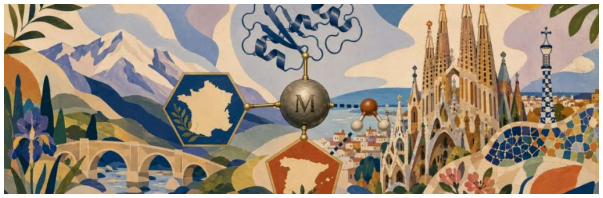

2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **María Concepción Gimeno**, Gold and Silver Chemistry Group, Instituto de Síntesis Química y Catálisis Homogénea (ISQCH), CSIC-Universidad de Zaragoza, Instituto de Síntesis Química y Catálisis Homogénea (ISQCH), CSIC-Universidad de Zaragoza

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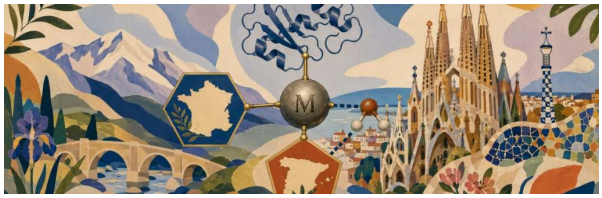
CODE: T1_1

Next-Generation Metal-Based Anticancer Agents: Organelle Targeting, Regulated Cell Death and Multitarget Strategies

Authors: Marta Redraro, María Gil-Moles, Elena Cerrada, M. Concepción Gimeno

Metal-based compounds remain highly attractive for anticancer therapy due to their unique structural, electronic and physicochemical properties. Our research focuses on the design, synthesis and biological evaluation of innovative metallodrugs based mainly on Group 11 metals, as well as ruthenium, iridium, rhenium and selected first-row transition metals, aiming to expand cancer treatment beyond the classical DNA-targeting paradigm. A central research line involves organelle-directed metal complexes that selectively accumulate in intracellular compartments such as the nucleus, mitochondria and endoplasmic reticulum. By targeting these organelles, the compounds disrupt key cellular processes, promoting oxidative stress, metabolic dysfunction, ER stress and regulated cell death pathways. Particular emphasis is placed on understanding apoptosis, ferroptosis, pyroptosis and immunogenic cell death (ICD), and their relevance in overcoming drug resistance and enhancing antitumour immune responses. We also develop metal complexes containing nucleoside and nucleobase analogues to improve cellular recognition, uptake and anticancer activity. In parallel, we investigate multifunctional mono- and bimetallic systems that combine complementary bioactive motifs within a single framework, enabling simultaneous modulation of multiple biological targets to enhance efficacy and combat resistance. Additionally, we study photoresponsive metal complexes activated by light, enabling precise spatiotemporal control of drug activity. These systems include agents for photodynamic therapy (PDT), photoactivated chemotherapy (PACT) and photocatalytic therapy (PCT), where light-triggered reactive oxygen species generation or activation of cytotoxic pathways improves tumour selectivity while reducing off-target toxicity.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Jose Ruiz, Metallodrugs discovery group, Universidad de Murcia, Universidad de Murcia

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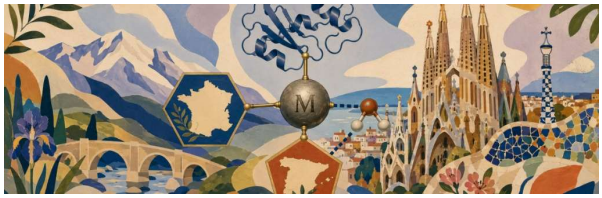
CODE: T1_2

Multifunctional Iridium complexes as novel photosensitizers for treating resistant tumors

Authors: Jose Ruiz, Pezhman Ashoo, Alba Hernández García, Eduardo Izquierdo García, Neus Santiago, Rebeca Mondaray Marín, Diego Abad Montero, Manel Bosch, Neus Isidro, Valentin V. Novikov, Josep Rocas, María Dolores Santana, Vicente Marchán

Cancer remains a major public health challenge, largely due to tumors that resist conventional treatments such as chemotherapy, radiotherapy, and immunotherapy. Photodynamic therapy (PDT) has emerged as a powerful alternative, leveraging light-activated photosensitizers to generate reactive oxygen species (ROS) that selectively eradicate tumor cells. Transition metal complexes (TMCs), especially cyclometalated iridium(III) complexes of the type $[Ir(C^N)_2(N^N)]^+$ (where C^N denotes a cyclometalated ligand and N^N a diimine ligand), stand out for their unique photophysical and photochemical properties, and have been widely explored as luminescent and photosensitizing agents. However, conventional Ir(III)-based photosensitizers suffer from low absorption at long wavelengths, limiting their efficacy against large, hypoxic tumors. This study reports the development of heteroleptic Ir(III) complexes activated within the phototherapeutic window, rationally tuned for lipophilicity, cytotoxicity, and multifunctionality through incorporation of coumarin-based COUBPY ligands. These complexes preferentially accumulate in the mitochondria of cancer cells, where light activation induces the photogeneration of a series of Type I ROS, including superoxide, hydroxyl radicals and hydrogen peroxide. Encapsulation in polymeric nanocarriers further improves delivery and therapeutic efficacy. Strikingly, these Ir(III)-COUBPY systems induce non-canonical cell death pathways, notably ferroptosis, as demonstrated by light-driven lipid peroxidation, glutathione oxidation and depletion, intracellular ATP photodepletion, and rescue by ferrostatin-1 (Fer-1). Photobiological studies in 3D tumor spheroids confirmed superior cellular uptake of the Ir nanoformulations, contributing to the overall improved phototoxic efficiency. This work establishes Ir(III)-COUBPY complexes as next-generation PDT agents capable of overcoming key limitations of current therapies.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Hélène Bertrand, METHROX Metals in Biology and redox homeostasis, Sorbonne University, Chimie Physique et Chimie du Vivant

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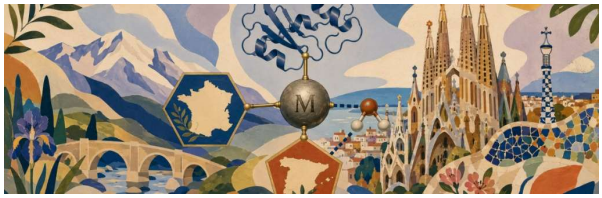
CODE: T1_3

Tackling systemic side effects of platinum based anticancer chemotherapies: a multiscale approach

Authors: Emmanuel Marcos, Alvaro Lopez-Sanchez, C. Policar, Christine Rampon, Hélène C. Bertrand

Platinum-based anticancer agents, such as oxaliplatin (Ox), are widely used in clinic (with a main indication in metastatic colorectal cancer for Ox),1 despite severe side effects. The Ox-induced peripheral neuropathy (OIPN) is a major hurdle limiting the clinical use of Ox and severely impacting patients' quality of life.2 It constitutes a major and critical societal issue. Its underlying molecular mechanisms are complex and no clinically effective treatment or prevention therapy exists.3,4 Among the explored strategies in the prevention of OIPN, modulators of oxidative stress are promising. In this context, we have explored small Mn complexes that mimic the superoxide dismutase (SOD), a metalloenzyme catalyzing the dismutation of the superoxide anion into H2O2 and O2.5 In association with Ox, derivatives of the MnSOD mimic Mn1 show encouraging results in the prevention of the appearance of neuropathy and neuromuscular disorders induced by Ox without affecting its antitumor activity in mice grafted with CT26 colon cancer cells.6 We develop Ox-based Pt(IV) complexes7 with redox modulators as axial ligands to achieve anticancer agents with reduced neurotoxicity and off-target effects. Our results in in vivo models, in mice8 and in zebrafish larvae, and our progresses along this multiscale approach against oxaliplatin-induced peripheral neuropathy using redox modulation will be presented.

1) Kee J. X. et al., Chem. Rev. 2025, 125, 21, 10248–10341, 10.1021/acs.chemrev.5c00041; 2) Saif M. W., Reardon J., Ther. Clin. Risk Manage., 2005, 1, 249-258; 3) Areti A. et al., Redox Biol., 2014, 2, 289-295; 4) Yang Y. et al., J. Exp. Clin. Cancer Res., 2021, 40, 331, 10.1186/s13046-021-02141-z; 5) Policar C. et al., Curr.Op.Chem.Biol., 2022, 67, 102109, 10.1016/j.cbpa.2021.102109; 6) Guillaumot M.-A. et al., Oncotarget, 2019, 10: 6418, 10.18632/oncotarget.27248; 7) Lopez-Sanchez A., Bertrand H. C., Inorg. Chem. Front, 2024, 10.1039/d3qi02602g; 8) Lopez-Sanchez A. et al. Adv.Healthc.Mater. 2025, 2501847, 10.1002/adhm.202501847



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Vicente Marchán, Light-activatable molecules for bioimaging and therapeutic applications, University of Barcelona, Department of Inorganic and Organic Chemistry

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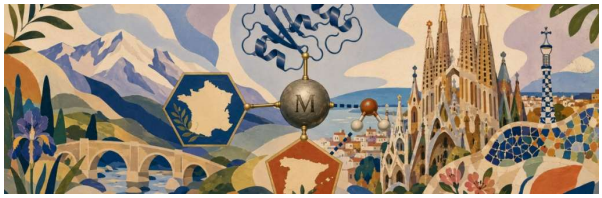
CODE: T1_4

NIR-activated peptide-targeted Ru-COUBPY photosensitizers for precision phototherapy of cancer

Authors: Elena de la Torre-Rubio, Diego Abad-Montero, Marc Suau, Alberto Cambra, Guillem Loren, Albert Gandioso, Vicente Marchán

Photodynamic therapy (PDT) is a minimally invasive anticancer modality that offers exceptional spatiotemporal control of therapeutic activity through light activation. Despite its clinical success, the effectiveness of PDT is limited in large or deep-seated tumors due to the weak absorption of most approved photosensitizers (PSs) in the deep-red and near-infrared (NIR) region, the restricted tissue penetration of activating visible light, and the strong dependence of photodynamic mechanisms on molecular oxygen, which compromises efficacy under hypoxic conditions. To address these challenges, we have developed a versatile platform of PSs based on Ru(II) polypyridyl complexes incorporating coumarin-derived COUBPY ligands, which display strong absorption within the phototherapeutic window and excellent phototoxicity both in vitro and in vivo. Within this platform, π-extended Ru-COUBPY complexes were engineered to enhance light harvesting and shift absorption into the NIR region through a vinylogation strategy combined with post-coordination assembly. These compounds exhibit potent light-induced cytotoxicity under deep-red and NIR irradiation, preserving activity under hypoxic conditions. Notably, the lead compound DAM15 produced strong tumor growth inhibition in mice bearing subcutaneous colorectal tumors upon irradiation with 780 nm NIR light, representing one of the few examples of Ru(II)-based PSs with robust antitumor efficacy under true one-photon NIR activation.

