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Book of Abstracts

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Foreword

Welcome to the XIII National Conference of BIFI 2026, held at the Institute for Biocomputation and Physics of Complex Systems (BIFI) in Zaragoza, Spain. This meeting is part of our long-standing series of national conferences and provides an open and stimulating forum for BIFI members to present recent advances, share perspectives, and strengthen interactions across the Institute's diverse research areas, as well as with colleagues from outside BIFI.

The scientific program includes a broad range of activities, such as short talks by students and early-career researchers, two poster sessions, and invited lectures by principal investigators leading most of BIFI's active research lines, complemented by contributions from researchers at other Spanish and international institutions.

We hope this conference will be both scientifically rewarding and enjoyable, offering a valuable opportunity for our community to reconnect, exchange ideas, and spark new collaborations. We wish you a productive and inspiring stay at the XIII National Conference of BIFI 2026.

The BIFI 2026 Organizing Committee
Zaragoza, 2026

Program

Legend
BIOCHEMISTRY AND MCB
BIOPHYSICS
COMPUTATION AND DATA SCIENCE
PHYSICS
EXTERNAL CONTRIBUTIONS

Wednesday January 14th

Session 1: 08:30 - 11:00

Chairperson: Pierpaolo Bruscolini

08:30-08:45	**REGISTRATION**
08:45-09:00	**OPENING**
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09:15-09:30	**Ariadna Fosch**: Diversification of global food trade partners increased inequalities in the exposure to shock risks
09:30-09:45	**Pietro Traversa:** Rumor propagation on hypergraphs
09:45-10:00	**THEORETICAL AND APPLIED MODELING OF COMPLEX SYSTEMS** **Santiago Lamata:** Temporal interactions in complex contagion
10:00-10:15	**Pablo Gallarta-Saénz:** The role of connectivity in the coevolutionary dynamics of antagonistic communities
10:15-10:30	**Francesca Dilisante:** In itinere contagions reduce epidemic robustness and drive delocalization in metapopulations
10:30-11:00	**SPECIAL PURPOSE COMPUTERS** **Sergio Pérez Gaviro:** Our upcoming Special Purpose Computing infrastructure at BIFI
11:00-11:30	**COFFEE BREAK**

Session 2: 11:30 - 13:45
Chairperson: Yamir Moreno

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12:15-12:30	**MOLECULAR DYNAMICS AND ELECTRONIC STRUCTURE** **Julen Munárriz:** Modelling Pt⍰ Sub-Nanocluster Electrocatalysts under Realistic Conditions
12:30-12:45	**Rubén Laplaza**: Exploring the energy landscape of metallic subnanoclusters using machine learning interatomc potentials
12:45-13:00	**Daniel Barrena:** Quantum Chemical Topology study of N–H bond activation via metal–ligand cooperation
13:00-13:30	**FUNDACIÓN IBERCIVIS (BIFI)** **Fermín Serrano Sanz:** RIECS-Concept: First Insights Towards a Pan-European Research Infrastructure for Excellent Citizen Science
13:30-13:45	**Francisco Sanz García**: Analysis of the evolution and collaboration networks of citizen science
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Session 3: 15:15 - 17:00
Chairperson: Ramón Hurtado

15:15-15:30	**Cancer Immunomics and Heterogeneity group (IISA)** **Eduardo José Aranda Cañada:** Unraveling Colorectal Cancer Lung Metastasis Through Spatial Transcriptomics and Single-Cell Analysis
15:30-15:45	**COMPUTATIONAL GENOMICS AND SYSTEMS BIO-MEDICINE** **Joaquín Sanz Remón:** Recent Advances in Computational Genomics and Systems Biomedicine: Exploring Host–Pathogen Interactions in Tuberculosis and Patient Heterogeneity in Autoimmunity
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16:15-16:45	**DATA ANALYSIS, ADVANCED VISUALIZATION & TECH. TRANSFER** **Francisco Bauzá Mingueza:** Towards a Non-Invasive Diagnosis of Huntington's Disease: A Machine Learning Approach with Random Lasing Spectroscopy
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09:15-09:30	**Miguel A. Vela Tafalla:** Linguistics becomes tips for scientists: Enhancing science communication skill development through interdisciplinary collaboration
09:30-09:45	**Rosana Villares:** Learn to engage in science dissemination online: An overview of DILAN's MOOC "Introduction to Online Science Communication Strategies"
09:45-10:00	**STOCHASTIC MODELS AND DATA ANALYSIS IN MEDICINE** **Javier Estéban:** Machine Learning Models Integrating Fetal Heart Rate Deceleration Dynamics to Predict Acidemia: A Tool for Optimizing Intrapartum Clinical Decisions
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10:15-10:30	**Sergio Sabroso**: How Missingness Patterns Affect Diagnostic Accuracy in Predictive Models
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12:30-12:45	**Hajar Jeblaoui Fattah:** Evaluating Enterotoxigenic Bacteroides fragilis Toxin as a Biomarker for Early Detection of Colorectal Cancer
12:45-13:00	**Francisco Javier Falcó:** Advanced Computational Characterisation of Protein Dynamics, Conformational Stability and Ligand Interactions, Illustrated Through the HDAC8 Case Study
13:00-13:15	**BIMOLECULAR INTERACTIONS** **Adrian Velazquez-Campoy:** Biomolecular Interactions: A journey Biophysics to Drug Discovery
13:15-13:30	**Paula María García Franco:** Targeting HDAC8: A Novel Approach to Overcome Drug Resistance in Melanoma Treatment
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16:00-16:15	**Blanca Viguri:** Structural requirements of the autophagy receptor p62 and polyubiquitin chains in biomolecular condensate assembly
16:15-16:45	**STATISTICAL-PHYSICS MODELING OF BIOMOLECULES** **Pierpaolo Bruscolini:** Ongoing research in the “Physical Modeling of Biomolecules” research line at BIFI
	Alessandro Fiasconaro: Synchronization features in a realistic model of CA1 pyramidal neurons
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09:15-09:30	**Iris del Val García:** Structural and Functional Determinants of Endocannabinoid Modulation at the hCB1 Receptor
09:30-09:45	**Sandra Arroyo Urea:** A ligand-triggered receptor conformation enables the design of selective agonists for the dopamine 3 receptor using a bitopic strategy
09:45-10:00	**STRUCTURAL BIOLOGY OF NEURONAL MEMBRANE RECEPTORS** **Beatriz Herguedas:** Dissecting Glutamate Receptors: structure, dynamics and biogenesis
10:00-10:15	**Irene Sánchez Valls:** From monomers to tetramers: ER-associated proteins drive AMPA receptor assembly
10:15-10:30	**Carlos Vega Gutiérrez:** GluA4 AMPA Receptors in Motion: Molecular Architecture Across the Gating Cycle
10:30-11:00	**HIGH PERFORMANCE COMPUTING** **Sergio Martínez-Losa:** Towards in Quantum Computing: The QuantumSpain Project
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Session 2: 11:30 - 15:15
Chairperson: Beatriz Herguedas

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12:00-12:15	**FUNCTIONAL GENOMICS OF THE OXPHOS SYSTEM** **Rocío Vázquez Martínez:** Magnetic Hyperthermia Directed to Mitochondria: Effects on OXPHOS Organization and Anticancer Response
12:15-12:30	**NEW DETERMINANTS OF MITOCHONDRIAL PROTEIN SYNTHESIS** **David Pacheu:** Molecular determinants of mitochondrial gene expression
12:30-12:45	**Aldara Mainé Rodrigo**: Kinase Regulation of Mitochondrial Translation: Functional Insights into eEF2K Silencing
12:45-13:00	**Ana Vela Sebastián:** Dissecting the tissue-specific mechanisms involved in mitochondrial protein synthesis defects
13:00-13:15	**PROTEIN FOLDING AND MOLECULAR DESIGN** **Javier Sancho:** Ongoing experimental and computational research on genes and proteins
13:15-13:30	**Antonio Hidalgo:** Rapid Protein Stabilization with Protposer: Flavodoxin and Aspergillopepsin I as models
13:30-13:45	**David Ros:** Toward First-Principles Folding Thermodynamics: Benchmarking Protein and Solvent Entropy Methods
13:45-15:15	**LUNCH**

Session 3: 15:15 - 19:30
Chairperson: Adrián Velazquez

15:15-15:30	**GENETIC REGULATION AND PHYSIOLOGY OF CYANOBACTERIA** **María F. Fillat Castejón:** Novel secondary regulators at the crossroad of nitrogen metabolism, stress response and biofilm formation in Anabaena sp. PCC7120
15:30-15:45	**Irene Oliván-Muro**: Nano-scale distribution of metals in filamentous cyanobacterium Anabaena sp. PCC7120
15:45-16:00	**Inés Federío Zalaya:** Analysis of structural and functional diversity of LinA and LinB dehalogenases for bioremediation of HCH isomers
16:00-16:15	**FLAVOENZYMES: ACTION MECHANISMS AND BIOTECHNOLOGY** **Milagros Medina:** Exploring Asymmetric Catalysis Mechanisms in Homodimeric Flavonzymes
16:15-16:30	**Victor Correa Pérez:** Functional and Structural Analysis of a Potential Alkene Reductase from Brucella ovis: toward the Development of a Novel Industrial Biocatalys
16:30-16:45	**Olga Soriano**: Dissecting the role of AIF dimerization in mitochondrial homeostasis through its interaction with CHCHD4
16:45-17:15	**APOPTOSIS Y METABOLISMO** **José Alberto Carrodeguas:** COTEGIN (Comprehensive Organized Tool for Expression and Gene Interaction Networks): An Integrated Bioinformatics Platform for Advanced Transcriptomic
17:15-17:30	**CLOSING REMARKS**

TALKS

A Complex Systems Approach: Theoretical and Data-Driven Advances and Interdisciplinary applications

Alejandro Tejedor[1,2], COSNET Group[2]

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2. Institute for Biocomputation and Physics of Complex Systems, University of Zaragoza.

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In this talk, we present an overview of recent theoretical and practical advancements developed within the COSNET group. Using a Complex Systems approach, and advancing both theoretical and data-driven methodologies, we address challenges across several core research areas. These include the characterization of the structure and dynamics of higher-order interaction systems (including information-theoretical approaches), the study of spreading dynamics (e.g., epidemics, diffusion) in networked systems, and methods for coarsening network structure to make large-scale system analysis more tractable while gaining insight into their behavior. We also investigate decision-making and behavioral science, combining game-theoretic experimental frameworks with the deployment of Large Language Models (LLMs) as agents capable of interacting among themselves and with humans. We further outline how the Complex Systems perspective has enabled COSNET members to engage in highly interdisciplinary research, addressing problems in fields as diverse as finance, sustainability, and sports.

As a case study of particular societal relevance, we present an end-to-end application that began with new theoretical insights in network theory and culminated in a framework to inform the placement of fuel-breaks to mitigate the spread and impact of wildfires. This example highlights how advances in fundamental theory can translate into potentially actionable strategies for real-world resilience.

Diversification of global food trade partners increased inequalities in the exposure to shock risks

Ariadna Fosch[1], Alberto Aleta[1], Roger Cremades[2], Yamir Moreno[1]

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2. Sustainability Research Institute — University of Leeds, UK.

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Recent disruptions in the food trade systems, have evidenced how quickly local shocks can spread until becoming global security threats. The capacity of these systems to absorb spillover cascades, their robustness, depends greatly on the structure of the trade networks. However, few studies have quantified how topological changes in these networks have shaped systemic vulnerability.

In this study, we use a combination of topological multiplex analysis and shock simulations to identify how changes in trade connectivity between 1986-2022 have reshaped global vulnerability to production shocks. Using trade data from FAO we built yearly multiplex representations of the food trade system and explored their temporal evolution. We also quantified robustness trends through a stochastic shock-propagation model where countries facing supply shortages impose dynamic export bans.

Our results show that increasing globalisation has strengthened interdependencies among countries, amplifying cascade magnitudes for most commodities. However, robustness trends are heterogeneous across food types: grain trade has become more decentralised and resilient to targeted shocks, while animal and vegetable fats exhibit growing centralisation and fragility around key exporters such as Indonesia and Malaysia. This also resulted in differential shifts in vulnerability, which increased the most in Central Asia for grains, and Eastern Europe for fats.

Rumor propagation on hypergraphs

Kleber Andrade Oliveira[1], **Pietro Traversa**[2,3], Guilherme Ferraz de Arruda[4], Yamir Moreno[2,3]

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2. Institute for Biocomputation and Physics of Complex Systems, University of Zaragoza, Zaragoza 50009, Spain.

3. Department of Theoretical Physics, University of Zaragoza, Zaragoza 50009, Spain.

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The rapid spread of information and rumors through social media platforms, especially in group settings, motivates the need for more sophisticated models of rumor propagation. Traditional pairwise models do not account for group interactions, a limitation that we address by proposing a higher-order rumor model based on hypergraphs. Our model incorporates a group-based annihilation mechanism, where a spreader becomes a stifler when the fraction of hyperedges aware of the rumor exceeds a threshold. The dynamics has two distinct subcritical behaviors: exponential and power-law decay, which can coexist depending on the heterogeneity of the hypergraph. Interestingly, in the set of parameters we analysed, we found continuous phase transitions in both homogeneous and heterogeneous hypergraphs. This finding aligns with the literature suggesting that real-world rumor propagation occurs near criticality. Finally, we validated our model using empirical data from Telegram and email cascades, which provides additional evidence and possible explanations for this criticality claim. These results open the door to a more detailed understanding of rumor dynamics in higher-order systems.

Temporal interactions in complex contagion

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3. Vermont Complex Systems Institute, University of Vermont
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Contagion in social systems is often driven by group interactions, where peer influence shapes the adoption of behaviors, ideas, and technologies. While previous studies have shown that higher-order group synergy can generate explosive transitions, most analyses assume static networks or rely on aggregated temporal data, obscuring the role of time-varying interactions. Here we introduce a mathematical framework that explicitly incorporates group annealing into complex contagion dynamics, allowing us to explore how temporal changes in group structure affect system-level transitions. Using Approximate Master Equations, we derive numerical and analytical results that reveal the central role of temporal variability.

For simple contagion, temporal annealing shifts the continuous activation transition toward lower spreading power. More strikingly, for complex contagion, increasing annealing transforms the transition from continuous to discontinuous, generating bistability whose width grows with the annealing rate. We obtain implicit analytical expressions for the invasion threshold and identify the tricritical point separating continuous and bistable regimes, smoothly bridging the quenched and mean-field limits. Finally, by comparing different empirical interaction datasets, we show that the continuity or explosiveness of transitions depends sensitively on group size, connectivity, and annealing rate. These results demonstrate that static, aggregated representations can substantially mischaracterize contagion dynamics.

The role of connectivity in the coevolutionary dynamics of antagonistic communities

Pablo Gallarta-Sáenz[1,2], Santiago Lamata-Otín[1,2], Jesús Gómez-Gardeñes[1,2], Cecilia de Andreazzi[3]

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Antagonistic interactions are fundamental to the structure and function of ecological communities, generating strong reciprocal selective pressures that shape the evolution of species. However, their coevolutionary dynamics remain far less understood than those of mutualistic systems, which have been more broadly studied through trait-based and fitness-centered models. In this work, we develop a novel framework that integrates network structure, trait evolution and species fitness within a unified formalism.

In our model, both exploiters and victims' dynamics are governed by two competing forces: a selection toward an environmental optimum and a selection arising from pairwise interactions. The antagonistic nature of these relationships introduces an asymmetry, since exploiters adapt to match the traits of their victims, whereas victims evolve to increase trait divergence and escape exploitation. Exploring the coevolutionary scenarios we characterize the different dynamical regimes: from rapid convergence toward the environmental optima under weak interaction pressures to complex behaviors that arise when species experience strong interaction selection.

Overall, our framework merges evolutionary theory and antagonistic interactions, highlighting how asymmetric coevolutionary strengths and connectivity heterogeneity of the network drive fitness imbalances and evolutionary divergence within antagonistic communities.

In itinere contagions reduce epidemic robustness and drive delocalization in metapopulations

Francesca Dilisante[1,2], Pablo Valgañón-Ruíz[2], David Soriano-Paños[2,4], Jesús Gómez Gardeñes[1,2]

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3. Pyrenean Institute of Ecology (IPE-CSIC), 50059 Zaragoza (Spain)
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Individuals utilizing mass transportation systems are disproportionately susceptible to contracting airborne diseases. However, many epidemic models incorporate human mobility as a single aggregate factor, overlooking the possibility of contagion during transit.

To address this limitation, this work proposes an extension to the Movement–Interaction–Return (MIR) metapopulation model with distinguishable agents [1]. This extension introduces a novel mechanism that specifically accounts for in itinere contagion. The existing mixing matrix formalism is expanded, and an analytical derivation within this new framework enables precise characterization of the epidemic threshold through spectral analysis. Furthermore, numerical simulations in synthetic metapopulations confirm that in itinere contagions reduce the epidemic threshold, increase disease prevalence, and attenuate the epidemic detriment phenomenon, wherein low mobility suppresses epidemic spread relative to no mobility. Therefore, this transmission route alters the critical conditions under which mobility either enhances or suppresses epidemic spread. Moreover, in-transit contagion drives epidemic delocalization, shifting the spatial profile of outbreaks from being confined to highly vulnerable patches to being uniformly distributed across the metapopulation.

These findings underscore the need to incorporate transportation-mediated contagion when modeling airborne disease propagation, as failure to do so can lead to underestimated epidemic risk and misinformed public health strategies.

