ARCANE SCIENTIFIC DAY

May 5, 2025

Maison de la Création et de l'Innovation (MaCI)
339, avenue centrale
38400 Saint-Martin d'Hères

9h00	**Welcome**
9h05	**KN1 – Bertrand Reuillard** *Electrocatalytic CO_2 conversion with a molecularly engineered Co cathode*
9h30	**OC1 – Quentin Laurent** *New aptamer conjugates mimicking monoclonal antibody activity*
9h45	**OC2 – Majd Khalife** *Peptide decorated amyloid fibrils and hydrogels as biomimetic olfactory cilia for sensitivity improvement of electronic nose*
10h00	**KN 2 – Galina Dubacheva** *Design of bio-targeted model systems using tunable surface chemistry and physico-chemical characterization tools*
10h25	**Presentation of the Pôle Universitaire d'Innovation**
10h30	**Coffee break**
10h50	**Isabelle Lémonon** *Gender equality: The Matilda effect*
11h50	**Poster Session**
12h30	**Lunch**
14h00	**PL – Gilles Guichard** *Chemical tools to structurally mimic protein domains and disrupt protein interactions*
14h45	**OC3 – Preslav Smits** *Synthesis, isolation and photophysics of the first stable carbene radical anion*
15h00	**OC4 – Léa Latour** *Exploring protein glycosylation via chemical tagging of methionines*
15h15	**OC5 – Guilherme Tripodi** *Electrochemical CO_2 Reduction by [FeFe]-Hydrogenase Models*
15h30	**Coffee break**
16h00	**KN3 – Xavier Le Guevel** *Development of nanomolecular theranostic agents and instruments for NIR/SWIR detection and therapy*
16h25	**OC6 – Digyash Kumar Bhattacharyya** *Light Driven Release: Exploring Photo-ejection in Ruthenium Complexes*
16h40	**OC7 – Mathis Gunther** *Strong C-H bond activation induced by immobilized copper-based molecular electrocatalyst*
16h55	**Conclusions & prizes**
17h10	**Beer session**

PLENARY LECTURE

Chemical Tools to Structurally Mimic Protein Domains and Disrupt Protein Interactions

Gilles Guichard*

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Protein structural elements at protein interfaces offer valuable starting points for designing effective modulators of protein interactions (PPIs) and to investigate biological functions. Research efforts have explored this concept by developing strategies to mimic protein surfaces while preserving the side-chain geometry of binding epitopes. Efficient recognition of protein surfaces can be achieved by stabilizing the structures of isolated peptides in their bioactive conformation through various conformational constraints. These include macrocyclisation (stapling), non-canonical amino acid replacements, non-natural backbones and foldamer strategies. Such chemical modifications not only stabilize the active conformation but also enhance properties such as stability in biological fluids, and cellular permeability. Our work has focused on foldamer-based approaches to stabilize secondary structures and reduce the peptide character of peptide inhibitors targeting PPIs. Structural analyses have validated the design of high-affinity foldamer-based binders for diverse protein targets that will be discussed in this presentation. Beyond the foldamer toolbox, we have developed novel macrocyclization strategies to efficiently introduce staples into peptides and foldamers, further stabilizing secondary structures. This strategy has been successfully applied to several proteins of interest. More recently, we have also explored molecular proximity to design peptide-based covalent protein inhibitors. This approach is exemplified by the structure-guided design of covalent inhibitors targeting the bacterial sliding clamp.

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KEYNOTE LECTURES

Electrocatalytic CO_2 conversion with a molecularly engineered Co cathode

Matthieu Haake,[1] Dmitry Aldakov,[2] Julien Pérard,[1] Giulia Veronesi,[1] Antonio Aguilar Tapia,[3] Bertrand Reuillard[1] and Vincent Artero[1]

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The electrochemical conversion of CO_2 into useful chemicals/fuels using decarbonised electricity is a promising strategy to close the carbon cycle.[1] To achieve this, the development of molecular catalysts and their integration at electrode surfaces have attracted a lot of attention.[2] These molecular cathodes combine the advantages of heterogeneous catalysts and the easy tuning of molecular catalysts which usually also showcase better selectivity at lower overpotentials.

Over the past 10 years, cobalt complexes with tetraaza macrocyclic based ligands (CoN_4H) have been extensively studied and have shown promising performance for CO_2 reduction to CO.[3] Our group recently reported the derivatization of this structure with a pyrene unit for its non-covalent integration at multi wall carbon nanotube (MWCNT)-based porous electrode. Electrocatalytic study of the molecular cathode in aqueous conditions in saturated carbonate electrolyte showed a very selective production of CO with faradaic efficiency for CO above 90% at very modest overpotential (–1 V vs SHE, pH 7.4) matching literatures' best performing molecular cathodes.[4] *Post operando* characterisation shows retention of the molecular structure of the Co complex with however clear changes of its redox activity, suggesting modification of the direct environment of the Co centre upon operation.

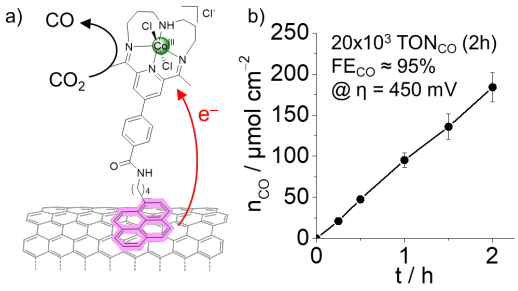

Figure: a) Scheme of the CoN_4H-Pyr|MWCNT modified cathode b) Production of CO overtime at –1 V vs SHE in CO2-saturated 0.5M $KHCO_3$, pH7.4

This work was supported by the INSTN at CEA, the Labex ARCANE and EUR at UGA and the ANR (reg. No. CBH-EUR-GS, ANR-17-EURE-0003, and ANR-21-CE50-0004)

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Design of bio-targeted model systems using tunable surface chemistry and physico-chemical characterization tools

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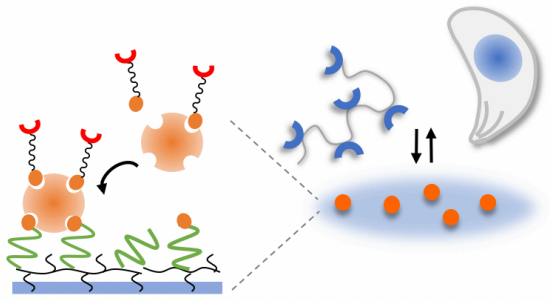
Developing biomimetic surfaces is pivotal across a wide range of disciplines, from fundamental research aimed at understanding the structure and function of biological systems to practical applications in biomedical engineering and the design of advanced materials. Our group combines surface chemistry approaches, including self-assembled monolayers, supported lipid bilayers, polymer coatings, and click chemistry, with a suite of complementary physicochemical characterization techniques such as ellipsometry, electrochemistry, QCM-D, and fluorescence microscopy. This integrated approach enables us to design model systems for studying supramolecular assembly at interfaces, with precise control over the nature, density, and lateral mobility of surface ligands. Two examples of model surfaces will be presented: the first based on streptavidin/biotin chemistry [1] and the second employing host/guest interactions [2]. The use of these platforms to study superselective multivalent interactions will then be demonstrated [3]. Our recent study, which involves the use of model streptavidin/biotin interfaces for in situ monitoring and understanding biological processes such as parasite/host adhesion, will also be discussed [4].



Acknowledgements
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Development of nanomolecular theranostic agents and instruments for NIR/SWIR detection & therapy

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In vivo optical imaging is nowadays widely used for cancer diagnosis and image-guided therapy with various devices that have already entered into the clinic. However, current fluorescence imaging is worth improving in spatial and temporal resolution in deep tissues. New approaches rely on collecting optical signal in the first (NIR-I, 700-900 nm) and the second near-infrared window (NIR-II, 900-1700 nm) called shortwave infrared (SWIR). The use of this wavelength range, especially in the SWIR range with appropriate probes, should considerably reduce light scattering and absorption by blood and tissues in vivo improving sensitivity and spatial resolution in depth. In addition, bringing therapeutic modalities to such contrast agents will offer high potential in the field of personalized nanomedicine. Among the large library of organic and inorganic nanosystems, noble metal nanoclusters—primarily gold—are ultra-small particles with sizes below 3 nm. These nanoobjects exhibit molecular-like properties, which include tunable photoluminescence ranging from UV to NIR/SWIR and photo/radiotoxicity[1]. These properties can be harnessed for diagnostic and therapeutic purposes and are closely linked to the nanoclusters' size and the precise design of ligand engineering[2]. Moreover, recent studies have reported new optical properties, such as striking enhancements in absorbance and photoluminescence, when these metal nanoclusters are organized in one, two, or three dimensions[3, 4]. We design biocompatible gold nanoclusters at the single level using short organic molecules or peptides and at assembly levels using polymers, and biomolecules (DNA, protein) as matrices. After characterizing their morphology, physico-chemical and optical properties[3-5], we investigate their potential as SWIR emitters. Recent advances in instrumentation design and image processing techniques—such as Monte Carlo restoration and deep learning—enable high-resolution, real-time visualization at sub-centimeter depths, supporting applications like vascular disorder diagnosis and tumor angiogenesis studies in small animal models. [1, 5-9]. In the context of cancer therapy, we also use these nanomolecular species to enhance their targeting of cancer cells and to induce cell death through combined strategies, including siRNA delivery and light/X-ray stimulation. We study the interactions of these nanosystems in 2D and 3D cancer cell cultures (including lung, breast, and glioblastoma). Additionally, we assess their biodistribution and therapeutic efficacy in tumor-bearing mice[10-13].