Recently, we have expanded this platform by conjugating Ru-COUBPY candidates to targeting peptides whose receptors are overexpressed in specific tumor types, enabling active tumor targeting through peptide–drug conjugates (PDCs). These Ru-based PDCs have been successfully validated both in vitro and in vivo, demonstrating enhanced tumor selectivity while maintaining excellent photoresponse, highlighting their potential as next-generation agents for precision phototherapy of cancer.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Carlos Sánchez Cano**, X-rays for Inorganic Biochemistry Laboratory, Donostia International Physics Center, Donostia International Physics Center

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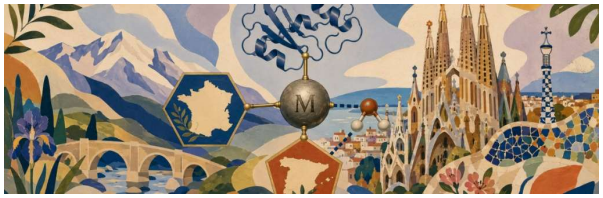
CODE: T1_5

Steps towards the in situ activation of anticancer drugs

Authors: Carlos Sanchez-Cano

Metal complexes are used as therapeutic drugs. Still, once inside the organism they suffer harsh environmental changes causing degradation and decrease in their therapeutic efficiency, but also unwanted toxicity upon release of non-natural components. A possible strategy to solve low biological stability of metal complexes is the use of ligands that coordinate to metals present in the organism with high affinity. They would form active drugs in situ and be available again after degradation. Here we show our efforts to form anticancer drugs inside the organism following this approach.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Raphael De Paiva**, , Universitat Autònoma de Barcelona, Department of Chemistry

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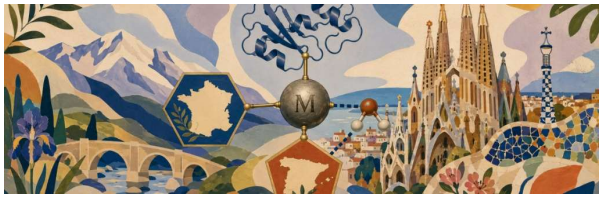
CODE: T1_6

What Lies Beyond TXNRD1? Cyclometallated Gold Compounds Reveal Sec Selectivity in Glutathione Peroxidases

Authors: Douglas H. NAKAHATA, Ioannis KANAVOS, Madeleine BARRETT, Ancély F. DOS SANTOS, Maria ZUBIRIA-ULACIA, German E. PIESLINGER, Ana B. S. TEIXEIRA, Clarissa R. R. ROCHA, Jonas EBERLE,5 Ryszard LOBINSKI, Jon M. MATXAIN,1,6 Matthew D. HALL, José Pedro FRIEDMANN ANGELI, Elias S.J. ARNÉR, Luisa RONGA, and Raphael E.F. DE PAIVA

The selenoenzyme GPX4 plays a central role in controlling ferroptosis, a regulated form of cell death driven by lipid peroxidation. Despite its biological importance, selective inhibitors of GPX4 are still scarce. In this work, we present a series of cyclometallated gold(III) compounds and explore their ability to promote C-Se coupling reactions under biocompatible conditions. Competitive reactions with selenium- and sulfur-containing substrates highlighted the preference for selenium, and this selectivity was further confirmed in selenopeptide models mimicking the GPx active site. The compounds were further investigated as inhibitors of the selenoproteins glutathione peroxidase GPX1 and GPX4. The six-membered metallacycles exhibited a potent inhibition of GPx1, while in vitro GPx4 inhibition was overall less pronounced. LC-MS studies identified selenocysteine (Sec51) as the primary arylation site on GPx1. Finally, we demonstrated that chemoselectivity could also be translated to an intracellular setting, using a A375 GPx4 WT cell line and an A375 GPx4 U46C mutant. Viability assays revealed a modest decrease in the IC50 for GPx4 WT cells compared to U46C mutants while a proliferation assay over six days showed a marked effect in GPx4 WT cells compared to the U46C mutant.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Òscar Palacios, UAB Bioinorganic group, Universitat Autònoma de Barcelona, Departament de Química

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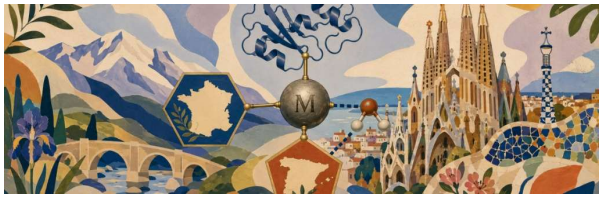
CODE: T1_7

Metal-Based Compounds and Smart Delivery Strategies as Potential Anticancer Agents

Authors: Òscar Palacios, Pau Bayón, Mercè Capdevila

Platinum-based chemotherapeutics remain a cornerstone in cancer therapy, yet their clinical efficacy is limited by systemic toxicity, poor selectivity, and drug resistance. To overcome these drawbacks, novel bioinorganic strategies involving alternative metals, light-triggered activation, and targeted delivery systems are being actively pursued. Here, we present three complementary strategies to develop targeted metal-based antineoplastic agents: Cu(II) Complexes: A series of novel Cu(II) N,N,O-chelating complexes were synthesized and characterized (NMR, ESI-MS, UV-Vis, EPR, voltammetry). Biomolecular interaction studies (DNA/proteins) and cell assays demonstrated efficient intracellular copper uptake, ROS generation, and potent cytotoxicity in cancer cell lines. Pt(II) Photocages & UCNPs: To achieve spatiotemporal control, photo-switchable Pt(II) complexes incorporating photosensitive ligands were developed. To overcome limited light penetration in deep tissues, upconversion nanoparticles (〖"LiYF" 〗_4:"Yb/Tm") coated with mPEG-ODA were integrated to convert NIR excitation into local UV/Vis light, triggering drug activation and enhancing cytotoxicity in melanoma cells upon NIR irradiation. Metallosomes: Liposomes incorporating Pt(II) and Cu(II) metallosurfactants were designed to improve solubility, biocompatibility, and cellular uptake while minimizing off-target toxicity. Combining targeted coordination chemistry, photo-responsiveness, and nanocarriers offers a highly promising platform for next-generation cancer therapies. Keywords: Bioinorganic Chemistry, Platinum, Copper, Photocages, UCNPs, Metallosomes, Cancer Therapy.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Ruben Pietro Vincenzo Di Fiore, , Universitat Autònoma de Barcelona, Department of Chemistry

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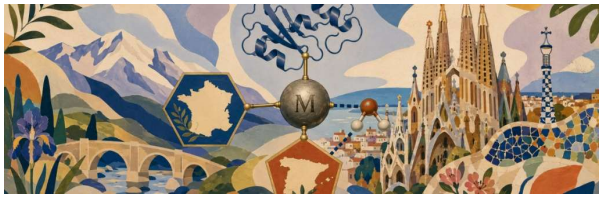
CODE: T1_E1

Covalent Inhibition of the Cancer-Associated Redox Enzymes ALDH1A1 and PRDX6 by Ligand-Tuned Cyclometallated Au(III) Complexes

Authors: Ruben Pietro Vincenzo Di Fiore, Raquel Pequerul Pavón, Martin Hugo Pereira, Jaume Farrés, Raphael Enoque Ferraz de Paiva*

Cellular defence against lipid peroxidation is distributed across structurally unrelated enzymes that converge on a single chemical feature: a catalytic cysteine held well below the normal thiol pKa. Aldehyde dehydrogenase 1A1 (ALDH1A1) employs Cys303 in NAD^+-dependent covalent catalysis to detoxify the reactive aldehydes released by peroxidised membrane lipids. Peroxiredoxin 6 (PRDX6), a 1-Cys peroxiredoxin regenerated through GSTP1-mediated glutathionylation rather than by thioredoxin, reduces hydroperoxides at Cys47 and carries a distinct phospholipase A2 site. Recent evidence reassigns much of its ferroptosis-suppressive function to selenium handling, with Cys47 forming selenium adducts that supply SEPHS2 for selenocysteine biosynthesis, such that PRDX6 loss depletes GPX4 and sensitises cells to ferroptosis. Both enzymes are redox-network nodes whose catalytic competence depends on a solvent-exposed, low-pKa thiolate, which represents a convergent vulnerability to soft, thiophilic metal centers. Gold compounds have gained attention as inhibitors of redox-active enzymes, though the field has focused overwhelmingly on linear, two-coordinate Au(I) complexes. C^N cyclometallated Au(III) complexes remain comparatively unexplored and offer a mechanistically distinct mode of action, with the chelating aryl-pyridine framework kinetically stabilizing the metal against biological reduction and enabling covalent modification of Cys and Sec residues. Here we evaluate a targeted library of cyclometallated C^N Au(III) complexes bearing systematically substituted phenylpyridine ligands, and we ask how electronic and steric tuning of the scaffold governs both the Au(III)/Au(I) reduction potential and the lability of the ancillary chlorides, and hence reactivity toward catalytic cysteines ofALDH1A1and PRDX6.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Célia Bonnet, Metal Complexes and MRI, Centre de Biophysique Moléculaire, CNRS Orléans

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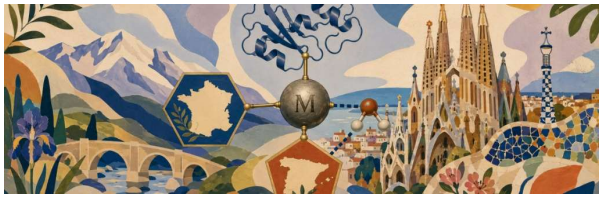
CODE: T2_1

Cation detection using responsive MRI contrast agents: from rational design to in vivo applications

