– Journée de Rentrée de l'ED406 – promotion 2022 –

Mercredi 8 mars 2023 à 9h15

Amphithéâtre Moissan – PSL, Chimie ParisTech

Livre des résumés

Jakhongir Bekmirzaev

Multicatalytic approaches to polymers upcycling

PhD advisor: Regis GAUVIN and Christophe Thomas

Laboratory: Organometallic chemistry and catalysis of polymerization,

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In recent years, the olefin metathesis reaction has been explored and used in polymer production as well as the construction of polymers with functionalized terminated groups. Besides that, the olefin metathesis shows great potential in the degradation of polymers with unsaturated backbones. Olefin metathesis is based on the trans-alkylidene of two double bonds using metal complexes as catalysts. The metathesis degradation can be completed within a short range of time, and especially a rapid breakdown can happen in the very early stage of the reaction with a decrease of Mn by approximately 70 times. Catalyst loading proves to be a crucial factor for the metathesis degradation as the conversion and the molecular mass of the final degraded species have a strong reliance on it. In this manner, we decided to degradation of nitrile butadiene rubber by using Ru based catalytic degradation. Thus, we have tried explore the decomposition reaction with different resins such as: ABS, HIPS, NBR and so on.

Natacha JEANSON

Polyurethane recycling

PhD advisor: Vincent SEMETEY

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Polyurethane is the sixth most used polymer in the world. They can be found in several applications, such as construction (isolation foam), automotive (foam), textiles (shoes) and medical advices. This diversity is due to the multiple types of monomers that can be used to form the polyurethane. The typical reaction implies a polyol and a polyisocyanate and the choice of both monomer allows to create a material with specific characteristics. Nowadays, polyurethanes are difficult to recycle due to their diversity and also because of their thermostability. My work focuses on the chemical recycling of polyurethanes, and particurlarly on the solvolysis of polyurethane by using methanol as solvent. The depolymerisation of polyurethane will be followed by the separation of the monomers and their reuse to form new polyurethanes.

Qing Liu

Mechanochemistry-assisted continuous catalysis in green solvent

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Abstract: The rapid depletion of non-renewable resources and the greenhouse effect have led to global environmental problems with an adverse impact on the quality of human life. In this urgent context, the search for new and greener strategies and alternative resources for the sustainable development has intensified within the scientific community and at the level of the citizen. In order to create sustainable processes in green chemistry and engineering, alternative intensification processes (continuous flow, ball-milling and mechanochemistry-assisted continuous flow) and green solvent have been explored. In this context, the development of homogeneous and heterogeneous catalysis for the production of high-value chemicals in a designed green solvent will be studied in a mechanochemistry-assisted continuous flow equipment as a high-throughput reaction platform for the first time. Insights on the mechanism will be then gained using modern modeling approach based on Density Functional Theory, with the aim to gain insights on the whole reaction mechanism and to give some indications on the process optimization.

Lamine SAADI

Catalytic Metalation of C–H bonds with Main Group Element-Based Diazenes

PhD advisor: Clément CHAUVIER.

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Organosilanes and organoboranes are versatile compounds used in drug discovery, polymer synthesis or as advanced materials. Therefore, developing new methodologies to access to these compounds in an efficient way is a major challenge in organometallic chemistry.

The main objective of my thesis is to obtain silylated and borylated compounds using molecules called diazenes (R'-N=N-E, E = SiR_3, $BR"_2$) substituted by different silylated groups (especially alkoxysilanes) or borylated groups. These diazenes are able, under mild and transition metal-free conditions, with an association with a s-block based catalyst, to metalate unactivated C–H bond. Then, the metalated substrate can be silylated or borylated in an overall catalytic process.

Olivier CHARRON

Asymmetric transfer hydrogenation : application to strained functionalized cycles

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Three- and four-membered cycles are attracting an increasing interest in medicinal chemistry. Their restricted conformation allows for a well-defined orientation of the substituents in space thereby resulting in improved affinities and selectivities toward the biological targets. Strained cycles are also often used to modulate the pharmacokinetic properties. In this context, the objective of this PhD thesis is to develop transition metal-catalyzed ATH reactions of new classes of substrates in order to efficiently access diversely substituted cyclopropanes, cyclobutanes, oxetanes and azetidines, incorporating several stereocenters, which are valuable building blocks in organic synthesis. The experimental conditions of the ATH reactions will be optimized for the different classes of unsaturated substrates with the goal of obtaining the resulting strained carbocycles and heterocycles with high enantioselectivities and diastereoselectivities. The substrate scope and post-functionalization reactions will be investigated to highlight the interest of the developed methods.