More detailed information about the model and the results in [2].

References

[1] Valgañón, P. et al. (2022). Contagion-diffusion processes with recurrent mobili-ty patterns of distinguishable agents. Chaos 32, 043102.

[2] Dilisante, F. et al (2025). In itinere infections covertly undermine localized epidemic control in metapopulations. Chaos 35, 051102.

Our upcoming Special Purpose Computing infrastructure at BIFI

S. Perez-Gaviro[1,2]

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Dedicated computing systems can improve performance by several orders of magnitude compared to conventional general-purpose computers for highly specialized tasks for demanding scientific research and industrial applications. This significant leap is achieved through hardware optimization designed for intensive computational workloads like high-throughput data processing, machine learning, or complex simulations.

A successful example is the Janus family [1] at BIFI-Institute. Our special purpose computers, *Janus* and *Janus II*, have been instrumental in achieving several significant scientific milestones in the study of spin glasses, the paradigm of complex systems.

To further enhance our BIFI research capacity, we have secured funding for a new, state-of-the-art dedicated computing cluster based on Field-Programmable Gate Arrays (FPGAs) processors. This powerful resource will be made available to both academic researchers and corporate partners, fostering collaboration and driving innovation across multiple scientific and technological domains like Complex Systems, Quantum Emulation and Quantum Algorithm Evaluation, AI inference, Molecular dynamics, Neural networks training, Language modeling and Propagation in large scale networks, among others.

[1] See https://www.janus-computer.com and references there in for details

Reducibility of higher-order to pairwise interactions: Social Impact Models on Hypergraphs

Jaume LLabrés[1], Federico Vázquez[1], Raúl Toral[1], Maxi San Miguel[1]

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The question of the reducibility of Higher Order Interactions is addressed. We show that general social impact models with Higher-Order Interactions (HOI) on hypergraphs can be mapped exactly onto a pairwise (PW) dynamics on a weighted projected network, while preserving the microscopic flipping probabilities. For Hypergraph Voter Models, we compute these weights analytically or numerically across several hypergraph ensembles, and we characterize their ordering dynamics through simulations of both the reduced PW system and the original HOI model. For a linear social impact function, the projected-network weights become time independent, allowing us to develop a Pair Approximation that predicts macroscopic observables independent of those weights—a prediction confirmed numerically-, yielding macroscopic dynamics equivalent to the classical Voter Model on the unweighted projected network. For a nonlinear social impact function, the weights of the reduced PW representation depend on the instantaneous system configuration; nevertheless, a much simpler Nonlinear Voter Model on the unweighted projected network still reproduces the main macroscopic trends.

Modelling Pt□ Sub-Nanocluster Electrocatalysts under Realistic Conditions

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The oxygen reduction reaction is of great relevance in renewable energy transformation processes. Unfortunately, the reaction kinetics are sluggish, which hinders its application at an industrial scale. Sub-nano-cluster-decorated electrode interfaces stand as promising candidates for overcoming such limitations [1]. However, the understanding of the nature of the active sites of these catalysts under electrocatalytic conditions is a challenge for both experiment and theory, due to their dynamic fluxional character. In this context, we combine global optimization techniques with the electronic Grand Canonical DFT to characterize the structure and dynamics of subnano Pt_n clusters deposited on electrified carbon-based interfaces (Figure 1).

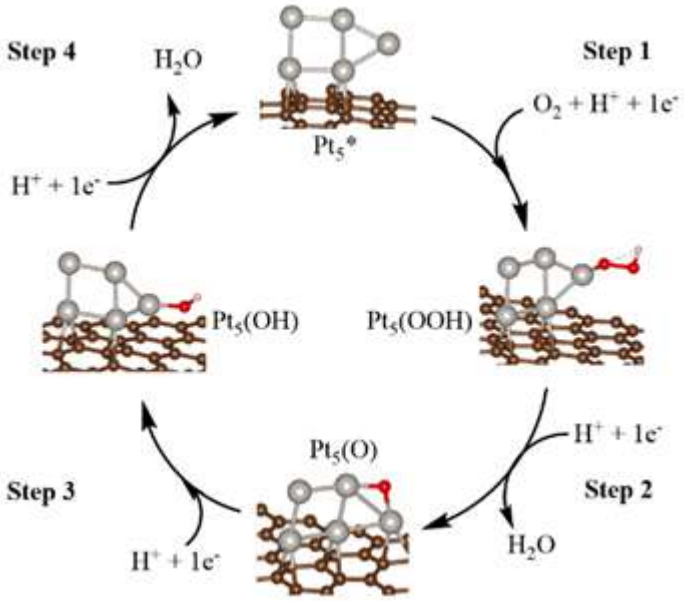

Figure 1. Schematic Representation of the Four-Electron Mechanism of ORR on Pt5/graphite systems.

We show that, under electrochemical conditions, the clusters exist as statistical ensembles of multiple states, whose composition is greatly affected by the potential. This way, the results reveal the presence of potential-dependent active sites and, hence, reaction energetics [2].

We also note that the methodological framework considered in the calculations has a huge impact on the relative energies of the various clusters forming the ensemble. This is especially relevant in C-defective interfaces, as it will be explained during the presentation.

[1] A. von Weber, S. L. Anderson. Acc. Chem. Res. 2016, 49, 2632−2639.

[2] J. Munarriz, Z. Zhang, P. Sautet, A. Alexandrova. ACS Catal. 2022, 12, 14517−14526.

Exploring the energy landscape of metallic subnanoclusters using machine learning interatomic potentials

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Metallic subnanoclusters (SNCs) can adopt many configurations, with the number of plausible stable arrangements scaling exponentially with the number of atoms involved. Under catalytic conditions with high temperature and applied potentials, SNCs may interconvert fluxionally. Thus, considering the full energy landscape of such systems is of interest to understand, rationalize and design SNC-based heterogeneous catalysts. In this work, we leverage foundation models for machine learning interatomic potentials in the global exploration of SNC configurations, and achieve an unprecedented coverage of all possible structures.

Quantum Chemical Topology study of N–H bond activation via metal–ligand cooperation

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The activation and functionalization of N–H bonds have long represented a fundamental challenge in chemistry, a fact that stands in noteworthy contrast with the remarkable range of applications exhibited by their derivatives. Amines, as primary substrates, display limited acidity and readily form stable Werner complexes, which hinder the effectiveness of many well-established coordination compounds.[1] Although several sophisticated strategies have been developed, they remain scarce compared with the more diverse methods available for analogous C–H or O–H bond activations. Within this context, metal-ligand cooperation (MLC) offers a promising approach by enabling N–H bond activation through the formation of metal-amido species, with a parallel process —such as ligand rearomatization— providing the driving force of the reaction.[2,3] In this work, we examine the details of the N–H activation mediated by Milstein's archetypal PNP-Ru(II) complexes.[3] Our analysis integrates Quantum Chemical Topology methods, including the Electron Localization Function (ELF) within the Bonding Evolution Theory (BET) framework, and the energetic counterpart provided by the Interacting Quantum Atoms (IQA) decomposition scheme. This combined approach affords an accurate description of the role of ligand rearomatization and provides new insights into the factors governing reactivity, thereby guiding the rational design of improved MLC systems.[4]

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RIECS-Concept: First Insights Towards a Pan-European Research Infrastructure for Excellent Citizen Science

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Citizen science has grown rapidly across Europe, but the landscape remains highly fragmented, with hundreds of platforms, tools, datasets and methodologies operating in isolation. This reduces scientific value, limits interoperability, and increases inequalities in access to technological and organisational capacity. RIECS-Concept (see concept.riecs.eu), a Horizon Europe project coordinated by Ibercivis and involving 13 partners, is developing the conceptual and technical foundations for the future Research Infrastructure for Excellent Citizen Science (RIECS), with the ambition to enter the ESFRI Roadmap. After one year of work, the project provides the first integrated analysis of needs, challenges and opportunities across scientific, technological, policy and societal dimensions.

We are mapping existing services and resources, identifying interoperability gaps, and analysing requirements related to data, metadata, sustainability, governance and ethics. Crucially, in parallel, we are deploying an open governance model with over 100 co-design and participatory actions involving researchers, citizens, citizen science networks, NGOs, technology providers, companies, policy makers and other research infrastructures. This large-scale engagement is generating a rich set of user stories and early insights that directly inform the preliminary RIECS conceptual design and its future implementation roadmap.

Our presentation will share these early findings, showing how a shared pan-European infrastructure can enhance scientific excellence, reinforce interoperability, support financial and organisational sustainability, and strengthen societal uptake of citizen science across Europe and beyond.

Analysis of the evolution and collaboration networks of citizen science

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This presentation explores the rapid growth and evolving dynamics of scientific publications in Citizen Science up to 2025. Building on the foundational 2020 study "Analysis of the Evolution and Collaboration Networks of Citizen Science Scientific Publications," our updated analysis captures the increase in publications, rising from 2,645 papers in 2018 to an estimated 13,000 in 2025. This trajectory underscores the rapid expansion and diversification of the field.

Using comprehensive bibliometric analysis, we identify significant growth trends across disciplines, geographic regions, and publication types, highlighting the integration of Citizen Science into previously underrepresented domains. We map the expansion of international and interdisciplinary collaboration, revealing patterns of knowledge exchange, key hubs of activity, and the pivotal role of funding agencies.

The study further evaluates the impact of Citizen Science through citation metrics and societal influence, particularly in policymaking and public engagement, alongside the technological innovations fueling the field. Visualizations, including growth curves and network diagrams, will illustrate these findings. The presentation concludes with projections for the next decade, discussing challenges and opportunities for democratizing science. These findings offer researchers, policymakers, and practitioners valuable insights to support strategic collaborations and the ongoing expansion of Citizen Science’s global impact.

Unraveling Colorectal Cancer Lung Metastasis Through Spatial Transcriptomics and Single-Cell Analysis

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Colorectal cancer (CRC) most often spreads to liver but also metastasizes to lung though less frequently. For this reason, lung metastases remain understudied. Previous studies from our group suggested that lung metastasis is more immunogenomic than liver metastasis. Understanding its immunogenicity could be key to treat these patients with immunotherapy. This study aims to deeply characterize CRC lung metastases by combining spatial and single-cell transcriptomics to decipher the molecular crosstalk between tumoral and immune cells. FFPE tissue samples from eight CRC lung metastasis were analyzed using Visium CytAssist Spatial Transcriptomics allowing the analysis of gene expression while preserving tissue structure. In four samples, scRNA-seq was performed using Chromium Fixed RNA Profiling solution. Libraries were sequenced using Illumina Hiseq 400 and data were processed with Space Ranger, Cell Ranger and Seurat. After rigorous quality control, gene expression was used for spatial clustering and TALKIEN software was used to identify molecular interactions between clusters. Spatial data were deconvoluted using CARD, leveraging our annotated single-cell data for cell-type annotation. Expression levels of stromal and epithelial cells overlap with stromal and tumor areas in the histological image. In conclusion, integrating these technologies provides powerful tool to deeper understanding the tumor microenvironment of lung metastases.

Recent Advances in Computational Genomics and Systems Biomedicine: Exploring Host–Pathogen Interactions in Tuberculosis and Patient Heterogeneity in Autoimmunity.

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Over the past five years, our Research line in computational genomics and systems biomedicine has consolidated its activity around two main research topics: the molecular cross-talk between *Mycobacterium tuberculosis* (Mtb) and its host, and the study of inter-individual transcriptomic variation in autoimmunity.

In the tuberculosis line, our most recent work has highlighted extracellular vesicles as key modulators of the host–pathogen interface. We have identified VirR as a central regulator of vesiculogenesis in mycobacteria and shown that vesicle-associated small RNAs engage TLR8, revealing a previously unrecognized signaling route relevant for early macrophage control of Mtb. In parallel, we are investigating the genetic architecture underlying the temporal dynamics of macrophage responses to intracellular infection, uncovering host genetic factors that shape the strength and timing of innate immune activation.

In the second axis, I will summarize the main conclusions of our recent work on the characterization of the sources and consequences of patient-to-patient heterogeneity in celiac disease. Using a large transcriptomic dataset of duodenal mucosa spanning active disease and gluten-free-diet remission, we characterize robust sex- and age-associated patterns: women display heightened immune activation during active disease; men show stronger epithelial regeneration alongside marked suppression of nutrient absorption and metabolic programs; and children exhibit the most pronounced immune reversal upon gluten withdrawal. We further introduce a statistical framework for stabilized inter-individual variability, identifying a 101-gene hypervariable signature strongly linked to mucosal damage, independent of sex or age.

Together, these studies illustrate how integrating systems biology, transcriptomics, and host genetics can uncover the mechanisms that drive heterogeneity in human immune responses, with implications for precision medicine in both tuberculosis and celiac disease.

Identification of putative sRNA-Interacting Proteins Implicated in Extracellular Vesicle Cargo Loading in *Mycobacterium tuberculosis*

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Small RNAs (sRNAs) are key regulatory molecules orchestrating diverse biological processes in bacteria. To exert their functions, sRNAs rely on protein partners that modulate their stability, structure, and subcellular localization. A relevant example is their selective incorporation into extracellular vesicles (EVs), which mediate bacterial communication and host-pathogen cross-talk. While RNA-binding proteins involved in these processes have been described in model prokaryotes, potential sRNA interactors in Mycobacterium tuberculosis (*Mtb.)* remain unknown.

To address this gap, we applied Gradient Fractionation and Sequencing (Grad-seq), a technique that profiles RNA and protein distributions by separating cellular components according to sedimentation properties, followed by RNA-seq and liquid chromatography-mass spectrometry (LC-MS) proteomics. Grad-seq, however, presents specific analytical challenges. Standard RNA-seq data normalization approaches assume that most features remain unchanged across samples, a premise violated by fractionation gradients. Moreover, correlations between protein and RNA profiles are distorted by coincident molecular masses, which can artificially inflate association signals.

To overcome these challenges, we developed an improved Grad-seq analysis pipeline that introduces tailored RNA normalization, protein imputation strategies, and a method to adjust for mass similarity bias. Using this framework, we identified putative interacting proteins that may function as candidate chaperones for EV cargo selection, providing a solid foundation for uncovering RNA-protein interactions in *Mtb.*

Taken together, these methodological refinements enhance Grad-seq resolution in *Mtb*. and open new avenues for investigating the mechanisms governing EV-mediated sRNA trafficking.

Characterization of multi-scale variation patterns in transcriptomics data: computational models and applications in immune responses and cancer

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Following a phase in which transcriptomics progress was driven by improvements in sequencing fidelity and cost-efficiency, the advent of single-cell and, more recently, spatial -omics technologies has expanded the resolution at which gene expression heterogeneity can be interrogated. These technologies enable the analysis of variation across cellular lineages, perturbational contexts and spatial microenvironments, motivating statistical frameworks that model further aspects of expression distributions than their means, or more generally, location parameters.

To meet this need, our group has developed *scdvar*, a GAMLSS-based method for detecting differential variability across groups of observations, applicable to both single-cell and bulk RNA-seq. To illustrate the utility of this approach across biological scales, we have applied it in two biomedical collaborations involving two markedly different diseases: a highly prevalent, autoimmune disorder -celiac disease- as well as an under-studied, cancer: vulvar Paget disease.

In what regards celiac disease, the characterization of a set of genes displaying pronounced inter-patient variability—yet comparatively coherent expression in healthy mucosa—led us to identify a dominant transcriptional signature that stratifies patients along a previously uncharacterized functional axis strongly associated with mucosal damage and independent of demographic determinants. Concerning Paget disease, we present preliminary analyses in which variation in gene expression is examined at both bulk and single-cell resolution to delineate tumor composition, oncogenic programs and potential drivers of severity.

Together, these studies demonstrate how multi-scale transcriptomic modeling can sharpen patient stratification and support precision medicine efforts in heterogeneous diseases.

Towards a Non-Invasive Diagnosis of Huntington's Disease: A Machine Learning Approach with Random Lasing Spectroscopy

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The early and non-invasive diagnosis of neurodegenerative diseases like Huntington's remains a significant challenge in medical science. Current reliable methods often involve invasive tissue sampling, highlighting the need for alternative approaches. This study explores the use of Random Lasing spectroscopy from blood samples as a minimally invasive diagnostic tool, coupled with machine learning for classification.

We analyzed a dataset of 10,500 light spectra obtained from the blood samples of 21 mice (10 healthy, 11 with Huntington's disease). The data, characterized by high dimensionality (1600 wavelengths), underwent a rigorous preprocessing pipeline. This included distribution inspection, outlier correction, and standardization at the wavelength level, followed by dimensionality reduction via Principal Component Analysis (PCA). A key methodological consideration was the nested structure of the data, where spectra are grouped by mouse. Consequently, model training and validation employed a 21-fold leave-one-group-out scheme, ensuring that all spectra from a single mouse were exclusively in the training or test set. We evaluated several classifiers, including Logistic Regression, k-Nearest Neighbors, and Support Vector Machines (SVM). Predictions at the individual mouse level were derived from spectrum-level classifications using a majority voting rule.

The results are highly promising. A Gaussian SVM classifier achieved the best performance, correctly identifying the disease status in 19 out of 21 mice (91% accuracy). This demonstrates the considerable potential of combining Random Lasing spectroscopy with machine learning for accurate, non-invasive disease detection. The main challenges involved handling the high-dimensional, group-structured data, which was successfully addressed through tailored preprocessing and validation strategies. This approach paves the way for a less invasive diagnostic methodology with potential for early risk prediction.