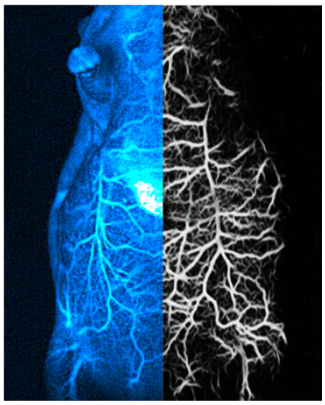

Figure 1: SWIR image of a mouse (left side) with post-treatment by deep learning (right) showing thevascularization in depth

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TOPIC OF THE YEAR

L'effet Matilda : quand la maternité d'une découverte scientifique échappe aux femmes

par Isabelle Lémonon-Waxin (Centre François Viète, Cermes3)

En 2024, en France, les femmes représentent environ 20 % des effectifs dans la recherche en mathématiques, physique ou informatique et environ 40 % en chimie. Pourtant, moins de 5 % de l'ensemble des lauréats du prix Nobel en physique ou en chimie, de la médaille Fields en mathématiques ou du prix Turing en informatique sont des femmes. Comment comprendre cette sous-représentation dans les sciences ? Les facteurs sont multiples et l'objectif de cette conférence est de s'attarder sur l'un d'entre eux : l'effet Matilda. Depuis les années 1990, de nombreux travaux de recherche en histoire des sciences ont permis de lever le voile sur ce mécanisme de minoration, d'invisibilisation et de dépossession de femmes qui ont été à l'origine de découvertes scientifiques. Pour mieux comprendre et déjouer l'invisibilisation des femmes dans les sciences, cette conférence propose un parcours historique qui suit les trajectoires de quelques *figures de l'ombre*.

Eléments biographiques :

Isabelle Lémonon-Waxin est professeure agrégée de sciences physiques et docteure en histoire des sciences de l'Ecole des hautes études en sciences sociales (EHESS). Elle est chercheuse associée au Centre François Viète de Nantes Université et au Cermes3 (CNRS/EHESS/Inserm/Université Paris Cité). Ses travaux de recherche visent à retrouver et analyser les pratiques scientifiques des femmes dans la France des Lumières et de la première moitié du XIX^{e} siècle.

ORAL COMMUNICATIONS

New Aptamer Conjugates Mimicking Monoclonal Antibody Activity

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Monoclonal antibodies (mAbs) are widely used for diagnostic, research, and therapeutic applications, but several limitations related to their nature limit their extensive clinical use. Developing new molecular systems that integrate the advantages of mAbs while circumventing their limitations is then highly advantageous. In this context, nucleic acid aptamers are a special class of biomolecules that are currently investigated for clinical use.

Herein, we are interested by the development of DNA aptamers that target the CD20 (Cluster of Differentiation 20) antigen. Among the key target of mAbs, the recognition of CD20 antigen, exclusively expressed on B cells, is used for the treatment of several pathologies including lymphoma and autoimmune diseases, by using for example the mAb Rituximab. Recently, the interaction between CD20 and Rituximab was shown to involve a dimerization of CD20 at the cell surface, which we have been able to recapitulate on a synthetic biomimetic surface.[1]

Based on this result, we selected DNA aptamers from a dimeric version of CD20 by using CE-SELEX (Capillary electrophoresis-systematic evolution of ligands by exponential enrichment)[2] and characterized them *in vitro* by various physico-chemical methods. The best aptamer candidates will then be integrated into multivalent systems by grafting several aptamers onto a molecular scaffold in combination with a fluorophore. The proof of concept in hands, this project may lead to the design of a therapeutic candidate.

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Peptide decorated amyloid fibrils and hydrogels as biomimetic olfactory cilia for sensitivity improvement of electronic nose.

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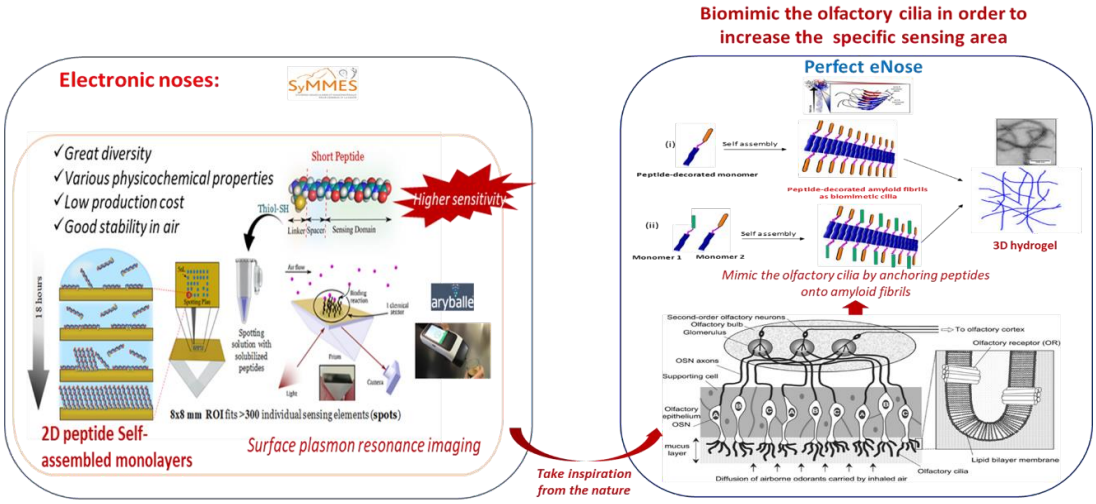
In recent years, the demand for rapid and accurate detection of volatile organic compounds (VOCs) has grown across various fields. Since VOCs play a crucial role in environmental monitoring, food safety, and the cosmetics industry. The traditional analytical methods are accurate and reliable but require expensive equipment and skilled personnel and are often timeconsuming and laborious. Electronic noses (eNs), are considered promising alternatives to traditional analytical methods. However, so far, their performance is still far behind that of the human nose, especially in terms of sensitivity.

Inspired by the biological olfactory system, we aim to develop an original bioinspired approach to mimic the olfactory cilia in human nose to greatly increase the specific sensing surface using amyloid fibrils. First, amyloid fibrils will be used alone as a sensing material to evaluate their intrinsic ability to capture and discriminate between different types of VOCs. Their structure and morphology were characterized using circular dichroism (CD) and transmission electron microscopy (TEM). These fibrils provide a highly stable and tunable scaffold, which makes them particularly well-suited for anchoring peptides. Accordingly, in the next step, peptides specifically designed for VOC detection, previously shown to be highly effective [1,2],will be anchored onto the fibrils. The performance of the fibrils alone will then be compared to that of the fibrils anchored with peptides.

The interaction of these biomimetic structures and VOCs is currently being studied through surface plasmon resonance imaging (SPRi). The results, though still preliminary, are quite promising and require further validation.



Acknowledgment: This work was supported by ARCANE and conducted within SYMMES and LCBM.

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Synthesis, isolation and photophysics of the first stable carbene radical anion

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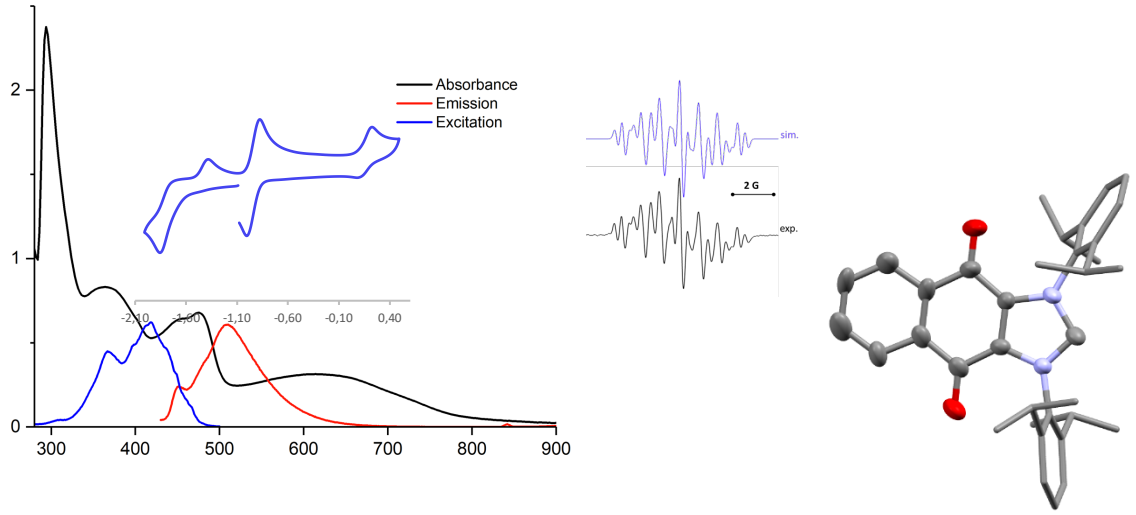
N-Heterocyclic carbenes (NHCs) have had incredible success as ligands in organometallic chemistry for various applications, such as catalysts, photosensitizers and others, due to their tunable electronic and steric properties. By comparison, their properties as free molecules have received much less attention. Advances in air-free synthesis techniques in the last 50 years have allowed for the isolation of a variety of stable carbenes[1], however the majority of studies involving NHCs still remain focused on their reactivity and use as covalent organocatalysts. In contrast, their redox properties are significantly less studied, even though short-lived oxidized or reduced carbene species have been proposed to act as intermediates in several well-known organic reactions[2]. It is precisely the difficulty in isolating the short-lived oxidized or reduced species that has hindered further study. In our group, through rational NHC design, (spectro)electrochemistry, and the aforementioned air-free synthesis techniques, we have achieved the isolation and crystallization of the first stable carbene radical anion. This radical species was subsequently found to be a strong absorber and emitter of light. Even more, while conventional radical species have excited states in the order of about 200 ps maximum[3], our radical carbene has an unprecedented long excited state lifetime of 21 ns. The application of these properties towards activation of aryl halides by photoinduced electron transfer, as well as the possible isolation of other carbene radical anions and their derivative adducts, are all underway.



