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JÓVENES BIOFÍSICOS

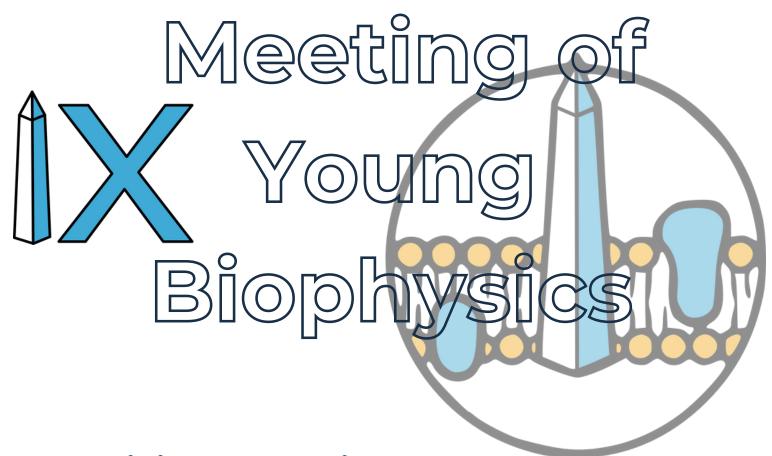
IX Meeting of The Young Initiative on Biophysics



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The Young Initiative on Biophysics

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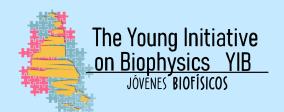
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Welcoming words by the organizing committee

Es un enorme placer darles la bienvenida al IX Encuentro de Jóvenes Biofísicos/Biofísicas. Poder reunirnos nuevamente, ver caras conocidas y muchas nuevas, es realmente una alegría que cobra un valor especial en este contexto tan desafiante que atraviesa hoy la ciencia argentina.

En tiempos donde la investigación y la educación pública enfrentan un fuerte desfinanciamiento, sostener espacios como este no es fácil. Por eso, este encuentro adquiere un sentido aún más profundo: demuestra que seguimos creyendo en la ciencia como un proyecto colectivo, en el valor de la colaboración, y en la fuerza de las y los jóvenes investigadores que, día a día, sostienen con compromiso el futuro del sistema científico nacional.

Desde el grupo Jóvenes Biofísicos/Biofísicas – The Young Initiative on Biophysics (YIB) queremos agradecerles sinceramente por estar aquí hoy, por acompañar, participar y darle vida a esta novena edición que tenemos el orgullo de realizar aquí, en Buenos Aires.

Nos gustaría recordar las palabras de Severo Ochoa, Premio Nobel en Fisiología y Medicina, quien decía que "en estos momentos, cuando la literatura científica ha crecido tanto que es imposible mantenerse al día incluso en el propio campo, los seminarios, conferencias y reuniones son esenciales para estar informado". Con ese espíritu, esperamos que este encuentro sea un espacio de intercambio, de aprendizaje mutuo y, sobre todo, de construcción de lazos humanos y profesionales que fortalezcan a toda nuestra comunidad biofísica.

Queremos compartir con ustedes algunos datos que reflejan el entusiasmo que impulsa esta iniciativa:

- · Este año contamos con 81 jóvenes científicas y científicos entre organizadores, invitados e inscriptos.
- · De los 69 inscriptos, la mayoría son becarias y becarios doctorales, junto a colegas de postdoctorado y estudiantes de grado que comienzan su camino en la biofísica.
- · Tendremos el privilegio de escuchar y dialogar con 9 invitadas e invitados que compartirán sus experiencias y conocimientos a lo largo de las actividades de hoy.

Queremos también agradecer profundamente al equipo que hace posible este encuentro año tras año. Gracias al esfuerzo sostenido de este grupo hemos logrado mantener viva esta iniciativa. Y con mucha alegría damos la bienvenida a Carolina Guamán y Juan José Alvear, quienes se sumaron este año al comité organizador.

Actualmente somos 8 integrantes del comité organizador aquí presentes, Nicole, Idalia, Francisco, Jan, María Julia, Carolina, Juan José y Stefanía; pero detrás de este evento hay muchas más personas que colaboraron de distintas formas para hacerlo posible. A todas ellas, y especialmente a ustedes por estar aquí, muchísimas gracias.

Esperamos que estos dos días sean una oportunidad para compartir ciencia, discutir ideas, descubrir nuevas perspectivas y, por supuesto, disfrutar de la biofísica y de la comunidad que la sostiene.

Con esa energía y entusiasmo, les presentamos el PROGRAMA de esta edición:

- · Comunicaciones orales
- · Talleres / Workshops
- · Y la 7ª edición de "Tu Proyecto en 2 Minutos", un espacio para divulgar y celebrar las ideas que nacen en nuestros laboratorios.

Les deseamos un excelente encuentro, lleno de inspiración, intercambio y nuevas conexiones.

¡Bienvenidas y bienvenidos al IX Encuentro de Jóvenes Biofísicos!





IX Meeting of Young Biophysics Scientific Program - Buenos Aires 2025



The Young Initiative on Biop	Scientific Program - Buenos Aires 2025 FUNDACION WILLIAMS
9:10- 10:50 h Session A	Talk 1: Unlocking the invisible: Structural biology with cryo-EM Dr. Germán Gustavo Sgro (Universidade de São Paulo) Talk 2: Structure and activities of the CEBEM (Centro de Biología Estructural del Mercosur) network Dra. Lucía Beatriz Chemes IB-INTECH. UNSAM
10:50-11:10 h	Coffee break
11:10-12:30 h Session B	Workshop 1: "Molecular dynamics simulations: hands-on". Dr. Ari Zeida - (CEINBIO-Departamento de Bioquímica, Facultad de Medicina, UDELAR) Dr. Gerardo Zerbetto de Palma (FFyB, UBA) y el Msc. Santiago Sastre (Facultad de Medicina, Udelar, Uruguay) Workshop 2: Transforming Data into Knowledge: Statistics Applied to Science Dra. Myriam Nuñez - Cátedra de Matemática Facultad de Farmacia y Bioquímica
12:30-14:00 h- Lunch	
14:00-15:15 h Session C	Talk 1: "Functional and Structural Characterization of Human PMCA3 and Its Pathological Variants Associated with Primary Aldosteronism" Cecilia Souto Guevara, IQUIFIB- CONICET UBA Talk 2: "Functional conformations of the human metallochaperone Cox17: from the apo to the holo state" Maura Gonçalves Da Cruz, Departamento de Ciencia y Tecnología - UNQ Talk 3: "Insights on Voltage Sensitivity in a Chromene-Based Near-InfraComputational red Dye Embedded in a Polarized Lipid Bilayer" Micaela Janeth Sosa, ICB-CONICET-FCEN-UNCUYO

15:10-17:00 h Session D

17:00-17:15 h

Session E

Round Table: "Beyond the Thesis: Opportunities and Challenges After the Doctorate"

Dra Daigna Candovilla - IIPRA (CONICET-Eupdación Instituto Lolair). Dra Cabriola

Dra. Daiana Capdevilla -IIBBA (CONICET-Fundación Instituto Leloir), **Dra. Gabriela Amodeo** - IBBEA (UBA-CONICET), **Dr. Fernando Baidnanoff** JOHNSON&JOHNSON - MARKET ACCESS, ITBA

16:00 My Two Minutes Project: 7th Edition

17:15-18:15 h Organization of transcription in living cells

Dra. Valeria Levi - Vicedecana Exactas, UBA IQUIBICEN - Departamento de Química Biológica

Coffee break

18:15-18:30 h Closing ceremony - Biobirra





OUR INVITED SPEAKERS





Dr. Germán Gustavo Sgro Universidade de São Paulo

I earned my PhD in Biological Sciences from the Universidad Nacional de Rosario (2014), studying the type III secretion system of Xanthomonas citri. I then completed postdoctoral training at the Universidade de São Paulo, focusing on structural and functional analyses of type IV secretion systems. During this period, I spent a year at Birkbeck, University of London, where I specialized in cryo-electron microscopy (cryo-EM) applied to membrane protein complexes—expertise that has guided my research ever since.