Authors: Célia Bonnet

Magnetic Resonance Imaging (MRI) has been devoted for a long time to obtaining anatomical and functional images. Recently, emerging applications in molecular imaging seek information at the molecular level, looking at the biochemical or physiological abnormalities underlying the diseases. Unlike anatomic imaging, molecular imaging always requires an imaging probe that is selectively responsive to the parameter to detect. Gd3+-based contrast agents are particularly well-adapted for this purpose and most often the changes on the efficacy (relaxivity) are based on changes of the hydration number and/or rotational dynamics of the complexes; these two parameters being the easiest to be tailored by the chemist. Among the biomarkers of interest, Zinc and Copper are particularly relevant. They are essential transition metal ions and their concentrations are tightly regulated. Disturbances in their homeostasis are implicated various diseases such as neurodegenerative diseases (Alzheimer, Parkinson), diabetes, cancers (prostate, pancreas and breast), Wilson and Menkes' diseases. Therefore, monitoring these in vivo by non-invasive technique such as MRI is important in biomedical research to better understand their biological role, and to provide earlier diagnosis for specific pathologies. We will present two approaches : (1) the use of small molecular Gd3+-based responsive contrast agents to which a cation complexing unit has been added through a linker, and (2) bioinspired approaches, based on zinc-finger peptides and the ATCUN motif, which binds Cu2+ in HSA (Human Serum Albumin). We will show how structural modifications can affect the response of the contrast agent, and help to understand the behaviour of these systems. Challenges in terms of selectivity, affinity, and quantification will be discussed, as well as in vivo results.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Thibault Troadec**, CEMCA Laboratory Brest, CNRS - University of Brest, CNRS

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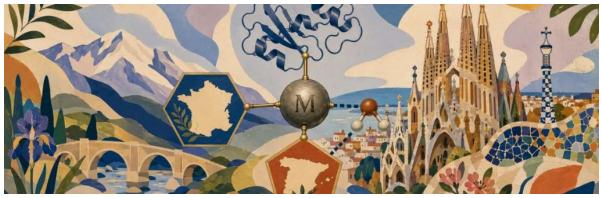
CODE: T2_2

Polyazamacrocyclic chelators : synthesis, coordination chemistry and applications in medical imaging, therapy and bioinspired catalysis

Authors: Thibault Troadec

Polyazamacrocyclic chelators (cyclen, cyclam, tacn, pyclen...) have been long known for their outstanding coordination properties, thanks to their rigidity and preorganization, towards a large range of cations (transition metals, lanthanides). In particular, as evidenced by the archetypal DOTA (tetraacetate cyclen), this class of ligands have found many applications in the medical imaging and nuclear medicine field for the chelation of cations of interest in MRI (Magnetic Resonance Imaging), PET (Positron Emission Tomography) or internal Radiotherapy for instance. Our group has strong expertise in organic and coordination chemistries, and develops synthetic tools for the selective functionalization of polyazamacrocyclic chelators, the optimization of their coordination properties, and their further grafting on biomolecules for medical applications. More recently, we have also focused on the use of such chelators as ligands for (bioinspired) catalysis and electrocatalysis.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Willem Kauffeld**, METHROX (Metals in biology and redox homeostasis), Laboratoire CPCV, ENS-PSL

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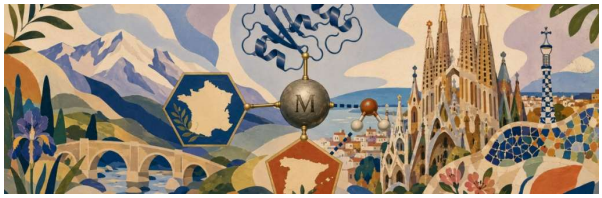
CODE: T2_E1

Re(CO)-based silica-nanoparticles as a multimodal platform for biological applications

Authors: Willem KAUFFELD, Bastien SIMONEAU, Suzanne FAUCHIER, Carole AIME, Clotilde POLICAR, Nicolas DELSUC

In the last decade, the emergence of nanomaterials as carriers for active biological compounds has shifted the paradigm on the development of novel treatments. Indeed, nanomaterials are a support for theranostics and increase the effectiveness of existing molecules. The combination of these materials with metal complexes, such as d^6 low-spin rhenium tricarbonyl compounds presenting unique luminescent, vibrational characteristics as well as X-ray fluorescence properties, creates promising candidates for multimodal imaging applications (including non-conventional imaging techniques)1-2 and for novel treatment in oncology. These complexes demonstrate robust photostability, in contrast to organic fluorophores, exhibit mid-infrared (mid-IR) absorption within the biological transparency window (1800-2200 cm-1) and X-ray specific fluorescence properties from the Re which is considered as an ultra-trace element in biological systems. This project aims to develop [$ReCl(CO)_3$(pyta)]-based silica nanoparticles (ReSiNPs) to achieve high-density multimodal probes for enhanced sensitivity in multiple imaging techniques including mid-IR imaging, two-photon imaging, fluorescence and synchrotron-based X-fluorescence microscopy. Moreover, the increased mid-IR response can be used to induce controlled cell death by rising their temperature above 47°C. Utilizing fed-batch co-polymerization methods, the synthesis is optimized to achieve high probe densities within nanoparticles while preserving the desired morphology. ReSiNPs are evaluated for cytotoxicity, mid-IR sensitivity, imaging efficacy across cellular models, and their penetration and diffusion in 3D spheroid cancer models are studied. Future work of functionalization of ReSiNPs with targeting peptides3-4 will enable organelle-specific delivery expanding their utility as versatile multimodal probes capable of thermometry as well as IR, XRF, and fluorescence imaging.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Sofiia Kulish, Metal Complexes and MRI, Centre de Biophysique Moléculaire (CBM), CNRS

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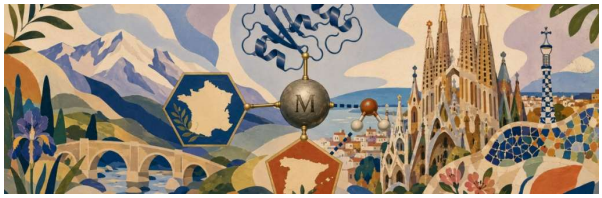
CODE: T2_E2

Development of contrast agents for selective Cu2+ detection via frequency-encoded ParaCEST/Parashift MRI

Authors: Sofiia Kulish, Jean-François Morfin, Harlei Martin, Elise Pidoux, Anne-Laure Barra, Jean-Marie Mouesca, Serge Gambarelli, Célia Bonnet

Copper is an essential microelement, and impairments in its homeostasis are suspected to be among the underlying causes of a number of neurodegenerative diseases, such as Alzheimer's or Parkinson's diseases, but also congenital syndromes like Wilson or Menkes diseases, as well as cancer. Magnetic resonance imaging (MRI) using responsive probes is a promising method for non-invasive and reliable copper level measurement. Currently, the majority of copper-responsive probes are based on Gadolinium(III) complexes. The main challenges to detect Cu(II) are related to the sensitivity of the probes, since Cu(II) is present in low concentrations, and their selectivity, particularly versus Zn(II), a cation that is more readily available. Here, we propose a new approach, relying on frequency-encoded MRI imaging and exploiting the paramagnetic properties of copper cations, aiming to obtain spectroscopic selectivity in the presence of other cations. To this aim, we have developed a series of Ytterbium(III) macrocyclic complexes, which possess exchangeable protons that can be detected by CEST (Chemical Exchange Saturation Transfer) experiments. These complexes also possess a binding site for divalent cation. We will present the influence of structural variations of the macrocyclic moiety, the chelating part and the linker on the CEST effect both in presence and absence of Cu(II) and other competing ions.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Patrick Gamez, nanoBIC, Universitat de Barcelona / ICREA, Department of Inorganic and Organic Chemistry, Inorganic Chemistry Section, nanoBIC Research Group

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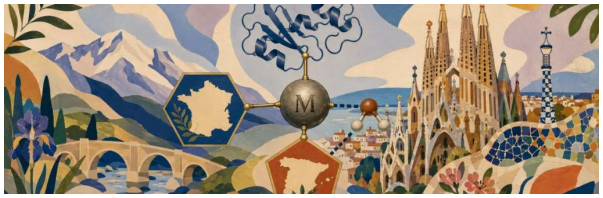
CODE: T3_1

Coordination Chemistry and Nanoscience for Medicine: Recent Advances from the nanoBIC Group

Authors: Ana B. Caballero, Patrick Gamez

The nanoBIC group (Nanoscience and Bio-Inorganic Chemistry, University of Barcelona) coordinated by Patrick Gamez combines coordination chemistry and nanoscience to develop new approaches for treating two major health challenges: cancer and amyloid diseases such as Alzheimer's disease. The group is organized into three closely connected teams: ChemDesign, Nano, and AmyloidTech (www.nanobic.eu). In cancer research, the group develops light-activated metal compounds, especially ruthenium (Ru(II)) complexes, that can release active molecules and produce reactive oxygen species when exposed to light. Some of the compounds have shown promising anticancer activity against pancreatic cancer cells (including in vivo). nanoBIC researchers also design ruthenium, osmium, rhodium, and iridium complexes containing pyrene-based ligands, which exhibit strong antiproliferative effects. In parallel, the Nano team is developing smart nanocarriers based on proteins, gold nanoparticles and superparamagnetic iron oxide nanoparticles (SPIONs) for targeted drug delivery and combined diagnostic and therapeutic applications. For amyloid diseases, researchers have created peptide-based metal chelators and functionalized nanoparticles, including Prussian blue nanoparticles, to regulate copper-induced amyloid-β aggregation and toxicity associated with Alzheimer's disease. In addition, organometallic "piano-stool" complexes have shown the ability to inhibit amyloid aggregation in both laboratory and animal studies. Together, these interdisciplinary efforts demonstrate nanoBIC's commitment to transforming advances in inorganic chemistry and nanoscience into innovative biomedical solutions.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Eva Royo, DISCOBAC Design, Interaction and Synthesis of Bioactive Compounds, Universidad de Alcala, AEBIN

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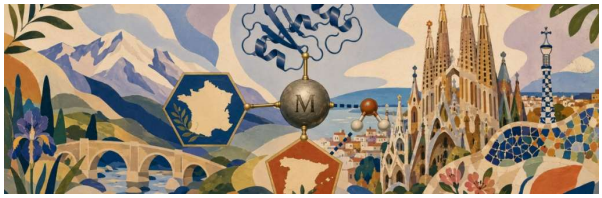
CODE: T3_2

