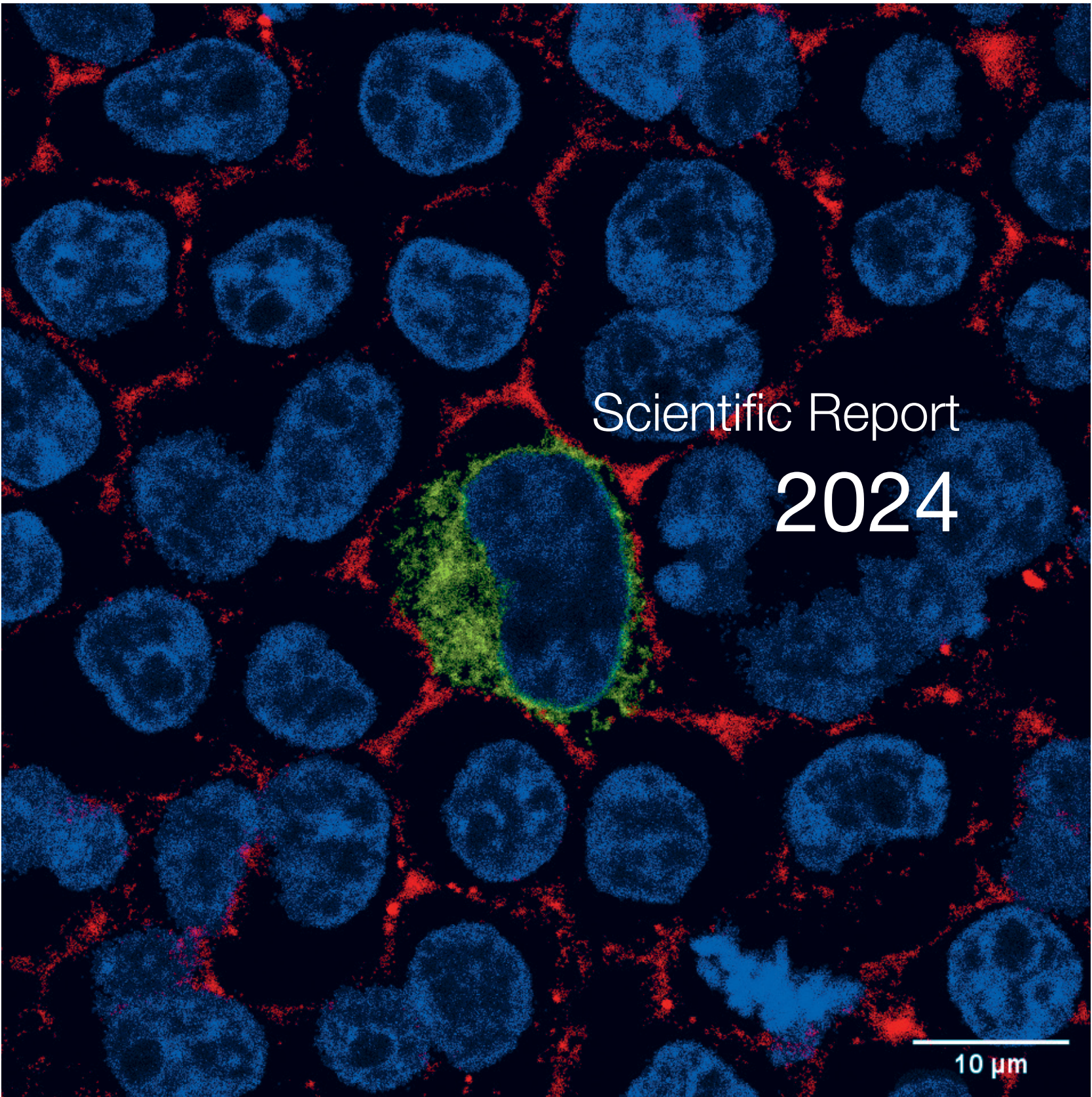




I E C B

Institut Européen de Chimie et Biologie
European Institute of Chemistry and Biology

A fluorescence microscopy image showing a dense population of cells. The nuclei are stained blue, and the cytoplasm or extracellular matrix shows red and green fluorescence. A single cell in the center is highlighted with a bright green outline.

Scientific Report 2024

10 μ m

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Inserm

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On June 27, 2024, IECB and CBMN co-hosted a mini-symposium to celebrate the 90th birthday of Professor Léon Ghosez—a pioneering figure in organic chemistry and one of the founding architects of the IECB. Professor Ghosez has had an exceptional career in Belgium and France, marked by his profound influence on the field and on generations of chemists. Over 300 doctoral and postdoctoral researchers have trained under his mentorship, and his legacy includes numerous prestigious awards—as well as a chemical reagent that bears his name. The symposium brought together former collaborators and long-time friends—including three past directors of the IECB. The event concluded with a special lecture by Professor Ghosez himself, offering a personal and inspiring reflection on his extraordinary “lifetime journey into the world of chemistry,” as he titled his 2019 article in *Tetrahedron*.



Publication director: Gilles Guichard & Antoine Loquet **Graphic design:** Delphine Fleury

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Yves Théobald (building), Marc Grémillon (portraits), Lionel Lizet (UAR3033/US01 IECB technology platform).



Institut Européen de Chimie et Biologie
European Institute of Chemistry and Biology

Scientific Report 2024

Director's Foreword

**Dr. Brice KAUFFMANN**

Deputy Director of the Unit UAR3033/US01 IECB

Dr. Antoine LOQUET

Director of the Unit UAR3033/US01 IECB

At the heart of our activities, the research team incubator continues to thrive as a hub of scientific excellence, driven by innovation, the emergence of new teams, and strong cross-disciplinary collaborations. The 15th “Looking to the Future” symposium, held in November, offered eight pre-selected candidates the opportunity to present their work to the Bordeaux scientific community, highlighting the vitality of the Institute ahead of their interviews with the Scientific Advisory Board (SAB).

This year was also marked by the final SAB meeting chaired by Moshe Yaniv. We warmly thank him for his long-standing dedication to the IECB and for his constant support, as recalled in his reflective letter included on pages 10 & 11 of this report. Looking ahead to 2025, we are pleased to welcome Bernard Paul Henrissat, CNRS Emeritus Research Director and Professor at the Technical University of Denmark, as the new Chair of the SAB. An internationally recognized leader in glycosciences and founder of the CAZy database, his expertise will be a major asset for the Institute.

Scientific animation remained particularly strong in 2024, with the resumption of the monthly IECB Seminar Series (eight invited speakers), the Chemistry Meets Biology seminars dedicated to young researchers, and several symposia at the chemistry-biology interface, including the Chemistry-Biology Interface Day (CBID 2024) co-organized by IECB group leaders from three different research units.

The year also included memorable moments, such as the celebration of the 90th birthday of Professor Léon Ghosez, one of the founders of the Institute, which brought together former directors and alumni. In recognition of scientific excellence at the IECB, Nicolas Reyes, CNRS Research Director and IECB team leader, was awarded the Molecular and Cellular Biology, Genomics medal by the Académie des Sciences.

Looking ahead, 2025 will see the revival of the Young Scientist Symposium (13th YSS). Together, these initiatives reflect the IECB's strong commitment to nurturing talent, fostering collaboration, and promoting interdisciplinarity at the heart of its scientific strategy.

This year has been particularly eventful for the IECB Unit (UAR3033/US01). New equipment funded by the CPER, Région Nouvelle-Aquitaine, the University of Bordeaux, and Inserm—dedicated to the structural characterization of biomolecular systems by electron microscopy (a 200 keV Glacios and a 120 keV Talos)—has been fully deployed and is now accessible to IECB researchers as well as to the wider regional and national scientific communities.

A long-standing project called ENAMAR (Euskadi Nouvelle-Aquitaine Magnetic Resonance), led by myself together with the local NMR community, has finally come to fruition. We are proud to announce that IECB will acquire a state-of-the-art 1 GHz NMR spectrometer for the NMR platform in 2027. This project will also involve collaborative work with the manufacturer Bruker to develop cryoMAS probes operating at 1 GHz, aimed at the characterization of low-sensitivity biomolecules by solid-state NMR. The ENAMAR project is supported by the Région Nouvelle-Aquitaine, FEDER, CNRS Chimie, and the University of Bordeaux.

In addition, our platform facility will be recognized as an “Associated Platform” of the national infrastructure FRISBI, further strengthening our visibility within the French structural biology and biophysics communities.

Significant rearrangement and space optimization efforts are currently underway within the IECB building, with strong support from the University of Bordeaux. These include the relocation of one of our main hosted companies, Aelis Farma, in 2026. Following the departure of Synboli, we are now actively seeking to host a new start-up.

**Dr. Gilles GUICHARD**

Director of the IECB Research Team Incubator

Dr. Frédéric FRISCOURT

Deputy Director of the IECB Research Team Incubator

Dr. Antoine Loquet

Director of the Unit UAR3033/US01 IECB

Dr. Gilles Guichard

Director of the IECB Research Team Incubator

Dr. Brice Kauffmann

Deputy Director of the Unit UAR3033/US01 IECB

Dr. Frédéric Friscourt

Deputy Director of the IECB Research Team Incubator

The Institut européen de chimie et biologie (IECB) is a research team incubator placed under the joint authority of the CNRS, the Inserm and the Univ. Bordeaux. It was created in 1998 with the support of the Aquitaine Regional Council to provide promising European chemists and biologists with an environment designed to facilitate the development of first-class interdisciplinary research programs, in collaboration with international public and private research centres.

IECB's International Scientific Advisory Board guides the selection and periodic evaluation of the team leaders. After a probative period of two years, research teams are then hosted for a maximum of 10 years. During their stay at IECB, teams enjoy full financial and managerial autonomy and benefit from state-of-the-art facilities and dedicated technical expertise through IECB's technology platforms in structural biology and preparative and analytical techniques.

The IECB is the largest research team incubator in France, with 13 research teams accounting for 141 researchers and expert technicians.

The IECB hosts a Unit (UAR3033, US01, CNRS, Inserm, Univ. Bordeaux) composed of 17 people, managing the platforms of the building (X-ray diffraction, NMR, mass spectrometry, electron microscopy, biophysics and biochemistry).

Synboli & AelisFarma are hosted at the institute.



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The IECB International Scientific Advisory Board, chaired by Dr Moshe YANIV, interviewed candidates from all over the world for group leader positions.



Dr. Moshe YANIV
Président, Institut Pasteur,
Paris, France



Dr. Stephen CUSACK
EMBL, Grenoble, France



Dr. Sabine FLITSCH
University of Manchester, UK



Dr. Anne HOUDUSSE JUILLE
Institut Curie, Paris, France



Dr. Jesús JIMENEZ-BARBERO
CIC bioGUNE, Bizkaia, Espagne



Dr. Claude SARDET
IRCM, Montpellier, France



Pr. Helma WENNEMERS
ETH, Zurich, Switzerland



Pr. Yves POMMIER
NCIB, USA

Organisational Structure



Moshe YANIV

Honorary Professor, Pasteur Institute
Emeritus Research Director, CNRS
Member, French Academy of Sciences

My contact with the IECB had its origin in my collaboration and friendship with the late Claude Hélène during my PhD work and later. I came to know Jean-Jacques Toulmé when he joined Claude in the laboratory in Orleans and later in Paris. These contacts and perhaps my initial training in chemistry followed by research on tRNAs, aminoacyl tRNA synthetases, gene expression and epigenetics where at the basis for the proposal to join the IECB SAB. I had also close contacts with Jean-Yves Lallemand, I believe one of the proponents of the initial project.

I accepted the invitation with pleasure not realizing that it will concern a rather long-term commitment. After several years with Daniel Louvard as the chair of the SAB, I accepted to take over the chairmanship for quite a few years.

I must admit that I liked the idea of a limited period of residency at the Institute with extensive turnover of groups. All of us know that this is not the typical tradition in the French system and that it creates enormous difficulties. Nonetheless, it follows examples that exist in very prestigious Institutions like EMBL, Max Planck Institutes junior fellow positions, the Crick Institute in London etc.

In my view, a great advantage for such a system is the atmosphere of an Institute where most of the PIs are young, roughly at similar stages of their career, they have total freedom to develop their own ideas and to blossom. In addition, there are no local mandarins who would not like to share the power and the allocations.

The annual SAB meetings were always exciting two days shared with wonderful SAB members dedicated to the success of the IECB. For me it was also an interesting coming back to chemistry that I studied as an undergraduate at the Hebrew University in Jerusalem several decades ago. It was also an opportunity to meet exceptional scientists from different countries and different horizons and take part in a common enterprise of selecting exceptional young scientists as group leader candidates for the IECB and reviewing and promoting excellent science by the members of the Institute. We were delighted to learn every year about the success of the PI's in securing permanent positions in the CNRS, INSERM or the University, about their high-profile publications and the exceptional rate of success in securing prestigious ERC grants, ATIP-AVENIR, FRM etc grants.

As a recompense for our contribution for the life of the IECB, we were invited to an excellent restaurant, I guess selected by Léon Chosez, with a competition among the wine connoisseur's, Léon, Daniel Louvard and Ivan Huc among others to identify the origin of the wines served with the different plates.

During these years the SAB greatly appreciated the build-up of an extremely strong cluster of structural biologists, certainly one of the best in France. It also contributed to increased collaboration between chemists and biologists, a major goal of the Institute.

We greatly appreciated the endless effort of the successive directors, Jean Jacques Toulmé, Jean-Louis Mergny, Rémi Fronzes, Valérie Gabelica and Gilles Guichard helped by co or deputy directors to direct the Institute both scientifically and administratively. We realized that the job was extremely difficult and required a great sacrifice and considerable time not available

for their own research. We always regretted that much of their occupation involved issues that should have been stream lighted by the trustees, the University of Bordeaux and the CNRS and INSERM.

These involved endless discussions of the exit of groups that terminated their ten years term at the Institute. This issue is certainly one of the weak points concerning this concept. It is evident that much better planning should be set up for the turnover, an essential principle for the success of this innovative system. It seemed to us that improved contacts, coordination and cooperation with the co-hosting CNRS or INSERM units should be achieved spanning from the initial selection procedure to the follow up and departure.

Another issue concerned the physical state of the building. We were upset that no repair was done for many years of the faulty wall in our annual meeting room. Similarly, we were astonished that renovation of space and its adaptation to receive new heavy and precious equipment took so long. The building is 25 years old and requires a better maintenance and renovation.

Reducing the burden of administrative work for the director and his deputy will enable them to spend more time on looking around for potential candidates especially in the fields that connect chemistry and biology.

The recruitment of young group leaders always involved an endless effort by the director and the PI's. The recruitment of young promising group leaders is a very competitive process at the international level. We regret that many excellent candidates recommended by the SAB accepted positions elsewhere. The absence of a solid recruitment package involving installation, initial running costs and salary strongly disadvantages the IECB when in competition with other Institutes or Universities around the world and create a terrible burden on the direction and the candidates in their effort to try to assemble the finance and salary to permit their installation. All possible efforts should be done by the trustees to change this unfavourable framework for an institute that depends on rapid turnover of young group leaders.

In conclusion, I believe that it is of interest for the University, the CNRS and INSERM to pursue this model of a highly performing incubator for young scientists who have the facility to develop innovative research projects in the interface between chemistry and Biology. All the efforts should be done to pursue this innovative model for research in close collaboration with the different partners at Bordeaux University, the CNRS and INSERM.

Moshe Yaniv

Honorary Professor, Pasteur Institute
Emeritus Research Director, CNRS
Member, French Academy of Sciences

Board Members

International scientific advisory board (ISAB)

Dr. Moshe YANIV President
Institut Pasteur, Paris, France

Dr. Stephen CUSACK
EMBL, Grenoble, France

Dr. Sabine FLITSCH
University of Manchester, UK

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Institut Curie, Paris, France

Pr. Yves POMMIER
National Cancer Research, NIH, Bethesda, USA

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Institut de Recherche en Cancérologie de Montpellier (IRCM), France

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Prof. Dinshaw PATEL
Memorial Sloan-Kettering Cancer Center, New York, USA (2009–2016)

Dr. Daniel LOUVARD
Institut Curie, Paris, France (1999–2014)

Pr. Iain D. CAMPBELL
Department of Biochemistry, University of Oxford, UK (1999–2013)

Dr. Simon CAMPBELL
Royal Society of Chemistry, London, UK

Pr. Claude HÉLÈNE
Muséum National d'Histoire Naturelle, Paris, France (1999–2003)

Pr. Georges HUEZ
Université Libre de Bruxelles, Brussels, Belgium (2000–2005)

Pr. Steven LEY
Department of Chemistry, University of Cambridge, UK (1999–2005)

Pr. Helmut RINGS DORF
Institut für Organische Chemie, Johannes Gutenberg Universität, Mainz, Germany (1999–2006)

Pr. Fritz ECKSTEIN
Max Planck Institute for Experimental Medicine, Göttingen, Germany (2003–2006)

Pr. Jack BALDWIN
Department of Chemistry, University of Oxford, UK (2005 – 2007)

Pr. Wilfred van GUNSTEREN
Laboratory of Physical Chemistry, ETH, Zürich, Switzerland (1999–2007)

Pr. François DIEDERICH
Department of Chemistry and Applied Biosciences, ETH, Zürich, Switzerland (2006–2008)

Pr. Jean-Yves LALLEMAND
Institut de Chimie des Substances Naturelles, CNRS Gif-sur-Yvette, France (1999–2010)

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Dr. Rémi FRONZES Former Executive Scientific Director (2019–2020)

Dr. Jean-Louis MERGNY Former Executive Scientific Director (2015–2018)

Dr. Jean-Jacques TOULMÉ Former Executive Scientific Director (2001–2014)

Pr. Jean-Yves LALLEMAND Former Executive Scientific Director (1998–1999)

Pr. Léon GHOSEZ Former Deputy Scientific Director (1998–2008)

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Associate professor (Univ. Bordeaux), UMR5255

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Research Director (CNRS), UMR5234

Dr. Gilles GUICHARD Team leader
Research Director (CNRS), UMR5248

Dr Yaser HASHEM Team leader
Research Director (Inserm), U1212

Dr. Brice KAUFFMANN Deputy Director of the UAR3033/US01 Unit

Dr. Antoine LOQUET Team leader. Research Director (CNRS), UMR5248 (Director of the UAR3033/US01 Unit)

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Univ. Bordeaux
35 Place Pey Berland, 33000 Bordeaux

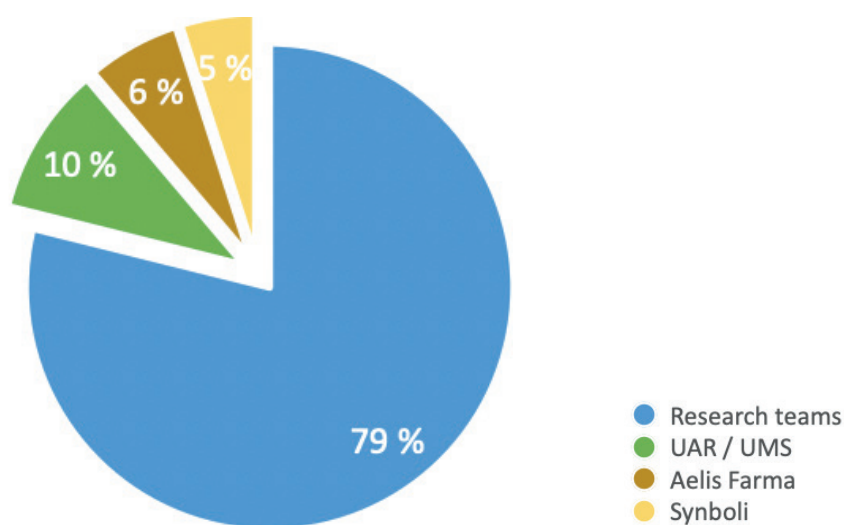
Organisational Chart



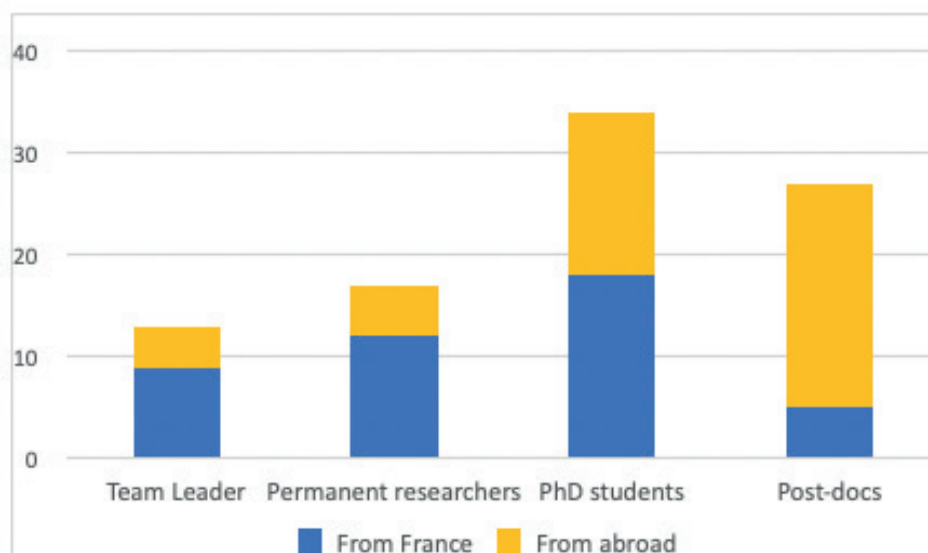
2024 Key Figures

In 2024, the IECB brought together 141 people: 107 research staff, 16 employees within the IECB UAR (platforms and administrative services), and 18 employees from start-ups (Aelis Farma, Synboli). Young researchers make up a large part of the research community, driving both gender balance and international visibility. With 18 nationalities represented, the institute reflects a vibrant and diverse environment that underscores its strong attractiveness.

IECB Staff by Professional Category



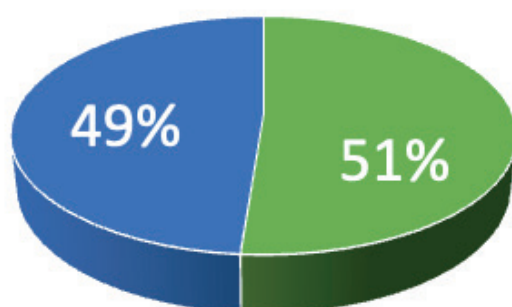
IECB researchers and students by nationality & Professional category



SUPPORT SERVICES (UAR3033 & US01)

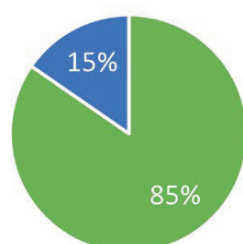
Support services at IECB consist of staff in administration and finance, infrastructure and maintenance, as well as engineers and technicians dedicated to IECB's technology platforms. The support services unit UAR3033 & US01 is jointly funded by the CNRS, the Inserm and the Univ. Bordeaux, and receives financial support from the Nouvelle Aquitaine Regional Council. Research teams also contribute to financing those general services.

Male/Female Distribution within IECB (& among Team Leaders)



■ male ■ female

Team Leaders



Administration and infrastructure

Administrative director

Fabienne LASTERE-ITCAINA, IE, CNRS

Executive assistant officer

Claire-Hélène BIARD, AI, Inserm

Accounting and administration officers

Sandra LAVENANT, Tech, Univ. Bordeaux

Amélie STOTZINGER, Tech, Inserm

IT management

Eric ROUBIN, AI, Inserm

Structural biology facilities

Head of structural biology facilities

and crystallography engineer

Brice KAUFFMANN, IR, CNRS

Crystallography engineer

Stéphane MASSIP, IE, Univ. Bordeaux

Nuclear magnetic resonance engineer

Estelle MORVAN, IE, CNRS

Mass spectrometry engineer

Corinne BURE, IR, CNRS

Surface plasmon resonance engineer

Jean-Michel BLANC, IE, Inserm

Electron microscopy engineer

Axel SIROY, IR, Inserm

Biochemistry and molecular biology engineer

Laure BATAILLE, IR, Univ. Bordeaux

Jean-Michel BLANC, IE, Inserm

Biochemistry and molecular biology technicians

Thierry DAKHLI, Tech, Inserm

Myriam MEDERIC, Tech, Inserm

Quality approach and peptide synthesis

Loïc KLINGER, AI, CNRS

Welcome



synboli



Cassandre Motte (AI), Dr. Marion Boyet (Chemistry), Dr. Maksym Odnoroh (Polymers), Dr. Mathieu Pucheault (co founder and CEO)

Accelerating Sustainable Polymer Innovation with Synboli

Synboli, a deep-tech startup born from a University of Bordeaux/CNRS patent, is based in Bordeaux and dedicated to reimagining the entire lifecycle of specialty polymers, from conception to industrialization. On January 13, 2025, Synboli officially launched its inaugural laboratory within the European Institute of Chemistry and Biology (IECB), gaining instant access to state-of-the-art analytical tools and a rich scientific community.

The core of Synboli's groundbreaking technology is a systematic polymer-synthesis platform designed for high-throughput production with precise reaction control. This robust hardware is complemented by exclusive machine-learning models. These models are meticulously trained on a curated database of thousands of validated polymers, a collection that is an order of magnitude larger and more diverse than any public dataset. Together, this powerful "hardware + software" loop drastically shortens the development timeline, compressing what once took years into mere months—a reduction factor of at least eight.

As a dedicated polymer foundry, Synboli offers industrial partners a rapid, IP-protected pathway to bespoke, regulation-compliant materials. Early efforts are concentrating on high-demand markets where swift innovation and stringent sustainability requirements converge, including biodegradable ingredients, PFAS-free high-performance plastics, and electrolytes for solid-state batteries. Crucially, environmental factors such as biocompatibility, recyclability, and carbon footprint are intrinsically woven into Synboli's discovery algorithms, guaranteeing that all new materials meet compliance standards from their inception.

At its IECB site, Synboli will commence operations with comprehensive synthesis capabilities, advanced characterization tools, and a dedicated data-engineering hub. This infrastructure will empower the company to conduct numerous polymer syntheses each week while fostering interdisciplinary collaborations in chemistry, biology, and data science. By seamlessly integrating advanced automation, predictive artificial intelligence, and responsible chemistry, Synboli is turning polymer innovation from a significant bottleneck into a vital competitive edge for European industries.