Since 2020, I have been a faculty member at the Faculdade de Ciências Farmacêuticas de Ribeirão Preto (USP), leading the Laboratório de Estudos Estruturais de Macromoléculas (LEEM). My group combines biochemistry, microbiology, and structural biology, with a strong emphasis on cryo-EM to study protein complexes central to microbial processes.

Current projects focus on bacteriophages, aiming to resolve infection mechanisms and virus—host interactions using single-particle cryo-EM and cryo-electron tomography. These efforts are supported by major FAPESP grants, including a Projeto Inicial award, and through participation in the CEPID B3 center.

I am also committed to expanding cryo-EM capacity in Latin America by organizing workshops and advanced schools in Brazil and Argentina, training young researchers and fostering regional collaborations.



Dra. Lucía Beatriz Chemes II

IB-INTECH, UNSAM

Dr. Chemes has contributed to understanding virus-host interactions, particularly the viral protein-mediated inactivation of key cell-cycle regulatory proteins, and has dissected these interactions at the biochemical, biophysical, and structural levels. In addition, Dr Chemes has contributed to understanding evolutionary mechanisms in viral proteins and linear motifs, demonstrating convergent evolution of these critical elements and providing evidence that linear motifs play a meaningful role in viral adaptive evolution. In recent years, Dr. Chemes' work has focused on disordered regions of viral proteins and their functions, with particular emphasis on the sequence features of linear motifs and the role of linker regions in the function of intrinsically disordered proteins.







Dr. Ari Zeida

CEINBIO, UDELAR

I am a biochemist from Montevideo, Uruguay, currently a professor at the School of Medicine, Universidad de la República. Since the very beginning of my scientific career, I've been fascinated by how protein dynamics shape biological function. This interest led me to explore the world of computer simulations during my Ph.D. studies at the Universidad de Buenos Aires, where I learned to see proteins as dynamic, ever-changing systems rather than static structures.

After completing my postdoctoral training, I returned to Uruguay to continue investigating how redox processes and structural flexibility influence protein activity. My current research combines Structural Bioinformatics with experimental approaches to understand how oxidative modifications regulate key enzymes at the molecular level. I am deeply committed to fostering interdisciplinary science, mentoring young researchers, and strengthening scientific collaboration across Latin America.



Dra. Myriam Nuñez

FFyB-UBA

Full Professor with exclusive dedication in the Mathematics Department. She holds a bachelor in Mathematical Sciences and a PhD from the University of Buenos Aires.







Dra. Daiana Capdevilla

IIBBA (CONICET-Instituto Leloir)

Daiana Capdevila is a Chemist and PhD in Chemical Sciences from the University of Buenos Aires, specializing in Inorganic, Analytical, and Physical Chemistry. Her early work examined bacterial stress responses in the human body. In 2018, she joined Northwestern University (Illinois, USA) as a postdoctoral fellow, contributing to "Rosalind," a protein-based biosensor platform for detecting over 15 water contaminants, including heavy metals and antibiotics. Since 2018, she has led the Physical Chemistry of Infectious Diseases Laboratory at the Fundación Instituto Leloir, studying the molecular evolution that enables bacterial pathogens to persist in human hosts. In 2019, she applied her expertise to monitoring pollution in the Matanza–Riachuelo Basin, developing cell-free sensors for rapid, low-cost metal detection in partnership with ACUMAR—work recognized with the 2020 L'Oréal–UNESCO "For Women in Science" Fellowship.



Dra. Gabriela Amodeo

IBBEA-UBA-CONICET

She is a Full Associate Professor at the Faculty of Exact and Natural Sciences of the University of Buenos Aires, where she had taught and mentored students across multiple stages of their scientific training. She also serves as a Full Principal Investigator at IBBEA (UBA-CONICET), leading research that integrates fundamental biological and biophysical questions to advance our understanding of hydraulic regulation in higher plants.







Dr. Fernando Baidnanoff

JOHNSON&JOHNSON - MARKET ACCESS, ITBA

I consider myself a curious person who thrives on challenges. My interest is to lead transformation processes in agile organizations with a focus on their customers and optimization of resources and processes. I seek to promote the development of high-performance projects and teams collaboratively and purposefully.



Dra. Valeria Levi Vice dean of Facultad de Ciencias Exactas, UBA IQUIBICEN

Valeria Levi earned her Licentiate in Chemical Sciences (1997) and her PhD (2001) from the University of Buenos Aires. From 2002 to 2006, she completed a postdoctoral fellowship at the Laboratory for Fluorescence Dynamics at the University of Illinois (USA), where she specialized in advanced fluorescence microscopy applied to biological systems. Upon returning to Argentina, she joined CONICET as a researcher and established the Intracellular Dynamics Laboratory at the Faculty of Exact and Natural Sciences, where she is now an Associate Professor. She has received distinctions from the Biophysical Society (2008 Young Fluorescence Award) and the L'Oréal–UNESCO "For Women in Science" program (2017). She is the author of 62 publications in international journals. In 2020, she contributed to the development of a kit designed to simplify COVID-19 sample processing, which was later transferred to an Argentine company





ORAL COMMUNICATIONS



Presenting: Valentina Abratti Bogdanich (valentina.abratti@gmail.com) CEFOBI- CONICET



Structural – kinectic characterization of the Malolactic Enzyme of Streptococcus mutans

Abratti Bogdanich, Valentina; ¹ Saavedra, D.D.; ¹ Lisa, M.N.; ² Alvarez, C.E.¹

1 Centro de Estudios Fotosintéticos y Bioquímicos (CEFOBI- CONICET), FBIOyF, UNR, Rosario, Argentina 2 Instituto de Biología Molecular y Celular de Rosario (IBR, CONICET-UNR), Rosario, Argentina.

Malolactic fermentation (MLF) is a secondary fermentation process that allows bacteria to convert Lmalate into L-lactate through the malolactic enzyme (MLE), in a reaction dependent on NAD+ and Mn2+. This process prevents cytosolic acidification and contributes to generating a proton gradient that drives ATP synthesis. MLF plays a crucial role in energy metabolism and has significant industrial importance in the production of wines, ciders, cheeses, and yogurts, where it improves both nutritional quality and organoleptic properties. In Streptococcus mutans, a key agent of dental caries, MLF is considered a virulence factor. Despite its biological and biotechnological relevance, MLF remains a spontaneous and poorly regulated process, largely due to limited information on the biochemical and structural properties of MLE. Currently, there are no published structures of MLE in the PDB, and its mechanism is poorly understood. An integrated biochemical and biophysical characterization of S. mutans MLE (SmMLE) was performed. The recombinant enzyme was obtained using a codon-optimized construct cloned in pET-22 for periplasmic expression in E. coli, which facilitated purification free of cytoplasmic contaminants. With this preparation, the first crystal structure of SmMLE was obtained in a quaternary complex with NAD+, Mn2+, and pyruvate, which was diffracted successfully. Recently, new crystals have also been grown in the presence of lactate or malate/lactate mixtures. The structural data revealed a dimeric conformation with two distinct Mn²⁺ binding sites—one at the catalytic site and another at the dimer interface—and provided the basis to explore conformational states associated with catalysis and product binding. An indirect measurement protocol was established, since MLE regenerates the NAD+ it uses, difficulting continuous monitoring. This protocol allowed the determination of optimal conditions and kinetic parameters of the enzyme, which were validated using HPLC. Under these optimal conditions, the enzyme showed pyruvate dehydrogenase-like activity in the presence of NADH, a result not previously reported in scientific literature. In addition, the potential regulatory roles of other metals besides Mn²⁺, including Na⁺, K⁺, Mg²⁺, and F⁻, were evaluated. The enzyme's stability was analyzed under different storage conditions, considering the effects of Mn²⁺ and glycerol addition, as well as storage time, through both activity assays and circular dichroism (CD) measurements. Thermal denaturation ramps by CD were performed to further assess structural stability. These results provide novel insights into the structure-function relationships of SmMLE and represent a key step toward identifying regulatory metabolites and potential inhibitors. Understanding these features could enable the rational modulation of MLE activity, contributing both to the development of controlled malolactic fermentation strategies and to the design of therapeutic approaches targeting dental caries.