Generating consensus and dissent on massive discussion platforms with an O(N) semantic-vector model

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Reaching consensus in massive discussion networks is critical for reducing noise and achieving optimal collective outcomes. However, the natural tendency of humans to preserve their initial ideas constrains the emergence of global solutions. To address this, Collective Intelligence (CI) platforms facilitate the discovery of globally superior solutions. We introduce a dynamic model based on the standard O(N) model to drive the aggregation of semantically similar ideas. The system consists of users represented as nodes in a lattice with nearest-neighbour interactions, where their ideas are represented by a semantic vector.

We analyse the system's equilibrium states as a function of the coupling parameter . Our results show that drives the system toward a ferromagnetic-like phase (global consensus), while induces an antiferromagnetic-like state (maximum dissent), where users maximize semantic distance from their neighbours. This framework offers a controllable method for managing the trade-off between cohesion and diversity in Collective Intelligence platforms.

Integrating network and linguist analysis to model research visibility and impact: A mixed-methods approach to academic ecosystems

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In our current research we have used network analysis to describe the academic ecosystems of four leading EU researchers. We have also supplemented the network analysis results with a textual analysis of the language used in the titles in order to bridge the social and the linguistic dimensions of research productivity and impact in today's increasingly competitive research world. In this presentation we share some interdisciplinary methodological reflections, highlighting the value of establishing synergies between network and text-linguistic perspectives are mutually beneficial. Specifically, in this presentation we explain how we have used network analysis to map social dimensions (i.e., collaboration structure) and linguistic data mining to analyze discursive dimensions (i.e., communicative effectiveness) influencing research productivity and visibility. The convergence of these quantitative and qualitative methodologies provides a more nuanced interpretation of scholarly performance, bridging the gap between collaboration and communication. We argue that to understand research visibility, it is necessary to move beyond single-domain analyses. Networks reveal structure, while language reveals meaning. Combining these two perspectives allows us to obtain a comprehensive account of how scientific knowledge is constructed socially, institutionally and discursively within the global research landscape.

Linguistics becomes tips for scientists: Enhancing science communication skill development through interdisciplinary collaboration

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This presentation stems from the joint work of a variety of specialists in the SCICOMM project at the University of Zaragoza, where linguists and scientists managed to create and test materials to support science students in communication skill development. In particular, our goal is to showcase the process of dialogue and collaboration through which expert knowledge from the field of English for Specific Purposes has been selected, repurposed and adapted to enhance undergraduate and master's students' training by integrating Digital Competence and Written/Oral Communication Competence into specialized content courses.

To illustrate this process, we focus on some of the handouts we produced detailing the creation and presentation of infographics. We explain the theoretical foundations that led to the choices made in the preparation of the materials, especially with relation to rhetorical and phonetic considerations, and provide commentary as to how they have been translated into manageable pieces of information for students. Our report includes data from both the students and the content teachers as to the students' level of attainment in terms of communication. Because of this, this work can be taken as good practice and as encouragement for teachers interested in this type of interdisciplinary collaboration.

Learn to engage in science dissemination online: An overview of DILAN's MOOC "Introduction to Online Science Communication Strategies"

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DILAN is an Erasmus + funded project that has developed a MOOC to support the development of EU researchers' online communication competences. In this presentation we seek to provide an overview of the DILAN MOOC: what will you learn; how will you learn; how will know that you have learned. The contents and competences of this course include writing texts to meet diversified online (i.e. experts and non-experts). Course participant will gain background knowledge on digital genres such as the lay summary, infographic, tweetorial, and graphic abstract including noticing their features and communication strategies for audience engagement. The learning experience is enhanced by grouping content into small, bite-sized, modules. This will facilitate integration of learning into everyday routine, as well as skills transfer by drawing on previous academic writing experience to craft new digital genres. A variety of resources enrich the learning itinerary: video tutorials, short explanations and up-to-date examples, among others. Learning assessment relies on short quizzes and wrap-up sections that foster reflection and awareness of skills. All in all, the DILAN MOOC is suitable for everyone: participants can choose their own path, move freely around the course and explore digital genres, or get started into their own project.

Machine Learning Models Integrating Fetal Heart Rate Deceleration Dynamics to Predict Acidemia: A Tool for Optimizing Intrapartum Clinical Decisions

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Based on electronic fetal monitoring (EFM) recordings from 868 infants, our work developed a machine learning model to predict fetal acidemia (pH < 7.10). Key parameters, including total reperfusion time, deceleration area, and the number and depth of decelerations, were extracted from the last 30 minutes of the fetal heart rate signal. These variables were used to train and validate three predictive models: logistic regression, random forest, and neural networks. The random forest model, comprising 100 trees, demonstrated the best overall performance, achieving an area under the ROC curve of 0.865. It also exhibited superior calibration and clinical utility, showing that a 33% probability threshold could prevent 46% of unnecessary cesarean sections while missing only 5% of acidotic cases. This approach provides a practical tool for improving intrapartum decision-making.

Explainable Machine Learning Models for the Prediction of Clinically Significant Prostate Cancer

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This study investigates the prediction of clinically significant prostate cancer (CsPCA) in a cohort of 1,327 patients, a major contributor to cancer-related mortality in men. The dataset originated from the AI4HealthyAging project. Missing values in clinically relevant variables, such as prostate volume, were addressed using two different imputation techniques.

Using multiple machine learning approaches, most models demonstrated strong predictive performance, with AUC values ranging from 0.834 to 0.910. Logistic Regression, Elastic Net, Random Forest, and Neural Networks showed comparable and superior performance to Classification Trees and XGBoost. The highest AUC was achieved by Elastic Net, whereas the Classification Tree performed worst and exhibited marked limitations at high sensitivity levels, classifying almost all patients as positive. Although XGBoost achieved acceptable performance, it did not outperform simpler models, which appeared to benefit from the structure of the data.

Model interpretability was enhanced through SHAP (SHapley Additive Explanations) analysis. PI-RADS emerged as one of the most influential features, with higher categories (4–5) contributing strongly and positively to the predicted probability of CsPCA. In addition, SHAP plots revealed relevant interactions between PI-RADS, PSA levels, and prostate volume, providing both global and individual-level explanations to support clinical decision-making.

How Missingness Patterns Affect Diagnostic Accuracy in Predictive Models

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The rapid expansion of large, complex datasets has made missing data a major challenge in statistical modeling, as the proportion and distribution of missing values can significantly affect the reliability of predictive analyses. Although the impact of different imputation methods on discrimination metrics such as the area under the ROC curve has been studied, their effect on the Youden Index, which combines sensitivity and specificity, remains poorly understood.

We conducted simulation studies under realistic conditions, including normally distributed and categorical variables, predefined correlation structures, and skewed distributions. Several imputation approaches were evaluated across missing data levels from 5% to 90%. Model performance was assessed using AUC, sensitivity, specificity, and the Youden Index.

Results showed a 20–30% decline in most diagnostic metrics compared to complete-data models. The correlation between imputed variables played a critical role, with slightly positive correlations mitigating performance loss and slightly negative correlations accelerating it. The Youden Index varied substantially as the proportion of missing data increased, complicating the identification of optimal cutoff values. These findings emphasize the need for improved imputation strategies that consider both the amount and structure of missing data to strengthen the reliability of predictive models.

Selective mucin adhesion by a microbial module that binds clustered saccharide patches of inner O-glycans

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Mucus covering the body's wet epithelial surfaces is built from large mucin proteins densely decorated with O-glycans. This complex glycocalyx shapes the microbiota, nourishes commensals, and protects tissues by preventing pathogen adhesion and biofilm formation. Yet the molecular logic by which microbes selectively recognize mucins has remained poorly understood. Here, we characterize a small mucin-binding module, X409, that binds with high specificity to clustered saccharide patches—rows of inner monosaccharides formed by adjacent O-glycans within STTT-like motifs. Using an integrated structural approach combining X-ray crystallography, NMR spectroscopy, molecular dynamics simulations, and mass photometry, we show that X409 recognizes a defined three-dimensional glycan epitope unique to mucins. Mass photometry was essential to detect and quantify X409 interactions with mucin reporters carrying the STTT motif, thereby helping to pinpoint the minimal sequence required for high-affinity binding. This binding strategy enables microbes to remain attached even as outer glycan chains are progressively trimmed during mucin degradation. The discovery of this "clustered saccharide patch" epitope highlights a previously underappreciated class of contextual glycan signals and provides a framework for identifying new mucin-binding proteins. These insights may inform future strategies to block pathogen colonization or to target therapeutics to mucin-rich niches.

Discovery of α(1,6)-Fucosyltransferase (FUT8) Inhibitors Using Machine Learning and Physics-Based In Silico Approaches

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Confidential abstract.

Atomic-level views of enzyme catalysis to guide biotechnology

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Carbohydrate-active enzymes (CAZymes), including glycoside hydrolases and glycosyltransferases, are the primary molecular machinery responsible for the degradation, synthesis, and modification of carbohydrates in nature. They underpin a wide range of industrial and biotechnological applications, from biomass conversion and biofuel production to the development of biotherapeutics. To use these enzymes in a controlled way and improve them for practical purposes, we need a detailed understanding of how enzymes recognize carbohydrates and how sugar units “move” through the catalytic cycle [1–4]. Such mechanistic insight can guide the design of new drugs and chemical probes for glycobiology and immunology [5]. In this talk, I will illustrate how modern computer simulations can reveal enzyme mechanisms at atomic resolution, and I will highlight computational approaches that are expanding what we can learn about CAZyme catalysis.

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Tracing Cancer: From Biophysical Patterns to Early Diagnosis

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Early detection and molecular stratification remain major challenges in pancreatic and colorectal cancer, where late diagnosis and biological heterogeneity still limit the success of current treatments. Our research line aims to develop minimally invasive diagnostic strategies by integrating Thermal Liquid Biopsy (TLB) with multi-omics data and machine-learning models to detect systemic proteome alterations related to tumor presence, progression and treatment response. TLB provides a rapid and low-volume biophysical measurement of serum protein stability, reflecting disease-associated changes in protein complexes and immune components. By combining these thermodynamic profiles with clinical variables, high-resolution proteomics and structural modelling, we aim to identify biomarker panels and understand key mechanistic features behind cancer phenotypes.

Our recent studies show that TLB-based signatures, together with selected clinical parameters, can discriminate early-stage tumors with high sensitivity and also indicate biological pathways underlying these observations. Current efforts focus on expanding validation to multicenter cohorts, improving interpretation of the molecular basis of TLB signals, and advancing structure-guided approaches to design inhibitors of epigenetic and bacterial targets relevant to digestive cancers.

Overall, this research line aims to connect biophysical diagnostics with computational biology and precision oncology, with the goal of providing useful tools and new insights for early detection and more targeted clinical interventions.

Evaluating Enterotoxigenic Bacteroides fragilis Toxin as a Biomarker for Early Detection of Colorectal Cancer

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Enterotoxigenic Bacteroides fragilis (ETBF) is known to produce the Bacteroides fragilis toxin (fragilysin), an extracellular zinc metalloprotease that disrupts the intestinal epithelial barrier by cleaving intercellular proteins. This activity is linked to acute diarrheal disease, inflammatory bowel disease, and colorectal cancer (CRC). Fragilysin's role in damaging the paracellular barrier and promoting fluid secretion highlights its involvement in inflammation and cancer transformation within the intestine. Recent studies suggest that BFT can serve as a biomarker for the inflammation-to-cancer progression in intestinal diseases.

Colorectal cancer, with rising incidence rates and younger onset, is the second leading cause of cancer-related death and the third most commonly diagnosed cancer globally. Population screening remains crucial for reducing disease incidence and mortality. However, conventional methods like the fecal occult blood test (FOBT) exhibit limitations, with a false positive rate of 48% as observed in previous studies conducted in Aragón. Introducing rapid, non-invasive diagnostic tools alongside FOBT could increase specificity and optimize patient management. Additionally, utilizing serum biomarkers like EBFT could enhance risk stratification, improve patient adherence, and contribute to personalized screening protocols.

The development of a sensitive and specific enzyme-linked immunosorbent assay (ELISA) for detecting BFT is underway. We have evidence of successful serum detection of EBFT in patients from CRC screening, using specific antibodies. The ultimate goal is to streamline healthcare resources by focusing on early detection and targeted interventions to mitigate the growing burden of CRC.

Advanced Computational Characterisation of Protein Dynamics, Conformational Stability and Ligand Interactions, Illustrated Through the HDAC8 Case Study

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Computational tools have become indispensable for the in-depth study of protein dynamics, conformational stability, and the influence of cofactors on structural integrity. In addition, these approaches provide a quantitative framework to characterize protein-ligand interactions and elucidate the mechanistic determinants of their impact on biological activity. HDAC8, a zinc-dependent histone deacetylase, exemplifies the utility of computational approaches. This enzyme adopts distinct conformational states depending on zinc coordination, which is essential for catalytic activity. Different 5-µs molecular dynamics replicas characterized structural dynamics and stability in zinc-bound and zinc-free states, revealing that zinc removal triggers widespread conformational changes, including reduced native contacts, altered secondary structure, and reorganization of catalytic residues, as well as higher heterogeneity and partial unfolding. Furthermore, selected molecules from in vitro screening were assessed through docking simulations to investigate whether stabilization of the inactive zinc-free state may function as an inhibition mechanism. This integrative strategy provides quantitative metrics and mechanistic insights into zinc-dependent stability and ligand-mediated modulation. By linking conformational dynamics with targeted small molecule binding, the approach illustrates the potential of advanced computational strategies for selective regulation of HDAC8 activity and rational inhibitor design.

Biomolecular Interactions: A journey Biophysics to Drug Discovery

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Current efforts in drug discovery and development benefit from the interplay of many disciplines. Thus, a comprehensive experimental biophysical characterization of a pharmacological protein target, together with thorough computational analysis, represent a suitable starting point for developing screening, validation, and optimization protocols to be applied throughout the complex and uncertain process of early drug discovery.

In the Biomolecular Interaction research line, we study the conformational and functional landscape of pharmacological protein targets to reveal crucial information that can later be used to identify small molecules capable of modulating the function of these targets and serving as candidates for the development of medicines for emerging diseases, rare diseases, neglected diseases, and aggravated diseases because of resistance or reduced efficacy.

We take advantage of LACRIMA, the Advanced Laboratory for Screening and Molecular Interactions of Aragon, which brings together advanced and unique experimental instrumentation in Biophysics, Biochemistry, Molecular Biology, and Cell Biology to gather valuable information through experiments, as well as CESAR, the Supercomputing Center of Aragon, with advanced computational resources to obtain information hardly accessible or inaccessible through experimentation on protein targets and their interactions.

Targeting HDAC8: A Novel Approach to Overcome Drug Resistance in Melanoma Treatment

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Melanoma is the deadliest form of skin cancer, and its incidence has been increasing significantly over the past few decades. Melanoma develops from melanocytes, which are highly differentiated cells producing melanin, a macromolecule that protects against UV induced damage. Despite advances in melanoma therapy, adverse effects from cumulative toxicity and reduced efficiency due to development of drug resistance represent considerable barriers for current melanoma treatment strategies. Hypoacetylation has recently been identified as a common characteristic of many cancers, including melanoma. Histone deacetylases (HDAC) are involved in the deacetylation of lysine residues of histones during chromatin remodelling. These epigenetic alterations supress transcription of diverse genes In particula r, h istone deacetylase 8 (HDAC8), a class I HDAC, has a fundamental role in the progression of melanoma by enhancing cell proliferation and metastasis , participating in cancer development by interacting with histone and non histone proteins. Exposure of melanoma cells to stress conditions (hypoxia, UV damage, etc. lead to an increase in HDAC8 expression and the adoption of a drug resistant phenotype. We have identified several compounds with potential HDAC8 inhibitory effects. All these compounds interact with HDAC8 and modulate its activity and conformational stability. The discovery of potent HDAC8 inhibitors is a promising strategy to limit melanoma cell s plasticity , thereby improving therapeutic responses.

Towards c-Myc inhibition

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The rising incidence of cancer and the urgent need for targeted therapies represent major global health challenges. The transcription factor c-Myc, a member of the MYC protein family, plays a central role in many cancers by regulating cell growth, proliferation, tumorigenesis, and stem cell processes. Its importance is underscored by the fact that c-Myc expression is deregulated in up to 70% of human cancers.

One promising therapeutic strategy is the inhibition of c-Myc using small molecules. However, this approach remains challenging due to its intrinsically disordered regions, the absence of well-defined hydrophobic binding pockets, and its complex interactions with partner proteins and DNA. Consequently, novel targeted molecular strategies are required to develop effective therapies with reduced side effects.

To this end, full-length c-Myc and selected truncated constructs have been expressed in E. coli and purified using fast-performance liquid chromatography. These proteins are being characterized using calorimetric and spectroscopic techniques. In parallel, a tailored high-throughput screening is being optimized for the full-length protein, and several small-molecule inhibitors targeting the c-Myc NLS have been identified. Their therapeutic potential is currently being evaluated in cellular models. Here, we present some of our results from this challenging endeavor.

Mimicking patient-derived polymorphs of tau and α-synuclein with recombinant full-length protein: cross-seeding in pathologies origin

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Protein misfolding into amyloid fibrils underlies multiple neurodegenerative disorders. Specific proteins form disease-linked aggregates: α-synuclein (α-syn) in synucleinopa-thies and tau in tauopathies. Advances in cryo-electron microscopy (cryo-EM) have re-vealed numerous polymorphs of both proteins, enabling correlations between patient-derived α-syn or tau structures and distinct diseases in each group. However, major structural differences between brain-derived and in-vitro aggregates highlight the diffi-culty of reproducing physiological aggregation pathways.

