative potential across various scientific and technological domains.

The "Physical Modeling of Biomolecules" research line at BIFI

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In this talk, I will present an overview of the research activity of the three different subgroups that contribute to this line, covering both published and ongoing studies. All of them share a common approach, based on the applications of theoretical and computational methods, from the non-linear and statistical-physics fields, to different biomolecules as well as biological processes.

CertPrime: a new oligonucleotides design tool for gene synthesis

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Gene synthesis is a fundamental technique in molecular biology that enables the creation of long, custom DNA sequences, driving advancements in genetic engineering and synthetic biology. The precise design of oligonucleotides is essential for successful gene synthesis, ensuring specificity and uniform hybridisation temperatures. However, existing computational tools for oligonucleotide design face significant limitations. These include difficulties in handling long DNA sequences, inadequate adaptation to specific experimental conditions, inability to effectively restrict oligonucleotide length, and issues with spurious dimer formation.

To overcome these challenges, we have developed CertPrime, a novel tool that offers excellent computational scalability for efficient processing of long DNA sequences. CertPrime allows precise adjustment of experimental parameters, including concentrations of ions, DNA, and dNTPs, and provides the ability to limit the maximum length of oligonucleotides. It achieves designs with lower deviations in melting temperatures of overlapping regions compared to existing tools, while maintaining a similar number of oligonucleotides required for synthesis. These features make CertPrime a powerful and versatile tool for oligonucleotide design in gene synthesis applications.

Polymer model for nuclear chromatin: simulation of chromatin structure and dynamics.

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Nuclear chromatin structure and dynamics play an important role in understanding processes such as gene regulation and cell fate decisions in developmental biology, as well as other processes such as epigenetic modifications.

In this communication, a polymer model of the structure and dynamics of chromatin is proposed. The dynamics of the model are implemented in a very efficient parallel computing code (based on GPU CUDA programming) for Langevin molecular dynamics, which allows us to simulate large polymers up to 30,000 beads. The model includes lamina-nucleosome interactions as well as hetero- (compacted and silenced genic region) and euchromatin (gene-expressing region) specific interactions. The model is able to capture key features of chromatin structure, such as the formation of chromosome and compacted regions, and reproduces the expected Hi-C experiments. We will also discuss the comparison of the simulation with other experimental results involving nuclear osmotic stress and nuclear shape deformation under mechanical forces.

Revealing Human G-quadruplex unfolding Intermediates through Complex Markov Networks

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G-quadruplexes are secondary, non-canonical RNA/DNA structures formed by guanine-rich sequences assembled into four-stranded helical structures by the progressive stacking of G-Tetrads, planar arrangements of guanines stabilized by monovalent ions such as K^+ or Na^+. Their stability plays a very important role in the prevention of DNA degradation, leading to the promotion or inhibition of specific biological pathways upon formation.

In this work we study the different conformations of these structures through their Free Energy Landscape at different temperatures. All-atom simulations are adopted according to a mesoscopic G-quadruplex model previously developed by our group. We use a small number of significant reaction coordinates to analyze the evolution of the system by applying two dimensionality reduction techniques: Principal Component Analysis (PCA) and time-Independent Component Analysis (tICA). The data of the trajectories of the system in this reduced space are encoded into a Complex Markov Network which, in conjunction with a Stochastic Steepest Descent, provides an hierarchical organization of the different nodes into basins of attraction, so revealing the main intermediate states and the most relevant transitions the system undergoes in its denaturation path.

Boundary conditions play a key role in pattern formation in nitrogen-fixing filamentous cyanobacteria

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Understanding multicellular pattern formation is key for the study of both natural and synthetic developmental processes. Arguably one of the simplest model systems for this is the filamentous cyanobacterium Anabaena, that in conditions of nitrogen deprivation undergoes a dynamical differentiation process that differentiates roughly one in every ten cells into nitrogen-fixing heterocysts, in a quasi-regular pattern that is maintained as the filament keeps growing. One of the most characteristic mutations affecting this process forms heterocysts mostly constrained to the terminal cells of the filament. We have used experimental observations to propose a mathematical model of heterocyst differentiation able to reproduce this striking phenotype. The model extends our understanding of the regulations in this pattern-forming system and makes several predictions on molecular interactions. Importantly, a key aspect is the boundary condition at the filament's ends: inhibitors of differentiation should be able to leakout of the filament, or otherwise the terminal cells would not differentiate. This highlights, in a very clear example, the importance of considering physical constraints in developmental processes.

Coculture with *Anabaena* PCC7120: a tool to mitigate lindane toxicity in rice (*Oryza sativa L.*) seedlings

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Lindane (γ-hexachlorocyclohexane, γ-HCH) is a broad-spectrum pesticide widely used since the 1950s until its inclusion in the Stockholm Convention Persistent Organic Pollutants (POPs) list for global elimination in 2009, together with its isomers α-HCH and β-HCH. The high persistence and mismanagement of the toxic wastes generated during its synthesis have led to serious environmental problems worldwide. In this work, we hypothesised that the co-culture of *Anabaena* sp. PCC7120 (a cyanobacteria capable of metabolising lindane) with rice (*Oryza sativa* L.) seeds could mitigate the toxic effects of pesticide on plants. Therefore, we first evaluated the toxicity of lindane in rice seeds and seedlings, proving that it especially affects root development. Then, we tested the growth of *Anabaena* cells on various concentrations of lindane, verifying its viability even at high concentrations of HCH. Lastly, we co-cultured rice seeds with cyanobacteria, applying two different methods (direct inoculation and biopriming). Our results show that soaking the seeds in a cyanobacteria solution (biopriming) before exposure to lindane helps plant development, significantly improving root development in lindane-treated seedlings.

To biofilm or not to biofilm: insights into biofilm formation and its link to stress response in cyanobacterium *Anabaena sp.* PCC7120

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Adaptation to different stresses is key for survival in hostile environments. A widespread bacterial resistance mechanism is the embedment in a complex extracellular matrix, forming communities known as biofilms. Although their undesired growth constitutes an environmental and sanitary hazard, they are also ecologically relevant and show considerable biotechnological potential in fields like bioremediation and biofertilization due to their resilience and the negative charge of their matrix, allowing removal of cationic molecules, among other applications.
Anabaena sp. PCC7120 is a model nitrogen-fixing cyanobacterium capable of forming biofilms. To advance in the understanding of phototrophic biofilm formation, we carried out comparative transcriptomic analysis of biofilm and planktonic *Anabaena*, observing vast alterations. Consistent with the role of biofilms in stress resistance, their expression profile partially overlaps with the transcriptional response to drought and nitrogen deficiency.

Growth assays under iron deprivation, saline stress and nitrogen-fixing conditions unveiled that, while the biomass obtained was slightly greater for the latter two, absence of iron practically voided biofilm formation. Lastly, nano-X-ray fluorescence allowed us to map metal distribution on sessile and planktonic cells, displaying differences of several orders of magnitude that showcase the relevance of metals in biofilm formation and strengthen their potential in heavy metal removal.

Understanding the AMPA receptor proteome: insights from structural studies

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Glutamate is the main excitatory neurotransmitter in the central nervous system, where it binds and activates ionotropic glutamate receptors (iGluRs). Glutamate binding to the AMPA receptor subtype of iGluRs (AMPARs) induces a fast depolarization of postsynaptic neurons, and therefore, it is crucial for the initiation of action potentials. Its disfunction is associated with epilepsy, brain cancer, and neurodegenerative diseases. AMPARs constitute a large family of receptors composed of a core ion channel interacting with more than 30 protein partners including (1) Transmembrane binders which modulate function and pharmacological properties (2) Extracellular protein partners which contribute to synapse anchoring (3) Endoplasmic reticulum partners which modulate AMPAR assembly and (4) intracellular partners that participate in trafficking. The variable subunit composition of AMPARs is crucial for signaling in the brain, as it determines the speed and frequencies of neuronal responses. Our group is focused in understanding the molecular variability of AMPARs as well as identifying the structural motifs involved in the regulation of their functional properties. Here we present our recent results. We generated a baculoviral library that permits the expression of most members of the transmembrane, ER and extracellular family of AMPAR binders. Using this library as starting point we produced and purified different AMPAR complexes, we obtained high resolution electron microscopy structures and we identified novel regulatory mechanisms of AMPARs and its proteins partners.

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Molecular architecture and gating of GluA4-containing AMPA Receptors

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AMPA receptors (AMPARs), members of the ionotropic glutamate receptor family, are ligand-gated cation channels that participate in fast-excitatory neurotransmission and synaptic plasticity. The tetrameric core of AMPARs is composed of various combinations of four subunits (GluA1-GluA4), whose expression is developmentally and regionally regulated. GluA2-containing AMPARs are calcium-impermeable, while GluA2-lacking receptors are calcium-permeable. Furthermore, AMPARs co-assemble with different auxiliary subunits (TARPs, CKAMPs, GSG1L and CNIH), resulting in receptor complexes with altered gating kinetics, pharmacology and pore properties. It is key to understand the architecture and functions of different AMPAR complexes, as they represent drug targets for treating neurological disorders.

Here we present the cryo-EM analysis of GluA4 containing complexes, both alone and in complex with the auxiliary subunit TARP2, trapped at three distinct functional states. In the resting state, GluA4 exhibits a classical Y-shape modular architecture and mimics GluA2-containing receptors, forming a dimer of dimers where Ligand Binding Domains (LBDs) and N-terminal Domains (NTD) form dimeric and tetrameric interfaces. However, differences emerge in the presence of TARP2 subunit and during the gating cycle. A subpopulation of resting and desensitized states, present a rupture of the LBD dimers, distorting the ion channel gating machinery and aligning more closely with GluA1 receptors. Additionally, we identified a novel regulatory site for TARP2 modulation.

