

DOCTORAL WORKSHOP PhD IN CHEMISTRY

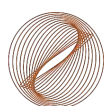
Scientific program and Book of abstracts

May 29 – 30th and June 2nd, 2023

Sala d'Actes
Faculty of Sciences

Department of Chemistry

UAB
Universitat Autònoma
de Barcelona



Facultat
de Ciències
UAB





WELCOME TO THE XII DOCTORAL WORKSHOP OF THE PHD PROGRAM IN CHEMISTRY

May 29 – 30th and June 2nd, 2023

It is our great pleasure to welcome you to the new Edition of the Doctoral Workshop of the PhD programme in Chemistry that is organized by the UAB's Department of Chemistry.

This year's workshop continues its tradition of providing supportive environment for doctoral students to present and discuss their dissertation with peers, members of the program and other experienced researchers, with the aim to strengthen the links and facilitating the exchange of research experiences and new ideas in the fields of entrepreneurship and small business.

During the event, 26 PhD students will have an excellent opportunity to share their projects. The Doctoral Workshop will also include an exciting series of plenary lectures given by international experts.

All the members of the PhD program in Chemistry and related programs, as well as other members of the research community are more than welcome.

We look forward to your participation in this event.

The Organizing Committee



Organizing, Scientific and Awards Committee:

Prof. Gregori Ujaque, Department of Chemistry, UAB.
Prof. Félix Busqué, Department of Chemistry, UAB.
Prof. Xavier Sala, Department of Chemistry, UAB.
Prof. Daniel MasPOCH, Catalan Institute of Nanoscience and Nanotechnology (ICN2)
Prof. Mireia Baeza, Department of Chemistry, UAB.
Prof. Rosario Núñez, Institute of Materials Science of Barcelona (ICMAB-CSIC)
Arnau Comajuncosa, PhD Student.
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Event sponsored by:

Real Sociedad Española de Química (RSEQ) – Secció Catalana de la RSEQ
Societat Catalana de Química (SCQ)



INVITED SPEAKERS

Prof. Javier García Martínez, IUPAC President
University of Alicante



President of the International Union of Pure and Applied Chemistry (IUPAC). Previously he served as vice president of the Division of Inorganic Chemistry and as a member of the IUPAC Executive Committee and Bureau <https://iupac.org/>

President of the Young Academy of Spain, which brings together 40 of the most talented young researchers in the country and works to promote science, research and innovation in Spain <https://academiajoven.es/>

Professor of inorganic chemistry and director of the Molecular Nanotechnology Laboratory, a research center

that works on the synthesis and application of nanostructured materials for the sustainable production of chemical products and energy at the University of Alicante, <http://nanomol.es/en/home/>

Since 2019, Rafael del Pino Professor and Director of the report 10 Technologies to Promote Spain. This work, which is published annually, identifies, explains and puts into context the 10 technologies that, in the opinion of a panel of experts, are key to improving the competitiveness of the Spanish productive sector.

Founder of Rive Technology, a technology-based company that markets nanostructured catalysts that significantly reduce CO₂ emissions while increasing energy efficiency. In 2019, W. R. Grace acquired this technology and now markets it globally <https://grace.com/industries/refining-technologies/fcc-catalyst-application/>

Founder and President of Celera, a talent acceleration program that supports and provides resources and mentorship to 10 young members each year. 80 young people have already benefited from this program. They have financed more than 10 companies valued at 500 million dollars and are mentoring other young people <https://www.acelerame.org/>

Contributions to chemistry, catalysis, and sustainable energy generation have been recognized with some of the most prestigious awards including King James I Award in 2014, Kathryn C. Hach Award for Best Entrepreneur in the Chemical Sector by American Chemical Society in 2018 is a Fellow of the Royal Society of Chemistry and the American Chemical Society and a Member of the Emerging Technologies Council of the World Economic Forum <https://www.weforum.org/agenda/authors/javier-garcia-martinez>

Information on: <http://nanomol.es/en/home/>

Prof. Katherine Villa , Group Leader
Institute of Chemical Research of Catalonia (ICIQ)



Dr. Villa obtained her PhD in Chemistry from the UAB. Then, she worked at the Catalonia Institute for Energy Research (IREC) and at the Institute for Bioengineering of Catalonia (IBEC). In 2018 she joined the Advanced Functional Nanorobots center at the University of Chemistry and Technology (Czech Republic). Since 2021, she is leading a research group on advanced photocatalytic materials for energy and environmental applications at the Institute of Chemical Research of Catalonia (ICIQ). She has received important recognitions such as the RSEQ Award 2023 for Young researchers (group leader) as well as competitive funding including an ERC Starting Grant 2022. Her research interests include photocatalysis, nanomaterials, renewable energy, micro/nanomotors, and environmental remediation.

Information on: https://www.iciq.org/research/research_group/dr-katherine-villa/

Prof. Ben Feringa, Nobel Prize in Chemistry
University of Groningen



Ben L. Feringa obtained his PhD degree at the University of Groningen in the Netherlands under the guidance of Professor Hans Wynberg. After working as a research scientist at Shell in the Netherlands and the UK, he was appointed lecturer and in 1988 full professor at the University of Groningen and named the Jacobus H. van't Hoff Distinguished Professor of Molecular Sciences in 2004. In 2008 he was appointed Academy Professor and was knighted by Her Majesty the Queen of the Netherlands. Feringa's research has been recognized with a number of awards including the Koerber European Science Award (2003), the Spinoza Award (2004), the Norrish Award of the ACS (2007), the Paracelsus medal (2008), the Nagoya gold medal (2013), ACS Cope Scholar Award 2015, Chemistry for the Future Solvay Prize (2015), The 2016 Nobel prize in Chemistry and the Euchems gold medal.

Feringa's research interest includes stereochemistry, organic synthesis, asymmetric catalysis, molecular switches and motors, self-assembly, molecular nanosystems and photopharmacology.

Information on: <http://www.benferinga.com/>



SCIENTIFIC PROGRAM

May 29th

09:30–09:45 Welcome and opening

09:45—10:45 Plenary Lecture

Chair: Gregori Ujaque

**Title: Chemistry beyond the Valence Shell
Prof. Javier García Martínez**

10:45— 11:45 Poster session and coffee break

11:45 - 13:00 Presentation's Session I

Chair: Xavier Sala

- 11:45-12:00** Machine Learning to Predict Adsorption Energies and Interatomic Potential Development. Usuga, Andrés Felipe 1.1
- 12:00-12:15** New plant-based nanovesicles based on alkyl polyglucosides surfactants and β -sitosterol as topical drug delivery Systems. Alcaina Hernando, Marta. 1.2
- 12:15-12:30** Polymerization of Porous Molecular Cages Through Covalent Chemistry: Synthesis, Functionalization, and Applications. Khobotov Bakishev, Akim. 1.3
- 12:30-12:45** Metal-Based Nanomaterials as Photo/Electro-Catalysts for Hydrogen Evolution Reaction and Intracellular Catalysis. Hou , Heting. 1.4
- 12:45-13:00** Industrial Process Development to Manufacture a Highly Potent Active Pharmaceutical Ingredient. Miranda Salinas, Ronnie Andres. 1.5

13:00 - 15:00 Break

15:00 - 16:00 Presentation's Session II

Chair: Mireia Baeza

- 15:00-15:15** Computational studies and developments for chemical glycobiology: an overview of results and current developments. Fernández-Luengo Flores, Xavier. 2.1
- 15:15-15:30** Cerium-doped Magnetite Nanoparticles: Synthesis, Characterization and Catalytic Activity. Mejía Carmona, Karen Stefanie. 2.2
- 15:30-15:45** Functionalized silica nanostructures and cotton fabrics for topical biomedical applications. Liu, Ming. 2.3
- 15:45-16:00** New sensors based on microelectronic technologies for cell culture monitoring. Moreno Díaz, Alexandre. 2.4

16:00 - 16:30 Break and poster session

16:30 - 17:30 Presentation's Session III

Chair: Félix Busqué

- 16:30-16:45** Synthesis of phosphorus dendrimers for applications in green solvent catalysis. Cejas Sánchez, Joel. 3.1
- 16:45-17:00** DELOS nanovesicles-based hydrogels as promising subcutaneous drug delivery systems. Castellar Alvarez, Carla. 3.2
- 17:00-17:15** Towards the photocontrol of biological activity under two-photon excitation with near-infrared light. Gómez Ventura, Marc.. 3.3
- 17:15-17:30** Multiscale Modelling of Heterogeneous Catalysts for CO₂ Conversion. Díaz López , Estefanía. 3.4



May 30th

09:30 - 10:45 Presentation's Session IV

Chair: Jose Maria Muñoz

- 09:30-09:45 Screening of a Feasible Synthetic Route for an API-A. Fazio Zalányi, Zeno. 4.1
- 09:45-10:00 Catalytic activity of Cu/Mo2CTx: hydrogenation of CO₂ and CO to methanol. Vidal López, Anna. 4.2
- 10:00-10:15 Microanalyzers' development for tracking key compounds in biotechnological processes for contaminants revalorization. Paré Estalella, Franc 4.3
- 10:15-10:30 Selenium biofortification of Wheat Plants by Foliar Application of liposomes. Viltres Portales, Marcia. 4.4
- 10:30-10:45 Development of a Portable Paper-Based Electrophoretic Bioassay with Simultaneous Electrochemical Readout. Maroli , Gabriel. 4.5

10:45 - 12:00 Poster session and coffee break

12:00 - 13:15 Presentation's Session V

Chair: Rosario Núñez

- 12:00-12:15 Catalysis in supercritical CO₂ with asymmetrically functionalized phosphorous dendrimers. Petriccone, Massimo. 5.1
- 12:15-12:30 Switchable MOP solubility through surface chemistry: engineering molecular self-sorting systems. Hernández López, Laura. 5.2
- 12:30-12:45 Green synthesis and processing of CaSyr-1 bioMOF: a potential drug delivery system with intriguing triple bioactivity. Rosado Morente, Albert. 5.3
- 12:45-13:00 Dithienylethene-based photoswitchable phosphines for in situ modification of catalysts. Sherstiuk, Anastasiia. 5.4
- 13:00-13:15 Novel bifunctional ligand scaffolds for stable and inert complexes as PET imaging contrast agents. Torralba Maldonado, Daniel. 5.5

13:15 - 15:30 Break

15:30 - 16:15 Presentation's Session VI

Chair: Carolina Gimbert

- 15:30-15:45 Se-biofortified microgreens as functional foods: phytochemical profile, bioactive properties, and Se speciation. García Tenesaca, Marilyn Mishelle. 6.1
- 15:45-16:00 Application of scale-up methodologies into industrial pharmaceutical processes. Suriñach Ros, Amando. 6.2
- 16:00-16:15 Theoretical Investigation on the Catalytic Performance of Pt₃Mn Alloys in Propane Dehydrogenation to Propylene. Zhang , Wenjuan. 6.3

16:15 - 16:45 Break and poster session

16:45 - 17:45 Plenary Lecture

Chair: Jose Peral

Title: Light-driven photocatalytic micromotors based on single-component semiconductors
Prof. Katherine Villa

17:45 - 18:00 Award ceremony

Doctoral Workshop 2023 distinguished Diploma, along with a gift, will be given to the two best Poster & Presentation.