Keywords. Malolactic fermentation; Crystal structure; Optimised protocol; Enzyme kinetics



Presenting: Maria Julia Maristany (mjm261@cam.ac.uk) University of Cambridge



The Multiscale Structure of Chromatin Condensates

Maristany, Maria Julia^{1,2,3}; Zhou, Huabin ^{3,4}; Huertas, Jan ^{1,3,5}; Russell, Kieran^{1,3}; Collepardo-Guevara, Rosana ^{1,2,3,5}; Rosen, Michael K. ^{3,4}

1 Yusuf Hamied Department of Chemistry, University of Cambridge, UK
2 Department of Physics, University of Cambridge
3 Marine Biological Laboratory Chromatin Collaborative, Marine Biological Laboratory, Woods Hole, MA
02543, USA

4 Department of Biophysics and Howard Hughes medical Institute, University of Texas Southwestern Medical Center, Dallas, TX, USA

5 Department of Genetics, University of Cambridge, Cambridge, United Kingdom Within the cellular environment, biomolecules can be selectively concentrated into compartments that lack a surrounding membrane: biomolecular condensates, integral to numerous cellular processes. However, the molecular determinants of their structure and physical properties remain unclear. To investigate the structure and dynamics of chromatin arrays within condensates, we combine cryoelectron tomography (cryo-ET) with our multiscale chromatin model. Our model enhances the resolution of cryo-ET, enabling us to characterize individual nucleosomes, resolving chromatin droplets at singleamino acid and base-pair resolution. By coupling these techniques, we show that linker DNA length is a key structural parameter controlling chromatin behavior across scales. Varying linker length reorganizes nucleosome geometry, histone tail bridging, and intra-versus inter-molecular interaction balance, determining whether individual chromatin chains remain compact or form extended networks. These microscopic differences propagate to the mesoscale, tuning condensate density, molecular connectivity, thermodynamic stability, and viscoelastic properties. Across a wide range of conditions, simulated condensates reproduce the heterogeneous nucleosome clusters observed by cryo-ET, demonstrating that the physical rules encoded at the single-molecule level are sufficient to explain emergent features of chromatin condensates—and suggesting how chromatin structure in vivo might arise from simple biophysical principles

Keywords. Biomolecular phase separation, cryo ET, chromatin, multiscale genome organization, molecular dynamics.



Presenting : Carolina Guamán (cguaman@ffyb.uba.ar) IQUIFIB- CONICET





Guamán, Carolina¹; Ontiveros, Mallku¹; Rossi, Rolando¹; Rossi, Juan Pablo¹; Mangialavori, Irene¹; Ferreira-Gomes Mariela¹

1 Instituto de Química y Fisicoquímica Biológicas. "Prof. Paladini". Departamento de Química Biológica, Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires, Buenos Aires.

Plasma membrane calcium ATPases (PMCAs) are crucial for maintaining intracellular Ca²⁺ homeostasis in eukaryotic cells by actively transporting Ca2+ out of the cytosol via ATP hydrolysis, essential for restoring low cytoplasmic calcium levels following cellular signalling events. PMCAs are regulated by Ca²⁺-Calmodulin (Ca²⁺-CaM) and natural phospholipids. Dysregulation of PMCA isoforms, characterized by changes in expression, localization, or activity, has been associated with a range of diseases, including neurodegenerative and cardiovascular disorders, hearing loss, and cancer. Despite their clinical relevance, key questions persist regarding PMCA structurefunction dynamics and physiological roles, underscoring the need for specific inhibitors to probe these mechanisms. Our prior studies identified flavonols as potential inhibitors of the PMCA4 isoform, focusing on gossypin—a flavonoid from Hibiscus plants (Malvaceae family) recognized for its antioxidant, antiinflammatory, and anticancer properties. We found that gossypin inhibits PMCA4 via a gossypinMg2+ complex, with minimal effects on other ATPases, suggesting gossypin's promise as a specific inhibitor. This study aims to characterize the inhibition mechanism of PMCA by gossypin and to identify a potential binding site. Our findings reveal that (1) gossypin enables precise measurement of PMCA4 activity in a complex system containing other ATPases from a microsomal sample of sf9 cells overexpressing the human isoform 4b; (2) gossypin inhibits PMCA4 independently of CaM, suggesting it does not interact with the CaM-binding site. (3) The presence of acidic phospholipids reduces PMCA4 inhibition, suggesting a possible interaction with the acidic phospholipid binding site; and (4) this effect was independent of both the molar fraction and the total amount of amphiphiles, indicating a direct action of gossypin on the enzyme. In conclusion, this study provides insights into the molecular basis of PMCA inhibition by gossypin, advancing our understanding of PMCA regulation and its potential as a therapeutic target.

Acknowledgment This work was supported by grants of ANPCYT (PICT-2021-I-A-00421), CONICET (PIP (2022) 11220210100103C0) and UBACYT (2023-2024: 20020220400129BA)





Presenting: Maura Gonçalves-Da-Cruz (goncalvesdacruzmaura@gmail.com) UNQ



Functional conformations of the human metallochaperone Cox17: from the apo to the holo state

Gonçalves-Da-Cruz, Maura¹; Gustavo Pierdominici-Sottile^{1,2}.; Agustín Ormazábal^{1,3}

1Departamento de Ciencia y Tecnología (UNQ), Buenos Aires, Argentina. 2CONICET, CABA, Argentina. 3Agencia I+D+i, CABA, Argentina.

Proteins are macromolecules essential to cellular processes. The dogma of Structural Biochemistry states that a protein's sequence determines its three-dimensional structure and that structure determines its function. However, this dogma has limitations, since there are proteins with essential functions that contain flexible motifs and intrinsically disordered regions (IDRs). The human metallochaperone Cox17 (63 amino acids) delivers Cu^{2+} to cytochrome c oxidase; its two α -helices plus an intrinsically disordered region make it an excellent model to compare ordered versus disordered conformations. It is implicated in diseases associated with impaired oxidative phosphorylation and problems in the assembly of Complex IV of the mitochondrial electron transport chain. The objective is to study Cox17's essential subspace using computational tools, including artificial intelligence (AI)-based methods, and to determine whether the same mechanisms used for proteins with defined structures can be applied.

Molecular dynamics (MD) simulations were performed on Cox17 in its apo form (without Cu²+), starting from structures reported by Nuclear Magnetic Resonance (NMR). Several systems were evaluated with the ff19SB force field and OPC water model; initial implicit-solvent (igb7/igb8) simulations displayed conformational bias, so explicit-solvent dynamics were run and better reproduced the diverse interactions that govern the protein's distribution and stability. To determine the essential subspace in which the protein resides, a Principal Component Analysis (PCA) and a novel adaptation for proteins with IDRs, like Cox17, were carried out. This new version was designed as a possible remedy for the fact that the average structure produced by conventional PCA results in an artificial conformation which—given the variability of the intrinsically disordered region—is not contained within the true conformational space. Thus, an algorithm was developed that references the governing PCA equation to the structure of the subspace with the lowest average RMSD.

Starting from this PCA, the dynamics were projected onto two subspaces: one generated from the NMR structures of the apo form, and another corresponding to the protein's holo state (with Cu^{2+}). The results were compared with those obtained using Al-based tools. The new PCA facilitated the interpretation of the structural families identified within Cox17 dynamics, comparable to those from standard PCA. Trajectory projections using the $C\alpha$ coordinates of the full protein versus only the IDR were similar, suggesting that the IDR contributes substantially to the essential subspace of the system; however, Al-based analyses point to the structured helices as modulators of collective motion. The apo-state trajectories sample conformations that resemble those of the Cu^{2+} -bound (holo) state, which Cu^{2+} likely stabilizes, supporting a conformational selection mechanism relevant to cytochrome c oxidase assembly.