Acknowledgements
P. Smits acknowledges Labex Arcane for funding.

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EXPLORING PROTEIN GLYCOSYLATION *VIA* CHEMICAL TAGGING OF METHIONINES

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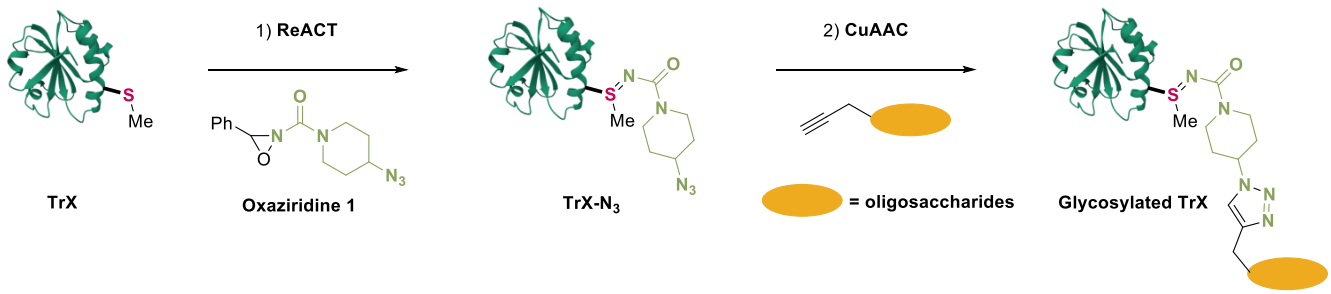
Glycosylation is a major post-translational modification that significantly impacts protein folding, distribution, stability and activity.[1] Despite significant advances in protein expression systems, the glycosylation profile remains unique to each host organism, often resulting in the production of heterogeneous glycoforms. Controlling protein glycosylation is thus a major challenge, particularly when therapeutic proteins are targeted. Chemical conjugation is an interesting alternative method to this purpose. Redox Activated Chemical Tagging (ReACT) has recently emerged as an efficient bioconjugation method for protein modification. This click chemistry reaction consists in the addition of methionine sulfur atom to an electrophilic oxaziridine leading to a sulfimide adduct.[2] In the present work, we combine ReACT and CuAAC reactions in a one pot sequence as a general strategy to access glycosylated proteins. To enhance the modest yield (30%) reported in the literature for the preparation of the azido-functionalized oxaziridine **1** (Scheme 1),[3] alternative synthetic routes were initially explored. Methionine glycosylation by the ReACT-CuAAC tandem approach was then applied to a pentapeptide selected from the sequence of thioredoxin, a model protein, before extending its application to the entire protein (Scheme 1).



Scheme 1 : General strategy towards protein glycosylation based on one-pot sequential ReACT-CuAAC reactions

Acknowledgements:
This work is supported by the French National Research Agency (ANR) through Labex ARCANE/CBH-EUR-GS (ANR-17-EURE-0003).

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THE SUF IRON-SULFUR CLUSTER ASSEMBLY MACHINERY : FROM *ESCHERICHIA COLI* TO *MYCOBACTERIUM TUBERCULOSIS*

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Iron-sulfur clusters (Fe-S) are among the most ancient and versatile inorganic cofactors in nature, playing a crucial role in fundamental biological processes. Various multi-protein machineries (NIF, ISC, SUF, MIS, and SMS) mediate Fe-S cluster biogenesis across archaea, bacteria, parasites, plants, and humans [1,2]. The SUF system is nearly ubiquitous in nature [3]. It plays a general role in many bacteria and is essential for the viability of organisms lacking the ISC or NIF systems, such as *Mycobacterium tuberculosis*, *Bacillus subtilis*, *Synechocystis*, and *Staphylococcus aureus* [4-7]. Furthermore, it has been identified in certain eukaryotic organelles (plastids), and a SUF-like ancient Fe-S cluster assembly machinery was recently proposed to have existed in the proto-eukaryotic cell [8]. This underscores the biological significance of the SUF system and fully justifies a comprehensive review of it. We have been studying the *Escherichia coli* SUF system for 20 years, yet several mechanistic questions remain unresolved. Recently, we expanded our research to the SUF system of the pathogen *M. tuberculosis* and obtained exciting results [9], particularly regarding the Fe-S scaffold $SufBC_2D$.

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Electrochemical CO_2 Reduction by [FeFe]-Hydrogenase Models

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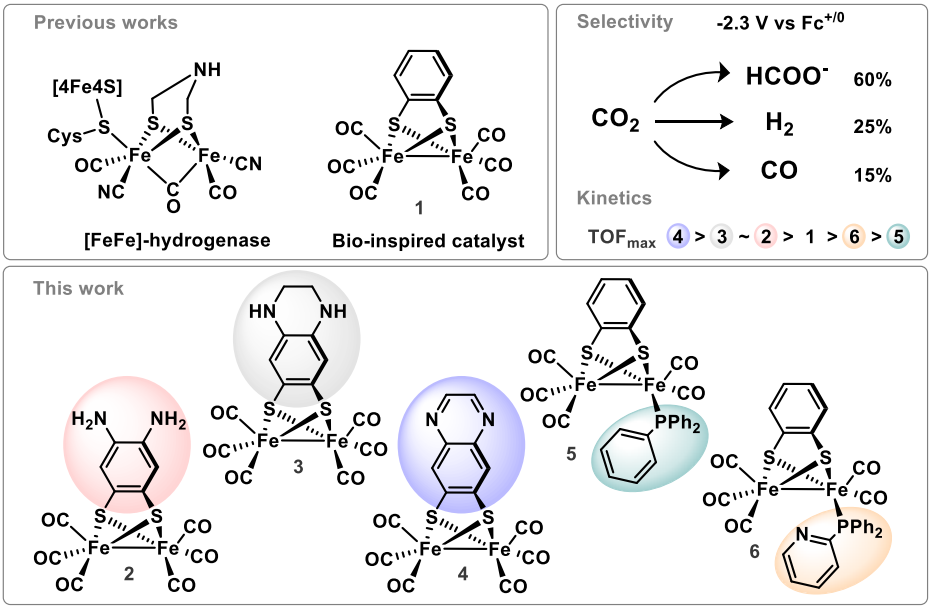
The electrochemical reduction of CO_2 to formate is a promising route for sustainable energy storage and renewable feedstock production. Inspired by [FeFe]-hydrogenases, we synthesized a series of [(μ-bdt)-$Fe_2(CO)_6$] (**1**) derivatives: three bearing nitrogen-functionalized bdt ligands (**2**–**4**) and two with a CO ligand replaced by phosphine-based ligands (**5**,**6**). Their catalytic activity for electrochemical CO_2 reduction was evaluated in acetonitrile solution with methanol as the proton source.



Functionalization of the bdt ligand with nitrogen-containing groups (**2**-**4**) enhances catalytic performance, as shown by increased maximum turnover frequencies (TOF_{max}). A similar enhancement is observed for complex **6**, which contains a pyridine-functionalized phosphine, despite the general decrease in reaction kinetics associated with CO substitution. We attribute the improved activity to secondary coordination sphere effects, wherein nitrogen groups facilitate local proton delivery through hydrogen bonding with methanol.

Despite variations in kinetics, all complexes exhibit comparable selectivity, reaching up to 62% Faradaic efficiency for formate production. Based on combined electrochemical measurements, infrared spectroelectrochemistry, and DFT calculations, we revised the previously proposed mechanism and suggest an alternative pathway involving the formation of a metal-hydride intermediate. These results provide new insights into the role of secondary-sphere interactions in modulating the activity of [FeFe]-based catalysts for selective CO_2 reduction.