Marharyta KOSIUHA

Asymmetric Transfer Hydrogenation: Toward Organic Molecules of Interest (Cyclic and Strained)

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Project: Development of new synthetic methodologies to access strained chiral hetero- and carbocycles using asymmetric transfer hydrogenation (ATH) as chemical tool. In this context, the objective of the thesis will be to study the asymmetric transfer hydrogenation (ATH) reaction of oxetan-3-ones and azetidin-3-ones derivatives, catalyzed by Ru(II) or Rh(III) complexes, in order to access via a dynamic kinetic resolution (DKR) process, respectively, to the corresponding diastereomerically and enantiomerically enriched oxetanols and azetidinols which are valuable building blocks in organic synthesis. The rhodium complex [Rh] developed in the team will be particularly studied in this transformation. These synthons of interest will also be valorized via various post-functionalization reactions and in the synthesis of biologically active compounds.

Lukmonjon MUTALLIEV

New Cross Coupling Reactions by Dual Photoredox/Ni Catalysis

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PhD co-supervisor : Dr. Cyril OLLIVIER

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Abstract. Many biologically significant compounds are synthesized employing at least one cross-coupling step, making transition metal-catalyzed cross-couplings one of the most significant groups of reactions for the creation of carbon-carbon bonds. Our goals are to explore new radical silicate precursors that present interesting biological properties that can be implemented in various platforms and develop a novel radical silylation reagent that will react via an unprecedented radical mechanism in order to prepare the branched regioisomers.

He WANG

Glycoengineering of monoclonal antibodies with therapeutic activity on Liver Cancers

PhD advisor: Dr. ZHANG Yongmin

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Primary liver cancers include hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA) and constitute the third cause of cancer mortality worldwide . Due to the limited efficacy of general treatment both in HCC and CCA, it is clear that primary liver tumors require novel and more effective treatment strategies. Natural killer cells (NK) cells are a major population of lymphocytes infiltrating HCC and CCA. They have the potential to kill malignant cells by a perforin-dependent pathway and by an antibody-dependent cellular cytotoxicity (ADCC). The carbohydrate moiety of Fc is involved in defining the ADCC activity promoted by the antibodies. However, monoclonal antibodies (mAbs) are heterogeneous mixtures of glyco-forms and only a small percentage has the optimal glycosylation required for the interaction with the FcyIIIa receptors of NK cells, which reduces the efficiency of ADCC. This project aims at the development of new mAbs carrying modifications of the Fc sugar chains able to optimize binding to the Fc receptors of NK and/or macrophage cells in order to optimize tumoricidal activity via a targeted ADCC.

Josue Arturo Ledezma Fierro

Valorization of lignin depolymerization products for the preparation of value-added chemicals

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The use of petroleum resources for the production of raw chemicals leads to CO_2 accumulation, which causes global warming. With nowadays urgent environmental issues, it becomes a necessity to find new sustainable resources. Lignocellulosic biomass, mainly composed of cellulose, hemicellulose, and lignin, is produced in large amounts in nature every year, making it a suitable candidate as a sustainable resource. Whereas the sugar part has been wildly studied for its transformation into low molecular mass chemicals, the lignin part remains underexplored. In this collaborative project, we want to create a connection between lignin depolymerization (German team in Technische Universität Braunschweig) and exploitation of the resulting monomers (French team in Sorbonne University). On one hand, enzymatic lignin depolymerization is being studied and scaled up in Germany focusing on monomers such as guaiacyl-3-hydroxypropanone (GHP) or syringyl-3-hydroxypropanone (SHP). On the other hand, our team will be developing emerging procedures for the conversion of these monomers into high added value chemicals such as 4-chromanones, neoflavanes, and indanone to serve as building blocks for the synthesis of molecules of interest.

Shuai ZHONG

Development of Antifungal Organometallic Drug Candidates

Kevin CARIOU and Gilles GASSER

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In recent decades, the antibacterial resistance crisis has caused reflection on many aspects of public health where weaknesses in our medicinal arsenal may potentially be present – including in the treatment of fungal infections, particularly in the immunocompromised and those with underlying health conditions where mortality rates can exceed 50%.