Keywords. Molecular Dynamics, Cox-17, Conformational Space.





Presenting: Micaela Sosa (smicaelajanet@gmail.com) ICB-CONICET



Insights on Voltage Sensitivity in a Chromene-Based Near-InfraComputational red Dye Embedded in a Polarized Lipid Bilayer

Sosa, Micaela^{1,2}; Sánchez, C¹; Del Pópolo, MG^{1,2}; Galassi, VV^{1,2}

1 Instituto Interdisciplinario de Ciencias Básicas (ICB-CONICET). 2 Facultad de Ciencias Exactas y Naturales (FCEN-UNCUYO)

A detailed molecular understanding of how voltage-sensitive dyes respond to membrane potentials is crucial for the rational design of next-generation probes and their application in biomedical imaging. ElectroFluor730 (EF7), a fluorescent molecule recently developed by the Loew laboratory, can resolve cardiac action potentials with a Δ F/F of 12% per spike. As the most red-shifted member of the hemicyanine family (λ_{ex} = 730 nm), EF7 represents a promising candidate for in vivo optical measurements of electrical activity. Nevertheless, the molecular origins of its voltage-dependent optical response remain to be elucidated.

We employed molecular dynamics simulations and electronic structure calculations to investigate the molecular basis of EF7's sensitivity to membrane voltage, aiming to elucidate the mechanisms underlying its voltage response and to provide insights for the rational design of new, improved voltage-sensitive dyes. We conducted three molecular dynamics (MD) simulations of EF7 embedded in lipid membranes using the CHARMM36 force field, corresponding to hyperpolarized (-1.3 V), depolarized (+1.3 V), and unpolarized conditions. Representative configurations from the trajectories were used to compute absorption spectra via LR-TDDFT, employing electrostatic embedding to account for the classical charge distribution of the aqueous and membrane environments.

We found that the transmembrane potential dictates the most stable localization and tilting of EF7 within the membrane. The polarization-dependent changes in these properties account for the shifts observed in the absorption spectra.

The computational approach proposed in this work enables us to capture the mechanistic details of this dye, which differs from other members of its family as it lacks charge-transfer characteristics and instead exhibits a $\pi \to \pi^*$ excitation.

Keywords. Voltage Sensitive dyes, Polarised Lipid Membranes, Absorption Spectra, LR-TDDFT.

Acknowledgements. All authors acknowledge financial support from the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina, and the allocation of computer time on the HPC clusters Toko (UN-CUYO), Mendieta and Serafín (CCAD-UNC). Also acknowledge funding from SIIP-UNCUYO and FONCyT.



Presenting : Cecilia Souto-Guevara (ceci.souto.98@gmail.com) IQUIFIB-CONICET





Souto-Guevara, Cecilia¹; Mariela Ferreira-Gomes¹; Pablo Artigas²; Hugo Adamo¹; Irene Mangialavori¹.

1 Instituto de Química y Fisicoquímica Biológicas Dr. A Paladini, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, CONICET. Buenos Aires. Argentina. 2 Department of Cell Physiology and Molecular Biophysics, Center for Membrane Protein Research, Texas Tech University Health Sciences Center, Lubbock, TX.

Plasma membrane Ca²⁺-ATPases (PMCAs) are PII-type ATPases crucial for maintaining intracellular calcium homeostasis by actively extruding Ca²⁺ from the cytosol. Of the four human PMCA isoforms (PMCA1-4), PMCA1 and PMCA4 are ubiquitously expressed, whereas PMCA2 and PMCA3 are restricted to specialized tissues. Recent studies have linked somatic mutations in the ATP2B3 gene, which encodes PMCA3, to aldosterone-producing adenomas (APAs)—the most common cause of primary aldosteronism, a form of secondary hypertension.

Unpublished results from our group suggest that the PMCA3 variant L425_V426del may contribute to hyperaldosteronism by generating a depolarizing, Na⁺-mediated current. In this context, our study aims to functionally and structurally characterize the human PMCA3 (PMCA3)—the least studied PMCA isoform—and to investigate how pathological variants, such as PMCA3L425_V426del and PMCA3G123R, may alter its behavior and contribute to disease mechanisms.

To this end, PMCA3 and its variants were heterologously expressed in Saccharomyces cerevisiae, purified, and reconstituted into lipid particles. Preliminary findings reveal isoform-specific differences in apparent Ca²⁺ and Mg²⁺ affinity, as well as distinct responses to calmodulin regulation and lipid environment. Notably, while PMCA3G123R displays reduced ATPase activity compared to the wild type, the PMCA3L425_V426del variant appears to lack Ca²⁺-ATPase activity altogether.

These observations provide insights into the functional divergence among PMCA isoforms and lay the initial groundwork for understanding the molecular basis of PMCA3-related pathologies.

Keywords. ATPases, membrane proteins, calcium, enzyme kinetics.





INVITED EVALUATORS BOARD

PHD. AITZIBER LÓPEZ CORTAJARENA

PHD. IRENE MANGIALAVORI

PHD. ARI ZEIDA







Topographic Labeling of TDP-43 Using Diazirine: A Novel Method to Study ALS Protein Behavior

Abadie Bottcher, Juana Manuela^{1,2}; Cortez, Leonardo M²; Delfino, José M¹; Gómez, Gabriela E.¹

Email: jabadiebottcher@gmail.com

1Departamento de Química Biológica e IQUIFIB, Facultad de Farmacia y Bioquímica, UBA-CONICET. Buenos Aires, Argentina. 2Centre for Prions and Protein Folding Diseases. University of Alberta. Edmonton. Alberta. Canada.

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease characterized by pronounced clinical and molecular heterogeneity, encompassing variable sites of onset, differential motor neuron involvement, and distinct rates of progression. A key pathological hallmark of ALS is the cytoplasmic aggregation of TAR DNA-binding protein 43 (TDP-43), which undergoes misfolding, prion-like propagation, and intercellular transmission. TDP-43 aggregates span a range of sizes, with oligomeric species being notably stable and neurotoxic.

Our laboratory focuses on elucidating protein conformational dynamics and their functional consequences through an integrated experimental and computational approach. We have developed a novel topographic labeling strategy employing diazirine (DZN), a photoactivatable gas that mimics the physicochemical behavior of water. Upon UV irradiation at 320 nm, DZN produces methylene carbene, a highly reactive intermediate that methylates residues located within its transient molecular cage. In this work, we explored the feasibility of DZN-based photolabeling to probe the conformational landscape and aggregation behavior of TDP-43. To this end, we expressed and purified a recombinant fragment of the TDP-43 C-terminal domain (residues 263–414), incubated it with increasing DZN concentrations, and subjected the samples to UV irradiation. Electrospray ionization mass spectrometry (ESI-MS) revealed concentration-dependent mass increases (M + n*14 Da), consistent with methylene incorporation. These results demonstrate that diazirine represents a valuable tool for mapping protein surfaces and interaction sites, with potential applications in therapeutic development and molecular probe design.

Keywords. Amyotrophic lateral sclerosis (ALS), TAR DNA-binding protein 43 (TDP-43), protein aggregates, Topographic Photolabeling, Diazirine (DZN).

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A study of the potential role of amyloid fibers of pancreatic hormones in catalytic reactions

Abate, MB ^{1,2,3}; Alvarez, RL ²; Melian, NA^{1,2}; Toledo, PL ^{1,2}; Ermácora, MR ^{1,3}; Vazquez, DS ^{1,2,3}.