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Light Driven Release: Exploring Photo-ejection in Ruthenium Complexes

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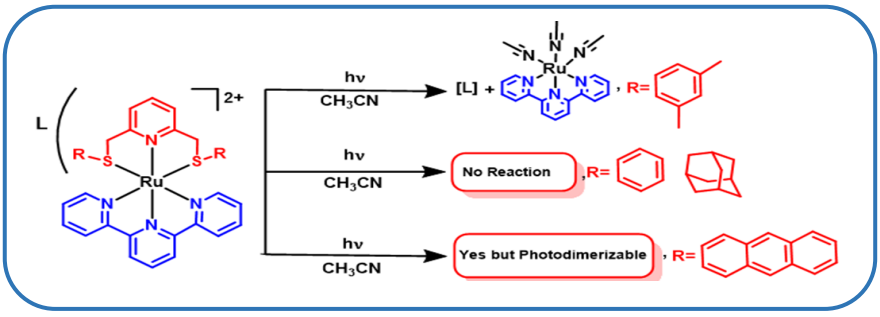
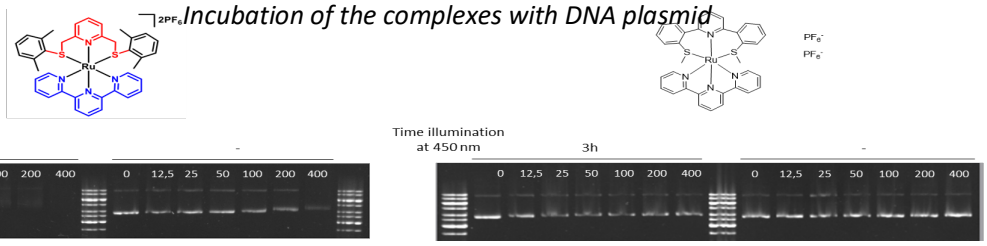
The rich and diverse chemistry of ruthenium complexes has been extensively studied due to their notable photophysical and photochemical properties. Photo-ejection of ligands from ruthenium core proposes exciting prospects for cancer treatment allowing localized release of bioactive compounds [(1)]. Recent achievements of application of Ru(II) complexes lie in photoactivated chemotherapy (PACT)[(2)]. In this strategy, the presence of oxygen is not required to achieve cell toxicity. Tridentate ligands photo-ejection is likely to produce more coordinating sites than bidentate ligands to interact with DNA/proteins [(3)]. $[Ru(tpy)SNS\ (R)]^{2+}$ (tpy = 2,2';6',2"-terpyridine; R = phenyl, xylene, anthracene) were synthesized and photochemical studies were carried out. No reaction was observed when $[Ru(tpy)SNS\text{-}phenyl]^{2+}$ was irradiated in degassed acetonitrile solution compared to $[Ru(tpy)SNS\text{-}xylene]^{2+}$ which showed efficient and rapid ejection. Steric hindrance around the ruthenium core proved to be an important aspect for efficient photoejection. Biological studies for $[Ru(tpy)SNS\text{-}xylene]^{2+}$ were carried out on DNA plasmid through gel electrophoresis under different conditions, clearly showing a great activity when illuminated with a 450 nm lamp for 3hrs.



Biological evaluation:

Incubation of the complexes with DNA plasmid



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Strong C-H bond activation induced by immobilized copper-based molecular electrocatalyst

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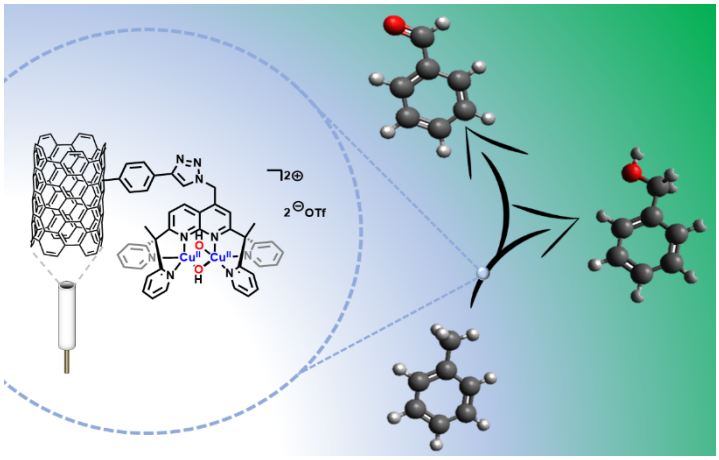
C-H bonds possess high activation energy (BDFE > 90 kcal/mol) [1] and therefore are very difficult to break. Consequently, their activation is needed in order to lower their energy and enhance their reactivity. Dicopper complexes have turned to be active for this purpose. Recently, novel dicopper complexes bearing a naphthyridine spacer scaffold have demonstrated catalytic activity towards the electrodriven toluene oxidation reaction in acetonitrile in the presence of a suitable base. Results showed that the catalytic behaviour of the complex is influenced by the solvent leading to the formation of side-products.[2]

Building upon this study involving a soluble molecular dicopper complex, the catalyst was modified by incorporating an azide function. Copper(I)-catalysed Alkyne-Azide Cycloaddition–(CuAAC) was employed to covalently immobilize this complex onto the surface of alkyne-modified multiwalled carbon nanotubes (MWCNTs) [3,4]. Optimization of the CuAAC conditions was performed as well as the evaluation of the activity of this new hybrid material towards the electrocatalytic toluene oxidation. The work performed on the synthesis of the new modified ligand, the different immobilization methods of the complexes on modified MWCNTs, their electrochemical characterizations and their catalytic activity will be presented.



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POSTERS

Dual-function *de novo* peptides: infection treatment and bacteria identification

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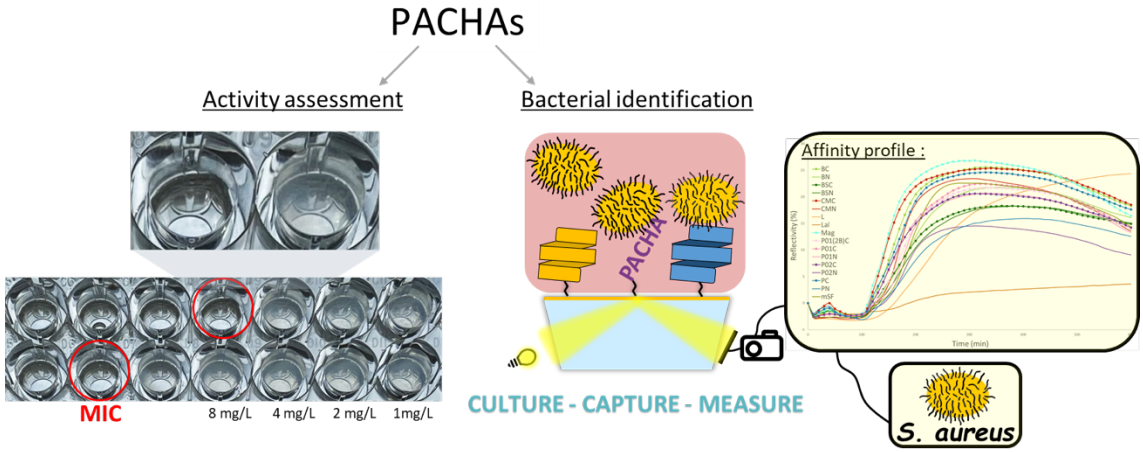
Antimicrobial resistance (AMR) drives the need for new therapeutic options and rapid diagnostics. Antimicrobial peptides (AMPs) are promising candidate to fight against AMR due to their broad-spectrum activity, unique mechanism, and low toxicity.

We designed *de novo* AMP sequences, PACHA01 and PACHA02 with the same composition of amino acids but featuring different primary sequences and secondary structures. While their lack of solubility in complex medium hampers accurate assessment of their antimicrobial activity by minimal inhibitory concentration (MIC) determination, these peptides hold strong potential for bacterial detection and identification on surfaces. Indeed, the diagnostic capability of AMPs is driven by their broad-spectrum interaction with bacterial membranes. PACHA01 and PACHA02 were employed among a panel of reported AMPs as probes to develop a biosensor thanks to surface plasmon resonance imaging (SPRi). This device enabled real-time bacterial identification and showed potential for rapid infection diagnostics.[1]

Références :



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Design and synthesis of redox active macrocyclic lanthanide complexes for medical imaging

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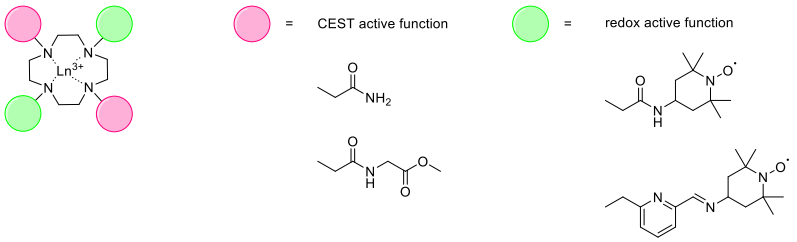
ROS play an essential role in important physiological processes such as signalling and immune response.[1] The over production of reactive oxygen species has been shown to be implicated in the development of illnesses such as cancers, diabetes and neurodegenerative disorders.[2] A challenge in medical imaging is the precocious detection of such elusive species. Intelligent contrast agents can allow a controlled response to these processes potentially allowing early diagnosis.[3]

Lanthanide complexes are fascinating for their optical and magnetic properties and so are widely used in imaging applications.[4] However, the lanthanide ions are very stable in their (+III) state and so cannot inherently be used as redox probes.