Targeted metal-organic bioconjugates

Authors: Eva Royo

Discobac (Design, Interaction and Synthesis of Bioactive Compounds, IPs L. Gude, E. Royo), focuses on the search for novel multifunctional metal-based compounds to improve the understanding of molecular mechanisms relevant to effective therapies for cancer and bacterial infections. Most recent project focuses on expanding current knowledge of biomolecule interactions, mechanisms of action, and potential applications of multi-targeted metal-organic bioconjugates. Our compounds are rationally designed to: a) selectively recognize secondary G-quadruplex (G4) DNA structures; b) potentially target glycan moieties. The presence of sugar can enhance G4 binding, but they could also act as glycan-recognition domains. Also, carbohydrate-binding protein interactions are involved in many metastasis-related processes and are essential for microbial growth and bacterial virulence. The presentation will highlight the group's expertise and recent advances in the design, synthesis, biological evaluation, and mechanistic characterization of some of these multifunctional metal compounds.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Miguel A. Galindo Cuesta**, Metal-DNA Lab, Universidad de Granada, Universidad de Granada

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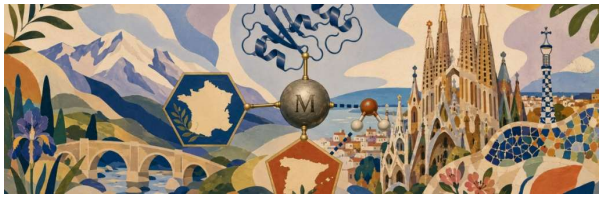
CODE: T3_3

DNA Architectures for the Controlled Positioning of Metal Ions

Authors: Miguel A. Galindo, María Rodríguez-Ruiz, Antonio Pérez-Romero

DNA provides a uniquely programmable molecular scaffold for the controlled organization of functional components, owing to its well-defined architecture, predictable base recognition, and structural versatility. In this communication, we present a general strategy to use both double-stranded and single-stranded DNA as platforms for the rational and site-selective incorporation of metal ions into nucleic acid architectures. In double-stranded systems, chemically modified nucleobases enable metal coordination to be introduced directly into defined positions of the duplex while preserving, to a large extent, the structural features of canonical Watson-Crick DNA. Such an approach allows metal ions to be placed within the interior of the helix, where coordination can modulate base pairing, enhance duplex stability, and introduce new chemical functionality without disrupting the overall DNA framework. In complementary single-stranded systems, nucleic acid sequences serve as programmable templates for the ordered assembly of metal complexes through a combination of coordination and non-covalent recognition, enabling controlled organization along the DNA backbone and the generation of hybrid supramolecular structures. Together, these approaches establish DNA as a versatile scaffold for positioning metal ions with high spatial control in both duplex and single-stranded environments. Beyond the specific systems described here, this concept opens the way to a broader family of metal-DNA architectures based on alternative nucleobase modifications and coordination motifs, including sulfur-containing nucleobases such as thioguanines, with potential applications in nanotechnology, supramolecular chemistry, and molecular electronics.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Ana Isabel González Garnica, Bionanometals, Universidad de Granada, Departamento de Química Inorgánica, Facultad de Ciencias, Universidad de Granada

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CODE: T3_4

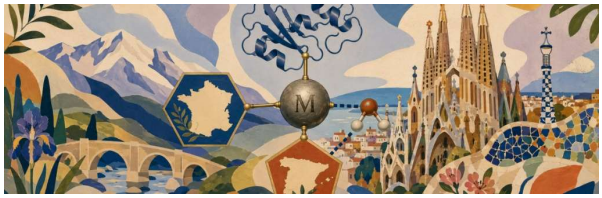
METALLIC BIONANOPARTICLES GROUP (BIONANOMET)

Authors: Ana González, Gloria B. Ramírez-Rodríguez, José M. Delgado-López, Natividad Gálvez, Jose M. Dominguez-Vera

Our research team is part of the Department of Inorganic Chemistry (University of Granada). The laboratory is a multidisciplinary one devoted to the Nano- and Bioinorganic Chemistry, and our research is centered on five different research areas:

1. Iron metabolism. Fe(III) hydrogels obtained from fruit waste for slow release of Fe(II) at duodenum.
2. Living materials with probiotics as antibacterials to combat antibiotic-resistant bacteria.
3. Sensors based on electrochromic molecules for biotechnological applications.
4. Protein-based materials and biopolymers self-organization for health applications and advanced materials design. 5. Biomineralization and Bio-Inspired Materials

Our team is formed by dynamical young scientists with a well-defined and promising area of research. We also have meaningful collaborations with other groups.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Miguel Vázquez López, Vázquez López Lab, CiQUS - Universidade de Santiago de Compostela, CiQUS - Universidade de Santiago de Compostela

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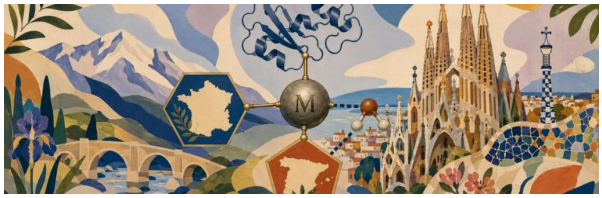
CODE: T3_5

Peptide helicates as versatile DNA three-way junctions binders

Authors: Miguez Vázquez López

DNA three-way junctions (3WJs) are non-canonical nucleic acid architectures that arise transiently during essential cellular processes, including DNA replication, recombination and repair. Their distinctive topology makes them attractive yet largely unexplored targets for selective molecular recognition. Here, we present our efforts toward the development of peptide-based metallosupramolecular helicates capable of selectively recognizing and modulating DNA 3WJs. Our approach relies on short peptide sequences engineered to undergo metal-directed self-assembly into well-defined dinuclear helicates. The resulting architectures combine the structural preorganization provided by metal coordination with the chemical versatility and biocompatibility of peptides. These systems display preferential binding to DNA 3WJs over duplex DNA and other nucleic acid structures, and their properties can be further modulated through peptide functionalization and metal-ion selection. Incorporation of specific metal-binding motifs provides additional functionality, including selective oxidative cleavage of 3WJs, while fluorescent derivatives enable the recognition of these structures to be investigated in living cells. More recently, we have developed strategies to regulate 3WJ recognition through external stimuli, including light, providing temporal control over the interaction between the helicates and their DNA targets. Together, these results establish peptide helicates as a versatile platform for the selective recognition, visualization and chemical manipulation of DNA three-way junctions, and illustrate the potential of metallosupramolecular chemistry for targeting dynamic non-canonical nucleic acid structures in biological environments.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Luisa Ronga**, IPREM, University of Pau, CNRS, IPREM, UPPA-CNRS

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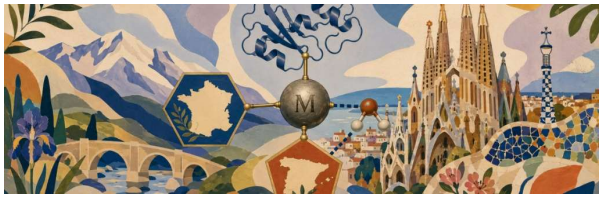
CODE: T4_1

Molecular insights into the role of selenoenzymes in the therapeutic and toxic activity of metals

Authors: Luisa Ronga

Mammalian selenoproteins containing selenocysteine (Sec), the sulfur-to-selenium substituted variant of cysteine (Cys), at their active site, play critical roles in redox homeostasis, antioxidant defense, and cellular signaling. Due to the high nucleophilicity and reactivity of selenocysteine, these proteins represent potential target of toxic trace metal (Hg) and metallodugs (Au, Pt)1. This presentation will elucidate the key role of Thioredoxin Reductases (TrxR) and Glutathione Peroxidases (Gpx), two main families of selenoenzymes, both in the toxicity of MeHg+, a potent neurotoxicant, and in the therapeutic activity of gold-based drugs. The reactivity of TrxR and Gpx with MeHg+ or gold(III) cyclometallated compounds was evaluated by an integrated experimental, theoretical and cellular approach. Our data offer a clear molecular explanation for the inhibition of the selenoenzymes TrxR1 and GPx1 by MeHg+, as well as for the associated toxic effects. This process involves MeHg+ preferentially reacting with SeCys, which is followed by the involvement of neighboring Cys residues2. We also provide mechanistic details and evidence supporting the use of selenopeptides for MeHg+ detoxification strategies3. Moreover, the intrinsic preferences of cyclometallated gold(III) compounds for Sec- over Cys-arylation was demostrated in peptide models4 and translated to functional inhibition of selenoenzymes5. This activity can mediate the cytotoxicity of these metallodrugs, highlighting their potential in anticancer therapy. References 1. Bernabeau de Maria M. et al. Coordination Chemistry Reviews (2023), 474, 214836. 2. Bernabeau de Maria M., Zangmo T. et al. Inorganic Chemistry Frontiers (2026), 13, 32. 3. Bernabeu De Maria M. et al. Inorganic Chemistry (2023), 62, 14980. 4. Nakahata D.H. et al. Chemistry a European J. (2024), 30, e202304050. 5. Kanavos I., Nakahata D et al. Free Radical Biololgy and Medicine (2026), 247, 139.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Maria Rosa Beccia, Human and Environmental Radiochemistry, Université Côte d'Azur, Institut de Chimie de Nice (ICN)

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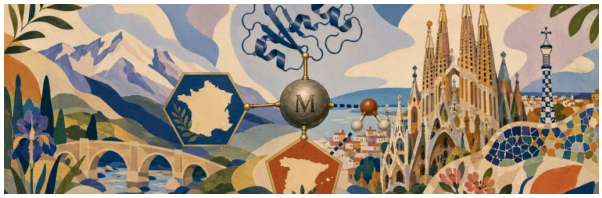
CODE: T4_2

Metallic radionuclides at the interface of environmental systems and living organisms

Authors: Maria Rosa Beccia

Metallic radionuclides are of particular environmental relevance due to their dual chemical and radiological toxicity, which makes their impact on ecosystems and organisms critical to understand and predict. Our research explores how chemical speciation governs the fate, transport, and biological impact of metallic radionuclides across environmental and living systems. Using a bioinorganic chemistry framework, we investigate metal-biomolecule interactions in marine organisms and human-relevant models, combining radiochemistry, spectroscopy, and molecular-level approaches to elucidate uptake pathways, transformation processes, and binding mechanisms. Particular attention is given to actinides and radionuclides related to the nuclear fuel cycle. By linking environmental chemistry with biological metal handling, our work aims to build a mechanistic understanding of radionuclide behavior from natural ecosystems to biological targets, opening new perspectives for interdisciplinary research at the interface of bioinorganic chemistry, environmental science, and health.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Jalila Simaan, BiosCiences, CNRS - Aix Marseille University, CNRS