Email: pamelaludmilatoledo@gmail.com and devazquez86@gmail.com
1Grupo de Biología Estructural y Biotecnología vinculado al IMBICE (UNLP-CIC-CONICET), Laboratorio de Expresión y Plegado de Proteínas, Departamento de Quilmes, Buenos Aires, Argentina. 2Laboratorio de Expresión y Plegado de Proteínas, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Buenos Aires, Argentina. 3Consejo Nacional de

Investigaciones Científicas y Técnicas (CONICET), Ciudad Autónoma de Buenos Aires, Argentina.

Protein aggregation has been linked to various diseases affecting the nervous system, such as Alzheimer's and Parkinson's, as well as metabolic disorders like type 2 diabetes. Previous studies have demonstrated that certain hormone peptides, including insulin (hlNS), human pancreatic islet amyloid polypeptide (hlAPP), and glucagon (hGCG), can form fibers under specific conditions.

Amyloid fibers are polymers formed from protein monomers that are assembled in a non-covalent and highly ordered manner. These bonds are arranged perpendicular to the fiber axis, forming a cross-beta structure. Because of their polymeric and ordered structure, amyloid fibers can arrange catalytic sites on their surface, allowing them to carry out metabolic transformations in vitro1. It was recently discovered that GCG amyloid fibers can catalyze biological reactions, including ester and lipid hydrolysis, as well as dephosphorylation2.

In our laboratory, we optimize the formation of amyloid-type hINS fibers3. Our goal is to obtain hIAPP and hGCG fibers for further study of peptide hormones related to glucose homeostasis. We evaluate the effect of temperature, incubation time, and agitation on fiber formation using fluorescence measurements with thioflavin T.

The main objective of this study is to determine if hIAPP and hINS fibers exhibit ATPase and/or phosphatase activity. We evaluate this activity using the malachite green colorimetric method and pnitrophenyl phosphate hydrolysis, respectively.

Keywords. Insulin, IAPP, Amyloids, Catalysis, Hydrolysis.

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- 1. Arad, E; Jelinek, R. Trends Chem. 4, 2022, 907-917.
- 2. Arad, E; et al.. ACS Nano. 2022, 16, 12889-12899.
- 3. Toledo PL; et al.. J. Biol. Chem. 2019, 294, 8564-8576







Biophysical characterization of polypeptide prohormones from the pancreatic islets

Alvarez, RL¹; Melian, NA^{1,2}; Abate, MB^{1,2,3}; Toledo, PL^{1,2}; Ermácora, MR^{2,3}; Vazquez, DS^{1,2,3}

Email: pamelaludmilatoledo@gmail.com and <a href="mailto:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:decom:

Glucagon1 (GCG) and human islet amyloid polypeptide-22 (IAPP) are two types of peptide hormones that are produced by pancreatic α and β cells, respectively. These hormones are closely linked to glucose homeostasis. Both are initially synthesized as prohormones that require proteolytic processing by specific enzymes to obtain their functional form. Previous studies have shown that GCG and IAPP can form amyloid-like aggregates under different physicochemical conditions. This has a significant impact on the development of type 2 diabetes mellitus and pharmacological formulations for its treatment.

In our laboratory, we demonstrated that the N-terminal domain of ICA512, a crucial transmembrane protein in the maturation of insulin secretion granules, inhibits the formation of insulin fibers in vitro3. Therefore, our hypothesis focuses on the potential of ICA512 to inhibit or retard the fibrillation of the prohormones and their derived peptides under study.

The overall objective of this work plan is the preliminary biophysical characterization of the prohormones IAPP (proIAPP) and glucagon (proGCG). In a first step, we designed the genetic constructs of proIAPP and proGCG fused to the Glutathione S-Transferase (GST) tag to obtain proteins with a high degree of purity. The next step will be to optimise the expression, purification, and removal of the GST tag. In a second stage, controlled proteolysis assays, thermodynamic stability analysis, structure, and oligomeric state analysis will be performed using spectroscopic techniques such as fluorescence, circular dichroism, and light scattering.

Keywords. amyloid fibers, ICA512, diabetes mellitus.

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- 1. Holst JJ.(2022) Glucagon and other proglucagon-derived peptides in the pathogenesis of obesity. Front Nutr.9:964406.
- 2. Westermark P, Andersson A, Westermark GT.(2011) Islet amyloid polypeptide, islet amyloid, and diabetes mellitus. Physiol Rev. 795-826.
- 3. Toledo PL, Torkko J, Müller A, Wegbrod C, Sönmez A, Solimena M, Ermácora MR.(2019) ICA512 RESP18 homology domain is a protein-condensing factor and insulin fibrillation inhibitor. Biol Chem. 294(21):8564-857.







Molecular dynamics simulations reveal hylin-Pul3 interactions at water-octanol interfaces and bacterial membrane model

Caliva, Victor Manuel ^{1,2}; ;Aguilar, Silvana ³; Marani, Mariela M.³; Di Lella, Santiago ⁴; Pickholz, Monica ^{1,2}.

Email: vcaliva@df.uba.ar

1Universidad de Buenos Aires, Facultad de Ciencias Exactas y Naturales, Departamento de Física. Buenos Aires, Argentina. 2CONICET - Universidad de Buenos Aires, Instituto de Física de Buenos Aires (IFIBA). Buenos Aires, Argentina. 3IPEEC-CONICET, Consejo Nacional de Investigaciones Científicas y Técnicas, U9120ACD Puerto Madryn, Argentina. 4IQUIBICEN-CONICET, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Argentina.

Antimicrobial peptides (AMPs) have the potential to be effective against harmful bacteria by disrupting the membranes that compose them. The mechanism through which these peptides could act may differ significantly. Completely mature peptides and selected fragments derived from the skin of Boana pulchella have been chemically synthesized and subjected to testing against Gram-positive and Gramnegative bacterial strains. The hylin-Pul3 mature peptide was the most active [1]. Looking forward to improving their action, several mutations were proposed. Six of them were synthesized and purified. In this work, we used Molecular Dynamics simulations to explore hylin-Pul3 in different environments. First, we simulated single hylin-Pul3 peptides and an array of ten peptides at the water-octanol interface. Overall, we found more affinity to the octanol phase with two preferential orientations. Furthermore, we investigated the process of peptide pore formation in simple bacterial model membranes. We found that hylin-Pul3 were able to disrupt membranes with 16 pore-forming peptides, and 18 arranged in square matrices. Besides, we calculated several properties. In particular, we used the SUAVE software [2] to calculate the density taking into account the effect of membrane curvature in the presence of peptides.

Keywords. Antimicrobial, Boana, Molecular Dynamics, pore, matrices.

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- 1. AGUILAR, Silvana, et al. Structure and function of cationic hylin bioactive peptides from the tree frog Boana pulchella in interaction with lipid membranes. Peptides, 2023, vol. 159, p. 170900.
- 2. SANTOS, Denys ES; COUTINHO, Kaline; SOARES, Thereza A. Surface assessment via grid evaluation (SuAVE) for every surface curvature and cavity shape. Journal of Chemical Information and Modeling, 2022, vol. 62, no 19, p. 4690-4701.







Structural analysis of a 2-cys peroxiredoxin from *Elizabethkingia* anophelis

Díaz, Carla¹; Santos, J²; and Vazquez, DS^{1,3}

Email: dsvazquez86@gmail.com

1Grupo de Biología Estructural y Biotecnología vinculado al IMBICE (UNLP-CIC-CONICET), Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Buenos Aires, Argentina. 2Instituto de Biociencias, Biotecnología y Biología traslacional (IB3), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, IArgentina. 3Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Av. Rivadavia 1917 Ciudad Autónoma de Buenos Aires, Argentina.

Elizabethkingia anophelis, an emerging pathogen, was first isolated from the gut of Anopheles gambiae, a primary malaria vector. This pathogen has been associated with meningitis and sepsis, resulting in high mortality rates among neonates and immunocompromised individuals 1. Peroxiredoxins (Prxs) are Cys-dependent antioxidant enzymes that catalyze the reduction of reactive oxygen and nitrogen species. Several studies have demonstrated the role of Prxs in the pathogenicity and virulence of clinically relevant microorganisms, such as M. tuberculosis and P. falciparum, as well as their ability to reduce or prevent induced oxidative stress in host cells. Therefore, studying the biochemistry of the Prx system of E. anopheles is important.