Our team focuses on the design of redox active ligands which can communicate the redox response to a lanthanide ion, allowing a response in both magnetic and luminescent properties. We herein report the design and synthesis of symmetrical lanthanide complexes containing a redox non-innocent ligand, capable of inducing a response from the coordinated lanthanide ion.[5] Electrochemistry and EPR are used to understand the interaction between metal and redox active ligand. The response of these complexes can be exploited in luminescent imaging or CEST imaging.



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New lanthanide complexes for in vivo luminescent biphotonic and MRI imaging

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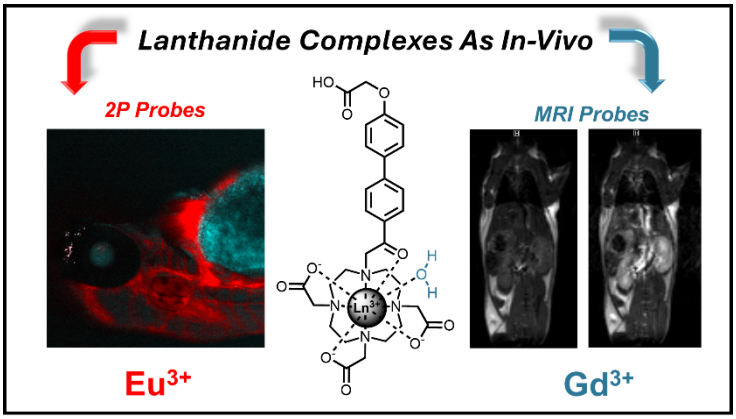
In recent decades, lanthanide(III) complexes have been widely used in medicine as MRI and nuclear imaging probes. These elements have similar coordination properties, making it possible to use a single complex for several applications. Despite their fantastic luminescent properties compared with conventional fluorescent probes (long luminescence lifetime, large stokes shift, fine emission band at fixed wavelengths from visible to near infrared, high photostability, low tendency to aggregation), they have not been widely explored for these applications. Indeed, these complexes require an antenna that absorbs and transfers its energy to the excited state of the lanthanide. They often require high-energy excitation (in the UV, <370nm), out of the optical transparency window of the biological samples and also damaging for cells. The two-photon absorption provide a solution to this issue: molecules are excited by the simultaneous absorption of two photons of half the energy, shifting the excitation in the near infrared, which is the appropriate range for a deeper and more accurate imaging.

Most luminescent lanthanide complexes optimized for microscopy imaging are based on a ligand that saturates the lanthanide coordination sphere, in order to suppress some non-radiative de-excitation due to water molecules. Consequently, their Gd(III) analogue cannot be used as an MRI contrast agent, as this technique requires exchangeable water molecules in the Gd(III) coordination sphere. Here we describe a new family of lanthanide complex that combines a DO3A macrocycle with a fourth substituted acetophenone that serves an antenna for 2P absorption. This system shows excellent 2P luminescence properties with Eu(III) despite a coordinating water molecule and good MRI properties with Gd(III) thereby opening the way to 2P luminescence/MRI bimodal imaging. This poster presents the synthesis, the optical and magnetic properties of theses complexes as well as their in-vivo imaging applications in zebrafish embryos and mice respectively.



Impact of CO_2 insertion in the 2nd coordination sphere of molecular electrocatalyst

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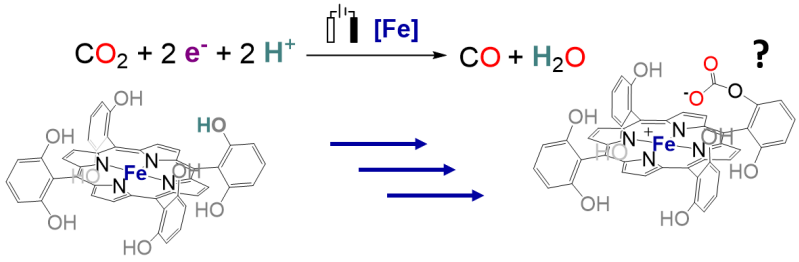
The electrification of chemical processes, combined with the use of renewable building blocks such as CO_2, is an important prerequisite for transitioning away from fossil fuels. Catalysis is needed in these approaches to achieve high reaction rates, selectivity and energy efficiency, and must be accompanied by a high level of understanding. Inspired by nature, the second coordination sphere of molecular electrocatalysts has been modified by the addition of functional groups to improve performance. However, the interaction or even modification during electrocatalysis of these groups in the presence of CO_2 (e.g. binding) has been largely unexplored to date (**Scheme 1**).

In this work, the impact of CO_2 on these functional groups was investigated using a synergistic experimental and theoretical approach. Iron porphyrins, although long discovered for this reaction, are still being extensively studied to reveal the mechanistic keys explaining their performance.[1] In particular, the phenoxy-containing iron porphyrin developed by the host team will be chosen as a model catalyst.[2] It is one of the best molecular electrocatalysts for the reduction of CO_2 to CO, with near-quantitative faradaic efficiency. These have so far been attributed to proton-relay and hydrogen bonding effects by the phenoxy groups in the second coordination sphere.[3] However, the role of these groups and the maintenance of their integrity during catalysis in the presence of CO_2 remain to be elucidated.



Scheme 1. *Impact on catalysis of CO_2 insertion in iron porphyrin complexes bearing phenoxy groups.*

Acknowledgements

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Electroreduction of CO_2 to CH_4 by copper nanoclusters

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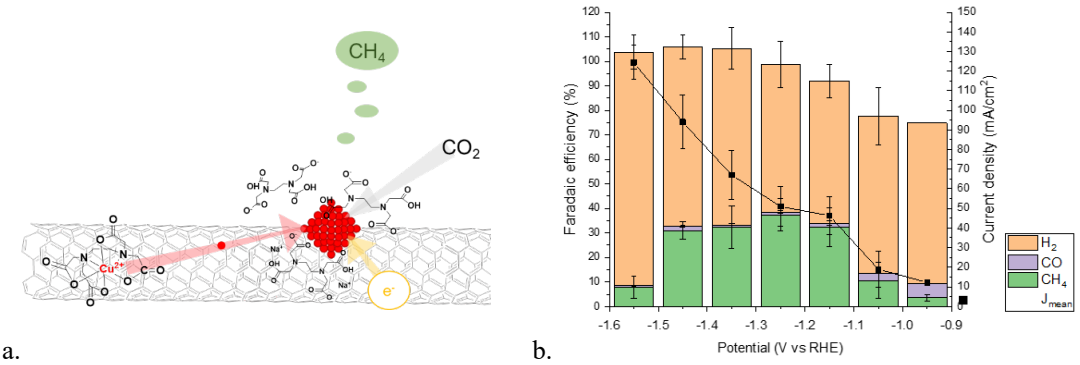
CO_2 reduction reaction (CO_2RR) is extensively studied as a means to use anthropogenic CO_2 to store renewable energy into value-added chemicals and fuels.[1-2] Methane is an interesting product to target from the CO_2RR as it is the main component of natural gas, accounting for a quarter of global electricity production, thus representing a market worth USD 4.3 billion per year.[3] CO_2RR using low-cost copper catalysts has shown great promise as a viable and scalable process for the industrial production of methane from renewable energies.[4]

In this context, we present here the study of a copper ethylenediaminetetraacetic acid complex (Cu-EDTA) acting as a low-cost precursor for the *in-situ* generation of copper nanoparticles highly active for the reduction of CO_2 into methane (Figure 1a). A faradaic efficiency of up to 40% was obtained at –1.15 V vs. RHE (Figure 1b), with a current density of –53 mA cm^{-2}, thus reaching a similar CH_4 current density than the Cu-Pc system[5] with a pre-catalyst 200 times less expensive. We also looked at the integration of this pre-catalyst on a gas diffusion layer to further study this system in more industrially relevant conditions. In a flow cell, under 3.4 volts, this cathode can generate 30% of CH_4, showcasing very promising performances for further CO_2-to-CH_4 electrolyzer design.



a. b.

Figure 1. a. Schematic representation of the atomic agglomeration from Cu-EDTA for selective reduction of CO_2 to CH_4. b. Impact of the applied potential on the faradaic efficiency and current density for CO_2RR catalyzed by Cu-EDTA/CNT in a 0.5 M $KHCO_3$ + 1 mM EDTA solution.