June 2nd

12.00 - 13:00 Plenary Lecture

Chair: Daniel Maspoch

Title: The Art of Building Small: from molecular switches to motors
Prof. Ben Feringa

Included within 2023 Manuel Cardona Lecture Series organized by the Catalan Institute of Nanoscience and Nanotechnology (ICN2).



13:00 - 13:15 Closing ceremony



Venue:

Plenary Lectures and PhD students' presentations: in the Auditorium of the Faculty of Sciences (*Sala d'Actes*).

Posters' Exhibition: in the Hall on the ground floor of the Faculty of Sciences (in front of *Sala de Graus I*).



ABSTRACTS

INVITED TALKS

Chemistry beyond the Valence Shell

Prof. Javier García Martínez

President of the International Union of Pure and Applied Chemistry, IUPAC

Chemistry plays a crucial role in tackling some of the most pressing global issues, including climate change, environmental degradation, resource depletion, and public health. While the study and manipulation of nature on a molecular level are central to these efforts, the impact of chemistry extends far beyond the laboratory. [1-2]

To fully leverage the potential of chemical research, it is essential to foster collaboration with other fields and disciplines while to fully realize its potential, new technologies should be made accessible through licensing or start-ups that can accelerate the translation of research findings into practical solutions. [3] Improving chemistry efficiency alone is not sufficient; we must fundamentally change the way we think, teach, and practice chemistry. [1] The current linear model of extraction, transformation, and emission is not sustainable and has negative consequences on the environment. During my presentation, I will highlight the concept of circular chemistry, which aims to convert waste into raw materials through sustainable practices. By prioritizing sustainability in the design of molecules and processes, rather than in recycling at the end of the process, circular chemistry reduces waste and minimizes environmental impact. (Figure 1).

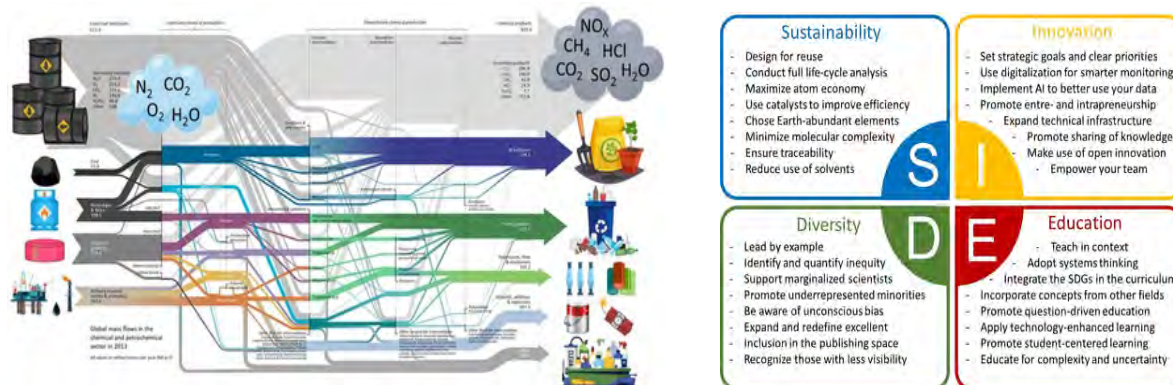


Figure 1. The Sankey diagram showing mass flow in the chemical and petrochemical sectors (left) and the SIDE vision for Chemistry 2030 comprising a series of recommendations aimed at moving towards more sustainable chemistry (right). From reference [1]

Furthermore, I will comment on how chemistry can contribute to addressing urgent global issues, including climate change, resource scarcity, and food security. Through cutting-edge research in chemistry, artificial intelligence, and new materials, we can unlock immense possibilities for achieving the Sustainable Development Goals.

Specifically, I will present some advances in heterogeneous catalysis applied to sustainable chemistry that allows toxic reagents to be replaced by more benign alternatives, eliminate the need for solvents, and allow for milder synthesis conditions while improving conversion and selectivity toward the formation of complex molecules (Figure 2). [4-5]

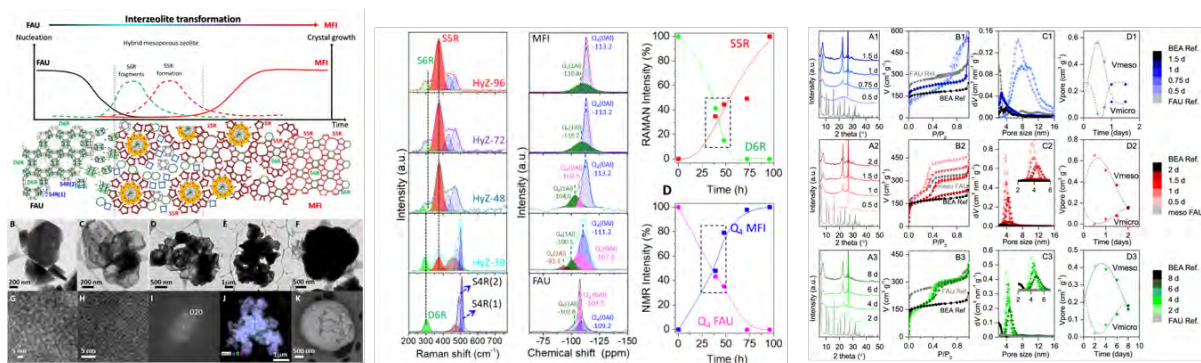


Figure 2. Characterization by transmission electron microscopy, Raman spectroscopy, and ^{29}Si NMR, and N_2 adsorption at 77 K of heterogeneous catalysts built via zeolite interconversion. From references [4-5]

Finally, I will present various activities led by IUPAC to promote scientific education, research, and international collaboration among scientists, academics, and industry professionals worldwide. Currently, IUPAC supports over 180 international projects, with many focused on sustainability and environmental protection. [6] These initiatives aim to encourage the use of renewable energy and promote the adoption of more sustainable practices in the chemical industry. Through these and other resources, IUPAC facilitates collaborative research and innovation that can advance scientific knowledge and address global challenges. By promoting international cooperation, we can foster the development of new technologies, materials, and processes that are more sustainable and contribute to a better future for all. [7]

References:

- [1] J. García-Martínez, *Angew. Chem. Int. Ed.*, **2021**, 60, 4956-4960
- [2] F. Gomollón-Bel, J. García-Martínez, *Nature Chemistry* **2022**, 14(2), 113-114
- [3] E. Li, J. García-Martínez, *Chemistry Entrepreneurship*, Wiley-VCH, **2021**
- [4] M. J. Mendoza-Castro, Z. Qie, X. Fan, N. Linares, J. García-Martínez, *Nature Communications* **2023**, 14, 1256-1260
- [5] M. Mendoza-Castro, E. De Oliveira-Jardim, N.T. Ramírez-Márquez, C. A. Trujillo, N. Linares, J. García-Martínez, *J. Am. Chem. Soc.* **2022**, 144(11), 5163-5171
- [6] J. García-Martínez, *Chemistry International*, **2022**, 44(1), 2-4
- [7] System Thinking for Education and Nature Sustainability <https://iupac.org/systems-thinking-for-education/>



Light-driven photocatalytic micromotors based on single-component semiconductors

Dr. Katherine Villa

Institute of Chemical Research of Catalonia (ICIQ),
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In recent years, there has been a growing interest in light-driven photocatalytic micromotors. This is mostly due to their fast motion activation under light stimuli, notable speeds, and remarkable chemical stability.^[1] The first part of this talk will focus on the fundamental principles of self-propelled photocatalytic micromotors. Then, the different approaches for diminishing the fabrication costs and enhance the synthesis yields will be presented as well as our efforts to design efficient visible-light-responsive micromotors.^[2,3] The capabilities of these micromotors to interact with the surrounding environment, *e.g.*, metal ions, microorganisms, and passive particles will be discussed. The versatility and potential of these photoactivated micromachines for removing microbial and chemical contaminants from liquid and solid matrixes under visible-light irradiation will be demonstrated as well.^[4-5] These approaches based on multifunctional photoresponsive micromotors hold promising applications in the fields of photocatalytic disinfection, water treatment, and the food industry.

References:

- [1] **K. Villa**, *et al.* Chem.Soc. Rev. **2019**, 48, 4966-4978.
- [2] **K. Villa**, *et al.* ACS Nano **2018**, 12, 12482–12491.
- [3] **K. Villa**, *et al.* ACS Nano **2019**, 13, 8135-8145.
- [4] **K. Villa**, *et al.* Chem. Eur. J. **2020**, 26, 3039-3043.
- [5] X. Yuan, *et al.* Small **2023**, 2207303.



The Art of Building Small **from molecular switches to motors**

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Beyond the current frontiers of chemical sciences there is vast uncharted territory to control dynamic function based on molecular and supramolecular approaches. Taking inspiration from Nature's design, the creative power of synthetic chemistry provides unlimited opportunities to realize our own molecular world as we experience every day with products ranging from drugs to displays. In the art of building small we explore the fascinating field of molecular nanoscience. Among the major challenges ahead in the design of complex artificial molecular systems is the control over dynamic functions and responsive behaviour. A major goal is to gain control over translational and rotary motion. The focus is on my journey in the world of molecular switches and motors creating opportunities for smart drugs, adaptive catalysts or responsive materials.

Information on <http://www.benferinga.com>



ABSTRACTS

PHD STUDENTS



Machine Learning to Predict Adsorption Energies and Interatomic Potential Development

1.1

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One strategy to mitigate CO₂ emissions is its conversion in the hydrogenation process, where Cu-based catalysts are the reference materials. However, finding the relation between the catalyst's nature and activity is challenging, hampering the design of better catalytic materials. Moreover, the dynamics of complex heterogeneous catalysts, such as Cu-based materials are rarely considered in the simulations, but even pure Cu-based catalysts undergo critical atomic transformation under H₂/O₂ atmospheres [1]. To that aim, in this talk, we will focus on both aspects aided by ML approaches. On one side, we will work on developing ML algorithms to predict adsorption energies on Cu-based bimetallic surfaces. The adsorption energy is a crucial parameter to screen catalytic materials but is costly to obtain at the DFT level. On the other side, we will present our work on developing interatomic potentials based on ML models to perform long-timescale dynamic simulations with DFT accuracy.

The first part of the talk will describe our work developing ML-based models to predict the adsorption energies of C, OH, and H among others on several facets of Cu-based bimetallic alloys, combined with elements such as Fe, Ni, Ru, Rh, and Ga among others. We start by presenting the workflow used to generate a database based on DFT calculations. Then we will show the best-performing ML model, an ExtraGradient Boost algorithm with a tree regressor. We used features that only require calculating properties related to the adsorption site for the clean surface and the free gas-phase adsorbate. The model gives a Mean Standard Error (MSE) of 0.012 and 0.307 eV for the train and test sets, respectively. Currently, we are working on improving the ML algorithm's performance further.