This study focused on the structural and functional characterization of 2-Cys thiolperoxidase (EaTPx) from E. anophelis. We synthesized the EaTPx gene with an N-terminal His-tag and TEV cleavage site, cloned it into pET-9a, and expressed in E. coli and purified using pseudoaffinity chromatography. We performed protease cleavage assays at different mass ratios. The protein was subjected to initial characterization of secondary structure by circular dichroism and determination of molecular weight and oligomeric state by size exclusion chromatography (SEC). Preliminary results showed that EaTPx was obtained with high purity and displayed spectroscopic properties consistent with a properly folded protein. Additionally, it was efficiently cleaved by TEV protease. Finally, SEC analysis revealed that EaTPx exists in a monomer-dimer equilibrium under native conditions.

Keywords. Peroxidase Activity, Peroxiredoxin, Oxidative Stress.

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- 1. Kämpfer P, et al., I. Int J Syst Evol Microbiol. 2011, 11, 2670-2675.
- 2. Perkins A, et al., Trends Biochem Sci. 2015, 8, 435-45.







Biochemical and biophysical characterization of the ICA512 Insulin Receptor Ectodomain of Human β-Pancreatic cells expressed in Pichia Pastoris

Ducloux, GM¹, Vazquez, DS^{1,2,3}, Ermácora, ME^{2,3} and Ferreyra, RG^{1,2,3}

E-mail: rferreyr@gmail.com

1Laboratorio de Expresión y Plegado de Proteínas, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Buenos Aires, Argentina. 2Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Av. Rivadavia 1917 Ciudad Autónoma de Buenos Aires, Argentina. 3Grupo de Biología Estructural y Biotecnología vinculado al IMBICE (UNLP-CIC-CONICET), Laboratorio de Expresión y Plegado de Proteínas, Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Buenos Aires, Argentina.

ICA512 (Islet cell antigen 512) is a transmembrane protein belonging to the family of receptor-type protein-tyrosine phosphatases, located in neuroendocrine secretory granules and insulin-producing β -pancreatic cells, and was identified as one of the main autoantigens associated with the development of autoimmune diabetes. ICA512 constitutes a 979 amino acid polypeptide that includes a signal peptide, an ectodomain (MPE), a single transmembrane segment and a cytoplasmic region. In our laboratory, we determined that MPE has a folding similar to ferredoxin and belongs to the SEA protein family, specialized in oligomerization and interaction with the extracellular matrix. The existence of post-translational modifications of the MPE domain had been predicted and suggested by the heterogeneity of the products visualized in immunoprecipitation experiments1. Our results demonstrated that glycosylations occur in regions critical for monomer association. In vitro studies with non-glycosylated MPE (expressed in Escherichia coli) showed that only the $\beta 2\beta 2$ dimer is significantly formed in solution. However, glycosylation of the Asn506 residue of MPE appears to inhibit its formation in vivo, possibly due to the resulting steric hindrance2.

Our working hypothesis is that post-translational modifications, primarily N-glycosylations, affect the architecture of the native state of MPE and therefore its biophysical and functional properties. The objective of this work is to deepen the structural characterization of the ICA512 receptor. To this end, recombinant variants of the MPE domain are being produced in the methylotropic yeast Pichia pastoris and the impact of these modifications on the structural properties of the protein will be characterized.

Keywords. Pichia pastoris, ICA512, glicoproteins.

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- 1. Noguera ME et al. J Struct Funct Genomics. 2015 Mar;16(1):1-9.
- 2. Primo ME et al. PLoS ONE 6, e24191.







A Computational Study on Post-Transcriptional Control by the RsmA-RsmZ System in Pseudomonas aeruginosa

Gagliardi, Federico¹;Palma, Juliana ^{1,2};Ormazabal, Agustín ^{1,3}

E-mail: federicogagliardi22@gmail.com 1 Departamento de Ciencia y Tecnología (UNQ), Buenos Aires, Argentina. 2 CONICET, CABA, Argentina. 3 Agencia I+D+i, CABA, Argentina.

The opportunistic pathogen Pseudomonas aeruginosa affects patients with immunodeficiency, cystic fibrosis, and cancer, among others. The virulence of this pathogen is regulated by quorum sensing through the dimeric protein RsmA. This protein controls the expression of target genes by altering their translation through sequence-specific interactions. Its function is, in turn, regulated by the small RNA (sRNA) RsmZ, which selectively sequesters the protein and inhibits its activity. RsmZ's structure comprises five stem-loops (SL1, SL2, SL3, SL4, and SL5) and three single-stranded regions (SSR), in addition to the sRNA terminator[1]. Given the relevance of the RsmA-RsmZ system as a potential therapeutic target against Pseudomonas aeruginosa, understanding the binding order within the complex is particularly important for designing inhibition strategies. With the aim of unveiling the molecular basis of the binding mechanism between RsmA and RsmZ, in this work, we study this system by employing molecular dynamics simulations. For these calculations, we started from the experimentally reported structure for the RsmA-RsmZ complex, in which two RsmA units bind to binding pockets formed by the SL1-SL5 and SL4-SSR pairs. Since the binding order for the complete RsmA-RsmZ complex has not been described, three strategies were used to simulate the free RNA: in the first case, both proteins were simultaneously removed; in the other two, removal was sequential, starting with the protein associated with the SL1-SL5 pair in one simulation, and with the SL4-SS site in the other. Simulation analyses were carried out using an adaptation of traditional Principal Component Analysis (PCA) proposed by our group. This adaptation arose from the need for an efficient method to address the high conformational freedom of RNA in the absence of protein interactions. Unlike globular proteins, RNA has numerous degrees of freedom that can introduce noise in a conventional PCA based on Cartesian coordinate transformations. As an alternative, we analyzed binding site availability, using the BaRNAba algorithm to compute the covariance matrix from a binary variable: the presence or absence of interactions in the binding motifs. In this way, PCA can capture the internal conformational changes that are relevant for protein binding. The results, based on the extent to which each binding site is available (i.e., not making contact with other regions of the molecule), suggest that all three RsmZ binding pockets have at least one of their sites available for a significant fraction of the concatenated trajectories. Thereby, none of the pockets has a predilection for being the first to bind RsmA, in line with recent experimental studies. Moreover, the exposure of the sites that form a single pocket is generally alternated, and they are not available simultaneously. This could prevent two sites in the same pocket from capturing different proteins. Taken together, our study provides a structural and dynamic characterization of RsmZ in its free state and establishes an innovative methodology for mapping functional motif accessibility in RNA.

Keywords. RsmA/RsmZ, Molecular Dynamics, Binari PCA.

References: 1. Jia X. et al. 2023. Nature.







Gossypin as a Selective Inhibitor of hPMCA4b: Potential Antimalarial Application

Guamán-Cañar CS¹; Ontiveros MQ¹, Marder M1, Rossi JP¹, Mangialavori IC¹, Alvarez C¹, Ferreira-Gomes MS¹

E-mail: cguaman@ffyb.uba.ar

1 Instituto de Química y Fisicoquímica Biológicas. "Prof. Paladini". Departamento de Química Biológica, Facultad de Farmacia y Bioquímica. Universidad de Buenos Aires.

ATPases play essential roles in the regulation of cellular ions through mechanisms coupled to ATP hydrolysis. Among them, the plasma membrane calcium pump (PMCA) constitutes only 0.1% of the total membrane proteins but plays a crucial role in intracellular signaling, muscle contraction, and other calcium-dependent processes. Despite its physiological relevance, no specific inhibitors have been identified that would allow PMCA to be considered a therapeutic target.