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Novel aqueous synthesis of $CuInGaS_2$ quantum dots for water splitting

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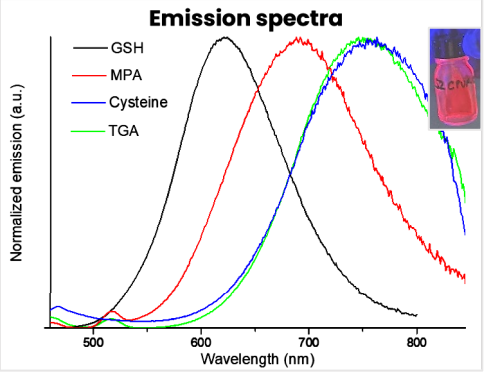
Abstract

Hydrogen is a well-known energy vector, fundamental for the transition from fossil fuels to green combustibles. It can be produced by environmentally friendly water splitting, which employs renewable energy sources such as solar light in a so-called photoelectrocatalytic (PEC) cell. In a PEC cell, the element responsible for light absorption and electron transfer to the catalyst is called sensitizer. For the role of sensitizer, inorganic semiconducting nanocrystals (quantum dots, QDs) have attracted increasing interest in recent years, thanks to their stability, high sunlight absorption and possibility to tune the bandgap as a function of the composition [1].

In our work, we chose to employ heavy-metal-free $CuInGaS_2$ QDs as sensitizers, for their low toxicity and proper band position for hydrogen production. For this purpose, we developed the first environmentally friendly microwave-assisted aqueous synthesis of $CuInGaS_2$ quantum dots [2], which has been upscaled in a flow synthesis setup [3]. QDs with different compositions, shells (GaS and ZnS), ligands (thioglycolic acid, mercaptopropionic acid, L-cysteine and glutathione) and surface treatments have been synthesized. The properties of the QDs have been studied by absorption and emission spectroscopy, differential pulse voltammetry (intrinsic bandgap determination), X-ray diffraction, energy dispersive X-ray spectroscopy, nuclear magnetic resonance (ligand detection), small angle X-ray scattering (size distribution study) and dynamic light scattering (hydrodynamic diameter determination).



These analytical techniques allowed the authors to optimize and select the best QDs candidates for water splitting. After depositing the QDs on a homemade TiO_2 electrode, they displayed a photocurrent of 1.7 mA/cm^2 (pH = 7, electrode surface = 2 cm^2) which remained stable for more than 8 hours, close to the best literature results for QD-sensitized TiO_2 electrodes.

Acknowledgements

The author would like to thank Peter Reiss and Vincent Artero for our fruitful scientific discussions over the last two years.

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Unveiling Perovskite Nanocrystal Surfaces with DNP-enhanced Solid-State NMR supported by DFT Simulations

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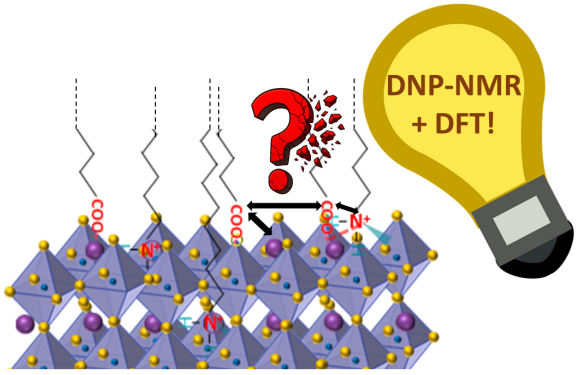
The surface chemistry of nanomaterials is one of the most important factors controlling their physicochemical properties, stability, and applicability. Magic angle spinning (MAS) solid-state NMR has proven to be the most versatile technique for surface-specific studies, providing both qualitative and quantitative information. The issue of the inherent low sensitivity of NMR can be overcome through hyperpolarization techniques such as dynamic nuclear polarization (DNP) [1]. This technique combined with ultra-low temperature measurements [2] has made it possible to study exotic and challenging materials such as perovskite nanocrystals at atomic-level resolution. $CsPbBr_3$ and other halide perovskite nanocrystals are of particular interest due to their myriad applications in optoelectronics, photovoltaics, and catalysis [3]. Their properties are governed by their surface chemistry, which is tunable by the organic ligands used during synthesis to passivate the ionic nanocrystal surfaces. As a consequence, the determination of the ligand stabilization mechanism is a highly impactful and pertinent problem to be solved with DNP-enhanced MAS solid-state NMR. This study delivers both qualitative and quantitative insights into ligand interactions with perovskite surfaces. Surface-ligand proximity has been quantified through advanced NMR techniques, supplemented by density functional theory (DFT) simulations of the ligand-surface interface. Additionally, this study provides the first experimental evidence of cooperative one-on-one interactions between the ligands. The results of this project provide much-needed clarity regarding ligand-surface interactions in perovskite nanocrystals that will be instrumental in improving their stability and enhancing their functional properties. In addition, the techniques explored and employed in this study form a versatile analytical framework that can be used to study similar nanomaterials.



Acknowledgements
I am sincerely grateful to the ARCANE program for their generous support in funding my PhD.

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Carbazole-based lanthanide luminescent bioprobes for live cell imaging

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Lanthanide(III) complexes have fantastic luminescent properties that make them very attractive for bioimaging. Classic lanthanide-based luminescent bioprobes require high energy excitation by UV-visible light (300-450 nm), which is absorbed and scattered by the biological tissues and causes photodamage1,2. Indeed, for cellular imaging applications, working with both excitation and emission in visible or, even better, in the near infrared is preferred to avoid these problems. This can be achieved by using Europium(III) as a red emitter or Terbium(III) as green emitters and a light-harvesting antenna (to sensitize Eu3+ or Tb3+ luminescence) that presents two-photon absorption properties3,4. During the past two years, we have developed a Eu3+ complex featuring a carbazole antenna that features interesting two-photon absorption properties. This complex was conjugated to a cell penetrating peptide (CPP), allowing its delivery to the cytosol. Despite a very low quantum yield (0.2%), this system was successfully used for two-photon imaging of living cells5. Now, our goal is to improve its optical properties and to develop novel responsive probes based on this first imaging probe.
In this poster we will present you how we optimized the luminescence properties of this Eu3+ and Tb3+ complex by tuning the photophysical properties of the carbazole antenna. Indeed, to improve its luminescence properties, we need to suppress an unproductive photoinduced electron transfer between the carbazole antenna and Eu3+. This was achieved by introducing electroactracting substituents on the carbazole unit. We will describe the synthesis of the CPP conjugates of this new lanthanide complex, their luminescence properties and two-photon microscopy imaging with these probes.

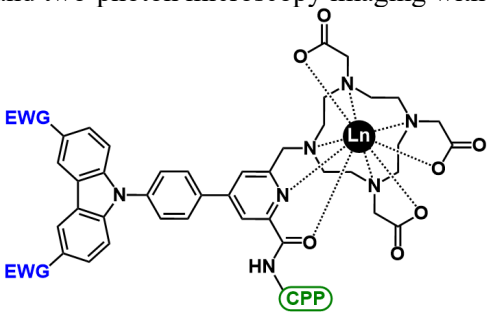

Figure 2:New two-photon luminescent lanthanide-based bioprobes with substituted cabarzoles

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Streamlined discovery of bioactive glycoconjugates using On-Chip synthesis and screening

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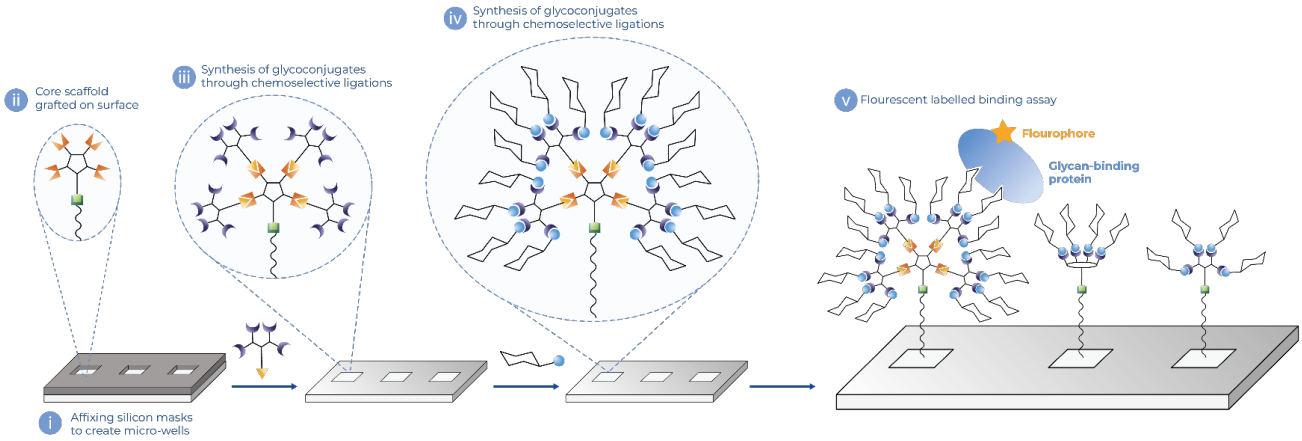
Carbohydrate-protein interactions between glycans and glycan-binding proteins (GBPs) play crucial roles in biological processes and are potential therapeutic targets. While multivalent interactions are necessary for high affinity and selectivity with target GBPs, designing effective multivalent glycan ligands involves complex structural parameters. Traditional methods requiring individual synthesis and study of various structures are timeconsuming and expensive due to extensive purification steps. This project developed a microarray-based tool using glycoconjugate arrays to rapidly evaluate multivalent architectures against carbohydrate-binding proteins using minimal material. The approach involves synthesizing glycoconjugates directly on surfaces using functionalized synthons through stepwise chemical ligations, reducing purification steps. These glycoconjugates can then be simultaneously screened for bioactivity against GBPs. Initial proof-of-concept involved solution-phase synthesis before surface immobilization to study the grafting process. Interaction assays were developed using fluorescent-labelled lectins for direct testing to identify anti-adhesive compounds, while indirect tests used human serum and secondary fluorescent antibodies to find high-affinity antibody-binding molecules. Our team successfully synthesized various glycoconjugates on surface using different chemo-selective ligation reactions. Several structures demonstrated promising bioactivity, with results comparable to classical physicochemical tests. This success enables exploration of more potential structures and ligation reactions using the microarray platform.