The second part of the talk will show our work in developing interatomic potentials for Cu-based systems based on a neural network (NN) architecture to predict the local energy. Here, we used the DeepMD-kit [2] package to design the potential, using a descriptor for the NN based on the local interaction for every atom, mapping atomic configuration that embeds the distances and angles between two or three atoms. The database is composed of a set of ab initio molecular dynamics simulations for a Cu nanoparticle that exposes (111), (100), and (211) phases. The total energy prediction is better for the angular descriptor. The Root-Mean-Square-Error (RMSE) of the test set for the total energy and forces were 0.003 eV and 0.125 eV/Å respectively, better than typically reported potentials [3].

Keywords: DFT, Machine Learning, bimetallic alloys, adsorption energy.

References:

- [1] Cao, J. et al. Nat. Commun. 11, 3554 (2020).
- [2] Wang, H. et al. Comput. Phys. Commun. 228, 178 (2018)
- [3] Smith, J. et al. Nat. Commun. 12, 1257 (2021).

New plant-based nanovesicles based on alkyl polyglucosides surfactants and β -sitosterol as topical drug delivery systems

M. Alcaina-Hernando^{1,2}; I. Malvacio¹; I. Ferraboschi³; S. Pescina⁴; L. Ferrer¹; S. Sala¹; C. Sissa³; N. Ventosa^{2,5}; A. Córdoba^{1*}

¹ Nanomol Technologies S.L, Bellaterra, Spain; ² Institut de Ciència de Materials de Barcelona (ICMAB-CSIC), Bellaterra, Spain; ³ ADDRes Lab, Department of Food and Drug, University of Parma, Parma, Italy; ⁴ Department of Chemistry, Life Science and Environmental Sustainability, University of Parma, Parma, Italy; ⁵ Centro de Investigación Biomédica en Red de Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, Bellaterra, Spain

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Most of the delivery systems (DSs) used in healthcare are not suitable for vegan consumers or patients, so there is the need of new DSs. We present here for the first time a new platform of nanovesicles (NVs) formed by self-assembly of β -Sitosterol (Sit) and alkyl polyglucosides, biodegradable and biocompatible components from vegetal origin, that can integrate a large variety of hydrophobic and hydrophilic payloads and deliver them topically.

These new NVs were formulated combining Sit and alkyl polyglucosides using DELOS technology, a sustainable production method based on compressed fluids [1,2]. Their physicochemical properties were studied: size, PDI, surface charge (DLS-ELS), morphology (CryoTEM and SAXS), and stability. For the first time, small unilamellar NVs were produced using Sit and Lauryl Glucoside (LGL) (1:1) as membrane components (size 217 ± 11 nm, PDI 0.22 ± 0.01) (Fig. 1) [3]. Addition of negatively charged surfactants, such as Lauryl Glucose Carboxylate (LGC), enabled to tune the surface charge of the NVs from -40 mV to -70 mV. NVs composed by Sit:LGL:LGC (1:0.8:0.2) (size 182 ± 9 nm, PDI 0.22 ± 0.01) were used to test their loading capacity with α -Tocopherol (TCP). They were successfully produced presenting similar physicochemical properties (size 131 ± 4 nm, PDI 0.19 ± 0.01) and maintaining the antioxidant capacity of TCP after encapsulation. Furthermore, In vitro assays with reconstructed human epidermis showed that the novel delivery platform is compatible with the skin and non-irritant. Finally, skin penetration in porcine ear explants was determined with multiphoton microscopy showing that the NVs can penetrate down to epidermis.

To summarize, a new drug delivery platform has been developed, using plant-derived ingredients that self-assemble in stable small unilamellar NVs [3]. This novel delivery platform is completely biocompatible with the skin and can help to the retention of loaded actives in the epidermis, important characteristics for topical delivery applications in pharma and cosmetics. Thus, it will cover an unmet need for vegan patients and consumers.



Figure 1. Schematic representation of the new DELOS-NVs and their composition.

Keywords: Delivery Systems; Nanovesicles; Plant-based components; Healthcare; DELOS technology

References:

- [1] Cabrera I, et al. Nano lett. 2013: 3766-3774
- [2] J. Merlo-Mas, et al. J. Supercrit. Fluids. 2021: 105204
- [3] European Patent, Application Number: EP22382751.0. A. Córdoba. (03 August 2022)

Polymerization of Porous Molecular Cages Through Covalent Chemistry: Synthesis, Functionalization, and Applications

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Metal-Organic Polyhedra (MOPs) are becoming a powerful building block for the synthesis of porous extended networks. [1] To date, most of these networks are formed by the polymerization of MOPs through coordination bonds with additional ligands. [2] With this strategy, however, the resulting materials usually have modest mechanical properties, and all their metal-open sites are saturated. In this Doctoral Workshop, I will present that the polymerization of MOPs can also occur through reversible covalent chemistry to form macroscopic gels and aerogels (Figure 1). The resulting aerogels are robust, porous, and stable under immersion in water. Another novelty of our strategy lies in the possibility of post-functionalizing the aerogels through coordination chemistry, allowing the modification of their macroscopic properties. I will show how we have taken advantage of the versatile nature and stability of our aerogels to develop a new modular adsorbent for the capture of pollutants in water.

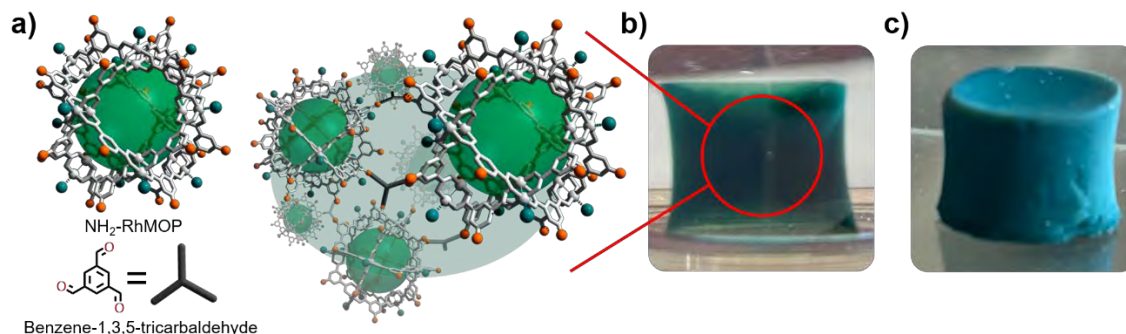


Figure 1 a) Schematic representation of covalent polymerization of MOPs to give b) gels and c) aerogels.

Keywords: Aerogels, Metal-Organic Polyhedra, Post-Synthetic Modification.

References:

- [1] A. Khobotov-Bakishev, L. Hernández-López, C. von Baeckmann, J. Albalad, A. Carné-Sánchez, D. Maspoch. *Adv. Sci.* **2022**, 9, 2104753
- [2] A. Carné-Sánchez, G. A. Craig, P. Larpent, T. Hirose, M. Higuchi, S. Kitagawa, K. Matsuda, K. Uruyama, S. Furukawa. *Nat. Commun.* **2018**, 9, 2506.

Metal-Based Nanomaterials as Photo/Electro-Catalysts for Hydrogen Evolution Reaction and Intracellular Catalysis

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Ultrasmall metal-based nanoparticles display an extremely high surface area to volume ratio and are excellent candidates for catalytic and biomedical applications. [1] The size, shape, structure, homogeneity, and surface properties of the nanoparticles are key characteristics for their activity and stability. [2] The organometallic approach allows to obtain ultra-small metallic nanoparticles with high homogeneity in size and shape, defined structures, and controlled surface state. [3]

In the present work, we present new materials based on isolated Ru NPs stabilized by pyridine ligands (Figure 1 left) and Pt nanoparticles supported onto the surface of carbon nitride (Figure 1 middle) used as photocatalysts. Both have been extensively characterized and used as hydrogen evolution catalysts. Additionally, Pt NPs prepared by the organometallic approach and stabilized with triglycine, have been used as intracellular catalysts for the deprotection reaction of anticancer pro-drugs (Figure 1 right).

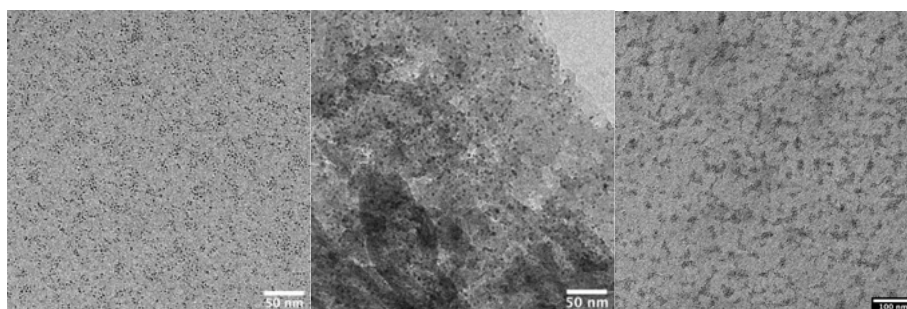


Figure 1. Ru NPs stabilized by pyridine-derived ligand (left), Pt NPs supported onto carbon nitride (middle), and Pt NPs stabilized by triglycine(right).

Keywords: organometallic approach, HER, electrocatalysts, photocatalysts, anticancer.

References:

- [1] Creus, J.; De Tovar, J.; Romero, N.; García-Antón, Jordi.; Philippot, K.; Bofill, R.; Sala, X.; *Chem. Sus. Chem.* **2019**, 12, 2493-2514.
- [2] G. Martí, L. Mallón, N. Romero, L. Francàs, R. Bofill, K. Philippot, J. García-Antón, X.r Sala, *Adv. Energy Mat.* **2023**, 2300282.
- [3] Amiens, C.; Ciuculescu-Pradines, D.; Philippot, K.; *Coord. Chem. Rev.* **2016**, 308, 409-432.



Industrial Process Development to Manufacture a Highly Potent Active Pharmaceutical Ingredient

1.5

R. Miranda; A. Corominas; B. López; I. Lloveras; H. Camps; P. Bayón.

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Commercializing new drugs is an extremely costly and time-consuming investment for a pharmaceutical company. The optimization of drug manufacturing has become critical for the commercial success of these high added-value products. The scope of this project is the development of a manufacturing process to commercial scale of a well-known API to be sold as a generic.

With the pass of the years, the pharmaceutical industry has developed more and more targeted therapies. Regarding small molecules, the active pharmaceutical ingredients (APIs) that show a very highly selectivity for its pharmacological target and exhibit a biological activity at extremely low concentrations, are known as Highly Potent APIs (HPAPIs).

The synthesis of our target HPAPI starts with the nucleophilic addition of the Grignard reagent prepared from an aryl halide to a nitrile imidazole derivate to afford, after acidic hydrolysis, the corresponding ketone. The ketone is subsequently alkylated and the tertiary alcohol formed is dehydrated to obtain the corresponding alkene. The alkene is asymmetrically hydrogenated to the enantioenrich alkane which is further purified as a diastereomeric salt with a enantiopure chiral acid as a resolution agent. The enantiopure alkane is then crystalized as a hydrochloride salt to obtain the desired HPAPI.