Several studies have shown that decreased PMCA expression in erythrocytes alters the host's susceptibility to Plasmodium falciparum infection, affecting and reducing parasite proliferation. This highlights the importance of characterizing compounds capable of inhibiting the activity of this enzyme. In this context, flavonoids have been shown to interact with various ATPases. In our laboratory, we identified that gossypin, in complex with magnesium, selectively inhibits the hPMCA4b isoform, with an inhibition constant of 5 μ M. Assays indicate that this compound does not affect the activity of other ATPases, such as SERCA, Na*/K*-ATPase, or ecto-ATPase, suggesting significant specificity. Our results show that gossypin selectively inhibits PMCA, possibly by interacting with the acidic phospholipid-binding site, displaying an interaction independent of amphiphilic content and micellar fraction. Moreover, its ability to reduce P. falciparum growth by 50% in in vivo assays supports its potential as a candidate for the development of antimalarial therapies.

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How Tiny Worms Reveal the Hidden Biophysics of Fat Storage in Cells

Guastaferri, Florencia¹; Delprato, C¹; Hernández Cravero, B¹; Lombardo, V^{2,1}; Vranych, C¹; De Mendoza, D^{3,1}; Binolfi, A^{1,4}

E-mail: guastaferri@ibr-conicet.gov.ar

1 Instituto de Biología Molecular y Celular de Rosario (IBR-CONICET-UNR), Rosario, Argentina. 2 Centro de Estudios Interdisciplinarios (CEI), Rosario, Argentina. 3 Facultad de Ciencias Bioquímicas y Farmacéuticas, Universidad Nacional de Rosario (FBIOyF - UNR), Rosario, Argentina. 4 Plataforma Argentina de Biología Estructural y Metabolómica (PLABEM), Rosario, Argentina

Lipid droplets (LDs) are essential organelles that store and regulate the use of fats in cells. Far from being static depots, they are dynamic structures whose composition fluctuate according to the metabolic needs of the organism. The molecular constitution of their lipid core determines its internal fluidity, which in turn influences protein binding to the droplet surface and modulate its functions. These interactions play a key role in maintaining cellular lipid balance under physiological conditions, and also contribute to metabolic dysfunction in disease (1). In this project, we aim to uncover how the internal biophysical properties of lipid droplets emerge from their lipid composition and how these properties affect protein association and cellular metabolism. To address these questions, we use the microscopic nematode Caenorhabditis elegans as a whole-animal model and apply nuclear magnetic resonance (NMR) spectroscopy directly to live organisms (2). This in vivo approach allows us to probe the chemical composition and dynamic behaviour of LDs in their native biological environment. By combining NMR-based biophysical measurements with genetic and dietary manipulations, we can systematically modulate the fatty acid profile of LDs and examine its impact on their internal mobility. Together, this integrative pipeline provides a powerful framework to link the molecular organization of lipid droplets to their physiological roles, offering insights into how altered lipid composition may influence metabolism and contribute to disease.

Keywords. in vivo NMR spectroscopy, Caenorhabditis elegans, Lipid Metabolism, Lipid Droplets, Structural Dynamics.

- 1. Henne, W Mike. "The (social) lives, deaths, and biophysical phases of lipid droplets." Current opinion in cell biology (2023).
- 2. Cravero, Bruno Hernández et al. "A high-resolution 13C NMR approach for profiling fatty acid unsaturation in lipid extracts and in live Caenorhabditis elegans" Journal of Lipid Research (2024).







Evaluation of bisphosphonates as species-specific inhibitors of Plasmodium falciparum Hypoxanthine-Guanine-Xanthine Phosphoribosyltransferase

Mancinelli, Paola^{1,2,3}; Alvarez, CL^{1,4}; Valsecchi, WM ^{1,2,3}

Email: paomancinelli2001@gmail.com, alvarezcora@gmail.com and wvalsecchi@ffyb.uba.ar 1 Inst. de Química y Fisicoquímica Biológicas (IQUIFIB-UBA-CONICET), 2Departamento. de Química. Biológica, Fac. de Farm. y Bioq. (FFyB-UBA), 3 Cátedra de Microbiología y Parasitología, Fac. de Odontología (FOUBA). 4 Departamento de Biodiversidad y Biología Experimental, Facultad de Ciencias Exactas y Naturales, (FCEN-UBA)

de Jovena

Malaria is a disease caused by the protozoan parasite Plasmodium falciparum, it remains a globally significant disease with high morbidity and mortality –more than 200 million cases and about 400.000 deaths are reported annually–. Due to the parasite's growing resistance to current therapies, there is an urgent need for new ones. Since P. falciparum is unable to synthetize purines de novo, it depends entirely on the purine salvage pathway, in which the enzyme hypoxanthine-guanine-xanthine phosphoribosyltransferase (PfHGXPRT) plays an essential role. PfHGXPRT catalyses the cleavage of the pyrophosphate (PPi) group from 5-phosphoribosyl- α -pyrophosphate (PRPP) via nucleophilic attack by a nitrogenous base (hypoxanthine (Hx), guanine, or xanthine) to generate the nucleotides (IMP, GMP, and XMP, respectively).

This project proposes the repurposing of bisphosphonates (BPs), structural analogues of PRPP, as potential PfHGXPRT inhibitors. Previously, we identified zoledronate (a BP) as a promising trypanocidal agent¹, supporting the feasibility of this strategy.

The objectives of this study include the expression and purification of PfHGXPRT, its structural and functional characterization, and the evaluation of the effects of BPs on both enzyme activity and P. falciparum growth in vitro. The methodology combines biochemical, biophysical, and cell culture techniques. By repurposing drugs with established safety profiles, this project aims to advance the development of selective and effective antimalarial therapies, addressing an urgent global health challenge.

Keywords. HGXPRT BIPHOSPHONATE MALARIA

References.

1. Valsecchi, W. M., Delfino, J. M., Santos, J., & Fernández Villamil, S. H. (2021). Zoledronate repositioning as a potential trypanocidal drug: Trypanosoma cruzi HPRT an alternative target to be considered. Biochemical Pharmacology, 188, 114524. doi:10.1016/j.bcp.2021.114524







Estructural and Functional Insights into Hypoxanthine-Guanine Phosphoribosyltransferase: Divergent Tetrameric Assemblies

Rengifo, M, 1,2; Fernández Bettelli, L, 1; Moscato F,1; Valsecchi WM, 1,2,3.

Email: wvalsecchi@ffyb.uba.ar

1 Inst. de Química y Fisicoquímica Biológicas (IQUIFIB-UBA-CONICET). 2Depto. de Química. Biológica, Fac. de Farm. y Bioq. (FFyB-UBA).3Cátedra de Microbiología y Parasitología, Fac. de Odontología (FOUBA).

Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) is a member of the phosphoribosyltransferase (PRT) family, a group of enzymes that play a central role in nucleotide biosynthesis and salvage pathways. Members of this family are essential for the survival of several pathogens responsible for endemic diseases such as Chagas disease, leishmaniasis, malaria, and tuberculosis1,2.3.

In humans, the purine salvage pathway prevents excessive uric acid accumulation, and its disruption is associated with gout. In HsHGPRT, a five-nucleotide deletion (TCGAG) combined with a six-nucleotide insertion (ACGAAA) gives rise to an inactive 153-residue protein instead of the normal 218-residue enzyme, ultimately causing Lesch—Nyhan syndrome.4

Members of the HGPRT family can assemble into both dimeric and tetrameric functional structures. While monomers and dimers display a high degree of structural similarity, tetrameric organisations differ significantly: TcHGPRT adopts a D1T1 arrangement, whereas HsHGPRT forms a D1T1' assembly3,5,6.

Additional arrangements, such as D2T2, D1, D2, and D3, have also been reported, all sharing superimposable monomeric units. Particular attention has been given to the C-terminal region (CTR) of TcHGPRT, whose removal causes the tetramer to dissociate into dimers, suggesting that CTR-mediated interactions are crucial for the formation and stabilisation of the D1T1 tetrameric assembly5,6. To elucidate the structural differences among HGPRTs from diverse organisms, we employ bioinformatic tools such as AlphaFold, CABS-flex, and RING. These approaches are also used to analyse the predicted structures of 148 HGPRTs from different species. In addition, we perform molecular dynamics simulations on the CTR of TcHGPRT to identify the interactions that sustain the tetrameric assembly.