Recently, in-vitro conditions have been established to aggregate recombinant tau frag-ments that mimic certain patient-derived polymorphs. We have now developed condi-tions that enable full-length recombinant tau to form aggregates closely resembling pa-tient-derived structures. This is important because tau's terminal regions critically influ-ence amyloid elongation, allowing these lab-generated polymorphs to be used in spreading studies.

For α-syn, we propose that cross-seeding of α-syn onto tau aggregates—more aggrega-tion-prone than α-syn—may initiate α-syn amyloid formation and propagation. Our la-boratory has tested the cross-seeding abilities of multiple tau polymorphs, aggregated in-vitro from full-length tau or tau fragments, with recombinant wild-type α-syn mono-mers and in HEK cells overexpressing wild-type α-syn. Using cryo-EM, we aim to identify tau structural features that enable cross-seeding and to assess the relevance of the re-sulting cross-aggregates.

Protein phase transitions in health and disease

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Protein phase transitions, i.e. changes in the physical state of proteins between soluble, condensed, and aggregated forms, have emerged as fundamental regulators of cellular organization and function. These dynamic transitions enable the formation of membraneless organelles and support key biological processes, yet their dysregulation can drive pathological aggregation implicated in numerous diseases such as Alzheimer´s and Parkinson´s disease. Understanding how proteins transition between functional soluble or condensated states and harmful assemblies is therefore crucial for uncovering the molecular underpinnings of both health and disease and for identifying new therapeutic strategies. Our lab is devoted to shedding 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.

Mechanical characterization of alpha-synuclein and Tau assemblies in cell models using Brillouin microscopy

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The study of macromolecular phase separation has transformed our understanding of cellular mechanisms involved in neurodegenerative disease development. Many intrin-sically disordered proteins can undergo phase separation, forming biomolecular con-densates through weak, multivalent interactions. The transition of these fluid-like con-densates into solid aggregates may represent an early step in the aggregation of amy-loid-prone proteins such as α-synuclein (αS) and Tau, contributing to disorders including Parkinson's and Alzheimer's disease.

The mechanisms driving these phase transitions remain poorly understood, and identi-fying such structures in cells is still challenging. Brillouin microscopy, a non-invasive op-tical technique that measures the interaction between light and acoustic phonons, of-fers a powerful way to quantify the mechanical properties of protein condensates, alt-hough its use has been limited.

Here, we established cellular models containing a spectrum of Tau and αS condensates and characterized them using Brillouin microscopy according to their mechanical prop-erties, including viscosity and elasticity. This approach allowed us to classify them as dynamic, fluid-like condensates or rigid, amyloid-like structures, providing insight into their pathogenic potential. Importantly, this is the first time that condensates of this size, approaching the optical resolution limit, have been mechanically characterized in cells, representing a significant advance for the cellular application of Brillouin micros-copy and for understanding the behavior of biomolecular condensates.

Structural requirements of the autophagy receptor p62 and polyubiquitin chains in biomolecular condensate assembly

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Cellular proteostasis is maintained by an elaborate network of protein quality control components, such as molecular chaperones, the ubiquitination machinery, the proteasome and the autophagy-lysosome pathway, to ensure the proper synthesis, folding and degradation of proteins. Particularly in autophagy, a membrane organelle termed the autophagosome engulfs cytoplasmatic material and subsequently fuses with the lysosome to degrade its content. Recently, phase separation has been proposed to be an important mechanism in this context since several components of the autophagy machinery concentrate in biomolecular condensates. One of the main drivers of this process is the autophagy receptor p62 which is believed to oligomerize in the cell forming filaments. However, it remains unclear how these filaments bind to polyubiquitinated proteins to mediate selective autophagy. Our aim is to decipher the interactions between p62 structural assemblies and polyubiquitin chains that drive biomolecular condensate formation. By structurally characterizing both components in vitro, we seek to define how multivalent p62-polyUb binding organizes and stabilizes autophagy condensates, which are key to preserve cellular homeostasis.

Ongoing research in the “Physical Modeling of Biomolecules” research line at BIFI

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I will overview the research activity of the three 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.

Synchronization features in a realistic model of CA1 pyramidal neurons

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The mammalian allocortical hippocampus plays important roles in cognitive function as in short-term and long-term memory and their connection with spatial navigation and emotional response.
The CA1 pyramidal neurons of the hippocampus are fundamental as communication junctions as they receive two different sets of inputs: those arriving directly from the entorhinal cortex (the so-called perforant path), and those from the CA3 neurons, which receive the signal from the granule cells (GD) that in turn receive the signals again from the entorhinal cortex, forming the so-called trisynaptic path. Here, a realistic model of CA1 neuron is presented both morphologically and dynamically under an Hodgkin-Huxley dynamics. The excitatory synapses are distributed along the spatially extended neuron in both proximal or distal areas with respect to the soma. The synchronization is studied by using a correlation function based on the phase-difference between spikes, and investigated as a function of various parameters such as the relative distance from the soma, the inhibition weight and its associated activation delays, and excitatory inactivation delay. We found that the neurons' spiking activity depends non-monotonically on the relative dendritic location of the synapses and their inhibition weight, while the synchronization strongly depends on the excitatory inactivation time.

Position-weighted sequence distance for LNA-aware alignment, genomic networks and probe design

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Locked nucleic acids (LNAs) strongly increase duplex stability and mismatch discrimination, so mismatches at LNA positions are far more critical than at unmodified sites. However, most alignment tools treat all positions equally. We present a position-weighted framework in which the user can decide which sites matter most, and the metric adapts accordingly.

We encode each sequence window into a short numerical vector using simple weights based on prime numbers. Positions assigned small primes (e.g. LNA sites) have a stronger impact on the distance between two sequences, so mismatches there dominate the comparison. Using this distance, we build genomic networks where nodes are windows and edges link pairs that share at least n important positions. The parameter n acts as a resolution knob: low n reveals broad similarity patterns, while high n isolates highly conserved or repeated motifs. A local, label-guided walk on this network allows us to quickly find genomic regions that match a given LNA-containing probe along the user-selected positions.

With this approach, we can use simulated annealing to design probes that avoid close matches anywhere in the genome. This provides an integrated, LNA-aware pipeline for both searching and designing oligonucleotides.

Modulating 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 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.

Structural and Functional Determinants of Endocannabinoid Modulation at the *hCB1* Receptor

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The *human cannabinoid receptor 1 (hCB1)* is a class A GPCR activated by endocannabinoids and phytocannabinoids, widely expressed in the PNS and CNS. Its central role in neurophysiological regulation makes it a key pharmacological target for treating addiction, pain, epilepsy, and obesity. To investigate how the endogenous ligands *2-arachidonoylglycerol (2-AG)* and *anandamide* may differentially modulate *hCB1* activity, this project aims to elucidate the structural and functional determinants underlying their engagement with the receptor. Because endocannabinoids are metabolically unstable and exhibit low potency, we also employ synthetic analogues with improved properties.

Our objective is to characterize how each ligand binds to *hCB1* and how these interactions translate into distinct activation outcomes. To this end, we combine cryo-electron microscopy, which provides high-resolution views of ligand-bound receptor conformations, with cell-based signaling assays that measure downstream pathway activation. Integrating these approaches allows us to directly connect binding modes with functional responses, providing molecular insights to understand differences in endocannabinoid signaling at *hCB1*.

By clarifying how *2-AG* and *anandamide*, despite their structural similarity, engage and modulate *hCB1* in different ways, this work aims to advance our understanding of endocannabinoid signaling. These insights may also guide the development of pharmacological probes and therapeutics inspired by endogenous ligand architectures.

A ligand-triggered receptor conformation enables the design of selective agonists for the dopamine 3 receptor using a bitopic strategy

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While G protein-coupled receptors (GPCRs) represent the largest drug target family, designing subtype-selective molecules is still a challenge, especially to distinguish among closely related subtypes. One of the most challenging cases is the distinction between dopamine D2R and D3R, pivotal receptors in motor functions and cognition, and targets of Parkinson's disease treatments, schizophrenia or substance abuse disorders. Attempts to design D3R selective molecules with ligands binding towards the first transmembrane helix (the most sequence diverse and conformationally flexible segment in GPCRs but rarely participating in ligand binding) allowed us to discover a ligand-induced ordering of TM1 unique to D3R, yielding an unexploited selectivity site for drug development. Using rational bitopic drug design and the ligand-triggered conformation of the D3R we designed, synthesized and characterized the most selective D3R agonists to date, >100,000s-fold more selective than available ligands. More specifically, we report D3R partial agonists AB12-82 (6d) and AB13-73A (6j), with >575,000- and >1,000,000-fold subtype selectivity, picomolar potency and 82% and 48% efficacy, respectively. We also present the most selective full agonists reported to date, AB13-08 (4b) and AB13-46A (9), presenting low and sub-nanomolar potencies with >2,800 and >6,300-fold selectivity for D3R. Overall, we introduce a first-in-class pharmacological toolbox to dissect the (patho)-physiology of D3R, open new avenues for the design of improved neurotherapeutics, and show that using ligand-induced TM1 reorganizations might represent a promising strategy for the design of subtype-selective molecules in other GPCRs.

Dissecting Glutamate Receptors: structure, dynamics and biogenesis

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In this talk I will summarize the recent advances of the research line “Structural Biology of neuronal membrane receptors”. The group is currently exploring the structure of AMPA-type Glutamate receptors, which are key mediators of fast excitatory neurotransmission and memory formation. Subunit composition determines the receptor gating properties, generating a plethora of receptor functions which profoundly impacts signal processing in the brain. The group has focused on GluA2-lacking AMPA receptors, which display unique structural properties, which mostly involve receptor dynamics. I present our current approaches to generate modulators trapping subunit-specific conformations, as well as the biochemical characterization of the AMPAR biogenesis pathway.

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From monomers to tetramers: ER-associated proteins drive AMPA receptor assembly

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AMPA receptors (AMPARs) are glutamate-gated ion channels essential for fast excitatory neurotransmission. Their assembly into functional tetramers occurs in the endoplasmic reticulum (ER), where ER-associated partners regulate receptor biogenesis. Among these, ABHD6, FRRS1L, and CPT1C modulate early oligomerization steps, yet their precise roles remain unclear. Here, we combine biochemical reconstitution and cryo-electron microscopy (cryo-EM) to characterize the molecular interactions driving AMPAR assembly.

Native gels show that ABHD6 recruits monomeric GluA subunits (GluA1–4), both full-length and ΔNTD (N-terminal domain) variants. However, ΔNTD constructs display weak dimer bands, indicating that the ligand-binding (LBD) and transmembrane (TMD) domains are sufficient for early GluA oligomerization and mediate the ABHD6–GluA interaction. Cryo-EM of ABHD6–GluA reveal heterogeneous particles, likely reflecting aggregation or dissociation upon vitrification, limiting high-resolution analysis. To stabilize these complexes, we have initiated the generation of anti-ABHD6 and anti-GluA4 nanobodies through Instruct-ERIC.

In contrast, purification of FRRS1L–GluA1 yields well-defined GluA1 tetramers. Particles classify into two populations: isolated GluA1 tetramers and FRRS1L–GluA1 complexes. Deletion of residues 30–93 together with the TMD in FRRS1L is sufficient for complex formation, indicating a minimal interaction interface. Ongoing surface-expression assays aim to determine whether this complex remains ER-retained.

Collectively, these data provide mechanistic insight into the ER-stage organization of AMPAR biogenesis.

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GluA4 AMPA Receptors in Motion: Molecular Architecture Across the Gating Cycle

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AMPA receptors (AMPARs), members of the ionotropic glutamate receptor family, are ligand-gated cation channels that mediate fast excitatory synaptic transmission and support synaptic plasticity. They assemble as tetramers from GluA1–GluA4 subunits and associate with auxiliary proteins such as TARPs, CKAMPs, GSG1L and CNIH, which fine-tune their gating kinetics and pharmacological properties. Because of their central role in excitatory synaptic function, AMPAR complexes are among the major therapeutic targets in neurological disease.

Here, we use cryo-EM to determine the structure of a relatively unexplored AMPAR subtype, GluA4-containing receptors, analysed both in isolation and in complex with the auxiliary subunit TARP-g2, and captured in multiple conformational states along the gating cycle. In the resting state, the GluA4 core adopts a modular Y-shaped architecture and assembles as a dimer of dimers, similarly to GluA2-containing receptors. However, we observe pronounced deviations from this canonical organization as the receptor progresses through the gating cycle. In particular, as reported for GluA1 and GluA3, we detect disruption of dimer interfaces within the ligand-binding domain (LBD) in particles corresponding to the desensitized state. This disruption is less pronounced in edited GluA4:g2 R/G receptors and markedly stronger in the absence of TARP-g2 than in unedited GluA4:g2 R/G receptors. In addition, we identify a previously unrecognized regulatory site involved in TARP-g2–dependent modulation of GluA4 receptors.

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Towards in Quantum Computing: The QuantumSpain Project

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Quantum computing harnesses quantum mechanics to solve certain problems exponentially faster than classical computers. This introduction covers fundamental concepts including qubits, superposition, entanglement, quantum gates, and measurement—the building blocks of quantum computation. We will explore how these principles enable quantum algorithms to efficiently tackle complex problems in cryptography, optimization, and simulation. The discussion includes major quantum computing architectures: superconducting qubits, trapped ions, and topological quantum computers. We examine the current state of quantum hardware and software development, along with practical applications and future directions for this emerging technology. The presentation uses intuitive explanations accessible to both physicists and non-physicists, requiring no prior quantum mechanics knowledge. This overview highlights quantum computing transformative potential across scientific and technological domains, providing a comprehensive introduction for experts and newcomers alike.

Launching MolSysSuite: Foundational Tools for a Modern, Unified Ecosystem for Working with Molecular System Models in Drug Design Workflows

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MolSysSuite is a new open-source ecosystem designed to modernize and streamline computational workflows for molecular modeling, molecular dynamics, and structure-based early drug discovery. In this presentation, we will introduce the foundational components that mark the beginning of the project: MolSysMT (Molecular Systems MultiToolkit) and MolSysViewer (Molecular Systems Viewer). MolSysMT provides a unified and consistent Python interface for loading, manipulating, transforming, and analyzing molecular systems and trajectories across a wide range of formats and software toolchains. MolSysViewer complements this core functionality with a modern Mol*-based interactive visualization environment fully integrated into Python, Jupyter notebooks, and web documentation. Together, they illustrate a contemporary alternative to the fragmented legacy workflows that have long dominated the field.

Additional modules currently in development, such as TopoMT for cavity and topography analysis, ElastNetMT for elastic network models, and PharmacophoreMT for pharmacophore extraction, further expand the analytical breadth of the ecosystem. By bringing these tools together within a coherent architecture, MolSysSuite aims to make advanced computational methods more accessible for researchers across computational biophysics, chemistry, and structural biology.

Magnetic Hyperthermia Directed to Mitochondria: Effects on OXPHOS Organization and Anticancer Response

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New therapeutic approaches are urgently needed in the fight against cancer, and a deeper understanding of tumor metabolism is essential. Hyperthermia (HT) directly targets the intrinsic thermal vulnerability of tumor cells, mitochondria, and cancerous tissues. Although HT is known to induce cytotoxicity and sensitize tumors to conventional therapies, its mechanisms of action remain only partially understood. In this work, we investigate the impact of HT from a mitochondrial perspective, focusing on how thermal stress affects OXPHOS organization and functionality, as well as broader tumor-associated processes that lead to regulated forms of cell death.

A central objective is the development of an intracellular and localized HT strategy. For this purpose, we employ iron oxide magnetic nanoparticles functionalized with antibodies and ligands to achieve selective targeting of cancer cells and mitochondrial accumulation. Upon exposure to alternating magnetic fields, these nanoheaters generate localized temperature increases, enabling controlled magnetic HT at the subcellular level.

In parallel, we implement nanothermometers consisting of lanthanide-based micellar probes (Sm^{3+}/Eu^{3+}) that can be internalized by cells. Their luminescent properties allow absolute temperature measurements with high spatial and temporal resolution. This system will enable precise mapping of intracellular thermal gradients, determination of mitochondrial thermal thresholds, and real-time monitoring of temperatures reached by nanoheaters during magnetic HT.

Molecular determinants of mitochondrial gene expression

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Mitochondrial translation is a key regulatory point for cellular bioenergetics, as the 13 mtDNA-encoded proteins are essential components of the OXPHOS system. The expression of these proteins inside the organelle is coupled with the import of nuclear encoded subunits and the assembly of respiratory chain complexes in the inner mitochondrial membranes. In addition, mitochondrial translation is integrated in the cellular context, not only in a physiological state but also in diseased conditions.

The last insights in molecular processes, within and outside mitochondria, that modulate mitochondrial gene expression in physiopathological conditions will be presented.

Kinase Regulation of Mitochondrial Translation: Functional Insights into eEF2K Silencing

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Mitochondrial translation is a key regulatory point for cellular bioenergetics, as the 13 mtDNA-encoded proteins are essential components of the OXPHOS system. Recent kinase-screening studies have revealed that multiple signaling pathways dynamically modulate mitochondrial protein synthesis. Among the identified regulators, the elongation factor 2 kinase (eEF2K) emerged as a modulator whose inhibition enhances mitochondrial translation.