The 3 main improvement of this work are the following:

1. Establishment of new conditions to synthetize the Grignard reagent and the nucleophilic addition to the nitrile, reducing costs, impurities and gaining yield and robustness. Safety issues are also studied and evaluated along these part of the study.
2. New hydrogenation conditions are proposed by changing the substrate to be hydrogenated. All other parameters involved in the hydrogenation regarding enantioselectivity are also studied and a new catalytic system is proposed.
3. New resolution conditions are proposed by eliminating the derivatization with an enantiopure chiral acid. This type of purification has not been reported before for this product and the mechanism throw which the resolution takes place is under current study.

The product obtained after the hydrogenation (racemic or enantiopure) is a HPAPI so the handling during the bench work must be carefully done in order to reduce exposure to the product. These considerations will be extended to the manufacturing process to be design.

Keywords: HPAPI, asymmetric synthesis, chiral resolution, Grignard reaction.



Computational studies and developments for chemical glycobiology: an overview of results and current developments

2.1

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The objectives of this thesis are twofold: the development of computational tools that aid the research of complex macromolecular systems and the application of wide array of computational techniques to glycobiological systems to elucidate mechanistic insights.

The development part consists of the programming of a multi-objective genetic algorithm, Gaudi2, which will be the successor of GaudiMM [1], a computational tool developed within JD Maréchal's group. The improvements made to the former GaudiMM are the implementation of an upgraded genetic algorithm, the optimization of the code and the addition of many objectives that include metal docking, NMR constraints, glycan specific score functions, etc. This platform allows for a novel and exhaustive exploration of the solution space for a given docking problem, using a variety of evaluators and modifiers to tailor the solving approach that better suits the system of study.

The applied part consists of the thorough study of glycobiological systems of interest. First, the computational study of a wild-type barley GH3 β -glucosidase protein and two of its mutants, including substrate and product diffusion. Glycoside hydrolases, found essentially in all domains of life, catalyze the hydrolysis of glycosidic bonds. A remarkable conclusion drawn from a recent collaboration with M. Hrmova's group [2], was that barley GH3 β -glucosidase may use a substrate-product assisted mechanism in which the hydrolysed product exits the active site through a newly-discovered cavity different from the one by which the substrate enters, which could be proved during our study [3]. As part of the analysis, we used the modeling tool Gpathfinder developed by the group of JD Maréchal to study product exit pathways [4]; molecular dynamics with AMBER force fields and Gaussian accelerated Molecular Dynamics (GaMD) to explore the conformational space and behavior of the protein under different time scales and with different substrates/products bound.

Secondly, a highly efficient di-C-glycosyltransferase (GgCGT) was discovered from the medicinal plant *Glycyrrhiza glabra*. GgCGT catalyzes a two-step di-C-glycosylation of flopropione-containing substrates with conversion rates of >98% [5] This project was conceived to elucidate the catalytic mechanisms of GgCGT, using the newly obtained crystal structures of GgCGT complexed with various glucose donors and an ensemble of computational techniques such as cMD, GaMD, docking and QM/MM. Currently, this is a work in progress and we have been able to thoroughly explore the dynamics of the enzyme and we are delving into the QM/MM analysis of the system.

Keywords: Chemical Glycobiology, Genetic Algorithm, Molecular Dynamics, QM/MM, Docking

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Cerium-doped Magnetite Nanoparticles: Synthesis, Characterization and Catalytic Activity

2.2

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Magnetic iron oxide nanoparticles (MNPs), particularly magnetite and maghemite NPs, have attracted significant interest because of their potential applications in catalysis, biomedicine, and environmental remediation [1]. The magnetic and chemical properties of MNPs, and consequently, their applications, are highly dependent on their size, morphology, atomic composition (such as doping) and surface [1,2]. Most synthetic magnetite is produced through the fast aqueous co-precipitation of Fe^{2+} and Fe^{3+} ions, where control over nucleation and growth is difficult to achieve and generally yields small Fe_3O_4 NPs (sub-20 nm). Herein, we present a co-precipitation method for synthesizing Fe_3O_4 NPs in the presence of a cerium-citrate complex, which allows size control of Fe_3O_4 NPs through lanthanide doping. By adjusting the cerium concentration, Cerium-doped Fe_3O_4 NPs of different sizes (9 – 46 nm) were obtained in aqueous media at room temperature. The cerium-doped Fe_3O_4 NPs were successfully characterized using high-resolution scanning transmission electron microscopy (HR-STEM), powder X-ray diffraction (XRD), X-ray photoelectron spectroscopy (XPS), and magnetometry analysis. The versatility of this synthetic procedure was demonstrated by expanding the use of other lanthanide ions for magnetite doping, thereby demonstrating its capability to obtain similar MNPs. Finally, the obtained Cerium-doped Fe_3O_4 NPs were tested as catalysts for mimicking peroxidase activity in the oxidation of 3,3',5,5'-tetramethylbenzidine (TMB) by H_2O_2 [3]. The synthesis was simple and adaptable for preparing lanthanide-doped Fe_3O_4 NPs of different sizes, demonstrating its potential for a wide range of applications.

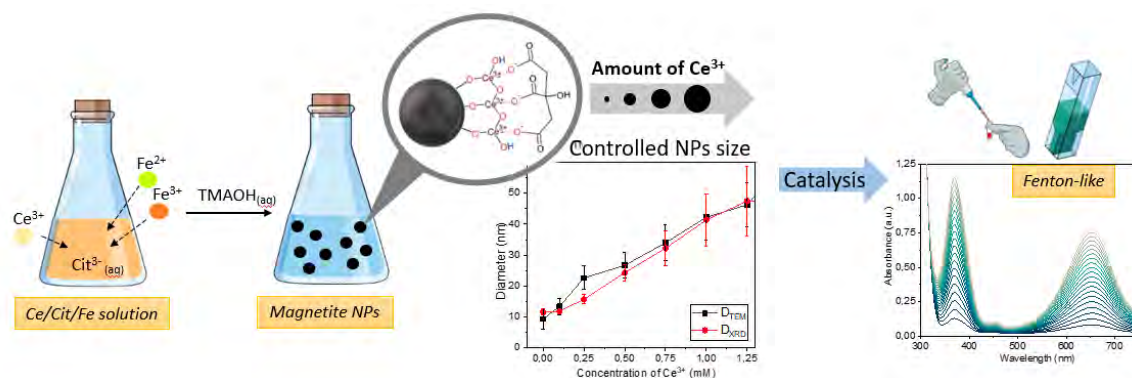


Figure 1. Schematic illustration of Magnetite synthesis and oxidation of TMB by H_2O_2 in the Fenton-like system.

Keywords: Magnetite, Cerium, Lanthanide doping, size control.

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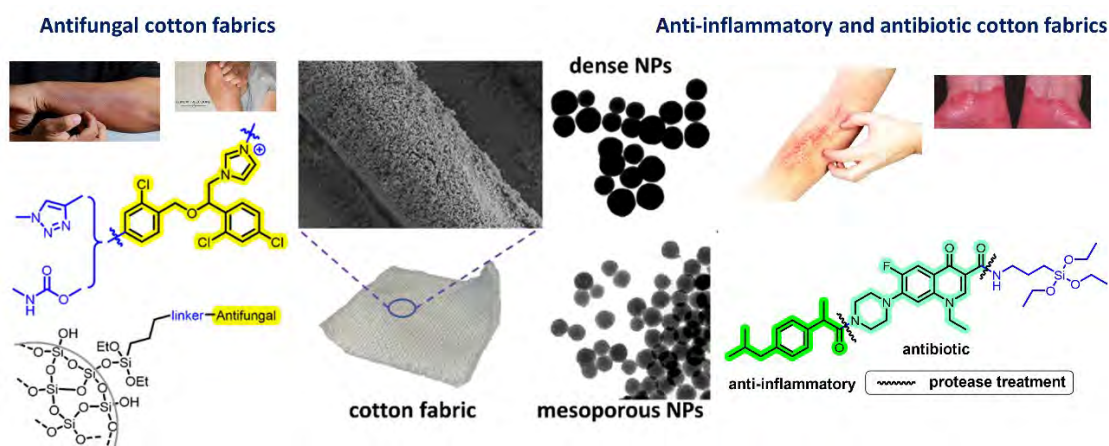
Functionalized silica nanostructures and cotton fabrics for topical biomedical applications

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Keywords: Functional coatings, nanoparticles, silica, antifungal, wound healing

In our daily life, we come into contact with a variety of microorganisms, which may rapidly grow and cause damage to people's health. Some hosts for the microorganism proliferation are food crops, animal species and textiles.^[1] Cotton fabrics are widely used materials because of their excellent properties including biodegradability, softness, permeability and hygroscopic capacity. However, cotton textiles can also be excellent substrates for microorganisms and can contribute to the spread of pathogen. Fungal infections represent a huge global problem resulting in over 1.7 million of deaths every year in humans and over one billion people suffer from severe fungal diseases.^[2] In the first part of the presentation, we describe the covalent anchoring of silylated derivatives based on topical antifungal agent Miconazole on silica nanoparticles (NPs). Grafting and co-condensation procedures are used to obtain mesoporous or dense functionalized NPs. Cotton fabrics have been coated with these antifungal-functionalized silica NPs under ultrasonic conditions, resulting in high effectiveness towards *Trichophyton mentagrophytes* and *Candida Albicans*.^[3] On the other hand, there is an increasing awareness of healthcare-related infections, with a strong demand to develop functional medical gauzes with broad-spectrum antibacterial and anti-inflammatory activities to prevent wound infection, promote wound healing and accelerate cicatrization. In the second part, we describe the preparation of silica NPs functionalized with a monosilylated precursor containing both anti-inflammatory and antibiotic moieties. These drugs are linked through amide bonds which can be cleaved by proteases to release the drugs. Cotton fabrics have been coated with these NPs and high expectations arise for topical cutaneous applications in wound dressings (bandages, gauzes, strips).



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New sensors based on microelectronic technologies for cell culture monitoring

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Cell culture monitoring is mostly conducted with bulky and expensive instrumentation, e.g. by microscopy or cytometry. Such methods are complex and tedious, requiring continuous manipulation of the cell culture and qualified staff for analysis. In opposition, it is the current tendency to integrate sensing elements inside the cell culture chamber, being thus possible to monitor the cells without human manipulation, in an automate and continuous manner providing precise analytical values in real time. This data is used to improve the control over the cell cultures and their environment.

This study involves the development and integration in neuron culture chambers of two types of (bio)sensors: amperometric, for the detection of metabolic indicators such as glucose and lactate, and Ion Sensitive Field Effect Transistors (ISFETs) for pH and ions of interest, including sodium, potassium and calcium. The challenge in the case of neuronal cultures is that the sensors and biosensors should remain stable and reliable for long-time periods (> 15 days). To achieve this, silk fibroin films are here employed to produce the (bio)sensors due to their long term thermal, mechanical and chemical stability, and capacity to retain biomacromolecules (e.g. enzymes, antibodies, etc.) for long time periods without compromising their integrity and functionality. Additionally, due to their low porosity, crystalline fibroin silk membranes overcome the biofouling of the sensor, which is one of the main drawbacks of electrochemical transducers when operating in real conditions, e.g. complex biological media.