Research Teams & Output



Dr. Rémi Fronzes
Research Director (DR1), CNRS

Rémi Fronzes has a long-term research experience in biochemistry and structural biology of macromolecular assemblies. He trained as a membrane protein biochemist during his PhD in Bordeaux (France). In 2005, he moved to Gabriel Waksman's laboratory at the Institute of Structural and Molecular Biology in London (UK) to work as a postdoctoral research associate. In 2009, he was appointed as a junior research scientist at the CNRS and as a group leader at Institut Pasteur, in Paris (France). In 2011, RF was awarded an ERC (European Research Council) starting grant. In 2015, Rémi Fronzes was awarded a "Chaire d'excellence Senior" by the university of Bordeaux and Aquitaine regional Council. He moved his research group to IECB and CNRS unit UMR 5234 « Microbiologie Fondamentale et Pathogénicité » in 2016. In 2017, RF was awarded an ERC consolidator grant. He is the coordinator of the EquipEx+ project NanoCryoCLEM awarded in 2020.

Research team

Dr. Rémi FRONZES Research Director DR1, (CNRS)
Dr. Esther MARZA Maître de conference (Univ. Bordeaux)
Dr. Gabriel OKA Post-doc (ANR)
Nathanaël BENOIT PhD student (Université de Bordeaux)
Louis ROUILLAN PhD Student (Université de Bordeaux)
Nicolas SOLA PhD Student (Université de Bordeaux)
Marie MANDART Research assistant AI (ANR)

This team is part of the unit "Microbiologie fondamentale et pathogénicité" (MFP), CNRS UMR5234/Univ. Bordeaux.

Structure and Function of Bacterial Nanomachines

Bacteria are extremely adaptable and able adjust their lifestyle very quickly when these changes occur. One dramatic illustration of this capacity is the spread of antibiotic resistance among bacterial pathogens. During the last decade, the emergence of multi-resistant bacteria, which are resistant to several treatments, led to increase mortality caused by common infections. The 2014 report on antimicrobial resistance from the World Health Organization warns against the beginning of a "post-antibiotic" era, when most of the bacterial pathogens will become resistant to all treatments available.

In this context, it is crucial to fully understand the molecular mechanism of bacterial adaptability to ultimately target and limit this ability. To survive in a changing environment, bacteria have to resist to stresses induced by these changes and ultimately to adapt their lifestyle if these changes persist. These two processes are almost contradictory since the first aims at maintaining cell integrity while the second allows long term variability through the acquisition of new traits.

For 10 years, the team engaged several lines of research on this topic in the lab, first at Institut Pasteur and from 2016 within the MFP unit and at the Institut Européen de Chimie et Biologie (IECB) in Bordeaux. Over the last 5 years, we focused our research on the main projects listed below. The lab has also been instrumental in setting up a state of the art cryo-electron microscopy (CryoEM) facility at IECB. We have several on-going collaborations related to our expertise in CryoEM. We are also involved in technological development projects such as the implementation of super-resolution correlative microscopy in cryo conditions.

Project 1: Natural transformation and gene repair in bacterial pathogens (Funded by ERC)

In this project, we want to understand how DNA can be uptaken and recombined in the bacterial genome during bacterial transformation.

Natural genetic transformation, first discovered in *Streptococcus pneumoniae* by F. Griffith in 1928, is observed in many Gram-negative and Gram-positive bacteria. This process promotes genome plasticity and adaptability. In particular, it enables many human pathogens such as *Streptococcus pneumoniae*, *Neisseria gonorrhoeae* or *Vibrio Cholerae* to acquire resistance to antibiotics and/or to escape vaccines through the binding and incorporation of new genetic material. While it is well established that this process requires the binding, internalization of external DNA and its recombination in the bacterial genome, the molecular details of these steps are unknown. In this project, we aim at acquiring a detailed understanding of each of these steps. We discovered a new appendage at the surface of *S. pneumoniae* cells and showed that this appendage is similar in morphology and composition to appendages called Type IV pili commonly found in Gram-negative bacteria. We demonstrated that this new pneumococcal pilus is essential for transformation and that it directly binds DNA (**PLOS Pathogens 2013 and 2015**). We are also actively studying the DNA translocation apparatus. We isolated most of its components and are in the process of determining their structure and studying their function *in vitro* and *in vivo*. Finally, we identified a new key ATPase involved in the recombination process. We determined the crystal structure of this protein and identified its function *in vitro* and *in vivo* in collaboration with Patrice Polard's team in Toulouse (France) (**Nature communications, 2017**). We also explored the initiation and molecular mechanism of the recombination event. We determined the structure of RecA filaments from *S. pneumoniae* and revealed the structural basis of its interaction with its loader on ssDNA during transformation (called DprA) (**Manuscripts in preparation**). Finally, we are also exploring the architecture of the transformation apparatus in its native cellular environment using Cryo-tomography and correlative microscopy approaches.

Project 2: Bacterial competition systems (Type 6 and type 7 secretion systems) (funded by the IDEX/regional Chair).

The bacterial Type 6 secretion (T6S) system is one of the key players for microbial competition, as well as an important virulence determinant during bacterial infections. It assembles a nano-crossbow-like structure that propels an arrow made of Hcp tube and VgrG spike into the cytoplasm of the attacker cell and punctures the prey's cell wall. The nano-crossbow is stably anchored to the cell envelope of the attacker by a membrane core complex. In collaboration with Eric Cascales' laboratory in Marseille (France), we recently have shown that this membrane complex is assembled by the sequential addition of three proteins –TssJ, TssM and TssL– and presented a structure of the fully assembled complex (**Nature 2015**). Since our arrival at IECB and MFP, we solved the cryoEM structure of this complex (**EMBO J. 2019**). We also solved the cryoEM structure of another key element of the T6S system, the baseplate (**Nature microbiology 2018**) and of the T6SS substrate from pathogenic *Escherichia coli* in complex with the T6SS spike (**EMBO J. 2020**).

While at institut Pasteur, our group started to work on type 7 secretion systems (T7SS). These systems are mostly found in mycobacteria and other Gram-positive bacteria such as *Staphylococcus aureus* or *Bacillus subtilis*. While it is well established that mycobacterial T7SS are directly used in virulence, their exact function in other Gram-positive bacteria was unclear. We recently revealed that the T7SS found in *B. subtilis* is an anti-microbiol device used by these bacteria to kill other Gram-positive bacteria (**BioRxiv 2020**). We also performed an in-depth biochemical study and solved the crystal structure of a key component of this system (YukC). Overall, our work shows that *B. subtilis* Yuk T7SS is a bona fide and functional T7SS that can be used a model system to study T7SSs.

Project 3: Metabolic adaptability of bacterial pathogens (funded by the ERC)

Acetaldehyde-alcohol dehydrogenase (AdhE) enzymes are a key metabolic enzyme in bacterial physiology and pathogenicity. They convert acetyl-CoA to ethanol via an acetaldehyde intermediate during ethanol fermentation in an anaerobic environment. This two-step reaction is associated to NAD⁺ regeneration, essential for glycolysis. The bifunctional AdhE enzyme is conserved in all bacterial kingdoms but also in more phylogenetically distant microorganisms such as green microalgae. It is found as an oligomeric form called spiroosomes, for which the function remains elusive. We used cryo-electron microscopy to obtain structures of *E. coli* spiroosomes in different conformational states. We showed that spiroosomes contain active AdhE monomers, and that AdhE filamentation is essential for its activity *in vitro* and function *in vivo*. The detailed analysis of these structures provides insight showing that AdhE filamentation is essential for substrate channeling within the filament and for the regulation of enzyme activity. This work was published in **Nature communications in 2020**.

Project 4: Structure and function of a mycoplasma antibody cleavage device (funded by the ANR, in collaboration Yonathan Arfi, INRA, Bordeaux)

Mycoplasmas cause various chronic diseases in animals and humans. They have evolved strategies to evade the host immune response, including the Mycoplasma Ig Binding (MIB)– Mycoplasma Ig Protease (MIP) antibody degrading system. The Fab domain of many types of immunoglobulins is recognized by MIB. This interaction allows the recruitment of the serine protease MIP, which cleaves the VH domain of the antibody. To understand the molecular basis of this system, we have solved the structure of the ternary complex Fab–MIB–MIP antibody degrading system by cryo-electron microscopy. The structure of the complex between MIB, MIP and the Fab fragment of a goat IgG has been solved to a 3 Å resolution, by single particle cryoEM. Together with biochemical and *in vivo* data, our work reveals very original binding mechanism of the complex to the antibody (**Science Advances, 2020**).

Project 5: Development of super-resolution cryo-correlative microscopy
The project 5 started very recently in collaboration with the laboratories of Daniel

Choquet (IINS), Brahim Lounis, (LP2N) Gregory Giannone (IINS), Bordeaux imaging center and the UMS of the IECB. The major challenge in cell and structural biology today is to combine two cutting-edge technologies, super-resolution fluorescence microscopy and cryoEM, to enable a new revolution in the determination of atomic structure and the understanding of the function of molecules in their natural context. Multimodal or correlative microscopy approaches combining the power of high-resolution optical and electronic microscopy are at the forefront of technology at the national and international level. This technological development will make it possible to go beyond the limits of existing technologies and will revolutionize our understanding of the molecular mechanisms of living organisms, particularly in the fields of neurobiology, cancerology and the study of pathogens such as parasites, bacteria that are multi-resistant to antibiotics or emerging viruses. Rémi Fronzes is the coordinator of an EquipEx proposal awarded in 2020 focusing on this project. He is also the coordinator of a CPER project for IECB, including equipment that will be essential to this project.

Selected publications

1. Hertzog, M.; Perry, T. N.; Dupaigne, P.; Serres, S.; Morales, V.; Soulet, A.-L.; Bell, J. C.; Margeat, E.; Kowalczykowski, S. C.; Le Cam, E.; Fronzes, R.; Polard, P. Assembly Mechanism and cryoEM Structure of RecA Recombination Nucleofilaments from *Streptococcus Pneumoniae*. *Nucleic Acids Res* **2023**, 51 (6), 2800–2817. <https://doi.org/10.1093/nar/gkad080>.
2. Blanc, M.; Lettl, C.; Guérin, J.; Vieille, A.; Furler, S.; Briand-Schumacher, S.; Dreier, B.; Bergé, C.; Plückthun, A.; Vadon-Le Goff, S.; Fronzes, R.; Rousselle, P.; Fischer, W.; Terradot, L. Designed Ankyrin Repeat Proteins Provide Insights into the Structure and Function of Cagl and Are Potent Inhibitors of CagA Translocation by the *Helicobacter Pylori* Type IV Secretion System. *PLoS Pathog* **2023**, 19 (5), e1011368. <https://doi.org/10.1371/journal.ppat.1011368>.
3. Rosa, L. T.; Vernhes, É.; Soulet, A.-L.; Polard, P.; Fronzes, R. Structural Insights into the Mechanism of DNA Branch Migration during Homologous Recombination in Bacteria. *EMBO J* **2024**, 43 (23), 6180–6198. <https://doi.org/10.1038/s44318-024-00264-5>.
4. Anger, R.; Pieuille, L.; Shahin, M.; Valette, O.; Le Guenno, H.; Kosta, A.; Pelicic, V.; Fronzes, R. Structure of a Heteropolymeric Type 4 Pilus from a Monoderm Bacterium. *Nat Commun* **2023**, 14 (1), 7143. <https://doi.org/10.1038/s41467-023-42872-5>.
5. Beauvois, S. G.; Flaugnatti, N.; Ilbert, M.; Boyer, M.; Gavello-Fernandez, E.; Fronzes, R.; Jurénas, D.; Journet, L. The Tip Protein PAAR Is Required for the Function of the Type VI Secretion System. *Microbiol Spectr* **2023**, 11 (6), e0147823. <https://doi.org/10.1128/spectrum.01478-23>.



Dr. Yaser Hashem
Research Director (DR2), Inserm

Yaser Hashem obtained his PhD in 2010 in Strasbourg (France) in computational structural biology where he developed computational approaches for the study of bacterial ribosomal RNA interactions with several antibiotics. After his PhD he went on for a Postdoc at Columbia University in the city of New York with Prof. Joachim Frank (Nobel Laureate for Cryo-EM, 2017) where he worked on understanding the mRNA translation regulation using Cryo-EM and more specifically the translation initiation step in mammals. In 2014, Y. Hashem started his research group in Strasbourg (France) where he became expert in translation regulation in pathogenic parasites and their mammalian hosts. In 2017, Y. Hashem was awarded with the ATIP-Avenir grant, the ERC (European Research Council) starting grant and the "Chair d'Excellence Junior" from the University of Bordeaux and joined the IECB as a Group Leader. More recently, Y. Hashem was awarded with the ERC (European Research Council) Consolidator Grant 2022.

Research team

Dr. Yaser HASHEM Research Director, DR2, (Inserm)
Mrs Stéphanie DURRIEU Ai (CNRS)
Dr José EDUARDO GOMEZ MC (UB)
Dr Mayara DEL CISTIA Postdoc (INSERM)
Dr Trung NGUYEN Postdoc (INSERM)
Ms Sramona BARUA PhD student (INSERM)
Ms Jessica DA CRUZ PhD student (INSERM)
Dr Rafael ROCHA Postdoc (INSERM)
Dr Yaser HASHEM DR2 (INSERM)

This team is part of the unit: This team is part of the unit "Acides Nucléiques: Régulations Naturelles et Artificielles" (ARNA), Inserm U1212/CNRS UMR5320/Univ. Bordeaux

RNA Processing and translation regulation in pathogens and hosts (RNA-PT)

The "mRNA translation regulation in pathogens and hosts" group endeavors to study at the molecular level the mRNA translation regulation in several species of pathogens, mainly eukaryotic (both cytosolic and mitochondrial mRNA translation), and their hosts. For several years already, the group has studies existing structural differences in the translation machinery between kinetoplastids and their mammalian hosts in order to discover new and more specific potential therapeutic targets that can be used for the development of safer therapeutic strategies against this family of dangerous parasites. One of the main focuses of the group is the translation initiation step that presents various important structural differences in kinetoplastids, such as Trypanosomes and Leishmanias, when compared to humans. The group is mainly specialized in cryo-electron microscopy, a technique that allows in principle to resolve molecular structures of large sizes to atomic resolutions.

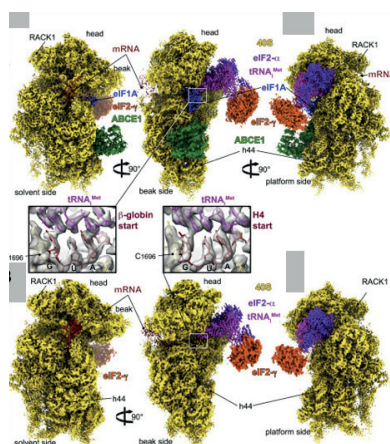


Figure1. Late-stage 48S initiation complexes (48SIC) from mammals. Thanks to grad-cryo protocol we were able to purify native IC in native conditions. A, β -globin IC. B, histon 4 IC. In boxes a blow up on the start-initiation codons for both complexes. From Simonetti & Guca at al. Cell Reports 2020.

We have solved the structures of two native translation initiation complexes with two archetype abundant cellular mRNAs, the β -globin and histon 4. Our structures are at near-atomic resolution (3.0 to 3.5 Å, respectively, Figure1) and reveal that depending on the mRNA sequence, its interactions with different components of the initiation complex such as eukaryotic initiation factors (eIFs) 1A, 2 and 3 can vary. These complexes can be directly compared

with those from several species of pathogenic protozoa.

Translation initiation in kinetoplastids: The initiation stage is expected to represent numerous variations in pathogenic protozoa such as kinetoplastids (like *T. cruzi*, *T. brucei* and *L. major*) compared to its mammalian counterpart because of the presence of several large rRNA expansion segments at the binding site of several initiation factors such as eIF3. Protozoa like kinetoplastids present a complex life cycle where the parasite spends most of its life in an insect vector before being transmitted to a mammalian host upon biting. Moreover, *in vitro* growth of the parasite reveals various population regulation points aimed at optimizing the environmental resources such as oxygen and carbon resources. Therefore, we first attempted to study their *in vitro* growth in order to retrieve the best conditions allowing the purification of canonical translation initiation complexes.

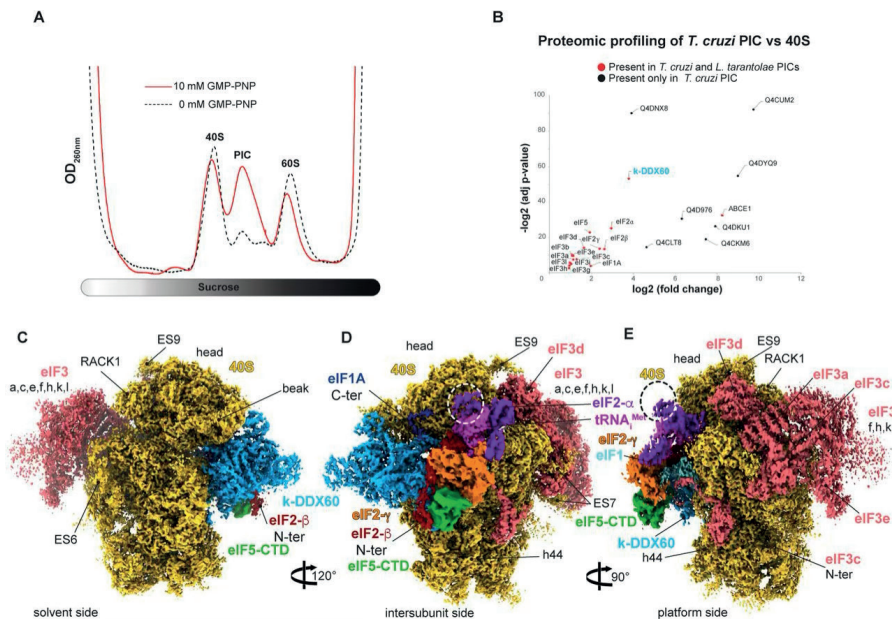


Figure 2. Composition and cryo-EM structure of the *T. cruzi* 43S PIC. (A) The effect of the GMP-PNP treatment on the 43S PIC stabilization in the *T. cruzi* lysate assessed by UV absorbance profile analyses (B) Proteomic profiling of the endogenous pre-initiation complex in comparison with native 40Ss purified from the *T. cruzi* cell lysate (see methods for the validation). (C) The overall structure of the *T. cruzi* 43S PIC shown from the intersubunit side. The initiation factors are colored variably. (D) The 43S PIC reconstruction focused on the solvent side. Extra density of eIF2 α corresponding to the kinetoplastid specific N-terminal insertion is encircled by a dashed line. (E) The 43S PIC reconstruction focused on eIF3 and the 40S platform. From Boehler et al. 2020 (Cell Reports).

The study of the dynamics of growth of epimastigote forms from *trypanosoma cruzi* and *Leishmania tarentolae* was carried out. After establishing the best growth conditions for both parasites, we have attempted the purification of initiation complexes using our grad-cryo protocol at different time-points of the growth curves and only at the 3rd growth day we were able to harvest the (pre)initiation complexes in sufficient yield to obtain a cryo-EM structure, the reason of which remains unknown.

The purified complexes were solved by cryo-EM at 3.3Å revealing the presence of several kinetoplastids-specific features such as the presence of an additional helicase involved in the initiation process that we have termed DDX60-like because of its faint homology to mammalian DDX60 (Figure2).

Mitochondrial translation regulation: In the past years the team has heavily invested in investigating translation regulation in mitochondria in both pathogens and hosts. Thus, we have recently published the cryo-EM structure of the plant mitoribosome, as plants are also known to be hosts for several species of kinetoplastids (Waltz et al. Nature plants 2019, Waltz & Soufari et al. Nature plants 2020, Figure 3), but also from green algae *Chlamydomonas reinhardtii* (Waltz et Salinas, Nature Comm. 2022) and *T. cruzi* and *L. tarentolae* (Soufari et al. PNAS plants 2020).

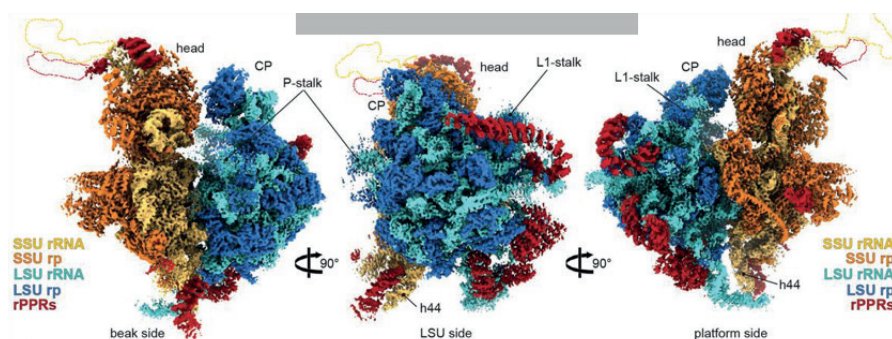


Figure 3. Overall structure of the plant mitochondrial ribosome. rRNAs are colored in light blue (LSU) and yellow (SSU) and ribosomal proteins in blue (LSU) or orange (SSU). A dozen pentatricopeptide repeat proteins (PPR), specific to the plant mitoribosome were discovered and termed ribosomal PPR (rPPR), shown in red. From Waltz & Soufari et al. Nature plants 2020.

Selected publications

- Wang, C.; Kassem, S.; Rocha, R. E. O.; Sun, P.; Nguyen, T.-T.; Kloehn, J.; Liu, X.; Brusini, L.; Bonavoglia, A.; Barua, S.; Boissier, F.; Lucia Del Cistia, M.; Peng, H.; Tang, X.; Xie, F.; Wang, Z.; Vadas, O.; Suo, X.; Hashem, Y.; Soldati-Favre, D.; Jia, Y. Apicomplexan Mitochondrion from Highly Fragmented rRNAs to a Functional Machine. *Nat Commun* 2024, 15 (1), 10689. <https://doi.org/10.1038/s41467-024-55033-z>.
- Guca, E.; Alarcon, R.; Palo, M. Z.; Santos, L.; Alonso-Gil, S.; Davyt, M.; De Lima, L. H. F.; Boissier, F.; Das, S.; Zagrovic, B.; Puglisi, J. D.; Hashem, Y.; Ignatova, Z. N6-Methyladenosine in 5' UTR Does Not Promote Translation Initiation. *Molecular Cell* 2024, 84 (3), 584-595.e6. <https://doi.org/10.1016/j.molcel.2023.12.028>.
- Fostier, C. R.; Ousaleem, F.; Leroy, E. C.; Ngo, S.; Soufari, H.; Innis, C. A.; Hashem, Y.; Boël, G. Regulation of the Macrolide Resistance ABC-F Translation Factor MsrD. *Nat Commun* 2023, 14 (1), 3891. <https://doi.org/10.1038/s41467-023-39553-8>.



Dr. Petya Violinova Krasteva
Research Director (DR2), CNRS
UMR5248 CBMN

Dr. Petya V. Krasteva joined the CBMN as an IECB group leader in October 2019.

Her research focuses on cyclic dinucleotide signaling and extracellular matrix secretion in bacterial biofilm formation and pathogenesis. Combining X-ray crystallography, biophysical and biochemical assays, cryo-electron microscopy and in cellulo/in biofilm structural and functional studies, her 'Structural Biology of Biofilms' team aims to provide a comprehensive view of bacterial social networks that spans the different resolution levels and present molecular blueprints for the development of novel anti-infectives and sustainable biomaterials.

Petya Krasteva completed her PhD in Molecular and Cell Biology at Ivy League's Cornell University in January 2011, after which she joined the editorial team of Nature Methods in New York. For her postdoc, she moved to the Institut Pasteur in Paris in 2012 and started her independent team as a CNRS CRCN and an ATIP-Avenir laureate in the end of 2016 at the I2BC, Gif-sur-Yvette.

For her work on bacterial signaling and biofilm formation, Petya Krasteva is the recipient of the Prix Jacques Monod (Fondation de France, 2016), the CNRS Médaille de Bronze (2019), an ERC Starting Grant (BioMatrix, 2018–2023) and an ERC Consolidator Grant (BacFilm, start December 2024).

Research team

Dr. Petya V. KRASTEVA PhD, HDR, DR2
CNRS, Principal Investigator / Group Leader
(CNRS)

Thibault SANA Research engineer (CNRS)

Itxaso ANSO PostDoc (CNRS)

Reem IWAZA PostDoc (CNRS)

Solène Lelievre Intern BTS (Lycée des Métiers
de la Biologie et de la Chimie – Saint-Louis |
Université Paris-Saclay)

Salomé CHADRIN Intern M1 (Univ. Côte d'Azur)

Tom TOUYA Intern L3 (Univ. de Besançon)

This team is part of the unit: This team is part of the unit "Chimie et Biologie des Membranes et des Nano-objets" (CBMN), CNRS UMR5248/INP/Univ. Bordeaux

Structural Biology of Biofilms

The Krasteva Lab's research focuses on cyclic dinucleotide signaling and extracellular matrix secretion in bacterial biofilm formation and pathogenesis. Combining X-ray crystallography, biophysical and biochemical assays, cryo-EM and in cellulo/in biofilm structural and functional studies, the 'Structural Biology of Biofilms' (SBB) team aims to provide a comprehensive view of bacterial social networks that spans the different resolution levels and presents molecular blueprints for the development of novel anti-infectives.