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Novel iron-based catalysts for photoinduced reversible hydrogen transfer reactions

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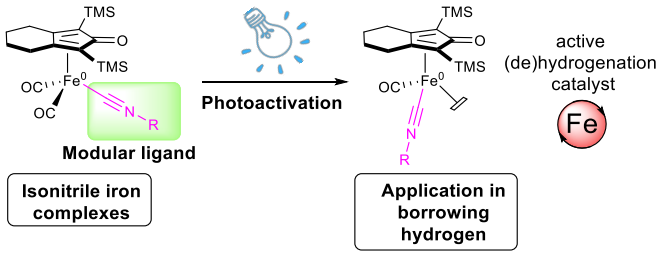
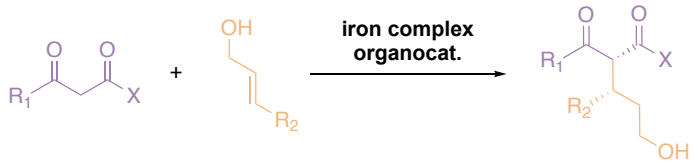
The quest for sustainable and cost-efficient synthetic processes has led to the development of iron cyclopentadienone catalysts, replacing costly noble metal complexes notably for hydrogen transfer reactions. These catalysts, featuring cooperativity between iron and the cyclopentadienone ligand, provided unique reactivities, particularly in borrowing hydrogen reactions.[1],[2] Modification of these catalysts has mainly focused on changing the cyclopentadienone core, but little has been done with the iron tricarbonyl structure. In order to potentially enhance the activity of these complexes and obtain different reactivities, the CO ligands were replaced by different isonitrile ligands, creating a library of modular complexes.[3]



These catalysts demonstrated notable activity, surpassing classical catalysts, in a photoinduced multicatalytic borrowing hydrogen process. This enabled easy enantioselective functionalization of allylic alcohols under mild conditions.



To gain a comprehensive understanding of these complexes' reactivity and establish a structure-activity relationship, their behavior was carefully investigated by spectroscopy and computational chemistry. This approach offers profound insights into the catalyst's activity origin and properties.

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Design of biomimetic surfaces with CD20 clusters for Rituximab recognition

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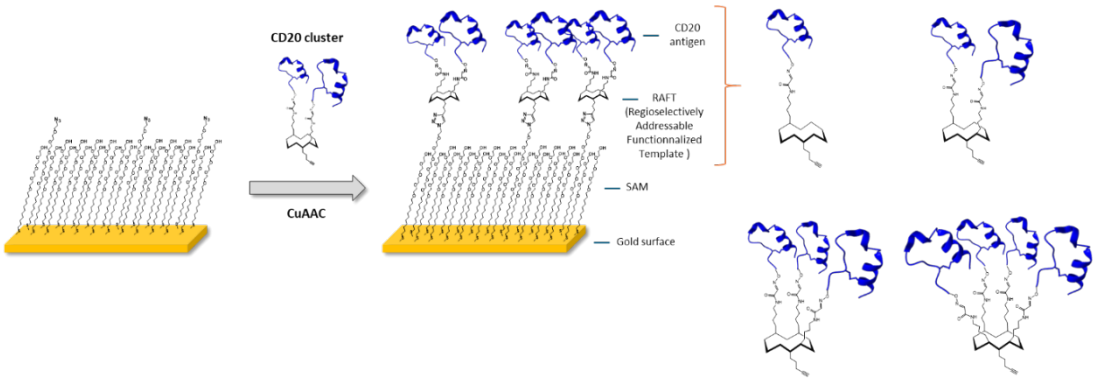
The human cluster of differentiation 20 (CD20) antigen, a protein overexpressed on mature B cells, is a key target for antibody drug therapy. Among the antibodies that target the CD20 antigen, rituximab (RTX) is routinely used to treat several cancers. It is well-known that the levels of antigen expression, in particular antigen clusters at the cell surface, has a clear effect on the efficacity of the therapy. In this context, our group reported the impact of CD20 density on RTX antibody. We found an average inter-CD20 spacing of nearly 2 nm that confers a binding constant (K_D= 100 nM) in accordance with values from *in vitro* analysis with B cells.[1] This study offers an interesting outlook in the understanding of the necessity of epitope clusters for effective mAb recognition. In the present work, we report new CD20 clusters (monomer, dimer, trimer, and tetramer). To systematically study these clusters on antibody recognition, we design self-assembled monolayer surfaces that display tunable CD20 cluster densities. The antigen-antibody interactions were studied by using sensitive surface techniques such as Surface Plasmon Resonance (SPR). This study revealed that a dimerization of CD20 on surfaces significantly enhanced the interaction with RTX (K_D = 10 nM). We reason that the design of such surfaces will pave the way for the discovery of mAb mimics, especially through the screening of peptides and nucleic acid aptamers.



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QM/MM Metadynamics Study of CO_2 Capture by Ethylenediamine: Toward an Accurate and Reliable Free Energy Protocol

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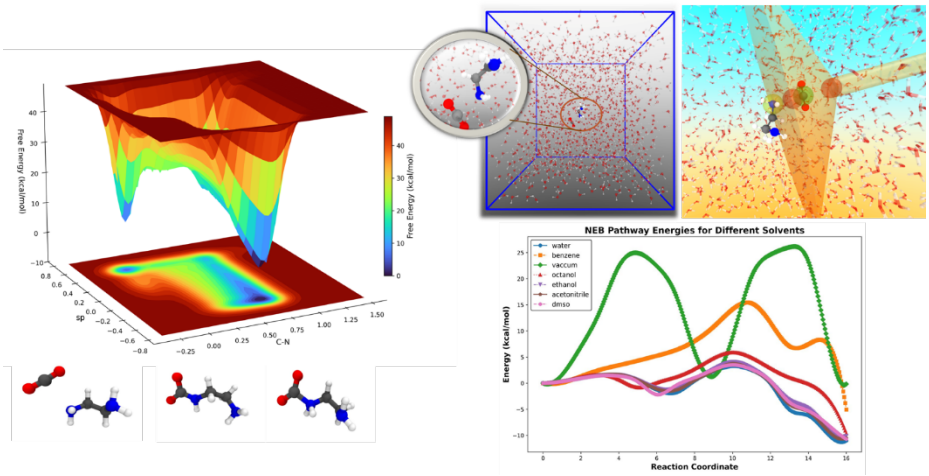
Direct CO_2 capture in aqueous solution using small amines such as Ethylenediamine (EDA) is a promising strategy in carbon capture technologies. However, accurately modelling the reaction mechanism and its free energy surface is a computational challenge. Here, we present a QM/MM-Metadynamics (QM/MM-MTD) protocol designed to model such systems in a realistic manner and produce accurate reaction free energy surfaces. For an explicitly solvated system, we perform Well-tempered (WT) QM/MM-MTD and study the free energy surface using carefully selected collective variables tailored for studying bond formation, tautomerism, and proton transfer in small-molecule systems [[1] To effectively sample both bound and unbound states, a funnel-shaped restraint potential [2] is used. Furthermore, we discuss a Δ-learning correction approach to improve the accuracy of QM/MM energies and forces, bridging the gap between semiempirical methods and higher-level DFT [3]. The resulting protocol implemented in ASH [4] offers a transferable and computationally efficient framework for studying CO_2 capture reactions, combining the cost of semiempirical methods with the accuracy of DFT.



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DISCOVERY OF NOVEL G4 BINDING PEPTIDIC DERIVATIVES USING DNA ENCODED CHEMICAL LIBRARIES

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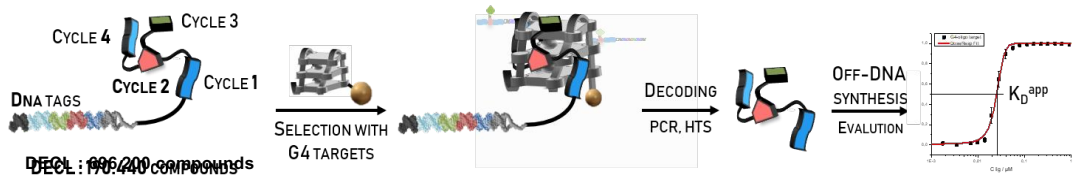
Beyond the known helix, there are now compelling evidences demonstrating that nucleic acids can form other secondary structures such as G-quadruplex (G4). G4 can arise through non-canonical nucleobase interactions within G-rich DNA and RNA sequences (a). Those G4, established in key regulatory regions of genomes and transcriptomes, are repeatedly identified to play pivotal roles in many biological processes.[1] Also involved in the molecular mechanisms of several diseases, G4 structures have become a major target for synthetic chemists aiming at the development of G4-targeted chemical probes and drug leads, notably capable of stabilizing the G4 structure.