During the second half of the 20th century, antifungal research mainly focused on an intensive derivatization of accepted compounds (e.g., from ketoconazole to fluconazole). Moreover, the benchmark drugs were all discovered almost 20 or more years ago and accounts of ineffective therapies have been reported for several of these agents especially towards Candida albicans and Aspergillus terreus. Combination of organic moieties with known antifungal properties and metal ions can lead to increased bioavailability, uptake and efficacy.

For these reasons, and encouraged by the spectacular results obtained with metal complexes (e.g. cisplatin, auranofin, ferroquine, etc.) in other medicinal fields, development of such organometallic drugs may alleviate pressure on existing antifungal medications.

Jules BRESSON

Synthesis of bis-β-lactam conjugates as narrow spectrum antibiotics to fight the emergence of antimicrobial resistance

PhD advisor: Dr. Kevin Cariou

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Antimicrobial resistance is a major public health issue. Today, most bacterial diseases can be treated thanks to discoveries made in the 20th century, but if nothing is done, by 2050, the number of deaths from bacterial infections could surpass those from cancer. This project aims to synthetize new conjugates of already existing β-lactams antibiotics to fight the increasing resistance of bacteria to those drugs. One of the main reasons of this resistance are enzymes called β-lactamases, which hydrolyzes the β-lactam antibiotic, thus disabling it. There are already multiple β-lactamases inhibitors on the market, but the mechanism of action of our molecule was designed differently, because we have chosen a pro-drug concept. A sacrificial β-lactam will be hydrolyzed in the presence of a β-lactamase, triggering a cascade that will then release the warhead antibiotic. Thus, this antibiotic will only be selective to resistant strains of bacteria expressing β-lactamases, and it avoids creating an unnecessary selection pressure that could see the emergence of new resistant species.

Namita Raju JOHN

Biological studies on mimics of the superoxide dismutase enzyme

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Reactive oxygen species (ROS) such as superoxide, hydrogen peroxide, hydroxide radical etc are produced in living organisms. Their internal concentration is regulated by several antioxidant defenses like superoxide dismutases, catalases, glutathione peroxidase etc. Oxidative stress reflects a situation of disruption of the balance of antioxidant defenses in relation to oxidant systems and it is associated with several diseases including Alzheimer's disease, cancer and inflammatory bowel diseases (IBD). Inspired by the active site of one of the naturally occuring superoxide dismutase enzymes, Clotilde Policar's team have developed mimic complexes of this enzyme, one of them called Mn1. There are studies that show that Mn1 has an antioxidant activity, as well as an anti-inflammatory activity. Thus, it could be a potential candidate for the treatment of IBDs, which at the moment are incurable. The aim of this project is to carry out proteomic studies to understand the role and biological activity of Mn1 at the proteome level and the link between oxidative stress, inflammation and the antioxidant and anti-inflammatory properties of this mimic.

Lorenzo LORENZINI

New radical based strategies for Ge-C bond formation

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Organogermanes have received far less attention than other group-14 congeners like organosilanes or organostannanes. In recent years, however, this class of compounds witnesses increasing interest from the synthetic community because of new applications of germanium derivates in material science and in the field of cross-coupling chemistry. In this context, the chemistry of germanium-centered radicals has also received attention. Notably, the ROCS group has developed radical-based inter and intramolecular germyzincation reactions leading to vinylgermanes and germoles. The objective of my research is to explore new strategies for the synthesis of germanium-substituted (hetero)arenes and alkenes through radical C-H germylation processes.

Clément SOEP

Study of ligand electronic effects in organometallic complexes using FT-ICR mass spectrometry

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I study tris-bipyridine Ruthenium complexes who were synthetized by chemist of the DCM from Grenoble Alpes University interested by the development of photosensitizers used in photo-induced redox catalytic reactions for hydrogen production and CO_2 reduction. The reactions catalyzed by these species imply reduced reaction intermediates which are difficult to characterize and to isolate. We are able to form them using an FT-ICR (Fourier-transform ion cyclotron resonance) mass spectrometer and an ETD (electron-transfer dissociation) setup. We are coupling this approach with the use of activation processes such as SORI-CID (sustained off-resonance irradiation - collision-induced dissociation), RE-CID (on-resonance excitation-CID), BIRD (Blackbody infrared radiative dissociation) which all have until now rarely been used in the context of our studies. In parallel to this experimental approach, calculations are performed to support the experimental results.