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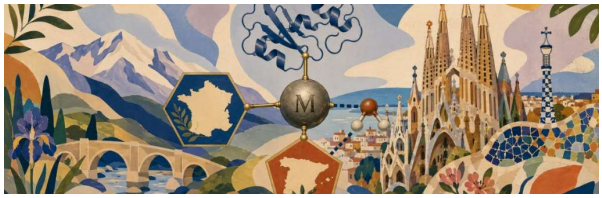
CODE: T4_3

LPMO-inspired functional copper complexes

Authors: R. Leblay, S. Sutradhar, N. Nova, B. Faure, M. Réglier, A. Jalila Simaan

Polysaccharides from biomass (e.g. cellulose or chitin) are increasingly considered as renewable feedstocks to produce chemicals, biomaterials and advanced biofuels. However, their recalcitrance to deconstruction is partly responsible for high conversion costs that currently limit their use for biobased chemistry. Lytic Polysaccharide Monooxygenases (LPMO) are copper enzymes that have attracted attention for their ability to promote polysaccharide cleavage using oxidative mechanisms with either O2 or H2O2 as oxygenated co-substrate. Our group combines studies on LPMO enzymes, and bioinspired model complexes. In particular, we have prepared synthetic and peptidic copper complexes which activities were studied on various substrates and we have obtained proof-of-concept that some bioinspired complexes are relevant for the oxidative depolymerization of insoluble polysaccharides. This presentation will highlight our latest findings, focusing on strategies to rationalize activities across different LPMO models and on mechanistic insights.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Feryanne Taroudjit, Human, Environment and Radiochemistry, Université Côte d'Azur, Institut de Chimie de Nice (ICN)

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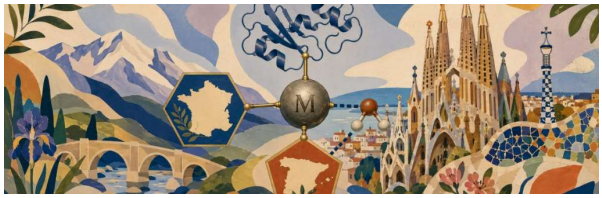
CODE: T4_E1

Speciation and transfert mechanisms of actinides in marine phytoplankton

Authors: F. Taroudjit, M-R. Beccia, C. Den Auwer, P. Crançon and M. Virot

Seawater constitutes both the final sink and the largest reservoir for contaminated waters, making it a key environmental compartment for monitoring radioactive metal contamination. Among these elements, actinides of natural or anthropogenic origin represent major radiotoxic pollutants whose bioaccumulation and transfer within marine ecosystems raise significant environmental concerns. [1] Phytoplankton is a particularly relevant model for studying the entry of these elements into the food chain. Located at the base of the marine trophic web, it can accumulate these contaminants and may therefore influence their transfer to higher trophic levels. Among the actinides present in the environment, plutonium-239 is of particular interest: it serves as a tracer of fallout from nuclear weapons testing and is among the most radiotoxic elements. [1] Understanding its behavior in the marine environment is therefore essential. However, experimental studies remain limited due to its high radiotoxicity and the constraint



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Pablo Macías Benítez, UMR 6521 CEMCA, Université de Bretagne Occidentale, UMR 6521 CEMCA

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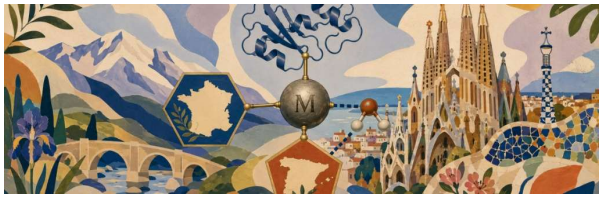
CODE: T4_E2

Cyclam-Based Nickel and Copper Complexes for the Electrocatalytic Activation of Small Molecules

Authors: Pablo Macías-Benítez, Thibault Troadec, Frédéric Gloaguen, Hélène Bernard, Raphaël Tripier, Nicolas Le Poul

The main focus of our research group is the development of novel azamacrocycles with applications in two main areas: medicinal chemistry and sustainable catalysis. The design of polyazacycloalkane based chelators with improved performance indeed requires a full understanding of the structural properties of the complexes at the molecular level. Thus, the introduction of pendant coordinating arms provokes dramatic changes in the structures and properties of the complexes. Moreover, the kinetic and thermodynamic stability of the corresponding metal complexes makes these ligands attractive molecular platforms for a wide range of catalytic applications simply by changing the metal center. These properties enable the activation of small molecules, such as carbon dioxide or water, and their catalytic transformation, contributing to pollution mitigation and the pursuit of environmental sustainability. The continuous increase in atmospheric carbon dioxide levels has become a major global concern in recent years because of the environmental and societal consequences associated with the greenhouse effect. As a result, there is growing interest in cost-effective and environmentally friendly catalytic systems capable of efficiently and selectively reducing CO2 into valuable industrial feedstocks such as CO, HCOOH, and CH3OH. Parallelly, water oxidation represents one of the main alternatives for the industrial production of hydrogen as a renewable and clean energy source. In this context, the search for suitable water oxidation catalysts (WOCs) that are efficient, robust and cost-effective is essential for future industrial applications and implementation. To summarize, we aim to develop new macrocyclic nickel and copper catalysts for the electrochemical conversion of small molecules. Herein, we report the synthetic methodologies used to access cyclam-based ligands, their nickel(II) and copper(II) complexes, and their catalytic activity.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Luca Salassa**, IPL - Salassa group, Donostia International Physics Center, Inorganic Photochemistry Labo

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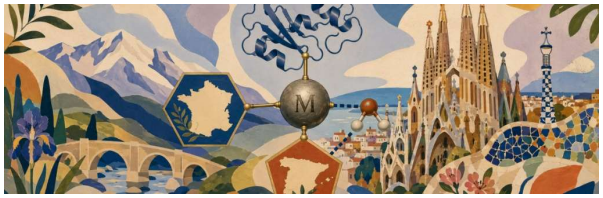
CODE: T5_1

Host-Directed Metal-Based Antivirals

Authors: Luca Salassa

Nucleoside analogues used to treat Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are frequently limited by the emergence of drug resistance and treatment-related adverse effects. As an alternative or adjunct strategy, host-directed antivirals represent a promising avenue for HSV management. In this setting, the immunomodulator imiquimod (IMQ) and related derivatives have been proposed for recurrent HSV infections, with clinical reports describing favorable outcomes in patients who failed or were refractory to standard antiviral therapy. Building on this premise, we synthesized a library of new imiquimod-based ruthenium complexes with strong antiviral activity. Among these, RM11, MAF09, and ACC71 (Figure) showed greater potency against HSV-1 and HSV-2 than IMQ in both primary and transformed cell lines, while also displaying reduced cytotoxicity relative to the parent organic drug. These metallodrug candidates were further assessed against HSV-1 in patient-derived human ectocervical organoids (PDOs), which reproduce key features of native epithelium, including tissue organization, cellular heterogeneity, and immune responsiveness. In PDO infection models, the Ru-IMQ derivatives markedly decreased viral load without disrupting epithelial integrity, outperforming IMQ. In this contribution, I will discuss these findings in detail and examine the biological mechanism(s) of action based on the evidence obtained to date.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Christelle Hureau, ALAMBIC, Laboratoire de Chimie de Coordination, CNRS

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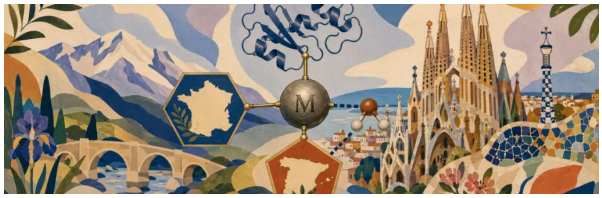
CODE: T5_2

ATCUN peptides to shuttle copper intracellularly

Authors: C. Hureau and coworkers.

Alzheimer's disease (AD) is characterized by extracellular deposits of aggregated amyloid-β (Aβ) peptides, which are a hallmark of the disease. Copper (Cu) and zinc (Zn) ions can bind to Aβs, modulating the peptide's propensity to self-assemble, and abnormal amounts of these ions are detected in the senile plaques.[1] This may eventually lead to overall metal dyshomeostasis, resulting in an intracellular Cu level that is too low.[2] Additionally, Cu bound to Aβs can contribute to oxidative stress by catalyzing the formation of reactive oxygen species (ROS).[3] Cu is therefore a prime therapeutic target, and over the last ten years we have focused on identifying the key parameters that drug candidates should meet.[4] In that context, ATCUN (amino-terminal Cu and Ni) sequences which are widely encountered in biology,[5] demonstrate promising potential as Cu-targeting molecules in the context of chelation therapy.[6, 7] Following an exhaustive study of the coordination-induced properties of a series of ATCUN peptides,[8] several sequences were tested in neuronal cell models and on organotypic hippocampal slices to determine their ability to restore cell survival and improve Cu homeostasis.[9]

[1] Coord. Chem. Rev. 2018, 375, 38.
[2] Transl. Neurodegen. 2025, 14, 42.
[3] Redox Biol. 2018, 14, 450 – ChemSocRev, 2023, 52, 6595.
[4] Inorg. Chem. 2019, 58, 13509.
[5] Chem. Eur. J., 2018, 24, 8029.
[6] Chem. Eur. J., 2021, 27, 1777
[7] Chem. Eur. J., 2016, 22, 7268
[8] Molecules, 2022, 27, 7903 –Biomolecules, 2022, 12, 1327.
[9] Chem. Sci., 2022, 13, 11829 - Inorg. Chem. Front., 2026, 13, 5701.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Santiago Gómez Ruiz**, COMET-NANO, Universidad Rey Juan Carlos, Instituto de Investigación de Tecnologías para la Sostenibilidad

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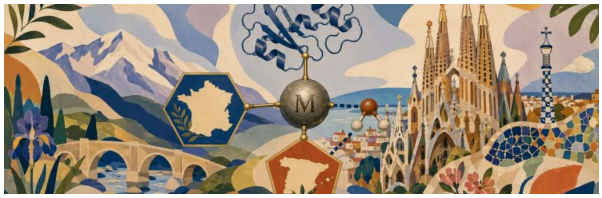
CODE: T5_3

From Metal Complexes to Intelligent Nanomedicines: Bioinorganic Platforms for Cancer, Infection and Neurodegeneration