Currently the team's research is focused on two main scientific questions: i) what are the intracellular signaling mechanisms that regulate bacterial biofilm formation and, ii) what are the structure, function and dynamics of the membrane-embedded biosynthetic platforms for the secretion of extracellular matrix components

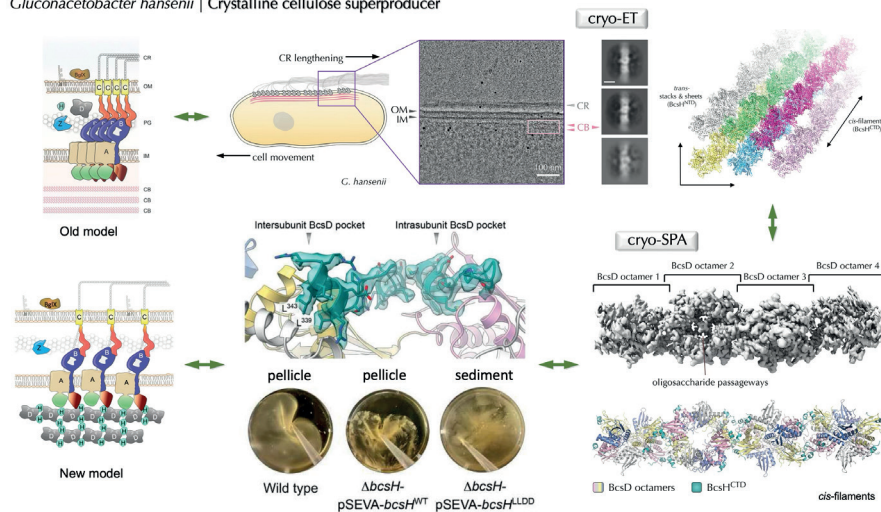
Recently, the 'Structural Biology of Biofilms' team provided unprecedented insights into the structural biology of bacterial cellulose secretion (BCS) systems in bacterial biofilms with complete structure-function analyses of the megadalton-sized membrane-embedded Bcs secretion macrocomplex of *E. coli* and other enterobacteria, as well as multiple regulatory subcomplexes (Zouhir *et al.* *mBio* 2020, Abidi *et al.* *Science Advances* 2021, Anso *et al.* 2024). In a separate studies, the group also discovered dedicated cytoskeletal scaffolds for exopolysaccharide secretion and provided atomic-resolution insights into the mechanism of synthase array assembly in the cellulose superproducer *Gluconacetobacter hansenii* and in a wide array of plant-colonizing Proteobacteria of substantial interest for industrial, agricultural and biomedical applications (Abidi *et al.* *Science Advances* 2022; Sana *et al.* *Current Biology* 2023). Finally, the team also deciphered cyclic dinucleotide-dependent mechanisms of transcription regulation of motility and biofilm formation in the ESKAPE pathogen *P. aeruginosa* (Torres-Sánchez *et al.* *PNAS* 2023)

In recent years, the Krasteva Lab made significant progress in the mechanistic unravelling of the enterobacterial cellulose secretion machinery. These include:

- Initial structural and mechanistic insights into the *E. coli*-like bacterial cellulose secretion (Bcs) systems revealing for the first time the assembly of a cooperative multi-component synthase-dependent system for exopolysaccharide secretion. Electron microscopy studies in negative stain of a megadalton-sized BcsRQABEFG membrane-extracted macrocomplex (Krasteva *et al.*, Bernal-Bayard *et al.*, *Nature Communications* 2017).
- Structure and multitasking of the c-di-GMP-sensing cellulose secretion regulator BcsE: Using a combination of single-particle EM, X-ray crystallography, phenotypic and *in vitro* biochemical assays, the team demonstrated that the hallmark for *E. coli*-like enterobacterial systems BcsE and BcsF proteins might have evolved to boost exopolysaccharide production through action at multiple levels: from regulating the expression and membrane protein sorting of essential for secretion components, to maintaining Bcs macrocomplex integrity and dimeric c-di-GMP complexation for processive synthase activation (Zouhir*, Abidi* *et al.*, *mBio* 2020).
- First cryo-EM structure of the assembled, megadalton-sized synthase-dependent cellulose secretion macrocomplex from *E. coli* and multiple crystal structures of regulatory protein subcomplexes (Abidi*, Zouhir* *et al.*, *Science Advances* 2021).
- Complete high-resolution cryo-EM structures of the Bcs secretory macrocomplex in discrete conformational states dependent on available c-di-GMP. In this most recent cryo-EM study the team revealed the molecular mechanisms i) for cellulose-modifying phosphoethanolamine (pETN)-transferase recruitment via the evolution of

The team therefore undertook a comparative structural biology approach to unveil determinants of crystalline

Gluconacetobacter hansenii | Crystalline cellulose superproducer



Finally, the team's contributions to the field go well beyond bacterial cellulose secretion. For example we recently provided an integrated model of the motile-to-sessile transition via the FleQN master regulator complex of flagellar vs. biofilm-promoting gene expression in *P. aeruginosa* (Torres-Sánchez *et al.*, **PNAS** 2023) and have several additional axes of research on flagellar motility (e.g. Altinoglu*, Abriat* *et al.*, **PLoS Genetics** 2022), bacterial shape-determining proteins and c-di-GMP-dependent regulation of bacterial adaptation and virulence.

7. Torres-Sánchez, L.; Géry Sana, T.; Decossas, M.; Hashem, Y.; Krasteva, P. V. Structures of the *P. Aeruginosa* FleQ-FleN Master Regulators Reveal Large-Scale Conformational Switching in Motility and Biofilm Control. *Proc. Natl. Acad. Sci. U.S.A.* **2023**, *120* (50), e2312276120. <https://doi.org/10.1073/pnas.2312276120>.



Dr. Pierre Maisonneuve
Research Scientist (CNRS)

Pierre Maisonneuve has completed his PhD in 2014 at the Pasteur institute in Paris. He then performed a postdoc at the Lunenfeld-Tanenbaum research Institute in Toronto (Canada) where he was supported by a postdoctoral fellowship from the Canadian Institutes of Health Research. In 2022, he was awarded a starting grant "Amorçage de Jeunes Équipes" from the "Fondation pour la Recherche Médicale" (FRM) to join the CBMN in Bordeaux and start as a group leader at the IECB. In 2023, he obtained a permanent position as a research scientist (CRCN) at the CNRS.

Research team

Dr. Pierre MAISONNEUVE Research Scientist (CNRS)

Dr. Marion DECOSSAS Research engineer (CNRS)

Dr. Baptiste FISCHER Lecturer (UB)

Dr. Margaux LUSTIG Postdoctoral fellow (CNRS)

Dr. Sandeep KN MULUKALA Postdoctoral fellow (INSERM)

Lou CAMOIN Master 1 Student (UB)

Alexandre DARRIUS-LAPLACE 2nd year BTS student (CNRS)

Jules POZZAR 2nd year BTS student (CNRS)

This team is part of the unit: "Chemistry and Biology of Membranes and Nano-objects" (CBMN), CNRS UMR 5248/INP/Univ. Bordeaux

Structural Biology of Signaling proteins

Pseudokinases are inactive kinases that influence cell signaling through non-catalytic mechanisms. Pseudokinases represent ~10% of all human protein kinases. Their dysregulation contributes to human diseases, including cancers. They represent a promising niche of therapeutic targets. Indeed, the first drug targeting a pseudokinase protein, i.e. Deucravacitinib, was approved by the FDA in 2022, paving the way for the development of new therapeutics targeting pseudokinases. However, pseudokinases remain challenging targets due to their lack of catalytic activity and our lack of understanding of how they function. Therefore, uncovering the molecular mechanisms of pseudokinases would not only improve our understanding of human signaling in health and disease, but would also allow us to better target them in the clinic.

The RAS-ERK signaling pathway is crucial for regulating cell proliferation, growth or differentiation. Activation of RAS in response to mitogenic stimulation triggers the activation of the RAF kinase family and downstream signaling. Efficient signaling through the RAS/ERK cascade requires the proper assembly of RAF, MEK and ERK proteins into a complex that facilitates a sequential phosphorylation cascade with RAF phosphorylating MEK and MEK phosphorylating ERK (Figure 1).

Unbridled activation of this pathway is a hallmark of cancer. RAS is the most frequently mutated oncogene (~27% of cancers), while RAF is the most mutated kinase family in cancer (8% of cancers) with the V600E mutation accounting for 92% of oncogenic RAF mutants. In fact, the RAS-ERK pathway is one of the most targeted in the clinic, but unfortunately resistance mechanisms limit drug efficacy. It is therefore crucial to improve our understanding of the regulation of the RAS-ERK pathway in order to develop new treatments.

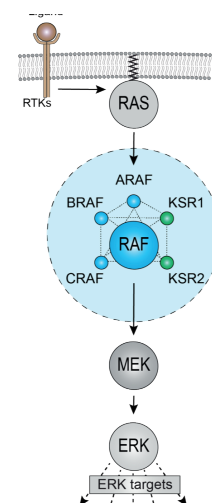


Figure 1: The RAS-ERK Pathway 22

Mammals express five RAF isoforms including three active kinases ARAF, BRAF, CRAF and two catalytically deficient pseudokinases KSR1 and KSR2. RAF family members assemble into distinct homo- or hetero- dimers and their biological relevance is still emerging. Despite recent progress, it is still unclear how specific homo- and heterodimer pairs are preferentially assembled and what their specific functions are. In this context, we aim to decipher the role of the inactive KSR pseudokinases in the activation of RAF protein kinases.

To dissect the molecular function of KSR in RAF activation, we investigated its interaction with MEK and BRAF. Contrary to the long-standing model in which KSR acts as a passive scaffold, we demonstrated that **KSR functions as an allosteric activator of BRAF**. MEK binding to KSR1 induces a conformational change that promotes heterodimerization with BRAF and its subsequent activation. We identified a previously uncharacterized **BRAF-specific region (BRS)** that binds directly to the **CC-SAM domain** of KSR1. This interface was structurally defined and functionally validated both in vitro and in cells, revealing its critical role in RAF signalling output (Figure 2). These results redefine the role of KSR from scaffold to **active regulator**, establishing a new allosteric mechanism by which KSR pseudokinases control signalling in the RAS-ERK pathway (Lavoie H, Sahmi M, Maisonneuve P, et al., Nature. 2018).

Selected publications

1. Ignatov, M.; Jindal, A.; Kotelnikov, S.; Beglov, D.; Posternak, G.; Tang, X.; Maisonneuve, P.; Poda, G.; Batey, R. A.; Sicheri, F.; Whitty, A.; Tonge, P. J.; Vajda, S.; Kozakov, D. High Accuracy Prediction of PROTAC Complex Structures. *J Am Chem Soc* **2023**, 145 (13), 7123–7135. <https://doi.org/10.1021/jacs.2c09387>.
2. Maisonneuve, P.; Sahmi, M.; Bergeron-Labrecque, F.; Ma, X. I.; Queguiner, J.; Arseneault, G.; Lefrançois, M.; Kurinov, I.; Fronzes, R.; Sicheri, F.; Therrien, M. The CNK–HYP Scaffolding Complex Promotes RAF Activation by Enhancing KSR–MEK Interaction. *Nat Struct Mol Biol* **2024**, 31 (7), 1028–1038. <https://doi.org/10.1038/s41594-024-01233-6>.
3. Mishra, V.; Sharma, K.; Bose, A.; Maisonneuve, P.; Visweswariah, S. S. The Evolutionary Divergence of Receptor Guanylyl Cyclase C Has Implications for Preclinical Models for Receptor–Directed Therapeutics. *J Biol Chem* **2024**, 300 (1), 105505. <https://doi.org/10.1016/j.jbc.2023.105505>.

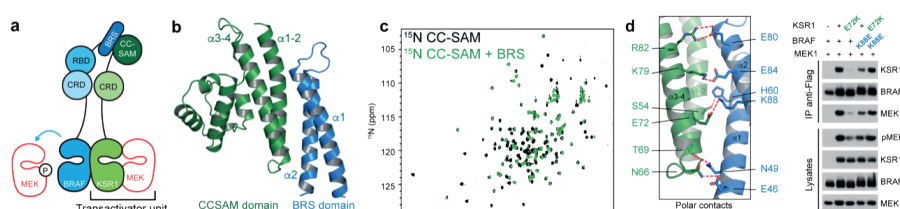


Figure 2: KSR allosterically activate RAF. **a.** Schematic of the updated models of KSR-mediated MEK phosphorylation by RAF. **b.** Crystal structure of the BRS:CC-SAM complex. **c.** Superposition of the $1\text{H } 15\text{N}$ HSQC spectra of 15N CC-SAM alone (black) or with BRS (green). **d.** Mutations at the BRS:CCSAM binding interface disturb RAF–KSR1 dimerization.

Building on this model, we next addressed how **scaffolding proteins CNK and HYP** enhance RAF activation in a KSR-dependent manner. Using X-Ray crystallography, we solved the structure of the CNK–HYP complex revealing a ring shape module, which was shown to be important for the KSR-dependent activation of RAF. To deepen our understanding on how this complex activates RAF, we solved the **cryo-EM structure of the CNK–HYP:KSR–MEK complex at 3.3 Å** using the 200kV Talos Artica microscope at the IECB facility to reveal how CNK and HYP bind simultaneously to KSR and MEK, thereby stabilizing the KSR–MEK complex. This stabilized complex facilitates **heterodimerization between KSR and RAF**, enabling allosteric RAF activation through the same allosteric mechanism that we previously described. This study provides a mechanistic explanation for how multimeric scaffolding complexes fine-tune RAF activation through the recruitment of pseudokinases and offers a **new regulatory axis** within the RAS–ERK pathway (Maisonneuve P, Sahmi M, et al., *Nat Struct Mol Biol.* 2024).

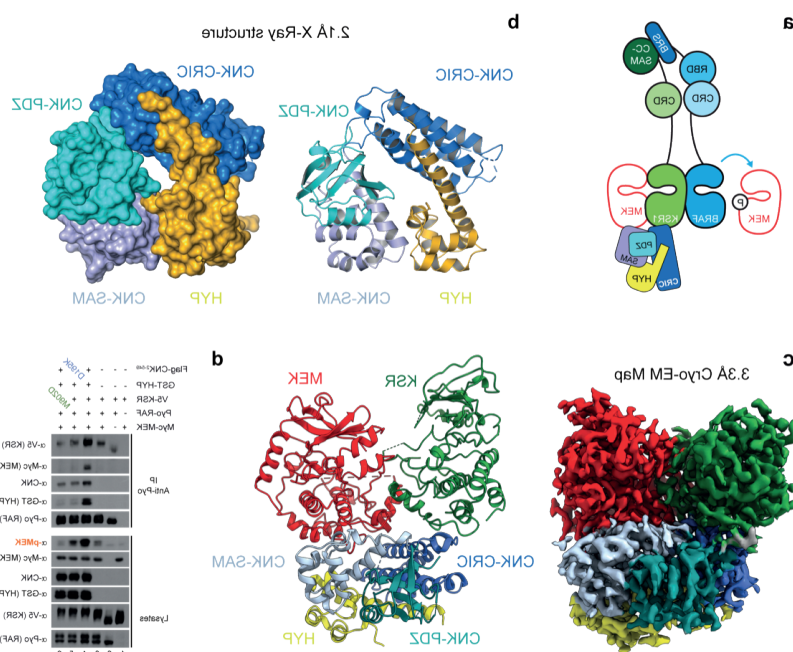


Figure 3: CNK–HYP binds to KSR–MEK to activate RAF. **a.** Schematics on how CNK–HYP regulate the RAS–ERK pathway. **b.** Crystal structure of the CNK:HYP complex in cartoon or surface representation. **c.** Cryo-EM map and structure of the CNK:HYP:KSR:MEK complex. **d.** The CNK–HYP complex promotes RAF–KSR heterodimerization and RAF activation.



Dr. Nicolas Reyes
Research Director (DR2),
CNRS/Univ. Bordeaux

My work focuses on the molecular mechanisms of human membrane proteins. I have a multidisciplinary background in membrane protein biophysics spanning from single-molecule electrophysiological measurements (*Nature* 2006; visiting PhD student at The Rockefeller University, USA) to atomic-resolution structure determination (*Nature* 2009; Postdoc at Weill Cornell, USA).

As an early-career independent researcher, my laboratory determined the first 3D structures of an essential synaptic component in the human brain, namely excitatory amino acid transporters, and a first-in-class allosteric inhibition mechanism (*Nature* 2017). More recently, we studied receptor (*Science* 2020; *Nature* 2022; *Nat. Struct. Mol. Biol.* 2022) and transport (*EMBO J.* 2022) mechanisms of different membrane protein systems with a focus on human solute carriers. Research in my lab has mainly been funded by international grants including ERC Starting and Consolidator grants.

Research team

Dr. Nicolas REYES Research Director, DR2 (CNRS)
Dr. Juan CANUL-TEC Postdoc (CNRS)
Dr. Miryam VILLALBA Postdoc (CNRS)
Dr. Sandeep MULAKALA Postdoc (CNRS)
Marie MANDART Engineer (CNRS)

This team is part of the unit: "Fundamental microbiology and pathogenicity" (MFP), CNRS UMR5234/Univ. Bordeaux

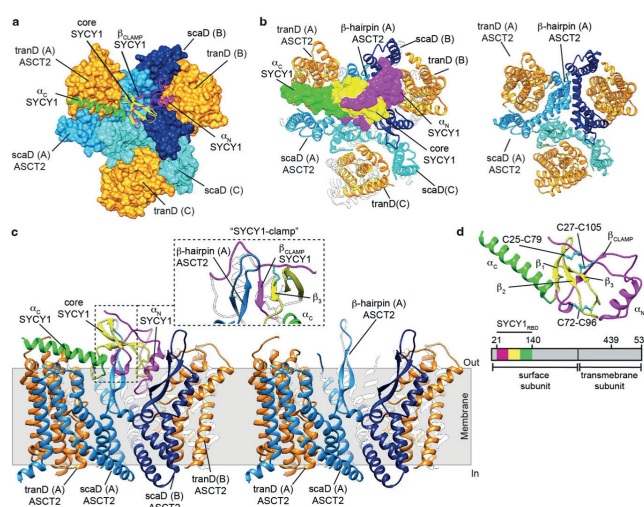
Membrane Protein Mechanisms

Human solute carriers (hSLC) form a superfamily of integral membrane proteins that transport essential molecules and ions across membranes, and are the cellular receptors of human and pathogenic proteins. Their transport and receptor functions are involved in a wide range of pathological conditions, making hSLCs important emerging drug targets in neurodegeneration, cancer, and infectious diseases, among others.

Our research program aims to unravel novel transport, receptor and pharmacological mechanisms of medically important hSLCs using a multidisciplinary biophysical approach. To achieve this, we combined high-resolution cryo-electron microscopy with functional approaches to probe hSLC complexes' structures, dynamics, and thermodynamics.

Figure 1: Cryo-EM structure of ASCT2WT-SYCY1RBD complex

a, Extracellular view of the ASCT2WT (surface representation) in complex with the SYCY1RBD (ribbon representation). The three ASCT2WT tranDs are in orange and the central "propeller-like" structure formed by the three scaDs in different tones of blue. The corresponding ASCT2 subunits are indicated in brackets. The SYCY1RBD N-terminal region is in pink, the core in yellow, and the α C in green. **b**, Extracellular view of the ASCT2WT (ribbon representation) in complex with the SYCY1RBD (surface representation). **c**, Membrane view of the complex. The ASCT2WT subunit C and some elements of the TM4 in the scaD in the subunit B were removed for clarity of display. The inset shows the details of the hybrid β -sheet clamp formed between the N-terminal β CLAMP of the SYCY1RBD (pink) and the extracellular β -hairpin of ASCT2 subunit A. **d**, Structure of the bound SYCY1RBD highlighting the different structural elements with the same color code as in (b). A linear diagram of the syncytin-1 architecture is shown.



Receptor-recognition and antiviral mechanisms of human placental proteins.

Human endogenous retroviruses (HERVs) constitute a significant part of the human genome (~8%), and originated from ancient infections of the germline. The human placenta expresses HERV-derived proteins syncytin-1 and suppressyn that catalyse the formation of the ultimate cellular interface between the mother and the fetus. Notably, those placental proteins restrict infections from the largest interference group of vertebrate retroviruses, known as the RDR interference group, which includes simian retroviruses that cause immunodeficiency in non-human primates and have zoonotic potential (<https://spillover.global/virus/141>). Therefore, syncytin-1 and suppressyn are regarded as host-immunity restriction factors expressed during development (Frank et al., *Science* 2022; 10.1126/science.abq7871).

At the core of the syncytin-1 and suppressyn morphological and immunological functions in placenta are poorly-understood molecular mechanisms by which they recognize a common cellular receptor, the membrane transporter ASCT2. In this project, we have determined cryo-electron microscopy structures of the human ASCT2 in complexes with the receptor binding domains (RBDs) of syncytin-1 and suppressyn. The structures reveal unexpected architectural similarities between the placental proteins and a common ASCT2-recognition mechanism, whereby one RBD bind a large vestibule

excavated on the extracellular surface of the receptor and is “clamped” at that binding site by the formation of a unique hybrid β -sheet with ASCT2 (Fig. 1). Structural modelling using artificial intelligence-based AlphaFold allows us to extend the observed ASCT2-recognition mechanism to the vertebrate retroviruses of the RDR interference group, and to reveal direct competition between the retroviruses and the placental proteins for the human receptor.

ASCT2 is overexpressed in several human cancers and is an emergent target for drug development. Our results also demonstrate that the SYCY1RBD and SUPYNRBD, as well as a newly developed nanobody act as first-in-class selective ASCT2 inhibitors. Hence, the mechanistic insight and structures that we present, including that of the ASCT2-nanobody complex, should facilitate the development of novel ASCT2 antagonists with improved selectivity and potency for cancer therapy.

Overall, our results unravel an ancient and universal structural mechanism that explains key morphological and immunological functions of retrovirus-derived proteins in human placenta, as well as receptor-interference phenomena observed in extant retroviruses. We also open new venues to develop pharmacological tools targeting ASCT2 for cancer therapy (Khare et al., Nat. Struct. Mol. Biol. 2024).

Transport and hepatitis-B-virus receptor mechanisms of a central liver carrier.

Bile salts could be regarded as detergent molecules secreted by our body to help us solubilize and absorb lipidic nutrients from the diet (fat and hydrophobic vitamins, for example vitamin D). However, they are a unique detergent type, as bile salts are made out of cholesterol, and therefore contribute to control cholesterol levels in our body. To act as efficient detergents, bile salts are concentrated in bile, a dark-green liquid produced in the liver, and then stored in the gallbladder for release into the intestine to aid our digestion. In order to avoid wasting energy to produce new bile salt molecules after their use in the intestine, our body recycles bile salts by transporting them back into the liver from blood.

This transport function is mainly carried out by a membrane protein called Na⁺-taurocholate co-transporting polypeptide (NTCP), that uses the energy stored in the sodium transmembrane gradient to efficiently take up bile salts into the liver for bile production. Importantly, NTCP plays a fundamental role in liver pathology, as it is the cellular entry receptor of human hepatitis B and D viruses (HBV/HDV). Despite efficient vaccination programs, chronic HBV infection is a major cause of hepatocellular carcinoma and liver cirrhosis that affects ~250 million people globally. NTCP has emerged as an important target to develop viral entry inhibitors.

In this project we aim to understand the molecular mechanisms underlying NTCP transport and HBV receptor functions. To this aim, we combine high-resolution cryo-EM and transport functional assays. Cryo-EM only works for relatively large proteins (> 50 kDa), and NTCP is only ~38 kDa. To overcome this problem, in collaboration with the laboratory of Jan Steyaert at VIB Brussels, we developed selective antibody fragments against NTCP that recognize its extracellular surface, and provide molecular features that enable cryo-EM structure determination. These antibody fragments, namely nanobodies, have an added advantage, as they stabilize different conformations of NTCP transport cycle (Fig. 2).

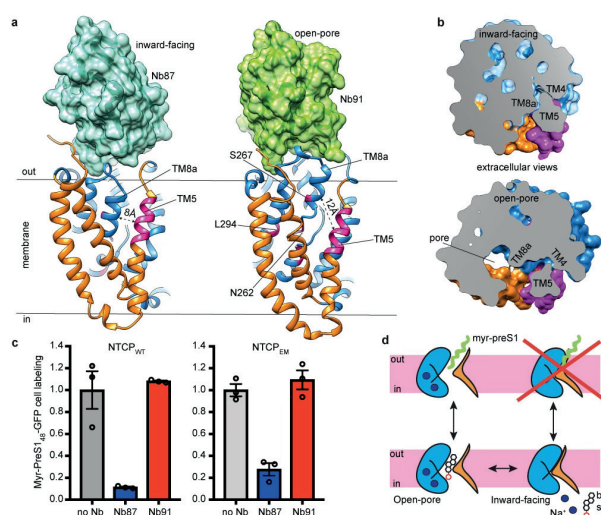


Figure 2 Structures of NTCP complexes with Nb87 and Nb91

a, Nb87 (left, cyan surface) and Nb91 (right, green surface) bind overlapping 3D epitopes on the extracellular surface of the core domain, distant from myr-preS1 binding-determinant TM5 region, and residues within the pore (highlighted in pink). In the inward-facing state (left) TM5 packs against the core domain (blue). In the open-pore state (right), the core domain moves outward and away from TM5 exposing important residues for myr-preS1 binding (pink). b, Extracellular view of cross-sections passing through the myr-preS1 binding determinant region in TM5 (highlighted in pink). Inward-facing (top), and open-pore (bottom) show TM5-core domain (blue) interfaces. c, Myr-preS148-GFP labelling of

cells expressing NTCP^{WT} (left) and NTCP^{EM} (right), respectively. Pre-incubation with Nb87, but not with Nb91, impaired myr-preS148-GFP labelling. Plots depict average of $n=3$ biologically independent experiments, and circles represent values from individual experiments. Error bars represent SEM. d, Cartoon representation of NTCP “gated-pore” transport mechanism and the relative movements of core (blue), and panel (orange) domains. Myr-preS1 domain of HBV/HDV (green) preferentially binds to open-to-outside states of NTCP transport cycle.

Selected publications

1. Khare, S.; Villalba, M. I.; Canul-Tec, J. C.; Cajiao, A. B.; Kumar, A.; Backovic, M.; Rey, F. A.; Pardon, E.; Steyaert, J.; Perez, C.; Reyes, N. Receptor-Recognition and Antiviral Mechanisms of Retrovirus-Derived Human Proteins. *Nat Struct Mol Biol* 2024, 31 (9), 1368-1376. <https://doi.org/10.1038/s41594-024-01295-6>.



Dr. Frédéric Friscourt
Associate Professor, ATIP-Avenir Fellow,
Univ. Bordeaux

Frédéric Friscourt received his PhD from the University of Glasgow, UK in 2009, under the guidance of Prof. P. Kočovský, on the development of novel chiral ligands for enantioselective catalysis. He then joined the group of Prof. G.-J. Boons at the Complex Carbohydrate Research Center, GA, USA, as a post-doctoral research associate (2009–2014) in order to transition to chemical biology research. There, he became involved in the design of probes for imaging the glycome. In 2014, he obtained a Junior Chair of Excellence from the University of Bordeaux and was soon after recruited as a group leader at the IECB in Bordeaux. He received the prestigious CNRS-ATIP-Avenir award (2017) and was recently promoted to Associate Professor in Chemical Biology at the University of Bordeaux, France (2021). His current research focuses on using organic chemistry to develop novel tools that can probe and control the influence of mammalian glycans physiologically and pathologically.