Alix DESJONQUERES

Photocatalyzed Alkane Conversion by Polyoxometalates

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Conversion of alkanes into chemical building blocks of higher added value represents a major challenge in homogeneous catalysis. Dehydrogenation of alkanes into olefins is a reversible, endothermic reaction with high kinetic barriers associated with C-H bond activations. The aims of this work are to develop robust catalysts: Metala-SiloxPolyoxometalates complexes, to study their redox properties and ability to promote photo-assisted C-H activation through Hydrogen Atom Transfer. The development of such catalysts would allow to couple in a single system the photochemical capacity of the POM to promote HAT in tandem with single electron transfer (SET) chemistries of first row transition metals (Fe and Co).

Kirill Kuznetsov

Novel PDT agents for Synetgetic and Theranostic applications

PhD advisors: Kevin Cariou and Gilles Gasser

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Due to the life-threatening impact of cancer and the growing resistance to clinically used anticancer drugs, searching for new alternative candidates to treat cancers is in progress. Among several clinically used techniques to treat cancers, viz. surgery, chemotherapy, radiation therapy, immunotherapy, etc., photodynamic therapy (PDT) appears as a frequently used and first line of therapeutic option for skin cancer. This is due to the very high spatial and temporal controlled activity with minimal side effects and low proximity of formation of resistance to this type of drug. Therefore, within the framework of the current doctoral project, we decided to obtain compounds of a new type for the purposes of photodynamic therapy.

Francesc Penas

Computational Chemistry of Functionalized MOFs for CO_2 transformations

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The current ecologic transition requires sustainable chemical processes for the transformation of small molecules into more valuable ones, especially in the case of CO_2. The reactivity of Frustrated Lewis Pairs (FLPs) for H_2 splitting and their large potential for the hydrogenation of CO_2, turns them into a good proposal to achieve the requirements mentioned before, while their immobilization inside the pores of Metal-Organic Frameworks (MOFs) allows circumventing the main limitations underlying homogeneous systems. In this PhD project, we will conduct a computational design of FLP@MOF catalysts with optimal activity for CO2 hydrogenation via the analysis and rationalization of the descriptors that describe their reactivity. The experimental group of Dr. Canivet (IRCELYON), will then synthesize, characterize and test the most promising candidate materials.

Yiqian WANG

NanoTheranostic Porphyrins for MRI Imaging, Photodynamic and Photothermal Therapy against Cancer in Preclinics

PhD advisor: Gilles GASSER and Bich-thuy DOAN

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Photodynamic therapy (PDT) is a promising, effective and non-invasive treatment for superficial cancers. It is based on the light irradiation of an injected photosensitiser (PS) generating reactive oxygen species (ROS) that can cause cell death. PTT is an emerging modality for the thermal treatment of cancer, and synergistic when combined with PDT. Alternatively, controlled release of a cytotoxic drug into a tumour can be achieved by a light irradiation such as NIR irradiation of photodynamic or photo thermosensitive compounds. Through many researches we seek to develop a synergy between PDT coupled with PTT based on a new formulation of theranostic agents with antitumor effect in vitro, with imaging features.

Nihal HADJ SEYD

Switchable molecular tweezers for multifunctional systems

Supervised by: Dr Guillaume Vives, Prof Bernold Hasenknopf

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Greatly inspired by biological molecular machines, artificial molecular devices such as motors or switches have been developed throughout the years. These machines produce mechanical movements in response to specific stimuli. Among them, molecular tweezers that can reversibly shift from an open to a closed state depending on the stimulus received. Our group has successfully developed over the past decade a series of switchable molecular tweezers based on coordination stimuli in order to modulate their luminescent, magnetic and catalytic properties. Going a step further away, the elaboration of multifunctional systems could be done by expanding their number of accessible states with the combination of orthogonal stimuli. To reach those multi-state systems, dissymmetric molecular tweezers, based on a terpyridine switchable unit substituted by two different metal-salphen complexes, will be developed. Those tweezers could thus acquire unprecedented luminescent, magnetic or catalytic properties either with the interaction between the two metallic centers or thanks to the orthogonal stimuli.