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Building of AMPA Glutamate receptors in the endoplasmic reticulum

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AMPA receptors (AMPARs) are glutamate gated ion channels that play a central role in excitatory neurotransmission and plasticity. AMPARs consist of combinations of four subunits (GluA1-4) that form homo- or hetero-tetrameric channels. It was recently shown that GluA core subunits associate at the endoplasmic reticulum with different protein partners that modulate the receptors' biogenesis and tetramerization. These interaction partners include ferric chelate reductase 1 like (FRRS1l), carnitine palmitoyl transferase 1c (CPT1c), and α/β-hydrolase domain-containing protein 6 (ABHD6).
Here, we focused on the characterization of the AMPAR biogenesis pathway at the structural level. We confirmed that GluA subunits interact with ABHD6, FRRS1L and CPT1c. ABHD6 recruits monomeric GluA and prevents its oligomerization into the functional tetrameric form, while the interaction with CPT1c depends on FRRS1L. GluA-ABHD6 and FRRS1L-CPT1c complexes can be isolated with detergents and purified at high yields, but size exclusion chromatography and negative staining EM reveal that the complexes are flexible and dissociate during the procedure. To obtain a suitable sample for cryo-EM, we are exploring reconstitution into lipidic nanodiscs, which provide a robust lipid environment and reduce complex dissociation. Using this approach, we obtained promising negative staining reconstructions for GluA:ABHD6, which will be used for further cryo-EM analysis.

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Addressing the IND problem (Institution Name Disambiguation) in affiliation data extracted from research production repositories

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The global growth in scientific production generates an immense volume of data, making its analysis increasingly complex. This output is published in diverse formats and standards across various repositories, such as Web of Science, Scopus, and emerging open platforms like OpenAlex. These repositories allow to perform searches using different criteria, providing valuable insights into collaboration patterns, influential works, and leading institutions. However, accurately linking this scientific production to researchers and institutions remains a major challenge due to inconsistencies in how this information is presented, whether by the researchers themselves, by the institutions that collect the data, or by the repositories that store and index it. In this presentation we will show different strategies to address the complexities of correctly identifying institutions from affiliations in publications. This problem is known as Institution Name Disambiguation (IND).

Predictive models for estimating the risk of bone mineral loss in Gaucher disease

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Bone health complications such as osteopenia and osteoporosis are significant concerns for patients with Gaucher disease, yet predictive models in this domain are underdeveloped. Current methodologies emphasize the integration of diverse data types, but often face challenges related to small sample sizes and high-dimensional data. While approaches such as logistic regression and decision tree classifiers show potential, their generalizability and robustness require further refinement.

In this study, we analyzed a dataset comprising 59 patients with Gaucher disease to assess the relationship between bone health conditions and various predictive factors. We conducted a descriptive statistical analysis, employing tests like the Brunnel-Munzel test and Fisher's exact test to identify significant associations. Key variables, including gender, S-MRI imaging results, and several microRNAs emerged as significant predictors. To develop a predictive model, we employed logistic regression, integrating dimensionality reduction through Principal Component Analysis (PCA) and standardization techniques.

Several challenges were encountered, including the limited dataset and the high dimensionality of genomic variables. These issues necessitated the application of dimensionality reduction and non-traditional data splitting methods, complicating the validation process. Nonetheless, the study underscores the potential for machine learning to provide insights into bone health risks in Gaucher disease and highlights the importance of overcoming data-related limitations for improved predictive accuracy.

Does Digitalization Enhance Firm Performance Among Science and Technology Park Enterprises?

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In the evolving digital landscape, understanding its impact on firm performance is crucial, especially in Science and Technology Parks (STPs). This study investigates this relationship in Spanish STPs firms, focusing on Smart and Non-Smart Technologies. Through a multilevel analysis, we evaluate how digitalization affects key performance indicators like profitability, productivity, market share, and sales. Our findings reveal significant positive relationships between Non-Smart Technologies adoption and firm performance, emphasizing the value of basic digital tools for competitiveness. Additionally, we identify specific digitalization dimensions that significantly influence firm performance in STPs. These insights have implications for policymakers, managers, and researchers interested in leveraging digitalization for economic growth and innovation within STPs and beyond.

From research papers to tweetorials: How researchers are transforming scientific publications into engaging social media narratives

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The need to promote research and make it visible to diverse audiences has given rise to innovative digital genres designed to draw attention to research publications. Among these, tweetorials—extended Twitter threads that communicate complex concepts—have become increasingly popular among researchers for reporting on and promoting their published articles and preprints. In this study, I analyzed a small-scale corpus of 50 publication-promoting tweetorials to understand how papers/preprints are recontextualized in this genre. The first part of the analysis focuses on the rhetorical structure of tweetorials to determine if they mirror the structure of traditional research articles. The second part examines recontextualizing strategies—techniques used to adapt the content of research papers to the tweetorial format. The analysis has identified five categories of strategies: strategies to establish the authors' authority and credibility; strategies to make claims and arguments convincing (e.g. the use of figures); strategies to engage the readers and attract their attention to the tweetorials (e.g. questions, gifs); strategies to facilitate quick processing of information; and strategies to deal with space constraints. The findings of this study are expected to help researchers who want to use Twitter to disseminate their research in a clear and engaging way.

From research to reach: How video abstracts connect science with broader Audiences

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Online videos are increasingly used by academics, universities and organizations to make scientific knowledge accessible to diverse audiences (Scotto di Carlo, 2014; Erviti & Stengler, 2016; León & Bourk, 2018; Luzón & Pérez-Llantada, 2019). Their multimodal nature provides an effective and accessible format for communicating complex scientific ideas to non-specialist audiences, serving purposes such as disseminating and promoting research findings (Pasquali, 2007). This study examines video abstracts published on the website Latest Thinking (lt.org), designed to engage both the scientific community and lay audiences. A small-scale corpus of 30 videos and their associated research articles from the fields of "Chemistry," "Medicine" and "Climate Change" has been compiled. The analysis focuses on how authors orchestrate diverse discourse strategies and semiotic modes to assert their voice and establish interpersonal meaning with viewers. Drawing on different proximity facets (Hyland, 2010) such as framing, stance, engagement and visual organization, the study explores how content is made more accessible and interactive. The findings reveal the use of three main strategies: simplifying information to match viewers' knowledge levels, constructing credibility and authority, and fostering connections with the audience by emphasizing shared relevance.

Beyond the Graph: Computational Perspectives on Human, Economic, and Animal Behavior

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In this talk, we explore the exciting frontiers our group is charting in the application of advanced computational tools to diverse challenges. First, we will explore how hypergraphs can be used to capture higher-order relationships, offering a lens for modeling complexity in ways that transcend traditional network structures. Next, we will examine social dilemmas through the lens of large language models (LLMs), investigating whether these systems can replicate and shed light on human behavioral patterns in cooperative and competitive scenarios. Finally, we highlight the versatility of graph neural networks (GNNs) across three distinct domains: understanding the dynamics of Spanish funds, in particular during crisis; predicting player interactions in football matches, to obtain information that goes beyond individual characteristics; and decoding how social relationships among cows influence milk production. Together, these projects showcase the interplay between innovative computational methods and pressing real-world problems, opening avenues for discovery and impact.

Rumor-Spreading Dynamics on Polarized Networks: Theoretical Predictions and Empirical Observations

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Historically, rumors have sparked revolutions, undermined political trust, and destabilized societies. Nowadays, their constant spread amplified by fake news poses growing risks to social harmony in increasingly polarized communities. Online communication networks frequently exhibits polarization, often evident with the appearance of echo chambers, wherein individuals tend to engage predominantly with peers of similar leanings. We investigate rumor-spreading models onto loosely connected modular networks forming echo chambers. Here, rumors are coupled with interacting agent's opinions according to different rules that alters spreading and stifling rates. We show that highly modular structures of opinion polarized networks strongly impairs rumor spreading, however, the introduction of opinion coupling has a striking effect on rumor-telling dynamics. In particular, a controversy-seeking mechanism, in which agents postpone their transitions to the stiffer state upon interactions with agents of confronting opinions, enhances rumor spreading suppressing the modularity bottleneck. Additionally, over a billion posts related to Brazilian politics were collected from the online social network X/Twitter from 2018-2022, a period marked by severe polarization and misinformation spreading. We reconstruct a multilayered networks of hashtags, re-posts, and mentions, providing empirical evidence of anti-echo chamber effects: users engaging in cross-ideological interactions with others outside their bubbles in a provocative, confrontational manner.

Consider a spherical cow...

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In this group, human social networks have been extensively studied for various purposes, including rumor spreading, echo chambers, and the diffusion of epidemics. However, it's time for a change. In this work, we will focus on analyzing the social networks of cows.

To do so, we will focus on their social dynamics in self-milking barns. In these barns, cows are automatically milked by a highly sophisticated machine that is only activated when the cows want (or are allowed to by other cows), and that tracks many characteristics of each cow. Given that several studies have confirmed the significant impact of cows' social networks on milk production, this setting provides a valuable opportunity to analyze these networks in relation to milk yield and quality.

There appears to be a strong hierarchy among certain cows, along with distinct friend groups—evidenced by the fact that some cows consistently go to be milked together, suggesting social bonds. Building on these observations, we plan to derive the social networks of the cows based on their milking events. To further explore these dynamics and potentially enhance milk quality, we propose using a Graph Neural Network for analysis and optimization.