Research team

Dr. Frédéric FRISCOURT Associate Professor, (Univ. Bordeaux)

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Dr. Jürgen SCHULZ IRCN (CNRS)

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Mathilde WILLIGENS Master student (M1) (Univ. Bordeaux)

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Ludovic HIRSOUX Undergraduate student (L3) (Univ. Bordeaux)

Kerstin MULLER PhD Student (KIT, Germany)

This team is part of the unit "Institut des Sciences Moléculaires" (ISM), CNRS UMR5255/Univ. Bordeaux

Chemical Glycobiology

Frédéric Friscourt received his PhD from the University of Glasgow, UK in 2009. Glycans are chains of monosaccharides that are covalently linked to cell surface proteins and lipids. They have been recognized as key participants in a variety of physiological processes, including angiogenesis, fertilization, cell adhesion and host-pathogen interactions. From a pathological point of view, changes in the glycome of cells are associated with developmental disorders, can mark the onset of cancer and inflammation. Despite these intriguing observations, the molecular mechanisms by which these complex carbohydrates influence cell functions are not well understood due to a lack of suitable biochemical methods. We aim at unravelling the functional roles of mammalian glycans by exploiting organic chemistry to develop novel tools that can probe and control them in living systems.

Tagging glycans.

The **bioorthogonal chemical reporter strategy**, which elegantly combines the use of metabolically labeled azido sugars and highly reactive cyclooctyne probes, through strain-promoted alkyne azide cycloadditions (SPAAC), is a versatile technology for labeling and visualizing glycans. However, the biological stability and chemical diversity of current bioorthogonal reporters is not always up to par.

To address these shortcomings, we are developing novel bioorthogonal reporters while maintaining high reactivity towards cyclooctyne probes, and exploit them in order to **control glycan-protein interactions**.

Sydnones as novel bioorthogonal chemical reporters.

Over the past few years, we have exploited **sydnones** (Figure 1), highly stable mesoionic 1,3-dipoles, as novel bioorthogonal chemical reporters for the challenging detection of modified-proteins in complex cellular extracts (*J. Org. Chem.* **2018**, 83, 2058), for the fast tagging of single-stranded DNAs both in vitro and in cells (*Chem. Eur. J.* **2021**, 27, 16093), as well as for the labeling of complex glycans in living cells (*Angew. Chem. Int. Ed.* **2019**, 58, 4281).

More recently, we started to investigate the impact of bioorthogonal tags on the activity of metabolic enzymes.

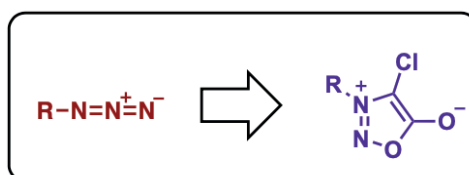


Figure 1. Bioorthogonal chloro-sydnone 1,3-dipole as opposed to the common azido-tag.

Impact of chemical reporters on the activity of glycan-processing enzymes.

Impact on Sialyltransferases

We recently showed that while sydnones could be employed for **tagging complex sialo-glycans in living mammalian cells**, their positioning on the sialic acid residue had a strong influence on sialyltransferases substrate recognition (*Angew. Chem. Int. Ed.* **2019**, 58, 4281). Unlike azido-sialic acid, which is well processed by all human sialyltransferases (hST), 9-sydnone modified sialic acid was found to be a good substrate for hST6GAL1 but not at all for hST3GAL4, consequently leading to the selective incorporation of the tag into linkage-specific α 2,6-N-linked sialoproteins.

Impact on Sialidases

We next turned our attention to exploit the impacted recognition of sydnone-modified sugars in a pathological context. We focused our attention on studying the activity of **bacterial sialidases**, enzymes expressed by bacteria during pathogenesis for cleaving sialic acid sugars from mammalian cell-surface glycans in order to adhere and infect the host.

By employing a multidisciplinary approach, including chemo-enzymatic synthesis for generating the unnatural sugars, enzymatic assays for probing *in vitro* the sialidase activity, cell imaging for visualizing glycans in living cells, and *in silico* modelling for rationalizing the observed molecular effects, we recently identified that pathogenic bacterial sialidases were unable to cleave sialosides displaying a sydnone *in vitro* as well as in living cells (*ACS Chem. Biol.* **2021**, 16, 2307) (Figure 2). We are currently studying the potential use of this novel strategy for protecting mammalian cells against bacterial invasion.

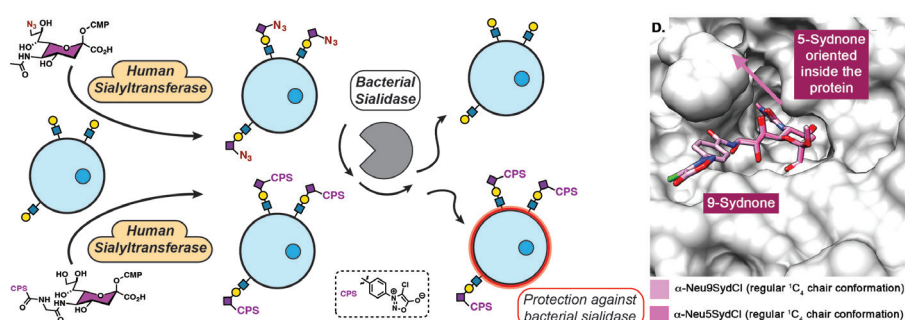
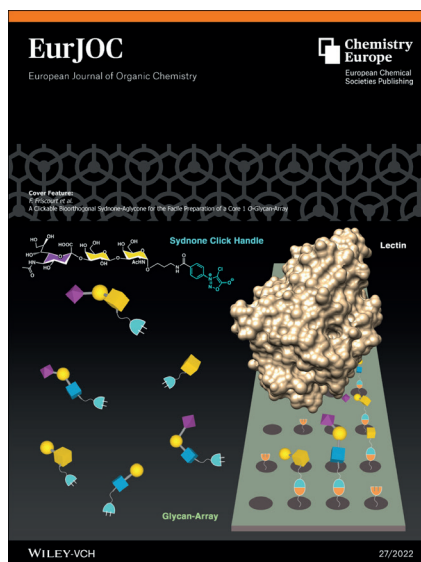


Figure 2. Glyco-edited mammalian cells with azide- or sydnone-modified sialic acids are not recognized similarly by bacterial sialidases and consequently exhibit different level of protecting effects against them. D. Sydnone-modified sialic acids modeled into the active site of *C. perfringens* sialidase

Exploiting sydnone tags for the facile preparation of a glycan-array.

At the molecular level, glycans have been shown to exert their functions through glycan-protein interactions. However, our understanding of the molecular cues that control these interactions is still in its infancy. Glycan-microarrays have revolutionized our knowledge of functional glycomics by allowing high-throughput study of glycan-protein recognition. However, their generation remains laborious.

Accordingly, we have recently exploited sydnone tags as an innovative technology for the facile preparation of glycan-microarray via Strain-Promoted Sydnone-Alkyne Cycloadditions (SPSAC) (*Eur. J. Org. Chem.* **2022**, 27, e202200271). We showed that sydnones, unlike azides, can be incorporated as an aglycon into core 1 O-glycans early-on in their synthesis since they are compatible with carbohydrate chemistry and enzymatic glycosylations. The sydnone-aglycon was then utilized for the preparation of an O-glycan array via SPSAC, which in turn was employed for the high-throughput screening of O-glycan-lectin interactions.



Selected publications

1. Chinoy, Z. S.; Friscourt, F. Expanding the Strain-Promoted 1,3-Dipolar Cycloaddition Arsenal for a More Selective Bioorthogonal Labeling in Living Cells. *Israel Journal of Chemistry* **2023**, 63 (1-2). <https://doi.org/10.1002/ijch.202200055>.



Dr. Gilles Guichard
Research Director (DR1), CNRS

Gilles Guichard graduated in chemistry from the Ecole Nationale Supérieure de Chimie in Toulouse (1991) and Univ. Montpellier (1992) in France. He received his PhD from the Univ. Strasbourg (1996) in the field of peptide science. Following post-doctoral research with Prof. Dieter Seebach at the ETH in Zürich (1997) working on the synthesis of β -amino acids and β -peptides, he joined the Institut de Biologie Moléculaire et Cellulaire (IBMC) in Strasbourg as a CNRS Chargé de Recherche (1998). Since 2006, he has been a CNRS Research Director. In 2009, he moved to Bordeaux and joined the Institut de Chimie et Biologie des Membranes et Nanoobjets (CBMN) and the Institut Européen de Chimie et Biologie (IECB). In 2019, he received the Grammaticakis-Neuman award from the Académie des Sciences for his work on foldamers and has been a member of the advisory board of Peptide Science since 2022. His research focuses on the biomimetic chemistry of peptides.

Research team

Dr. Gilles GUICHARD DR1 (CNRS)
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Dr. Morgane PASCO CRCN (CNRS)
Dr. Guillaume COMPAIN MCU (Univ. Bordeaux)
Dr. Claire SARAGAGLIA AI (CNRS)
Dr. Sandeep Mummadi Postdoctoral fellow (CNRS)
Naveen Gupta Postdoctoral fellow (CNRS)
Chenxiao Qi Postdoctoral fellow (CNRS)
Pierre Dubois-Geoffroy Postdoctoral fellow (CNRS)
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Veeresh Kuruva Postdoctoral fellow (CNRS)
Anaïs LUTON PhD student (CNRS)
Jiao WANG PhD student (CSC)
Laetitia VARAJAO PhD student (Univ. Bordeaux)
Fabian SOULARD PhD student (Univ. Bordeaux)

This team is part of the unit "Chimie et Biologie des Membranes et Nanoobjets" (CBMN), CNRS – Université de Bordeaux – Bordeaux INP (UMR 5248)

Peptidomimetic Chemistry

Our main line of research is biomolecular and bioinspired chemistry. We are interested in designing synthetic molecular systems that structurally and functionally mimic protein domains. The group is well recognized for its work in foldamer chemistry and current research effort include applications such as catalysis, nanostructure formation and selective protein surface recognition. More recently, the group also broadened its scope in peptide chemistry by developing new chemical tools such as covalent inhibitors, macrocyclization techniques, and the enantioselective synthesis of fluorinated amino acids. In parallel, we are conducting projects that focus on the identification of modulators of protein interactions to target key biological processes, such as transcription regulation (nuclear receptors, p53), epigenetics (histone chaperones), and bacterial replication (the sliding clamp).

Our research primarily focuses on the chemistry of amino acids, peptidomimetics and foldamers with three selected highlights corresponding to new approaches to design peptides with improved properties for therapeutic interactions. As part of our research on foldamers, we discovered that short helical oligoureases can serve as capping motifs to stabilize peptide α -helices which may be of practical use to stabilize bioactive peptides (*ChemBioChem* 2024, **Highlight #1**). We also investigated new stapling approaches to generate macrocyclic helical peptides through the introduction of guanidinium crosslinks (*Angew Chem Int Ed*, 2025, **Highlight #2**). Finally, as part of our efforts to design peptide ligands targeting the bacterial sliding clamp, we reported the first covalent peptide inhibitors of this protein by selectively targeting a conserved histidine residue at the edge of the binding site (*JACS Au* 2024, **Highlight #3**).

Highlight #1: Short oligourea foldamers as capping motifs for promoting α -helix formation in water (*ChemBioChem* 2023)

While foldamers have been extensively studied as α -helix mimics, their use as capping motif to enhance α -helix propensity remains comparatively much limited. We leverage the structural similarities between urea-based helical foldamers and α -helix to investigate the efficacy of oligoureases as N- or C-caps for reinforcing α -helical structures in water. This research identifies specific foldamer sequences capable of promoting α -helicity when incorporated at either terminus of the peptides (Fig. 1). The findings presented in this study may have implications for peptide design and the development of bioactive foldamer-based peptide mimics.

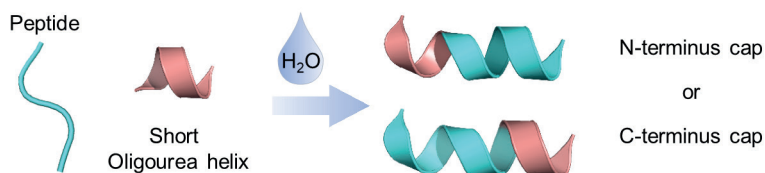


Fig. 1.

Highlight #2: Guanidinium-stapled helical peptides for targeting protein interactions (Angew Chem Int Ed, 2025)

Peptide stapling has emerged as a versatile approach in drug discovery to reinforce secondary structure elements especially α -helices and improve properties of linear bioactive peptides. Inspired by the prevalence of arginine in protein-protein and protein-DNA interfaces, we investigated guanidinium-stapling as a means to constrain helical peptides. Guanidinium stapling was readily achieved on solid support, utilizing two orthogonally protected lysine or unnatural α -amino acid residues with an amino function. This method allows for easy modulation of the nature and size of the staple as well as helix propensity. Evaluating a set of guanidinium-stapled peptides for their interaction with different protein targets identified several binders with increased target affinity. X-ray structure determination of four complexes revealed that all stapled peptides adopt a helical conformation upon protein binding. This research significantly expands the repertoire of α -helix stapling techniques for the creation of useful protein mimics (see Fig. 2).

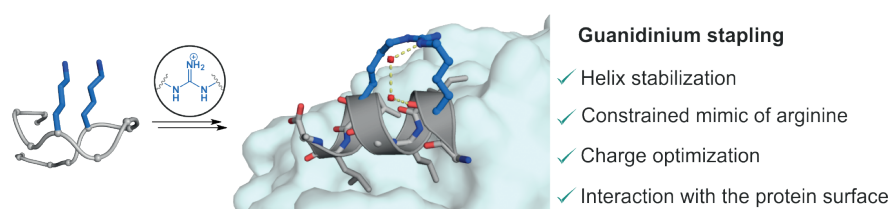


Fig. 2.

Highlight #3: (JACS Au, 2024)

This work is part of our ongoing effort to design inhibitors of the bacterial sliding clamp (SC) and target Gram-negative pathogens. Using a structure-guided approach, we developed effective and selective covalent peptide inhibitors by targeting a conserved histidine residue adjacent to the DNA polymerase-binding region (Fig. 3a). Remarkably, His175—despite its lower intrinsic reactivity compared to nucleophiles like cysteine—readily engages mild electrophiles such as chloroacetamide and acrylamide, when precisely positioned on the peptide ligand near the imidazole side chain. Two high-resolution X-ray crystal structures of the covalent protein–ligand adducts reveal that the canonical binding mode is fully preserved upon covalent bond formation (Fig. 3b). These results, along with the higher prevalence of His at ligand-binding sites compared to Lys and Cys, highlight histidine potential as a nucleophile for designing covalent inhibitors of protein–protein interactions.

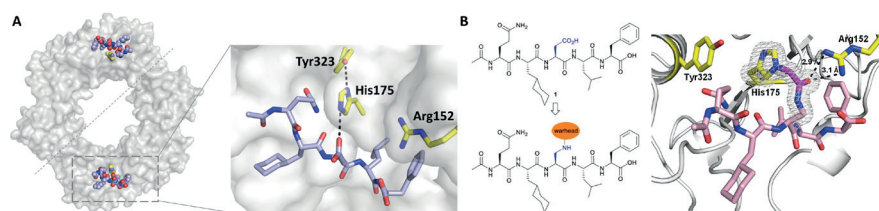


Fig. 3.

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1. Neuville, M.; Bourgeois, M.; Li, B.; Varajao, L.; Hallé, F.; Goudreau, S. R.; Thion, E.; Pasco, M.; Khatib, A.-M.; Guichard, G. Cell-Permeable Peptide Inhibitors of the P53–hDM2 Interaction via Foldamer Helix Mimicry and Bis-Thioether Stapling. *J. Med. Chem.* **2025**, 68 (1), 236–246. <https://doi.org/10.1021/acs.jmedchem.4c01762>.
2. Perdriau, C.; Luton, A.; Zimmer, K.; Neuville, M.; Saragaglia, C.; Peluso-Iltis, C.; Osz, J.; Kauffmann, B.; Collie, G. W.; Rochel, N.; Guichard, G.; Pasco, M. Guanidinium-Stapled Helical Peptides for Targeting Protein–Protein Interactions. *Angew Chem Int Ed* **2025**, 64 (5). <https://doi.org/10.1002/anie.202416348>.
3. Dutta, C.; Krishnamurthy, P.; Su, D.; Li, J.; Yoo, S. H.; Collie, G. W.; Pasco, M.; Fan, J.; Luo, M.; Barboiu, M.; Guichard, G.; Kini, R. M.; Kumar, P. Innovative Self-Assembly of 15-Mer Chimeric α -Peptide–Oligourea Foldamers toward Cl[−]-Selective Ion Channels. *Small Science* **2024**, 4 (8). <https://doi.org/10.1002/smssc.202300352>.
4. Yoo, S. H.; Buratto, J.; Roy, A.; Pasco, M.; Pulka-Ziach, K.; Collie, G. W.; Guichard, G. Oligourea Helix Bundle Binds Detergents with Diverse Polar Head Groups. *Org. Biomol. Chem.* **2024**, 22 (4), 731–734. <https://doi.org/10.1039/d3ob01873c>.
5. Compain, G.; Monsarrat, C.; Blagojevic, J.; Brillet, K.; Dumas, P.; Hammann, P.; Kuhn, L.; Martiel, I.; Engilberge, S.; Oliéric, V.; Wolff, P.; Burnouf, D. Y.; Wagner, J.; Guichard, G. Peptide-Based Covalent Inhibitors Bearing Mild Electrophiles to Target a Conserved His Residue of the Bacterial Sliding Clamp. *JACS Au* **2024**, 4 (2), 432–440. <https://doi.org/10.1021/jacsau.3c00572>.
6. Mauran, L.; Assailly, C.; Goudreau, S. R.; Odaert, B.; Guichard, G.; Pasco, M. Short Oligourea Foldamers as N- or C-Caps for Promoting α -Helix Formation in Water. *ChemBioChem* **2024**. <https://doi.org/10.1002/cbic.202400427>.
7. Pendem, N.; Nelli, Y.; Cussol, L.; Didierjean, C.; Kauffmann, B.; Dolain, C.; Guichard, G. Synthesis and Crystallographic Characterization of Helical Hairpin Oligourea Foldamers. *Chemistry A European J* **2023**, 29 (39). <https://doi.org/10.1002/chem.202300087>.



Dr. Emmanuelle Thinon
Research scientist (CRCN), CNRS

Emmanuelle Thinon completed her PhD in Chemical Biology at Imperial College London in 2014, under the supervision of Prof. Ed Tate. For her postdoc, thanks to a Marie Skłodowska-Curie Global fellowship, she worked at the Rockefeller University (USA) with Prof. Howard Hang and The Francis Crick Institute (UK) with Dr. Sharon Tooze. In 2019, she was recruited as a research associate (chargé de recherche, CRCN) within the French National Centre for Scientific Research (CNRS), to join the CBMN (Institute of Chemistry & Biology of Membranes & Nanoobjects) in Bordeaux. In November 2019, she joined IECB as a group leader.

Research team

Dr. Emmanuelle THINON Research scientist
CRCN, (CNRS)
Chloé FREYERMUTH PhD student (CNRS)
Santiago LEIVA Postdoctoral scientist (UB)

This team is part of the unit "Chimie des membranes et des nanoobjets" (CBMN), CNRS UMR5248/INP/ Univ. Bordeaux

Chemical Biology of membrane proteins

The study of small transmembrane proteins can often be challenging. In particular, it can be difficult to tag these proteins with a fluorophore *in cellulo* without perturbing the proteins localization and function, or to extract and purify them from membranes, without disturbing their structure or interactions with other proteins, for structure determination or for mass spectrometry interaction proteomics. Additionally, these proteins can be post-translationally modified by lipids, but proteomics methods to precisely identify and quantify some of these modifications are noticeably lacking. The "Chemical Biology of membrane proteins group" endeavours to develop and/or apply a combination of chemical and biological approaches to facilitate the study of these small membrane proteins (Figure 1).

The first aim of our work is to use a combination of chemical approaches (chemical proteomics, site-specific chemical labelling, crosslinking interaction proteomics, solid state NMR) to characterize small transmembrane proteins involved in viral infections. Some of these proteins are post-translationally modified by S-palmitoylation, which corresponds to the reversible addition of a C16 fatty acid to Cys, often adjacent to the protein transmembrane domain. S-palmitoylation is essential for protein localization and regulation, but its precise function, notably during viral infection, remains unknown for some proteins.

Using a combination of methods, we are currently characterising a small protein involved in viral infections by studying the role and regulation of its S-palmitoylation, its structure in interaction with membranes and by identifying its interaction partners. These studies will help us to understand if this protein could be a new antiviral drug target.

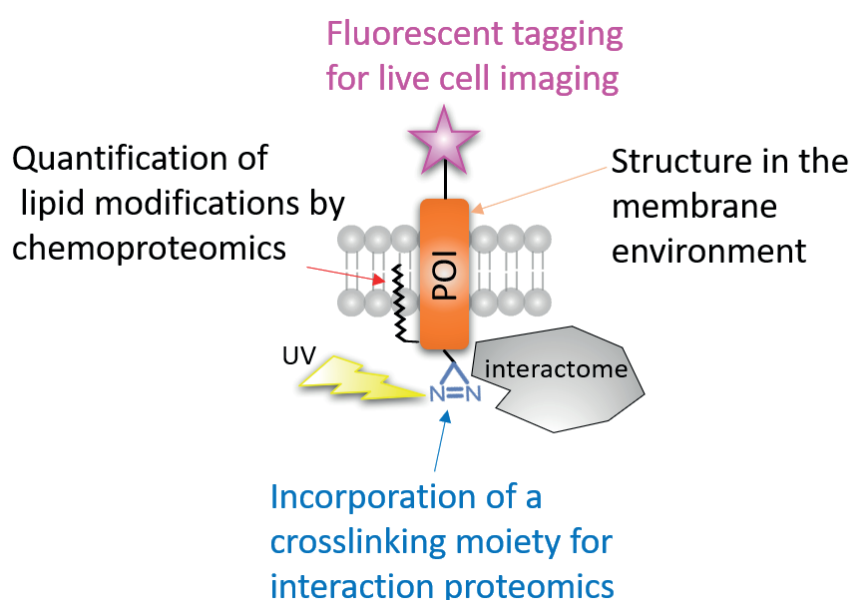


Figure 1. Characterization of small membrane proteins using a combination of chemical and biological methods.

Selected publications

1. Leiva, S.; Freyermuth, C.; Claverol, S.; Mantione, D.; Thinon, E. Affinity-Based Protein Profiling of the Antiviral Natural Product Nanchangmycin. *American Chemical Society (ACS)* May 14, 2025. <https://doi.org/10.26434/chemrxiv-2025-rlkss>.
2. Neuville, M.; Bourgeais, M.; Li, B.; Varajao, L.; Hallé, F.; Goudreau, S. R.; Thinon, E.; Pasco, M.; Khatib, A.-M.; Guichard, G. Cell-Permeable Peptide Inhibitors of the P53-hDM2 Interaction via Foldamer Helix Mimicry and Bis-Thioether Stapling. *J Med Chem* **2025**, 68 (1), 236–246. <https://doi.org/10.1021/acs.jmedchem.4c01762>.
3. Neuville, M.; Bourgeais, M.; Buratto, J.; Saragaglia, C.; Li, B.; Galeano-Otero, I.; Mauran, L.; Varajao, L.; Goudreau, S. R.; Kauffmann, B.; Thinon, E.; Pasco, M.; Khatib, A.-M.; Guichard, G. Optimal Stapling of a Helical Peptide–Foldamer Hybrid Using a C-Terminal 4-Mercaptoproline Enhances Protein Surface Recognition and Cellular Activity. *Chemistry* **2025**, 31 (19), e202403330. <https://doi.org/10.1002/chem.202403330>.

The second aim of our work is to develop new methods to tag proteins at the endogenous level (no overexpression). The addition of a tag to a protein, such as GFP (Green Fluorescence Protein) for immunofluorescence studies, can sometimes perturb the protein biophysical properties, localization and/or function. The tag is often added by overexpressing the protein of interest, which can sometimes lead to toxicity, hence the development of new methods to tag proteins at the endogenous level is essential. The tag could be a small fluorophore (BODIPY etc) for live cell imaging studies or with a crosslinking moiety to enable the identification of the interactome of the protein of interest by mass spectrometry-based proteomics. These new methods will be applied to facilitate the study of small membrane proteins.

Finally, we recently studied the mode of action of natural product, nanchangmycin, known to inhibit Zika viral infection, using chemical proteomics and photo-affinity labelling. We designed a photoreactive clickable nanchangmycin probe and employed chemical proteomics to identify protein targets of nanchangmycin related to Zika virus infection in human cells. Among the most prominent targets was the protein SEC11A, a key component of the signal peptidase complex, which is essential for cleaving and processing Zika virus polyproteins. We showed that Nan blocks the cleavage of a Zika virus polyprotein (2K-NS4B), suggesting a novel mechanism for Nan-mediated inhibition of Zika virus infection (Figure 2).

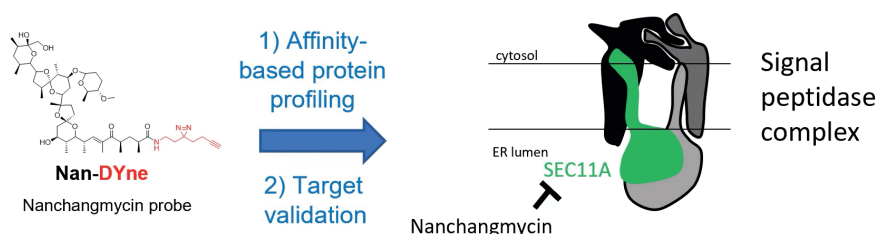


Figure 2. Identification of the protein target(s) of the antiviral compound nanchangmycin using a photoreactive clickable chemical probe.



Dr. Mikayel Aznauryan,
Research scientist (CRCN), Inserm

Mikayel Aznauryan obtained his PhD from Yerevan State University in Armenia (2008–2011). Then, he moved to Switzerland (2012–2014) as a postdoctoral researcher at the Department of Biochemistry of the University of Zurich (Group of Prof. B. Schuler), to work on protein folding and dynamics with single-molecule FRET spectroscopy. Afterwards, Mikayel Aznauryan did a second postdoc (2014–2018) at the Department of Chemistry and the Interdisciplinary Nanoscience Center of Aarhus University in Denmark, where he used single-molecule methods to study the dynamics of nucleic acid structures. Mikayel Aznauryan has joined IECB at the end of 2018 and has been awarded FRM Jeune equipe and IdEx Chaire Junior grants to start his group. Shortly after, he obtained INSERM researcher position (CRCN) within ARNA laboratory.