Zhimei Xiao

Photocatalysis in Living Cells with Earth Abundant Metals for Cancer Therapy

Advisors: Gilles GASSER and Bich-thuy DOAN

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Photodynamic therapy (PDT) is an approved technique which relies on the use of photosensitizers (PSs) that accumulate in certain organs after systemic intravenous injection, but whose cytotoxicity is activated only locally by illumination with low powered laser light. The advantages of PDT over other therapies are therefore the high spatiotemporal control and the low systemic toxicity of the treatment. However, most metal-based PSs contain heavy metals such as Ru, Os, Ir, Pt or Au, which are expensive and non-earth abundant, contrary to first-row transition metals. In this context, the exploration of the photochemical properties of complexes based on first-row transition metals appears to be extremely promising. We envision to further design and synthetize new PDT PS based on cheap and abundant first-row transition metals for optimized photophysical and phototoxic features dedicated to in vivo applications.

Luis CANO-GONZALEZ

Designing New Cell-Penetrating Peptides and Homeoproteins for Therapeutic Applications

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Cell-penetrating peptides (CPPs), some of them being derived from homeoproteins (HPs), constitute a promising approach for the delivery of therapeutic molecules inside living cells. In addition, *Engrailed-2* HP, involved in neuronal survival, has recently been identified as a potential therapeutic target for Alzheimer's disease. The main goal of this PhD project is to design a new generation of CPPs and HPs with improved cell penetration efficiency. We seek to introduce by native chemical ligation (NCL), combining expressed and synthetic fragments, targeted side-chain and/or structural modifications to improve *Engrailed-2* HP therapeutic applications by generating a novel analog capable of entering cells in a more efficient way.

Sarah MEHDI

Peptide inhibitors of RED-SMU1 interaction as a new anti-viral agent against Influenza A viruses using Dynamic Combinatorial Chemistry

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In recent years, the concept of host-directed therapies, has been rapidly expanding. Naffakh *et al* have recently characterized the structure of a human splicing factor, RED-SMU1, which is essential for influenza A virus (IAV) life cycle and investigated this cellular factor as a potential target for IAV therapy. They have shown that disrupting this protein-protein complex allow decreasing the level of endogenous RED-SMU-1 levels, and inhibiting viral mRNA splicing, and viral multiplication while preserving cell viability. Interfering with this complex represents thus a potential strategy for the development of new antiviral therapy. In this project, we wish to downsize the RED protein into a short helical peptide corresponding to RED amino acids 211-222, that retains the target affinity and activity of the whole protein and is embedded with pharmacological properties favorable for its *in vivo* use, particularly cell membrane permeability and stability toward proteolytic degradation. For this purpose, different strategies combining rational design and libraries screening will be explored.

Farah Tazi

Dissecting cell-penetrating peptides systems for cytosolic delivery of therapeutic proteins

PhD advisor: Sandrine SAGAN et Astrid WALRANT

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Delivering biologics into the cytosol would represent a major step to reach the panel of intracellular therapeutic targets. This delivery is limited by the toxicity or the lack of efficiency of current vectors. To overcome those defects in the used systems, many studies took an interest in cell-penetrating peptides (CPP), which are defined as peptides able to internalize into cells and to transport cargo molecules. Many CPP sequences have been identified with different internalization efficacy and mechanisms that are not fully understood. The main objective of the project is to study and compare cell uptake mechanisms of a bispecific protein when conjugated to various types of CPPs, in order to give clues for the design of efficient systems to deliver therapeutic proteins inside cell cytosol. To do so, different CPPs will be conjugated to a nanobody that will be tagged to evaluate the intracellular delivery. The cellular uptake will be assessed using mass spectrometry-based method for absolute quantification and fluorescence-based method for an orthogonal internalization quantification.

Faycel DJEBBAR

Synthesis of iron complexes featuring redox active ligands for catalysis.

PhD advisor: Guillaume LEFEVRE

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This PhD project will be focused on the synthesis and characterization of new iron complexes involving non-innocent coordination frameworks, as well as an unsaturated functional group based on the presence of a main-group element (mostly from groups XIII and XIV). Physicochemical properties of those new species along with their reactivity in organometallic catalysis will be investigated.