The Role of Higher-Interactions in the Processes of Opinion Formation

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The processes of opinion formation have been traditionally addressed attending only to pairwise interactions, but human interaction usually takes place in groups that act as major drivers of opinion change via phenomena like group polarization: a group of people can end up with a more extreme opinion that they started with before interacting. This behavior, widely documented in real-world situations, cannot be accounted for if only pairwise interactions are considered.

We propose a model of opinion formation that includes this mechanism, together with homophily (the tendency of individuals to interact with similar people) in the context of higher-order contact structures. Our results show that, even in the case of weak higher-order interactions, the processes of opinion formation vary greatly, and the emergence of opinion polarization can become widespread in societies where, if higher-order interactions are ignored, consensus emerges as the only possible final state. Our results show the importance of considering network structures beyond the traditional pairwise approach, especially in contexts where human sociality comes into play.

Emergence of technological innovations under reputation-driven interactions

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The development of novel technologies is strongly shaped by interactions between individuals, and one effective approach to study these interactions is through networked structures that mimic real human societies. In this work, we explore the role of reputation-based interactions using a dynamic agent-based model. Additionally, we introduce the concept of reputation to examine how prestige influences the accumulation of human culture and knowledge.

To study reputation-driven contacts, we consider not only the knowledge of agents, but also its social influence, represented by its degree in the network structure. This distinction allows us to explore three types of interactions: random, degree-driven (DD) and score-driven (SD) contact. To validate our results, we derived a macroscopic observable to quantify the technological trapping of the society. This metric, combined with the time to crossover, provides a good way of characterizing our model.

The results show a notorious effect: while preferential engagement with prestigious individuals speeds up innovation, an excessively exclusive focus of interactions among them can actually hamper the discovery of new technologies. This inequality highlights the complex dynamics of reputation-driven interactions, finding a balance between the benefits of prestige contacts and the side effects of an excessive focus.

Group overlap drives explosive collective behaviors in dynamical systems

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Recent studies have shown that novel collective behaviors emerge in complex systems due to the presence of group interactions. However, how the collective behavior of a system is influenced by the microscopic organization of its group interactions is not fully understood. In this talk [1], we introduce a way to quantify the overlap among the groups of a system, and we show that real-world systems exhibit different levels of overlap. We then study two types of dynamical processes, namely complex contagion and synchronization, finding that group overlap plays a universal role in determining the collective behavior in a variety of systems. Our results demonstrate that the presence of group interactions alone does not guarantee abrupt transitions. Rather, explosivity and bistability require a microscopic organization of the structure with a low value of group overlap.

Protein phase transitions in neurodegenerative diseases: from basic research to diagnosis

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A number of neurodegenerative diseases, including Alzheimer´s and Parkinson´s disease, are associated to protein amyloid aggregation, a process involving the transition from the functional, soluble state of a particular protein into insoluble amyloid fibrils. While there has been significant progress in understanding certain aspects of the amyloid aggregation process, particularly elongation and spreading of aggregates, we still do not know the details of the early steps of oligomerization. Emerging evidence supports the hypothesis that aberrant protein-driven liquid-liquid phase separation and the transition of the liquid droplets to solid-like structures might be a relevant cellular pathway leading to the formation of amyloid fibrils and neurodegeneration. Our lab is devoted to the shed light into the factors governing protein phase transitions particularly those related to neurodegenerative diseases with the aim of designing novel strategies for the diagnosis of some of these devastating diseases. In this talk, I will summarize some of our recent advances towards these aims.

Dynamic arrest in protein phase separation: the case of tau and alpha synuclein complex coacervation

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Protein phase separation, responsible for the formation of membraneless organelles, has drawn significant attention due to its unique properties, such as viscoelasticity, intracellular homeostasis, metabolic catalysis, and free molecular exchange without a lipid membrane. Protein coacervates are increasingly recognized as key players in human diseases, especially those involving protein aggregation. Intrinsically disordered proteins like tau and alpha-synuclein, linked to Alzheimer's and Parkinson's diseases, respectively, can both aggregate into amyloids and form coacervates under pathological conditions. Remarkably, these proteins undergo electrostatic phase separation when mixed, resulting in coacervates whose viscoelastic properties change over time. Our observations indicate that aging coacervates develop a reinforced polypeptide network, with a dynamical arrest of the proteins, leading to gelation and diminished liquid-like behavior. To better understand and potentially manipulate this phenomenon, we are employing advanced fluorescence spectroscopy and microscopy techniques to track the viscoelastic dynamics of these systems in vitro and in vivo. Our goal is to uncover ways to modulate the mechanical properties of protein coacervates, providing new insights into their biological roles and implications for disease.

Development and characterization of cellular models for studying the formation of molecular condensates in neurodegenerative diseases

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Alpha-synuclein (αS) and tau protein inclusions are key features of neurodegenerative diseases like Parkinson's and Alzheimer's. Co-aggregates of these proteins have been found in the brains of patients with synucleinopathies, yet the molecular mechanisms behind their formation remain unclear. Recent studies indicate that molecular condensates—membraneless organelles formed through liquid-liquid phase separation—play a crucial role in the pathogenesis of these disorders. Our research shows that the interaction between αS and tau is electrostatically driven, leading to the formation of liquid condensates that can mature into gel-like structures or amyloid hetero-aggregates (Nat Commun 13, 4586, 2022).

In this study, we aim to investigate the behavior of these condensates in cellular systems by developing models that mimic phase separation with varying material properties. We utilized two approaches: internalization of preformed condensates and de novo formation within cells. We successfully created distinct cellular models featuring αS and tau condensates, each with unique mechanical properties, ranging from fluid and gel-like to more solidified forms. By studying these models, we hope to gain insights into how the physical properties of αS and tau condensates contribute to neurotoxicity in neurodegenerative diseases.

A family of di-glutamate mucin-degrading enzymes that bridges glycan hydrolases and peptidases

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In this talk, I will present our recent discovery of microbial mucinases—enzymes specifically designed to cleave mucins. Microbes use polysaccharides to protect their surfaces and form biofilms, while metazoans rely on large, O-glycan-rich mucins to shield their epithelial surfaces and maintain a safe distance from microbes. However, in the gut, microbes within the mucus layer feed on host mucins, creating a need for continuous mucus renewal to uphold protection, clearance, and homeostasis.
While we've known about glycopeptidases that can degrade mucins, true mucinases that specifically target intact mucins have remained elusive—until now. I'll discuss how these newly identified microbial mucinases are able to selectively cleave mucins with trimmed glycans by recognizing dense clusters of O-glycans. Structurally, they use a fold and catalytic machinery reminiscent of glycan hydrolases and peptidases, and interestingly, we've found that similar di-glutamate mucinases are also present in eukaryotes. I propose that these enzymes play a role in clearing mucins after O-glycan scavenging, thereby supporting healthy gut–microbiome homeostasis.

Recognizing Tn and STn Epitopes in Protein Context

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Confidential Abstract

Spin glass traveller guide for a Janus journey

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Spin glasses are the paradigm of complex systems. They have been studied during the last 70 years from both experimental and theoretical approaches. Over time, computation has been revealed as a fundamental tool in this research field. And our special purpose computers, *Janus* and *Janus II* [1], located at the BIFI Institute*, have been crucial milestones in the study of spin glasses, spanned simulation times and system sizes never accomplished before.

In this contribution I will briefly explain what spin glasses are for a non expert audience in this field and their relevance not only in the complex system research environment, I will show how our Janus machines work and I will highlight some of the key breakthroughs achieved with them in the spin glass world.

[1] See https://www.janus-computer.com and references there in for details
* *Janus*, nowadays retired, can be seen at the Science Faculty hall at the University of Zaragoza.

Memory in spin glasses: overview of results by the Janus Collaboration

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Spin glasses have long been considered paradigmatic complex system, combining a rich phenomenology with the existence of well-defined theoretical models. Despite this relevance, experimental and theoretical research on spin glasses largely progressed along separate lines for decades. The starkest example of this disconnect is the study of memory and rejuvenation, which remained unassailable by numerical simulations for 20 years despite being the most striking experimental features of spin glasses. In this talk I will review the first reproduction of the memory and rejuvenation effects on the computer, which was made possible by the Janus II special-purpose supercomputer, hosted at the BIFI Institute, and by the insight on the nature of the spin-glass phase obtained in the last 15 years by the Janus Collaboration. The main result of this work is that aging dynamics is ruled by at least three different length scales.

Numerical evidences of a second order phase transition in the six-dimensional Ising spin glass on a field

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The study of spin glasses has been tackled from many different points of view. On the theoretical side, great efforts have been dedicated to studying and classifying the phase transition. Specifically, for the Sherrington-Kirkpatrick mean field model of a spin glass, Parisi's Replica Symmetry Breaking solution[1] provides an exact description of the system.

For the finite-dimensional models, however, we have no exact solution and the standard way to study them is the Wilsonian Renormalization Group[2]. Systems with no external magnetic field have been widely studied, both by theory and by simulations. Nevertheless, the scenario for systems with an external magnetic field is completely different. It is not clear if there is a phase transition to a spin-glass phase at all.

We discuss here[3] the value of the upper critical dimension by means of massive numerical simulations for the six-dimensional spin glasses in the presence of an external field. We simulate the Edwards-Anderson model and study the phase transition through different estimations of the magnetic susceptibility.