Keywords.

HGPRT; purine salvage; C-terminal region; tetramer stability; molecular dynamics

- 1. RL. Berens, et al. (1981). DOI: 10.1016/0166-6851(81)90049-9.
- 2.DT. Keugth, et al. (2017). DOI: 10.1021/acschembio.7b00916.
- 3. WM. Valsecchi, et al. (2021). DOI: 10.1016/j.bcp.2021.114524.
- 4. KV. Nguyen et al. (2017). DOI: 10.1080/15257770.2015.1014492.
- 5. J. Santos, et al. (2023) DOI: 10.1016/J.abb.2023.109550.
- 6. WM. Valsecchi, et al. (2016). DOI: 10.1016/j.bbapap.2016.03.005.





YIB ORGANIZING COMMITTEE



Stefanía Vargas Vélez

UNC, Córdoba



I hold a degree in Chemistry from the University of Quindío (2020) in Armenia, Quindío, Colombia. I am currently pursuing a PhD in Chemical Sciences at the "Ranwell Caputto" Department of Biological Chemistry at the National University of Córdoba (UNC), under the supervision of Dr. Natalia Wilke. Additionally, I serve as an assistant professor in the Faculty of Chemical Sciences. Our research focuses on analyzing the interaction between antimicrobial peptides and bacterial membranes, investigating how these peptides alter the biophysical properties of the membranes and exploring the role of membrane lipid composition in peptide selectivity. This work is particularly important because antimicrobial peptides represent a promising therapeutic alternative to conventional antibiotics. I began my PhD in 2022, and since then, I have been an active member of the Young Biophysicists initiative. This experience has given me the opportunity to connect with incredible people and broaden my academic network, significantly enriching my training in a meaningful way.



Nicole Cerf

UBA, Buenos Aires

I am a Biochemist with orientation in Basic Research (University of Buenos Aires). I joined IQUIFIB in 2017 as an intern in the laboratory of Dr. Rolando Rossi and later in the framework of a CIN grant. Since that year, until now, I work at the Department of Biological Chemistry of FFyB-UBA as an assistant in the subject Biological Chemistry.

In 2020, I started my PhD under the direction of Mónica Montes and Santiago Faraj in the area of biophysics of membrane proteins with a CONICET grant.



Francisco Feito

UNT, Tucumán



I hold a Bachelor's degree in Biotechnology obtained from the National University of Tucumán (2019), in San Miguel de Tucumán, Argentina. I am currently in the final year of my PhD in Biological Sciences at the Higher Institute of Biological Research (INSIBIO – CONICET – UNT), under the supervision of Dr. Fernando Dupuy.

Our research focuses on studying the interactions of antimicrobial peptides, such as Colistin and Enterocin CRL 35, with biological membrane models including lipid monolayers and solid-supported membranes, aimed at developing and designing new peptides in response to the growing problem of bacterial resistance to traditional antibiotics. During my doctoral studies, I have taken several postgraduate courses and participated in conferences organized by the Argentine Biophysical Society in different parts of the country.



Maria Julia Maristany Cambridge University, Cambridge

have a Licentiate Degree in Physics from the National University of Córdoba (2018) and completed my MSc degrees at the Institute for Quantum Computing and the Perimeter Institute in Canada. I earned my PhD in Physics from the University of Cambridge in 2025, where I studied how molecular interactions drive the self-assembly and phase behaviour of chromatin and other biomolecular systems. My research combines theoretical physics and molecular simulations to uncover the physical principles underlying genome organization. I am passionate about interdisciplinary science and mentoring young researchers, and I have been involved in outreach initiatives promoting diversity and inclusion in STEM across Latin America and the UK."



Juan José Alvear Arias

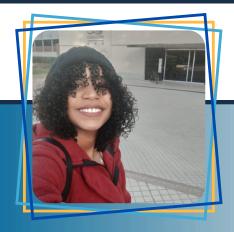
UBA, Buenos Aires



I have been a postdoctoral fellow at the University of Buenos Aires since 2023. I earned my degree in Biology, my MSc in Neuroscience, and my PhD in Biophysics at the University of Valparaíso (Valparaíso, Chile).

My training has centered on biophysical approaches to investigate the gating mechanisms of ion channels and aquaporins (AQPs). My current research focuses on elucidating the principles underlying proton conduction in the voltage-gated proton channel (Hv1) and the mechanical gating of both plant and animal AQPs.

Since 2025, I have been an active member of the YIB initiative.



Idalia Herrera Estrada

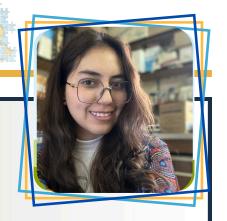
UNR, Rosario

I completed my Bachelor's degree in Biology at the University of Havana in Cuba. I currently hold a CONICET scholarship, and I am a fourth-year Ph.D. student in Biological Sciences at the Institute of Molecular and Cellular Biology in Rosario, Argentina. My current research, which utilizes microscopy and fluorescence techniques, is centered on the influence of oxidative stress on heart looping in the zebrafish model, with a primary focus on cardiovascular research and heart development. I joined the Young Initiative on Biophysics (YIB) members in 2023, which is an opportunity for interdisciplinary exchange and allows me to provide a physical perspective to biological topics



Carolina Guamán

UBA, Buenos Aires



Lam a Biotechnology Engineer, graduated in 2023 from the Universidad de las Fuerzas Armadas "ESPE" (Ecuador), and a member of the iGEM Synthetic Biology Team Ecuador. In 2024, I began my Ph.D. in Biochemistry and Pharmacy at the University of Buenos Aires (Argentina), within the Institute of Biological Chemistry and Physicochemistry (IQUIFIB), supported by a scholarship from the National Agency for the Promotion of Research, Technological Development and Innovation (ANPCyT). I am currently conducting my research under the supervision of Dr. Mariela Ferreira and serve as a teaching assistant for the Advanced Biological Chemistry course at the same university. My research focuses on studying the effect of flavonoids on the plasma membrane calcium pump, both

in purified systems and in complex cellular models.





SUPPORTING AND HONORARY MEMBERS



The Young Initiative on Biophysics



FOUNDING MEMBERS

Agustín Mangiarotti

UNC, Córdoba



I hold a Ph.D. in Chemical Sciences from the National University of Córdoba (Argentina). My background is in membrane biophysics, with experience in teaching and science outreach. After several postdoctoral positions in Argentina and Germany, I became an Assistant Researcher at CIQUIBIC (CONICET) and an Assistant Professor at FCQ-UNC.

My current research explores how biomolecular condensates interact with lipid membranes, using in vitro and cellular assays combined with biophysical and advanced microscopy techniques. This work aims to clarify the mechanisms governing membrane-condensate interactions and their roles in cellular organization, organelle remodeling, and phagocytosis, while also informing potential applications in disease and bioinspired technologies.



Macarena Siri

IIByT-UNC-CONICET

I am a biotechnologist from Quilmes National University, place where I also did my PhD thesis which encompassed the biophysical and biochemical characterization of an albumin-based nanoparticle. It was during this time, that we started The Young Initiative in Biophysics with a group of friends. I slightly changed fields for my postdoc at CIQUIBIC in the city of Córdoba where I deepened my knowledge in protein biophysics and discovered my interest for amyloid fibers and how they are influenced by their biological environment. Afterwards, I did a 4-year postdoc at Max Planck Institute of Potsdam, Germany, focusing on how amyloids fibers contribute to the architecture and mechanical properties of bacterial biofilms.

I returned to Argentina this year to establish as an Assistant Researcher at IIByT Institute in Córdoba. My research will focus on how the climate change affects soil biofilms at the macroscopic and molecular level and their impact in crop yield and health.,





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