Milan INNOCENT

Photoinduced iron-catalyzed decarboxylative reactions

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The objective of this PhD project is to develop alternative visible light-induced decarboxylative reactions based on earth-abundant iron photocatalysts allowing the conversion of simple carboxylic acids into attractive compounds. The success of the project will be based on an original combinatorial approach for the photocatalyst (metal/ligand) selection through the simultaneous recording of multiple absorbance spectra, the measurements of redox potentials and the synthesis of a molecular probe. Several decarboxylative reactions will be optimized for the synthesis of valuable building blocks or the late-stage functionalization of complex molecules. Mechanistic studies of the developed transformations will be conducted.

Hang LI

New Allene bis-Phosphine Ligands. Applications in Catalysis and Materials Sciences

PhD advisor: Louis Fensterbank

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My project is based on the bisphosphine 1,3-bis(diphenylphosphino)-1,3-diphenylallene. Then this project aims at examining new coordination complexes from 1,3-bis(diphenylphos- phino)-1,3-diphenylallene and also exploiting the full potential of the allene gold or rhodium complexes (rac- or enantiopure) for other applications. We will study the ability of these new bis-phosphine allene to coordinate other transition metals. In order to study the reactivity of the new chiral complexes in enantioselective [2+2+2] and cycloisomerization reactions. We also plan to substitute the chloride atom on the gold(I) with alkyne, alkene, arene moieties and study the properties of these new complexes. Coordination chemistry with other metals of these organometallic platforms will be examined. And we will considerer the synthesis of supramolecular assembly by *p*-stacking interactions or based on cation coordination processes.

Ashmi RODRIGUES

Self-adaptative peptidic libraries for protein-protein interaction inhibition

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This project consists in combining two different approaches, *i.e.,* peptide stapling and hot-spots grafting, by the use of dynamic combinatorial chemistry (DCC), allowing the screening of candidates in the context of finding inhibitors for protein-protein interactions (PPI). Thanks to DCC, large libraries of thermodynamically stable constructs can be generated with reversible covalent reactions, *i.e.,* thiol-thioester exchanges. Thus, in presence of a biological target, self-reorganization of the libraries can be observed, leading to the amplification of the best-bound species. This strategy would allow the simultaneous screening of lateral residues of amino acids as well as different tridimensional peptidic structures generated by the use of two sets of orthogonal reactions without facing difficulties related to rational design and synthesis. Therefore, to prove this concept, the project will focus on p53-MDM2 PPI known to play a crucial role in cell apoptosis. So far, promising results were obtained as stapled peptides with linkers of different geometries were generated by DCC through thiol-thioester exchanges.

Océane RONDOT

Design and pharmacological optimization of N,N,N-triacylamines, as kallikrein-8 inhibitors for the treatment of Alzheimer's disease

PhD advisors: BOTUHA Candice ; CORCE Vincent, THORIMBERT Serge

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Alzheimer disease (AD) is a most common progressive neurodegenerative disease with devastating effects on cognition and memory function. About 2 million people suffer from Alzheimer's disease type dementia and 55 million patients worldwide. Currently, there is no treatment nor pre-mortem diagnosis with specificity and selectivity. Recently, studies underlined that kallikrein 8 (KLK-8), a serine protease, would be involved in the development of different pathophysiology associated with this disease. Despite a growing interest in this target, no potential therapeutic inhibitor has been identified to date. The aim of this work is to design and synthetize the first organic KLK-8 inhibitors with high selectivity. In collaboration with the team Adaptation Biologique et Vieillissement at SU, triacylamines (T2A) were identified as promising hit compounds with IC_{50} in a range of submicromolar with modest selectivity. In first assays, we have developed a structure-activity relationship approach using pharmacomodulation on triacylamines to design structural analogs with improved activity.

Valérian LIBERIOUX

Structure-activity of virus-like supramolecular assemblies of cyclodextrins resolved by cryo-EM

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Nature builds beautiful hierarchical architectures such as microtubules, fibrils or viruses having specific roles in the life machinery. These structures precisely engineered by nature are directly linked to their function. In the course of our study on DNA transfection using modified cyclodextrins, our lab has observed micrometric fibers. Through 3D reconstruction of these fibers, the structure appeared to be constituted of a co-assembly of both partners. These modified cyclodextrins are known to form polycationic supramolecular polymers favoring the electrostatic interaction with polyanionic DNA. The assembly displays a controlled diameter, around 6 nm, of various length under a wide array of conditions. We thus propose to study the rules governing the assembly to bring control over the morphology, length, width of these artificial architectures. Such assemblies can be very sensitive to conditions, we thus plan to explore the effect of conditions such as the pH of the solution, the oligonucleotide scaffold or the structure of the cyclodextrin monomer which already exhibits a degree of control. Our goal here is first to elucidate the atomic-scale structure and understand the assembly mechanism of such artificial assemblies using cryo-EM combined to image analysis and 3D-reconstruction. We also wish to characterize the thermodynamic and kinetic aspects of these mechanisms.