We identify a continuous phase transition and we also estimate the critical temperature, significative smaller than the critical temperature of the model with no external magnetic field. We also computed the critical exponents η and ν.

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Insights into functional and structural features of Ferredoxin NADP+ Reductase (FPR) from *Brucella ovis*

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Bacterial flavoproteomes, which comprise all flavin-dependent proteins in an organism, are valuable sources for the identification of antimicrobial targets and industrial biocatalysts. Flavoenzymes also serve as models to study poorly understood processes such as flavin cofactor homeostasis, flavin channeling, and metabolic control via allosteric and cooperative mechanisms.

Our research investigates flavoproteomes of pathogenic microorganisms, including *Brucella ovis*, a causative agent of ovine brucellosis. We are characterizing several of the 78 flavoproteins from this organism identified in a previous study [1].

Here, in particular, we will show a functional and structural approach to the characterization of ferredoxin-NADP$^+$ reductase (FPR), a key enzyme in oxidative stress response in bacteria, supporting oxidoreductive metabolism and potentially regulating reactive oxygen species. Here, we demonstrated that FPR is active with the endogenous [2Fe-2S]Fdx ferredoxin and binds DNA non-specifically, suggesting a potential protective role against oxidative damage. Using serial femtosecond crystallography, we have solved the first room-temperature structures of FPR, revealing increased flexibility at the FAD and C-terminal tail. A modeling study predicts the FPR:Fdx:NADP$^+$/H ternary interaction, offering insights into the simultaneous binding of the Fdx redox partner and the NADPH coenzyme. These findings enhance our understanding of the role of FPR in *B. ovis* physiology as well as of its molecular mechanisms of action from a structural approach.

[1] M. Minjárez-Sáenz, M. Martínez-Júlvez, I. Yruela, M. Medina, Mining the Flavoproteome of Brucella ovis, the Brucellosis Causing Agent in Ovis aries, Microbiol Spectr 10(2) (2022) e0229421.

Two novel Bacterial Aryl-Alcohol Oxidases: Expanding the Toolbox for Greener Synthesis

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The development of novel synthetic tools for safer and more sustainable chemical production is a key goal in synthetic chemistry. Here, we report the discovery, characterization, and synthetic utility of two novel bacterial aryl-alcohol oxidases, *Sh*AAO and *Sd*AAO (1). These enzymes efficiently oxidize a broad range of aliphatic and aromatic alcohols, achieving catalytic efficiencies of up to 4970 min^{-1} mM^{-1}. Both enzymes exhibit moderate thermostability, exhibiting thermal melting temperatures of 50.9 °C and 48.6 °C for *Sh*AAO and *Sd*AAO, respectively. Structural analysis revealed an unusually wide-open active-site entrance, distinct from traditional fungal AAOs, which may correlate with enhanced substrate versatility and catalytic performance.
Preparative-scale reactions confirmed their robustness under high substrate loadings, achieving total turnover numbers >38000. Furthermore, their production as soluble and active recombinant proteins facilitate their application in cell-free systems for scalable carbonyl compound synthesis. These findings position bacterial AAOs as promising tools for greener industrial processes, offering improved efficiency and versatility compared to traditional biocatalysts.

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Non-equivalent active sites in homodimeric flavoenzymes

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Homodimeric flavoenzymes are composed of two identical subunits, each containing a flavin cofactor, and both come together to form each of the two active sites within the dimer. Despite being identical, in some cases the two active sites appear to work independently or non-cooperatively during catalysis, showing non-equivalent behaviour. Here, we will focus on the kinetic characterization of two homodimeric flavoenzymes, NAD(P)H:quinone oxidoreductase 1 (NQO1) [1] and pyridox(am)ine 5'-phosphate oxidase (PNPOx) [2], showing that they behave non-equivalenty regarding catalysis at each of their flavin active sites. The molecular basis of such behaviour is still far to be understood, but it might involve conformational changes, substrate/product binding or be induced by the redox state of the flavin cofactor. Nonetheless, investigation into the kinetics and molecular mechanisms underlying the dynamics of these systems helps us to understand how protein dynamics influence enzyme kinetics or substrate specificity, and how it provides additional layers of regulation of metabolic fluxes within cells. Such knowledge can offer valuable insights for the use of these flavoenzymes in drug development, disease intervention strategies or biocatalyst.

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2. Rivero, M., Boneta, S., Novo, N., Velázquez-Campoy, A., Polo, V., & Medina, M. (2023). Riboflavin kinase and pyridoxine 5'-phosphate oxidase complex formation envisages transient interactions for FMN cofactor delivery. Frontiers in Molecular Biosciences, 10.

Posters

No.	Title	Author(s)
1	Building the digital presence of BIFI researchers: Connecting science with society	Eva María Navarro Pena
2	Enhancing MUMAX3 software for Magnon-Cavity Interactions	Sergio Martínez-Losa *et al.*
3	A new drawing tool for Qibo circuits	Sergio Martínez-Losa
4	Characterization of ABHD6: an enzyme involved in AMPA Glutamate receptor assembly	Ribón Fuster *et al.*
5	Neuroblastoma molecular therapy based on NLS n-Myc	Gema Merino Loma *et al.*
6	Characterization of Transcriptomic Changes in *Bacteroides fragilis* Induced by Antibacterial Compounds	Hajar Jeblaoui *et al.*
7	Molecular insights on the role of AIF dimerization in its interaction with CHCHD4 in the mitochondria	Olga Soriano *et al.*
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21	Identification of a histidine and glutamine transporter in *Streptococcus suis*	Carla García *et al.*
22	Hierarchization and critical mass for survival due to pathogen spread in ant societies	Francesca Dilisante *et al.*
23	The interrelationship between epidemic spreading and game-theoretic modelling of collective behavior	Junfeng Fan *et al.*
24	Detection of fungal Epichloë endophytes in model Brachypodium grasses	Diana Calderón *et al.*
25	Genome assembling of polyploid genomes of perennial Brachypodium model grasses	Wenjie Mu *et al.*
26	Enhancement of mRNA translation efficiency through 5’ UTR engineering via Kozak’s motif additions	Irene Blasco-Machín *et al.*
27	Evaluating the Effects of MTBVAC on Trained Immunity in a Mouse Sepsis Model: Insights from Single-Cell Transcriptomics	Noelia Ferrer-Luzón *et al.*
28	Dynamic arrest in protein phase separation: the case of tau and alpha synuclein complex coacervation	David Polanco *et. al.*
29	Development and characterization of cellular models for studying the formation of molecular condensates in neurodegenerative diseases	Laura Asín *et. al.*

Poster 1

Building the digital presence of BIFI researchers: Connecting science with society

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In today's digital age, it is crucial for researchers to establish a robust online presence and draw attention to their investigations and research outcomes. The aim of this project is to draw attention to the work of the BIFI Institute while simultaneously enhancing its visibility across digital media. This will foster greater engagement with both expert and public audiences. The project has involved the creation and management of an individual profile for each BIFI member, with relevant information about the researcher, and their research outreach and societal impact. The profiles have been designed taking into account the corporate image of the Institute and they have been formatted to ensure consistency in both language and rhetoric, as well as in multimodal content. Furthermore, to enhance visibility and reach, each researcher profile will be presented alongside an appealing infographic. The content and language of the infographic have been adapted to make scientific content accessible to non-expert and diverse audiences, particularly internet audiences (Wickman and Fitzgerald, 2019). Helping society to understand what researchers do and how it benefits everyone breaks down barriers and contributes to the appreciation of BIFI's research activities and work.

Poster 2

Enhancing MUMAX3 software for Magnon-Cavity Interactions

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MUMAX3 is an open-source software which is GPU-accelerated and it is used to perform micromagnetic simulations, it was developed and maintained at the DyNaMat group at Ghent University (The design and verification of MuMax3 [1]).

We implement a new feature that extends the current capabilities of MUMAX3 by including the effects of coupling a given magnetic material to an electromagnetic cavity. This will enable the study of analytically-intractable models in the field of magnetic cavity QED materials.

To implement these modifications, a fork of the MUMAX3 code was created. The Landau–Lifshitz–Gilbert (LLG) equation that MUMAX3 solves is understood as a phenomenological analogue of the Heisenberg equations of motion of the spin degrees of freedom of the magnetic material. These are extended to include the coupling to the cavity and then the equation of motion of the cavity is integrated out, giving rise to an effective term for the spins. The effect of the cavity is thus included in MUMAX3 as a new contribution to the effective field given by the cavity's zero-point field times a memory factor.

As a benchmark, we simulate the dynamics of the Dicke model, which serves as an analytically-solvable toy model of a paramagnetic material interacting with a single-mode cavity (Photon Condensation and Enhanced Magnetism in Cavity QED [2]). Preliminary results show promising signs, with the observation of two resonant peaks at the polaritonic frequencies of the Dicke model.

In addition, we simulate the coupling between different shaped ferromagnets and cavity photons yielding results comparable with recent experiments.

[1] A. Vansteenkiste et al., AIP. Adv. 4 (2014) 107133
[2] J. Román-Roche, F. Luis, D. Zueco, Phy. Rev. Let. 127 (2021) 167201

Poster 3

A new drawing tool for Qibo circuits

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Qibo framework, which is a well know library for Quantum Computation, had (until now) a lack of drawing tools to display quantum circuits. This poster shows a new drawing class based on Matplotlib which is highly customisable and it is now part of Qibo from version 0.12.2 onwards Also, as the new drawing tool is part of Qibo anybody can enhance its functions and expand the drawing tool capabilities.
This new drawing tool born as an answer to the feedback given by the Qibo users which made use of BSC Quantum Computer. The current circuit drawer has gate symbols that can confuse the user and this can be solved with a new drawing tool.