In this project, we investigated the functional consequences of eEF2K silencing in human HEK293T cells, with a focus on mitochondrial performance and cellular processes relevant to tumor biology. Given that eEF2K is overexpressed in several cancers and supports survival under metabolic stress, we aim to determine whether its inhibition alters mitochondrial activity and the expression of cancer-associated markers.

Our work provides initial insight into how eEF2K connects cytosolic translation control with mitochondrial function and may contribute to understanding its role in cancer metabolism and potential therapeutic targeting.

Dissecting the tissue-specific mechanisms involved in mitochondrial protein synthesis defects

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Mitochondrial DNA (mtDNA) encodes for thirteen protein subunits that are part of the oxidative phosphorylation system (OXPHOS) as well as other components involved in their synthesis within the organelle (2 rRNAs and 22 tRNAs). These proteins play an essential role in the production of cellular energy in the form of ATP. Mutations in different steps of the mitochondrial protein synthesis are associated with severe disorders commonly characterized by a multisystemic phenotype. However, despite the presence of mitochondria in all the cells of the human body, there are patients in whom only a specific group or a single tissue is affected and contributes to the patients´ phenotype. This is the case of certain mutations in the mitochondrial translation elongation factor (*TSFM*) gene, associated with ataxia and cardiomyopathy. The causes of this tissue specificity are still under debate. By using different cell models, including fibroblasts, induced pluripotent stem cells (iPSCs) and iPSCs-derive cardiomyocytes cells among others, we characterized the molecular and biochemical defects behind a specific mutation at mitochondrial protein synthesis level and the possible compensatory mechanisms behind the tissue specificity.

Ongoing experimental and computational research on genes and proteins

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I will provide an overview and summary of experimental and computational research done in my group for the past year. This will include advances in protein stability design, phenotypic variant interpretation, simulation of protein folding thermodynamics and experimental approaches to develop novel therapeutics for phenylketonuria.

Rapid Protein Stabilization with Protposer: Flavodoxin and Aspergillopepsin I as models

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Improving protein stability is essential for applications in biotechnology, industry and biomedicine, where proteins must operate reliably under demanding conditions. Computational methods play a key role in predicting mutations likely to enhance conformational robustness. Protposer is a practical tool that ranks probable stabilizing mutations, enabling the efficient design of improved protein variants.

Protposer was applied to apoflavodoxin, a flavoprotein already extensively stabilized in our laboratory. Starting from the engineered 6M variant, we introduced top-ranked Protposer mutations individually and in combination. This workflow generated several more stable constructs, including the 10M mutant, which showed an increase of nearly 9 °C in melting temperature. Optimized variants 3M and 4M exhibited ΔTm values of 6-8 °C, strong refolding reversibility and retention of electron-transfer activity.

The same strategy was applied to aspergillopepsin I, an acid protease used in food processing. Protposer-selected mutations generated single-mutant variants with measurable thermal improvements, including Tm increases of 1.1 °C and 0.9 °C relative to the wild type. These constructs maintained catalytic activity under acidic conditions and showed improved resistance to process-relevant temperatures. Because each stabilized variant carries only one mutation, their effects can now be combined to produce more robust variants, underscoring the versatility and industrial relevance of Protposer-guided protein engineering.

Toward First-Principles Folding Thermodynamics: Benchmarking Protein and Solvent Entropy Methods

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Protein folding is driven by a delicate balance of enthalpic and entropic contributions, yet computational studies have not fully dissected their individual roles. In prior work, our group calculated ΔH and ΔCp from molecular dynamics simulations combined with experimental melting temperatures (Galano-Frutos et al., 2024), enabling reliable estimates of ΔG. However, a first-principles description of folding energetics also requires ΔS, which must be computed by estimating the conformational space rather than output directly by MD engines.

Here, we benchmark several computationally intensive approaches to estimate conformational entropy changes during protein folding, considering the protein, the surrounding solvent, and the system as a whole. We evaluate methods such as quasiharmonic analysis and elastic network models for the protein, permutation-reduction combined with mutual information expansion, as well as Density of States, for water, and Multiscale Cell Correlation for both components. For each technique, we assess accuracy, convergence behavior, and computational cost. Together, these results lay the groundwork for an automated pipeline enabling comprehensive enthalpy–entropy analyses in biomolecular simulations of folding proteins and their solvent.

Novel secondary regulators at the crossroad of nitrogen metabolism, stress response and biofilm formation in *Anabaena* sp. PCC7120.

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The filamentous cyanobacterium *Anabaena* sp. PCC7120 is an established system for studying prokaryotic multicellularity and biological nitrogen fixation. To simultaneously perform oxygen-evolving photosynthesis and atmospheric nitrogen fixation *Anabaena* develops specialized cells called heterocysts. Additionally, *Anabaena* is able to develop biofilms, a way of growth that confers increased resistance to adverse conditions. Transcriptome analysis comparing sessile and planktonic cultures of *Anabaena* showed that the biofilm state induces a widespread transcriptional reprogramming coupled with broad metabolic alterations, displaying a gene expression signature that mirrors multiple stress responses.

Biological nitrogen fixation and biofilm development are controlled by a plethora of transcriptional regulators, two-component systems and sigma factors. The roles of key players, such as the master regulator of nitrogen metabolism NtcA, and the stress-response FUR (ferric uptake regulator) family proteins are well documented. However, the definition of NtcA and FUR regulons have unveiled numerous uncharacterised secondary regulators that intertwine the modulation of biofilm formation, nitrogen metabolism and the response to several stresses. Our group has identified and characterized several novel regulators linking NtcA and FUR control of nitrogen metabolism and biofilm formation, including the novel secondary regulators NsrM, NsrX, and CalB, which contribute to the intertwining of regulatory and signaling pathways in cyanobacteria.

Nano-scale distribution of metals in filamentous cyanobacterium *Anabaena* sp. PCC7120

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Filamentous cyanobacterium *Anabaena* sp. PCC7120 is capable of fixing atmospheric nitrogen by differentiating specialized cells known as heterocysts, when combined sources are scarce [1]. Since oxygen-evolving photosynthesis is incompatible with nitrogen fixation by the nitrogenase complex, these two processes are compartmentalized in different cell types, each containing specialized protein machinery with specific and extensive metal cofactor requirements. The FUR (Ferric Uptake Regulator) transcriptional regulators of *Anabaena* (FurA, Zur and PerR) manage metal homeostasis [2], but they have also been described to participate in the regulation of photosynthesis, nitrogen fixation or redox homeostasis, processes which engage multiple metal cofactors [3–5]. In this work, synchrotron radiation X-ray fluorescence nano-imaging has been applied to wild-type *Anabaena* filaments under standard and nitrogen-fixing conditions, as well as filaments of FUR deregulation variant strains. Furthermore, samples grown as biofilms, sessile microbial communities embedded in a self-produced matrix, were analyzed to determine differences between cellular and matrix-bound metal content. Our results shed light on the spatial organization of essential trace elements under different metabolic needs, as well as the impact of the FUR regulators on both metal content and its distribution.

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Analysis of structural and functional diversity of LinA and LinB dehalogenases for bioremediation of HCH isomers

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The persistent and toxic organochlorine pesticide lindane (γ-HCH) and its recalcitrant isomers remain a global environmental challenge. Enzymatic bioremediation offers a sustainable solution, with the upstream dehalogenases LinA and LinB catalyzing the crucial initial steps of aerobic hexachlorocyclohexane degradation. These cofactor-free enzymes have diversified rapidly, giving rise to variants with distinct catalytic properties.

To leverage LinA variant diversity, we performed a comprehensive bioinformatics analysis of all UniProt entries annotated as LinA dehydrochlorinase, classifying them into different types based on sequence features. Experimentally verified sequences were used as templates in BLAST-P searches against bacterial, fungal and metagenome databases. All hits with significant homology were retrieved for multiple sequence alignments and phylogenetic tree construction, confirming the LinA type classifications.

Representative canonical and mutant variants from each group were selected for cloning and recombinant expression. Our ongoing work aims to purify these proteins and perform an in-depth biochemical characterization, comparing their catalytic efficiency, substrate range and enantioselectivity toward different HCH isomers. Parallel analysis of LinB variants will clarify upstream pathway diversity.

Our long-term goal is to define an optimized enzymatic cascade capable of efficiently degrading complex mixtures of HCH isomers, contributing to scalable and green bioremediation strategies.

Exploring Asymmetric Catalysis Mechanisms in Homodimeric Flavonzymes

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Homodimeric flavoenzymes consist of two identical subunits, each housing a flavin cofactor. The dynamics and synchronicity at the two active sites in these enzymes are critical for their functional regulation, impacting substrate binding kinetics and catalytic activity. In such enzymes, the subunits can operate either independently or in a coordinated manner during catalysis, with both subunits contributing to the formation of the active sites. A notable phenomenon in these enzymes is negative cooperativity, where substrate binding to one subunit reduces the affinity of the other subunit for the same substrate. This suggests a form of communication between the active sites, as binding alters the conformation or chemical environment of the other site. The molecular basis for this cooperative behaviour remains poorly understood, but it likely involves conformational changes driven by protein dynamics, substrate interactions, or the redox state of the flavin cofactor, which propagate throughout the protein structure. This discussion will highlight prominent examples of homodimeric flavoenzymes where allosteric behaviour significantly influences enzymatic activity, catalytic asymmetry and substrate turnover rates. By integrating multiscale molecular dynamics simulations with kinetics studies through time-resolved stopped-flow absorption spectroscopy and time-resolved serial femtosecond X-ray crystallography dynamic behaviours essential for catalysis will be revealed.

Functional and Structural Analysis of a Potential Alkene Reductase from Brucella ovis: toward the Development of a Novel Industrial Biocatalyst

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Brucella ovis, a Gram-negative bacterium causing ovine brucellosis, contains in its flavoproteome a predicted alkene reductase (BoAKR). Spectroscopic characterization revealed that BoAKR contains a redox-active FMN as a cofactor, which can be photoreduced. Its redox potentialwas determined by both xanthine oxidase method and cyclic voltammetry. Fluorescence and circular dichroism spectroscopies provided further insights into the protein's folding, environment and thermal stability. BoAKR was also successfully crystallized, and its structure was solved in the presence and absence of substrates.

Importantly, BoAKR shows the capacity to accept hydride from NAD(P)H, with NADH serving as the more efficient donor. The enzyme can be reduced in presence and absence of hydride acceptors. Catalytic activity was detected with sixteen out of the thirty tested compounds as potential hydride acceptors, all containing a C=C double bond conjugated to an electron withdrawing group. In addition, it is also able to reduce both aromatic and aliphatic compounds. For the most efficient compounds, we have also stablished kinetic parameters, both under steady-state and pre-steady-state conditions.

The broad substrate scope of BoAKR can be attributed to its large solvent-accessible active-site pocket which enables catalytic promiscuity while maintaining stereoselectivity. This propertymakes BoAKR a promising versatile biocatalyst for asymmetric reductions of diverse compounds.

Dissecting the role of AIF dimerization in mitochondrial homeostasis through its interaction with CHCHD4

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The mitochondrial disulfide relay system is essential for the import and oxidative folding of certain oxidative phosphorylation (OXPHOS) subunits within the intermembrane space (IMS)1. This process is mediated by the chaperone CHCHD4 (coiled-coil-helix-coiled-coil-helix domain-containing 4)1, which forms a stable complex with the apopto-sis-inducing factor (AIF), a moonlight flavoenzyme that displays a monomer–dimer equi-librium in the IMS2. This equilibrium is modulated by NADH oxidation, stabilization of a long-lived $FADH^-/NAD^+$ charge transfer complex (CTC), and subsequent AIF structural rearrangements3. AIFred-CHCHD4 interaction has been shown to serve as a platform to ensure CHCHD4 correct mitochondrial localization and competent substrate recogni-tion2, 4, 5.

In this study, we have provided a new perspective through biophysics and cellular ap-proaches about of the functional significance of AIF dimerization in its interaction with CHCHD4 and its influence on AIF redox properties, conformational state, stability and binding. For that we use the engineered AIF E413A/R422A/R430A variant (unable to di-merize upon NADH binding)3, and the H454A variant (with a dimer conformation in the absence of NADH)6. Furthermore, we evaluated a peptide derived from the CHCHD4 N-terminal domain as an attractive therapeutic tool to diminish the redox effects associ-ated with the pathogenic R422Q variant.

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COTEGIN (Comprehensive Organized Tool for Expression and Gene Interaction Networks): An Integrated Bioinformatics Platform for Advanced Transcriptomic Analysis

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COTEGIN (Comprehensive Organized Tool for Expression and Gene Interaction Networks) is an integrated bioinformatics platform designed to streamline all major stages of RNA-seq analysis within a single, user-friendly Python interface. The system unifies alignment, quantification, filtering, differential expression, correlation, and differential coexpression (Δ-coexpression) into a fully reproducible workflow powered by Docker containers and scalable to HPC environments such as BIFI-Colossus.

COTEGIN provides advanced analytical modules including automated Ensembl metadata enrichment, PCA-based exploratory analysis, and construction of gene coexpression and Δ-coexpression networks using NetworkX with real-time visual previews. Networks can be exported directly to Cytoscape for downstream structural and functional analyses. The platform also incorporates a project-oriented architecture with persistent settings, progress monitoring, multi-thread management, and compatibility with large-scale datasets.

By lowering technical barriers, COTEGIN enables researchers with limited computational background to perform robust transcriptomic analyses while maintaining full reproducibility and methodological transparency. Its design is especially suited for studies focused on cancer, lncRNA biology, immune–tumor interactions, and complex cellular phenotypes, where network-level insights are essential for identifying regulatory modules and generating biologically meaningful hypotheses.

COTEGIN aims to bridge experimental biology with modern computational genomics, accelerating discovery and improving the interpretability of high-dimensional transcriptomic data.

POSTERS

Wednesday January 14th

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2	Alejandra Carrancho	Mechanical characterization of alpha-synuclein and Tau assemblies in cell models using Brillouin microscopy
3	Alejandra Rada	Information Theory in Opinion Dynamics Modeling Considering Polarization
4	Alejandro Sáinz Agost	Study of the dynamic structure of a polymer model of chromatin in mechanically deformed nucleus.
5	Alicia Mairo	Understanding the Molecular Determinants that Drive Aging in Tau Condensates
6	Ángela Carrión Antolí	Ligand Binding Induces a Disorder to Order Activation Switch in GPR15
7	Blanca Viguri	Structural requirements of the autophagy receptor p62 and polyubiquitin chains in biomolecular condensate assembly
8	Carlos Bruno de Araujo	Structural insights into the neuroprotective potential of hydroxytyrosol and its metabolites: a molecular docking and dynamics study
9	Cristina Lázaro	A Conformation-altering Mutation in TXDNC15 Linked to the Joubert Syndrome
10	Daniel Muñoz Reyes	Decoding constitutive activity in orphan GPCRs: basal activation GPR26 and GPR78
11	David Ortega Alarcón	Expanding the Druggable Proteome: High-Throughput Identification of Inhibitors Against Relevant IDPs
12	David Polanco	Assessing network stabilization of aging Tau/α-Synuclein biomolecular condensates
13	Diego Morales	Identification, purification, and characterization of enzymes involved in the lindane degradation pathway.
14	Ester Raigón Gómez	Metastatic homing shapes gene expression and immune infiltration in colorectal cancer
15	Guillermo Gil Martín	AI-driven protein binder design targeting GPCRs using BinderFlow
16	Irene Blasco Machín	Cancer targeting through rationally designed EGFR-binding peptides
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19	Jorge Arruego	Impact of the deletion of calB on the physiology of Anabaena sp. PCC7120
20	Ana Flores Charlez	GlobalPred: A user-friendly tool for the interpretation of single nucleotide variants in coding regions
21	Alejandro Pérez LaTorre	From bacterial to fungal mucinases: discovering a new Beauveria enzyme with broad O-glycan specificity

Thursday January 15th

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23	Karinna Pele	Mechanisms of Phase Separation and Ageing in Multicomponent Protein Condensates
24	Laia Mata Ríos	Unraveling the role of accessory proteins in G-protein coupled receptor signalling
25	Laura Asín	Developing cell models to study condensate formation and maturation in neurodegeneration via Brillouin microscopy.
26	Luis Mariano Esteban Escaño	Impact of Comorbidity Clusters on Survival in Patients Awaiting Liver Transplantation: A Sex-Stratified Analysis
27	Marco Fernández da Silva	COARSENET
28	María Gabriela Álvarez-Rodríguez	Salvianolic acid: an effective natural enhancer of PADI4 activity
29	María Martínez	Unravelling the Molecular Drivers of α-Synuclein Nucleation into Amyloid Aggregates in Parkinson´s disease
30	María Martínez Alfaya	Negative modulation of mitochondrial gene expression by cellular kinases
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32	Marta Acero Enguita	The alr7637 gene of Anabaena (Nostoc) sp. PCC 7120 is a MerR family regulator of FUR regulatory network that responds to heavy metals
33	Marta Asencio del Rio	Identification of Novel Antibiotics Targeting Zinc-Dependent Vulnerabilities of LpxC
34	Marta Espejel	AI-Enhanced Detection of α-Synuclein Aggregates for Parkinson's disease Diagnostic Applications
35	Miguel Ferrer	Integrated Mechanistic Characterization of the Pathogenic AIFM1 Variant E336K
36	Mónica Bescós Zaborras	Tissue-specificity of cellular kinases regulating mitochondrial translation
37	Paula Cinca	Bacterial Aryl-Alcohol Oxidases as Emerging Biocatalysts for Selective Oxidations
38	Pierpaolo Bruscolini	Biotechnological applications of 1D exactly solvable models
39	Rocío Aznar Gimeno	AI Models for Detecting Diseases and Conditions Using Sensor Fusion
40	Teresa Bes Fustero	Disentangling the metalloregulatory interconnections of (FUR) proteins in the control of biofilm generation and nitrogen metabolism in Anabaena sp. PCC7120
41	Victoria Ribón Fuster	Development of AMPA Receptor nanobodies: capturing functional states for modulation and structural analysis
42	Helena García Cebollada	reMoDA: A Python library for automatic relaxation Molecular Dynamics Analysis
43	Mateo Bouchet	Directed Interlayer Diffusion Generates Superdiffusion and Jamming in Multiplex Networks

Poster 1
Dynamics of Defensive and Malicious Worm Co-Propagation across Networked Systems

Andreia Sofia Teixeira[1,2], Ignacio Echegoyen[3], Rasha Shanaz[4], Alberto Aleta[5]

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The rapid growth of the Internet of Things (IoT) has expanded the attack surface of networked systems. To counter self-propagating malware ("black worms"), researchers have proposed using "white worms"—benign, self-replicating programs that move through networks to alert owners, assist with patching, and autonomously secure vulnerable devices. This concept highlights a key tension: the more a defensive agent adheres to ethical limits on autonomy and system modification, the less effective it may be at stopping malicious activity. This work formalizes and quantifies that trade-off.