In order to quickly identify molecules capable of binding with high affinity and specificity against such structures[2], we are building combinatorial libraries of potential G4 ligands, by means of a DNA-encoded technology (DEL). Thanks to the DEL approach, the identity of each compound within a combinatorial library is recorded by a unique DNA barcode, to allow for the high-throughput and quantitative identification of the best G4 ligands, isolated through *in vitro* selections between the library and G4 targets.[3,4]



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AI assisted design of artificial metalloenzymes for enantioselective sulfoxydation

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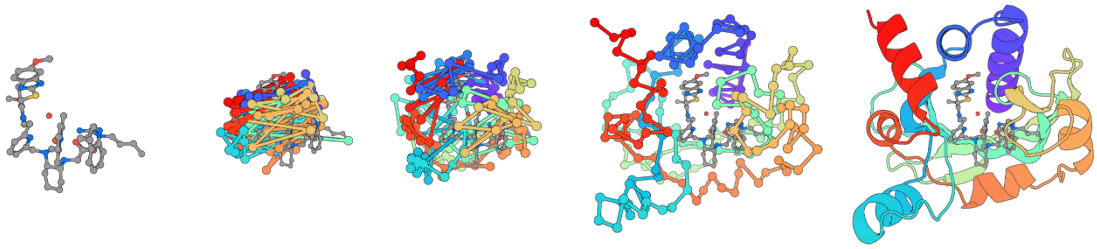
Natural enzymes are exceptional catalysts with high selectivity and efficiency under mild conditions. However, their industrial application is limited to natural transformations. This work presents an innovative approach to expanding the enzyme repertoire by using artificial intelligence to design artificial metalloenzymes for stereoselective sulfoxidation reactions.

Our research focuses on developing artificial metalloenzymes capable of highly enantioselective oxidation of thioethers to sulfoxides—a transformation critical in pharmaceutical synthesis, particularly for proton pump inhibitors like Esomeprazole®.

We pursue two complementary strategies: (1) engineering the bacterial nickel transporter NikA to accommodate iron complexes as artificial metal active sites[1] with enhanced stereoselectivity using active learning assisted directed evolution[2], and (2) designing from scratch artificial proteins around inorganic complexes. In the first approach, we implement an iterative computational pipeline that begins with QM/MM transition state modeling, followed by targeted mutations of key residues around the binding site. Our active learning algorithm prioritizes mutations based on their predicted impact on stereoselectivity, allowing efficient exploration of the vast sequence space. For the second approach, we leverage a set of calculations using RFdiffusion[3] to generate backbone scaffolds around the catalytic iron center, followed by ProteinMPNN[4] for sequence design and AlphaFold2 validation, creating entirely novel protein/peptide structures optimized for the target reaction.



In both approaches, computational modeling begins with an optimized transition state for the sulfoxidation reaction, followed by the design of protein scaffolds that stabilize this conformation. Preliminary in silico designs for strategy (1) have allowed us to identify new binding modes in NikA yielding promising candidates that are being expressed, purified, and evaluated for catalytic performances.

This research represents a significant advancement in applying artificial intelligence to biocatalyst design, potentially enabling greener pharmaceutical manufacturing processes by replacing conventional methods that rely on toxic reagents, organic solvents, and metal catalysts with selective enzymatic alternatives operating under mild conditions.

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Design and synthesis of advanced photosensitizers for multi-electron oxidations

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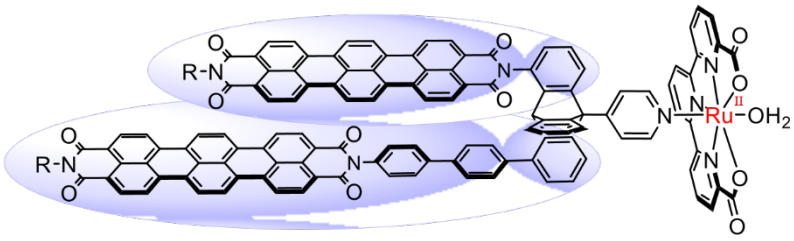
The development of sustainable pathways for the production of basic and commodity chemicals is a topic of increasing importance in the context of the current environmental crisis. Taking inspiration from Nature, and more specifically from photosynthetic organisms that are able to harvest solar energy to drive the primary reactions supporting their thriving, is of particular interest. Thus, the development of molecular photocatalytic systems coupling photosensitizers to a desired catalyst is a great challenge for the scientific community. A specific point to consider is the development of efficient antennas able to activate the catalyst under low-light (solar) irradiation. To achieve this goal, the implementation of multichromophoric photosensitizers can provide an enhanced absorption capability.

In this work, we will present our efforts toward designing multi-terrylene arrays, based on a rigid triptycene scaffold, and their coupling to well-established Ru-based catalysts for 2-electron alcohols oxidation. The choice of the terrylene core was driven by its exceptional (photo)chemical stability, its good absorption in the visible range[1] as well as its appropriate redox properties. The triptycene scaffold will provide a highly tunable base to spatially organize 2 terrylene moieties around a catalytic center.

In this poster, we will discuss different synthetic strategies for constructing precisely defined architectures that feature two terrylene units arranged co-facially around a robust triptycene core. [1]



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Development of DNP-enhanced solid-state NMR for protein investigation in complex environment

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Dynamic Nuclear Polarization (DNP) has revolutionized the scope of many solid-state NMR experiments by enabling new sensitivity-limited experiments to be recorded. For the field of structural biology, it bears great promise for the study of biomolecular systems diluted in their native environment, such as lipid membranes or in cells[1]. Indeed, studying the structure of proteins in their natural context is key to understand how they function, but it has strong limitations in sensitivity, that DNP can in principle overcome. The use of DNP for biomolecular systems is however often limited by the necessity to run experiments at cryogenic temperatures, which can induce line broadening and loss of spectral resolution resulting from frozen local motion.

In this context, our group developed over the past years a new methodology called Selective DNP (*Sel*DNP), which allows recovering high-resolution DNP spectra specific to a protein region in uniformly labeled samples[2].This approach is based on differential spectroscopy between a uniformly polarized spectrum (obtained from conventional DNP) and a spectrum in which a localized paramagnetic bleaching of resonances is produced by a paramagnetic spin label introduced at a specific protein site. It results in sensitive, highly resolved spectra, which are specific to the tagged region and provide distance information relative to the spin label[3].
So far, *Sel*DNP has only been demonstrated on a purified small protein of 12 kDa, to identify its binding site for a carbohydrate ligand. Despite its relevance, it is unclear whether *Sel*DNP can still be applied to larger proteins or extended to in cell studies. Since specific methyl labelling has been shown to be useful for approaching larger biomolecular systems by solution NMR, we investigate here its compatibility with the *Sel*DNP concept. The on-going methodological development is demonstrated on a large protein of 58 kDa, a chondroitin-4endosulfatse (PLM13) that plays a key role in regulating sulfation state of a complex cellsurface polysaccharide, chondroitin sulfate (CS). The CS binding site of this newly discovered endosulfatase (PLM13) is yet unknown. Once developed, our methodology will be used to probe PML13's binding site to contribute to the elucidation of the mechanistic details of the interaction of this human gut microbiota protein with the host cells.

References

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Le Pôle Universitaire d'Innovation Grenoble Alpes

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Le Pôle Universitaire d'Innovation Grenoble Alpes fait partie des 29 PUI créés dans le cadre de France 2030labellisant des sites universitaires de 2023 à 2027 dans le but d'améliorer l'impact socio-économique dela recherche. Porté par l'Université Grenoble Alpes, le PUI unit tous les acteurs de la recherche publique avec la SATT Linksium. Il est organisé en 5 filières dont une est dédiée à la Santé. Sa mission est de coordonner les actions des acteurs, de conseiller les porteurs de projets et de fournir des parcours optimisés pour les entreprises. Le PUI apporte une aide aux porteurs de projets innovants (personnel de recherche, étudiants) par des actions d'information, de formation, de conseil et d'accompagnement. L'accès pour les entreprises sera facilité par une offre filière intégrant l'ensemble des acteurs publiques. Pôle Universitaire d'Innovation Grenoble Alpes fait partie des 29 PUI créés dans le cadre de France 2030 labellisant des sites universitaires de 2023 à 2027 dans le but d'améliorer l'impact socio-économique de la recherche. Porté par l'Université Grenoble Alpes, le PUI unit tous les acteurs de la recherche publique avec la SATT Linksium. Il est organisé en 5 filières dont une est dédiée à la Santé. Sa mission est de coordonner les actions des acteurs, de conseiller les porteurs de projets et de fournir des parcours optimisés pour les entreprises. Le PUI apporte une aide aux porteurs de projets innovants (personnel de recherche, étudiants) par des actions d'information, de formation, de conseil et d'accompagnement. L'accès pour les entreprises sera facilité par une offre filière intégrant l'ensemble des acteurs publiques.