Poster 4

Characterization of ABHD6: an enzyme involved in AMPA Glutamate receptor assembly

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α/β hydrolase domain-containing protein 6 (ABHD6) is a membrane lipase that hydrolyzes 2-arachidonoylglycerol (2-AG) and plays a crucial role in the regulation of the endocannabinoid system. It modulates energy metabolism, release of neurotransmitters and biogenesis of AMPA-type glutamate receptors, working alongside other proteins such as CPT1c and FRRS1L.

Here we have characterized ABHD6 activity and its modulation by its protein partners GluA4 (an AMPA receptor subunit) and CPT1c. We cloned and purified different ABHD6 variants and optimized an enzymatic activity assay protocol. We evaluated the activity of soluble variants (produced in *Escherichia coli*), full-length variants (produced in mammalian cells) and membrane extracts from mammalian cells. Although the soluble variants were active, they exhibited substrate inhibition and lower enzymatic activity compared to the full-length protein isolated in detergents, suggesting that the transmembrane region is crucial for catalysis. Strikingly, activity assays in membrane extracts expressing ABHD6 and AMPAR subunit GluA4, demonstrated that GluA4 may reduce ABHD6 activity. However, CPT1c does seem to modulate ABHD6 activity, in contrast with previous reports that suggest that CPT1c inhibits ABHD6 activity in the presence of Malonyl-CoA. To confirm these results, we need to analyze the activity of pure complexes. We are producing ABHD6:CPT1C and ABHD6:GluA4 at high protein yields, which will allow us to confirm the regulatory role of CPT1c and GluA4 subunits.

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Poster 5

Neuroblastoma molecular therapy based on NLS n-Myc

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Neuroblastoma is one of the most common childhood cancers, characterized by a poor prognosis and high clinical heterogeneity. Despite the advances in treatment, side effects and recurrent cases persist. This underscores the need to develop more specific targeted therapies.

Neuroblastoma cells overexpress and heavily rely on n-Myc protein, a member of the MYC family. These proteins act as transcription factors, regulating genes involved in cell proliferation, death and play a critical role in tumor development. Synthesized in the cytosol, these proteins must translocate to the nucleus via their specific nuclear localization sequences (NLS) to function. However, designing inhibitors for MYC proteins is challenging due to their structural similarities, intrinsically disordered domains, lack of hydrophobic binding pockets, and complex interactions with other proteins and DNA.

This study proposes targeting n-Myc's NLS to block its nuclear translocation. First, small-molecule inhibitors will be identified through high-throughput screening based on the thermal shift of NLS sequences. These inhibitors will then be biophysically characterized using calorimetric and spectroscopic techniques. Finally, their therapeutic potential will be evaluated using cellular and animal models. The goal is to develop molecular therapies that enhance treatment efficacy while minimizing side effects for neuroblastoma patients.

Poster 6

Characterization of Transcriptomic Changes in *Bacteroides fragilis* Induced by Antibacterial Compounds

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Bacteroides fragilis is considered the most virulent species and the most common clinical isolate of Bacteroides. *B. fragilis* is a pathogen divided into enterotoxigenic B. fragilis (ETBF) and non-enterotoxigenic *B. fragilis*. The pathogenicity of ETBF is attributed to *B. fragilis* toxin (BFT), a zinc-dependent metalloprotease toxin. ETBF can induce clinical pathologies such as acute diarrhea, bacteremia, inflammatory bowel disease, and colorectal cancer. The objective of this study is to analyze variations in the transcriptome of *B. fragilis* after treatment with the compounds MOA4, MOA9, and MOA10.

MOA4, MOA9, and MOA10 showed promising results for advancement into further assays to analyze their potential as antibacterial compounds. For these reasons, the in vitro biological effect of these compounds was characterized on *B. fragilis* cultures. MIC90 determination and transcriptomic analyses demonstrated that MOA4, MOA9, and MOA10 exerted antimicrobial effects on both enterotoxigenic and non-toxigenic strains of *B. fragilis*.

Poster 7

Molecular insights on the role of AIF dimerization in its interaction with CHCHD4 in the mitochondria

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The human apoptosis-inducing factor (hAIF) is a mitochondrial flavoenzyme with a dual role in cell survival and programmed cell death(1). In the mitochondrial intermembrane space (IMS), hAIF exists in a monomer-dimer equilibrium, which is shifted towards the dimer by NADH oxidation, stabilization of a long-life $FADH^-/NAD^-$ charge transfer complex (CTC), and conformational remodeling(2). hAIF also participates in the mitochondrial disulfide relay system by promoting the import and proper localization of the chaperone CHCHD4 (coiled-coil-helix-coiled-coil-helix-domain containing 4), forming a long-lived stable complex(3,4). This interaction may be crucial for the efficient functioning of CHCHD4 with its specific substrates.

This study aims to decipher the role of hAIF dimerization in its interaction with CHCHD4, as well as its influence on hAIF redox properties, stability, and conformation. To this end, we utilized the E413A/R422A/R430A variant, designed to prevent dimerization in the presence of NADH. For that, we analyzed *in vivo* and *in vitro* effects on AIF:CHCHD4 interactions and AIF redox properties. Furthermore, we explored the potential of a peptide derived from the N-terminal domain of CHCHD4 as a therapeutic candidate to restore *in vitro* the function of the pathogenic R422Q AIF variant, which displays defective dimerization.

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[2] Ferreira P, Villanueva R, Martínez-Júlvez M, Herguedas B, Marcuello C, Fernandez-Silva P, et al. Structural insights into the coenzyme mediated monomer-dimer transition of the pro-apoptotic apoptosis inducing factor. Biochemistry. 2014;53(25):4204-15. doi: 10.1021/bi500343r. PubMed PMID: 24914854.
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Poster 8

Expression of Cytochrome P450_1AB from the marine hydrocarbon-degrading bacterium *Alcanivorax borkumensis*

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Cytochrome P450 constitutes a superfamily of enzymes present across all domains of life including bacteria, archaea and eukaryotes, and even viruses. These hemeproteins catalyze a wide range of reactions involving substrates and products, such as dealkylations, dehalogenations, epoxidations, and sulphoxidations. These reactions play essential roles in biological processes like detoxification, drug activation and biosynthesis of fat-soluble vitamins. Understanding these processes has significant implications for biotechnology, enabling advances in pharmacology, veterinary, medicine or pest control, among other fields.

Here we focus our efforts on the expression and purification of a cytochrome P450 from the marine bacterium *Alcanivorax borkumensis*, with projection to bioremediation. *A. borkumensis* is naturally highly specialized in alkane degradation, suggesting that its cytochromes play a role in the hydroxylation of these compounds. We present a strategy to express one of these cytochromes, CYP450_1AB (ABO_0201), through the coexpression of a protein regulated by the same promoter under slow growth and production conditions. Specifically, coexpression was performed with the ferredoxine (fdx, ABO_0200) to provide adequate redox support, while ensuring proper supplementation for the synthesis of the heme group and the iron-sulfur cluster.

Poster 9

A potential alkene reductase in *Brucella ovis*: spectroscopic, kinetic and structural characterization

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Brucella ovis is a gram-negative bacterium responsible for a reproductive disease affecting all breeds of sheep. Among its flavoproteins, there is a predicted alkene reductase (BoAKR), which holds significant potential as a biocatalyst.

We have established solid protocols for BoAKR overexpression in *E. coli* and its purification. Spectroscopic characterization revealed that BoAKR has a redox active FMN as a cofactor, which can get reduced through photoreduction. Furthermore, its redox potential has been determined by both the xanthine oxidase method and cyclic voltammetry.

Additionally, fluorescence and circular dichroism spectroscopies have been used to gain further insight into the protein folding, as well as about the protein thermal stability. BoAKR was also successfully crystallized, and its structure was solved.

Furthermore, BoAKR has shown the capacity to accept hydride from NAD(P)H, being NADH more efficient as a hydride donor. Catalytic activity was observed with five out of the seventeen compounds tested as potential hydride acceptors. All of them have a C=C double bond conjugated with a carbonyl group. Reactivity is observed both in aromatic and aliphatic compounds.

Kinetics and dissociation constant were calculated for four of these six active compounds. Furthermore, their effect on the spectroscopic properties and on the thermal stability of BoAKR were also evaluated.

Poster 10

Biomarker-Based Non-Invasive Molecular Diagnostic Method for Early Detection of Parkinson's Disease Using Flow Cytometry

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Parkinson's disease (PD) is one of the most prevalent age-related neurodegenerative disorders, affecting 2-3% of individuals over 65. To date, PD diagnosis relies on clinical evaluation, as no molecular biomarker-based methods exist. This limitation often results in delays in diagnosis, administration of treatment and misclassification with other parkinsonian syndromes. A hallmark of PD is the presence of aggregated alpha-synuclein (aS) in dopaminergic neurons of the substantia nigra pars compacta, forming Lewy bodies that drive neurodegeneration and motor symptoms among others.

During aggregation, various aS species emerge and each contributes differently to neurotoxicity and disease progression. These include physiological monomers, early benign oligomers, highly structured toxic oligomers with β-sheet-rich conformations, and ultimately fibrils. Toxic oligomers are thought to play the most significant role in PD pathogenesis [1]. In this study we propose a novel diagnostic method to detect these toxic aggregated aS species in easily accessible biological fluids (blood and nasal swabs). This approach uses paramagnetic beads functionalized with a nanobody specific to aggregated aS, combined with a fluorescently labeled secondary nanobody to quantify toxic aggregates via flow cytometry. This sensitive methodology enables early detection of PD, facilitating routine diagnostics and effective therapeutic interventions in clinical institutions.