We develop a co-propagation model for a malicious worm and an ethically constrained white worm using a network epidemiology framework. Under homogeneous mixing, we derive expressions for reproduction numbers and thresholds for botnet emergence. We then analyze spread on networks with different topologies and show that structure strongly shapes outcomes. In heterogeneous networks, the malicious worm's advantage on high-degree nodes increases defensive burden, producing larger and longer-lived botnets under the same ethical constraints. However, if white worms reach hubs early and act quickly, they significantly reduce botnet size and duration.

Overall, the results expose a design dilemma: effective autonomous defense may require levels of initiative that challenge the goal of minimally invasive agents.

Poster 2

Mechanical characterization of alpha-synuclein and Tau assemblies in cell models using Brillouin microscopy

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The study of macromolecular phase separation has transformed our understanding of cellular mechanisms involved in neurodegenerative disease development. Many intrinsically disordered proteins can undergo phase separation, forming biomolecular condensates through weak, multivalent interactions. The transition of these fluid-like condensates into solid aggregates may represent an early step in the aggregation of amy loid-prone proteins such as α-synuclein (αS) and Tau, contributing to disorders including Parkinson's and Alzheimer's disease.

The mechanisms driving these phase transitions remain poorly understood, and identifying such structures in cells is still challenging. Brillouin microscopy, a non-invasive optical technique that measures the interaction between light and acoustic phonons, offers a powerful way to quantify the mechanical properties of protein condensates, although its use has been limited.

Here, we established cellular models containing a spectrum of Tau and αS condensates and characterized them using Brillouin microscopy according to their mechanical properties, including viscosity and elasticity. This approach allowed us to classify them as dynamic, fluid-like condensates or rigid, amyloid-like structures, providing insight into their pathogenic potential. Importantly, this is the first time that condensates of this size, approaching the optical resolution limit, have been mechanically characterized in cells, representing a significant advance for the cellular application of Brillouin microscopy and for understanding the behavior of biomolecular condensates.

Poster 3

Information Theory in Opinion Dynamics Modeling Considering Polarization

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We present a computational model that uses information entropy and the Jensen–Shannon divergence to simulate the diffusion of opinions under conditions of distortion and polarization. The model reveals that without exposure to competing views, a non-polarized population tends to adopt the bias of a single influential group. This dynamic mirrors the formation of echo chambers, where a lack of opposing information leads to ideological conformity.

Poster 4

Study of the dynamic structure of a polymer model of chromatin in mechanically deformed nucleus

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Understanding nuclear chromatin structure and dynamics is important for gaining insight into processes such as gene regulation and cell fate decisions in developmental biology, as well as other processes such as epigenetic modifications [1]. This motivates us to study how chromatin changes when the nucleus deforms under mechanical forces, with a particular focus on cell migration. This is a fundamental physiological function that also plays a central role in pathological processes, particularly in cancer metastasis, where cancer cells deform extensively to pass through narrow constrictions and invade distant tissues. In this poster, we present and analyze a polymeric model of chromatin with the aim of understanding some of the changes in its structure and dynamics when the nucleus undergoes this kind of deformations [2]. We analyze changes in chromatin structure in relation to the different interactions present in the model. This enables us to determine which interactions are most relevant when interpreting the experimental results of cell migration [3].

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Poster 5
Understanding the Molecular Determinants that Drive Aging in Tau Condensates

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Protein phase separation is a key mechanism for cellular organization, and many intrinsically disordered proteins, such as Tau, can form condensates whose dynamic behavior is relevant for understanding their function and their possible involvement in neurodegenerative diseases. Since Tau can aggregate into amyloid structures associated with these disorders, it is important to characterize how the properties of its condensates influence their stability and temporal evolution.

In this work, we analyze the aging of condensates formed by full-length Tau and by truncated variants that preserve the same overall valency but differ in length and in the distribution of charged regions. This approach allows us to evaluate how these structural differences modulate the changes experienced by the internal network during the progressive stabilization of the condensate. Using confocal fluorescence microscopy and time-resolved stability assays, we characterize their dynamic behavior and evolution over time.

These findings provide a broader perspective on the aging process of protein condensates and on how certain molecular properties may influence their overall behavior.

Poster 6

Ligand Binding Induces a Disorder to Order Activation Switch in GPR15

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GPR15 is a G protein-coupled receptor (GPCR) involved in immune system regulation, including lymphocyte homing to epithelial barriers and modulation of inflammatory responses. Despite its physiological significance, the structural basis of GPR15 signaling remains poorly understood.

Using cryo-electron microscopy, we determined the structure of GPR15 in complex with a heterotrimeric GαO protein, revealing unique features that distinguish it from other GPCRs. Notably, the G protein engages the receptor at an atypical angle, differing from canonical coupling modes. Meanwhile, the peptide ligand binds in a distinctive “hook-like” configuration.

In the absence of ligand, the orthosteric pocket, especially in the extracellular regions of TM1 and TM7, exhibits increased flexibility, as shown by poor cryo-EM density and elevated root mean square fluctuations (RMSF) from molecular dynamics simulations. Ligand binding stabilizes this region, suggesting that ligand–receptor interactions play a key role in shaping the orthosteric site.

These findings provide new insights into the structural and functional biology of GPR15, offering a framework for therapeutic development.

Poster 7

Structural requirements of the autophagy receptor p62 and polyubiquitin chains in biomolecular condensate assembly

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Cellular proteostasis is maintained by an elaborate network of protein quality control components, such as molecular chaperones, the ubiquitination machinery, the proteasome and the autophagy-lysosome pathway, to ensure the proper synthesis, folding and degradation of proteins. Particularly in autophagy, a membrane organelle termed the autophagosome engulfs cytoplasmatic material and subsequently fuses with the lysosome to degrade its content. Recently, phase separation has been proposed to be an important mechanism in this context since several components of the autophagy machinery concentrate in biomolecular condensates. One of the main drivers of this process is the autophagy receptor p62 which is believed to oligomerize in the cell forming filaments. However, it remains unclear how these filaments bind to polyubiquitinated proteins to mediate selective autophagy. Our aim is to decipher the interactions between p62 structural assemblies and polyubiquitin chains that drive biomolecular condensate formation. By structurally characterizing both components in vitro, we seek to define how multivalent p62-polyUb binding organizes and stabilizes autophagy condensates, which are key to preserve cellular homeostasis.

Poster 8

Structural insights into the neuroprotective potential of coffee metabolite Chlorogenic Acid: a molecular docking and dynamics study

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Coffee is widely consumed worldwide and contains bioactive metabolites that have been associated with protective effects in several pathological conditions. In this study, we use in silico approaches to investigate the potential role of coffee metabolite chlorogenic acid in mechanisms related to Alzheimer's disease. We are using structural biology tools such as molecular docking and molecular dynamics simulations to explore direct interactions between chlorogenic acid and amyloid beta (Aβ) peptides. Docking results revealed a preferential binding region on Aβ, with ligands consistently interacting with the Met35 residue. Molecular dynamics simulations suggested that chlorogenic acid induces structural perturbations in Aβ, affecting β-structure organization and aggregation-related behavior. These findings support previous reports on the neuroprotective potential of coffee-derived biomolecules and provide molecular-level insights into possible mechanisms underlying their interaction with amyloid beta.

Poster 9
A Conformation-altering Mutation in TXDNC15 Linked to the Joubert Syndrome

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Ciliopathies are genetic disorders caused by abnormalities in primary cilia, a microtubule-based organelle that extends from various human cell types. Ciliopathies are classified into distinct syndromes according to clinical features, often overlapping genetically and phenotypically. Here, we report an infant with a phenotype compatible with Joubert Syndrome, including neurological, ocular, renal and respiratory manifestations. Genomic analyses reveal that the patient carries two compound heterozygous mutations in the TXNDC15 gen: a missense p.(R235W) mutation and an intronic deletion. This is among the first studies linking TXNDC15 to Joubert Syndrome, previously associated only with Meckel-Gruber syndrome. We here focus on the evaluation of the structural impact of the R235W mutation in TXNDC15. Bioinformatic analysis indicates that this protein presents a Thioredoxin domain, preceded by an intrinsically disordered region (IDR), and linked to a transmembrane helix through a second IDR, that is broken by a short α helix (residues 305-313). Molecular dynamics simulations show that the R235W mutation has a minimal impact on the Thioredoxin domain folding, where the mutation is located. However, it prevents formation of the Arg235-Asp309 salt bridge, contributing to the short α-helix stabilization and inducing its unfolding. This indicates that Arg235 contributes to maintain the conformational ensemble of TXNDC15.

Poster 10
Decoding constitutive activity in orphan GPCRs: basal activation GPR26 and GPR78

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Orphan G protein–coupled receptors (oGPCRs) remain unexplored despite their potential to reveal general rules of GPCR activation. In class A GPCRs, inactive-state motifs like the TM3-TM6 ionic lock and the Na+ pocket oppose activation, whereas microswitches (DRY, CWxP/PIF, NPxxY) enable the active state. GPR26 and GPR78 are orphan paralogs GPCR that carry a non-canonical DRY motif, and GPR78 additionally lacks the acidic residue at 6.30, precluding the ionic lock formation. We hypothesize that non-conserved deviations in these inactive-state brakes may encode constitutive activity by destabilizing the inactive ensemble and favoring active-like conformations, consistent with reported basal Gs signaling in heterologous systems.

We aimed to determine cryo-EM structures of GPR26 and GPR78. We have obtained a low-resolution cryo-EM map of GPR26 at 4.9 Å that allows the positioning of the transmembranes helices and suggests an unusual arrangement of intracellular loops, potentially underlying constitutive G-protein coupling. Ongoing efforts aim to achieve atomic resolution for both receptors and structure-guided mutagenesis that restores consensus brake. These studies would establish a generalizable blueprint to mechanistically decode basal signaling in orphan GPCRs and accelerate deorphanization.

Poster 11
Expanding the Druggable Proteome: High-Throughput Identification of Inhibitors Against Relevant IDPs

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Intrinsically disordered proteins (IDPs) have gained attention as unconventional yet compelling drug targets, owing to their conformational plasticity and central roles in transcriptional control, cellular stress adaptation, and disease progression. In pancreatic cancer, several IDPs- including c-MYC, NUPR1 and MeCP2- participate in tumor initiation, malignant progression and resistance to chemotherapy, positioning them as candidates for therapeutic modulation.

In this work, we describe an integrated workflow designed to discover and validate small molecules capable of interacting with these highly dynamic proteins. The platform combines a customized thermal shift-based primary screen with a suite of biophysical assays-such as isothermal titration calorimetry, fluorescence-based readouts and circular dichroism-to identify binding events and ligand-induced structural rearrangements.
Compounds that show promise in vitro are subsequently assessed in cellular or animal models to determine their impact on protein localization, transcriptional programs and phenotypes relevant to pancreatic cancer biology.

By tailoring both screening and validation approaches to the particularities of IDPs, this study contributes to broadening the landscape of druggable targets and supports the development of innovative therapeutic strategies for pancreatic cancer.

Poster 12
Assessing network stabilization of aging Tau/α-Synuclein biomolecular condensates

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Biomolecular condensates fulfill different functions in cells, and there is an increasing interest regarding their physiological and pathological relevance. In the case of condensates formed by amyloid-prone proteins, assessing the formation and maturation processes under cytomimetic conditions is key to understand the underlying cause of neurodegenerative diseases. Nonetheless, there is a lack of non-invasive, high throughput methods aiming to follow the maturation processes of a condensate's network. Here, we developed fluorescence-based approaches to measure network strengthening and stabilization rates of Tau/α-Synuclein complex condensates. We were able to assess inter-system differences between condensate stabilization rates using a high-throughput ionic strength assay. Then, we found that condensate aging results in a dynamic arrest and a decrease of the monomer exchange rate using single-droplet, 2-color colocalization imaging. Finally, we developed a time-resolved intermolecular FRET methodology with a dark acceptor, which allows to directly assess the peptide/peptide interaction strength as condensates age. Combining these three approaches, we measured significant differences in condensate network strength at starting times and also between stabilization rates among systems, ionic strengths and droplet size, shedding light on how molecular grammar and environmental conditions govern condensate maturation.

Poster 13

Identification, purification, and characterization of enzymes involved in the lindane degradation pathway.

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Lindane (γ-hexachlorocyclohexane) is a chemical compound obtained through the photochlorination of benzene and was widely used as a pesticide. Its synthesis generates several isomers with no industrial use that exhibit high environmental toxicity and pose a risk to human health. Numerous microbial genera capable of degrading these isomers to CO_2 and water through the Lin catabolic pathway have been identified; this pathway involves the sequential action of various enzymes and represents a promising bioremediation strategy.

In the present study, framed within the project 'New strategies for the elimination and valorization of lindane waste and development of a biosensor for its detection', Lin enzymes were identified in different microbial genomes using bioinformatic tools, and for each enzyme a canonical sequence was selected for starting further characterization. These models were heterologously produced in E. coli BL21, and their optimal overexpression conditions were experimentally determined in order to enable their overproduction, purification, and subsequent functional and structural characterization through activity assays and using various biophysical techniques. Enzymatic isoforms from different microorganisms will also be evaluated to establish differences and correlate sequence-level variations with biochemical and kinetic changes.

Overall, this work contributes to advancing strategies for the remediation of sites contaminated with lindane.

Poster 14

Metastatic homing shapes gene expression and immune infiltration in colorectal cancer

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Colorectal cancer (CRC) disseminates in different organs. Liver metastases, the most frequent, has been extensively studied whereas the pulmonary remains poorly characterized. The objective of this study is to search for biomarkers of specific relapse and for differences in immune infiltration that could be used as therapeutic targets.

To do this, a transcriptomics approach to understand CRC progression and how it changes from primary location to the metastatic one was performed. A total of 140 matched samples from 60 patients with 76 primary and 64 metastatic samples were profiled by Affymetrix Clariom microarrays. Firstly, limma was used to perform differential expression analysis between different tumour samples. To infer immune cell infiltration, transcriptomic data was also used to make an immune-deconvolution using ConsensusTME.

Specific genes associated with distinct tumour conditions across sample groups were found which correlate with the metastatic patterns of dissemination. Moreover, the immune-cell type infiltration shows that lung metastases tend to have a higher immune-profiling compared to the liver metastases, suggesting an organ-specific tumour microenvironment (TME) adaptation.

These findings support the role of immune system shaping metastatic homing from primary stages of the disease. Moreover, biomarkers useful for patients' management have been identified; although further validation is needed.

Poster 15

AI-driven protein binder design targeting GPCRs using BinderFlow

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G protein-coupled receptors (GPCRs) constitute one of the most pharmacologically relevant protein families, yet their structural flexibility and membrane-embedded nature make the rational design of selective binders particularly challenging. Recent advances in AI-based protein modeling suggest new opportunities for generating de novo binders with high affinity and specificity. In this proposal, we outline the potential use of BinderFlow, a modular, automated workflow integrating structure prediction, interface optimization, and sequence redesign in an iterative pipeline. BinderFlow combines generative modeling and physics-informed scoring to design structurally robust and diverse binder scaffolds. This approach is particularly suited for GPCRs with peptidic ligands, including chemokine receptors like GPR15, where it could be applied to diversify known peptide sequences, design mini-protein or peptide scaffolds, and iteratively optimize interface interactions. The ultimate goal is to experimentally validate the most promising BinderFlow-generated candidates (hits) through high-throughput screening, enabling the identification of selective and high-affinity binders. This approach will establish a scalable AI-driven platform for designing and validating selective protein binders against GPCR targets.

Poster 16

Cancer targeting through rationally designed EGFR-binding peptides

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Active targeting decorates drug carriers with receptor-specific ligands to concentrate therapeutics in diseased tissue while limiting systemic exposure. In oncology, this increases intratumoral delivery and lowers off-target toxicity. To develop new therapies against tumors, we have selected the epidermal growth factor receptor (EGFR) as the molecular target because it is ubiquitously expressed across cancers.