To produce the silk-modified electrochemical transducers, silk fibroin films are deposited by drop casting on the transducer surface, and recrystallized by water vacuum annealing in a water-saturated atmosphere. These functionalised transducers were studied in cell culture media, showing better performances than other methods: reduction of biofouling (5 times reduction), long-term stabilization of biorecognition elements (8 months stability), etc. These new sensors are precise, robust, stable, reproducible and can be integrated in a multi-sensor platform.

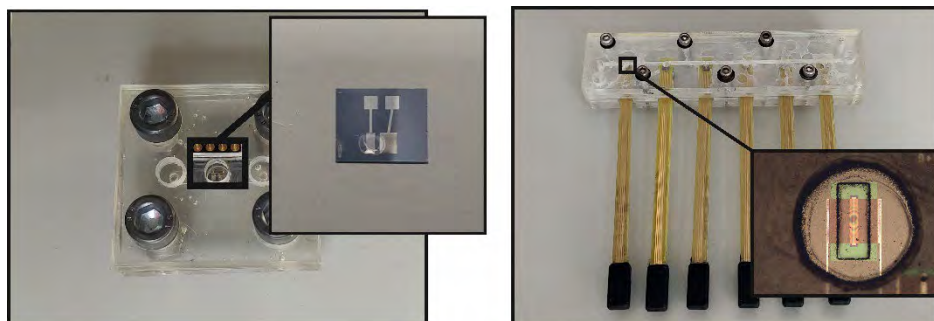


Figure 1: Devices used to monitor biomarkers (left) Amperometric biosensor (right) silk ISFET

Keywords: ISFET, Biosensor, ISE, Cell Culture, Fibroin

Synthesis of phosphorus dendrimers for applications in green solvent catalysis

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Society's increased demand for a green industry has led to the development of tailor-made catalysts that offer enhanced reactivity and stability in non-harmful solvents as well as the efficiency of post-reaction treatment.^[1] One of the novel approaches to overcome this limitation is the introduction of functionalities in the ligands, enabling their grafting to new-fashion supports, which can help to an easy recovery of the catalyst while avoiding metallic contamination in the products.^[2] In this regard, dendrimers have emerged as a valuable and innovative support for

olefin metathesis, concerning the huge tailoring that these hyperbranched macromolecules allow in regards to their properties (such as surface functionality or solubility in suitable media).^[3ab]

Among all types of dendrimers, Janus type are particularly appealing as they exhibit two different patterns within their structure enhancing the possibilities of the above-mentioned modulations.^[3c]

The present work aims to show the properties of a novel phosphorus-based Janus dendrimer containing in its structure both solubility modulation chains on one side, and metallic centres—or their corresponding ligands—on the other side (Figure 1), to be applied as metal@dendrimer systems to perform the desired catalytic processes in environmentally friendly solvents

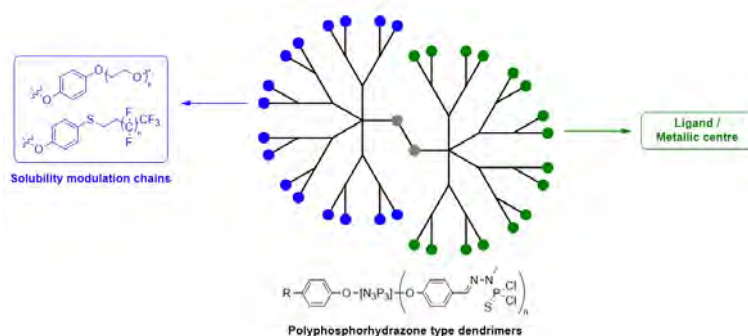


Figure 1: Representation of a metal@dendrimer system for catalysis in green solvents

Keywords: Phosphorus dendrimers, Catalysis, Green solvents

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DELOS nanovesicles-based hydrogels as promising subcutaneous drug delivery systems

3.2

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Hybrid systems composed of colloidal nanocarriers and hydrogels can combine the benefits of both drug delivery systems. Herein, we describe the development of an advanced hybrid formulation based on the so-called DELOS nanovesicles (DELOS-NVs) and thermo-reversible Poloxamer 407 (Plx407) hydrogel as a sustained delivery system for subcutaneous administration (Figure 1).

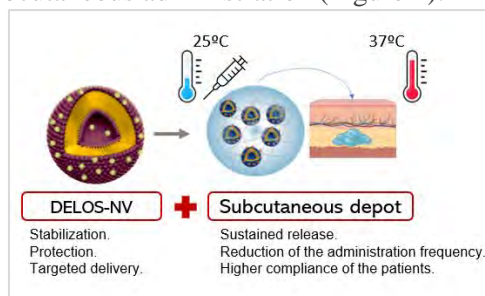


Figure 1: Figure illustrating the advanced hybrid formulation based on DELOS nanovesicles and Poloxamer 407 hydrogel.

The DELOS-NVs are composed of a mixture of sterols and ionic surfactants [1] and are produced in liquid form by a scalable and eco-efficient method based on compressed CO₂, named DELOS-SUSP [2]. In the present work, a Design of Experiments (DoE) was performed to select the best conditions to prepare DELOS-NV formulations based on cetylpyridinium chloride, a specially selected surfactant for subcutaneous injection. Next, the novel DELOS-NVs were gellified at different concentrations of Plx407, from 18% to 30% w/w. The integrity of these DELOS-NVs within the hydrogels was demonstrated by Cryo-Transmission Electron Microscopy (Cryo-TEM) [3]. The deep rheological characterization of these DELOS-NVs-based hydrogels showed that the 18% and 20% w/w Plx 407 hydrogels presented a desired rheological behavior to be injected at room temperature and to form a depot at 37 °C, while the 25% and 30% w/w Plx407 hydrogels were discarded for presenting a very low transition temperature from liquid to gel (Tsol-gel). More specifically, the 18% w/w Plx407 concentration presented a Newtonian and low viscosity behavior at 25 °C, while the 20% w/w concentration behaved as a plastic non-Newtonian hydrogel, which thinned in response to shear, thus presenting very low viscosities at shears like the ones applied in injections. In contrast, at 37 °C both hydrogels presented significantly higher viscosities and a very low thixotropy which results in a quick recovery of the inner structure after the injection. The presence of DELOS-NVs on the hydrogels slightly decreased the loss modulus, indicating higher cohesivity of the hydrogels with DELOS-NVs. Finally, an *in vitro* release test demonstrated sustained release of the DELOS-NVs for 24 h and the stability of these DELOS-NVs after this test was also confirmed by Cryo-TEM.

To conclude, these results provide evidence that DELOS-NVs can be successfully gellified in Plx407, maintaining their structure and stability, to obtain a promising formulation for the subcutaneous sustained delivery of therapeutic molecules.

Keywords: Nanovesicles; Subcutaneous drug delivery; Hydrogel; Rheology; Nanomedicine

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Towards the photocontrol of biological activity under two-photon excitation with near-infrared light

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Nowadays, light is being widely studied as a tool to control biological activity. In this context, two main techniques stand out: photopharmacology, which makes use of synthetic photoswitches appended to biologically active moieties, and optogenetics, which takes advantage of naturally photosensitive proteins bearing the photoswitching moiety in their structure.^[1]

Aiming to develop biological applications using low-energy light, the Two-Photon Absorption phenomenon (TPA) could become a seminal advantage compared with the typical one-photon absorption processes. By means of TPA, photopharmacology and optogenetic tools could be operated under simultaneous absorption of two photons of near-infrared light (NIR), which should lead to minimal photodamage, higher penetration depth and better excitation resolution. However, only a limited number of molecules can work efficiently under TPA conditions.^[2] For this reason, we are developing a modular approach to make TPA generalizable to any photopharmacology and optogenetics system.

In terms of optogenetics, the proposed approach is inspired by the pigment arrangement of light-harvesting complexes in photosynthesis. The aim is to decorate the vicinity of the photoswitchable site of optogenetic proteins with TPA photosensitizing chromophores, which should then funnel electronic excitation towards the protein photochrome (Fig. 1).

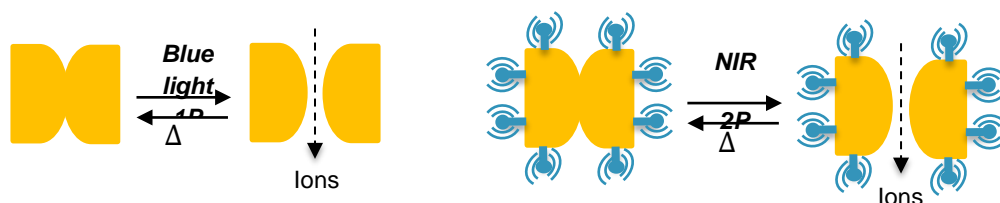


Figure 1.
Optogenetic approach. Proteins behaviour with (right) and without TPA (left) antenna.

About photopharmacology, the target is to prepare stilbene-based non-destructive caged ligands (NDCLs) as photomodulators of glutamate ionotropic receptors and neuronal activity. By incorporating a TPA antenna to these systems, we aim to accomplish a quantitative uncaging of the initial inactive *cis* isomeric form to the active *trans* counterpart using NIR light (Fig. 2).

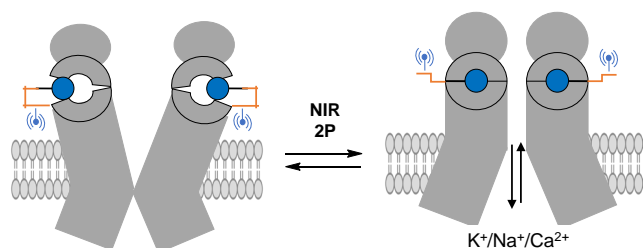


Figure 2. Photopharmacology approach (NDCL's Glu).

Keywords: Two-photon Absorption, Optogenetics, Photopharmacology

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Multiscale Modelling of Heterogeneous Catalysts for CO₂ Conversion

3.4

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Due to the increase in CO₂ anthropogenic emissions, there is a strong demand for its conversion into value-added chemicals. Strategies like the hydrogenation of CO₂ to methanol over Cu-based catalysts^[1] and the dry reforming of methane (DRM) forming syngas (H₂/CO) from CO₂ and CH₄ are promising possibilities for this purpose.^[2]

In this contribution, we combined density functional theory (DFT) calculations with kinetic Monte Carlo (kMC) simulations to study the reactions above. We evaluated the DRM reaction for temperatures ranging from 700-973 K catalyzed by the Ru (0001) and Rh (111) surfaces, as Ru and Rh are DRM's most active monometallic catalysts. For CO₂ hydrogenation to methanol, a non-precious-based catalyst based on a single-atom Cu catalyst supported on Mo₂CT_x was studied since it displays higher activity than the industrial Cu/ZnO/Al₂O₃ reference system.