[1] Cascella, R., Chen, S.W., Bigi, A. et al. The release of toxic oligomers from α-synuclein fibrils induces dysfunction in neuronal cells. Nat Commun 12, 1814 (2021).

Poster 11

Understanding phase separation driven by polyubiquitin chains in autophagy

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Cellular proteostasis relies on a network of protein quality control systems, including molecular chaperones, ubiquitination machinery, the proteasome, and the autophagy-lysosome pathway, to ensure proper protein synthesis, folding, and degradation. Particularly in autophagy, a membrane organelle termed the autophagosome engulfs cytoplasmatic material and subsequently fuses with the lysosome to degrade its content. Recent studies highlight liquid-liquid phase separation (LLPS) as a key mechanism in this pathway, where essential components of the autophagy machinery assemble into biomolecular condensates. Growing evidence suggests that these membraneless compartments serve as substrates for autophagy and are essential for autophagosome formation. The autophagy receptor p62 is a major driver of this process, as it facilitates the phase separation of ubiquitylated proteins into condensates. However, the molecular mechanisms by which these condensates recruit and organize the autophagy machinery remain poorly understood. Our recent findings focus on the role of different polyubiquitin chains in the formation and maturation of these biomolecular condensates involved in autophagy. Expanding the knowledge of the ability of these specific proteins to promote LLPS is essential to better understand the autophagy regulation, a fundamental pathway for maintaining cellular homeostasis.

Poster 12

From soluble to pathological: molecular mechanisms of α-synuclein nucleation into amyloid aggregates

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Misfolding of α-Synuclein (α-Syn) into amyloid aggregates is a hallmark of a group of neurodegenerative disorders known as synucleinopathies, including Parkinson's disease (PD). α-Syn is an intrinsically disordered protein that remains soluble under physiological conditions. Primary nucleation is the functional event that initiates aggregation, prompting the conversion of soluble monomers into small misfolded clusters called nuclei, which act as seeds for further aggregation of additional monomers into larger amyloid structures, which are the pathological hallmark of disease. In vitro, hydrophobic/hydrophilic interfaces have been shown to catalyse this process, but their exact role remains elusive. While interfaces may concentrate the protein to reach a critical aggregation threshold, our findings suggest that aggregation does not occur under quiescent conditions, even in the presence of such interfaces. We propose that proper protein conformation and orientation at the interface are also crucial for nucleation. To explore this, we have generated several α-Syn variants with specific truncations to study the interaction of the different protein domains with the interface. This project aims to uncover the molecular mechanisms underlying α-Syn primary nucleation, providing insights into the first pathological events that trigger the onset of synucleopathies, paving the way for the development of effective and more precise therapeutic approaches for these devastating diseases.

Poster 13

MOLECULAR INSIGHTS INTO GPR37 SELF-ACTIVATION MECHANISM: FROM BRAIN NECROPSIES TO CRYO-EM STRUCTURE

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GPR37 is an orphan G protein-coupled receptor which has gained attention due to its implication in the pathogenesis of Parkinson's disease (PD). Interestingly, the N-terminus of the receptor (ecto-GPR37) is subject to metalloproteinase-mediated proteolysis, which leads to several receptor forms at the cell membrane. In addition, PD patients have increased amounts of ecto-GPR37 in the cerebrospinal fluid, thus showing an increased expression of GPR37 cleaved forms in the brain. Here, we aimed at investigating the impact of ecto-GPR37 on receptor's function. To this end, we generated two GPR37 N-terminally truncated constructs ($GPR37^{\Delta 1\text{-}171}$ and $GPR37^{\Delta 1\text{-}219}$) based on the receptor forms found in brain necropsies. GPR37 wild-type and, particularly, $GPR37^{\Delta 1\text{-}171}$ show high constitutive coupling to $G\alpha_O$ and the arrestin machinery, an effect lost when the receptor is truncated beyond aminoacid 219. To unravel the molecular mechanisms underlying GPR37 constitutive activity, we sought to determine the cryo-electron microscopy structure of $GPR37^{\Delta 1\text{-}171}$-$G\alpha_O$ signalling complexes. The structure reveals that the second extracellular loop is buried inside the receptor transmembrane domain, possibly contributing to constitutive activity. Overall, the first structure of GPR37 to date may enable the identification of endogenous ligands, and guide drug discovery efforts that target the receptor.

Poster 14

Targeting the Neuronal Calcium Sensor 1 to modulate dopamine D2 receptor function: A structure-based drug repurposing approach

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The Neuronal Calcium Sensor 1 (NCS-1) is a key calcium-signaling protein that integrates Ca^{2+} and G-protein pathways by selectively interacting with partners such as the molecular chaperone Ric-8A and the dopamine D2 receptor (D2R), both implicated in neurodevelopmental disorders and neurodegeneration. Previous studies demonstrated that NCS-1 is a druggable target, allowing therapeutic modulation of its interaction with Ric-8A while elucidating its regulatory mechanism at the atomic level. However, the molecular details of NCS-1's role in modulating D2R activity remain unclear.

To address this, a structure-based drug repurposing strategy was employed using the crystallographic structure of the NCS-1/D2R complex. Virtual screening of FDA-approved molecules identified promising candidates, which were experimentally validated for their affinity and protein-protein interaction modulatory activity in vitro and in vivo. Co-crystallization of NCS-1 with five ligands revealed diverse mechanisms of action: FDA-02 emerged as the first competitive inhibitor of the NCS-1/D2R complex, while FDA-16 and FDA-18 showed dual modulatory activity, stabilizing NCS-1/Ric-8A and inhibiting NCS-1/D2R. FDA-10 and FDA-12 inhibited both PPIs.

These molecules provide therapeutic potential and serve as biomedical tools to understand how NCS-1 regulates the activity of the dopamine D2 receptor. Functional assays suggest that NCS-1 regulates D2R trafficking enhances G-protein signaling, and recruits β-arrestin.

Poster 15

Susceptibility to general anesthetics in cell cultures with OXPHOS deficiency

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General anesthetics have produced adverse effects in certain patients with diseases of the oxidative phosphorylation system (OXPHOS). Mutations in respiratory complex I (CI) genes that reduce OXPHOS function could increase susceptibility to general anesthetics such as propofol and sevoflurane.

In this study, the effects of exposure to propofol and sevoflurane were analyzed using several doses, including those within the range typically found in patients' plasma, across different cell lines. Cybrids, or transmitochondrial cell lines that share a common nucleus but with their own distinct mitochondrial DNA (mtDNA), were compared. Specifically, a control cybrid, a cybrid with a deletion in the mtDNA (derived from a patient with Kearns-Sayre syndrome), and a cybrid with an uncommon complex I mutation were analyzed.

The growth rates of the cell in galactose based media, which forces cells to rely on the OXPHOS system for energy production, were compared to those in glucose-based media. These growth rates provided an indication of the severity of respiratory deficiency. Three doses of propofol and two doses of sevoflurane were tested in the media with different energy sources. Interestingly, differences in sensibility to the effects of the anestetics were observed among the analyzed cybrids.

Poster 16

Effect of hyperthermia on the function and organization of the OXPHOS system in tumor cells

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In the fight against cancer, new therapeutic strategies need to be developed, with hyperthermia emerging as a promising approach. This strategy consists of increasing the temperature of the tumor tissue, thereby inducing cell death or sensitizing cancer cells to other therapies. This study investigates hyperthermia from the point of view of mitochondria. We consider targeting mitochondria a promising strategy because these organelles play a central and multifunctional role in tumor progression, and in this specific case, because they represent an important source of heat via the OXPHOS system. In this work, we have evaluated how hyperthermia affects cell viability, cellular stability, the organization and activity of the OXPHOS system and gene expression in the MDA-MB-468 breast cancer cell model. Our results demonstrate that hyperthermic treatment, especially at temperatures above 45 °C, leads to a significant reduction in cell viability, compromises mitochondrial function, and affects gene expression. This study contributes to figure out the molecular mechanisms by which hyperthermia induces cancer cell death and raises new questions for future investigations.

Poster 17

Interaction of mutations in proteins of the mtDNA replication machinery

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Mitochondria are organelles responsible for providing the majority of energy for the cell in the form of ATP. They have their own genome, mitochondrial DNA (mtDNA), which is replicated thanks to proteins coded in nuclear DNA. The main ones are DNA polymerase γ, mitochondrial helicase (TWINKLE), mitochondrial single-strand DNA binding proteins (mtSSB), and mitochondrial RNA polymerase (POLRMT). Mutations affecting these proteins may cause depletion in mtDNA levels or an increase in deletions and mutations. Eventually, this can damage the oxidative phosphorylation machinery (OXPHOS) and, if defects cannot be compensated, cellular energy levels may be compromised, causing mitochondrial disease. Tissues with high energy demands, such as the brain, muscle, or liver, are especially affected. In this work, we have correlated the symptoms of a girl with Alpers-Huttenlocher syndrome with the effect of two heterozygous mutations in POLG and TWNK. Using fibroblast models generated through overexpression and gene editing, we analyzed these models and concluded that overexpression of the POLG variant causes mitochondrial dysfunction, which is more pronounced in cells with the TWNK variant in heterozygosity.