Accordingly, we engineer EGFR-binding peptides to display them on the surface to lipid nanoparticles (LNPs) that encapsulate the therapeutic payload, enabling receptor guided uptake into EGFR-positive cells. The goal is to get “two-stage” designed peptides: high-affinity capture at the surface (pH 7.4) and weakened binding in the early endosome (pH 6) to enable LNP disengagement and cargo release.

Our methodology first screened peptide sequences by pH-dependent charge. At pH 7.4, mildly cationic sequences aid membrane approach while at pH 6.0 increase cationicity, reducing receptor affinity. Designed peptides are further examined using molecular dynamics (GROMACS) with protonation states mimicking pH 7.4 and 6.0, and binding free energies estimated by gmx_MMPBSA. Candidates were synthesized and subjected to SPR to assess interaction profiles. This integrated computational-biophysical workflow prioritizes peptides for LNP conjugation and will guide subsequent in vitro and in vivo evaluations, with the objective of achieving effective cancer targeting.

Poster 17
Recognizing Tn and STn Epitopes in Protein Context

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Traditional antibody therapies struggle to distinguish healthy from cancerous cells, partly because most monoclonal antibodies (mAbs) recognize only glycans rather than the combined glycan–peptide structures that truly define tumor-associated carbohydrate antigens (TACAs) like Tn and STn.

In this study, crystal structures of Tn- and STn-targeting mAbs revealed a cooperative binding mechanism: the VH domain recognizes the glycan, while the VL domain interacts with the peptide backbone. This division of labor enables highly selective recognition of tumor-specific “combotopes.” We also found that subtle VH CDR3 mutations can shift specificity between bis-Tn and bis-STn O-glycans.

Using these structural insights, we designed phage display libraries focused on the key residues involved in glycan and peptide recognition. By panning these libraries against Tn- and STn-modified MUC1 and CD43, we enriched antibodies that bind the full glycopeptide epitopes rather than glycans alone.

This tailored phage display strategy provides a powerful route to generate more precise, cancer-selective antibodies with reduced off-target effects.

Poster 18
Connecting metal homeostasis and biofilm formation in cyanobacterium Anabaena sp. PCC7120: a potential tool for the bioremediation of contaminated waters

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Cyanobacteria are photosynthetic prokaryotes which colonize any sun-irradiated niche, allowing the development of multispecies phototrophic biofilms and soil crusts (1). Biofilms are microbial communities that embed themselves in a complex self-produced matrix, highly resilient and commonly induced in response to stresses (2). Interaction with multivalent cations can alter biofilm architecture, while the matrix acts as a nutritional sieve and a barrier for toxic compounds, including metals, mainly thanks to its polysaccharidic content (3). Cyanobacterial polysaccharides are characterized by their anionic nature, making them attractive for applications such as heavy metal removal (4).

In this work, we sought to investigate the role of metals on biofilm formation by filamentous and nitrogen-fixing cyanobacterium Anabaena sp. PCC7120. Comparative transcriptomics of biofilm and planktonic cells and biofilm formation assays under iron starvation revealed the impact of metal homeostasis on biofilm formation and maintenance. Additionally, we employed synchrotron radiation X-ray fluorescence nano-imaging analysis to determine differences in metal density between the filaments and matrix component of biofilms. Lastly, we compared the potential in heavy metal bioremediation of biofilms compared to planktonic cultures based on their differential ability to remove an excess of zinc from the media.

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Poster 19

Impact of the deletion of calB on the physiology of Anabaena sp. PCC7120

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Cyanobacteria are highly versatile photosynthetic microorganisms that are found across diverse ecosystems due to their remarkable metabolic plasticity, including the ability to fix inorganic carbon and, in some species, atmospheric nitrogen. This flexibility relies on complex regulatory networks that coordinate global metabolic responses and abiotic stress adaptation. In the model of filamentous cyanobacterium, Anabaena sp. PCC 7120, stress responses are orchestrated by global regulators such as FUR proteins and NtcA, which control extensive regulons comprising transcription factors, two-component systems, and sigma factors. Among the genes controlled by FurA and NtcA regulators is all2080 (calB) which functional contribution to global regulation has yet to be fully defined.

To elucidate its physiological role, differential transcriptomic analyses were performed with a ΔcalB mutant. The resulting dataset revealed broad transcriptional changes suggesting that CalB participates in key pathways linked to stress adaptation and nitrogen metabolism. Building on these findings, we carried out physiological characterizations to validate predicted phenotypes and assess the impact of calB deletion under selected abiotic stresses. Together, these analyses enhance our understanding of CalB function and provide new insights into how FurA and NtcA integrate environmental signals to finely tune gene expression in Anabaena.

Poster 20

GlobalPred: A user-friendly tool for the interpretation of single nucleotide variants in coding regions

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Variant interpretation involves determining the clinical impact of changes in the DNA sequence, but predicting these effects is still difficult and often inaccurate. This is a challenge to precision medicine, which aims to tailor treatments to each patient, including their genomic profile.

Bioinformatics is essential in this process, as computational predictions are accepted as supporting evidence for variant classification in the Standards and Guidelines for the Interpretation of Sequence Variants published by the American College of Medical Genetics and Genomics (ACMG).

GlobalPred will be a comprehensive web server for the interpretation any protein variant caused by a single nucleotide variant (SNV) in the approximately 20,000 human genes. It will integrate a metapredictor—a classification model trained on multiple pathogenicity predictors—to provide a consensus classification of each variant as benign, pathogenic, or variant of uncertain significance (VUS). Following the recommendations of the ACMG of consulting more than one prediction tool, GlobalPred will also display the classification of the individual predictors included in the metapredictor. As a result, GlobalPred will provide a very useful and user-friendly tool to facilitate the interpretation of coding-region SNVs in the healthcare and research fields.

Poster 21

From bacterial to fungal mucinases: discovering a new Beauveria enzyme with broad O-glycan specificity

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Confidential abstract.

Poster 22
Collective interactions in ion pairs

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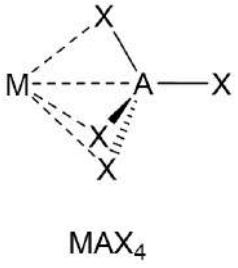
We report herein a quantum-chemical investigation into whether nominally ionic ion pairs can display collective bonding, a stabilization mode arising from distributed exchange-correlation interactions rather than a single two-center bond. Using Penetration Indices and Interacting Quantum Atoms (IQA) energy decomposition, we examined a series of ion pairs M[AX_4] (Fig. 1; M = Li^+–Cs^+; A = B, Fe, Co, Zn, Cd; X = –CH_3, –CO, –CCH, –OCH_3, –Cl). We found that alkali-metal tetramethylborates and several transition-metal tetrahedral anions show clear signatures of collective behavior: the direct M···A interaction is weakly covalent or even repulsive, while stabilization is dominated by exchange–correlation contributions distributed over multiple M···X contacts.



MAX_4

Figure 1. Structural motif of the studied ion pairs (MAX_4).

Systems bearing polarizable or electron-rich ligands (–CCH, –OCH_3, –Cl) exhibit low interaction-collectivity indices ($ICI_{XC} \lesssim 0.07$), whereas carbonyl-containing complexes show substantially higher values (> 0.25), consistent with more localized bonding. These results extend the concept of collective bonding into ionic environments and suggest that ion pairing, solvation, and reactivity may often be governed by multicenter exchange-correlation effects rather than purely electrostatic or classical two-center interactions.

Poster 23

Mechanisms of Phase Separation and Ageing in Multicomponent Protein Condensates

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Amyloid aggregation of α-Synuclein (αSyn) is closely linked to Parkinson's disease, while Tau is central to Alzheimer's pathology. Tau has been found co-localized within αSyn-rich inclusions, suggesting functional interplay between both proteins. Because aSyn and Tau can undergo electrostatic coacervation, they form liquid-like condensates that gradually age, a process shaped by the molecular interactions stabilizing their internal protein networks.

In collaboration with Dr. Shakhnovich (Harvard University), we investigate the mechanisms regulating phase separation and ageing by integrating theoretical predictions with experimental observations. Our system includes ΔNt Tau, a positively charged Tau variant lacking the N-terminal region, along with the negatively charged proteins αSyn and Nt Tau terminal region. ΔNt Tau acts as a common scaffold capable of binding both partners. Recombinant proteins were purified, fluorescently labelled, and imaged by confocal microscopy at different time points.

Initially, the condensates show a homogeneous mixture of proteins. As ageing progresses, they demix, developing regions enriched in Nt-Tau. Because αSyn preferentially coacervates with ΔNt Tau, Nt Tau becomes partially excluded, forming distinct "patches". Combined with theoretical insights, these results help elucidate the mechanisms driving phase separation and ageing in multicomponent protein condensates.

Poster 24

Unraveling the role of accessory proteins in G-protein coupled receptor signalling

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G protein-coupled receptors (GPCRs) constitute one of the most pharmacologically relevant protein families and control cellular communication within the human body. Recently, a set of accessory membrane protein subunits have been shown to modulate trafficking and pharmacology of GPCRs, however it is unclear the mechanisms and which receptors are modulated. In this work we aim to characterize the functional impact of accessory membrane proteins (MRAPs and RAMPs) on the function of GPCRs, taking as model system the adrenergic receptors. For this purpose, we will use molecular cloning, baculovirus generation, protein expression, biochemistry and cell signaling assays to define which accessory subunits modulate which adrenergic receptor and how. We hope the results aid in understanding fundamental aspects of adrenaline biology as well as opening new routes for drug design.

Poster 25

Developing cell models to study condensate formation and maturation in neurodegeneration via Brillouin microscopy.

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The pathological buildup of alpha-synuclein (αS) and tau inclusions is a defining feature of Parkinson's and Alzheimer's disease, yet the mechanisms driving their assembly remain poorly understood. Emerging evidence indicates that many early protein assemblies arise as biomolecular condensates formed through phase separation before transitioning into gel-like structures and eventually pathological aggregates. A key barrier to progress is the lack of precise, non-destructive measurements capable of distinguishing these states in living cells and linking their material properties to cellular toxicity.

In-Vivo Brillouin Microscopy (IVBM) provides a promising solution by enabling label free, high-resolution mapping of mechanical properties within intact biological systems. To deploy this technology effectively, suitable cellular models covering a range of condensate states are required. This work establishes such models by generating αS and tau condensates in cells through two complementary approaches: uptake of pre assembled condensates and de novo intracellular formation. Both methods yielded distinct condensate populations with measurable differences in dynamics and mechanical behavior.

These models will support rapid optimization of IVBM for live-cell and tissue imaging and, ultimately, enable deeper insight into how the evolving physical properties of αS and tau assemblies influence neuronal dysfunction and neurodegeneration.

Poster 26

Impact of Comorbidity Clusters on Survival in Patients Awaiting Liver Transplantation: A Sex-Stratified Analysis

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Comorbidities are key determinants of mortality in patients on the liver transplant waiting list and have a significant impact on post-transplant outcomes. Since biological mechanisms and clinical manifestations of liver disease differ between males and females, sex-disaggregated analyses are essential to identify inequalities in the effects of comorbidities. In this multicenter prospective study, 1,504 consecutive patients listed for liver transplantation in 18 Spanish hospitals were included. An intention-to-treat approach was used to evaluate the effect of comorbidities on overall survival. Unsupervised agglomerative hierarchical clustering algorithms were applied to identify patterns of comorbidities, and all analyses were stratified by sex. Comorbidities were significantly more prevalent in males than in females, with distinct profiles observed between sexes. The most frequent comorbidities and risk factors were smoking, arterial hypertension, obesity, and diabetes. Statistically significant sex-based differences were found in the prevalence of diabetes, renal insufficiency, cardiovascular disease, smoking, obesity, chronic obstructive pulmonary disease, obstructive sleep apnea, atrial fibrillation, and connective tissue disease. The resulting clusters exhibited different compositions and were associated with significantly different overall survival in both males and females. Integrating these comorbidity profiles with other key clinical variables may contribute to the development of a decision-support tool for liver transplantation.

Poster 27
COARSENET

Marco F. da Silva[1,2], Marcus Engsig[3], Alberto Aleta[1,2], and the AccelNet-MultiNet Collabathon

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As systems grow in size and complexity, tracking individual components becomes intractable, necessitating simplified versions that preserve inherent properties. Coarse-graining methods address this by reducing dimensionality, aggregating microscopic details into macroscopic network representations while retaining key topological and dynamical features.

We introduce CoarseNet, a Python library built upon the NetworkX package that provides a versatile collection of coarse-graining methods. This user-friendly tool allows researchers to easily apply techniques such as Spectral clustering, K-means, and Laplacian renormalization to complex networks. CoarseNet outputs the coarsened graph alongside nodal mappings to the original network, comparative visualizations, and quantitative metrics for evaluation. By integrating seamlessly into existing workflows, CoarseNet enables users to explore the effective scale of complex systems in a way that is computationally feasible and conceptually meaningful.

Poster 28

Salvianolic acid: an effective natural enhancer of PADI4 activity

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In recent years, interest in identifying natural compounds with therapeutic potential has grown significantly. PADI4, one of the five human isoforms capable of converting arginine to citrulline (citrullination), is involved in the development of autoimmune diseases, such as rheumatoid arthritis or psoriasis and different types of cancer, as glioblastoma. Salvianolic acid A (SAA), a natural stilbenoid extracted from the root of Salvia miltiorrhiza¸ exhibits antiinflammatory and anticarcinogenic effects. In this study, we investigated the interaction between SAA and PADI4, characterizing the in vitro binding by using fluorescence, ultraviolet (UV), nuclear magnetic resonance (NMR), and isothermal titration calorimetry (ITC). The affinity of SAA for PADI4, determined by fluorescence and ITC, was 620 ± 40 nM. The 2D 1H-15N HSQC NMR experiments, performed in the presence of a reporter protein (RING1B), indicated that binding occurred at an allosteric site. Colorimetric assays (UV) suggested that binding between PADI4 and SAA enhanced citrullination, acting as an activator. Cell-based assays revealed a reduction in viability across several cancer cell lines upon SAA administration. Moreover, the interaction between PADI4 and RING1B in cells decreased markedly and was almost completely abolished after 24 h. Overall, we conclude that SAA was bound to PADI4.

Poster 29

Unravelling the Molecular Drivers of α-Synuclein Nucleation into Amyloid Aggregates in Parkinson´s disease

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Misfolding and aggregation of α-Synuclein (α-Syn) are key pathological events in Synucleinopathies, such as Parkinson's disease (PD). α-Syn is an intrinsically disordered protein (IDP) that remains soluble under physiological conditions. Amyloid aggregation initiates through primary nucleation, where soluble monomers convert into small nuclei that catalyse the growth and propagation of pathological amyloid structures. The exact molecular mechanisms underlying these initial events remain unclear. While it has been recently recognised that hydrophobic/hydrophilic interfaces accelerate primary nucleation in vitro, their presence alone is insufficient, and other factors are likely involved. We hypothesize that specific protein conformation and orientation at the interface are also critical. Building on our previous work, we refined an in vitro model combining aggregation assays with Langmuir surface-pressure measurements. Using truncated α-Syn variants, we have determined the relative affinity of different protein regions for an air/water interface and found that this hierarchy strongly correlates with aggregation kinetics. In parallel, we established a cellular model of secondary nucleation using fluorescently labelled monomers and preformed fibrils (PFFs), enabling direct visualization of intracellular propagation. Together, these results provide critical insights into the earliest molecular events that trigger the onset of Synucleinopathies, paving the way for the development of more effective therapeutic approaches.

Poster 30

Negative modulation of mitochondrial gene expression by cellular kinases

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Mitochondrial translation is a key regulatory point for cellular bioenergetics, as the 13 mtDNA-encoded proteins are essential components of the OXPHOS system. Recent kinase-screening studies have revealed that multiple signaling pathways dynamically modulate mitochondrial protein synthesis.

In this project, we present the first steps in the analysis of the effect of cellular kinases that regulate negatively mitochondrial gene expression. This will provide insights into cellular processes that might be critical for proper mitochondrial function and therefore gain knowledge in the relevance of mitochondria within the cellular context.

Poster 31

Pyridoxal 5’-Phosphate Biosynthesis by Pyridox(am)ine 5’-Phosphate Oxidase: Species-Specific Features

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Pyridoxal 5’-phosphate (PLP) acts as a cofactor in nearly 200 enzymatic activities involved in a wide range of reactions, including amino acid, lipids and neurotransmitters metabolism. Its biosynthesis is catalyzed by pyridox(am)ine 5’-phosphate oxidase (PNPOx) in prokaryotes and eukaryotes. Human PNPOx has been extensively characterized due to its association with neurological disorders resulting from enzyme dysfunction and PLP deficiency. However, little is known about PNPOx from pathogenic microorganisms, despite PLP metabolism being crucial for their survival and virulence. This study characterizes PNPOx from Brucella ovis – a non-zoonotic bacterium that causes contagious epididymitis and infertility in rams – and from Mycobacterium tuberculosis, the causative agent of human tuberculosis. Recombinant PNPOx enzymes from B. ovis, M. tuberculosis and H. sapiens PNPOx were subjected to comparative analyses of their spectroscopic properties, catalytic activity and structural features. Such evaluations offer insights into species-specific mechanisms underlying catalysis and PLP mediated inhibition, contributing to a better understanding of PLP metabolism in both pathogenic and human contexts.