The kMC results for the DRM reaction reveal that the Ru (0001) catalyst is more active, according to a higher TOF (turnover frequency, s⁻¹) than Rh (111) for the DRM reaction. However, the Ru (0001) catalyst deactivates faster due to the high CH* and C* coverage from CH₄ activation. For both metals, it is evident that the O* is the main oxidant of these CH*/C* species, discarding the OH* as one of the primary oxidants due to its low concentration on the surface. The source of O* on the surface is the CO₂ direct dissociation, which is the most favorable way to activate CO₂ with practically negligible formation of COOH*. The main products of the DRM reaction (H₂/CO) are obtained following the CH* oxidation pathway (CH* + O*) for the Rh (111) catalyst, while for Ru (0001), the preferred route goes via the direct C oxidation path (C* + O*). Finally, we found that the CO₂ dissociation step is the only rate-determining step of the DRM catalyzed by Rh (111).^[3]

On the other hand, the results of CO₂ conversion to methanol show the crucial role played by the Cu@Mo₂C interface in providing a low-energy pathway for CO₂ hydrogenation to methanol. Both the Cu atom and Mo₂CT_x participate in the reaction mechanism and allow the successive heterolytic cleavages of H₂ required to form HCOO*, H₂COO*, and H₂COOH* species, simultaneously with adsorbed H*. CH₃OH forms easily, together with CO, under reaction conditions. Further, we investigated the kinetics of the mechanism to find the main routes operating over CO₂ hydrogenation catalyzed by Cu/Mo₂CT_x.^[4]

Keywords: kMC Simulations, Heterogeneous Catalysts, Dry Reforming of Methane, CO₂ hydrogenation, Reaction Mechanisms

References:

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Screening of a Feasible Synthetic Route for an API-A

4.1

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The objective of this project is to develop a new manufacturing procedure for *Active Pharmaceutical Ingredient A* (**API-A**, as shown in **Figure 1**), in order to enter the global generic market once the product patent has expired.

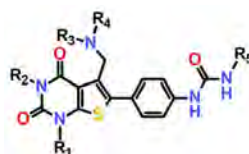
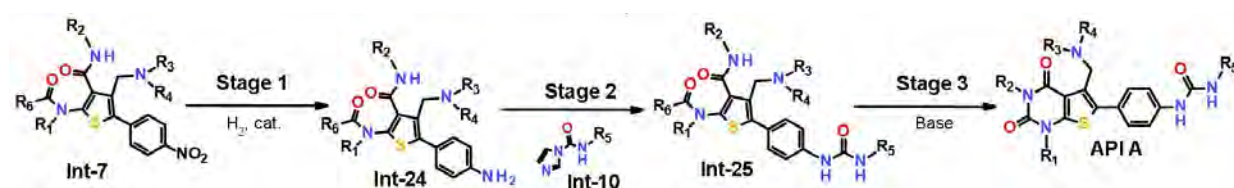


Figure 1: API-A drug.

Our objective is to identify a feasible and non-infringing synthetic route for **API-A**, optimizing each synthetic stage to achieve a cost-effective and industrially scalable manufacturing procedure that meets safety and quality requirements. Various routes of synthesis (RoS) have been proposed and tested, building upon the knowledge and experience gained in previous RoS attempts. Only **RoS B** (**Scheme 1**) has successfully completed Phase I verification and it has proven to be a competitive, suitable for industrialization, environmentally friendly route that meets safety and quality requirements for **API-A**. In the Phase II, the most critical stages have been optimized through the use of *Design of Experiments* (DoEs) in order to identify critical process parameters, adjusting the optimal conditions, to minimize impurity formation and to guarantee the correct scalability of process. **API-A** has been isolated as a non-infringing polymorphic form, and it complies with the drug substance related specifications. Non-GMP scale-up batches were produced in 10-30 L reactors at the pilot plant using the optimized procedures developed in Phase III.



Scheme 1: RoS B.

Keywords: MOEHS, API, synthesis, small molecule drug, Industrial PhD.

Catalytic activity of Cu/Mo₂CT_x: hydrogenation of CO₂ and CO to methanol

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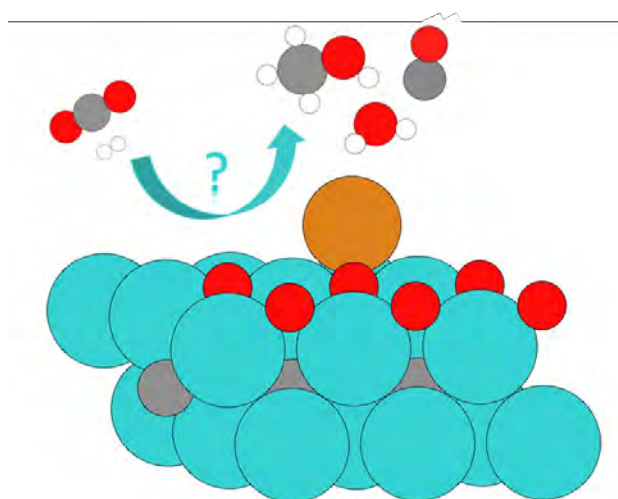
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CO₂ emissions are harmful to the environment, given their role in climate change and ocean acidification. A keyway to harness CO₂ is to use it as a precursor to high-energy density materials [1] to facilitate the energy transition. Hydrogenation of CO₂ to methanol is a promising option for this purpose.

The silica-supported Cu/Mo₂CT_x (MXene) catalyst shows higher activity than the industrial reference system Cu/ZnO/Al₂O₃. To better understand CO₂ hydrogenation in Cu/Mo₂CT_x, we performed DFT calculations to evaluate the reaction mechanism using a theoretical model previously calibrated by benchmarking it against the experiment. [2]

At a mechanistic level, our results [3] show the crucial role played by the Cu/Mo₂CT_x interface in providing a low-energy pathway to facilitate the hydrogenation of CO₂ to methanol. Both the Cu atom and the Mo₂CT_x support participate in the reaction mechanism. Both allow the successive heterolytic cleavages of molecular hydrogen (H₂) necessary to form HCOO*, H₂COO*, and H₂COOH* species, simultaneously with adsorbed H*. CH₃OH is readily formed together with CO under reaction conditions. In addition, the formation of CO through the reverse water-gas shift reaction (RWGS) facilitates its hydrogenation to methanol. These findings open new avenues for the hydrogenation of CO₂ and CO by exploiting metal-support interactions and considering the role of Cu/MXenes interfaces.



Keywords: CO₂ hydrogenation, climate change, methanol, MXene, DFT calculations.

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Microanalyzers' development for tracking key compounds in biotechnological processes for contaminants revalorization

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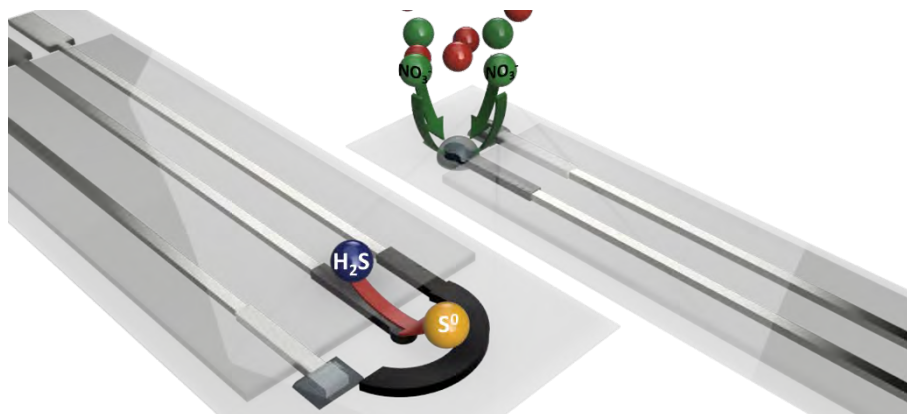
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With a severe lack of resources and serious environmental damage projected for the upcoming decades, wastewater treatment and chemical revalorization systems are in urgent requirement. One of the most dangerous contaminants, hydrogen sulphide (H_2S), is a toxic gas, soluble in water, commonly found in industrial and urban effluents. Another worrying one is nitrate ion (NO_3^-), which causes the acidification and eutrophication of aqueous ecosystems. Both need to be eliminated from urban and waste waters. To establish a proper control on the removal of contaminants, these need to be constantly tracked at several steps along the process, for prolonged amounts of time and with fast analysis. Consequently, the characteristics of the chemical analytical system prioritized are selectivity, stability, portability, and cost-efficiency over sensibility and limit of detection. Thus, the best suited analytical tools for this job are electrochemical sensors.

With the improvement of rapid-prototyping technologies in recent years it is now possible to mass-produce electrochemical devices with high reproducibility at a low cost. Compared to others, digital printing has the appropriate combination of ease of manufacturing, range of materials and geometry and size versatility for the tunability required to fabricate effective and innovative electroanalytical sensors.

In this thesis, graphite-based inks have been used as the base for the innovation of two printed sensors: a potentiometric ion-selective microelectrode for NO_3^- tracking and a three-electrode integrated amperometric microsensor for H_2S quantification. Using Direct Ink Writing to fabricate them, both sensors have high stability (over 20 days), pH robustness (7.5-11 pH for H_2S and 3-11 for NO_3^-), good reproducibility in fabrication (18% RSD for H_2S and 1.3% RSD for NO_3^-), and repeatability in consecutive measurements (2.5% RSD for H_2S and 0.98% RSD for NO_3^-). They have been tested successfully in synthetic and real samples, making them suitable for on-site applications.



Keywords: Printed Microelectrodes; Carbon-based Electrodes; Amperometric Sensor; Potentiometric Sensor; Ion-Selective Electrode

Selenium biofortification of Wheat Plants by Foliar Application of liposomes

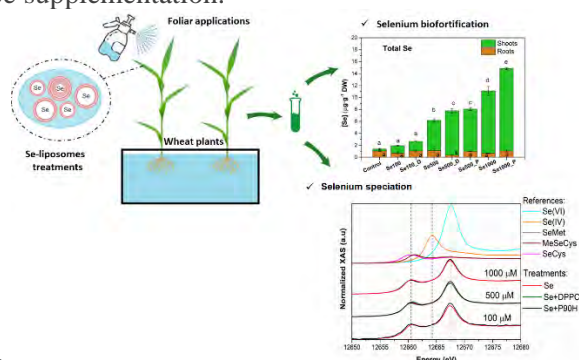
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Selenium (Se) is an essential micronutrient for humans with a key role in several physiological processes. Worldwide, the Se deficiency is considerable, and it has been estimated that 1 billion people have a scarce Se dietary intake due to the low concentrations in soils. To overcome this issue, Se agronomic biofortification practices are extensively investigated. To enhance the yield of foliar feeding and to minimize the stress or toxicity to crops, nanocarrier delivery technologies have been proposed. This last one is considering that only 0.1% of applied crop protection agents reach their biological target, whereas the majority are lost to the environment.