Poster 18

All0345: a novel transcriptional regulator of the FurC (PerR) regulatory network involved in nitrogen metabolism in *Anabaena* sp. PCC 7120

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Cyanobacteria are photosynthetic prokaryotic microorganisms with great ecological and economic importance as they can fix atmospheric nitrogen and CO_2.
The FUR (Ferric Uptake Regulator) family in *Anabaena* sp. PCC 7120 consists of three paralogs: FurA (Fur), FurB (Zur) and FurC (PerR), considered global regulators in this cyanobacterium where they play key roles in nitrogen metabolism. Recently, FUR proteins have been found to constitute transcriptional regulatory networks endowed with the ability to control different cellular processes indirectly through other transcriptional regulators.
All0345, annotated as transcriptional regulator, is a member of the FurC regulatory network. Although its regulon is unknown, some evidence point to its relationship with genes involved in nitrogen metabolism. Specifically, *all0345* shows differential transcription between the wild-type strain and a FurC-overexpressing variant only under nitrogen deficiency.
In the present work, we have established optimal conditions for All0345 binding to DNA using electrophoretic mobility shift assays (EMSA). All0345 implication in the control of genes related to nitrogen metabolism, has been confirmed by EMSA and qRT-PCR. Moreover, the ability of an *all0345*-deletion mutant to develop heterocysts has been analyzed.
Our results point to the participation of All0345 in the regulation of nitrogen metabolism and heterocyst development in *Anabaena* sp. PCC 7120.

Poster 19

Development of a whole-cell biosensor for lindane detection

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Lindane is a broad-spectrum organochlorine insecticide whose production and indiscriminate use have caused severe global environmental issues. It is produced by isolating the active γ-HCH isomer through an inefficient process that generates large amounts of toxic and bioaccumulative persistent organic pollutants (POPs). Inquinosa, a lindane factory established in Sabiñánigo (Aragón), operated for nearly 20 years without environmental safeguards, dumping massive amounts of organochlorine waste into the Sardás and Bailín landfills, near the Gállego River. Leachates from these sites have contaminated inland waters with DNAPL, an immiscible dense phase of high toxicity and difficult to manage. Groundwater and surface water contamination is currently monitored using sensitive but complex and costly chromatographic methods.

As a more practical alternative, bioanalytical techniques are proposed for *in situ* monitoring. Existing biosensors for lindane, based on *lin* pathway enzymes in *Sphingomonas*, face limitations such as low specificity and sensitivity. This study presents a whole-cell biosensor for lindane detection, based on the fusion of the green fluorescent protein (GFP) to the promoter of the putative *linC* gene from *Anabaena sp.* PCC 7120, inducible by HCH. A triparental conjugation protocol was optimized for DNA transformation in *Anabaena*, along with a cryopreservation method to improve the cyanobacteria's long-term viability.

Poster 20

Biofilm formation and exopolysaccharide synthesis in cyanobacterium *Anabaena* sp. PCC7120: novel insights into the genes involved and their regulation

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Bacterial biofilms are microbial communities that grow attached to a surface, often in response to stresses, embedded in a complex extracellular matrix with a relevant exopolysaccharide (EPS) content. Photosynthetic microorganisms, such as cyanobacteria, are essential components of biofilms in light-exposed environments, playing critical ecological roles. Additionally, the unique nature of cyanobacterial EPS, rich in negatively charged groups, makes them highly suitable for applications such as chelation of positively-charged contaminants, among others.

Despite their relevance, regulation of cyanobacterial biofilm formation and exopolysaccharide synthesis isn't well understood. In this work, we identified 183 novel genes associated with EPS biosynthesis and biofilm formation in model cyanobacterium *Anabaena* sp. PCC7120, based on homology to proteins known to be involved in these processes in different bacteria. Furthermore, we describe the regulation of a vast amount of these genes by FUR proteins, key transcriptional regulators in the response to numerous stresses, both *in vitro* through bioinformatic identification of FUR-binding boxes in their promoter sequences and protein-DNA binding evaluation by electrophoretic mobility shift assays, and *in vivo* by Real Time RT-PCR analysis of their differential expression in FUR-deregulation strains compared to the wild-type. These findings link the control of biofilm formation in *Anabaena* to different environmental cues.

Poster 21

Identification of a histidine and glutamine transporter in *Streptococcus suis*

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Streptococcus suis is a Gram-positive bacterium and a relevant pathogen for pigs and humans. The objective of this study was to characterize a putative lipoprotein (ShbP), presumably functioning as a substrate-binding protein of an ABC transporter involved in amino acid uptake. Genetic comparisons within public genomes revealed a high conservation of this transporter in strains of *S. suis* and across different *Streptococcus* species. A mutant derivative of *shbP* in *S. suis* reference strain P1/7 showed a reduced ability to grow in chemically defined medium with restricted concentrations of histidine and glutamine. Western blotting assays, using a specific antibody against ShbP, revealed an overexpression of ShbP approximately two-fold higher when the bacterium grew under low histidine conditions but not under glutamine restriction. Isothermal titration calorimetry assays demonstrated that ShbP binds histidine (K_d=0.17 µM) and glutamine (K_d=3.5 µM). In silico docking experiments identified five (Gly107, Ser109, Arg114, Ser157 and Asp202) and six (Asn106, Gly107, Ser109, Arg114, Ser157 and Asp202) amino acids that may provide interaction with histidine and glutamine, respectively, through polar or hydrogen bonds. In summary, this study identified, for the first time, a substrate-binding protein that is part of a transporter for histidine and glutamine in *S. suis*.

Poster 22

Hierarchization and critical mass for survival due to pathogen spread in ant societies

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Social insect colonies, such as ant societies, exhibit striking parallels to the immune responses of individual metazoans when faced with pathogens. These colonies display collective disease protection beyond individual-level defenses, termed social immunity. At low pathogen loads, the colony prioritizes protecting all members, with ants performing sanitary care behaviors towards infected nestmates. However, at higher loads, the strategy shifts: infected ants may be sacrificed to ensure the colony's survival. This change, termed the kill-care switch, mirrors the sacrifice of somatic cells in animals to protect healthy tissue.

Focusing on fungal pathogens, this poster will introduce a model capturing the microscopic mechanisms underlying pathogen propagation and sanitary care behaviors in ant colonies. First, the model is analytically characterized for the simplest scenario: an infected ant cared for by nestmates with a non-infectious pathogen. Afterwards, for pathogens with varying infectivity, we determine the critical mass of ants required to contain outbreaks. Finally, to round off the poster, we show how sanitary care behaviors induce hierarchical structures in social networks, enabling the isolation and protection of critical members, such as the queen.

All in all, we believe these insights have broader implications for epidemiology, as ant societies can provide controlled systems to study disease dynamics, overcoming the limitations of most outbreak-focused data.

Poster 23

The interrelationship between epidemic spreading and game-theoretic modelling of collective behavioral changes on multiplex networks

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Human behavior plays a critical role in controlling infectious disease outbreaks by influencing epidemic dynamics. However, this relationship is often overlooked in epidemic studies. To explore the interplay between disease spread and collective behavior, we model individual decision-making using bounded rationality. Key factors influencing decisions include risk perception (awareness of infection or preventive measures), government interventions, and the cost of self-protection. As a modeling framework, we chose to integrate the susceptible-infectious-susceptible model with game-theoretic behavioral dynamics.

Our results show periodic oscillations in epidemic and behavioral coevolution. As more individuals adopt preventive actions or become infected, awareness increases, prompting others to act. However, widespread prevention reduces infections, lowering the perceived need for action and leading to a resurgence of cases. If preventive measures are highly effective, fewer people adopt them, paradoxically increasing infections.

These dynamics explain recurrent outbreaks and highlight the importance of balanced policy interventions.

Poster 24

Detection of fungal Epichloë endophytes in model Brachypodium grasses

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The current plant biodiversity of the planet is the result of symbiotic interactions between plants and fungi that act as a spatiotemporal evolutionary unit: the holobiont. The capacity for evolutionary and ecological adaptation of wild plant species and the productivity of cultivated varieties have been related to this type of symbiotic interactions. Grasses form the botanical family of greatest ecological and economic importance worldwide, which makes them a system of interest for studying adaptation mechanisms to environmental stresses and biotic interactions and for their use and commercial exploitation. Perennial grass species of the model genus Brachypodium establish symbiosis with fungi of the genus Epichloë, which confers benefits to the holobiont, such as the production of herbivore-deterring alkaloids and greater tolerance to various abiotic stresses. In this study we are analyzing the presence and characteristics of Epichloë species and races in species of the genus Brachypodium. We have started screening eight perennial species (Brachypodium phoenicoides; B. boissieri; B. pinnatum; B. retusum; B. rupestre; B. sylvaticum; B. mexicanum) transplanted from the field to the greenhouse. The plant species with the highest presence of the endophyte is B. sylvaticum infected by Epichloë sylvatica. The analysis and identification of the symbiont in the rest of the species is being carried out.