Research team

Dr. Mikayel AZNAURYAN Research associate CRCN (Inserm)
Dr. Carmelo DI PRIMO Research associate CRHC (Inserm)
Mme. Sabrina ROUSSEAU Engineer, IE (Inserm)
Dr. Bikash Chandra SWAIN Postdoc (Inserm)
Mme Pascale SARKIS PhD student (Univ. Bordeaux)
Mme Paramita CHAUDHURI M1 student (UBdx/BBM)
Mme. Ani MELTONYAN Engineer, AI (Inserm)

This team is part of the unit: "Acides Nucléiques: Régulations Naturelles et Artificielles" (ARNA), Inserm U1212/CNRS UMR5320/Univ. Bordeaux

Single-molecule spectroscopy of disordered protein dynamics and interactions

Intrinsically disordered proteins (IDPs) or proteins containing intrinsically disordered regions (IDRs) are ubiquitous in eukaryotic proteome. They typically lack persistent structure in their native form and do not necessarily require defined structure for molecular recognition and specific function. They are frequently involved in liquid-liquid phase separation (LLPS) driven assembly of various cellular condensates. We use a large variety of biochemical and biophysical tools, among which particularly single-molecule FRET spectroscopy, in order to understand the mechanisms of IDP interactions and to reveal the basis of specificity for molecular recognition and particular function of IDPs, as well as uncover how certain IDP interactions define and modulate the LLPS and formation of cellular condensates.

The key expertise of the group is centered on *in vitro* and *in-cell* single-molecule FRET spectroscopy, which is our main tool to look at IDPs and their interaction. For this purpose, we also use a variety of other state-of-the-art biochemical and biophysical techniques, such as biomolecular nuclear magnetic resonance (NMR) spectroscopy, surface plasmon resonance (SPR), isothermal titration calorimetry (ITC), live-cell imaging and others, to obtain a comprehensive picture of mechanisms of IDP interactions and to reveal the basis of specificity for molecular recognition and particular function of IDPs.

Currently, in the group we are working on the following research projects:

- investigation of eukaryotic translation initiation and especially the role of disordered translation initiation factors in this process;
- understanding the behavior and molecular mechanisms of function of disordered RNA-binding proteins in LLPS and cellular condensates.

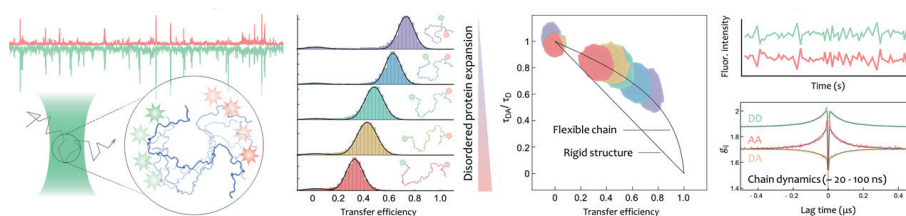


Figure 1. From detection of single biomolecules to characterization of their conformational distributions, fluctuations and dynamics

Disordered initiation factors – fine-tuners of the early steps of translation initiation

Translation initiation is directly regulated by the cap-binding complex (eIF4F), which recognizes and associates with the 5' terminal cap of mRNA and prepares it for the recruitment of the ribosome. eIF4F consists of three different proteins, so called translation initiation factors eIF4E, eIF4G and eIF4A. eIF4E is responsible for direct recognition of mRNA methyl-guanosine cap. eIF4A is an ATP-driven RNA helicase that unwinds secondary structures surrounding the 5'-end of mRNA. eIF4G serves as a scaffold for assembly of eIF4F, directly interacting with both eIF4E and eIF4A (Jackson, Hellen et al. 2010). In addition, eIF4F complex associates with eIF4B and eIF4H, which possess several crucial regulatory roles in translation initiation (Parsyan 2014). In a concerted action, these factors prepare the mRNA and facilitate the recruitment of the 43S pre-initiation complex to it, followed by scanning the mRNA towards the start-codon recognition. Despite the large number of binding partners (initiation factors, mRNA,

Selected publications

1. Mondal, S.; Rousseau, S.; Talenton, V.; Thiam, C. A. B.; Aznauryan, M.; Mackereth, C. D. Backbone Resonance Assignments of the C-Terminal Region of Human Translation Initiation Factor eIF4B. *Biomol NMR Assign* **2023**, 17 (2), 199–203. <https://doi.org/10.1007/s12104-023-10141-7>.
2. Swain, B. C.; Sarkis, P.; Ung, V.; Rousseau, S.; Fernandez, L.; Meltonyan, A.; Aho, V. E.; Mercadante, D.; Mackereth, C. D.; Aznauryan, M. Disordered Regions of Human eIF4B Orchestrate a Dynamic Self-Association Landscape. *Nat Commun* **2024**, 15 (1), 8766. <https://doi.org/10.1038/s41467-024-53136-1>.
3. Dobrovodský, D.; Di Primo, C. Do Conformational Changes Contribute to the Surface Plasmon Resonance Signal? *Biosens Bioelectron* **2023**, 232, 115296. <https://doi.org/10.1016/j.bios.2023.115296>.
4. Aznauryan, M.; Birkedal, V. Dynamics of G-Quadruplex Formation under Molecular Crowding. *J Phys Chem Lett* **2023**, 14 (46), 10354–10360. <https://doi.org/10.1021/acs.jpclett.3c02453>.

rRNA) and important function, eIF4B (and eIF4H) are predicted to be predominantly disordered (Uversky 2014) and can be termed as disordered translation initiation factors (DisIFs). We focus on investigation of these proteins, and aim at understanding their behavior, interactions and mechanistic basis for function in translation initiation.

Disordered initiation factors and their relation to LLPS and stress granules

It is currently emerging that many aspects of intracellular organization are performed through formation of membrane-less condensates (Banani, Lee et al. 2017). The main driving force for condensate assembly is believed to be the intracellular LLPS (Shin and Brangwynne 2017). Currently many independent observations point that IDPs or proteins with long IDRs can contribute to the cellular LLPS (Dignon, Best et al. 2020).

Cellular condensates form under action of various stimuli. For example, stress granules (SGs) form during cellular stress and are responsible for subcellular storage of stress-inhibited translation machinery and stabilization of naked mRNAs (Protter and Parker 2016).

Recent evidences indicate an enrichment of translation initiation factors, among which DisIFs (eIF4B, eIF4H, eIF4G, etc.), within the proteome of SGs (You, Huang et al. 2020), nevertheless their exact roles therein are currently unknown. We primarily focus on understanding of the behavior and function of DisIFs in LLPS and assembly of SGs. Our recent work shows that eIF4B is able to undergo LLPS in vitro at close to physiological conditions, i.e. at protein concentration comparable to endogenous levels and physiological ionic strength. Interestingly, prior to phase separation, eIF4B forms a range of high-molecular “fuzzy” oligomers. Our single-molecule and bulk phase separation assays allow to map the eIF4B self-association landscape both at the nanoscale and the mesoscale.

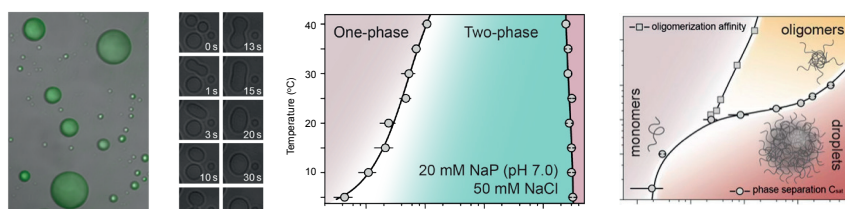


Figure 2. The self-association behavior of eIF4B at nanoscale and mesoscale



Dr. Sébastien Campagne
Research scientist (CRCN), Inserm

Sébastien Campagne undertook his PhD on the structural biology of a novel family of human transcription factors, the THAP protein family at the Institute of Pharmacology and Structural Biology and the University of Toulouse under the supervision of Prof. Alain Milon and Dr. Virginie Gervais. He then joined ETH Zurich in the group of Prof. Julia Vorholt to identify the molecular mechanisms triggering transcription rewinding in α -proteobacteria. In 2014, he joined the group of Prof. Frédéric Allain at ETH Zurich to start working on the regulation of mRNA splicing where he did important contributions in the field of RNA splicing correction. He joined IECB in October 2021 as Research officer in the group of Cameron Mackereth and was appointed group leader in February 2023.

Research team

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Sabrina ROUSSEAU IE (INSERM)

This team is part of the unit: "Acides Nucléiques: Régulations Naturelles et Artificielles" (ARNA), Inserm U1212/CNRS UMR5320/Univ. Bordeaux

Structure, Mechanism and RNA Therapeutics

RNA splicing is key step of gene expression that shapes the transcriptional output by regulating mRNA translation, localization and decay. This process is tightly regulated and from a given precursor messenger RNA, different mRNA associated with different proteins can be generated via alternative splicing. Although the splicing cycle has been deciphered at atomic level, splicing regulation is still poorly understood. Furthermore, many human diseases are linked to non-physiological splicing patterns. In this context, the SMaRT lab aims to decipher the molecular mechanisms controlling RNA splicing regulation and design synthetic splicing switches to correct rationally RNA splicing with therapeutic purposes in the context of inherited diseases and cancers.

Exploring the diversity of small molecule splicing modifiers.

A major revolution in the field of specific splicing correction was the discovery of the first gene specific small molecule splicing modifier that switches the splicing of the *SMN2* gene. The small molecule (SMN-C5) acts as a molecular glue between the first particle of the spliceosome (U1 snRNP) and the A-1 bulged 5'-splice site of *SMN2* exon 7. It binds the RNA duplex formed upon 5'-splice site recognition and stabilizes the unpaired adenine in position -1 to allosterically activate the inclusion of exon 7 in the *SMN2* transcript (Fig. 1A,B). We coined this mechanism "5'-splice site bulge repair" (Campagne S. *et al.*, Nat. Chem. Biol. 2019). However, SMN-C5 did not passed the clinical evaluation and raised a safety issue. Optimization of SMN-C5 triggers the discovery of other small molecules associated with similar activities and the molecule called risdiplam passed the clinical evaluation to become the first orally available treatment against Spinal Muscular Atrophy. To understand the chemical diversity of A-1 splicing modifiers, we investigated whether risdiplam and three other A-1 splicing modifiers also act through the bulge repair mechanism. By solving the solution structures of the four small molecules bound to the RNA helix (U1:A-1 bulged 5'-splice site), we could show that the four small molecules bind the same cavity than SMN-C5 and act through the bulge repair mechanism (Fig. 1C-E; Malard F. *et al.*, Nucleic Acids Res. 2024). These structures pinpointed the common pharmacophores required to correct splicing on an A-1 bulged 5'-splice site and paves the way towards the rational development of novel splicing modifiers associated with different gene selectivity (project funded by the FRM, 2024-2027).

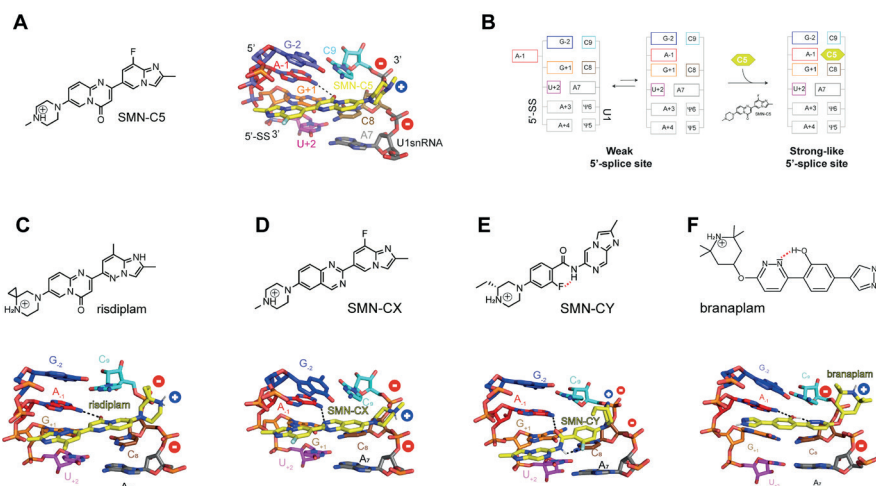


Figure 1 – Structures of A-1 splicing modifiers bound to the RNA epitope and concept of bulge repair. A) structure of SMN-C5 bound to its RNA epitope. B) Schematic representation of the bulge repair mechanism. C-F) Structures of risdiplam C), SMN-CX D), SMN-CY E) and branaplam F) bound to the RNA epitope.

Molecular Basis for the Calcium-Dependent Activation of the Ribonuclease EndoU.

Ribonucleases (RNases) are ubiquitous enzymes that process or degrade RNA, essential for cellular functions and immune responses. The EndoU-like superfamily includes endoribonucleases conserved across bacteria, eukaryotes, and certain viruses, with an ancient evolutionary link to the ribonuclease A-like superfamily. Both bacterial EndoU and animal RNase A share a similar fold and function independently of cofactors. In contrast, the eukaryotic EndoU catalytic domain requires divalent metal ions for catalysis, possibly due to an N-terminal extension near the catalytic core. In this study, we used biophysical and computational techniques along with in vitro assays to investigate the calcium-dependent activation of human EndoU. We determined the crystal structure of EndoU bound to calcium (Fig. 2A) and found that calcium binding remote from the catalytic triad triggers water-mediated intramolecular signaling and structural changes, activating the enzyme through allostery. Calcium binding involves residues from both the catalytic core and the N-terminal extension, indicating that the N-terminal extension interacts with the catalytic core to modulate activity in response to calcium. We also propose and validate a structural model explaining how EndoU achieves selectivity for U-containing RNAs (Fig. 2B-D). Our findings suggest that similar mechanisms may be present across all eukaryotic EndoUs, highlighting a unique evolutionary adaptation that connects endoribonuclease activity to cellular signaling in eukaryotes. These results have been first published in a pre-print and were recently accepted for publication in Nature communications (F. Malard et al., Nature Comm., accepted).

Selected publications

1. Malard, F.; Karginov, F. V.; Campagne, S. 1H, 13C and 15N Backbone Resonance Assignment of the Calcium-Activated EndoU Endoribonuclease. *Biomol NMR Assign* **2024**, 18 (2), 263-267. <https://doi.org/10.1007/s12104-024-10198-y>.
2. Malard, F.; Dias, K.; Baudy, M.; Thore, S.; Vialet, B.; Barthélémy, P.; Fribourg, S.; Karginov, F. V.; Campagne, S. Molecular Basis for the Calcium-Dependent Activation of the Ribonuclease EndoU. *Res Sq* **2024**, rs.3.rs-4654759. <https://doi.org/10.21203/rs.3.rs-4654759/v1>.
3. Bouton, L.; Ecoutin, A.; Malard, F.; Campagne, S. Small Molecules Modulating RNA Splicing: A Review of Targets and Future Perspectives. *RSC Med Chem* **2024**, 15 (4), 1109-1126. <https://doi.org/10.1039/d3md00685a>.
4. Malard, F.; Wolter, A. C.; Marquevielle, J.; Morvan, E.; Ecoutin, A.; Rüdisser, S. H.; Allain, F. H. T.; Campagne, S. The Diversity of Splicing Modifiers Acting on A-1 Bulged 5'-Splice Sites Reveals Rules for Rational Drug Design. *Nucleic Acids Res* **2024**, 52 (8), 4124-4136. <https://doi.org/10.1093/nar/gkae201>.
5. Malard, F.; Massman, L.; Campagne, S.; Olivier-Van Stichelen, S. The O-GlcNAc Database: Introducing New Features and Tools Developed from Community Feedback. *Anal Bioanal Chem* **2025**, 417 (5), 879-884. <https://doi.org/10.1007/s00216-024-05571-8>.
6. Campagne, S. U1 snRNP Biogenesis Defects in Neurodegenerative Diseases. *Chembiochem* **2024**, 25 (9), e202300864. <https://doi.org/10.1002/cbic.202300864>.



Dr. Yann Fichou
Research Scientist (CRCN), CNRS

Yann Fichou got an engineering degree in physics and material sciences from the Institut National des Sciences Appliquées (INSA) in Rennes in 2011. He received in 2015 his PhD from the Université Grenoble Alpes where he studied protein and hydration dynamics by neutron scattering and MD simulations, under the supervision of Martin Weik at the Institut de Biologie Structurale (IBS). He carried out a first postdoc in the lab of Martina Havenith at Ruhr-Universität Bochum (RUB, Germany) before going to the University of California Santa Barbara (UCSB) in the group of Songi Han. Since 2020, Yann Fichou is a CNRS Chargé de Recherche at the institut de Chimie et Biologie des Membranes et Nano-objets (CBMN) in Bordeaux and he became group leader at the IECB after obtaining a ERC starting grant in 2021.

Research team

Dr. Yann FICHO CRCN (CNRS)
Clara PIERSSON PhD student (CNRS)
Julien BROCCASALENGO PhD student (CNRS)
Dr. Vicoria LUBLIN Engineer (CNRS)
Finn SOMBROZKY PhD student (ILL)

This team is part of the unit: "Chimie et biologie des membranes et nanoobjets" (CBMN), UMR5248 CNRS/UB

Molecular mechanisms of amyloid diseases

The aggregation of the protein tau is involved in several neurodegenerative diseases, termed tauopathies, such as Alzheimer's disease. In different tauopathies, tau aggregates adopt different structures, emphasizing a causal link between the nature of tau aggregates at a molecular level and the associated pathology. Our research aims at understanding the molecular rules governing aggregate structural differentiation and propagation. Using biophysical and biochemical techniques, we study the mechanisms of tau aggregation across different pathways. We investigate different modulators of tau aggregation such as disease-associated mutations and interaction with various biomolecular cofactors (GAG, nucleic acids and lipids...). We also study liquid-liquid phase separation and its relationship to protein aggregation. Although the group uses a multi-technique approach, we have a particular interest in applying advanced electron paramagnetic resonance (EPR) spectroscopy to address different biological and chemical questions.

The tau protein is involved in several neurodegenerative diseases, termed tauopathies, including Alzheimer's disease (AD), Pick's disease (PiD), chronic traumatic encephalopathy (CTE) and corticobasal degeneration (CBD). Despite the heavy societal burden that they represent, to date no drugs have been brought to market to cure or even slow down tauopathies, revealing a lack of understanding of their onset and progression.

Our contribution to the field is to investigate the molecular mechanisms that lead disease-specific tau assemblies. We have written a perspective discussing a general framework that is suitable to present the current challenges in understanding tau aggregation and to critically analyze the current state of the art of in vitro studies (DOI).

In last 10 years, there has been a major shift in the understanding of tau amyloid assemblies. This shift originates from the clear demonstration that there is no one tau amyloid but rather different tau amyloid aggregates, which have different structures at a molecular level, are involved in diseases, tauopathies, with very different clinical and present various biological activity. Thus, the already-complex question of "how tau forms an amyloid?" becomes "how tau form a disease specific amyloid?". And the answer to this question is likely to be multifold and disease specific.

Recreating pathological assemblies *in vitro*, i.e. in a simple environment, is essential not only to understand the process of formation, but also to study how specific molecules (chaperones, metabolites, drugs, etc...) interfere with this process. Many protocols have been developed to form amyloid aggregates in vitro with recombinant protein. These artificial models aim at mimicking what is found in the brains of patients affected with various tauopathies. Then, it is essential to question how close these models are to what is actually present and pathologically active in the brain.

The first difficulty in defining the relevance of an in vitro model is to find the properties against which the model should be benchmarked. In other words, what criteria must be fulfilled by a recombinant aggregate to be an accurate pathological strain of tau. We propose that there are 3 features that should be considered to evaluate the quality of an in vitro model (figure 1):

- The structure of the assembly. This should not be limited to the amyloid nature but more precisely the conformation of the protein within the amyloid, which has now been established to be disease-specific (Shi et al. 2021b)

- The “pathological activity”. What is the toxicity of the assembly? How does it spread in a complex biological environment? What is its bioreactivity (e.g. capacity to sequester specific molecules, to interact with membranes...)?

- The composition of the amyloid. Pieces of evidence point to the presence of foreign molecules within the amyloid core of tau fibrils, which should also be recapitulated in the in vitro models.

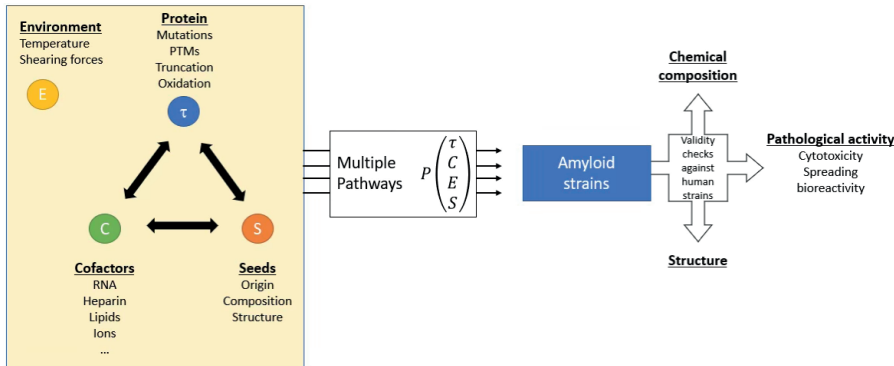


Figure 1: Framework to generate a biologically relevant amyloid strain of tau. Multiple parameters – namely the state of the protein (τ), the presence of seeds (S), the presence of cofactors (C), and the environmental conditions (E) – determine the aggregation pathways toward amyloid strains. The biological relevance of a given pathway leading to a given strain should be evaluated against several features: The pathological activity, the structure of the amyloid core, and the chemical composition of the amyloid aggregate.

Overall, a lot of work is needed to assess the relevance of amyloid model in vitro. The high-resolution structure should be assessed and the factors influencing this structure must be rationalized. In that direction, encouraging results show that in a simple in vitro experiment containing one recombinant version of tau, deprived of PTMs, could recapitulate the structure of AD aggregate. Nevertheless, the structural aspect is not sufficient and we argue that more studies are needed to characterize the pathological and biological activities of the amyloid models and compare them with disease-derived strains. Figure 1 proposes a global framework encompassing the properties to consider when forming the amyloid model in vitro, as well as the feature that should be benchmarked to assess the relevance of these models.

Selected publications

1. Broc, J.; Piersson, C.; Fichou, Y. Making Tau Amyloid Models *in Vitro*: A Crucial and Underestimated Challenge. *FEBS Letters* 2025. <https://doi.org/10.1002/1873-3468.70022>.



Dr. Elia Stahl

Research Scientist (CRCN), CNRS

Elia Stahl received his PhD from the Heinrich-Heine-University (Düsseldorf, Germany) under the supervision of Jürgen Zeier. In his PhD he worked on functional and regulatory aspects of plant stress-inducible metabolic pathways. His PhD project was embedded in the CEPLAS (Cluster of Excellence on Plant Science) graduate school. He afterwards joined the laboratory of Philippe Reymond in the Department of Plant Molecular Biology (DBMV) at the University of Lausanne (Switzerland) as a postdoctoral fellow. During his PostDoc he worked on how plants perceive insect eggs and respond to insect oviposition.

Since December 2023, Elia Stahl is a CNRS Chargé de Recherche at the Laboratory of Membrane Biogenesis (LBM, UMR5200).

Research team

Dr. Elia STAHL CRCN (CNRS)

Dr. Dikki PEDENLA BOMZAN Postdoctoral Fellow (CNRS)

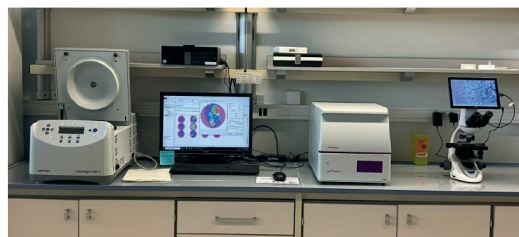
Brian VUE Collaborating PhD student (UB)

This team is part of the unit: Laboratory of Membrane Biogenesis (LBM, UMR5200) / Univ. Bordeaux.

Lipid-mediated signalling mechanisms in plant innate immunity

Our work aims on the identification of novel microbial derived lipidic elicitors of plant immune signalling and their perception mechanism in *Arabidopsis thaliana*. In order to achieve this, we use analytical chemistry methods (chromatography, lipidomics, MS, NMR) and classical molecular biology and biochemistry methods. We are moreover interested in how plant endogenous lipid homeostasis in the plasma membrane and lipid signalling affect and contribute to plant immunity.

Throughout their lifecycle plants interact with a multitude of biotic stressors and have therefore evolved an elaborated immune system to counteract such threats. Induction of robust plant immunity relies on pathogen and herbivore recognition. Plants activate immune signalling upon perception of non-self herbivore- and pathogen-associated molecular patterns (HAMPs, PAMPs) and self-derived damage-associated molecular patterns (DAMPs), a process called pattern triggered immunity (PTI). Perception of those patterns is ensured by plasma membrane-localized pattern recognition receptors (PRRs). We previously discovered that phospholipids from eggs of the large white butterfly *Pieris brassicae* act as elicitors of plant immune signalling in the model plant *Arabidopsis thaliana*. The ubiquitous presence of lipids in biological membranes and as storage lipids of organisms which interact with plants led to the question whether lipidic compounds from different sources might be detected by plants as conserved features from potential enemies. Our research therefore aims on (i) **the identification of novel microbial-derived immunogenic lipids**, (ii) **the study of the signalling mechanism activated in response to their perception** and (iii) **the perception mechanisms of those lipids in plants itself**.



Our group officially started in January 2024. A main achievement in 2024 was the establishment of plant growth facilities at IECB and to set up the laboratory space for our needs. We are currently investigating lipidic immunogenic patterns isolated from the plant pathogenic fungus *Botrytis cinerea*. The ascomycete *Botrytis cinerea* a necrotrophic

plant pathogen, causing the grey mould disease which is characterized by rotten above ground grown plant tissues. Botrytis has a wide range of host plants and is described to infect over 500 plant species worldwide, including important crops such as grape vine and wheat, and is therefore considered as one of the most important plant pathogens worldwide. Understanding how plants perceive initial attacks of this fungal pathogen is crucial to develop novel strategies for plant protection, a key challenge in agriculture and from particular interest in the Bordeaux area. In order to achieve this, we established a set of methods needed for our work, including the measurement of H₂O₂ production in plants, quantification of the plant defence hormone salicylic acid, determination of growth of bacterial and fungal plant pathogens and the visualisation and quantification of the plant hypersensitive response, a rapid localized programmed cell death response in plants.