Poster 32

The alr7637 gene of Anabaena (Nostoc) sp. PCC 7120 is a MerR family regulator of FUR regulatory network that responds to heavy metals

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Cyanobacteria are photosynthetic prokaryotic microorganisms with great ecological and economic importance as fixers of atmospheric nitrogen and CO2. Nitrogen fixation in Anabaena sp. PCC7120 takes place in specialized cells called heterocysts, when combined nitrogen is scarce. Heterocysts differentiation is mainly regulated by NtcA and HetR transcriptional regulators. However, a role of the ferric uptake regulator homologue FurC in controlling the expression of secondary regulators of nitrogen assimilation and heterocyst differentiation has recently been described. Deletion of a secondary regulator, all1651, alters the expression of 19 genes with known function, but only one of them, alr7637, is annotated as transcriptional regulator. This singularity prompted us to study the biochemical characteristics of Alr7637.

Our bioinformatic study indicates that Alr7637 belongs to the MerR family of transcriptional regulators that responds to heavy metals. Employing electrophoretic mobility shift assays (EMSA) and bioinformatic tools, we show that Alr7637 binds to its own promoter, in which we have identified a potential binding box of Alr7637. By combining analysis of alr7637 genetic context and Alr7637 binding box, we have identified potential targets of Alr7637 related to copper homeostasis, which have been confirmed by EMSA.

Our results point to Alr7673 as a member of FUR regulatory network, playing a role in keeping copper homeostasis during Anabaena cells acclimatation to changing nitrogen availability.

Poster 33
Identification of Novel Antibiotics Targeting Zinc-Dependent Vulnerabilities of LpxC

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LpxC is an essential zinc-dependent deacetylase involved in lipid A biosynthesis and represents a promising target against multidrug-resistant gram-negative bacteria. We purified LpxC from E. coli and assessed its structural stability using several biophysical techniques in the presence and absence of zinc. The enzyme remains well folded and active only when zinc is present, while zinc-free forms shift toward partially unfolded, inactive states. This vulnerability could be exploited by small molecules that stabilize the inactive conformation and block LpxC function.

After biophysical characterization, a screening using the Prestwick Chemical Library was carried out to identify compounds capable of modulating LpxC stability. A preliminary assay at two fixed concentrations (120 and 4 µM) was performed to confirme whether the selected compounds had a biological effect. Compounds showing activity were then tested across broader concentration ranges to determine MIC_{90} values.

Their effects were further evaluated in E. coli ATCC 25922 and a hyperpermeable strain to distinguish truly inactive compounds from those with poor cellular uptake. When reduced activity was linked to poor permeability, improving compound delivery into the cell may be required to achieve their full antibacterial potential.

Poster 34

AI-Enhanced Detection of α-Synuclein Aggregates for Parkinson's disease Diagnostic Applications

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Sensitive detection of α-synuclein (aSyn) amyloid aggregates is essential for developing reliable diagnostic assays for Parkinson’s disease. Fluorescently labeled nanobodies provide specific binding to aSyn aggregates, generating discrete events within time-resolved fluorescence traces. Because aggregate concentrations in human biofluids are extremely low, robust signal-processing strategies are required to discriminate true molecular events from noise and artifacts.

We present two complementary analytical approaches for aSyn aggregate detection: single-molecule analysis in a microfluidic flow system and a cytometry-based method. In the microfluidic platform, aggregates are identified using objective criteria based on signal intensity, minimum consecutive data points, and tolerated gaps between valid detections. To enhance reproducibility and reduce manual parameter tuning, we are developing a deep-learning model trained directly on fluorescence traces to automatically optimize detection parameters. In the cytometry workflow, machine-learning algorithms are employed to uncover subtle aggregate-associated patterns. Together, these approaches aim to improve the sensitivity and reliability of aSyn aggregate detection in clinically relevant samples.

Poster 35
Integrated Mechanistic Characterization of the Pathogenic AIFM1 Variant E336K

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The pathogenic AIFM1 variant E336K is shown to disrupt a core pro-survival function of Apoptosis-Inducing Factor (AIF), thereby broadening the mechanistic and phenotypic spectrum of AIF-related mitochondrial disease. A clinical presentation characterized by progressive axonal sensorimotor neuropathy and sensorineural hearing loss, with preserved cognition, places this case within the established CMTX4/Cowchock syndrome. At the cellular level, patient-derived fibroblasts exhibit reduced AIF abundance, impaired OXPHOS capacity, and defective assembly of respiratory chain supercomplexes, accompanied by decreased CHCHD4 expression and reduced mitochondrial mass. These alterations converge on a consistent mitochondrial maintenance defect rather than an enhancement of apoptotic signaling. Biochemical and structural analyses show that E336K destabilizes AIF and weakens FAD/NADH-dependent dimerization, impairing the CHCHD4–AIF redox relay. Collectively, the data indicate that the pathogenic impact of E336K arises primarily from the loss of AIF's bioenergetic support functions. This integrated clinical, cellular and molecular characterization underscores the functional heterogeneity of AIFM1 mutations and highlights the relevance of variant-specific analyses for refining genotype–phenotype correlations in mitochondrial neuropathies.

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Poster 36

Tissue-specificity of cellular kinases regulating mitochondrial translation

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Mitochondrial translation is a key regulatory point for cellular bioenergetics, as the 13 mtDNA-encoded proteins are essential components of the OXPHOS system. Recent kinase-screening studies have revealed that multiple signaling pathways dynamically modulate mitochondrial protein synthesis.

Interestingly, mitochondrial dysfunction caused by either mtDNA or nDNA mutations and present in all body cells, affects only distinct tissues and organs. To identify if cellular kinases modulating mitochondrial gene expression may account for this tissue specificity of mitochondrial disorders, we will analyze expression of those cellular kinases in different cell types. We present the design and first steps of this project.

Poster 37
Bacterial Aryl-Alcohol Oxidases as Emerging Biocatalysts for Selective Oxidations

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Aryl-alcohol oxidases (AAOs) are flavin-dependent oxidoreductases of the glucose-methanol choline (GMC) oxidoreductase superfamily that catalyze the oxidation of primary alcohols into the corresponding aldehydes. Their ability to selectively oxidize a broad range of aromatic and aliphatic alcohols makes them attractive biocatalysts for greener chemical synthesis, including the production of fine chemicals, pharmaceuticals, and polymer precursors. While fungal AAOs are well studied, their bacterial counterparts remain largely unexplored.

In this study, we performed a comprehensive bioinformatic screening across bacterial genomes to identify novel AAO candidates. Sequences were selected based on the conservation of GMC characteristic motifs and key catalytic residues of fungal AAOs. Phylogenetic and structural analyses exposed the existence of distinct bacterial AAO clades, supporting their independent evolutionary diversification (1).
Two enzymes, SdAAO and ShAAO, were recombinantly expressed and characterized. Both displayed broad substrate specificity and moderate thermostability, featuring an unusually open active site that may explain their substrate promiscuity (2). In particular, ShAAO has demonstrated outstanding biocatalytic potential, efficiently catalyzing diverse oxidations and enabling tandem organocatalytic processes for the synthesis of valuable chiral compounds (3).

These results expand the known diversity of AAOs and establish bacterial members as promising, sustainable biocatalysts for selective oxidation chemistry.

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2. Cinca-Fernando P, Ascaso-Alegre C, Sevilla E, Martínez-Júlvez M, Mangas-Sánchez J, Ferreira P. Discovery, characterization, and synthetic potential of two novel bacterial aryl alcohol oxidases. Appl Microbiol Biotechnol. 2024;108(1):498.
3. Ascaso-Alegre C, Cinca-Fernando P, Roberts TL, López-Fernández P, Herrera RP, Cosgrove SC, Mangas-Sánchez J, Ferreira P. Scope and Synthetic Applications of the Aryl-Alcohol Oxidase from Streptomyces hiroshimensis (ShAAO). Org Lett. 2025;27(43):12086-91.

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Poster 38
Biotechnological applications of 1D exactly solvable models

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Industrial biotechnological processes face several challenges of different natures at various stages along the pipeline, from research through development to production. While many challenges are related to experimental and wet-lab protocols, some are intrinsically theoretical, as they involve searching for an optimal configuration in a high-dimensional space. These types of challenges are typically addressed from a bioinformatics standpoint; however, ofter a statistical-physics approach can complement and enhance purely algorithmic solutions.

Here, I will analyze two examples that emerged during a collaboration with the company Certest Biotech. The first addresses codon optimization in mRNA within a research effort to improve protein expression [1]. The second deals with the optimal design of the partitioning of a gene into overlapping oligonucleotides [2], ensuring that its characteristics meet the constraints imposed by the production protocol. Both problems can be approached by recasting them as discrete, one-dimensional, nearest-neighbor interaction models, which are therefore exactly solvable. While the physics methods involved in solving them are straightforward, defining the problem and handling the associated subtleties are not. In turn, the results obtained improve upon standard bio-informatics approaches and highlight the value of bidirectional collaboration between academic research -including theoretical work- and industrial R&D departments.

[1] D. Luna-Cerralbo et al., A statistical-physics approach for codon usage optimisation, Comput. Struct. Biotech. J. 23, 3050 (2024).
[2] D. Luna-Cerralbo et al. In preparation.

Poster 39
AI Models for Detecting Diseases and Conditions Using Sensor Fusion

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The analysis of human movement allows the detection of motor alterations associated with neurodegenerative diseases, movement disorders, or aging-related conditions. In this context, the use of human activity recognition (HAR) techniques and gait analysis can help identify these alterations and enable early detection before they cause irreversible damage.
The presentation will cover the work carried out within a national project aimed at developing AI algorithms to detect sarcopenia and cognitive decline in older adults. The methodology used and the main results and conclusions obtained will be presented.

The methodology included the collection of multimodal data from two sources (inertial sensors and computer vision), the analysis of sensor signals, and the application of human pose estimation algorithms to extract key gait features, as well as the development of ML and DL models tailored to the study's objectives.

In addition, tools developed and used in the project, such as BodyFlow, a modular platform for HAR, will be showcased. Finally, future lines of work will be discussed, including multi-camera pose estimation for applications in preventive care and health.

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Disentangling the metalloregulatory interconnections of (FUR) proteins in the control of biofilm generation and nitrogen metabolism in Anabaena sp. PCC7120

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Cyanobacteria are oxygenic photosynthetic prokaryotes that can perform atmospheric CO2 and N2 fixation. Their unique adaptations to abiotic stresses and biofilm formation capacity have allowed them to succeed in varied habitats.

The cyanobacterium Anabaena sp. PCC7120 FUR (Ferric uptake regulator) paralogs are global regulators that control transcription of genes involved in maintaining metal homeostasis, nitrogen metabolism, stress responses and biofilm formation[1,2]. However, there is growing evidence that they may indirectly govern the transcription of many other genes by modulating the expression of different transcriptional regulators, thereby expanding their regulons[3].

Differential transcriptomics of Anabaena biofilms vs. planktonic cultures combined with bioinformatic analyses, qRT-PCR and gel shift assays, allowed identification of several novel secondary regulators in the biofilm formation regulatory network controlled by FUR proteins. From them, NsrM (Nitrogen secondary regulator of MerR family) requires reducing conditions for in vitro activity and is modulated by both, PerR (FurC) and the master regulator of nitrogen metabolism NtcA. We also found several regulators and two-component systems modulated by FUR paralogs that were also operated by NtcA. Some of them are metal-related proteins or metal-dependent regulators. Apparently, FUR proteins intertwine transcriptional regulatory networks tightly related to nitrogen control and biofilm development that depend on metals.

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Development of AMPA Receptor nanobodies: capturing functional states for modulation and structural analysis

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AMPA receptors (AMPARs) exhibit extensive molecular diversity arising from multiple post-transcriptional processes and the association with more than 30 auxiliary subunits, which affect key functional properties. Recent cryo-EM studies have revealed unique ligand-induced conformations in GluA3 and GluA4 receptors, suggesting that specific AMPAR assemblies adopt distinct extracellular states. These findings motivate the development of nanobodies capable of capturing and modulating conformation- and subunit-specific functional states.

The objective is to establish a robust workflow for generating synthetic nanobodies (sybodies) against AMPAR subunits and associated proteins using the Seeger synthetic library. The soluble form of ABHD6 and the ligand-binding domains (LBDs) of GluA4 and GluA2 have been successfully expressed and purified as targets. Sybody selection relies on biotinylated variants; for this purpose, the BirA enzyme has been purified and the in vitro biotinylation reaction is being optimized. Biotinylated targets will be used in ribosome and phage display panning, followed by ELISA-based screening and sequence analysis to identify high-affinity binders capable of recognizing specific receptor conformations. In parallel, ABHD6 and the GluA4 LBD have been submitted to the Instruct-ERIC platform for llama immunization to obtain high-affinity nanobodies. Together, this dual approach aims to produce conformationally selective binders to probe AMPAR functional mechanisms and lay the groundwork for future receptor modulation.

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reMoDA: A Python library for automatic relaxation Molecular Dynamics Analysis

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The current trend towards personalized medicine highlights some of the challenges we are facing in molecular diagnosis. Many of the variants found using next generation sequencing techniques have not been previously described, and experimental approaches can be inappropriate in terms of costs and time. Computational approaches, whether based on sequence homology or structural features, show limitations in the need of previously analyzed data and lack information about the dynamics of the protein, key to their function. To overcome these limitations, relaxation Molecular Dynamics (rMD) simulations have been developed, in order to understand the dynamics of a protein upon mutation and its effect in protein stability. However, rMD interpretation relies heavily on the detection of unfolding events, for which a standard metric or procedure has not been established. For this reason, we developed reMoDA, a Python library that executes four different kinds of analysis (classical metric multianalysis, energetics, clustering and PCA) both in the local and global scale to detect unfolding. It has been successfully tested in several real-case scenarios with promising results and is freely available at GitHub: https://github.com/elhectro2/reMoDA

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Directed Interlayer Diffusion Generates Superdiffusion and Jamming in Multiplex Networks

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Diffusion on multiplex networks exhibits a rich phenomenology arising from the interplay between network topology and interlayer coupling. While previous studies have shown that directionality within layers can induce superdiffusion and prime regime (optimal coupling), the role of directionality in the interlayer connections themselves has remained largely unexplored. Here we investigate diffusion dynamics in multiplex networks with directed interlayer couplings. Using a combination of analytical derivations and numerical experiments, we show that interlayer directionality alone, even when all layers are undirected, can reproduce both superdiffusion and the prime. More importantly, we uncover a previously unreported dynamical phase, which we term **jamming regime**, in which strong asymmetric interlayer couplings hinder diffusion, dynamically fragment the system, and prevent convergence to the steady state. We characterize this regime through the spectral properties of the supra-Laplacian, showing that the smallest nonzero eigenvalue vanishes asymptotically as the interlayer coupling increases. We demonstrate the directionality-induced jamming both in synthetic multiplex network and also in real-world systems. Our results identify interlayer directionality as a fundamental control parameter governing transport, relaxation, and connectivity in multiplex systems, with implications for the design, optimization, and control of interconnected infrastructures.

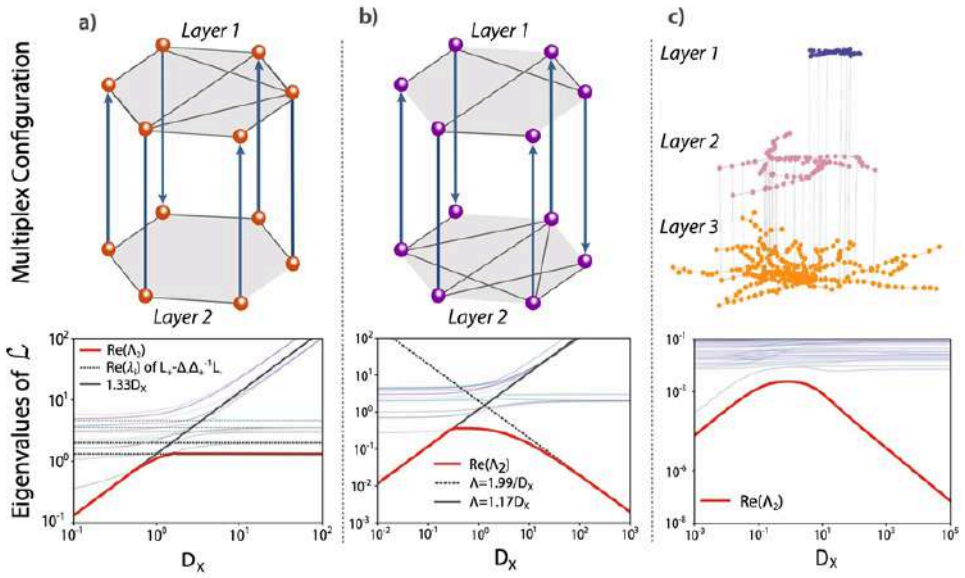

Figure 1: Diffusion Dynamics and Directionality-Induced Jamming. Panel **(a)** shows a simple synthetic multiplex configuration (N=6) with directed interlayer links and the corresponding evolution of the supra-Laplacian eigenvalues (real part) as a function of the interlayer coupling strength, superimposing the analytical asymptotic regime for $Dx \to 0$. Panels (b) and (c) shows for synthetic toy network and a real-world multiplex configuration (London transport multiplex), configurations that lead to the vanishing of the smallest non-zero eigenvalue (Re(Λ2)) as the coupling DX increases stalling the diffusion process.


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