Authors: Lucía Jiménez-Gómez, Nagore Grasa-Gude, Laura Kanon, Javier La O Bonet, Julia D. Magdaleno, Blanca Parra-Cadenas, Miguel Díaz-Sánchez, María Jesús Morán, Inés García-Benito, Josefa Ortiz-Bustos, Diana Díaz-García, Sanjiv Prashar, Isabel del Hierro, Santiago Gómez-Ruiz

COMET-NANO at Universidad Rey Juan Carlos (URJC) develops therapeutic bioinorganic systems at the interface of coordination chemistry, nanomaterials and biomedicine. We exploit redox-active and biologically relevant metal centres (including Cu, Zn, Ru, Ti, Sn and some others) integrating them into mesoporous silica nanoparticles, carbon dots, graphene-derived materials, nano-oxides and biocompatible hydrogels. These platforms enable controlled metal release, modulation of reactive oxygen species (ROS), redox homeostasis, cellular uptake and biological targeting. Our objective is to turn metallodrugs and hybrid nanoplatforms into more selective tools against cancer, bacterial infection and neurodegeneration. In this context, we are working in several projects in the field, for example, ROS-FUN engineers multifunctional systems that use controlled ROS generation for antitumour and antibacterial action. Brain-MIND focus on brain diseases including neurodegeneration (especially amyotrophic lateral sclerosis) thro



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Myriam Seemann**, Chimie Biologique et Applications Thérapeutiques (CBAT), Université de Strasbourg/Institut de Chimie de Strasbourg (UMR CNRS 7177)/ CBAT, CNRS

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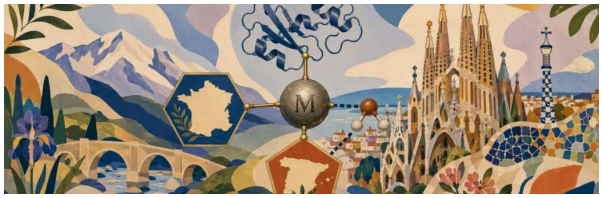
CODE: T5_4

From metalloenzyme mechanisms to novel antibacterial strategies

Authors: Myriam Seemann

Keywords: Metalloenzymes, MEP pathway, Fatty acid biosynthesis, enzyme inhibitors, antibacterial agents Link: https://institut-chimie.unistra.fr/equipes-de-recherche/chimie-biologique-et-applications-therapeutiques-cbat/ Antibiotics save millions of lives each year. However, antibiotic resistance is one of the biggest threats to public health as some bacterial infections impossible to treat with the existing therapeutic repertoire are emerging everywhere. The research activities of the Biological Chemistry and Therapeutic Applications team focus on the study of enzymes with medical potential, particularly for antibacterial applications. Targets that could be explored to combat antibacterial resistance are unstable and difficult-to-isolate essential bacterial enzymes, including certain metalloenzymes, that were not previously discovered due to lack of knowledge and technology to characterise them. Such enzymes are investigated in our team in order to combat bacteria for which current treatments are scarce or ineffective. IspG is an oxygen-sensitive enzyme essential for the survival of numerous bacteria. It is involved in the methylerythritol phosphate pathway that provide Isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP), key compounds for the synthesis of terpenoids. Importantly, this enzyme does not exist in humans and is therefore a valuable target for the development of new specific antibacterial drugs. It contains a [4Fe-4S] centre and catalyses an unprecedented reaction that is a source of inspiration for new antibacterial strategies. In this talk, the discovery, characterisation and breakthroughs made in the elucidation of the catalytic mechanism of some metalloenzymes as well as the exploitation of the first results to discover highly efficient inhibitors will be presented. C. Witjaksono, V. Herrscher, H. Jobelius, N. Noël, F. Massicot, J.-L. Vasse J.-B. Behr, M. Seemann, Chem. Eur. J. 2025, 31, e02471



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Nicolas Delsuc, MTHROX, CPL lab, ENS

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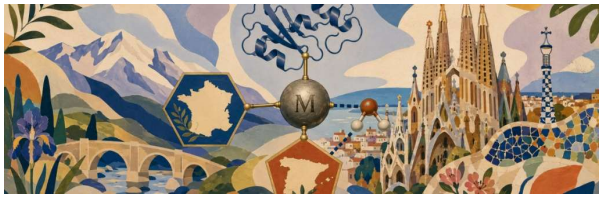
CODE: T5_5

Antioxidant metalloenzyme mímics delivery to mitigate symptoms in inflammatory bowel diseases

Authors: Nicolas Delsuc, Emilie Mathieu, Amandine Vincent, Koudedja Coulibaly, Gabrielle Schanne, Yaqine Ben Hadj Hammouda, Florian Chain, Sylvie Demignot, Philippe Seksik, Clotilde Policar

Inflammatory bowel diseases (IBD), which include Crohn's disease and ulcerative colitis represent a global health issue as a prevalence of 1% is expected in the western world by the end of this decade. These diseases are associated with a high oxidative stress that induces inflammatory pathways and severely damages the gut tissues. IBD patients suffer from antioxidant defenses weakening, though, for instance, an impaired activity of superoxide dismutases (SOD) — that catalyze the dismutation of superoxide — or other endogenous antioxidant enzymes including catalase (that catalyzes the dismutation of hydrogen peroxide). Metal complexes mimicking such antioxidant enzymes are thus interesting drug candidates to reduce the symptoms of IBD patients. Toward this goal we have designed, synthesized, characterized and studied in vitro SOD and catalase mimics, in which ligands are either functionalized polyamines or peptides. A main challenge for oral administration of these catalytic drugs in vivo is to protect this metal complexes from the stomachal acidic pH responsible for decoordination and thus drug inactivation. To achieve this, we have investigated innovative delivery systems based on food grade lactic acid bacteria. These delivery systems were further improved to be able to, at the same time, produce and deliver the antioxidants at the inflammation site.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Albert Gandioso, Light-activatable molecules for bioimaging and therapeutic applications - Marchan Group, Universitat de Barcelona, Universitat de Barcelona

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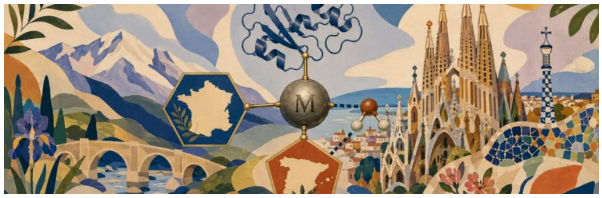
CODE: T5_E1

Tuning Photodynamic Therapy via Metal-Ligand Engineering: From Ruthenium(II)- to Osmium(II)-COUBPY Complexes

Authors: Samaya Ali-Hassan,Vicente Marchán and Albert Gandioso*

Hypoxia and the limited penetration of light through biological tissues remain major obstacles to the effective application of photodynamic therapy (PDT) against deep-seated tumors. To address these challenges, we developed a series of ruthenium(II)- and osmium(II)-based photosensitizers incorporating coumarin-derived COUBPY ligands and systematically investigated the influence of metal-center substitution and ancillary ligand engineering on their photophysical, photochemical, and biological properties. Replacement of Ru(II) by Os(II) induced a pronounced bathochromic shift, introducing low-energy absorption bands that enabled efficient photoactivation within the deep-red and near-infrared (NIR) regions. In parallel, incorporation of the π-extended ancillary ligand 4,7-diphenyl-1,10-phenanthroline (DIP) enhanced visible-light absorptivity, cellular uptake, and Type I reactive oxygen species (ROS) generation. These effects translated into improved photocytotoxic performance, particularly at longer wavelengths and under hypoxic conditions. Among the series, Os-2 displayed the most balanced photobiological profile, combining broad visible-to-NIR photoactivation, sustained photocytotoxicity at wavelengths up to 740 nm, and remarkable oxygen tolerance. Whereas the bpy-containing complexes Ru-1 and Os-1 exhibited pronounced sensitivity to hypoxia (HI = 19.7 and 10.4, respectively), the corresponding DIP-containing derivatives showed substantially improved oxygen independence, with Os-2 displaying a hypoxia index of only 1.4. These findings demonstrate that metal-center substitution and ancillary ligand engineering act synergistically to modulate PDT performance and provide valuable design principles for the development of next-generation metal-based photosensitizers for the treatment of hypoxic solid tumors.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Emmanuel Marcos, , École Normale Supérieure - PSL, Laboratoire Chimie Physique et Chimie du Vivant CPCV, UMR-8228, Département de chimie, École Normale Supérieure, PSL Université, Sorbonne Université, CNRS

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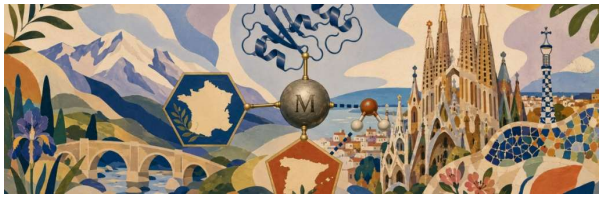
CODE: T5_E2

Investigating oxaliplatin-induced peripheral neuropathy and evaluating novel Pt(IV) prodrugs designed to reduce neurotoxicity using the zebrafish model.