In a second line of research, we investigate how plant endogenous lipid homeostasis in the plasma membrane affect and contribute to plant immunity. We thereby focus on the role of plant specific sphingolipids, in particular on glycosylinositol phosphorylceramides (GIPCs). In plants GIPCs are major components of the plasma membrane and enriched in the outer leaflet of the membrane, where they can make up 60 to 70% of the full lipid mass. In addition to be structural components of the plasma membrane, GIPCs are known for their crucial role in environmental interactions (biotic and abiotic). Novel genetic tools allow us to study the effect of modified sphingolipid homeostasis in plant biotic interactions without pleiotropic developmental phenotypes.

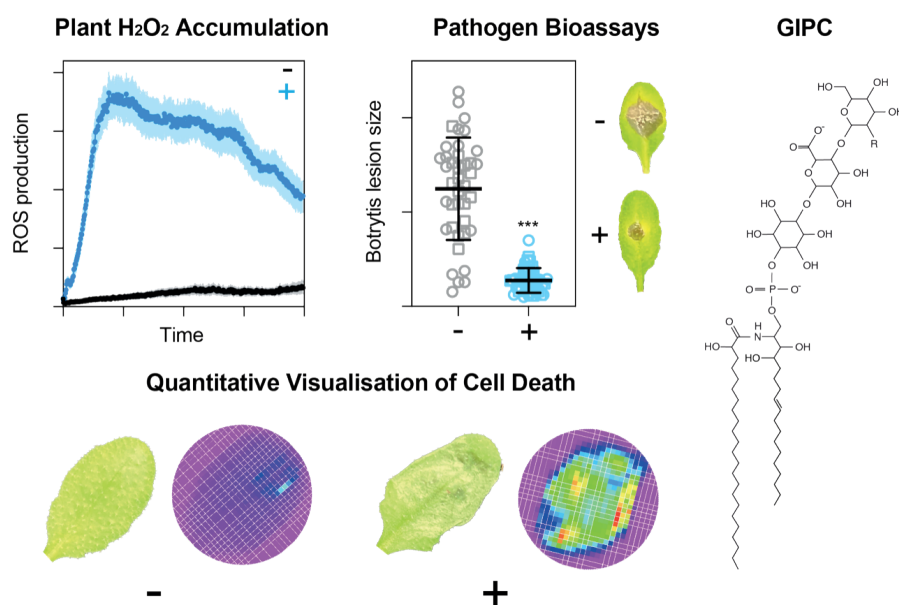


Figure: Examples of methods currently used and topics currently studied within the team.

Selected publications

1. Stahl, E.; Hartmann, M.; Scholten, N.; Zeier, J. A Role for Tocopherol Biosynthesis in Arabidopsis Basal Immunity to Bacterial Infection. *Plant Physiol.* **2019**, 181 (3), 1008–1028. <https://doi.org/10.1104/pp.19.00618>.
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3. Stahl, E.; Brillatz, T.; Ferreira Queiroz, E.; Marcourt, L.; Schmiesing, A.; Hilfiker, O.; Riezman, I.; Riezman, H.; Wolfender, J.-L.; Reymond, P. Phosphatidylcholines from *Pieris Brassicae* Eggs Activate an Immune Response in Arabidopsis. *eLife* **2020**, 9. <https://doi.org/10.7554/elife.60293>.
4. Stahl, E.; Fernandez Martin, A.; Glauser, G.; Guillou, M.-C.; Aubourg, S.; Renou, J.-P.; Reymond, P. The MIK2/SCOOP Signaling System Contributes to Arabidopsis Resistance Against Herbivory by Modulating Jasmonate and Indole Glucosinolate Biosynthesis. *Front. Plant Sci.* **2022**, 13. <https://doi.org/10.3389/fpls.2022.852808>.



Dr. Antoine Loquet
Research Director (DR2), CNRS

Antoine Loquet graduated from the University of Lyon / Ecole Normale Supérieure de Lyon. He did his PhD (2006–2009) under the guidance of Anja Böckmann (IBCP Lyon), working on the development of Solid-State NMR to solve protein structures. In 2008 he joined the group of Beat Meier (ETH Zürich) to study prion fibrils by Solid-State NMR. He then focused his research on molecular assemblies by Solid-State NMR as an EMBO postdoctoral fellow with Adam Lange at the Max Planck Institute for Biophysical Chemistry (Göttingen, Germany). There, he developed Solid-State NMR methods to determine atomic structures of large biological supramolecular assemblies. He obtained a CNRS position in 2013 at the CBMN (Institute of Chemistry & Biology of Membranes & Nanoobjects) in Bordeaux. In 2014, he was recruited as a group leader at the IECB and since 2016, he is leading the group “NMR of Membranes and Protein Assemblies” at CBMN. He obtained an ERC Starting Grant in 2015. His current research concentrates on the structural investigation of molecular assemblies using Solid-State NMR. He is CNRS Research Director since 2020, Co-director of IECB (2021–2023), Co-director of UAR3033/US01 IECB (2021–2023), Director (by interim) of IECB 2023–2024, and since 2024 Unit Director of UAR3033/US01 IECB.

Research team

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Dr. Erick DUFOURC Emeritus Research Director, (CNRS)
Bilal MUHAMMED PhD (Univ. Bordeaux)
Loïc DELCOURTE PhD (CNRS)
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This team is part of the unit “CBMN UMR5248 CNRS/Univ. Bordeaux /Bordeaux INP

NMR of Molecular Assemblies

Self-assembly is a fundamental process by which individual subunits assemble into ordered macromolecular entities, such as filaments, fibrils, oligomers, tubes or nanomachines. In biology, protein assemblies are involved in crucial cellular processes, ranging from the propagation of neurological disorders to viral and bacterial infections. The group aims at investigating atomic structures, and assembly processes of such sophisticated assemblies. We develop and apply solid-state NMR to capture structural and dynamic details at the atomic scale. Our group is also involved in the production of large protein assemblies to solve their structures based on solid-state NMR methods. Molecular assemblies either involved in cellular processes or engineered by supramolecular chemistry constitute the current research activities.

Examples of projects developed in 2024: 1. The cell wall and the capsule of *Cryptococcus neoformans* (Lends, ..., Loquet*, JACS 2025)

We addressed an innovative approach to detect, identify, quantify and measure dynamics, in an “in-situ” manner, of polysaccharides in intact cryptococcal cells. *Cryptococcus neoformans* is one of the three major human fungal pathogens responsible e.g. to cryptococcal meningitis. This pathogen is unique in the fungal kingdom, because in addition to its cell wall, it possesses an intriguing external capsule made of polysaccharides which are the main virulence factors. *C. neoformans* resists to most anti-fungal drugs and our knowledge on drug resistance is limited by the lack of analytical techniques to investigate the capsule in native conditions. State-of-the-art approaches rely on the use of harsh chemical treatment to solubilize cell wall polysaccharides, or mutants lacking the crucial capsule. There is therefore an urgent need to develop innovative methods to investigate polysaccharides directly on intact cryptococcal cells.

In this study (Figure 1), we report the development of an approach that employs magic-angle spinning solid-state NMR (MAS NMR) to decipher the *C. neoformans* cell-wall and capsule structure at atomic resolution. Our approach is innovative since it demonstrates that advanced proton-detected MAS NMR techniques, combined with fast MAS frequencies, give access to an arsenal of NMR techniques enabling the spectroscopic distinction of capsular polysaccharides to their counterparts found in the cell wall. Our data show a striking dynamical behavior between rigid polysaccharides associated to various level of structural polymorphism in the cell wall, to highly mobile polysaccharides forming the capsule. We also demonstrate that our approach can track the presence of triacylglycerol molecules, in form of lipid droplets, directly on intact cells.

Our study provides an unprecedented biophysical tool to monitor, at atomic resolution, the cell envelope of *cryptococcus*. Our method does not require sophisticated purification or extraction protocols to isolate different cell-wall and capsular components for detailed analysis, contrary to state-of-the-art methods currently applied in the field. Exemplified here on intact *C. neoformans* cells, our work opens an avenue to apply the methodology to investigate the response of the *cryptococcus* cell wall and capsule to antifungal drugs.

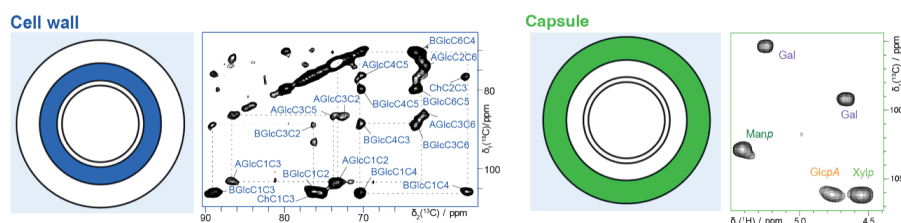


Figure 1: Atomic resolution study of the cell wall and the capsule of *cryptococcus neoformans* by solid-state NMR (adapted from Lends et al., JACS 2025).

Selected publications

2. Analytical framework to understand the origins of methyl side-chain dynamics in protein assemblies (Zumpfe, ..., Loquet*, Smith*, JACS 2024)

Side-chain motions play an important role in understanding protein structure, dynamics, protein-protein, and protein-ligand interactions. However, our understanding of protein side-chain dynamics is currently limited by the lack of analytical tools. Here, we present a novel analytical framework employing experimental nuclear magnetic resonance (NMR) relaxation measurements at atomic resolution combined with molecular dynamics (MD) simulation to characterize with a high level of detail the methyl side-chain dynamics in insoluble protein assemblies, using amyloid fibrils formed by the prion HET-s. In this work in collaboration with Albert Smith at Leipzig University, MD simulations were used to interpret experimental results, where rotameric hops, including methyl group rotation and χ_1/χ_2 rotations, cannot be completely described with a single correlation time but rather sample a broad distribution of correlation times, resulting from continuously changing local structure in the fibril. Backbone motion similarly samples a broad range of correlation times, from ~ 100 ps to μ s, although resulting from mostly different dynamic processes; nonetheless, we find that the backbone is not fully decoupled from the side-chain motion, where changes in side-chain dynamics influence backbone motion and vice versa. While the complexity of side-chain motion in protein assemblies makes it very challenging to obtain perfect agreement between experiment and simulation, this analytical framework improves the interpretation of experimental dynamics measurements for complex protein assemblies.

3. New solid-state NMR methods to detect chitin in intact cells (Delcourte, ..., Loquet*, Methods 2024).

Most bacterial, plant and fungal cells possess at their surface a protective layer called the cell wall, conferring strength, plasticity and rigidity to withstand the osmotic pressure. This molecular barrier is crucial for pathogenic microorganisms, as it protects the cell from the local environment and often constitutes the first structural component encountered in the host-pathogen interaction. In pathogenic molds and yeasts, the cell wall constitutes the main target for the development of clinically-relevant antifungal drugs. In the past decade, solid-state NMR has emerged as a powerful analytical technique to investigate the molecular organization of microbial cell walls in the context of intact cells. ^{13}C NMR chemical shift is an exquisite source of information to identify the polysaccharides present in the cell wall, and two-dimensional ^{13}C - ^{13}C correlation experiments provide an efficient tool to rapidly access the polysaccharide composition in whole cells. In this study, we investigate the use of the adiabatic DREAM (for dipolar recoupling enhancement through amplitude modulation) recoupling scheme to improve solid-state NMR analysis of polysaccharides in intact cells. We demonstrate the advantages of two-dimensional ^{13}C - ^{13}C experiments using the DREAM recoupling scheme. We report the spectral editing (Figure 2) of polysaccharide signals by varying the radio-frequency carrier position. We provide practical considerations for the implementation of DREAM experiments to characterize polysaccharides in whole cells. We demonstrate the approach on intact fungal cells of *Neurospora crassa* and *Aspergillus fumigatus*, a model and a pathogenic filamentous fungus, respectively. The approach could be envisioned to efficiently reduce the spectral crowding of more complex cell surfaces, such as cell wall and peptidoglycan in bacteria.

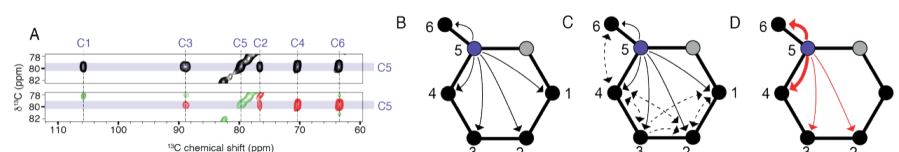


Figure 2: Spectral editing of nitrogen-containing polysaccharides in intact cells by solid-state NMR (adapted from Delcourte et al., Methods 2024).

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Pr. Léon Ghosez

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Léon Ghosez was born in Aalst, Belgium, in 1934. He studied at the University of Louvain where he got a PhD in 1958 under the supervision of Prof. G. Smets. He then spent 2 years as postdoctoral researcher at Harvard University (Prof. R.B. Woodward) and also collaborated for a few months with Prof. R. Huisgen in the Department of chemistry of the University of Munich. He got his "Habilitation" at the age of 32 for his independent work on the stereochemistry of synthesis and rearrangement of halocyclopropanes. In 1969 he became "Professeur Ordinaire" at the University of Louvain where he created the laboratory of organic synthesis. During his career in Louvain (1963–1999) he supervised the research of 125 PhD students and 135 postdoctoral associates. He also held appointments at the University of Liège (1969–1999) and the Ecole Polytechnique in Palaiseau (1993–1999). He took an active part in the creation of IECB where he established a research group in 1998. Since 2000, he shared the directorship of IECB with Dr J.J. Toulmé. Since 2011 he is an invited scientist in the same Institute. His current research interests include the design and total synthesis of biologically active molecules and the search of mild, efficient and "green" Lewis acid catalysts. In 2007, he received the medal of the Société Française de Chimie as a recognition of his support to the development of organic chemistry in France. Léon Ghosez is an emeritus member of the Royal Academy of Sciences of Belgium and a fellow of the Royal Society of Chemistry. In 2017 he received the title of "Chevalier de la Légion d'Honneur".

Research team

Dr. Léon GHOSEZ Prof. Emeritus, Invited scientist (CNRS–Univ. Bordeaux)

The team is part of the CNRS/University of Bordeaux UMR 5144 CBMN.

Organic & Medicinal Chemistry

1. Sustainable electrophilic catalysts for the activation of highly functionalized and sensitive molecules

The project aims at finding solutions to the often encountered problems associated with the use of many electrophilic catalysts: chemoselectivity, low turnover, too high molecular weight, in particular for asymmetric catalysis, toxicity and generation of much waste. New ionic solvents and silicon-derived Lewis superacids have been found to provide solutions to these problems. New electrophilic catalysts for cycloaddition and alkylation reactions involving highly functionalized acid-sensitive molecules have been developed.

2. Deoxysubstitution of hydroxyl-containing compounds under mild and sustainable conditions : a possible practical and sustainable substitute for the Mitsunobu reaction.

The project aims at finding milder conditions for the replacement of a hydroxyl group by a nucleophile. present methods often required acidic conditions or the use of toxic reagents or (and) lead much waste (eg Mitsunobu reaction) The concept is based on earlier findings of the group on the deoxychlorination-, bromination- and iodination reactions with the readily available haloenamines : conditions are mild, atom economy is high and no reagent is toxic. The reaction was recently extended to the often pharmacologically interesting replacement of an hydroxyl group by fluorine. The plan is to extend the method to a wide variety of nucleophilic reagents including carbon nucleophiles.

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44. Haidar, R.; Compant, S.; Robert, C.; Antonielli, L.; Yacoub, A.; Grélard, A.; **Loquet, A.**; Brader, G.; Guyoneaud, R.; Attard, E.; Rey, P. Two Paenibacillus Spp. Strains Promote Grapevine Wood Degradation by the Fungus Fomitiporia mediterranea: From Degradation Experiments to Genome Analyses. **Sci Rep** **2024**, 14 (1). <https://doi.org/10.1038/s41598-024-66620-x>.

Invited Peer-Reviewed Articles

1. Krasteva, P. V. Bacterial Synthase-Dependent Exopolysaccharide Secretion: A Focus on Cellulose. **Current Opinion in Microbiology** 2024, 79, 102476. <https://doi.org/10.1016/j.mib.2024.102476>.
2. Alfano, C.; Fichou, Y.; Huber, K.; Weiss, M.; Spruijt, E.; Ebbinghaus, S.; De Luca, G.; Morando, M. A.; Vetri, V.; Temussi, P. A.; Pastore, A. Molecular Crowding: The History and Development of a Scientific Paradigm. **Chem. Rev.** 2024, 124 (6), 3186–3219. <https://doi.org/10.1021/acs.chemrev.3c00615>.
3. Delamare, A.; Naulet, G.; Mummadi, S.; Guichard, G.; Compain, G. One-Step Introduction of the Hexafluoroisobutyl Group, Synthesis of (S)-5,5,5,5',5'-Hexafluoroleucine, and Its Incorporation into Peptides and Proteins. **Comptes Rendus. Chimie** 2024, 27 (G1), 385–394. <https://doi.org/10.5802/crchim.362>.
4. Bouton, L.; Ecoutin, A.; Malard, F.; Campagne, S. Small Molecules Modulating RNA Splicing: A Review of Targets and Future Perspectives. **RSC Med Chem** 2024, 15 (4), 1109–1126. <https://doi.org/10.1039/d3md00685a>.
5. Campagne, S. U1 snRNP Biogenesis Defects in Neurodegenerative Diseases. **Chembiochem** 2024, 25 (9), e202300864. <https://doi.org/10.1002/cbic.202300864>.

Other Publications

1. Anso, I.; Gayral, D.; Krasteva, P. V. Cellulose and Cellulose Secretion in Bacterial Biofilms. In **Biofilm Matrix**; Reichhardt, C., Ed.; Springer Series on Biofilms; Springer Nature Switzerland: Cham, 2024; Vol. 13, pp 215–258. https://doi.org/10.1007/978-3-031-70476-5_7.
2. Zouhir, S.; Abidi, W.; Krasteva, P. V. Large Complexes: Cloning Strategy, Production, and Purification. In **Bacterial Secretion Systems**; Journet, L., Cascales, E., Eds.; Methods in Molecular Biology; Springer US: New York, NY, 2024; Vol. 2715, pp 395–413. https://doi.org/10.1007/978-1-0716-3445-5_25.
3. Anso, I.; Zouhir, S.; Sana, T. G.; Krasteva, P. V. Structural Basis for Synthase Activation and Cellulose Modification in the *E. Coli* Type II Bcs Secretion System. June 5, 2024. <https://doi.org/10.1101/2024.06.05.597511>.

Patent

1. Renaud, B.; Buda, M.; Lewis, B. D.; Pujol, J. F. Effects of 5,6-Dihydroxytryptamine on Tyrosine-Hydroxylase Activity in Central Catecholaminergic Neurons of the Rat. **Biochem Pharmacol** 1975, 24 (18), 1739–1742. [https://doi.org/10.1016/0006-2952\(75\)90018-0](https://doi.org/10.1016/0006-2952(75)90018-0).

Prizes, Awards

- Médaille Biologie Moléculaire et Cellulaire. Académie des Sciences, 2024, [N. Reyes](#)
- Best poster prize at the SCF Chemical Biology Symposium 2024, Royal Society of Chemistry, 2024, [C. Freyermuth](#)
- Best oral presentation for the CBMN day, CBMN, 2024, [C. Freyermuth](#)

Journal & Scientific Society Boards

- Advisory Board Member, Peptide Science (Wiley), 2023, [G. Guichard](#)
- Scientific Council, Société de Chimie Thérapeutique (SCT), 2023, [G. Guichard](#)
- Member, SCT Young MedChem Forum – YMcF, 2023, [G. Compain](#)
- Communication manager, Société Chimique de France – Division Chémobiologie, 2024, [E. Thinon](#)
- Board member, Société Chimique de France – Section Aquitaine, 2024, [E. Thinon](#)
- Editorial board member, Proceedings of the Yerevan State University B: Chemical and biological sciences (Armenia), 2024, [M. Aznauryan](#)
- Board member, French EPR society, 2022, [Y. Fichou](#)
- Mid-Thesis Committee, Sramona Barua (Université de Bordeaux), 2023–2025, [P.V. Krasteva](#)
- Thesis Committee – Reviewer, Thibault Bongiovanni (Aix Marseille University), 2024, [P.V. Krasteva](#)
- Thesis Committee – President, Franck Martin (Université de Strasbourg), 2024, [P.V. Krasteva](#)
- Member of the IECB Steering Committee, CoDir IECB, Since 2024, [P.V. Krasteva](#)

Evaluation Boards

- Scientific advisory board, Cancerpole GSO, Health and Technologies, 2024, [F. Friscourt](#)
- Member of a focus group on how to improve interdisciplinary research at the University of Bordeaux, InterD at the University of Bordeaux, 2024, [F. Friscourt](#)
- Member of Research evaluation panel, HCERES, 2024, [G. Guichard](#)
- Member of Research evaluation panel, ANR, 2024, [G. Guichard](#)
- Thesis committee of darko mitrovic at the school of Engineering Sciences at the KTH Royal Institute of Technology in Stockholm, [N. Reyes](#)
- Referee HDR – Clement Charenton, CRCN CNRS – IGBMC Strasbourg, HDR Jury, 2024, [S. Campagne](#)
- Scientific committee – SifrARN 2024, SifrARN 2024, 2024, [S. Campagne](#)
- Examineur, PhD Thesis committee, 2024, [E. Stahl](#)
- Board member, Swiss National Science Foundation, 2022–2024, [A. Loquet](#)
- Co-president, ANR, 2024–2025, [A. Loquet](#)

Teaching

- Microbiology 2H, Cours de microbiologie générale Institut Pasteur 2020, [R. Fronzes](#)
- Chemical Biology class: Structure and biological roles of glycans and lipids – Total of 11h, Master Level (M1 Chemistry), 2024, [F. Friscourt](#)
- Biocatalysis class – Total of 28h, Master Level (M2 Biochemistry and molecular biology), 2024, [F. Friscourt](#)
- Organic Chemistry Classes: Structure– reactivity in organic chemistry (Alkane, Alkene and Aromatic chemistry, SN, E, organometallic reagents, Alcohols, Thiols, Amines and Carbonyl reactivity) as well as thermodynamic and kinetic aspects of organic reactions – Total of 151h, BSc Level (L1–L3 Chemistry & L1 Biology), 2024, [F. Friscourt](#)
- Chimie générale, Chimie organique, RMN, Biomolécules du vivant, Biologie Chimique : 192 HETD, BSc Level (L1 SVSTC Chimie, L2 SVSTC Chimie), MSc Level (M1 MMF/COVAN Chimie du vivant, M2 COVAN biologie chimique), 2024, [C. Dolain](#)
- Chimie générale, chimie organique, vectorisation, peptides bioactifs, sondes en imagerie, ciblage, chimie thérapeutique : 192 HETD, PASS (Parcours Accès Santé Spécifique) du collège santé, cursus pharmacie 2ème année et 3ème année, module chimie du double cursus "Ecole Santé Sciences" (équivalent M1 recherche) Coordinateur du module de chimie du double cursus "Ecole Santé Sciences", 2024, [G. Compain](#)
- 2nd year ENSTBB – 8h30, Characterization of biomolecules by SPR, 2024, [Di Primo](#)
- Master 1 Biochimie Univ. Bordeaux – 4h, Analysis of the interactions by SPR, 2024, [Di Primo](#)
- L3 TecSan Univ. Bordeaux – 14h, Instrumentations: SPTR technology, 2024, [Di Primo](#)
- Master 1 Biochimie Univ. Bordeaux – 4h, smFRET for biomolecular structure and interactions, 2024, [M. Aznauryan](#)
- Master 1 Chimie SiTH Univ. Bordeaux – 4h, Analysis of the biomolecular interactions by smFRET, 2024, [M. Aznauryan](#)
- M1 BBM – 2h, Génie génétique, 2024, [F. Malard](#)

PhD Theses

- Pascale SARKIS, "Dynamique conformationnelle et interactions de l'IDR de l'eIF4B et de ses mutants phosphomimétiques", Univ. Bordeaux, MESRI, [M. Aznauryan](#), 2024
- Loïc Delcourte, "Solid-state NMR-based studies of bacterial signalosomes and fungal cell walls » Univ. Bordeaux, ANR, [A. Loquet](#), 2024
- Zeren Xu, "Role and assembly mechanisms of Remorin », Univ. Bordeaux, ANR, [B. Habenstein](#), 2024

Science & Society

- Fête de la science, Bordeaux, octobre 2020, [R. Fronzes](#)
- Fête de la Science (Hands-on Activities on Chirality), Pessac, November 2024, [M. Pasco](#)
- Forum des métiers de l'industrie pharmaceutique animée par le cluster santé ALLIS-NA (presentation of research activities in medicinal chemistry), Bordeaux, novembre 2024, [G. Guichard](#)
- Happy hour de la recherche en pharmacie, Bordeaux, mars 2024, [G. Compain](#)



Team Funding

European and International fundings

Coordinated by IECB researchers/IECB researchers as participants

IECB Researcher(s)	Funding body	Research project	Period
R. Fronzes	ERC	Structure and Function of the Bacterial Transformosome	2017-2024
Y. Hashem	ERC	Translation regulation in eukaryotic pathogens and hosts	2018-2023
Y. Hashem	ERC	Species-specific aspects in eukaryotic mRNA translation modulation and their implications in diseases	2023-2028
P.V. Krasteva	ERC	BacFilm	2024-2029
P.V. Krasteva	ERC	Advancement Grant	2024-2025
P.V. Krasteva	ERC	BioMatrix	2018-2024
P.V. Krasteva	H2020 ERASMUS	ERASMUS+	2022-2023
N. Reyes	NIH	The mechanism of allosteric modulation of glutamate transporters	2019-2024
G. Guichard	PHC STAR	Peptidomimetic Oligocarbamate-Urea Hybrids Exhibiting Stable Helical Conformation in Solution	2025-2026
G. Guichard	EU	Bioinspired Foldamer-based Asymmetric Catalysis at low catalyst loading	2023-2026
G. Guichard	China Scholarship Council	Conception et synthèse de mimétiques enzymatiques à base de foldamères	2022-2026
C. Di Primo	Euskampus	LTC INCUBATOR	2023-2024
C. Di Primo	EIC	Functional Nucleic Acids as Versatile SMart BUilding BLocks in Non-Conventional SolvenTs	2023-2026
S. Campagne	NIH	Function and structure of EndoU	2024-2028
Y. Fichou	ERC	Cofactors at the core of tau prion behavior	2022-2027
Y. Fichou	FEBS	Tau protein structural differentiation guided by aggregation cofactors	2022-2025
B. Habenstein	EU-SUDOE	RePo	2024-2027