In the present work, liposomes have been used as nanocarriers in the biofortification of wheat plants (*Triticum aestivum* L. cv. *bancal*) with selenium by foliar application. Liposomal formulations based on 1,2-dipalmitoyl-sn-glycero-3-phosphocholine 16:0 PC (DPPC) or hydrogenated Phospholipon®90H (P90H) were prepared with different selenium concentrations. The treatments were applied at the plants' vegetative stage of growth. After the harvest, total Se was determined in the wheat plants showing that this element was successfully incorporated without affecting their biomass, other macro and micronutrients uptake and photosynthetic pigments production. Also, Se chemical speciation was studied by X-Ray Absorption Spectroscopy (XAS) using synchrotron radiation. Results showed that Se can be accumulated more efficiently in the plant tissues when liposomes treatments are used. Also, P90H can be considered a better alternative than DPPC, since similar results were obtained with both and the price of P90H phospholipid is considerably lower. Liposomes treatments do not cause negative effects on wheat plants concerning their vegetative growth. The speciation analysis revealed that Se is mainly present in wheat plants as organic selenium and the application using liposomes influences the proportion of these organic Se species. This information will be useful to minimize both plant toxicity and economic costs toward a more effective Se supplementation.



Figure/Scheme:

Keywords: selenium, biofortification, foliar application, liposomes, speciation

Development of a Portable Paper-Based Electrophoretic Bioassay with Simultaneous Electrochemical Readout

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Keywords: Portable Device, Electrophoresis, Electrochemical, Lateral Flow

Biosensors, especially lateral flow assays (LFAs), have become increasingly popular in point-of-care (PoC) diagnosis due to their versatility and affordability. However, their sensitivity and quantification capabilities are limited by their principle of operation, which can result in inaccurate or inconclusive results, especially when complex samples such as blood, serum, and plasma are involved. To address these challenges, our team has developed a new approach for the next generation of paper-based biosensors that combine LFA automation, electrophoresis separation, and electrochemical readout sensitivity.

In our recent work, we have successfully patterned conductive reduced graphene oxide electrodes on a nitrocellulose substrate, which, when coupled with electrophoretic separation up to 300 V, allows for electrochemical detection and eliminates unwanted interferences. Furthermore, our device is powered by a smartphone and takes advantage of near-field communication technology as an electrochemical reader, making it a viable PoC device that overcomes the limitations of traditional LFAs while remaining cost-effective.

Our approach, despite adding more complexity to the system, offers improved sensitivity and accuracy over traditional LFAs, making it a promising tool for diagnosing various diseases at the PoC. Our work builds upon the latest research in the field, including Parolo et al.'s (2020) comprehensive review of biosensors and their applications in diagnosis [1], recent advancements in LFA automation [2], and electrochemical readout sensitivity [4], as well as the successful implementation of electrophoresis separation in nitrocellulose substrates [3]. Additionally, our device benefits from the expertise and methods described in Giacomelli et al.'s (2020) study on the patterning of reduced graphene oxide electrodes [5].

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Catalysis in supercritical CO₂ with asymmetrically functionalized phosphorous dendrimers

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Phosphorus dendrimers, which are robust monodispersed hyperbranched polymers, are of keen importance for catalytic processes in organic synthesis because they are conveniently functionalizable with a wide range of organometallic functionalities on their surface.^{[1][2]} Furthermore, it is known that functional groups on the surface of phosphorus dendrimers can be used to control their solubility in various media.^[3] When phosphorus dendrimers have the terminal group -P(S)Cl₂ on their surface, they can be functionalized by replacing chlorine atoms with different amines or phenols.^[4] As shown in Figure 1, we intend to perform an asymmetrical substitution on the surface of phosphorus dendrimers with two different phenolic substituents, an organometallic moiety to act as a catalyst, and a polyfluorinated moiety to provide solubility in special media such as supercritical CO₂. We will present our latest results in catalysis.

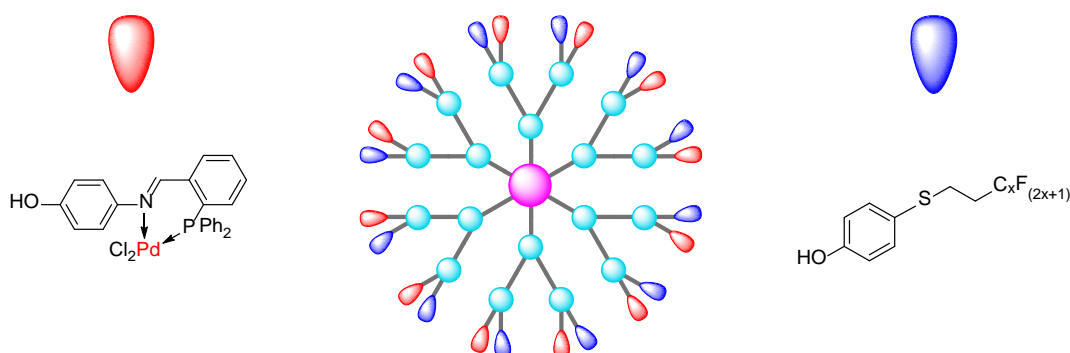


Figure 1: Scheme of asymmetrical substitution of phosphorus dendrimers, on the left the catalytic moiety and on the right the moiety that provide solubility of phosphorus dendrimers in supercritical CO₂.

Keywords: Phosphorus dendrimers, Catalysis, Palladium, supercritical CO₂.

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Switchable MOP solubility through surface chemistry: engineering molecular self-sorting systems

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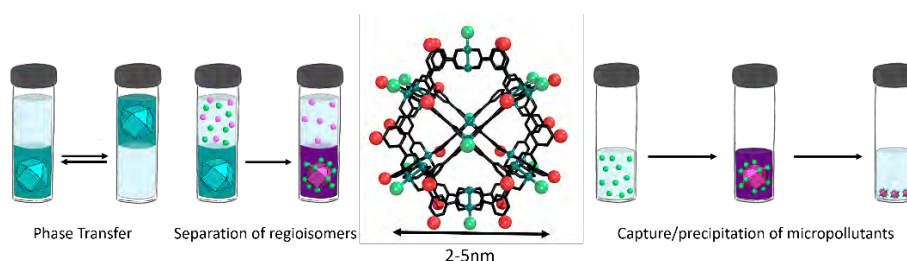
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Metal-organic polyhedra (MOPs) represent the ultimate miniaturization of a metal-organic material with intrinsic porosity as they can be conceptualized as the isolation of a sub-5 nm single cavity of an extended metal-organic framework.^[1] Moreover, the combination of their discrete nature and nano-sized scale endows them with properties tied to macromolecules, such as solubility and stoichiometric reactivity, or ultrasmall nanoparticles, as densely functionalized and highly reactive surfaces. This unique entanglement of properties opens up the possibility to post-synthetically modify their properties in solution with stoichiometric control through ionic exchange, organic covalent reactions or supramolecular chemistry, both orthogonally and synergistically.^[2]

Here we show how the role of these abovementioned properties gives rise to the possibility to modulate intrinsic physicochemical molecular properties such as solubility. MOPs solubility can be post-synthetically modulated through simple protonation/deprotonation and ionic exchange reactions and this behavior can be exploited to design phase transfer systems.^[3] We will show how this control over the MOP solubility can be coupled with the MOP coordination capabilities to undergo molecular transport and separation processes of regioisomeric mixtures in which the MOP governs the solubility of a molecule coordinatively bounded to the MOP surface.^[4] Moreover, we will discuss about the possibility of using such control of the solubility not only in solution, but also in heterogeneous conditions by using the MOP as a coordinatively capture agent to remove organic micropollutants from water by pH-controlled precipitation.^[5]



Keywords: Metal-Organic polyhedra, molecular cages, separation, selectivity, coordination chemistry.

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Green synthesis and processing of CaSyr-1 bioMOF: a potential drug delivery system with intriguing triple bioactivity

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Metal organic frameworks (MOFs) are a unique class of porous crystalline materials with exceptional versatile chemistry that have shown promising applicability in several and diverse fields [1]. One of the deeply investigated areas is biomedicine, where they have been mostly conceived as platforms for drug loading and delivery [2]. For this bio-related application it is meaningful to construct the MOF as a nano-particulate biological MOF (bioMOF), *i.e.*, constituted of endogenous cations and naturally occurring ligands, in order to reduce the global cytotoxicity. However, the overall processing of drug nanocarrier MOFs, including the synthesis of the framework, the encapsulation of the active ingredients and the required post-synthetic modifications, generally involves harsh reaction conditions, long reaction/activation periods and large amounts of hazardous solvents that hinder not only their biomedical application, but also their scale-up production [3].

Currently, the development of green technologies to produce and process MOFs is under survey [4]. Recently in our group, we have synthesized a new bioMOF called CaSyr-1 that meets numerous properties, *i.e.*, high surface area with large micropores, nano-particulate size and biocompatibility, commonly sought in systems designed for drug loading and delivery. Remarkably, CaSyr-1 constituents, *i.e.*, calcium and syringic acid, possess certain bioactivity that could complement the medical action of the contained drug, hence, affording a triply bioactive system (Figure 1). In this work, two model drugs,

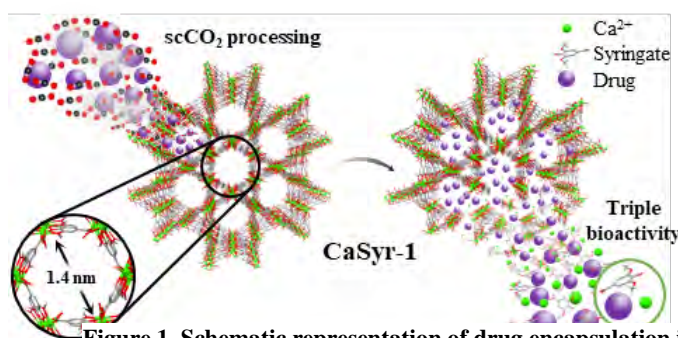


Figure 1. Schematic representation of drug encapsulation in CaSyr-1 after scCO₂ processing and subsequent triply bioactive release.

i.e., ibuprofen and isoniazid, have been separately encapsulated within CaSyr-1 voids. In both cases, the global effect of the drug could merge positively with the biomedical activity of both calcium and syringic acid. The entire processing of CaSyr-1(drug), considering the bioMOF synthesis, the drug impregnation and the post-synthetic modifications, relies on the combination of scCO₂ and EtOH as operation solvents, thus involving a fully eco-friendly procedure.

In conclusion, CaSyr-1 bioMOF has emerged as an ideal platform for drug loading and delivery. In this work, the development of CaSyr-1(drug) is accomplished by following a completely green approach.

Keywords: BioMOF, green chemistry, drug delivery, supercritical CO₂.

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Dithienylethene-based photoswitchable phosphines for in situ modification of catalysts

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Photoswitchable catalysts that are capable of toggling between active and inactive states upon irradiation are of high interest, as they allow the optical control of catalytic reactions on demand.^[1,2] The preparation of phosphines containing photoisomerisable backbones will likely enable light-controlled changes in their coordination behaviour and, as such, variation of the catalytic activity of the corresponding complexes.^[3] With this aim, we are currently exploring the use of dithienylethenes (DTEs) as light-responsive cores for the preparation of photoswitchable phosphines.