Authors: Emmanuel Marcos, Kadda Medjoubi, Hélène C. Bertrand, Christine Rampon

Platinum-based chemotherapeutics remain essential in the treatment of colorectal cancer (CRC)1, but their use is frequently limited by dose-limiting toxicities. Among them, oxaliplatin-induced peripheral neuropathy (OIPN) is one of the most debilitating side effects, occurring as both acute and chronic forms and significantly impairing patients' quality of life. Despite extensive research into its underlying mechanisms, no preventive treatment is currently approved2, and clinical management remains largely symptomatic.3 Oxaliplatin accumulates in the components of the peripheral nervous system, particularly in the dorsal root ganglia (DRG), where it induces oxidative stress and other cellular alterations. Developing relevant and accessible in vivo models is therefore essential for investigating OIPN mechanisms and evaluating new therapeutic strategies. In this work, we establish the zebrafish as a reliable in vivo model to study oxaliplatin-induced neurotoxicity and to screen candidate compounds. Using behavioral assays, including escape response4 and automated locomotion tests, we characterized the functional consequences of oxaliplatin exposure and investigated their relationship with neuronal alterations through confocal microscopy. The zebrafish model further enabled mechanistic investigations of oxaliplatin-induced toxicity. Using this model, we evaluated novel platinum(IV) prodrugs5 bearing antioxidant moieties6 designed to reduce the neurotoxicity associated with oxaliplatin treatment. Behavioral and mechanistic studies were performed to assess their effects and potential protective properties. In addition, X-ray fluorescence spectromicroscopy performed at the NANOSCOPIUM beamline at the SOLEIL synchrotron7 provided insights into platinum distribution and accumulation in neuronal tissues. Overall, our results support the use of zebrafish as an in vivo model for investigating OIPN and for the preclinical evaluation of novel platinum-based strategies with reduced neurotoxicity.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Diana Díaz García, COMET-NANO, Universidad Rey Juan Carlos, Universidad Rey Juan Carlos

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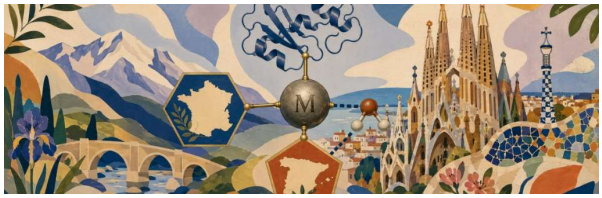
CODE: T5_E3

Metal-Based Multifunctional Nanocarriers for Brain-Targeted Therapy in Amyotrophic Lateral Sclerosis

Authors: Diana Díaz García, Javier Álvarez Conde, Julia Díaz Magdaleno, Miguel Díaz Sánchez, Inés García Benito, Nagore Grasa Gude, Isabel del Hierro, Laura Kanon, Josefa Ortiz Bustos, Blanca Parra Cadenas, Sanjiv Prashar, Santiago Gómez Ruiz

Amyotrophic lateral sclerosis (ALS) is a severe neurodegenerative disorder characterized by progressive motor neuron degeneration, with limited therapeutic options currently available. A major challenge in ALS treatment is the development of efficient strategies to deliver therapeutic agents into the central nervous system while overcoming the restrictive properties of the blood–brain barrier (BBB). Bioinorganic approaches combining metal-based therapeutics and advanced nanomaterials offer promising solutions for next-generation treatments. Herein, we describe the development of multifunctional nanoplatforms based on mesoporous silica nanoparticles (MSNs), carbon quantum dots (CQDs), and hybrid nanostructures for brain-targeted delivery in ALS. These systems are designed to incorporate therapeutic metal complexes and biologically active molecules through covalent attachment or adsorption, enabling controlled functionality and improved selectivity. Metal compounds capable of modulating biologically relevant G-quadruplex (G4) DNA/RNA structures are explored as innovative therapeutic components due to their potential involvement in pathways related to neurodegeneration and protein aggregation. The nanocarriers are further modified with biomolecules and biocompatible coatings to enhance stability, BBB permeability, and neuronal interactions. Their physicochemical characterization includes TEM, XRD, BET, thermogravimetric analysis, spectroscopy, and chromatographic techniques, complemented by biological evaluation through stability studies, drug release assays, and permeability tests using artificial BBB models. This interdisciplinary strategy integrates coordination chemistry, nanomaterials science, and biomedical applications to generate multifunctional platforms for targeted delivery. Metal-functionalized nanocarriers represent a promising approach for overcoming current limitations in ALS therapy and developing advanced treatments for neurodegenerative diseases.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Isabelle Vieira de Almeida, Chimie Biologique et Applications Thérapeutiques (CBAT), Université de Strasbourg/Institut de Chimie de Strasbourg (UMR CNRS 7177)/CBAT, Université de Strasbourg

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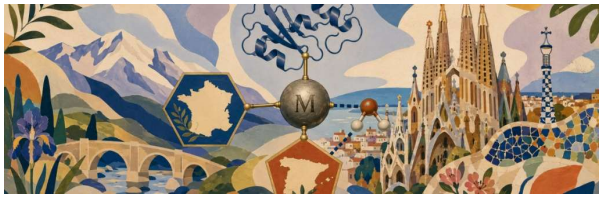
CODE: T5_E4

Towards new inhibitors of the IspH metalloenzyme, a target for the development of new antibiotics

Authors: Isabelle Vieira De Almeida, Philippe Chaignon, Myriam Seemann

IspH, an oxygen-sensitive [4Fe-4S] enzyme, catalyses the last step of the methylerythritol phosphate (MEP) pathway involved in the biosynthesis of isoprenoids. IspH converts (E)-4-hydroxyl-3-methylbut-2-enyl diphosphate (HMBPP) into a mixture of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP).[1] This enzyme is essential for the survival of most bacteria, including several WHO priority pathogens, while being absent in humans.[2] Therefore, IspH emerged as a promising therapeutic target for the development of novel antibiotics with new modes of action. Two HMBPP analogues were synthesized by the team by replacing the alcohol group by thiol or amino groups affording respectively TMBPP (Ki = 24 nM) and AMBPP (Ki = 54 nM), the two most potent IspH inhibitors.[3] The crystal structure of IspH in complex with the TMBPP or AMBPP lead us to design and synthesized new inhibitors with potentially enhanced binding properties. The molecules possess a thiol and an amine function, predicted to bind respectively, to the apical iron of the [4Fe-4S]2+ center and to glutamate 126 present in the active site of E. coli IspH. The multi-step synthesis of the candidate molecules as well as their preliminary biological evaluations on the oxygen sensitive E. coli IspH metalloenzyme will be presented. References : [1] H. Jobelius, G. I. Bianchino, F. Borel, P. Chaignon, M. Seemann, Molecules 2022, 27, 708. [2] Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial reisstance (World Health Organization Bacterial Priority Pathogens List, 2024). [3] K. Janthawornpong, S. Krasutsky, P. Chaignon, M. Rohmer, C. D. Poulter, M. Seemann, J. Am. Chem. Soc. 2013, 135, 1816. Keywords : IspH, metalloenzyme, inhibitors, multi-step synthesis, enzymatic assays. Website : https://institut-chimie.unistra.fr/equipes-de-recherche/chimie-biologique-et-applications-therapeutiques-cbat/



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Melanie Rossotti, ALAMBIC, Laboratoire de Chimie de Coordination, CNRS

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CODE: T5_E5

Oxidative stress tolerance studies on LPMO.

Authors: M. Rossottia*, E. Falconea, A. J. Simaanb, C. Hureaua

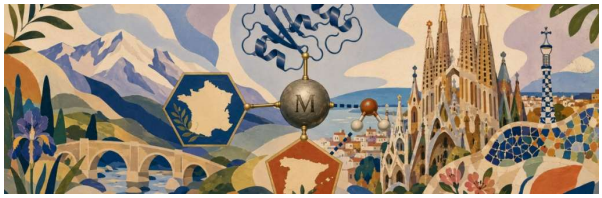
Lytic Polysaccharide Monooxygenases (LPMO) are bacterial and fungal enzymes able to cleave recalcitrant polysaccharides, such as cellulose and chitin, through oxidative mechanisms.1,2 Today, LPMOs have become essential tools in biorefineries for biomass valorisation, including biofuels and biochemicals production.

The active site of LPMOs features a copper ion in a unique “His-brace” coordination, comprising three nitrogen atoms from two highly conserved His residues. This solvent-expose site is located in a protein flat surface which is ideal for polysaccharide interactions.3,4 Additionally, the 2nd coordination sphere also cover an important for LPMO activity, either by tuning the Cu(II) electronic properties or by enabling the substrate binding 5. Their catalytic mechanism, in which the glycosidic bond is hydroxylated via short-lived Cu-oxygen intermediates, as well as the nature of the co-substrate (O2 or H2O2), are still under debate.6

Despite their industrial use, LPMOs feature a major limitation: oxidative auto-inactivation. This off-pathway process, which is faster when H2O2 is used as cofactor6, is driven by highly reactive oxygen species (ROS) generated during the LPMO reaction. Fully understanding this inactivation mechanism is crucial to improve LPMO longevity and enhance biomass valorisation yield.

In this context, we aim to evaluate the impact of 1st and 2nd coordination sphere mutations on the oxidative self-inactivation of LPMOs, using the well characterized chitin-active LPMO from Serratia marcescens, SmAA10, as a model.

To monitor hydroxyl radical generation, we set up an assay based on 3-coumarin carboxylic acid (3-CCA) which traps hydroxyl radicals to form fluorescent hydroxy-CCA. Experiments were conducted both in absence and presence of chitin to evaluate LPMO robustness against oxidative stress during catalysis. Additionally, this assay provides qualitative insights on relative chitin affinity and relative catalytic activity.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Caroline Marchi-Delapierre, LCBM, UGA_CNRS_CEA, LCBM

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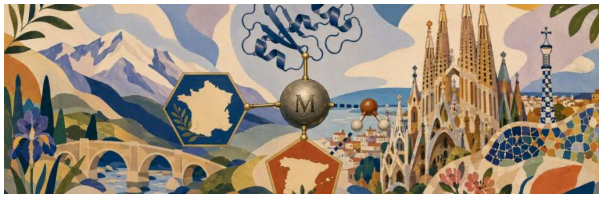
CODE: T6_1

Artificial metalloenzymes: from molecular design to catalysis

Authors: Caroline Marchi-Delapierre, Christine Cavazza, Stéphane Ménage

Can we create enzymes capable of carrying out reactions that do not exist in nature? Artificial metalloenzymes explore this idea by combining proteins and metal complexes to design novel catalysts. At the interface of chemistry, biology, and artificial intelligence, this field offers exciting opportunities in chemical synthesis, energy, and biocatalysis. This presentation will introduce the key concepts of the field before highlighting some recent results from our research team.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Thierry Tron**, BiosCiences, CNRIS Aix Marseille Univ, CNRS

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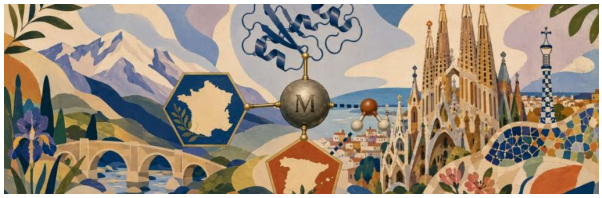
CODE: T6_2

Multi-Copper Oxidases in Hybrid Catalysis

Authors: I. Modenez, C. Righetti, P. Chakraborty, Y. Mekmouche, A. Ciaccafava, J. Simaan, T. Tron