National funding

Coordinated by IECB researchers/IECB researchers as participants

IECB Researcher	Funding body	Research project	Period
R. Fronzes	ANR	Dissecting the Antibody Cleavage System of Mycoplasmas	2018-2021
R. Fronzes	ANR	Structural basis of Helicobacter pylori type IV secretion system	2019-2022
R. Fronzes	ANR	Une approche multidisciplinaire pour comprendre la structure et la dynamique du système de sécrétion de type VI	2020-2024
R. Fronzes	EquipEX+	Microscopie corrélative à haute résolution en conditions cryogéniques	2021-2027

IECB Researcher	Funding body	Research project	Period
R. Fronzes	ANR	Nanoscale organization and dynamics of the molecular machinery that drives cell migration	2022-2026
P.V. Krasteva	ANR	BacFilm	2024
P.V. Krasteva	ANR	CelluSec	2024-2027
P.V. Krasteva	ANR	ROCKET	2022-2026
P. Maisonneuve	CRNS	Intestinal Guanylyl Cyclase Receptor Structure	2024-2025
P. Maisonneuve	ANR	Intestinal Guanylyl Cyclase Receptor Structure	2024-2028
F. Friscourt	ANR	Atypical N-glycosylation of the neuronal surface and its impact on synaptic transmission and plasticity	2022-2026
F. Friscourt	French Ministerial Scholarship	Development of unnatural sugars for controlling glycan-protein interactions in living cells	2023-2026
Z. Chinoy	CNRS	Synthesis of Siglec-specific glycans for targeted therapies	2024
G. Guichard	ANR	Precise pore-forming Assemblies of bioinspired foldamers for selective water translocation	2024-2027
G. Guichard	Ministry of Research	Synthesis of proteomimetic structures based on foldamers	2023-2026
G. Guichard	ANR	Fragment-based design of Irreversible Inhibitors of the Bacterial Replication	2023-2027
G. Guichard	ANR	Mode d'action dual: Nouveaux antimicrobiens ciblant la réplication et la traduction	2022-2025
G. Guichard	ANR	Selective and directional supramolecular interactions based on highly polar fluorinated synthons	2021-2024
G. Guichard	ANR	Therapeutic targeting and chemical biology of histone chaperone using rationally designed medium-size inhibitors	2021-2025
G. Guichard	ANR	Low Loading Asymmetric Catalysis with Helical Chiral Oligoureas	2019-2024
E. Thinon	ANR	Chemical approaches to study the S-palmitoylation of a host factor in Influenza A virus infection	2021-2024
M. Aznauryan	ANR	Probing the molecular mechanisms of function of disordered translation initiation factors: from in vitro to in-cell	2021-2026
S. Campagne	ANR	Rational development of small molecule splicing modifiers	2024-2028
S. Campagne	INSERM	AML-Killer : from in vitro to in vivo	2024-2025
Y. Fichou	ANR	En route to amyloid formation: Protein and hydration-water dynamics under liquid-liquid phase separation	2024-2028
E. Stahl	ATIP-Avenir	Lipid-mediated signalling mechanisms in plant innate immunity.	2024-2028
A. Loquet	ANR	Transkingamyloid	2021-2025
A. Loquet	ANR	API-NMR	2023-2027
A. Loquet	ANR	Ultimo	2021-2025
A. Loquet	ANR	ROSANE	
A. Loquet	ANR	FunWallEVs	

IECB Researcher	Funding body	Research project	Period
A. Loquet	ANR	Sorcelhub	
A. Loquet	ANR	BACdomain	

Regional funding

Coordinated by IECB researchers/IECB researchers as participants

IECB Researcher	Funding body	Type of funding	Period
Y. Hashem	ANR	ARchitecture of Algae Mitochondria translation System and its interplay with mRNA maturation	2021-2025
Y. Hashem	ANR	Dynamic And regulation of the Mitochondrial translational Apparatus in Arabidopsis	2020-2024
Y. Hashem	ANR	Deciphering the ABC-F protein mechanism of antibiotic resistance	2018-2022
Y. Hashem	ANR	Structural and molecular characterization of mRNA translation in colorectal cancer	2021-2023
Y. Hashem	INSERM	Rôle structural et régulatrice des G-quadruplexes dans le promoteur du proto-oncogène KRAS	2024-2028
N. Reyes	IDEX	Membrane protein mechanisms	2019-2024
N. Reyes	Region	Membrane protein mechanisms	2020-2025
N. Reyes	ANRS	Receptor-recognition and neutralization mechanisms of human HBV	2024-2026
F. Friscourt	Univ. Bordeaux / InnovationS	Novel bioorthogonal fluorogenic probes for the fast and precise labeling of biomolecules	2023-2025
G. Guichard	Univ. Bordeaux (Programme RIE)	poptotic Death Receptor 5 targeting for Theranostics. Ciblage du récepteur de mort DR5 pour des applications théranostiques	2024-2025
G. Guichard	Univ. Bordeaux (GPR PPM)	Bioplastics from Biomimetic Organocatalytic Stereocontrolled Polymerization	2024-2025
G. Guichard	Region Nouvelle Aquitaine	Nouveaux Antimicrobiens Ciblant La Réplication et la Traduction	2023-2025
G. Guichard	Region Nouvelle Aquitaine	Interactions supramoléculaires sélectives et directionnelles basées sur des synthons fluorés hautement polaires	2022-2024
G. Guichard	Region Nouvelle Aquitaine	Nouveaux outils pour l'optimisation et le développement de peptides thérapeutiques : Application au ciblage thérapeutique des chaperons d'histones	2022-2024
E. Thinon	University of Bordeaux	Chemical approaches to decipher the role of a host factor in Influenza A virus internalization	2019-2025
E. Thinon	Region Nouvelle Aquitaine	Caractérisation d'une nouvelle cible thérapeutique antivirale	2020-2025
M. Aznauryan	Region Nouvelle Aquitaine	Caractérisation des mécanismes moléculaires gouvernant la fonction d'eIF4B : vers de nouvelles cibles contre le cancer	2020-2025
S. Campagne	University of Bordeaux	Molecular mechanisms of disrupted spliceosome homeostasis during Alzheimer disease.	2024
Y. Fichou	UB	Photoswitches for the Control of tau Protein Liquid-Liquid Phase Separation	2023-2025
Y. Fichou	UB	Molecular basis for the interaction between Tau and U1 snRNP in the context of Alzheimer's disease	2023-2024

IECB Researcher	Funding body	Type of funding	Period
E. Stahl	GPR-BPS	Novel lipidic immunogenic patterns from Botrytis cinerea.	2024
E. Stahl	AAP Projets émergents	TNT: Réponse des plantes aux Toxines NécroTiques	2024
A. Loquet	UB	PhD	2023-2025

Charity-funded research projects

Coordinated by IECB researchers/IECB researchers as participants

IECB Researcher	Charity	Research project	Period
P. Maisonneuve	Foundation pour la Recherche Médicale (FRM)	Uncovering the mechanism of action of pseudokinases in human health and diseases	2022-2025
P. Maisonneuve	ARC	Deciphering mechanisms of regulation of RAF kinases in higher-order protein complexes	2024-2025
G. Guichard	Ligue Contre le Cancer	Protéinomimétiques se liant à l'ADN avec une activité anticancéreuse	2024-2026
E. Thinon	AFAF- FRM	Protein palmitoylation in Friedreich ataxia	2024-2025
M. Aznauryan	FRM	Probing interactions of eukaryotic initiation factor 4B (eIF4B): towards new anti-cancer targets	2022-2024
S. Campagne	FRM	Fundamental basis for specific splicing correction by small molecules	2024-2028
S. Campagne	Ligue Contre le Cancer	Splicing modulation of mTOR mRNA as a novel anti-cancer strategy	2024
S. Campagne	Fondation Alzheimer	Molecular mechanisms of disrupted spliceosome homeostasis during Alzheimer disease.	2025-2027
Y. Fichou	Fondation Vaincre Alzheimer	Tau aggregation cofactors	2023-2026

Contracts with the industry

Coordinated by IECB researchers/IECB researchers as participants

IECB Researcher	Company	Research contract	Period
G. Guichard	Ureka Pharma	Developpement de Peptidomimes Contraints Ciblant la Surface de Proteines	2022-2025
A. Loquet	BioLaffort		2024-2027
A. Loquet	AstraZeneca		
A. Loquet	Lallemand		2023-2024

Collaborations

Pole 1 – Structural biology

Structure and Function of Bacterial Nanomachines

Dr. Rémi Fronzes

- Dr. Yonathan Arfi, INRAE, Biologie du Fruit et Pathologie, UMR 1332, Villenave D'ornon, France
- Dr. Eric Cascales, LISM CNRS UMR7255, Marseille, France
- Dr. Laure Journet, LISM CNRS UMR7255, Marseille, France
- Dr. Laurent Terradot, IBCP, Lyon, France
- Dr. Thomas Henry, CIRI, Lyon, France
- Dr. Gregory Giannone, IINS, Bordeaux, France
- Dr. David Perrais, IINS, Bordeaux, France
- Dr. Raffaele Ieva, CBI, Toulouse, France
- Dr. Patrice Polard, CBI, Toulouse, France
- Dr. Vladimir Pellicic, LCB, Marseille, France

RNA Processing and translation regulation in pathogens and hosts

Dr. Yaser Hashem

- Dr. Zoya Ignatova, University of Hamburg, Hamburg, Germany
- Dr. Jody Puglisi, Stanford University, Stanford, USA
- Dr. Gregory Boël, CNRS, Université de Paris, Paris, France
- Dr. Axel Innis, Inserm, Université de Bordeaux, Bordeaux, France
- Dr. Dominique Favre-Soldati, Université de Genève, Suisse

Structural Biology of Biofilms

Dr. Petya Krasteva

- Dr. Yaser HASHEM, IECB, Pessac, France
- Dr. Aurélien Carlier, LIPME, CNRS, INRAE, Toulouse, France

Structural Biology of (Pseudo) Kinase proteins

Dr. Pierre Maisonneuve

- Dr. Sandhya Visweswariah, Department of Developmental Biology and Genetics, Indian Institute of Science, Bengaluru, India
- Dr. Marc Therrien, Institute for Research in Immunology and Cancer, Laboratory of Intracellular Signaling, Université de Montréal, Montreal, Quebec, Canada

Membrane Protein Mechanisms

Dr. Nicolas Reyes

- Prof. Jan Steyaert, VIB/VUB Brussel, Brussels, Belgium
- Prof. Camilo Perez, University of Georgia, Athens, EEUU

Pole 2 – Organic & bioorganic chemistry

Peptidomimetic Chemistry

Dr. Gilles Guichard

- Dr. Gavin Collie, Discovery Sciences, R&D, AstraZeneca, Cambridge, UK
- Prof. Prakash P. Kumar, National University of Singapore (NUS), Singapore
- Prof. R. Manjunatha Kini, National University of Singapore (NUS), Singapore
- Prof. Karolina Pulka-Ziach, University of Warsaw, Warsaw, Poland
- Prof. Sung Hyun Yoo, Chonnam National University, Gwangju, Republic of Korea
- Dr. Mihail Barboiu, Institut Européen des Membranes, Montpellier, France
- Dr. Natacha Rochel, Institute of Genetics and of Molecular and Cellular Biology, Illkirch, France
- Dr. Dominique Burnouf, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France
- Dr. Jérôme Wagner, Institut de Biologie Moléculaire et Cellulaire, Strasbourg, France
- Dr. Abdel-Majid Khatib, Univ. Bordeaux, INSERM, BRIC, U 1312, Bordeaux, France
- Dr. Cameron Mackereth, Univ. Bordeaux, CNRS, INSERM, ARNA, UMR 5320, U1212, Pessac, France
- Dr. Sébastien Campagne, Univ. Bordeaux, CNRS, INSERM, ARNA, UMR 5320, U1212, IECB, Pessac, France
- Dr. Emmanuelle Thinon, Univ. Bordeaux, CNRS, Bordeaux INP, CBMN, UMR 5248, IECB, Pessac, France
- Dr. Brice Kauffmann, Univ. Bordeaux, CNRS, INSERM, IECB, UMS 3033, Pessac, France

Chemical Biology of membrane proteins

Dr. Emmanuelle Thinon

- Dr. Gilles Guichard, CNRS UMR 5248 (CBMN), Pessac, France
- Dr. Daniele Mantione, POLYMAT, University of the Basque Country UPV/EHU, Donostia-San Sebastian, Spain
- Dr. Stéphane Claverol, Univ. Bordeaux, Bordeaux Proteome, Bordeaux, France



Pole 3 – Biophysics

Single-molecule Biophysics

Dr. Mikayel Aznauryan

- Dr. Cameron, INSERM, ARNA U1212, Bordeaux, France
- Prof. Davide Mercadante, University of Auckland, Auckland, New Zealand
- Prof. Victoria Birkedal, INANO, Aarhus University, Aarhus, Denmark
- Dr. Harald Wodrich, MFP, CNRS, Univ. Bordeaux, Bordeaux, France

Structure, Mechanism and RNA Therapeutics

Dr. Sébastien Campagne

- Prof. Frédéric HT Allain, ETH Zurich, Zurich, Switzerland
- Prof. Fedor Karginov, UC Riverside, Riverside, USA
- Prof. Jean-Marc Campagne, ENSCM, Montpellier, Montpellier, France
- Prof. Stéphanie Olivier-Van Stichelen, Medical College of Wisconsin, Madison, USA

Solid-state NMR of Molecular Assemblies

Dr. Antoine Loquet

- Prof. Fandrich, Ulm, Germany
- Prof. Smith, Leipzig U., Leipzig, Germany
- Prof. Ventura, Universitat Autònoma de Barcelona, Barcelona, Spain
- Dr. Saupe Sven, IBGC, Bordeaux, France
- Prof. Rey Patrice, IPREM, Pau, France
- Dr. Daskalov Asen, Immunoconcept, Bordeaux, France
- Prof. Delhaes Laurence, CHU Bordeaux / CRCTB, Bordeaux, France

Invited Conferences

Pole 1 – Structural biology

RNA Processing and translation regulation in pathogens and hosts

- The sifARN 2022 Meeting, Bordeaux, France, 2023, October 3rd–5th, [Y.Hashem](#)
- Société Française des Microscopies, Rouen, France, 2023, July 3rd–7th, [Y.Hashem](#)
- FEBS 47th Meeting, Tour, France, 2023, July 8th–12th, [Y.Hashem](#)
- Israeli RNA Society Meeting, Weizmann Institute, Rehovot, Israel, 2023, October 16–18th, [Y.Hashem](#)
- INT. CONFERENCE ON MICROBIOLOGY & ONE HEALTH, Quy Nhon, Vietnam, 2024, August 11th – 14th, [Y.Hashem](#)
- ZOMES XII CONFERENCE, Shenzhen, China, 2024, October 31–November 3, [Y.Hashem](#)
- GRC Translation and Disease, Los Angeles, California, USA, 2025, February 23rd–28th, [Y.Hashem](#)
- Ribosome Meeting 2025, Pacific-Grove, California, USA, 2025, June 22nd–24th, [Y.Hashem](#)
- FEBS meeting 2025, Istanbul, Turkey, 2025, July 5th–9th, [Y.Hashem](#)

Structural Biology of Biofilms Group

- GRC Carbohydrate-Active Enzymes for Glycan Conversion, Proctor Academy, USA, July 2025, [P.V. Krasteva](#)
- From Single Molecules to Cell Functions in Biomembranes, HHU Düsseldorf, Germany, April 2025, [P.V. Krasteva](#)
- CSSB Symposium: Charting the landscape of infection, Hamburg, Germany, May 2023, [P.V. Krasteva](#)

Structural Biology of (Pseudo) Kinase proteins

- Oncosphere Nouvelle-Aquitaine, Bordeaux, France, January 2024, [P. Maisonneuve](#)

Pole 2 – Organic & bioorganic chemistry

Chemical Glycobiology

- Société Chimique de France, Grand-Sud-Ouest 2024, Bordeaux, France, February, 2024, [F. Friscourt](#)
- Institut de Chimie de Nice, Department Seminar, Nice, France, September, 2024, [F. Friscourt](#)
- Chemistry-Biology Interface Day, Bordeaux, France, November, 2024, [ZS. Chinoy](#)

Peptidomimetic Chemistry

- Foldamer Conference, Bordeaux, France, September, [G. Compain](#)
- 9th EuChemS, Dublin, Ireland, July/2024, [G. Guichard](#)
- 2024 Foldamer Workshop, New York, USA, June/2024, [G. Guichard](#)
- KAIST-Univ Bordeaux Joint Symposium, Pessac, France, Mai/2024, [G. Guichard](#)
- SCF Chemical Biology Symposium 2024, Saclay, France, January/2024, [G. Guichard](#)
- Séminaire interdisciplinaire de l'oncosphère de bordeaux, Bordeaux, France, [G. Guichard](#)

Conference Organisation

Pole 3 – Biophysics

Single-molecule Biophysics

- Single-molecule FRET of non-globular proteins, Lisbon, Portugal, Sept 2024, [M. Aznauryan](#)

Molecular mechanisms of amyloid diseases

- “Tau protein phase separation”, Medyna online seminar, Virtual, 2024, [Y. Fichou](#)
- “Understanding the modulators of tau amyloid aggregation pathways” 1st FEBS excellence award meeting, Pavia, Italy, 2024, [Y. Fichou](#)
- “Tracking the Transition of the Intrinsically Disordered Protein Tau Toward Amyloid Aggregate by ESR”, Advances in ESR, ACERT, Cornell University, USA, 2024, [Y. Fichou](#)
- “Modulators of tau aggregation”, European South Atlantic Biophysics congress 2024, San Sebastian, Spain, 2024, [Y. Fichou](#)
- “Structure – aggregation relationship revealed by tau mutations”, 5th International symposium on pathomechanisms of amyloid diseases, Bordeaux, 2023, [Y. Fichou](#)
- “Deciphering protein amyloid formation by EPR spectroscopy”, Journée scientifique de l'ARPE, Paris, France, 2023, [Y. Fichou](#)

Lipid-mediated signalling mechanisms in plant innate immunity

- CUSO PhD Retreat, Murten, Switzerland, June 2024, [E. Stahl](#)
- Cycle de Séminaires – Biologie Agrosience 2024, Bordeaux, France, November 2024, [E. Stahl](#)
- Réunion plénière 2024 du réseau ENVIE, Bordeaux, France, November 2024, [E. Stahl](#)
- Chemistry Biology Interface Day 2024, Bordeaux, France, November 2024, [E. Stahl](#)

NMR of Molecular Assemblies

- Symposium Cell wall, Paris, 2024, [A. Loquet](#)
- Biomolecular assemblies symposium, Bordeaux, 2024, [A. Loquet](#)

- Gordon Conference on Mechanisms of Membrane Transport (Vice Chair), 2025, [N. Reyes](#)
- 4th National Chemical Biology Symposium (GDR ChemBio), Bordeaux, France, June, 2024, [F. Friscourt](#) & [ZS. Chinoy](#)
- 58th International Conference on Medicinal Chemistry: Interfacing Chemical Biology and Drug Discovery, RICT 2024, Bordeaux, France, July, 2024, [F. Friscourt](#)
- Chemistry Biology Interface Day CBID 2023, Bordeaux, France, November, 2023, [F. Friscourt](#)
- EFMC-ISMIC 2024 (XXVIII EFMC International Symposium on Medicinal Chemistry), Roma, Italy, September/2024, [G. Guichard](#)
- RICT 2024 – 58^{èmes} Rencontres Internationales de Chimie Thérapeutique, Bordeaux, France, July/2024, [G. Guichard](#), [G. Compain](#), [M. Pasco](#)
- « Celebrating Professor Léon Ghosez's 90th Birthday », Bordeaux, France, July/2024, [G. Guichard](#)
- 4^{ème} journées scientifiques du GDR ChemBio 2024, Bordeaux, France, July/2024, [G. Guichard](#)
- Gordon Conference on Mechanisms of Membrane Transport (Vice Chair), 2025, [S. Campagne](#)
- CBID 2024, Pessac, France, November 2024, [E. Thinon](#)
- Journées du Grand Sud-Ouest de la SCF, Pessac, France, February 2024, [E. Thinon](#)
- GDR Chémobiologie, Pessac, France, June 2024, [E. Thinon](#)
- Molecular Biophysics Week, IECB, Bordeaux/France, December 2024, [M. Aznauryan](#)
- 13th SifrARN 2024, Lyon, FR, November 2024, [S. Campagne](#)
- The sifrARN 2022 Meeting, Bordeaux, France, 2023, October 3rd–5th, [Y. Hashem](#)



Access to the platform:

The platform is accessible to researchers from the public and from the private sector. All information on available equipment and process to request services or contact experts can be found on the BPCS web page:

<http://www.iecb.u-bordeaux.fr/index.php/en/structural-biophysico-chemistry>

Three types of services are offered:

- (1) Instrument access time: duly trained users can request machine time, perform the experiments, and interpret the data. Office space is available to accommodate external users.
- (2) Routine services: samples are submitted, the platform personnel performs the assays and sends the analysis report to the user. Experiments for which the data interpretation is routine fall into this category.
- (3) Collaborative projects: all requests that require the platform personnel's scientific expertise and/or methodological developments in instrumentation, experiment design, or data interpretation, fall into this category.

Technology Platforms



Dr. Brice Kauffmann

Head of IECB's Biophysical and Structural Chemistry platform, IR, CNRS

Head of IECB's Biophysical and Structural Chemistry platform, IR, CNRS. After a PhD in protein crystallography (2003, University of Nancy I), Brice Kauffmann spent three years at the European Molecular Biology Laboratory (EMBL) in Hamburg (Germany) working on the development of a new macromolecular crystallography beamline (X12, DESY). He joined the European Institute of Chemistry and Biology in January 2006 as a staff Scientist.

Selected publications

1. Xu Z, Schahl A, Jolivet MD, Legrand A, Grélard A, Berbon M, Morvan E, Lagardere L, Piquemal JP, Loquet A, Germain V, Chavent M, Mongrand S, Habenstein B. Dynamic pre-structuration of lipid nanodomain-segregating remorin proteins. *Commun Biol.* 2024 Dec 5;7(1):1620.
2. Malard F, Wolter AC, Marquieville J, Morvan E, Ecoutin A, Rüdisser SH, Allain FHT, Campagne S. The diversity of splicing modifiers acting on A-1 bulged 5'-splice sites reveals rules for rational drug design. *Nucleic Acids Res.* 2024 May 8;52(8):4124-4136.
3. Yu L, Li D, Ma C, Kauffmann B, Liao S, Gan Q. Redox-Regulated and Guest-Driven Transformations of Aromatic Oligoamide Foldamers in Advanced Structures. *J Am Chem Soc.* 2024 May 15;146(19):12907-12912.
4. Saryeddine L, Hadnutt J, Grélard A, Morvan E, Alies B, Buré C, Bestel I, Badarau E. Design of light-responsive amphiphilic self-assemblies: A novel application of the photosensitive diazirine moiety. *J Colloid Interface Sci.* 2024 Jan;653(Pt B):1792-1804.
5. Maisonneuve P, Sahmi M, Bergeron-Labrecque F, Ma Xi, Queguiner J, Arseneault G, Lefrançois M, Kurinov I, Fronzes R, Sicheri F, Therrien M. The CNK-HYP scaffolding complex promotes RAF activation by enhancing KSR-MEK interaction. *Nat Struct Mol Biol.* 2024 Jul;31(7):1028-1038.

Biophysical & Structural Chemistry platform (BPCS)

IBISA-labelled since 2011, IECB core facility provides privileged access to state-of-the-art instruments and dedicated scientific expertise from scientists leading research programs either at IECB or in partner labs on the Bordeaux campus. The BPCS serves to nucleate the development of a supportive local community with expertise in structural biology, structural chemistry and biophysics to increase the attractiveness of the University of Bordeaux for talented scientist from all over the world.

In 2019, the IECB core facility has joined the new "Core Facilities" department at Bordeaux University. At the forefront of methodological developments in Structural (Bio) Chemistry and Biophysics, the facility is gathering on the same site a coherent set of techniques and expertise to investigate molecular recognition processes and structure of supramolecular assemblies from a structural and biophysical perspective.

Importantly, the facility stands at the frontiers between chemistry and biology, by focusing both on biological molecules and on synthetic molecules conceived to fold and self-assemble like biological molecules and/or interact with biological systems. It is indeed not sufficient to determine simply the structure and biochemical properties of macromolecules in vitro. In line with the trend towards systems biology and integrated structural biology initiatives in Europe (Instruct), a major challenge now is to understand how macromolecules functions dynamically within a larger macromolecular assembly or in a cellular pathway or even at the organism level. Understanding dynamical processes is not possible using a single technology, but becomes potentially accessible through the integration of a number of approaches, spanning different resolution scales.

The IECB facility follows that development strategy by regrouping expertise and state-of-the-art instruments in Biochemistry (production and purification of recombinant proteins, peptide synthesis...), NMR spectroscopy (liquid and solid state with 8 spectrometers from 100 MHz to 800 MHz), X-ray crystallography (from crystallization to atomic resolution structure on single crystals or powder samples with a high flux X-ray source and Hybrid direct detector), Cryo-EM (with a 200kV FEI Talos Arctica microscope equipped with a GATAN K2 summit camera), mass spectrometry (Bruker Solarix 7T ETD), surface plasmon resonance and spectroscopy (absorption and circular dichroism spectroscopy, SPR exploiting a T200 instrument from Biacore and Octet8 BLI).