Christian CARIÑO

Photoactive polyoxometalate-based molecular hybrids for solar energy conversion

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To effectuate fuel generation from sunlight, artificial photosynthetic devices must reproduce the key steps of photosynthesis in natural systems: light-harvesting, charge separation, charge accumulation, and multielectron redox catalysis. Polyoxometalates (POMs) are attractive candidates for the development of such devices owing to their electron storage properties. When covalently associated to a photosensitizer, the molecular hybrid displays a fast light-induced electron transfer from the chromophore to the POM resulting in a long-lived charge-separated excited states and subsequent charge accumulation in the presence of a sacrificial electron donor. In this thesis, a generation of hybrids of POM and photosensitizing dyes (e.g., bodipy, push-pull dyes) will be developed, and their photophysical properties and photoinduced charge accumulation in solution will be investigated through spectroscopic and electrochemical methods. POM-dye hybrids with anchoring groups will then be grafted onto photocathodes (e.g. NiO, ITO) that will be integrated in a photoelectrochemical device.

Hiba KHELIFA

Morphology-controlled nanomaterials to understand protein corona

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Following exposure to biological fluids, nanomaterials (NM) with a synthetic identity immediately acquire a new identity. In fact, thousands of blood proteins will competitively bind to NM surface leading to the formation of a protein corona. This biological identity completely changes NM properties and critically affects biological outcomes. Among criteria defining synthetic identity, NM morphology was more recently considered as a key attribute to control in vivo behaviors. Understanding of the fundamental mechanisms governing kinetics, composition and conformation of proteins adsorbed on NM with non-spherical morphology have been under-studied. In this context, our project aims to understand all these fundamental mechanisms of protein corona formation not only by handling NM morphology but also 3D dimensions, surface properties and mechanical behaviours, because those parameters are interconnected. This strategy offers insights on the most important parameters involved in the protein corona and will allow accurate prediction of the in vivo fate of NM leading to their rational design.

Fabio MOCCIA

Study of Indolizy ligand coordination and new applications

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To implement gold-catalysed asymmetric synthesis processes, the Pr.Mansuy and Pr.Fensterbank group developed a new family of C-ligands, known as 'Indolizy ligands'. These CAACs (cyclic amino alkyl carbenes) ligands have a chiral centre and a phosphin oxide branch, which can be exploited to limit the degrees of freedom of the system. Moreover, they are rapidly obtained by gold-promoted cyclization of allenepyridine, which directly gives the gold complexes. This project aims to expand the range of these ligands by performing several modifications of the scaffold. In particular, we want to explore the possibility of extending the arm length to evaluate the effect in asymmetric catalysis. Modifications to obtain bifunctional ligands able to complex other TMs is another main goal. The resulting complexes will be tested in gold-promoted asymmetric synthesis.

Adrien TINTAR

Synthesis of active pheromones by organometallic catalysis : development, methodology and applications in flow synthesis

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Public health issues related to environmental problems, particularly pollution and soil persistence, led in recent years to a decrease in the use of so-called conventional plants protection products for the protection of crops and plants. In this context, the development of more eco-friendly solutions for the protection of crops and plants is a major challenge, from a national to an international perspective. Consequently, the M2i development company has specialized in the synthesis and formulation of insect pheromones as eco-friendly pesticides alternatives. The objective of the thesis responds to a simple observation : currently, few methods for the synthesis of pheromonal active agents reported in the literature are suitable at the industrial scale. Taking this into account, this thesis project aims to develop new and more eco-friendly synthetic pathways of insect pheromones that are applicable to the industrial scale. To achieve this goal, this project is centered on iron-catalyzed cross-coupling reactions as key steps, due to the low eco-toxicity and low cost of this metal.