Hybrid catalysis exploit synergies that can appear between different catalysts, e.g. chemo- and bio-catalysts. Combining catalysts makes it possible both to carry out several stages of transformations and to offer new opportunities in terms of selectivity, efficiency and type of transformations. Understanding the contribution of each partner when associating a synthetic catalyst, an enzyme and a material is necessary to benefit from the best synergy. Laccases are biocatalysts with great robustness, high oxidation power and substrate versatility. Their unique set of copper centres - a near-surface located mononuclear type 1 and an embedded tri-nuclear cluster (TNC) made of a type 2 and a binuclear type 3 - couple the oxidation of substrates (organic or metal ions) to dioxygen reduction. We shape new catalysts based in particular on oriented functionalization of a laccase surface with different “plug-ins”. From our initial demonstrations on bi-molecular systems - a sensitizer/laccase system coupling the light driven four-electron reduction of dioxygen to water3 to the photo-oxidation of styrene or a Pd(II)/ laccase system competent for the aerobic oxidation of alcohol in mild conditions - we will present architectures based on the oriented grafting of the enzyme surface. Our most recent results on improved hybrid photocatalysts and functionalized laccase will be discussed.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Christophe Léger, Reaction dynamics of multicenter redox enzymes, electrochemical kinetics, Laboratoire de Bioénergétique et Ingénierie des Protéines, CNRS/AMU

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CODE: T6_3

Electrochemical studies of enzymes involved in the production of solar fuels

Authors: Christophe Léger

We study structure-function relationships in enzymes that catalyse reactions that are important in the bacterial bioenergetic metabolism and in our economy: the production of H2 and the reduction of CO2, by interpreting direct electrochemistry measurements [1] and extensively using protein engineering. That homologous metalloenzymes, in which the same inorganic active site is surrounded by a variable protein matrix, may have very distinct catalytic properties demonstrates the importance of residues that are remote from the active site [2]. We shall summarise recent findings on the diverse molecular mechanisms by which the protein matrix may define the oxygen tolerance, catalytic directionality and catalytic reversibility of hydrogenases, which catalyse H+/H2 conversion. These mechanisms involve residues in the second coordination sphere of the active site metal ion [3], more distant residues affecting protein flexibility [4], residues lining the gas channel and even accessory clusters [5].

[1] V. Fourmond et al. « Direct electrochemistry of enzymes that use and produce solar fuels: hydrogenase, formate dehydrogenase, CO-dehydrogenase and nitrogenase » Chem. Rev. (2026) doi: 10.1021/acs.chemrev.5c01110

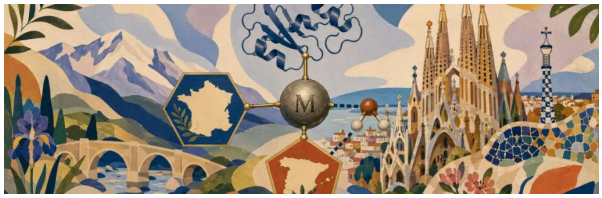
[2] A. Fasano, et al, « Outer-sphere effects on the O2 sensitivity, catalytic bias and catalytic reversibility of hydrogenases », Chem. Sc. (2024). doi: 10.1039/D4SC00691G

[3] A. Fasano et al. « Kinetic modeling of the reversible or irreversible electrochemical responses of FeFe-hydrogenases », JACS (2024) doi: 10.1021/jacs.3c10693

[4] Filmon et al. « Turning the FeFe hydrogenase from Clostridium beijerinckii into an efficient H2 oxidation catalyst using a redox-active matrix », PNAS (2025) doi: 10.1073/pnas.2514698122

[5] A. Fasano et al. « A chimeric NiFe hydrogenase heterodimer to assess the role of the electron transfer chain in tuning the enzyme's catalytic bias and oxygen tolerance », JACS (2023) doi: 10.1021/jacs.3c06895

See https://bip.cnrs.fr/groups/bip06/



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Jean-Didier Maréchal, InSiliChem, Universitat Autònoma de Barcelona, Department of Chemistry & Institute of Biomedicine and Biotechnology

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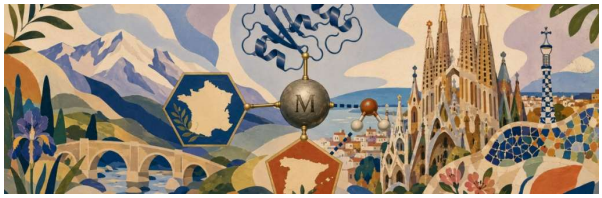
CODE: T6_4

Computational multiscale approaches in bioinorganic chemistry: recognition and catalysis

Authors: Maria Fernanda Morales Peralta, Mercè Alemany Chevarria, Yassir Boulaamane, Weifeng Gao, Raul Peña, Giuseppe Sciotino, Jean-Didier Maréchal

Over the last 20 years, our group has become an expert in developing and using computational strategies to study bioinorganic systems, with a particular focus on designing artificial metalloenzymes and developing metal-based drugs. Our work primarily relies on molecular modeling, including QM, QM/MM, docking, and molecular dynamics; however, in recent years, because modeling metal-protein interactions is challenging, we have developed statistics-based methods, including AI-driven software. In the talk, I will briefly overview the key components of our strategies and then give examples of recent successful applications and ongoing projects.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: **Laura Opdam**, Reaction dynamics of multicenter redox enzymes, electrochemical kinetics, Laboratoire de Bioénergétique et Ingénierie des Protéines, CNRS/AMU

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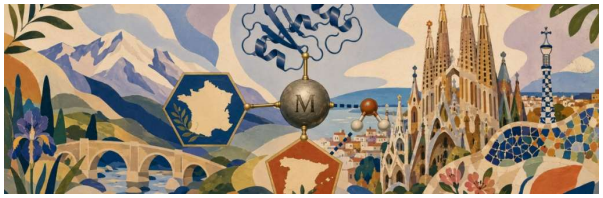
CODE: T6_E1

The impact of substrate channel mutations on the O2-sensitivity of CODH

Authors: Opdam L, Gebhardt P, Fasano A, Benvenuti B, Meneghello M, Chargelègue J, Guendon C, Bailly A, Léger C, Dobbek H, Fourmond V

To address these challenges, we have developed a versatile platform of PSs based on Ru(II) polypyridyl complexes incorporating coumarin-derived COUBPY ligands, which display strong absorption within the phototherapeutic window and excellent phototoxicity both in vitro and in vivo. Within this platform, π-extended Ru-COUBPY complexes were engineered to enhance light harvesting and shift absorption into the NIR region through a vinylogation strategy combined with post-coordination assembly. These compounds exhibit potent light-induced cytotoxicity under deep-red and NIR irradiation, preserving activity under hypoxic conditions. Notably, the lead compound DAM15 produced strong tumor growth inhibition in mice bearing subcutaneous colorectal tumors upon irradiation with 780 nm NIR light, representing one of the few examples of Ru(II)-based PSs with robust antitumor efficacy under true one-photon NIR activation.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: Stann Van Baaren, BioCE, UGA/CNRS/CEA, LCBM

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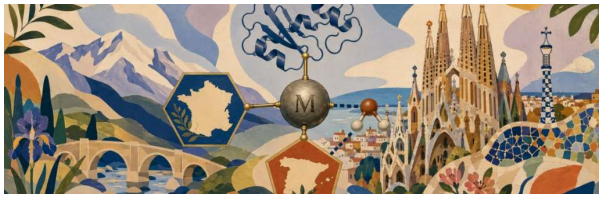
CODE: T6_E2

Design of artificial metalloenzymes for enantioselective sulfoxidation

Authors: S. Van Baaren, C. Cavazza, C. Marchi Delapierre, S. Ménage, Y. Moreau

Natural enzymes are exceptional catalysts with high selectivity and efficiency under mild conditions. However, their industrial application is limited to natural transformations. On the other hand, artificial metalloenzymes allow for a larger range of reactivities but often lack enantioselectivity. This work presents an innovative approach to improving artificial metalloenzymes stereoselectivity by using artificial intelligence for their design. Our research focuses on developing artificial metalloenzymes capable of enantioselective oxidation of thioethers to sulfoxides, a transformation critical in pharmaceutical synthesis, particularly for proton pump inhibitors like Esomeprazole. The strategy we use consist of designing from scratch artificial proteins around an ideal active site containing an inorganic complex. This presentation will explain the construction of the design pipeline and its different inputs. Starting from the theoretical active site construction and optimization with QM tools, it will address the AI assisted design of the backbone containing this theoretical active site using a RFdiffusion, the generation of corresponding sequences, their computational testing and filtering that lead to the selection of 24 candidates. Finally, we will present data on the high-throughput expression of these proteins from synthetic genes and discuss preliminary findings regarding their catalytic performance.



2nd Bilateral French-Spanish Meeting in Bioinorganic Chemistry

Presenting: María Fernanda Peralta Morales, InSiliChen,
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CODE: T6_E3

Modelling Au-Based Asymmetric Catalysis in Artificial Metalloenzymes: Mechanistic Insights into Gold-Catalyzed Alkenynone Cyclization

Authors: M. Fernanda Peralta-Morales, Agustí Lledós, Giuseppe Sciortino, Jean-Didier Maréchal

Artificial metalloenzymes (ArMs) are engineered biocatalysts that incorporate non-native metal ions or synthetic cofactors into protein scaffolds, combining enzymatic selectivity with the catalytic versatility of transition metals. Among emerging scaffolds, the Lactococcal multidrug resistance regulator (LmrR) has gained prominence as a versatile scaffold for ArM design. Recently, targeted mutations (such as V15pSHF) enabled site-specific Au(I) coordination, yielding a gold–LmrR system capable of catalyzing complex organic transformations. In this study, the reaction mechanism for the synthesis of highly substituted furans was evaluated using a single-cysteine LmrR variant. While the initial LmrR_V15C scaffold provided a water-compatible catalytic environment, achieving high enantioselectivity remained challenging due to unrestricted solvent accessibility. Through directed evolution, an optimized variant (LmrR_CVITQ) was developed, establishing a tailored asymmetric microenvironment that markedly enhances enantioselectivity. To gain deeper mechanistic insights, a multiscale computational protocol was implemented to elucidate the structural differences between LmrR_V15C and LmrR_CVITQ. Our analysis reveals that the most active evolved mutant has altered properties regarding the LmrR_V15C in terms of substrate orientation preference, distinct hydrophobic profiles, active-site cavity reconfiguration, and the formation of specific water channels that redirect solvent molecules to preferentially favor one face of the substrate.This localized control over solvation dynamics may explain the mechanistic origin of the observed enantiopreference.