Access to the platform:

The platform is accessible to researchers from the public and from the private sector. All information on available equipment and process to request services or contact experts can be found on the BPCS web page:

<http://www.iecb.u-bordeaux.fr/index.php/en/structural-biophysico-chemistry>

Three types of services are offered:

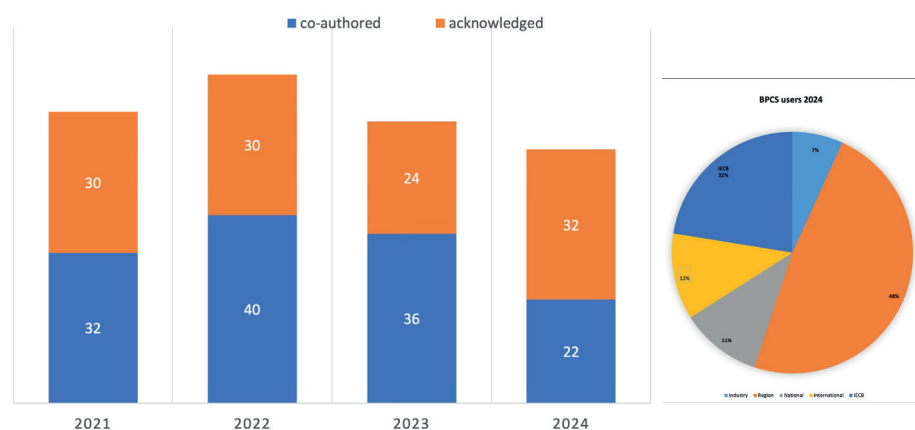
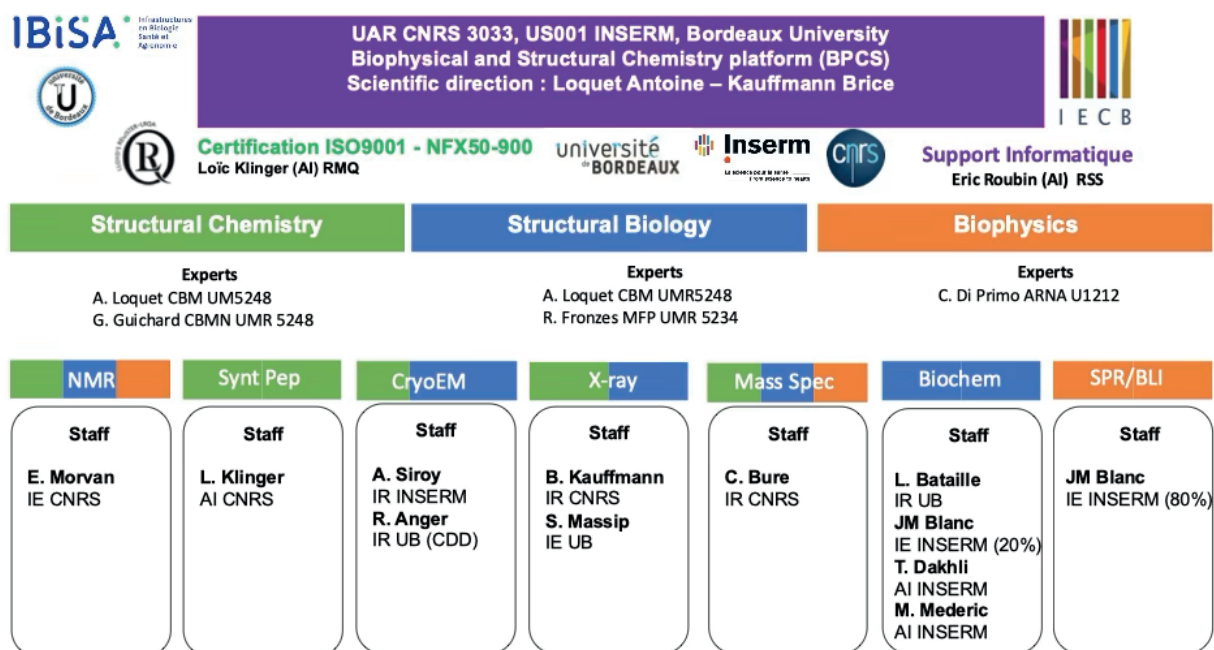
1. **Instrument access time:** duly trained users can request machine time, perform the experiments, and interpret the data. Office space is available to accommodate external users.
2. **Routine services:** samples are submitted, the platform personnel performs the assays and sends the analysis report to the user. Experiments for which the data interpretation is routine fall into this category.
3. **Collaborative projects:** all requests that require the platform personnel's scientific expertise and/or methodological developments in instrumentation, experiment design, or data interpretation, fall into this category.

Scientific and Quality policies:

To fulfill these missions, the BPCS is committed to:

- Support the research of IECB teams by providing them with:
 - Privileged access to a high-level platform (instruments and expertise) for physico-chemical and structural characterization of synthetic molecules, biomolecules and their assemblies.
 - Opportunities for collaboration in methodological research.
- Pursue opening policy to external academic and industrial teams. In particular, the strategic objectives are to:
 - Strengthen the positioning of the structural chemistry cluster, focused on the characterization of biomolecules and bio-inspired assemblies.
 - Strengthen the structural biology cluster through developments in cryo-electron microscopy, at the interface with cellular imaging.
 - Restructure a biophysics cluster to characterize molecular interactions.
- Reinforce best practices related to scientific ethics in experimental research (traceability, reliability).
- Contribute to the training of students and scientific and technical staff in the platform's areas of expertise.
- Continue the improvement process following ISO 9001:2015 and NF-X50-900.

Organization



Users of the platform: In 2024, the platform contributed to 147 projects for more than 40 different public or private laboratories or companies.

Key figures:

- **More than 100 people trained** per year (students, technicians, researchers)
- **60 publications** with staff members as co-author or with acknowledgments for the BPCS.



2024 Highlights:

A new state-of-the-art instrument is now available for use at the cryo-electron microscopy facility of the UAR IECB. This latest-generation automated transmission electron microscope – a ThermoFisher Glacios2 – was funded by the Nouvelle Aquitaine region via the CPER and EquipEx+ NanoCryoClem grant. Installed during the second semester of 2024, this Glacios2 is now fully operational. The Glacios2 is accessible for national and international users. It is the latest addition to a range of equipment for high-resolution screening and structural analysis of biological and synthetic macromolecules, including a ThermoFisher Talos L120C (morphological analysis, at room temperature or cryogenically) and a ThermoFisher Talos Arctica (cryo-SPA of proteins).



Technology Transfer & Start-ups

The scientific breakthroughs achieved at IECB are meant to nurture technological innovation. The skills, knowledge and technologies developed at the institute are transferred to economic players via different routes:

Collaborative research

Servier, UreKa, DART Neurosciences... Several key industry players work with IECB teams.

Contract services and consulting

The IECB brings together a wide range of scientific equipments and expertise in chemistry and biology. Such resources are made available to public and private research centers through IECB's Biophysical and Structural Chemistry platform.

Technology transfer

IECB researchers are strongly encouraged to patent their discoveries.

The technology transfer unit Novaptech that was hosted at IECB in 2008–2013 is now a promising biotech company headquartered in Bordeaux.

Incubating start-ups

IECB has 300 m² work space dedicated to start-ups. Ureka created in 2010 is located at the institute since 2014. Until 2018, a part of this area was also occupied by Fluofarma, created in 2003 by two team leaders from IECB.





Founded in Bordeaux in 2013, Aelis Farma is a biopharmaceutical company that is developing a new class of drugs, the Signaling-Specific inhibitors of the CB1 receptor of the endocannabinoid system (CB1-SSi). CB1-SSi have been developed by Aelis Farma based on the discovery of a natural regulatory mechanism of CB1 hyperactivity made by the team led by Dr. Pier Vincenzo Piazza, the Company's CEO, when he was the director of the Neurocentre Magendie of INSERM in Bordeaux.

By mimicking this natural mechanism, CB1-SSi appear to selectively inhibit the disease-related activity of the CB1 receptor without disrupting its normal physiological activity. CB1-SSi have consequently the potential to provide new safe treatments for several brain diseases.

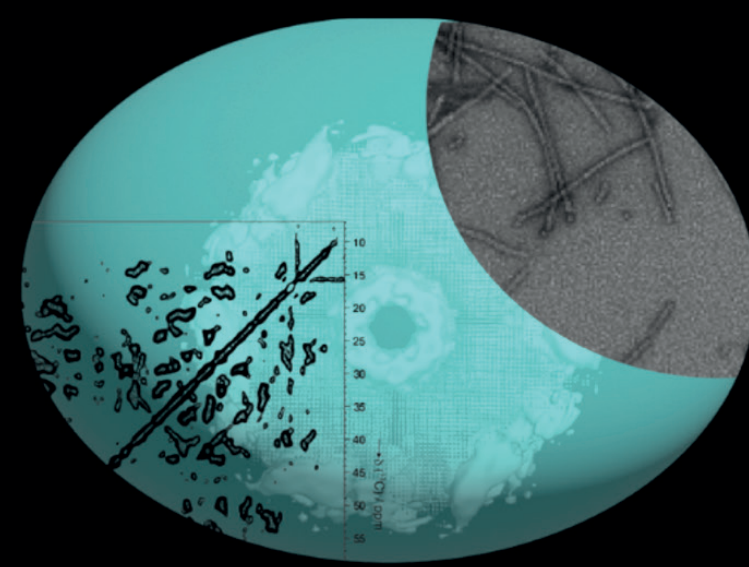
Aelis Farma is currently developing two first-in-class clinical-stage drug candidates: AEF0117 for the treatment of cannabis related disorders, that has just completed a Phase 2B study in the United States in CUD, and AEF0217 for cognitive disorders, including those of Down syndrome (Trisomy 21), that has just completed recruitment in a Phase 1/2 study in Spain in people with Down syndrome, with results expected in Q4 2024.

The Company also has a portfolio of new innovative CB1-SSi for the treatment of other disorders associated with a dysregulation of the activity of the CB1 receptor. The different drugs developed by the Company belong to the same general pharmacological class, the CB1-SSi, but have distinct functional effects allowing to target different types of dysregulations of the CB1 receptor.

Aelis Farma draws on the talents of more than 25 highly qualified employees.

Scientific Events

Workshops & symposia held at IECB



**Mini-symposium
Molecular
assemblies in health
and disease**

**April 4th
from 2 pm - 6 pm, IECB**

2 rue Robert Escarpit
Pessac

Wednesday May 22thSession Chair: *tbd*9:00-9:15 **Welcome address**

- 9:15-9:40 **C1 Hee-Seung Lee (KAIST)**
Chiral Metal-Peptide Networks from Helical Foldamers
- 9:40-10:05 **C2 Céline Olivier (UB)**
Linear and Nonlinear Chiroptical Properties of Helically Chiral Molecular Architectures
- 10:05-10:30 **C3 Sunkyu Han (KAIST)**
Natural Product's Inspired Chiral Molecular Photoswitch

10:30-11:00 **Coffee Break**Session Chair: *tbd*

- 11:00-11:25 **C4 Eiji Yashima (Nagoya)**
Control of One-Handed Helicity in Poly(biphenylacetylene)s: Impact of an Extremely Small Amount of Chiral Substituents
- 11:25-11:50 **C5 Sang Woo Han (KAIST)**
Thermally Responsive Liquid Crystal-Mediated Chiral Plasmonic Films with Strong Chiroptical Response and Dynamic Tunability
- 11:50-12:15 **C6 Reiko Oda**
Chirality can be transmitted between objects between different size range

12:15-14:30 **Lunch break**Session Chair: *tbd*

- 14:30-14:55 **C7 Byeong-Su Kim (Yonsei)**
Rapid and Enantioselective, Ring-Opening Polymerization of rac-Lactide Enabled by a Chiral Cyclopropenimine-Thiourea Catalyst
- 14:55-15:20 **C8 Sébastien Lecommandoux (UB)**
Harnessing Biomimicry with Self-Assembled Biohybrid polymers: from Nanomedicines to Protocells
- 15:20-15:45 **C9 Haeshin Lee (KAIST)**
Polyphenolic Adhesive Polymers for Biomedical and Cosmetic Applications

15:45-16:15 **Coffee Break**Session Chair: *tbd*

- 16:15-16:40 **C10 Dong Ki Yoon (KAIST)**
Fabrication of chiral structures based on liquid crystal materials in confined geometries and their application (Physically Unclonable Function: PUF)
- 16:40-17:05 **C11 Gilles Guichard (UB)**
Foldamer Nanostructures as Protein Structure Mimics



Looking to the Future Workshop Program Wednesday 13th November, 2024

09.45 – 10.00 Introduction

10.00 – 10.40 Spatiotemporal Control of Biological Events Using Photo-Uncaging Systems.

Dr. Dalu CHANG

EPFL, Lausanne, Switzerland / University of Oxford, UK.

10.40 – 11.10 Chemical approaches for microbial modulation and drug discovery.

Dr. Kyong T. FAM

Scripps Research, La Jolla, California, USA.

11.10 – 11.50 Functional Soft Materials from Complex Chemical Systems.

Dr. Jianwei LI

MediCity Research Laboratory, University of Turku, Finland.

11.50 – 13.30 *Break*

13.30 – 14.10 Polymer-Cell Interactions for Controlled Biological Systems.

Dr. Andrea BELLUATI

Darmstadt University of Technology, Darmstadt, Germany.

14.10 – 14.50 Surface-based cell-free platform to characterize host-pathogen interactions.

Dr. Aurore DUPIN

Weizmann Institute of Science, Rehovot Israel.

14.50 – 15.30 Crosstalk between membrane-bound organelles mRNA and the cytoskeleton in neurons.

Dr. Loïc BROIX

RIKEN Center for Biosystems Dynamics Research, Kobe, Japan.

15.30 – 16.00 *Break*

16.00 – 16.40 The archaeal core replisome: many ways to look at it

Dr. Markel MARTINEZ

Pasteur Institute, Paris, France.

16.40 – 17.20 Structurally characterising the phenuivirus replication machinery.

Dr. Harry M. WILLIAMS

Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany.

THURSDAY 27 JUNE 2024 • IECB AUDITORIUM

Special Event



Celebrating Professor Léon Ghosez's 90th Birthday

A tribute to a tireless chemist and a founding member of IECB

Lunch buffet 12:00

Scientific presentations 13:30

- 13:30 - 13:40 Welcome address
- 13:40 - 14:05 Jean-Jacques Toulmé (Novaptech, Bordeaux)
- 14:05 - 14:30 Ivan Huc (LMU, Munich)
- 14:30 - 14:55 Stéphane Quideau (Univ Bordeaux)
- 14:55 - 15:20 Dominique Lesuisse (BBB/Med Chem Consulting)
- 15:20 - 15:45 Jean-Louis Mergny (Ecole Polytechnique, Palaiseau)
- 15:45 - 16:10 Michal Hocek (IOCB & Charles Univ., Prague)
- 16:10 - 16:35 Janine Cossy (ESPCI, Paris)
- 16:35 - 16:50 Léon Ghosez (Univ Bordeaux)



Happy Hour 17:00



This event is open to all and free but registration is mandatory using the link below:

<https://framaforms.org/celebrating-professor-leon-ghosezs-90th-birthday-1714583983>

6-7 juin 2024

ATTENTION ! Changement de site

**Institut Européen de
Chimie et Biologie**

Pessac

4^{èmes} Journées du GDR ChemBio

Ne manquez pas les journées scientifiques du GDR ChemBio 2024 qui auront lieu les **6 et 7 juin 2024** à l'Institut Européen de Chimie et Biologie, de l'**Université de Bordeaux**.

Si vous êtes chercheurs, enseignants-chercheurs, ingénieurs, techniciens, post-doctorants ou doctorants, cet événement vous offre l'opportunité de présenter vos travaux via des présentations orales ou des affiches.

La participation à ces journées est gratuite. Nous vous demanderons simplement de vous inscrire pour faciliter l'organisation.

Attention : Les places seront limitées à 120 !

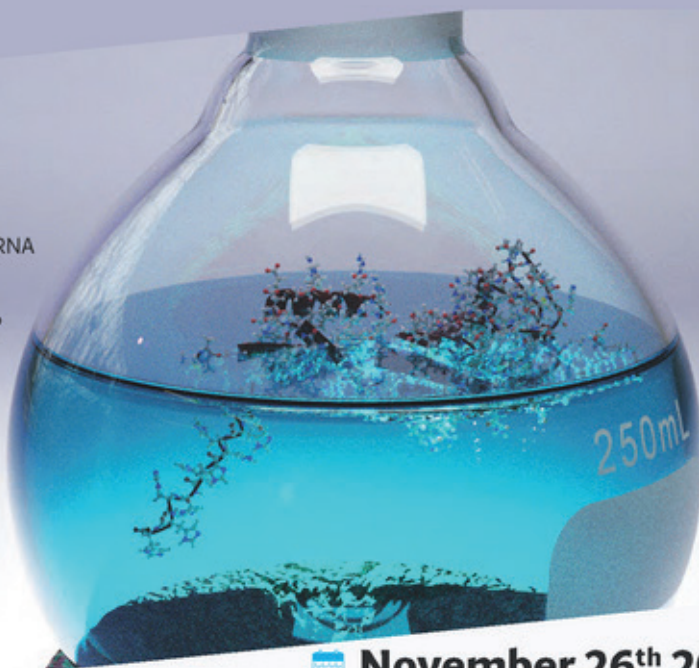
Les inscriptions sont désormais ouvertes jusqu'au **1er mai 2024** !

CBID 2024: Chemistry Biology Interface Day

- » A scientific meeting aiming at promoting research at the interface between chemistry and biology in the Nouvelle Aquitaine region.
- » Open to all from master student to researcher.

Speakers:

Sébastien Campagne - ARNA
Hugo De Oliveira - Biotis
Estelle Rascol - CBMN
Thomas Beneyton - CRPP
Sébastien Papot - IC2MP
Clément Morgat - INCIA
Anna Brachet - IINS
Laure Béven - INRAE
Zoeisha Chinoy - ISM
Elia Stahl - LBM
Colin Bonduelle - LCPO



 **November 26th 2024**
9h00-18h00

 **at IECB**
2, rue Robert Escarpit, Pessac

Registration before November 15th

<https://framaforms.org/cbid2024-chemistry-biology-interface-day-1722509840>



free but mandatory

Organizers:

Frederic Friscourt (IECB/ISM) / Elisabeth Garanger (LCPO)
Jeanne Leblond-Chain (ARNA) / Nicolas Martin (CRPP)
Matthieu Sainlos (IINS) / Elia Stahl (IECB/LBM)
Emmanuelle Thinon (IECB/CBMN)

Contact:

e.thinon@iecb.u-bordeaux.fr

université
de BORDEAUX

IECB Seminars Series

1. Dr. Ludger Johannes from Institut Curie, Paris, France hosted by Gilles Guichard March 15th. Title : Glycosylation in endocytosis and therapeutic intracellular delivery.
2. Dr. Steven Moussu from the Laboratoire de Recherche en Sciences Végétales Toulouse, France hosted by Elia Stahl, April 5th. Title : Plant cell wall patterning and expansion mediated by protein-peptide-polysaccharide interaction.
3. Pr. Sandhya S. Visweswariah from the Departments of Bioengineering and Genetics Indian Institute of Science (IISc, India) hosted by Pierre Maisonneuve May 3rd. Title: Gut reactions and gut instincts : the role of cGMP.
4. Drs. Slavica Pavlovic-Djuranovic & Sergej Djuranovic from Washington University, St. Louis, Missouri, USA hosted by Yaser Hashem June 21st. Titles : Exploration of the mRNA surveillance mechanism within the AU-rich transcriptome of malaria parasites & polyA track associated frameshifting in control of environmental stress survival and development.
5. Pr. Vincent Conticello from the Department of chemistry of Emory university (GA, USA), hosted by Gilles Guichard September 13th. Title : Peptide-based Nanomaterials: Progress from Structural Analysis to Design.
6. Pr. Jonathan Clayden from Bristol School of Chemistry (UK) invited by Yann Ferrand, October 4th. Title : Applications of conformational control : defluorination, deracemization and directional motion.
7. 1st Ambassadeur Tour des Sciences Chimiques du Professeur Ayyalusamy RAMAMOORTHY (Department of Chemical and Biochemical Engineering National High Magnetic Field Laboratory Florida State University, Tallahassee, USA), November 12th. Title: Probing Membrane-Assisted Protein-Protein Interactions by NMR
8. Dr. Yvon Jaillais from the Laboratoire Reproduction et Développement des Plantes (Lyon, France) hosted by Birgit Habenstein, December 6th. Title : Anionic phospholipids across scales: from plasma, membrane nanodomains to plant development.

Other Seminars

1. Prof. Yoshihiko Togawa, (Osaka Metropolitan University) hosted by Reiko Oda, July 5th. Title: A role of chirality: Generation and transfer of spin and phonon angular momenta
2. Prof. Matthew J. Harrington, Dept. of Chemistry, McGill University, Montreal, Quebec, Canada hosted by Yann Fichou, July 9th. Title : Biological fabrication of hierarchically structured materials from protein condensates
3. Prof. Steven Ballet, Vrije Universiteit Brussel, hosted by Guillaume Compain, October 22nd. Title : Peptide-based hydrogels for sustained drug release"
4. Prof. Sébastien Thibaudau, University of Poitiers UMR 7285 (IC2MP), hosted by Guillaume Compain, October 22nd. Title : Charge-driven reactivity in superacid"
5. Dr. Benoît Crousse, University of Paris-Saclay BioCIS UMR, hosted by Guillaume Compain, October 22nd. Title : Different Approaches to Fluorinated Amino Units"
6. Prof. Sébastien Papot, University of Poitiers UMR 7285 (IC2MP), hosted by Guillaume Compain, October 22nd. Title : Understand and manipulate biological processes via the controlled formation and/or breaking of chemical bonds"
7. Prof. Frances Separovic, Univ. Melbourne, November 21st. Title : Breaking barriers with antimicrobial peptides
8. Dr. Sandrine Sagan, CNRS Paris, November 21st. Title : Ins and outs of cell-penetrating peptides : bridging the gap of cell penetration mechanisms.
9. Prof. Burkhard Bechinger, Univ. Strasbourg, November 21st. Title : Biophysical investigations of the membrane interactions of antimicrobial peptides and their mimetics.
10. Dr. Sophie Lecomte, CNRS CBMN, Bordeaux, November 21st. Title : Vibrational spectroscopy to probe the structure of amyloid peptides and their interaction with membranes.
11. Dr. Birgit Habenstein, CNRS CBMN, Bordeaux, November 21st. Title : Assembly mechanisms of the plant protein remorin into membrane nanodomains
12. Dr. Antoine Loquet, CNRS CBMN, Bordeaux, November 21st. Title : Molecular Distinction of *Cryptococcus neoformans* Cell Wall and Capsular Polysaccharides by In Situ Magic-Angle Spinning NMR.
13. Prof. Michael Molinari, Univ. Bordeaux, November 21st. Title : Atomic Force Microscopy as a tool to investigate the morphology and structure of amyloid peptides and their interactions with model membranes.
14. Dr. Lucie Khemtouri, CNRS CBMN, Bordeaux, November 21st. Title : Understanding the first and second events of the islet amyloid polypeptide binding to lipid membranes.
15. Prof. Ayyalusamy Ramamoorthy, NHMFL Tallahassee, USA, November 21st. Title : Probing Membrane-Assisted Protein-Protein Interactions by NMR.
16. Prof. Birgit Strodel, Univ. Heinrich Heine, Germany, November 21st. Title : Decoding the Interaction of Amyloid Peptides with Lipid Membranes through Molecular Simulations.
17. Prof. Isabelle Marcotte, Univ. Québec, Montréal Canada, November 21st. Title : Probing (unwanted) interactions of antimicrobial peptides in situ with red blood cell membranes.
18. Prof. Victoria Birkedal, Aarhus University, Denmark, hosted by Mikayel Aznauryan, December 9th. Title : Conformational dynamics of G-rich DNA knots with single molecule FRET.
19. Prof. Michael Schlierf, Technical University of Dresden Germany, hosted by Mikayel Aznauryan, December 10th. Title : Molecular mechanisms of the bacterial integron revealed with single molecule biophysics.
20. Prof. Andrea Soranno, Washington University in St Louis USA, hosted by Mikayel Aznauryan, December 11th. Title : Single-molecule fluorescence measurements of disordered proteins and nucleic acid interactions.
21. Dr. Sigrid Milles, FMP Berlin, Germany, hosted by Mikayel Aznauryan, December 12th. Title : Intrinsically disordered regulators of endocytosis – an integrated NMR/single molecule fluorescence approach
22. Dr. Isabel Alves, CBMN Bordeaux, France, hosted by Mikayel Aznauryan, December 13th. Title : The modulation of the Dopamine D2 receptor activity by membrane poly-unsaturation.



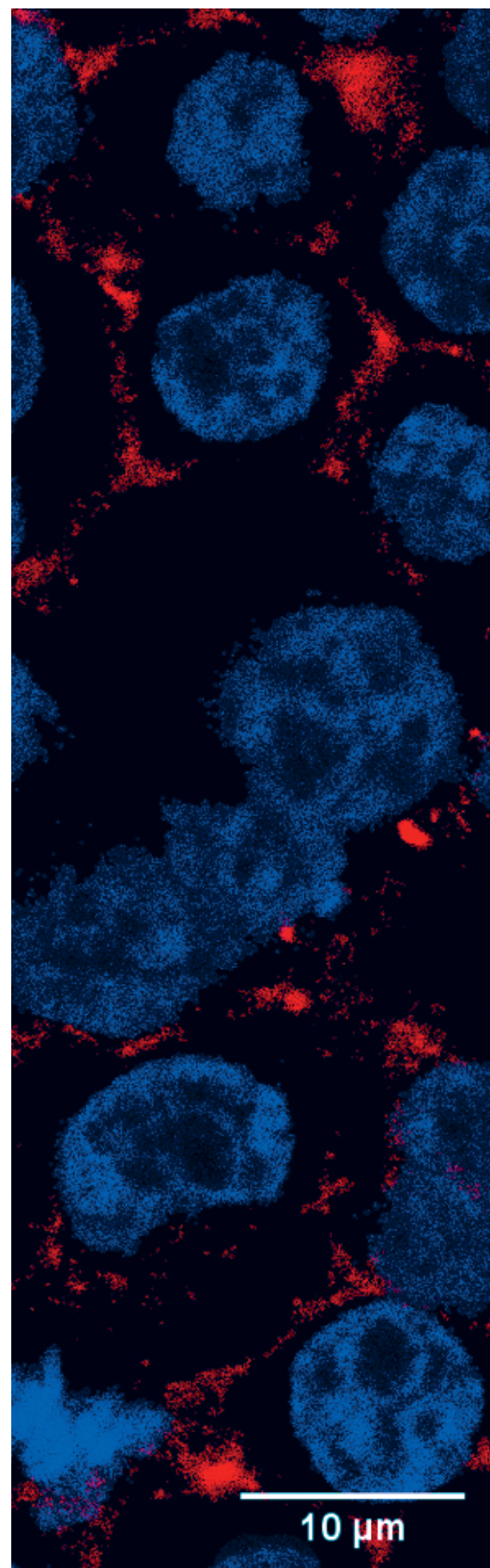
I E C B

Institut Européen de Chimie et Biologie

European Institute of Chemistry and Biology

Cover image: image credit: antiago Leiva.

Confocal immunofluorescence assay to detect the expression of the protein RNaseK-FLAG in HEK cells. Blue color is associated with the DNA of the cell nuclei. Red color is associated with the cell membranes of HEK cells. Green color is associated with the expression of the protein RNaseK-FLAG.



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