Jingjing REN

Co-immobilization of polyoxometalates and organic cations onto (mesoporous) silica for supported CO_2 cycloaddition onto epoxides

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The objective of this project is to valorise CO_2 by using it as an elementary C1 brick for the formation of (biosourced) cyclic carbonates. One of the most desirable routes to achieve this goal involves a CO_2 cycloaddition onto an epoxide. To reach these objectives, we propose to develop and further immobilize molecular transition-metal substituted polyoxometalates complexes. All the catalysts will be anchored at the surface of silica supports to allow their subsequent recyclings. The anchoring will be obtained by strong ionic interactions using imidazolium or tetraalkylammonium-functionalized silica supports that will avoid their lixiviation during the catalytic process.

Basile WEYL

Heterogeneous catalysis in flow: multicomponent reactions and photochemistry

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The synthesis of fine chemicals is traditionally achieved by discontinuous batch processes, enabling a myriad of transformations and complex bioactive product formation. However, the current environmental awareness and socio-economical stakes call for more sustainable and efficient ways for chemical manufacturing. In this context, continuous-flow chemistry represents a powerful synthetic tool to develop efficient, sustainable and industrially viable transformations under safe conditions. When combined with heterogeneous catalysis and atom-economical reactions, flow chemistry becomes an ideal strategy to achieve waste-limited reactions enabling telescoped multistep processes without need for purifications of intermediates.

Caitlan Vervisch

Impact of redox modulation on the fate of Pt anticancer drugs and tumor targeting using extracellular vesicles

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Oxaliplatin, a Pt(II)-based anticancer agent is widely used for colorectal cancer despite severe side effects and the emergence of resistance. Platinum tissue distribution, the sites of intracellular accumulation and their roles in the therapeutic effects and resistance still uncertain. Some metallic salts can mineralize in the form of nanoparticles in the lysosomes of the exposed cells in a process that involves key regulators of the intracellular redox state. Such redox-modulated intracellular transformations might profoundly impact their therapeutic activity and systemic toxicity. In addition, the major dose-limiting adverse side effect of oxaliplatin (peripheral neuropathy) is linked to the oxidative burst generated when oxaliplatin is applied. The use of redox modulator (as Manganese Super Oxide Dismutase mimics) may prevent the appearance of peripheral neuropathy induced by oxaliplatin without affecting its antitumor activity. Therefore, my PhD project is to unravel the interplay between oxidative stress, the role of redox regulators, intracellular Pt-mineralization and anticancer therapeutic activity of Pt drugs.

ROUX Arthur

Studying the interaction between Polyoxometalates and Amyloid peptides in the context of Alzheimer's disease and Diabetes

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The formation of Amyloid β peptide aggregates has clearly been identified as a key feature of Alzheimer's disease, although its exact role in the development of this pathology has not been clearly deciphered so far. This aggregation results from a very complex interaction process involving monomers, soluble oligomers and solid fibrils. The intermediates species (soluble oligomers) are proposed to be the most toxic forms for the brains. To better understand this mechanism, we are studying Polyoxometalates (POMs) as aggregation modulator agents. POMs or molecular oxides are stable inorganic, highly soluble and tuneables nanomolecules. They can have different geometries and sizes ranging from tenths of nanometers to a few nanometers for nano wheels. POMs have recently started to be studied for their influence on peptide aggregation.

Huiyin LIU

Magnetic Molecularly Imprinted Polymers in Organic Synthesis: From Standard to Dynamic Kinetic Resolution

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Enantiomers, despite their identical chemical formulation and structure, often exhibit different biological activities or toxicology profiles *in vivo*. This is why it is important to collect the enantiomer of interest from its chiral mixture. In this context, our work aims to develop an efficient method based on a stepwise conversion of enantiomers using magnetic molecularly imprinted polymers (MIPs). Indeed, MIPs are the sorbents with the ability to recognize a given molecule. Magnetic MIPs are obtained by implementing its polymerization on the surface of Fe_2O_3 nanoparticles, which allows the recycle and reuse of MIPs using a magnet. The target enantiomer can thus be selectively adsorbed on the MIP from a racemic mixture. Thereupon, racemization of the other remaining enantiomer allows to reproduce the racemic mixture, leading to its complete conversion to the target enantiomer through the cycle of adsorption and racemization steps.