Dithienylethenes^[4] are well-known photoswitches that have already been applied to control chemical reactivity with light based on the geometrical and electronic changes that occur upon reversible open-closed photoisomerisation.^[5] In particular, we are herein interested in exploiting the drastic variation in electronic communication that takes place between the external 5- and 5'-substituents of the DTE thiophene rings, which are not conjugated in the open isomer but become electronically connected after ring closing (Figure 1). Therefore, by introducing one phosphine moiety in one of the thiophenes and electron-withdrawing groups in the other, a control of the phosphine's electronic properties upon DTE photoswitching is expected, thus leading to different catalytic activity of their transition metal complexes.

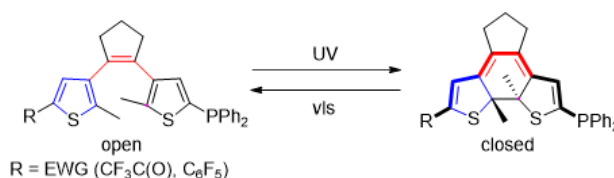


Figure 1: Photoswitchable ligands based on dithienylethene cores

Keywords: photoswitchable phosphines, organometallic catalysis, dithienylethenes.

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Novel bifunctional ligand scaffolds for stable and inert complexes as PET imaging contrast agents

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Keywords: Contrast agent, PET, bifunctional ligand

Nuclear medicine is a powerful tool to image metabolic processes by injecting a radioactive isotope fused to a targeting moiety that has the ability to transport the radionuclide specifically to the diseased tissue. To achieve this, the use of radiometals has grown rapidly in imaging techniques such as single-photon emission computed tomography (SPECT) or **positron emission tomography (PET)**. Traditionally, isotopes such as ^{13}F , ^{15}O , ^{13}N and ^{11}C have been incorporated into nuclear medicine agents; however, their production relied upon an on-site cyclotron, making PET an expensive imaging technique. In addition, the short half-lives of the organic nuclides limited the use of PET for imaging biological processes that occurred over a short time scale.¹

To overcome these disadvantages, much effort has been put towards the production of β^+ emitting radioisotopes of metals such as Ga, Y, Zr and Cu, that can circumvent some of the synthetic limitations.^{2,3} Moreover, their longer half-lives make them a more attractive option for their incorporation into radiopharmaceuticals. Despite the effort, there is currently no FDA-approved metal-based PET imaging agent; however, many are in early late-stage clinical trials.

Both ^{64}Cu ($t_{1/2} = 12.7$ h) and ^{68}Ga ($t_{1/2} = 68$ min) are very attractive β^+ emitters for application in PET imaging. The design of molecules that can chelate these metals is vital to keep developing this technique and to make it more accessible and inexpensive. Based on the bifunctional chelate (BFC) method,^{2,4} a 1,3-diaminocyclobutane scaffold that bears an additional functional group that will allow their conjugation with targeting peptides of clinical interest was recently developed (**Figure 1**). The objective of the design of these new ligands is to afford complexes with Ga^{3+} and Cu^{2+} with an enhanced stability due to the rigidity of the cyclobutane moiety, overcoming toxicity problems due to metal leaching and lowering the required concentration for the acquisition of molecule imaging through PET technique.

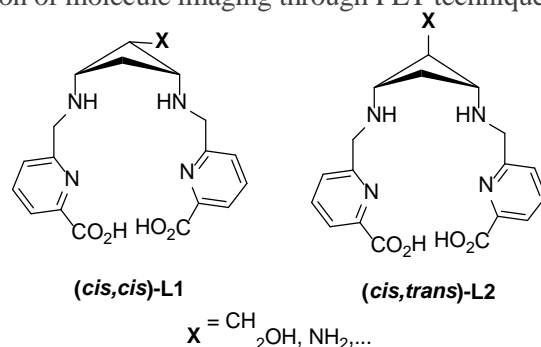


Figure 1. Structure of the new 1,3-diaminocyclobutane ligands

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Se-biofortified microgreens as functional foods: phytochemical profile, bioactive properties, and Se speciation

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An appropriate selenium (Se) intake can be beneficial for human health due to its antioxidant, antiviral, and anticarcinogenic properties. Se-biofortification of plants has been suggested as a method to overcome Se-deficient diets while avoiding toxic intake levels. Regarding plant-based food, microgreens have recently increased their popularity because of their high nutritional value and their distinctive flavours and textures. In this work, Se-biofortified microgreens (green pea, red radish, and alfalfa) have been grown at a semi-industrial vertical hydroponic cultivation system using a Se-formulation with a balanced combination of Se inorganic salts. The impact of the Se enrichment on the bioactive compounds, minerals, sugars and pigment concentration, and the antioxidant status of the plants have been evaluated. The species of Se present in the plant's tissues have been determined by X-ray absorption spectroscopy. The results have shown a noticeable concentration of Se in the biofortified microgreens, (40-90 $\mu\text{g}\cdot\text{kg}^{-1}$ Se). In addition, no negative impact on the bioactive constitution and nutritive value has been found. Under Se exposure, chlorophyll and carotenoid levels increased in green pea, while chlorophyll decreased in alfalfa. However, in red radish, the concentration of both pigments was not affected by the application of Se. Se treatment increased the amount of soluble sugars (glucose and fructose) in green pea and alfalfa, but no significant changes were found in radish. The speciation analysis showed that radish was the microgreen with the highest content of Se-amino acids (59.2%), followed by alfalfa (33.6%), and green pea (27.8%). Overall, Se-biofortified microgreens, which are culinary and nutritionally interesting, are a potential functional food for enhancing Se intake, and as a rich source of other dietary minerals to benefit human health.

Keywords: Biofortification, bioactive compounds, microgreens, selenium, speciation.



Application of scale-up methodologies into industrial pharmaceutical processes

6.2

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Esteve Company is a CDMO (Contract Development and Manufacturing Organizations) which produces Active Pharmaceutical Ingredients (API) during both clinical development and commercial stages. Esteve have more than 1000 m³ of reaction volume, distributed into 5 production plants around the world. Esteve works on many processes at the same time, targeting a 75-80% of plants occupancy during the whole year. However, these multiple projects are in different stages (early development, pre-validation studies, commercial production, etc.). Thus, multipurpose plants are required to deal with different projects stages. Furthermore, plant schedule is difficult as it is being constantly updated due to unexpected events such as starting material delay, customer decisions or problems during process scale-up. Some of these unexpected events are not avoidable, neither predictable, but ensure a right first time scale-up could be assessed from early development studies in R&D. On the other hand, a proper scale-up assessment could also ensure that process can fit as much reactors as possible, obtaining more flexible processes which would be less dependent on unexpected schedule changes.

This PhD Thesis has as a main objective the creation and implementation a scale-up assessment methodology in Esteve Company. This ambitious goal has been tackled from three different scopes: firstly, from a troubleshooting perspective of those process that fails during scale-up; secondly, by assessing new projects at R&D stage in terms of scale-up factors determination via scale-down strategy implementation; and thirdly, by applying a scale-up risk assessment of all those processes that are starting the process validation stage.

The background of these objectives is a mind-set change of R&D development teams and plant production teams, who may introduce the process scale-up factors consideration in their daily work. In this sense, the first objective of plant troubleshooting is a reactive solution which is targeted to be prevented by second and third thesis objectives. However, plant troubleshooting may be the most valuable examples to prove mixing calculations importance, as it can be easily quantified how much time and money would have been earned if previous scale-up assessment had been carried out. The implementation of the second objective requires the acquisition of simulation softwares, but also the creation of new laboratory and kilolab reactors setups that mimics Esteve plant reactors geometries. Geometrical similarity may facilitate the scale-up assessment as the more similar reactor geometry, the more accurate calculations can be done. Moreover, to bring these engineering angle to chemistry development a standardized work-flows have been generated to guide chemists in the scale-up factors detection, without software calculations. Once chemists detect a possible scale-up factor, then process chemical engineers may perform the required calculations to plan new laboratory trials applying the scale-down strategy. Finally, the third objective implementation is totally dependent on second objective success as Scale-up Risk assessment of the whole process, previous to be validated, may require laboratory trials information to perform a robust assessment.

Keywords: Scale-up, stirred vessel, batch mixing, API, pharmaceutical.

Theoretical Investigation on the Catalytic Performance of Pt₃Mn Alloys in Propane Dehydrogenation to Propylene

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Direct propane dehydrogenation (PDH) is a promising approach to producing propylene due to its raw material abundance, low cost, high yield, and excellent product purity. Currently, the commercial catalysts for PDH are mainly Pt-based, but they are expensive and suffer from rapid deactivation during the reaction. Other metals, such as Sn, Ga, and Fe, have been introduced into Pt-based catalysts to enhance active sites' stability while reducing the Pt loading amount. In this presentation, we report our recent work on the catalytic performance of PtMn alloys, namely Pt₃Mn, in the PDH reaction based on density functional theory (DFT) calculations.

By exchanging Mn atoms on the surface and Pt atoms from deep layers and comparing the energies of segregated structures with non-segregated ones, we find that the Pt atoms' segregation to the top layer is energetically favored. Then, we evaluate the catalytic performance of the most stable resulting Pt₃Mn surface by inspecting the reaction energetics and barriers. We locate three transition states: TS1 and TS2 for activating propane's 1st and 2nd C-H bonds, respectively, and TS3 for forming H₂. The reaction barriers are 1.04 eV (TS1), 1.11 eV (TS2), and 0.52 eV (TS3) for pure Pt catalyst. On Pt₃Mn, they are 1.21 eV (TS1), 1.48 eV (TS2), and 0.55 eV (TS3), which are slightly higher than those of pure Pt. We also evaluate the reaction barrier of coke formation, an undesirable side-reaction that poisons the active sites. The barrier is 2.13 eV on pure Pt, while it is much higher on the segregated Pt₃Mn system: 2.79 eV, indicating that coke formation will be suppressed. Our results demonstrate the potential of Pt₃Mn alloy in PDH.

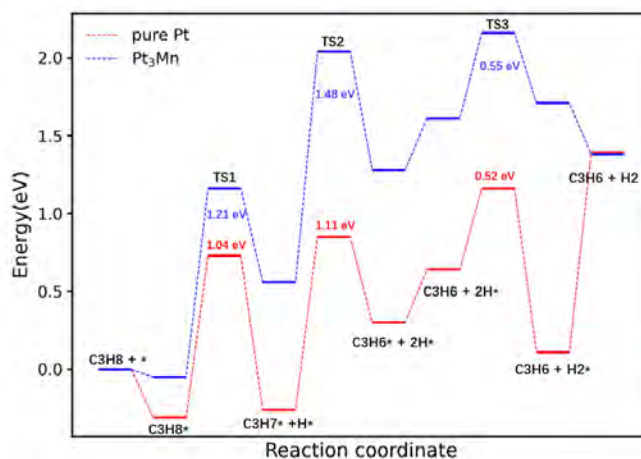


Fig. 1 Energetics of the Energy profile for the PDH catalyzed by Pt and Pt₃Mn catalysts.

Keywords: propane dehydrogenation, catalysis, Pt₃Mn Alloy, density functional theory



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