Poster 25

Genome assembling of polyploid genomes of perennial Brachypodium model grasses

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Polyploidy is a major driver of plant diversification, and understanding its genetic consequences and mechanism is crucial for exploring plant evolution. In the model plant *Brachypodium*, recurrent polyploidy events have been reported in both annual and perennial species. However, the lack of genomic resources has hindered further studies on polyploid perennial *Brachypodium* speciation. In this study, we present chromosome-level assemblies for the perennial species *B. rupestre* (allotetraploid), *B. phoenicoides* (allotetraploid), and the *B. phoenicoides*-6x (allo-autohexaploid), based on PacBio HiFi sequencing and chromosome conformation capture data. All three species have high levels of heterozygosity and complex polyploid genomic backgrounds, which challenge genome assembling. Using sequence homology with closely related diploid reference genomes and chromatin interactions information, we manually curated the assemblies to remove redundant sequences caused by high heterozygosity between haplotypes and corrected imbalanced haplotype phasing. The final genome assemblies of *B. rupestre*-4x, *B. phoenicoides*-4x, and *B. phoenicoides*-6x comprise complete E2 and G subgenomes, with total assembly sizes of 663.38 Mb, 607.84 Mb, and 1251.20 Mb, respectively, and contig N50 values of 29.31 Mb, 22.59 Mb, and 18.26 Mb. These genomic resources provide a valuable foundation for further research on perennial *Brachypodium* species and their polyploid evolution.

Poster 26

Enhancement of mRNA translation efficiency through 5’ UTR engineering via Kozak’s motif additions

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In recent years, mRNA-based therapeutics, including vaccines and gene therapies, have revolutionized clinical practice. However, there remains significant room for improvement to enhance translation efficiency. Modifying the 5’ untranslated region (5’-UTR) is one of the strategies that has garnered significant attention due to its crucial role in translation initiation (1-3). A key regulatory element within the 5’-UTR is the Kozak sequence (4, 5), a highly conserved consensus sequence in vertebrates positioned upstream of the ATG start codon. This sequence is critical for efficient ribosomal scanning and initiation of translation. In this study, we hypothesized that introducing tandem Kozak sequences upstream of the start codon could further enhance translation efficiency. To test this hypothesis, we engineered mRNAs with varying numbers of Kozak motifs in the 5’-UTRs of the APOA2 and HBB genes. These constructs were evaluated for translation efficiency in HeLa and HEK293T cells as well as in vivo using murine models. Among the tested designs, mRNAs containing three tandem Kozak motifs (3*k) consistently exhibited the highest levels of luciferase expression, outperforming both native 5’-UTRs and those used in the Spikevax vaccine. These findings underscore the potential of tandem Kozak motifs to enhance translation efficiency, offering a promising approach for optimizing protein production.

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Poster 27

Evaluating the Effects of MTBVAC on Trained Immunity in a Mouse Sepsis Model: Insights from Single-Cell Transcriptomics

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Trained immunity is a form of innate immune memory that, through epigenetic modifications, enables more efficient and robust responses to unspecific immune challenges. Among the most potent inducers of trained immunity is the BCG tuberculosis vaccine, making it essential to assess whether other candidate tuberculosis vaccines in development elicit comparable or more potent effects. One such candidate is MTBVAC, the first life vaccine based on an attenuated strain of the pathogen *Mycobacterium tuberculosis,* developed by the University of Zaragoza and BIOFABRI.

In this poster, we examine the effects of MTBVAC on an animal model of sepsis, analyzing single-cell transcriptomic data from PBMCs of vaccinated and unvaccinated mice challenged with lipopolysaccharide (LPS). We employ Seurat, an R package specifically developed for the analysis of single-cell RNA sequencing (scRNA-seq). The analytical workflow encompasses multiple stages, including data normalization, integration, and dimensionality reduction, which facilitate an accurate clustering of the cells. This allows for subsequent differential expression (DE) analysis, to identify and characterize the modulatory effects exerted by MTBVAC, on the immune response to the LPS challenge unfolded by the different cell populations present in mice peripheral bloods.

Poster 28

Dynamic arrest in protein phase separation: the case of tau and alpha synuclein complex coacervation

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Protein phase separation, responsible for the formation of membraneless organelles, has drawn significant attention due to its unique properties, such as viscoelasticity, intracellular homeostasis, metabolic catalysis, and free molecular exchange without a lipid membrane. Protein coacervates are increasingly recognized as key players in human diseases, especially those involving protein aggregation. Intrinsically disordered proteins like tau and alpha-synuclein, linked to Alzheimer's and Parkinson's diseases, respectively, can both aggregate into amyloids and form coacervates under pathological conditions. Remarkably, these proteins undergo electrostatic phase separation when mixed, resulting in coacervates whose viscoelastic properties change over time. Our observations indicate that aging coacervates develop a reinforced polypeptide network, with a dynamical arrest of the proteins, leading to gelation and diminished liquid-like behavior. To better understand and potentially manipulate this phenomenon, we are employing advanced fluorescence spectroscopy and microscopy techniques to track the viscoelastic dynamics of these systems in vitro and in vivo. Our goal is to uncover ways to modulate the mechanical properties of protein coacervates, providing new insights into their biological roles and implications for disease.

Poster 29

Development and characterization of cellular models for studying the formation of molecular condensates in neurodegenerative diseases

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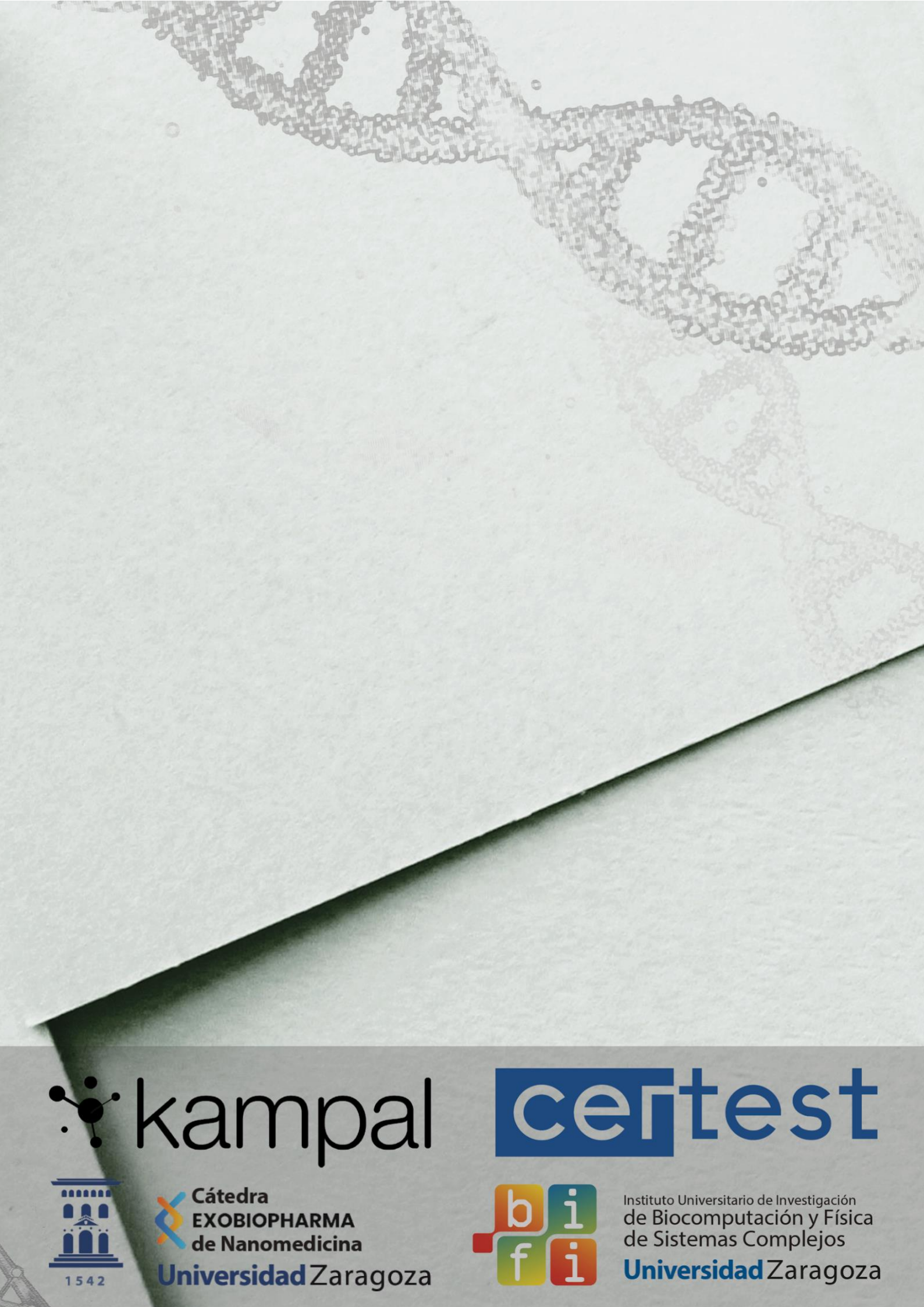
Alpha-synuclein (αS) and tau protein inclusions are key features of neurodegenerative diseases like Parkinson's and Alzheimer's. Co-aggregates of these proteins have been found in the brains of patients with synucleinopathies, yet the molecular mechanisms behind their formation remain unclear. Recent studies indicate that molecular condensates—membraneless organelles formed through liquid-liquid phase separation—play a crucial role in the pathogenesis of these disorders. Our research shows that the interaction between αS and tau is electrostatically driven, leading to the formation of liquid condensates that can mature into gel-like structures or amyloid hetero-aggregates (Nat Commun 13, 4586, 2022).

In this study, we aim to investigate the behavior of these condensates in cellular systems by developing models that mimic phase separation with varying material properties. We utilized two approaches: internalization of preformed condensates and de novo formation within cells. We successfully created distinct cellular models featuring αS and tau condensates, each with unique mechanical properties, ranging from fluid and gel-like to more solidified forms. By studying these models, we hope to gain insights into how the physical properties of αS and tau condensates contribute to neurotoxicity in neurodegenerative diseases.



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